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THE UNIVERSITY OF OKLAHOMA

GRADUATE COLLEGE

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# III. THE X-RAY CRYSTAL STRUCTURE OF *TRANS*-1,3-CYCLOBUTANEDICARBOXYLIC ACID

A DISSERTATION

SUBMITTED TO THE GRADUATE FACULTY

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DAVID STANLEY SEIGLER

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APPROVED BY:

DISSERTATION COMMITTEE

To

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# THE KINETICS OF THE EPIMERIZATION OF DIMETHYL CIS AND TRANS-1,2-CYCLOALKANEDICARBOXYLATES

## CHAPTER I

## INTRODUCTION

Much effort has been expended in recent years to establish energetic and stereochemical relations of alicyclic rings and their substituted derivatives. In the last decade large numbers of papers on this subject have been published. Advances in the theoretical treatment and in technological methods which allow the measurement of physical and chemical properties of these systems and the importance of many naturally occurring alicyclic systems have provided a driving force for these studies. The present work is intended to amplify the understanding of base catalyzed epimerizations of selected diesters of alicyclic rings, especially with respect to ring strain and substituent effects.

The anomolous behavior of alicyclic rings led Baeyer to propose his classical "strain theory."[1] His calculations of bond angles, based on simple geometry, assumed the planarity of the alicyclic rings. He postulated that deviation of bond angles from tetrahedral value of 109° 28′ would introduce strain in the system, (frequently called angle strain) and was able to account for many properties of these systems with this approach.

However, the Baeyer theory failed to explain other data, e.g., heats of combustion, which showed cyclohexane to have no significant deviation from the value calculated with the assumption that there was no strain in the system.

In 1890 Sachse proposed two puckered structures for cyclohexane (a chair and a boat form) in which all angles were tetrahedral and no strain existed.[2,3] (Fig. 1)



Boat form Chair form

Figure 1. The boat and chair forms of cyclohexane.

These structures did account for data such as the heats of combustion. Largely because of the preëminence of the Baeyer theory, Sachse's ideas were not generally accepted for many years. The proposed structures were revived when Mohr[4] predicted the cis-trans isomerism of decalin, and this was experimentally verified by W. Hückel.[5]

Although there is no angle strain in the boat form, there are bond opposition strains, similar to those in an eclipsed ethane structure and 1,4-hydrogen interactions caused by the close approach of these two hydrogens. However, the boat form is not rigid and some of the interactions may be decreased by conversion into a mobile form called a skew-boat. Despite this relief of interactions, the chair form is more stable than the boat form (at 25°) by 4 kcal/mole.[6a,b,c,12]

Sachse's structures further predicted two types of bonds for the cyclohexane system, now known as axial and equatorial. A substituent in an axial position suffers 1,3-diaxial hydrogen interactions, as well as two gauche butane interactions, and in the absence of other stabilizing factors, the most stable arrangement of a single substituent will be an equatorial position. Equatorial methycyclohexane is preferred over axial by 1.8 kcal/mole.[7]

The situation becomes more complex when one considers disubstituted cyclohexanes. The 1,2-, 1,3-, and 1,4-disubstituted cyclohexanes may exist in two geometric forms. Trans-1,2-dimethylcyclohexane is readily interconvertible from the diaxial to the diequatorial conformation. The diaxial form has four gauche butane interactions and the diequatorial, only one. Thus, the diaxial form is less stable by 2.7 kcal/mole. Cis-1,2-dimethylcyclohexane must have one substitutent axial and one equatorial. Therefore the two conformers are of equal energy and half the molecules exist in one and half in the other. Three gauche butane interactions are present in cis-1,2-dimethylcyclohexane making it 1.8 kcal/mole less stable than the diequatorial trans isomer.[8a,b] In 1,3-dimethylcyclohexane the diequatorial cis isomer is more stable than the trans by 1.8 kcal/mole;[9] and for 1,4-dimethylcyclohexane the diequatorial trans is preferred by 1.8 kcal/mole.[9]

The introduction of a double bond into a cyclohexane ring alters the configuration from that of the normal chair. The hydrogens of atoms 4 and 5 occupy normal axial and equatorial positions, but those

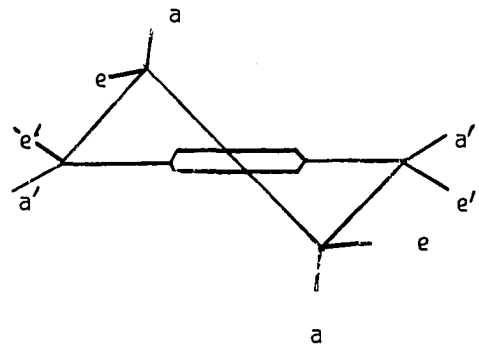



Figure 2. The pseudochair of cyclohexene.

of atoms 3 and 6 are imperfectly staggered and termed pseudoequatorial and pseudoaxial. The energy barrier between the "half-chair" form and the boat form has been calculated to be 2.7 kcal/mole.[10] The cis-4,5-dimethylcyclohexane compound may only exist in the axial-equatorial configuration but the trans isomer can exist in two conformations. Two of the 1,3-diaxial interactions are removed in this system and the diaxial conformer is stabilized with respect to the diequatorial. The diequatorial conformer is still preferred over the trans by 1.1 kcal/mole.[11]

Cycloheptane, in analogy to cyclohexane, has been postulated to exist in two forms: a pseudoboat and a pseudochair.[12] However,

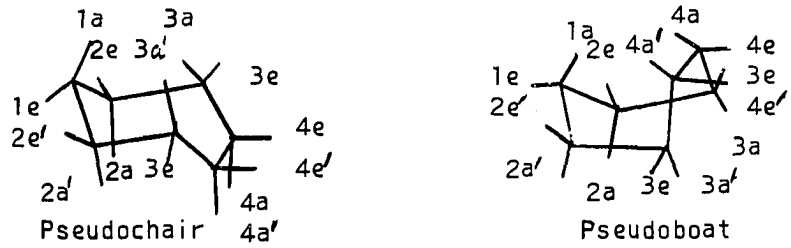
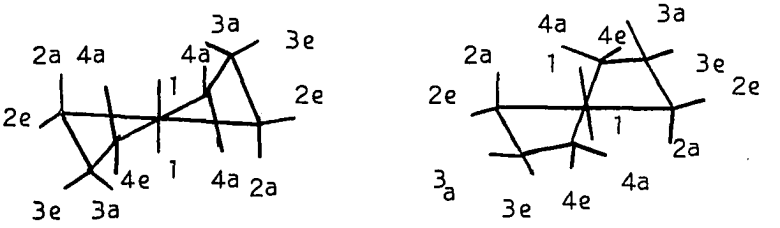



Figure 3. The pseudochair and pseudoboat forms of cycloheptane.

both of these forms (unlike those of cyclohexane) are mobile and both exist in a "twist" configuration to decrease 3,6-dihydrogen interactions. The bond angles, especially the 4,5-bond angles, are




"twist" chair "twist" boat

Figure 4. "Twist" forms of chair and boat cycloheptane.

distorted somewhat to assist in this removal of strain. The twist boat is less favorable than the twist chair by 2.16 kcal/mole. In contrast to the cyclohexane case there are seven positions in each twist form and eight each in the chair and boat form.

A monosubstituted cycloheptane will exist preferentially with the substituent in a twist chair in the 2e, 3e, or 4e position, which are of similar energies. Isolation of the conformers of cycloheptanes will likely be difficult, as they are all interconvertible by a combination of pseudorotations and flipping, as only a small energy barrier exist between conformers.

For 1,2-disubstituted cycloheptanes one can distinguish two cis and two trans conformers. With 2,3-substitution the two cis forms (2e-3a) and (2a-3e) are different, as are the trans forms (2e-3e) and (2a-3a). Both the cis and trans conformers are readily interconvertible. The cis dihedral angles vary from 0 to 97°, and the trans from 23 to 217°.

In cyclopentane the deviations from tetrahedral angles would be very small did not eclipsing between adjacent hydrogen atoms force cyclopentane to assume a puckered form. The configuration of cyclopentane is not fixed but the puckering moves around the ring. This is called pseudorotation.[13]

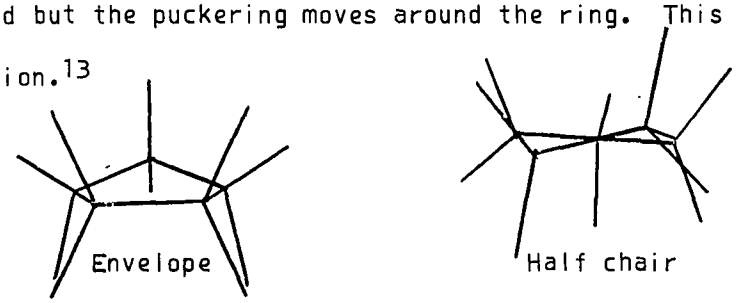



Figure 5. Two puckered forms of cyclopentane.

In substituted cyclopentanes these changes often involve sufficient energy differences so that one form or the other will have greater stability. Methyl cyclopentane exists in an envelope form with the methyl in a pseudoaxial position. This form has been calculated to be the most stable form by 0.9 kcal/mole.[14a,b] Many

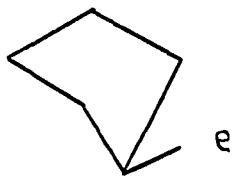



Figure 6. Methycyclopentane.

cyclobutanes are nonplanar. The cyclobutane ring is "butterflied" to remove strains between the 1,3-carbon atoms and eclipsed hydrogen atoms, even though this increases angle strain.

Cyclopropanes must be planar. Cyclopropyl hydrogens are largely eclipsed, only further angle distortion can ease bond oppositions here.

The relations between conformation, steric factors, and chemical reactivity have long posed problems of theoretical interests. Barton pointed out the difference in reactivities of substituents in axial and in equatorial positions.[15] Substituents in an axial position are more crowded (steric interactions) than in the corresponding equatorial conformers, and this is a principal factor controlling their reactivities. Reactions which proceed with a relief of strain are generally facilitated and those with transition states involving increases in strains are hindered.

Esters of cyclohexanol saponify more slowly than those of cyclohexanecarboxylic acids. In both cases a discrete intermediate is involved, which necessitates a change from trigonal to tetrahedral bonding, with a concurrent increase in crowding. In the cyclohexanol esters the crowding occurs farther away from the cyclohexane ring and causes less crowding in the intermediate state.[16]

Trans-4-t-butylcyclohexyl acetate (acetate equatorial) saponifies seven times more rapidly than the corresponding cis-4-t-butylcyclohexyl derivative (acetate axial). The more crowded axial isomer reacts more slowly than the equatorial.

In cases where a common intermediate is formed the difference in reactivity becomes the difference between the free energies of the two ground states. Examples of this type are the elimination of cis

and trans-4-t-butylcyclohexyl tosylates, of which the less stable cis isomer reacts more rapidly.[17]

As mentioned previously, many reactions involve the change in the transition state at the reaction site from trigonal to tetrahedral hybridization or vice versa. Displacement reactions of the $S_N1$ and $S_N2$ types are common examples of this effect. H. C. Brown has pointed out that if either of these changes occurs with a concomitant decrease in strain, the change should be facilitated; but if an increase in strain is encountered, the reaction is hindered.[18a,b]

Eliel is careful to note that this is always provided there are not other effects of a steric or polar nature more important than the above effect.[19] Changes in angle strain, bond opposition strain and transannular strain may occur simultaneously with changes in hybridization.

The effect of ring size in reactions of various types has been the subject of many studies. In small rings (3,4) the principal rate determining factor is angular strain. In normal rings (5,6,7) bond opposition strains play a large role but angular strain is still important. In seven membered rings transannular effects become a factor to be considered.

Many solvolysis reactions involve a change from tetrahedral to trigonal bonding as discussed previously. Solvolyses of cycloalkyl tosylates, brosylates, and halides show similar trends of reactivity. The rate of solvolysis via an $S_N1$ (or $S_N2$) mechanism should be slow for substituted cyclopropanes as this reaction involves change from an already distorted tetrahedral angle (60°) to a trigonal angle

(120°) which introduces even more strain into the ring.

The solvolyses of cyclobutyl esters and halides should also be a rather slow reaction, by the same assumptions. However, at least in the case of the tosylate, an ion intervenes which is more stable than the expected cyclobutyl carbonium ion and these solvolyses are very rapid.[20]

In cyclopentane systems solvolyses involving a trigonal carbonium ion are facilitated by the relief of bond eclipsing, (approximately 4 kcal/mole.) Thus the solvolysis of cyclopentyl tosylate is rapid.[20] This relief of bond opposition strains is enough to easily offset the change from a tetrahedral to a trigonal configuration.

Similar considerations apply to the cycloheptyl system, which contains many bond oppositions and the solvolyses of cycloheptyl esters are also rapid.

In cyclohexane systems, however, the ground state has no angle strains and no bond opposition strains. Any attempt to change the hybridization of a ring atom is resisted as it increases eclipsings (and introduces some angular strain, although in this case angle strain is probably a minor factor).

Plots of rate constants, Fig. 7, 8, 10, (or equilibrium constant Fig. 9) for several reactions versus the number of ring atoms illustrate some effects of ring size on reactivity.

Other influences of reactivity which are not observable from the plots may be seen for five, six, and seven ring compounds in some reactions which demand a specific configurational arrangement.

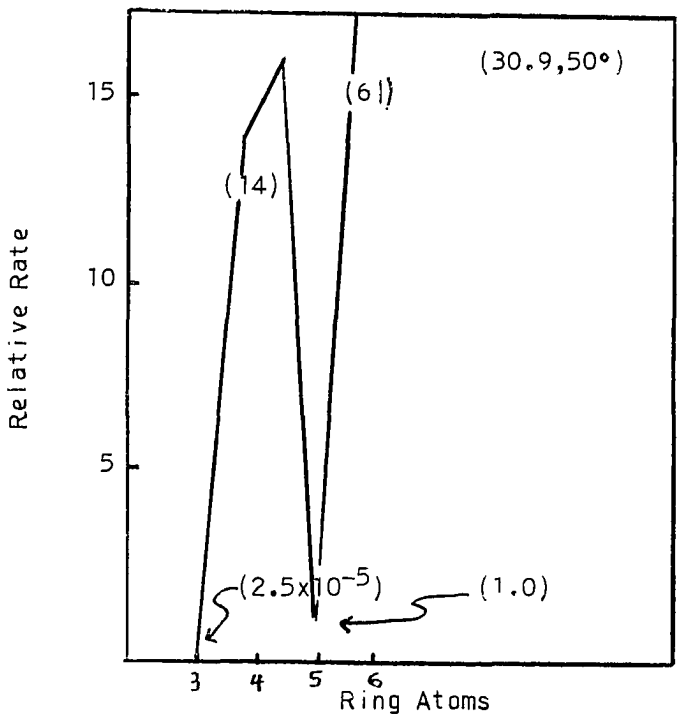



Figure 7. Solvolyses of cycloalkyl tosylates in acetic acid.[20,21]

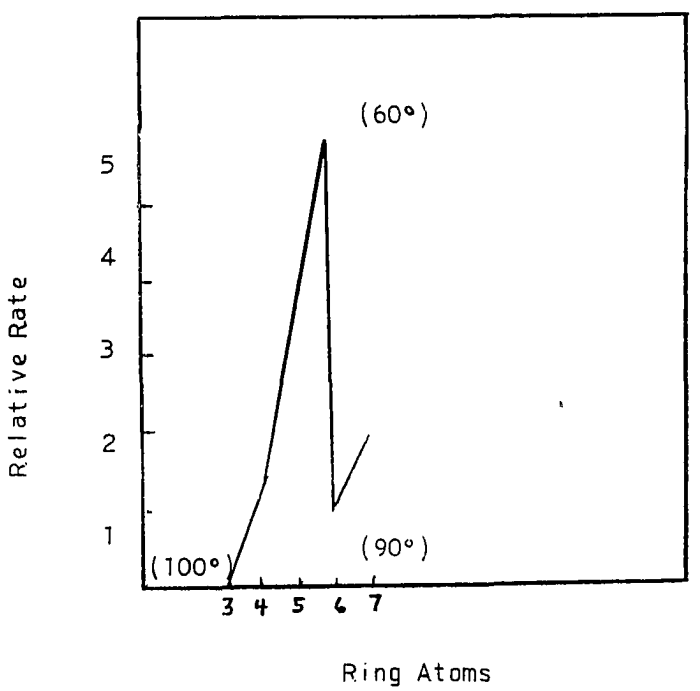



Figure 8. The $S_N2$ displacement of cycloalkyl bromides by potassium iodide in acetone.[20]

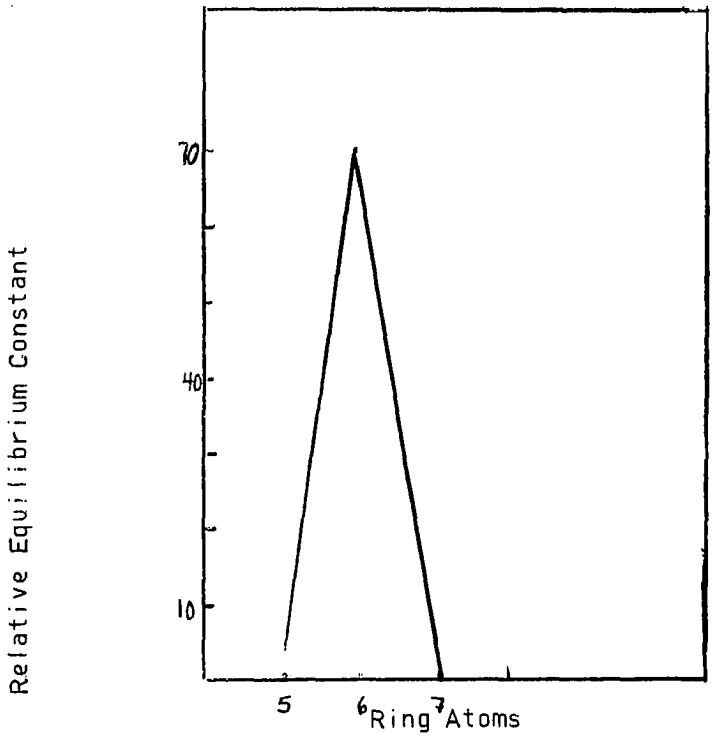



Figure 9. The relative equilibrium constant for cyanohydrin formation from cycloalkanones.[22]

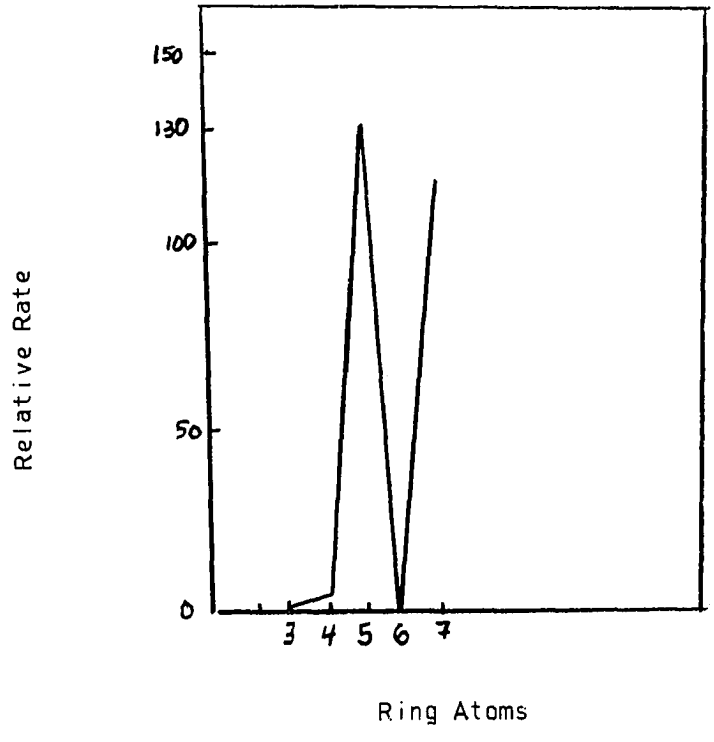
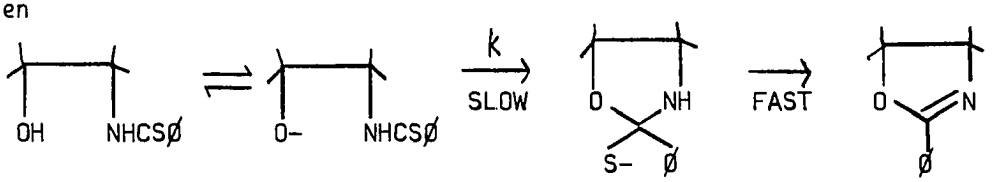



Figure 10. The solvolysis of 1-chloro-1-methylcycloalkanes in 80% ethanol at 25°.[23]

The cyclization of the N-thiobenzoyl derivatives of cis and trans-2-aminocycloalkanols and 2-benzamidocycloalkane methane - sulfonates have been studied by several Czech workers.[24,25]

The first of these reactions involves almost complete retention of configuration, the latter almost complete inversion.

Plots of the rate constants versus ring size illustrate the dependence on configuration. For the first series of reactions (Fig. 11) the cis cyclopentane isomer must have a ground state orientation similar to the requirements in the ground state. Again cyclohexanes are seen




to resist any change from the perfectly staggered ground state. The cyclization of the trans systems involves an increase in ring puckering with a concomitant increase in 1,3-interactions, whereas the cis encounters only ring flattening, and the ratio of $k_{trans}$ / $k_{cis}$ is increased.

In cycloheptanes the eclipsings produced are apparently negligible in comparison to those already present, and the more mobile system of both cis and trans reacts more rapidly.

In the second series of reactions (Fig. 12) the trend is reversed, the trans compounds react more rapidly than the corresponding cis. The trans compounds must become diaxial to react.

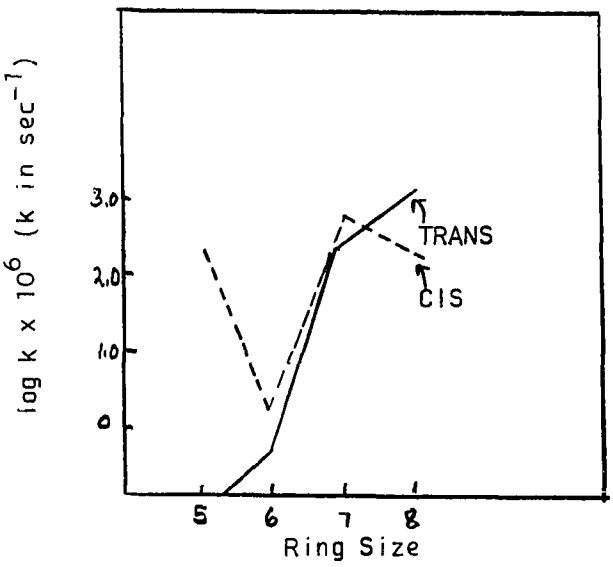



Figure 11. The effect of ring size upon the rate of cyclization of the N-thiobenzoyl derivatives of cis and trans-2-aminocycloalkanols.

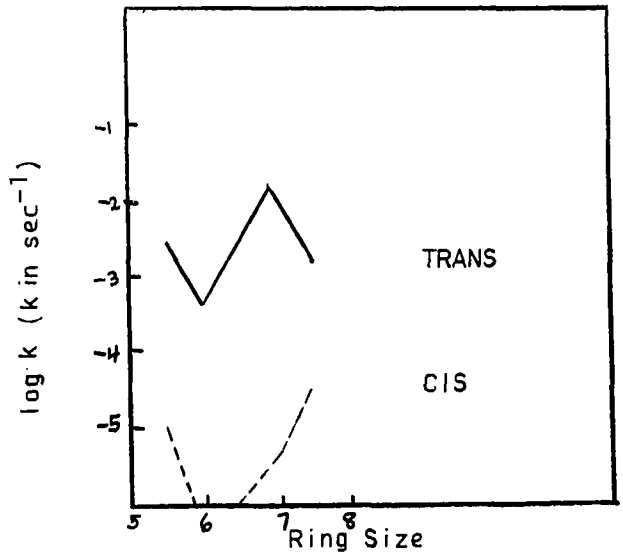
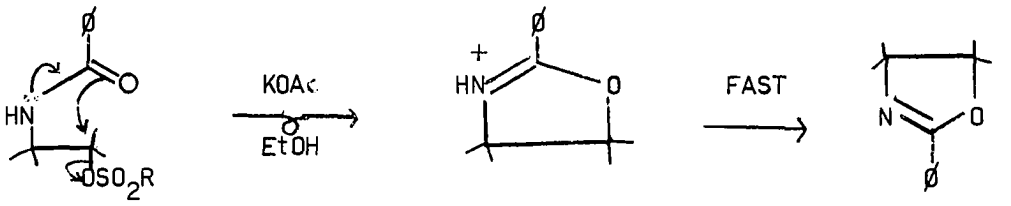



Figure 12. The effect of ring size on the rate of cyclization of cis and trans-2-benzamidocycloalkane methanesulfonates.




This arrangement is energetically unfavorable in the cis-cyclopentane and cyclohexane cases and these compounds fail to react at all. The ratio of the rates of the cycloheptanes is 6200 indicating some degree of flexibility in this system.

The configuration of cyclohexanedicarboxylate, cycloheptanedicarboxylate and cyclopentanedicarboxylate esters greatly affects the rate of both acid and base catalyzed hydrolysis. In acid catalyzed hydrolysis the principal effect is steric. In basic hydrolysis one observes a combination of steric and polar effects.[26]

Table 1

The Kinetics of the Acid Catalyzed Hydrolysis of cis and trans-1,2-cyclohexanedicarboxylates.

| Ester | $k_1/10^4$ ($l\ mole^{-1}sec^{-1}$) | $k_2$ ($l\ mole^{-1}sec^{-1}$) | T (o) | Ea (kcal/mole) |
|---|---|---|---|---|
| Dimethyl trans-1,2-cyclohexanedicarboxylate | 4.6 | 2.2 | 90.3 | 17.7 |
| Dimethyl cis-1,2-cyclohexanedicarboxylate | 4.3 | 7.5 | 90.3 | 18.8 |

The carbomethoxy groups are probably diequatorial in the trans and are necessarily axial-equatorial in the cis epimer. The trans epimer, with less steric hindrance, is seen to hydrolyze more rapidly. In the monoester the cis isomer hydrolyses more rapidly, possibly because of hydrogen bonded structures facilitating attack by water.

Similar effects were observed in the hydrolyses of 1,2-cis and trans-cyclopentanedicarboxylates, but in the corresponding 1,3-compounds the rates of hydrolysis are almost identical for both cis and trans diesters and cis and trans monesters.[27]

The base catalyzed hydrolyses of dimethyl cis and trans-1,2-cyclohexanedicarboxylates are similar except the trans monester saponifies more rapidly than the cis. The anion likely repels the attack of the incoming hydroxyl group.[28] The rates also provide evidence for hydrogen bonded structures in the acid catalyzed reaction.

Systems containing a carbonyl group and at least one alpha hydrogen undergo enolization, with either acid or base catalysis. This process is influenced greatly by steric and polar effects.

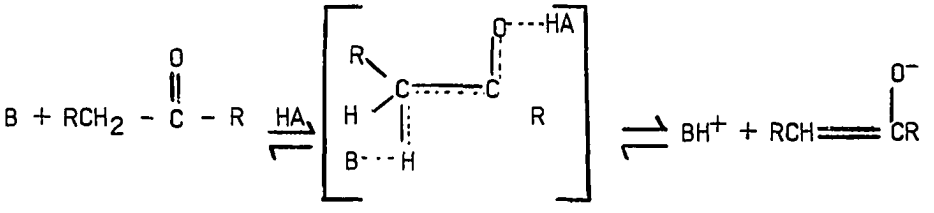



Figure 13. Proposed mechanism of the base catalyzed enolization of a ketone.

In general the enols that are stronger acids enolize more rapidly than those that are weaker.[29] Any structure which will stabilize the transition state should stabilize the product, as they resemble each other with respect to planarity, conjugation, or the presence of electron attracting groups. Substitution of alkyl groups for the alpha hydrogens tends to accelerate enolization.

Ring size plays a large role in the rate of enolization of alicyclic ketones and cycloalkylphenyl ketones. The rates of base catalyzed enolization are summarized in the table below.[30]

Table 2

The Effect of Ring Size on the Rate of Enolization of Cycloalkanones by NaOD

| Ring Size | $k_1 \times 10^{7}$(40°) ($sec^{-1}$) | E (kcal/mole) | $\Delta S^{\neq}$ (e.u.) |
|---|---|---|---|
| 4 | 2300 | 12.3 | -31 |
| 5 | 680 | 15.9 | -26 |
| 6 | 100 | 12.2 | -42 |
| 7 | 19 | 14.6 | -37 |

The results of an acid catalyzed rate study (data not shown) have been interpreted to indicate that the rate is influenced primarily by steric factors, but the base catalyzed rates are controlled by the s character of the carbon orbital directed toward the enolizable hydrogen.[30]

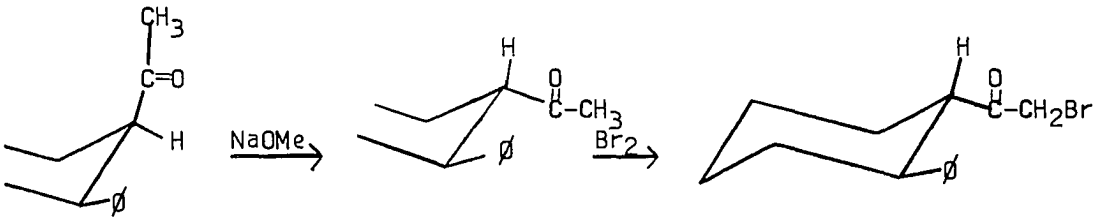
Table 3

The Effect of Ring Size on the Rate of Enolization of Phenylcycloalkyl Ketones Catalyzed by NaOD

| Ring Size | $k_1 \times 10^{7(40°)}$ ($sec^{-1}$) | E (kcal/mole) | $\Delta S^{\ddagger}$ (e.u.) |
|---|---|---|---|
| 3 | 10.0 | 15.7 | -38 |
| 4 | 8.4 | 16.8 | -35 |
| 5 | 2.9 | 13.1 | -48 |
| 6 | 0.5 | 17.0 | -39 |

In enolizations of steroid systems an unstable kinetic product is sometimes observed. The formation of these products is explained by the concept of stereoelectronic control.[31] There is better overlap in the transition state for enolization when the leaving alpha hydrogen possesses the axial orientation rather than the more stable equatorial. In some cases this effect is large enough to overcome steric factors favoring equatorial attack.

However, if the carbonyl function is on the carbon alpha to the ring, stereoelectronic control is no longer observed.[32] Zimmerman showed that cis-phenyl-2-acetylcyclohexane epimerized readily with sodium methoxide to give the trans ketone. This epimerization necessitates removal of an equatorial hydrogen. Further enolization in the bromination of the trans derivative occurs by removal of the methyl alpha proton rather than the axial proton. These effects are observed,



probably not because of the absence of stereoelectronic control but by the ability of the carbonyl group to orient itself for the maximum overlap in the transition state.

The carbonyls of ester groups are, in general, not as effective in enolization reactions as are ketones. With base catalysis one obtains reactions of esters such as the Claisen condensation which involve anions. Most of these anions are at least partially stabilized by enolate ion formation.

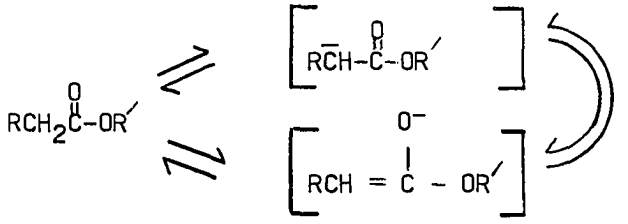


Figure 14. Proposed mechanism of Enolate Formation in the Claisen Condensation.[33]

These enolizations are accompanied by complete racemization of products (as are the products involving enolization of ketones). If only an intermediate carbanion is involved, racemization is thought

to occur via a rapid flipping of the pair of electrons to give equal quantities of each enantiomer.

If a carbanion is not involved, the planarity of the enolate ion destroys asymmetry, as attack may occur from either face.

Base catalyzed equilibrations of esters yield an equilibrium mixture which reflects the relative stabilities of these products. The first synthetic use of this reaction was by Hückel and Goth in 1925, in their preparation of diethyl trans-1,2-cyclohexanedicarboxylate.[34]

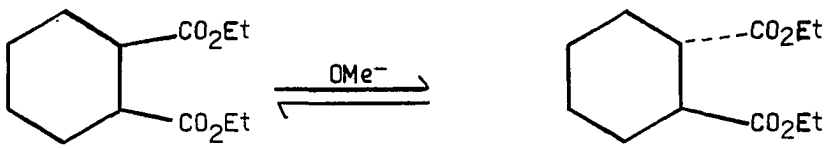



Figure 15. Base Catalyzed Epimerization of Diethyl 1,2-cyclohexanedicarboxylate.

The equilibration of dimethyl cis and trans-1,3-cyclohexanedicarboxylate has been studied by Allinger and Curby.[35] Conformational analysis of this system suggests the trans epimer is less stable than the cis. Equilibration of the esters with sodium methoxide in methanol yields a mixture of trans isomer (30%) and cis isomer (70%), corresponding to a free energy difference of 0.58 kcal/mole. The enthalpy is estimated to be -1.05 kcal/mole, smaller than the value for a methyl group, probably because the carbomethoxy group is planar and when in the axial position can avoid some axial hydrogen interactions.

The equilibrations of cis and trans-2-(2-thienyl)cyclopropanecarboxylic acid ethyl esters have also been studied.[36] McFarland studied this epimerization to clarify which acid was cis and which was trans, a point of some confusion in the literature. At equilibrium he found 6% of the cis isomer (equilibrating from both cis and trans isomers). This compares well with his value of 4.5% obtained for the corresponding phenylcyclopropylcarboxylate esters, as the steric requirements of the thienyl and phenyl groups should be similar.

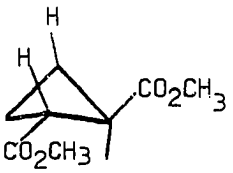
The effect of ring size on the equilibrium position of epimerization reactions of the preceding type has been studied by Fonken and Shiengthong.[37,38] Dimethyl cis and trans-1,2-cycloalkanedicarboxylates were equilibrated from both directions with sodium methoxide in methanol.

Table 4

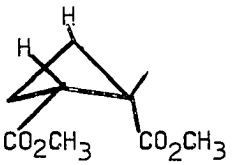
The Composition of Equilibrium Mixtures of Cycloalkanedicarboxylates from Base Catalyzed Epimerization

| Ester | % trans | % cis |
|---|---|---|
| Dimethyl 1,2-cyclopropanedicarboxylate | 99 | 1 |
| Dimethyl 1,2-cyclobutanedicarboxylate | 90 | 10 |
| Dimethyl 1,2-cyclopentanedicarboxylate | 90 | 10 |
| Dimethyl 1,2-cyclohexanedicarboxylate | 93 | 7 |

The equilibrium percentages for the different esters are rather similar, except for the cyclopropane case, where the trans epimer is overwhelmingly preferred. This is reasonable, as in the cis isomer the carbomethoxy groups are eclipsed and they are not in the trans. The position of equilibrium for the cyclobutane case is more similar to the cyclopentane and the cyclohexane case. This fact provides evidence for puckering in the cyclobutane rings. If puckering were not present the carbomethoxy groups would be eclipsed as in the cyclopropyl esters and a substantially different position of equilibrium would be observed. Puckering of the ring produces structures as those below.




trans




cis

# CHAPTER II

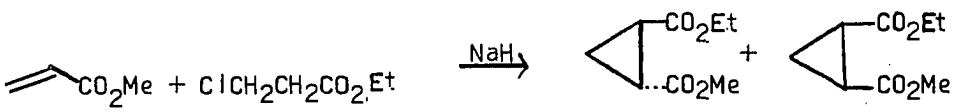
# DISCUSSION

The effects of substituents, sites of unsaturation, ring size, configuration, conformation, and other factors upon reaction rates need further study. The thermodynamics and kinetics of many reactions especially those involving enolization and epimerization are relevant. The present work is a study of the kinetics of the base catalyzed epimerization of dimethyl cis and trans-1,2-cycloalkanedicarboxylates. This work includes the study of the 1-methylcyclohexane, 1-methylcyclohex-4-ene, and the cyclohex-4-ene systems, as well as the homologous series of 1,2-cycloalkanedicarboyxlates containing three membered to seven membered rings.

## The Syntheses of Substrates

The substrates necessary for this study are, for the most part, not commercially available. The syntheses of the esters are described in the literature, although in several cases significant modifications are necessary to obtain reasonable quantities of materials.

Epimeric 1,2-cyclopropanedicarboxylic acid was synthesized by the method of McCoy.[39]

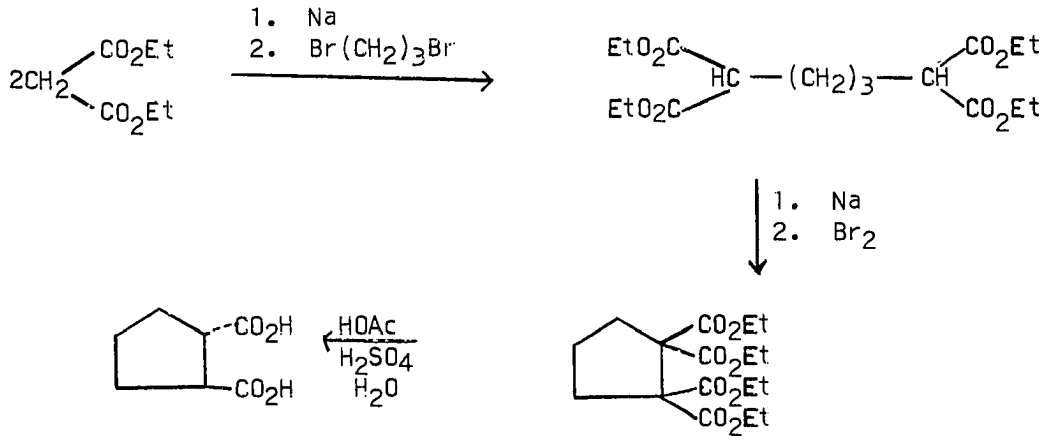


The ester obtained was saponified and the acid which resulted was converted to the cis anhydride with acetic anhydride. The pure cis acid was obtained upon treatment with water. The trans acid was prepared by epimerization of the dimethyl cis ester, followed by saponification and recrystallization. The dimethyl ester was synthesized with Fischer esterification conditions, in good yield.[40]

All esters prepared by this method are listed in Table 13, p. 46. The corresponding cis ester prepared in this manner was largely epimerized. Pure cis ester was synthesized by use of diazomethane in ethereal solution. All esters prepared by this method are listed in Table 12, p. 44.

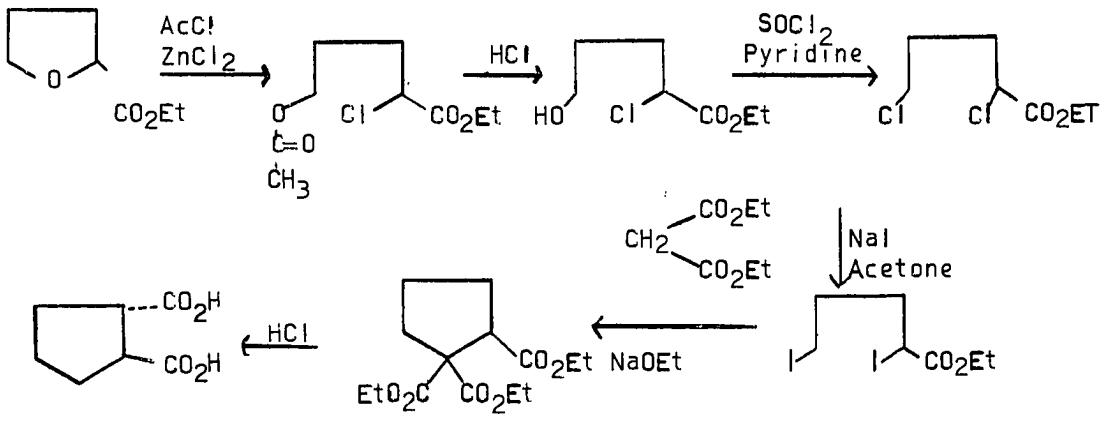
Cis and trans-cyclobutanedicarboxylic acids were prepared in a similar manner to the corresponding cyclopropyl acids from cis-1,2-cyclobutanedicarboxylic anhydride.[41]

The synthesis of cis and trans-1,2-cyclopentanedicarboxylic acid proved to be lengthy and good yields were difficult to obtain. These preparations were largely based on the work of Bailey and Sorenson[42] and Birch, Dean, Hunter, and Whitehead.[43] The synthesis used by Bailey and Sorenson is outlined below:




The yield of the first step of the series was increased from 36% to 70% theoretical by the use of sodium hydride in DMSO. The decarboxylation step, however, proves to go in poor yields (less than 21%) and only small quantities of the trans acid were prepared in this manner.

A second synthetic route with ethyl tetrahydrofuroate offered a more feasible approach. The impetus for use of this route was enhanced by the availability of a large sample of ethyl tetrahydrofuroate (Quaker Oats Company).



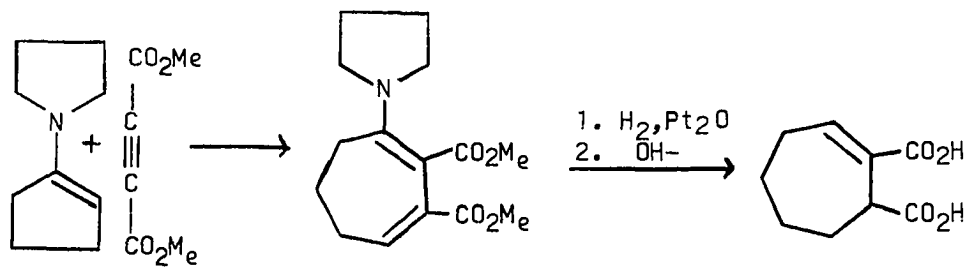
Although the procedure outlined above required more steps, the overall yields were good, and, in particular, a fair yield, 43%, was obtained in the decarboxylation step. The crude trans-1,2-cyclopentanedicarboxylic acid was converted to the cis anhydride with acetic anhydride. Pure cis and trans acids and their corresponding esters were prepared as described previously for the cyclopropyl and cyclobutyl cases from this precursor.

The synthesis of the 1,2-cyclohexanedicarboxylic acids, the 1,2-cyclohex-4-enedicarboxylic acids and their corresponding esters were performed as those described above from commercially available starting materials.

Cis-1,2-cyclohexanedicarboxylic esters were prepared by Fischer esterification; concurrent epimerization was not observed.

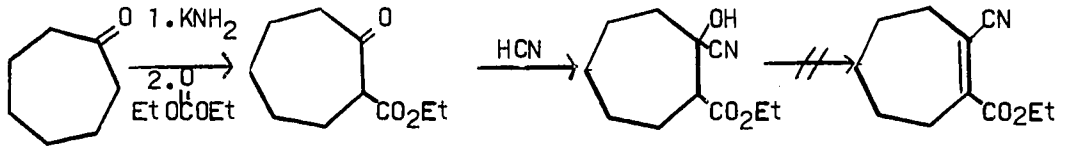
Cis and trans-1-methyl-1,2-cyclohex-4-enedicarboxylic anhydrides were hydrogenated to yield the cis and trans-1-methyl-1,2-cyclohexanedicarboxylic anhydrides respectively. The cis and trans dimethyl esters were prepared from all four anhydrides by treatment of the appropriate acid with diazomethane.

The synthesis of the cycloheptyl system was begun with the method of Brannock, Burpitt, Goodlet and Thweatt.[44] This method



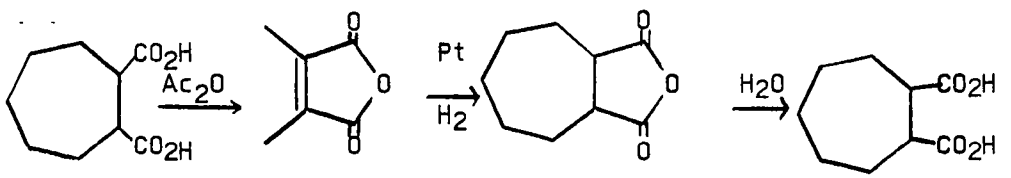
provided good intermediates for preparation of both cis and trans-1,2-cycloheptanedicarboxylic acids. 1,2-cyclohept-2-enedicarboxylic acid was hydrogenated in basic solution under moderate pressure with Raney nickel to yield predominantely trans acid. This method has been used as a synthesis for the cis acid, although, in this case epimerization occurred rapidly.[44] The dimethyl trans ester was prepared by esterification of the epimeric acid and purification by fractionation.

An attempt to prepare cis-1,2-cycloheptanedicarboxylic acid was made from cycloheptanone based on the work of Sicher, Sipos, and Jonas[45] and La Font and Bonnet.[46]




The cyanohydrin resisted dehydration with phosphorus oxychloride and pyridine. After each attempt only 2-carbethoxycycloheptanone could be recovered. Sicher, Sipos and Jonas reported good yields (90%) for the dehydration of the corresponding cyanohydrin of 2-carbomethoxycycloheptanone.[45]

Another synthetic scheme was envisioned to prepare the cis acid.



1,2-cyclohept-1-enedicarboxylic anhydride was formed by treatment of 1,2-cyclohept-2-enedicarboxylic acid with acetic anhydride. The hydrogenation step proceeded in only fair yield (50%) to produce the cis anhydride. The pure cis acid was prepared from this anhydride by hydrolysis with water.

## The Experimental Method

Samples of pure cis and trans esters in methanol were allowed to equilibrate at constant temperature with sodium methoxide. The concentrations of both base and substrate, and temperature were varied for different runs. Duplicate samples were epimerized for all runs. Close temperature control was maintained. Aliquots were removed at various times and titrated with hydrochloric acid. The quenched samples were then extracted and the relative percentages of esters in the samples were determined gas chromatographically. Each sample was determined three times and the average value was used in the calculations. Determination of known samples of esters showed no correction factors were necessary. The error of the relative percentages is estimated to be $\pm 1\%$.

## Thermodynamic Data

By measurements of the relative percentages of each pair of esters at equilibrium, the equilibrium constant and the free energy value may be calculated for the epimerization reaction.

As previously mentioned, thermodynamic stability has been related to conformation for the cyclobutane system.[37] The present study reveals some interesting conformational information for cyclic systems.

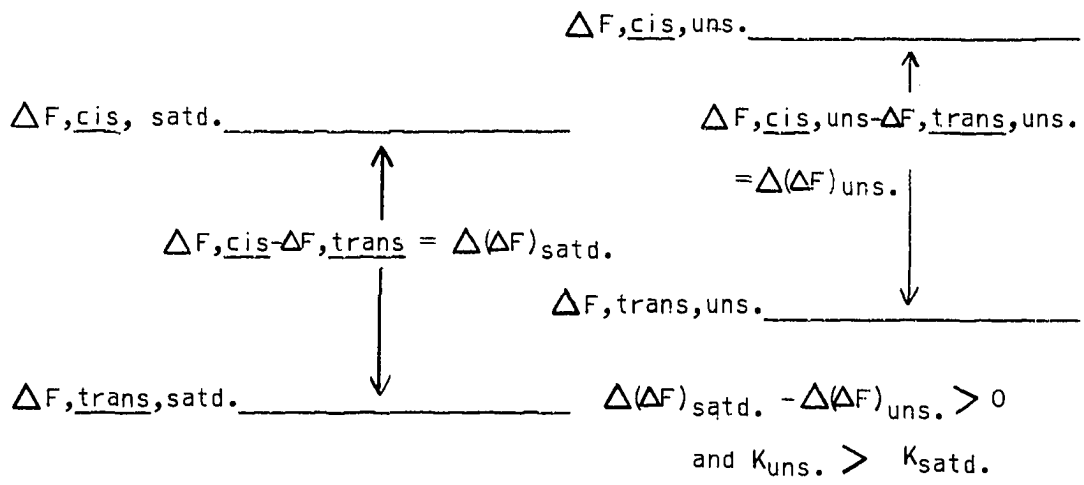
In trans cyclohexane systems the diaxial conformer is generally less stable than the diequatorial because of 1,3-diaxial interactions. In a system such as trans-4,5-dimethylcyclohexene, the diaxial conformer is stabilized with respect to the diequatorial by the removal of two 1,3 interactions.[11,47]

Dimethyl cis-1,2-cyclohexanedicarboxylate must contain one equatorial and one axial carbomethoxy group. The corresponding trans ester by analogy with 1,2-dimethylcyclohexane, should largely exist in the diequatorial conformation.[45] If a double bond is introduced into the four position, some 1,3 interactions are removed. As the cis ester must have one axial bond, the cis ester will be stabilized with respect to the trans. A stabilization, as predicted, is observed in the present work.

Table 5

Thermodynamic Data for the Equilibration of Dimethyl-cyclohexane- and Dimethyl Cyclohexenedicarboxylate Esters

| Compound | $\Delta F$ (kcal/mole) | K (trans/cis) |
|---|---|---|
| Dimethyl 1,2-cyclohexenedicarboxylate | -1.45 | 11.7 |
| Dimethyl 1,2-cyclohex-4-enedicarboxylate | -0.61 | 2.8 |




---

Allinger determined the interactions of a carbomethoxy group to be smaller than those of a methyl group. The carbomethoxy group is planar and can avoid some 1,3 interactions.[35]

In dimethyl trans-1-methyl-1,2-cyclohexanedicarboxylate the diequatorial conformation (carbomethoxy groups) should again be preferred. The cis ester may exist in two conformations. The carbomethoxy groups are axial and equatorial and the methyl group may be either axial or equatorial. The preferred conformation has the methyl group in an equatorial position. Conformational analysis reveals that the two isomers differ slightly. There is a difference of two 1,3-interactions and two gauche butane interactions with the methyl groups in the trans isomer whereas in the cis isomer these interactions are with a carbomethoxy group. As the interactions of a carbomethoxy group and a methyl group are similar, the cis should be stabilized with respect to the trans in this system.

Table 6

Thermodynamic Data for the Equilibration of the 1-Methylcyclohexane and Cyclohexanedicarboxylate Esters

| Compound | $\Delta F$ (kcal/mole) | K (trans/cis) |
|---|---|---|
| Dimethyl 1-methyl-1,2-cyclohexanedicarboxylate | -0.36 | 1.84 |
| Dimethyl 1,2-cyclohexanedicarboxylate | -1.45 | 11.7 |

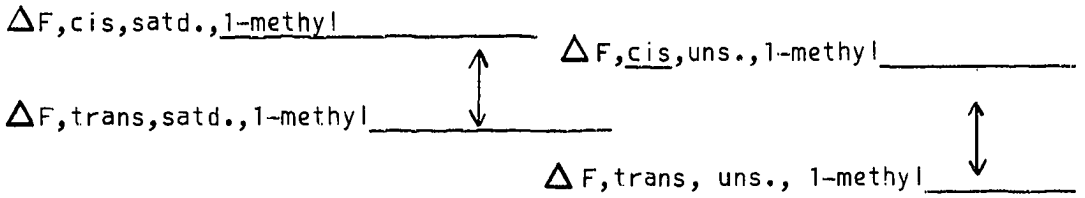
If one introduces a double bond into the system the trans diequatorial conformer becomes stabilized with respect to that of the saturated 1-methyl ester by a factor of one methyl-ring gauche butane interaction and one 1,3 methyl-hydrogen interaction. The cis ester (with the equatorial methyl) will be stabilized with respect to the unsaturated ester by one carbomethoxy-ring gauche butane interaction and one 1,3 carbomethoxy-hydrogen interaction. Since the interactions of carbomethoxy groups are slightly less than those of methyl groups, the trans ester should be stabilized with respect to the cis.

Table 7

Thermodynamic Data for the Equilibration of the Saturated and Unsaturated 1-Methyl Cyclohexanedicarboxylic Esters.

| Compound | $\Delta F$ (kcal/mole) | K(trans/cis) |
|---|---|---|
| Dimethyl 1-methyl-1,2-cyclohexanedicarboxylate | -0.36 | 1.84 |
| Dimethyl 1-methyl-1,2-cyclohex-4-enedicarboxylate | -0.80 | 3.90 |

A shift in the proper direction is again noted.




$$\Delta F,\underline{cis},satd.,1\text{-methyl} - \Delta F,\underline{trans},satd.,1\text{-methyl} = \Delta(\Delta F)_{satd.,1\text{-methyl}}$$

$$\Delta F,\ \underline{cis},\ uns.,1\text{-methyl} - \Delta F,\underline{trans},\ uns.,1\text{-methyl} = \Delta(\Delta F)_{uns.,1\text{-methyl}}$$

$$\Delta(\Delta F)_{uns.,\ 1\text{-methyl}} > \Delta(\Delta F)_{satd.,1\text{-methyl}}$$

---

The cis diester of cycloheptanedicarboxylic acid is stabilized with respect to that of the corresponding cyclohexane system because of a degree of flexibility in the ring which allows the substituents to decrease 1,3 diaxial and gauche butane interactions. The trans ester is affected less by this flexibility, although some gauche butane interactions are undoubtedly relieved. Again one observes a shift in the predicted direction.

Table 8

Thermodynamic Data for the Equilibration of Cyclohexyl and Cycloheptyl Esters

| Compound | $\Delta F$ (kcal/mole) | K (trans/cis) |
|---|---|---|
| Dimethyl 1,2-cyclohexanedicarboxylate | -1.45 | 11.7 |
| Dimethyl 1,2-cycloheptanedicarboxylate | -0.82 | 3.99 |

Small variations in the equilibrium constants were observed for changes in temperature and concentration. The equilibrium is shifted slightly toward the less stable cis isomer by an increase in temperature. This results because the overall energy of the system is increased and the formation of cis isomer becomes energetically more favorable.

The changes produced by concentration are much smaller than those of temperature. The effect is observed to vary so as to reduce the cis isomer in some systems and increase it in others. The differences, however, are probably not significantly different than the standard deviation of the rate constants and it is doubtful that a rigorous treatment would be meaningful.

## The Rate of Epimerization

The rates, $k_c$ and $k_t$, are reported for the epimerizations of both cis and trans esters. All calculated rates are expressed in the units ($l\ sec^{-1}\ moles^{-1}$) and are corrected for base concentration. As

the trans runs involve small changes of concentration, in most cases, the data derived from them is less accurate.

Plots of log $k_c$ for the homologous series of esters resemble the plots discussed in the introductory section. (Tables 7-10).

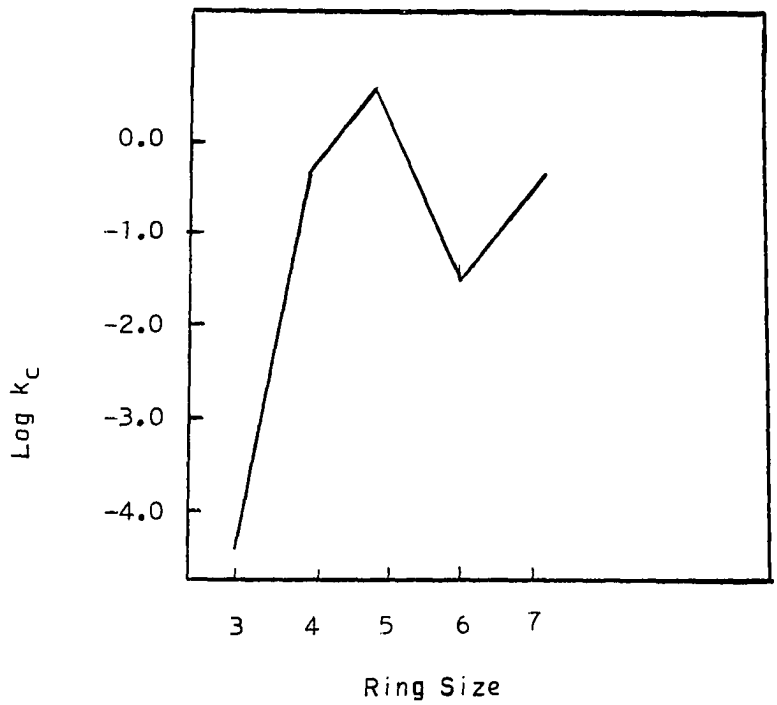



Figure 16. Plot of log $k_c$ Versus Ring Size for the Epimerization of cis-1,2-cycloalkanedicarboxylates.

The rates of the epimerization of the simple esters are explained by factors presented in the introduction.

The cyclopropyl ester requires a large amount of energy to distort the bond angles from tetrahedral to trigonal. The cyclohexane system is reluctant to be removed from its strain-free conformation.

The cyclobutyl, cyclopentyl, and cycloheptyl systems can change to a trigonal configuration more readily and are thus epimerized more rapidly.

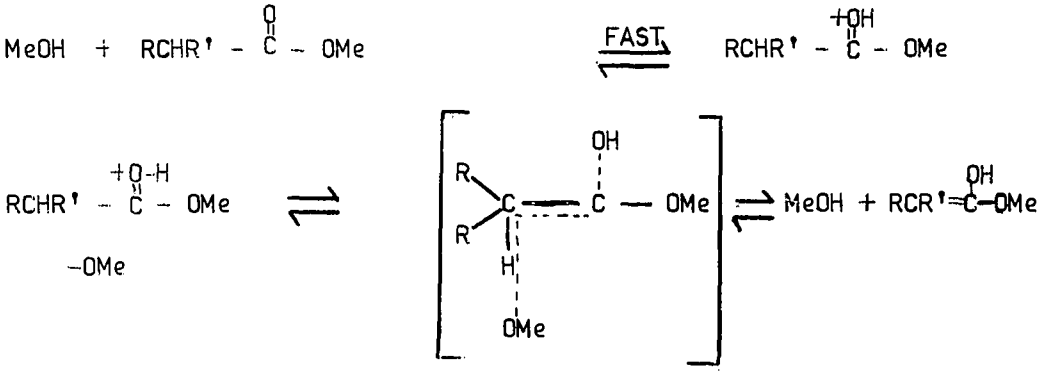
The rates of the 1-methyl substituted cyclohexyl and unsaturated cyclohexanedicarboxylates require a more complex explanation. Even assuming a statistical factor will decrease the rate of epimerization by one half, nevertheless the 1-methyl ester is still slower by a factor of ten than the unsubstituted ester. This effect is partially because of the added steric effects of the methyl group.

The rate of epimerization of dimethyl cis-1,2-cyclohex-4-enedicarboxylate is 1.8 times faster than that of the corresponding saturated compound. The approach to the hydrogen atom is much easier as there are less steric effects, i.e., less crowding in the unsaturated systems.

A similar effect is observed in a comparison of the rates of epimerization of dimethyl 1-methyl-1,2-cyclohex-4-enedicarboxylate and the corresponding saturated compound where the relative rate ratio is 2.5.

## The Mechanism

The mechanism of this epimerization reaction has not been examined closely. The removal of an acidic proton has been considered the rate controlling step. The mechanism must involve an enolization and the following mechanism explains certain features of the reaction. The mechanism in essence, was proposed by Shechter for the base catalyzed enolization of cycloalkanones and phenylcycloalkyl ketones.[30] He concluded that the rates of the base catalyzed process



Proposed mechanism for the base catalyzed epimerization of 1,2-cycloalkanedicarboxylates.

were primarily controlled by the s character of the carbon orbital directed toward an enolizable hydrogen. The transition states are fairly close to the enolate ion in character. It is of interest to note that the energies of activation of this reaction are all nearly the same (± 2 kcal). In the epimerization reaction of cycloalkanedicarboxylates a similar situation is observed.

Table 9

Energies and Entropies of Activation for the Epimeriation of 1,2-Cycloalkanedicarboxylates.

| Ester | $E_a$ (kcal/mole) | $\Delta S^{\ddagger}$ (e.u.) |
|---|---|---|
| Dimethyl 1,2-cyclopropanedicarboxylate | 20.8 | -23.1 |
| Dimethyl 1,2-cyclobutanedicarboxylate | 19.2 | -10.1 |
| Dimethyl 1,2-cyclopentanedicarboxylate | 19.9 | -10.5 |
| Dimethyl 1,2-cyclohexanedicarboxylate | 22.2 | -23.1 |
| Dimethyl 1-methyl-1,2-cyclohexanedicarboxylate | 20.7 | -19.6 |
| Dimethyl 1,2-cyclohex-4-enedicarboxylate | 19.8 | -14.8 |
| Dimethyl 1-methyl-1,2-cyclohex-4-enedicarboxylate | 24.3 | - 5.7 |
| Dimethyl 1,2-cycloheptanedicarboxylate | 20.3 | -11.0 |

Large negative entropies of activation are observed in both Shechter's and in the present study.

A negative entropy of activation is predicted for a reaction in which two substrates are brought together in the rate controlling step. However, the rather large differences in the two cases indicate a decided increase in ordering necessary in the transition state for certain esters.

The combination of a constant enthalpy of activation (or energy of activation) reflects a balance of the entropy and free energy factors, which may be expressed as:

$$\text{Constant} = \Delta H^{\ddagger} = \Delta(\Delta F)^{\ddagger} + T\,\Delta(\Delta S^{\ddagger}).$$

If the transition state located at the top of the $\Delta F^{\ddagger}$ "hill" of the reaction, is compared to that of a similar transition state atop an even higher hill; more energy is necessary to "order" the transition state of the higher hill. Thus, assuming the transition states to be of similar energies, an "ordering" or negative entropy contribution should be observed.

Based on these assumptions, the rates will be chiefly determined by this entropy factor. A plot of $\Delta S^{\ddagger}$ versus ring size is quite similar to the plot of log $k_c$ versus ring size (Figure 16).

The question now arises as to why the transition states are similar in these examples. The hydrogens alpha to a carbomethoxy group are all slightly acidic. The effect of the carbonyl group must tend to overshadow the effects of ring strain and other interactions, which may be present (as changes in hybridization). Further, the degree of

bond breaking and of bond making must be the same in all the transition states.

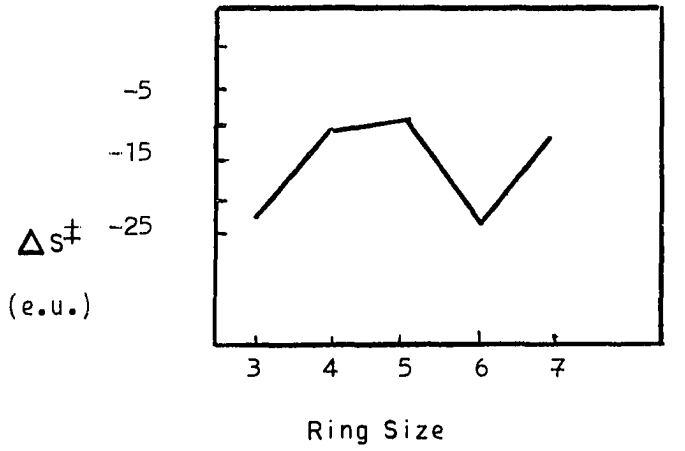
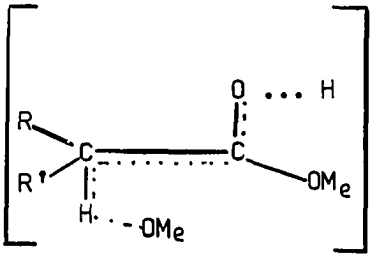



Figure 17. Plot of $\Delta S^{\ddagger}$ Versus Ring Size for the Epimerization of 1,2-cycloalkanedicarboxylates.

The transition state probably does not involve complete removal of the proton but looks more like:




The mechanism could be further investigated by substitution of deuterium in the alpha position. The ratio of $k_H/k_D$ should remain constant (from ester to ester) if the above state exists.

## CHAPTER III

## Conclusions

The kinetics of base catalyzed epimerization of dimethyl cis and trans-1,2-cycloalkanedicarboxylates has been shown to be a pseudo-first order process. The effect of ring strain, unsaturation, and methyl substitution upon the rates of base catalyzed epimerizations of these esters has been shown to be largely an entropy of activation effect. The activation energies of the reactions are approximately constant. This reflects a similarity in the transition states, which closely resemble the enolic forms of the esters. The differences in the rates of reaction are primarily determined by the entropy of activation effect. Steric interferences, which are probably manifestations of this entropy effect can qualitatively account for the relative rates of the cyclohexyl systems studied.

The relative rates of the homologous series (ring size 3 to 7) are accompanied by factors given in the following table. The stabilities of several cyclohexyl systems are examined by conformational analysis and found to agree in a qualitative manner with the observed equilibrium constants for the equilibration reaction.

Table 10

A Summary of the Rate Determining Factors for the Epimerization of 1,2-Cycloalkanedicarboxylates.

| Ester | Rate Determining Factor |
|---|---|
| Dimethyl 1,2-cyclopropanedicarboxylate | A distortion of $sp^3$ to $sp^2$ bonding in the transition state is unfavorable. |
| Dimethyl 1,2-cyclobutanedicarboxylate | The cyclobutyl system is assumed to be nonplanar and as it resembles the cyclopentane ring similar rates are observed. |
| Dimethyl 1,2-cyclopentanedicarboxylate | A change from $sp^3$ to $sp^2$ removes interactions and is favorable. |
| Dimethyl 1,2-cyclohexanedicarboxylate | Changes of hybridization introduce interactions into the perfectly staggered ground state and are unfavorable. |
| Dimethyl 1,2-cycloheptanedicarboxylate | A change from $sp^3$ to $sp^2$ hybridization removes interactions and is favored. |

# CHAPTER IV

## EXPERIMENTAL

All melting points and boiling points are uncorrected. Diazomethane was prepared from EXR-101 (DuPont trademark) (N,N'-dinitroso-N,N'-dimethylterephthalamide).[48] N.m.r. spectra were obtained with a Varian A-60 instrument, using tetramethylsilane as an internal standard. Chemical shifts are reported in δ-values (p.p.m. from TMS) and are followed by the multiplicity of the signals. Infrared spectra were recorded on a Beckman IR-8 spectrophotometer.

Thin layer chromatography was performed on glass plates (5 by 20 cm) coated with Merck (Darmstadt) silica gel H. The plates were placed in iodine vapor for visualization of the chromatogram.

Gas chromatographic analyses were conducted on a MicroTek, GC-1600 instrument with a flame ionization detector. Separations were done on stainless steel columns (1/8 inch, O.D., 10 feet in length) packed with 20% Carbowax 20M or 20% QF-1 on Anakrom ABS (80-100 mesh) and operated at temperatures between 115 and 140°. Helium was used for the carrier gas. A summary of conditions for the separations is given in the table below.

Known analytical samples of gas chromatographically pure esters were prepared and analyzed. The relative percentages corresponded within

TABLE 11

Conditions Used to Separate Epimeric Esters.

| Ester | Column | Temperature °C |
|---|---|---|
| Dimethyl 1,2-cyclopropanedicarboxylate | QF-1 | 140 |
| Dimethyl 1,2-cyclobutanedicarboxylate | Carbowax 20M | 140 |
| Dimethyl 1,2-cyclopentanedicarboxylate | Carbowax 20M | 130 |
| Dimethyl 1,2-cyclohexanedicarboxylate | Carbowax 20M | 130 |
| Dimethyl 1-methyl-1,2-cyclohexanedicarboxylate | QF-1 | 135 |
| Dimethyl 1,2-cyclohex-4-enedicarboxylate | Carbowax 20M | 130 |
| Dimethyl 1-methyl-1,2-cyclohex-4-enedicarboxylate | QF-1 | 115 |
| Dimethyl 1,2-cycloheptanedicarboxylate | Carbowax 20M | 135 |

experimental error to those of the known analytical samples, and no correction factors for the relative responses were necessary. The relative percentages of epimers were calculated using the method of half peak heights.[49] Samples of dimethyl 1,2-cyclohexanedicarboxylate which contained less than 12% of the cis ester were determined by the ratio of peak heights, which were compared with the relative heights of known samples.

Methylethyl 1,2-cyclopropanedicarboxylate[39]

Toluene (200 ml) and sodium hydride (25 g, 51.7% suspension in oil, 1.04 moles) were added to a one liter three neck flask equipped with a stirrer, addition funnel, and a Friedrich condenser with a drying tube, all flushed with nitrogen. After further flushing a mixture of ethyl chloroacetate (1 mole, 122 g) and methyl acrylate (1 mole, 86g) was added dropwise. The temperature was kept between 20 and 40°. The mixture was stirred until gas evolution was complete. Small amounts of methanol were then added until gas evolution again ceased. After the addition of sufficient water to dissolve the sodium chloride formed, the phases were separated, and the organic phase was washed three times with water (25 ml) and once with saturated sodium chloride solution (25 ml) and dried overnight with anhydrous magnesium sulfate. After removal of the magnesium sulfate by filtration, the toluene was distilled. (b.p. 109°). The remaining oil was rapidly distilled, b.p. 62-100°/0.4mm. The liquid which resulted was redistilled to give 70.2 g (40.8%) b.p. 52-54°/0.35 mm, $n_D^{24}$ 1.4416 (lit.[39] b.p. 104-114°/15mm, $n_D^{25}$ 1.4411).

Cis-1,2-cyclopropanedicarboxylic acid

Methylethyl 1,2-cyclopropanedicarboxylate (70.2g,0.41 mole) was heated for three hours with 50% excess of a 15% sodium hydroxide solution to effect saponification. Alcohols and water were removed under vacuum, and the salt was acidified with concentrated hydrochloric acid. The solution which resulted was continuously extracted with ether for three days. Removal of the ether left a solid which was then treated

with excess acetic anhydride. After the solution had refluxed overnight, the acetic anhydride was distilled leaving an oil which produced cis-1,2-cyclopropanedicarboxylic anhydride upon distillation, b.p. 97°/0.3 mm. The anhydride was hydrolyzed by warming with water. By removal of the water a slightly yellow solid was obtained, (52.5g, 92%). White crystals were obtained by recrystallization from ethyl acetate, m.p.139-140° (lit.[50], m.p.139°).

Dimethyl cis-1,2-cyclopropanedicarboxylate

Dimethyl cis-1,2-cyclopropanedicarboxylate was prepared by treating the cis acid dissolved in ether with a solution of diazomethane in ether. The results of this and other syntheses of esters by this method are summarized in Table 12.

Trans-1,2-cyclopropanedicarboxylic acid

A solution of sodium methoxide (0.43 M) was prepared by dissolving sodium (1 g., 0.043 mole) in methanol (100ml) which had previously been dried by reaction with magnesium. To this solution was added dimethyl cis-1,2-cyclopropanedicarboxylate (34g, 0.22 mole) and the mixture was heated for ten hours.

The ester was saponified by refluxing for eight hours with 10% potassium hydroxide solution (150 ml).

The saponification mixture was acidified with concentrated hydrochloric acid and then continuously extracted with ether for eight hours. The ether was removed by distillation to yield a crystalline material (23.3 g, 83%), which was recrystallized from an ether-pentane mixture to give the trans acid, m.p. 175° (lit.[51] m.p. 175°).

Table 12

Dimethyl Esters Prepared by Esterification with Diazomethane Solution

| Ester | Yield (g) | Yield (%) | $n_D$ | $n_D$(lit.) | Ref. | b.p. (°C) | b.p. (lit., °C) | Ref. |
|---|---|---|---|---|---|---|---|---|
| Dimethyl cis-1,2-cyclopropane-dicarboxylate | 32.3 | 97.5 | 1.4434 (27°) | -- | -- | 59/0.6mm | 200-202 | 61 |
| Dimethyl cis-1,2-cyclobutane-dicarboxylate | 31.6 | 88.5 | 1.4453 (27°) | 1.4430 (18°) | 62 | 56/0.5mm | 85/3mm | 41 |
| Dimethyl cis-1,2-cyclopentane-dicarboxylate | 24.1 | 91.5 | 1.4512 (27°) | 1.4528 (20°) | 63 | 68-70/ 0.7mm | 116-117/ 112mm | 27 |
| Dimethyl cis-1,2-cyclohex-4-enedicarboxylate | 31.6 | 94.0 | 1.4708 (26°) | 1.4700 (25°) | 40 | 77/0.7mm | 110-113/ 3mm | 69 |
| Dimethyl cis-1-methyl-1,2-cyclohexanedicarboxylate | 30.1 | 90.0 | 1.4588 (27°) | 1.4625 (20°) | 59 | 69-71/ 0.5mm | 98/2mm | 59 |
| Dimethyl trans-1-methyl-1,2-cyclohexanedicarboxylate | 24.0 | 92.5 | 1.4594 (25°) | 1.4639 (20°) | 59 | 54-55/ 0.2mm | 95/2mm | 59 |
| Dimethyl cis-1,2-cycloheptane-dicarboxylate | 2.7 | 82.0 | 1.4651 (26°) | 1.4659 (20°) | 45 | 85/0.4mm | 143-144/ 15mm | 45 |

### Dimethyl trans-1,2-cyclopropanedicarboxylate

Dimethyl trans-1,2-cyclopropanedicarboxylate was prepared from the trans acid with Fischer esterification conditions.[40] The results of syntheses of esters by this method are listed in Table 13.

### Cis-1,2-cyclobutanedicarboxylic Acid

Cis-1,2-cyclobutanedicarboxylic anhydride (62.2 g, 0.49 mole) (sample provided by Dr. J. J. Bloomfield) was allowed to react overnight with water. The mixture was extracted three times with ethyl acetate (25 ml) and the ethyl acetate solution was dried over anhydrous magnesium sulfate. The dried solution was filtered and then the solvent was removed by distillation. The acid crystallized (62.9 g, 89%) and after recrystallization from an ether-pentane mixture gave m.p. 139-140°. (lit.[52] m.p. 138°).

### Dimethyl cis-1,2-cyclobutanedicarboxylate

Dimethyl cis-1,2-cyclobutanedicarboxylate was prepared by esterification of the cis acid with diazomethane. The results are shown in Table 12. Ester prepared in this manner was shown to be 96.0% cis, 4% trans by gas chromatography.

### Trans-1,2-cyclobutanedicarboxylic Acid

A solution of sodium methoxide was prepared (0.2 M) by dissolving sodium (0.5 g, 0.02 moles in dry methanol (100 ml). Dimethyl cis-1,2-cyclobutanedicarboxylate (25 g,0.17 mole) was added and the solution was refluxed for twelve hours. Potassium hydroxide (150 ml of 10% solution) was added and the mixture heated at reflux

Table 13

Dimethyl Esters Prepared by Use of Fisher Esterification Techniques[40]

| Ester | Yield (g) | Yield (%) | $n_D$ | $n_D$(lit.) | Ref. | b.p. (°C) | b.p. (lit., °C) | Ref. |
|---|---|---|---|---|---|---|---|---|
| Dimethyl trans-1,2-cyclopropane-dicarboxylate | 18.1 | 64.0 | 1.4523 (26°) | 1.4472 (18°) | 71 | 61-63/ 0.5mm | 219-220 | 64 |
| Dimethyl trans-1,2-cyclobutane-dicarboxylate | 1.0 | 58.0 | 1.4430 (25°) | --- | --- | 53/0.4mm | 114/ 20mm | 62 |
| Dimethyl trans-1,2-cyclopentane-dicarboxylate | 7.5 | 54.0 | 1.4482 (25°) | 1.4491 (21°) | 63 | 59/0.7mm | 119-120/ 16mm | 27 |
| Dimethyl cis-1,2-cyclohex-anedicarboxylate | 192.5 | 64.0 | 1.4578 (25°) | 1.4570 (25°) | 40 | 73-75/ 1.3mm | 136.2/ 18mm | 28 |
| Dimethyl trans-1,2-cyclohex-anedicarboxylate | 24.0 | 80.0 | 1.4518 (25°) | 1.4539 (24°) | 56 | 58/1.3mm | 72-75/ 5-8mm | 56 |
| | | | | | m.p. | 33.5-35 | m.p.33° | 57 |

for an additional 10 hours. Alcohols and water were then removed under reduced pressure. The solution was acidified with concentrated hydrochloric acid and continuously extracted with ether for 36 hours. The ethereal solution was dried, filtered and then stripped leaving a yellow solid. White crystals were obtained by recrystallization (12.1 g, 58%) m.p. 131° (lit.[52] m.p. 131°).

Dimethyl trans-1,2-cyclobutanedicarboxylate

Dimethyl trans-1,2-cyclobutanedicarboxylate was prepared by esterification of the trans acid with Fischer esterification conditions. The results are listed in Table 13. The trans ester prepared in this manner was shown gas chromatographically to be 96.5% pure.

1,2-Cyclopentanedicarboxylic Acid

Tetraethyl-1,1,5,5-pentanetetracarboxylate. Sodium (5 g, 0.22 mole) was dissolved in absolute ethanol (100 ml), and the solution was cooled. Diethyl malonate (194 g., 1.2 moles) was added at a rate sufficient to keep the sodium enolate in solution by the heat generated. The solution was stirred and heated under reflux, and trimethylene bromide (20 g, 0.1 mole) was added dropwise over a thirty minute period. The solution was then refluxed for twelve hours. Ethanol was removed by distillation under vacuum. Water (80 ml) which contained sulfuric acid was added to the concentrated residue, to remove the sodium bromide and excess base. After separation of the phases, the aqueous layer was extracted three times with ether (100 ml) and the ether washings combined with the organic phase. The ethereal phase was dried over anhydrous sodium sulfate. The solution was filtered and the

ether was stripped. The remaining oil was distilled through a six inch Vigreux column to give tetraethyl-1,1,5,5-pentanetetracarboxylate, (13.2 g, 36.4%), b.p. 157-160°/0.5 mm, (lit.[42], b.p. 198-202).

The above ester was prepared by a modified reaction in substantially better yield.

Sodium hydride (20 g, 0.85 mole) was washed four times with dry benzene in a two liter three necked flask with a sintered glass filter sealed in the bottom, and fitted with a stirrer, Friedrich condenser, and addition funnel. Dimethyl sulfoxide (400 ml) was added to the washed sodium hydride, followed by the addition of diethyl malonate (384 g, 2.4 moles). After the mixture had been cooled, trimethylene bromide (40.4 g, 0.2 mole) was added dropwise while heat was supplied by a steam bath. After the addition was almost complete, the reaction mixture turned white and became viscous. This mixture was stirred vigorously for one hour at about 95° and then poured onto ice (1 liter). After the mixture had been stirred for ten minutes, the phases were separated and the aqueous layer was washed three times with ether (100 ml). The ether washes were added to the organic phase and it was washed three times with water (100 ml). The organic phase was dried with magnesium sulfate. After filtration of the magnesium sulfate, the ether was removed. The organic phase was fractionated to yield three fractions:

Fraction I: b.p. 60-70°/0.8 mm, recovered diethyl malonate, (300 ml).

Fraction II: b.p. 120-140°/0.8 mm, $n_D^{25}$ 1.4505, 8 ml. monoaddition product.

Fraction III: b.p. 160-164°/0.8 mm, $n_D^{25}$ 1.4439. (lit.[42] b.p. 198-202°/ 2.5 mm). (50.0 g, 70%) consisted of the desired ester.

Tetraethyl-1,1,2,2-cyclopentanetetracarboxylate. Sodium (6.44 g, 0.28 mole) was added to absolute ethanol (200 ml). After the reaction had ceased tetraethyl-1,1,5,5-pentanetetracarboxylate was added slowly. After the reaction mixture had cooled, bromine (49.0 g, 0.32 mole) was added with stirring and cooling. When addition was complete ethanol was removed under vacuum. The residue was triturated with water and the phases separated. The aqueous phase was washed with ether (25 ml) three times and the combined ether phases were also washed with water (50 ml). The ethereal phase was dried over anhydrous magnesium sulfate. After filtration of the magnesium sulfate, the ether was removed, and the residue was distilled to yield tetraethyl-1,1,2,2,-cyclopentane-tetracarboxylate (30.2 g, 60.0%), b.p. 138°/0.4mm.

Trans-1,2-cyclopentanedicarboxylic acid.

Tetraethyl-1,1,2,2-cyclopentanedicarboxylate. (30.2 g, 0.09 mole) was heated with a mixture of concentrated sulfuric acid (50 ml), glacial acetic acid (50 ml), and water (150 ml), with concurrent distillation of ethyl acetate. When formation of ethyl acetate ceased the mixture was continuously extracted with ether for 24 hours. The mixture was then neutralized with sodium bicarbonate, and then made barely acidic with hydrochloric acid. Trans-1,2-cyclopentanedicarboxylic acid was extracted from the solution with ethyl acetate. Upon removal of the ethyl acetate, crystals of crude product were formed, which were recrystallized from water, and decolorized with Norite to

yield white crystals, (3.2 g, 21.0%), m.p. 159-160° (lit.[53], m.p. 160°). Of several attempts this proved to be the best yield.

Trans-1,2-cyclopentanedicarboxyclic Acid

Ethyl 2-acetoxy-5-chloropentanoate. Acetyl chloride (redistilled, 316 g, 4.0 moles) was added over a period of an hour to ethyl tetrahydrofuroate (b.p. 188-189°, $n_D^{25}$ 1.433, 291 g, 2 moles, sample provided by the Quaker Oats Company) and fused zinc chloride (1 g) at 50-65°. After addition of the acetyl chloride, an additional quantity of zinc chloride (1 g) was added and the solution was refluxed for five hours. The acetyl chloride was removed by distillation and the solution was filtered to remove suspended solids. The material was then crudely distilled to yield a pink, viscous liquid (400 ml). The oil was distilled through a one foot Vigreux column and yielded 385.8 g, (86.8%), ethyl 2-acetoxy-5-chloropentanoate, b.p.75°/0.25 mm, and $n_D^{25}$ 1.4410 (lit.[43] b.p.120-132°/7.0 mm, $n_D^{20}$ 1.4428).

Ethyl 2-hydroxy-5-chloropentanoate. Ethyl 2-acetoxy-5-chloropentanoate (386 g, 1.74 moles) in methanol (700 g) and concentrated hydrochloric acid (7 ml) was refluxed ten hours. The methyl acetate and methanol azeotrope b.p. 54° (lit.[43] b.p. 54°) was removed as formed. The alcohols and methyl acetate were removed under vacuum to yield ethyl 2-hydroxy-5-chloropentanoate (265.4 g, 84.0%, calculated as the ethyl ester.)

Ethyl 2,5-dichloropentanoate. Ethyl 2-hydroxy-5-chloropentanoate (265.4 g, 1.47 moles) was dissolved in pyridine (180 g, 2.3 moles) and cyclohexane (600 ml). The solution was cooled to 15°. Thionyl chloride (320 g, 2.5 moles) was added, and the temperature carefully maintained

from 15-20°. After addition of the thionyl chloride was complete, the temperature was raised to 75° for thirty minutes. The reaction mixture was poured over one liter of ice. The phases were separated. The organic phase was dried over anhydrous magnesium sulfate. The cyclohexane was removed under vacuum and the residual oil distilled, to yield the desired ester (194.9 g, 73%), b.p. 66°/0.4mm and $n_D^{27}$ 1.4575, (lit.[43] b.p. 77-79°/2mm and $n_D^{20}$ 1.4610).

Ethyl 2,5-diiodopentanoate. Ethyl 2,5-dichloropentanoate (195 g, 1.07 moles) was refluxed with two liters of acetone containing sodium iodide, (400 g, 2.67 moles) for 18 hours. Sodium chloride was removed by filtration, and the acetone was removed under vacuum. The diiodo-ester was taken up in ether, dried over anhydrous magnesium sulfate, and filtered. The ether was removed to yield 354 g (84.5%), ethyl 2,5-diiodopentanoate, $n_D^{25}$ 1.5672.

Trans-1,2-cyclopentanedicarboxylic acid. A mixture of diethyl malonate (142 g, 0.88 moles) and ethyl 2,5-diiodopentanoate (354.0 g, 0.86 moles) and a solution of sodium ethoxide (prepared by addition of sodium (32.5 g, 1.42 moles) to absolute ethanol (800 ml) were added concurrently to a stirred solution of the diiodo ester (30 g) in anhydrous ethanol (100 ml) at a rate so that addition was completed in the same length of time (45 minutes). The solution was then refluxed ten hours. The crude ester was extracted with ether and the ether was then removed by distillation. The crude ester was hydrolyzed and then decarboxylated by heating with concentrated hydrochloric acid for 96 hours. The solution was decolorized while hot with activated charcoal. Upon cooling the solution was extracted with ethyl acetate and the combined

ethyl acetate solutions were dried over anhydrous magnesium sulfate. Upon filtration and removal of the ethyl acetate, light purple crystals were obtained, 59.5 g (43%). The acid was washed with benzene to remove the purple color. The white crystals from this treatment had m.p.164° (lit.[43] m.p. 162-163°).

### Cis-1,2-cyclopentanedicarboxylic Acid

Trans-1,2-cyclopentanedicarboxylic acid (25 g, 0.16 mole) was refluxed with excess acetic anhydride for 24 hours. The acetic anhydride was then removed by distillation, and the residue distilled. The distillate was heated with water for two hours. The solution was then extracted with ethyl acetate and the ethyl acetate solutions were dried over anhydrous magnesium sulfate. After filtration of the magnesium sulfate and removal of the ethyl acetate, crystals of acid remained, (22.7 g, 90.8%). The acid was recrystallized from acetone to m.p. 140° (lit.[54] 141°).

### Dimethyl cis-1,2-cyclopentanedicarboxylate

Dimethyl cis-1,2-cyclopentanedicarboxylate was prepared by esterification of the cis acid with diazomethane. The data are listed in Table 12.

### Dimethyl trans—1,2-cyclopentanedicarboxylate

This ester was prepared using the same conditions as the trans cyclopropyl ester. The results are in Table 13.

### Cis-1,2-cyclohexanedicarboxylic Acid

Cis-1,2-cyclohexanedicarboxylic acid anhydride (77.0 g, 0.5 mole) was heated with water overnight to yield cis-1,2-cyclohexane-

carboxylic acid (86.0 g, 100%). The acid had m.p. 194° (lit. 194°) when recrystallized from water-acetone.

Dimethyl cis-1,2-cyclohexanedicarboxylate

Dimethyl cis-1,2-cyclohexanedicarboxylate was prepared with Fischer esterfication conditions. The data from this synthesis is in Table 13.

Trans-1,2-cyclohexanedicarboxylic Acid

A solution of sodium methoxide was prepared by dissolving sodium (1 g, 0.04 mole) in dry methanol (200 ml). Dimethyl cis-1,2-cyclohexanedicarboxylate (60 g, 0.3 mole) was added and the solution was refluxed for eleven hours. Potassium hydroxide solution (300 ml of 12%) was added and reflux was continued for twelve hours. The alcohols and water were removed under reduced pressure, and the solution was made acidic with hydrochloric acid. The acid (52 g, quantitative yield) was removed by filtration and had m.p. 216-217°. Upon recrystallization from water-acetone the acid gave m. p. 221° (lit.[55], m.p. 215°).

Dimethyl trans-1,2-cyclohexanedicarboxylate

The preparation of this ester utilized the same reaction conditions as the cyclopropyl ester. Fractional distillation gave the desired ester (24.0 g, 80%) in two fractions:

Fraction I, b.p. 54-58°/1.1mm, $n_D^{25}$ 1.4518

Fraction II, b.p. 58°/1.25mm, $n_D^{25}$ 1.4519 (lit.[56] b.p. 72-75°/ 0.5-0.7mm, $n_D^{24}$ 1.4539) and m.p. 33.5-35° (m.p. 33°, lit.[57]).

Cis-1,2-cyclohex-4-enedicarboxylic acid

Tetrahydrophthalic anhydride (76.0 g, 0.5 mole) was heated with water overnight. Upon cooling, crystals of the cis acid (80.0 g, 94.0%) formed. These crystals were recrystallized from water. After the crystals were dried in a vacuum desiccator they had m.p. 173-174° (lit.[58] m.p. 174°).

Dimethyl cis-1,2-cyclohex-4-enedicarboxylate

Dimethyl cis-1,2-cyclohex-4-enedicarboxylate was prepared from the corresponding cis acid with diazomethane. The data for this synthesis is in Table 12.

Dimethyl trans-1,2-cyclohex-4-enedicarboxylate

A sample of the trans ester provided by Dr. J. J. Bloomfield was used without further purification. This ester was shown to be gas chromatographically pure trans.

Dimethyl Cis-1-methyl-1,2-cyclohexanedicarboxylate

Cis-1-methyl-1,2-cyclohex-4-enedicarboxylic anhydride (83 g, 0.5 mole) (sample provided by Dr. J. J. Bloomfield) and 5% palladium on charcoal (2 g) were added to hexane (150 ml) and the mixture shaken under hydrogen until absorption of hydrogen ceased (30 minutes). The mixture was filtered to remove the catalyst and upon cooling the saturated anhydride precipitated. The hexane was removed under vacuum. The residual solid was allowed to stand overnight with water and upon cooling, crystals were obtained (74.0 g, 80.5%) with

m.p. 164-165° (m.p. 158°).[59]

Dimethyl cis-1-methyl-1,2-cyclohexanedicarboxylate was prepared by esterification of the corresponding acid with diazomethane. The data for this reaction is in Table 12.

### Trans-1-methyl-1,2-cyclohexanedicarboxylic Acid

Trans-1-methyl-1,2-cyclohex-4-enedicarboxylic anhydride (32 g, 0.19 mole), (sample provided by Dr. J. J. Bloomfield), and 5% palladium on charcoal (1 g) were added to hexane (200 ml) and the mixture was shaken under hydrogen until absorption of hydrogen ceased (2 hours). Upon filtration of the mixture and removal of the hexane under vacuum, the anhydride remained. This residue was allowed to stand with water overnight, and crystals of the trans acid (29.3 g, 83.2%) were formed. The acid, after recrystallization from a water-acetone mixture, had m.p. 210-212° (lit.[59], m.p. 210-212°).

### Dimethyl Trans-1-methyl-1,2-cyclohexanedicarboxylate

Dimethyl trans-1-methyl-1,2-cyclohexanedicarboxylate was prepared by esterification of the corresponding acid with diazomethane. The data for this reaction is listed in Table 12.

### Dimethyl cis and trans 1-methyl-1,2-cyclohex-4-enedicarboxylates

Samples of dimethyl cis and trans-1-methyl-1,2-cyclohex-4-enedicarboxylates provided by Dr. J. J. Bloomfield were used without further purification.

### Trans-1,2-cycloheptanedicarboxylic Acid

*The Pyrrolidine Enamine of Cyclopentanone.* Cyclopentanone (168

g, 2 moles), pyrrolidine (142 g, 2 moles), toluene (600 ml), and Dowex 50-W-X-8 Ion Exchange resin were refluxed for 24 hours. Water was removed as it was formed using a Dean-Stark trap. The toluene and pyrrolidine were removed by distillation at atmospheric pressure. The residual brown oil was fractionated to produce Fraction I, b.p. 66-90°/2.5 mm, 99.0 g; and Fraction II, b.p.90-150°/2.5-4.0 mm, 68 g. These fractions were stored under dry nitrogen. The infrared spectra showed the absence of carbonyl and nitrogen-hydrogen bands in both fractions, and the presence of double bond absorptions (1640 $cm^{-1}$). In addition fraction I showed a band corresponding to the band for the monosubstituted phenyl group of toluene (740 $cm^{-1}$). The total yield (fractions I and II) was 167 g (61.0%).

1-(N-pyrrolidino)-2,3-dicarbomethoxy-1,3-cycloheptadiene. Dimethyl acetylenedicarboxylate (130 g, 0.92 mole) was added dropwise to a solution of the above enamine (167 g, 1.21 moles) dissolved in toluene (500 ml) which had been cooled to 10°. Care was taken so the reaction temperature was kept below 50°. After addition was complete the solution was refluxed for twelve hours. The solution was cooled and two liters of ether were added. After standing in the refrigerator overnight the enamine adduct precipitated as brown crystals. The solid material was removed by filtration, and recrystallized from acetone to give white crystals (115.8 g, 44.3%) m.p. 144-146° (lit.[60], m.p. 145-146°).

1,2-Cyclohept-2-enedicarboxylic acid. 1-(N-pyrrolidino)-2,3-dicarbomethoxy-1, 3-cycloheptadiene (115.0 g, 0.39 mole) was dissolved in glacial acetic acid. Adams Catalyst (3 g) was added, and the mixture was hydrogenated overnight. Hydrogen uptake ceased when 0.62 moles (80% of theoretical) had been absorbed. The solution was filtered to

remove the catalyst and the acetic acid was removed under reduced pressure. The residue was heated for two hours with excess aqueous 20% sodium hydroxide solution. Enough methanol was added to make the solution homogeneous. The mixture was acidified with concentrated hydrochloric acid, and extracted with ether (150 ml). The ethereal solutions were dried with anhydrous magnesium sulfate. After filtration of the solids the ether was removed by distillation to yield the unsaturated acid (26.2 g, 36.6%). The acid was recrystallized from water, m.p. 158–160° (lit.[44] m.p. 168–170°). This acid probably contained some 1,2-cyclohept-1-enedicarboxylic acid which produced a low melting point.

Dimethyl trans-1,2-cycloheptanedicarboxylate

1,2-Cyclohept-2-enedicarboxylic acid (26.2 g, 0.14 mole) was placed in a Parr hydrogenation bomb with water (170 ml), sodium hydroxide (11.4 g, 0.30 mole) and Raney nickel catalyst (8.7 g). When the mixture had been heated to 125°, the pressure was adjusted to 600 p.s.i., and the mixture was allowed to shake for twelve hours. The bomb was cooled and opened. The mixture from the bomb was filtered to remove the catalyst. The filtrate was concentrated to one-third its original volume and acidified with concentrated hydrochloric acid. The precipitate was removed by filtration and the solution was extracted with ether. Upon removal of the ether crystals were obtained which were combined with those removed by filtration. The total yield of acid (mixed cis and trans-) was 20.0 g (76.0%) which had m.p. 135–137° (lit.[44] m.p. (cis) 130–131°, 133–135°).

A mixture of cis and trans-1,2-cycloheptanedicarboxylic acid (10.0 g, 0.054 mole) in ether was added to an ethereal solution of diazomethane sufficient to completely esterify the acid. After removal of the ether, the residual oil was distilled to yield the ester, (9.8 g, 85%) b.p. 110-120°/3.5 mm, $n_D^{28}$ 1.4596. (lit.[45] (trans) b.p. 140-141°/ 10mm, $n_D^{20}$ 1.4630). The mixture of dimethyl cis and trans-1,2-cycloheptanedicarboxylate (9.0 g) was fractioned on a two foot spinning band column. Five fractions were collected:

Fraction I, b.p. 113-119°/4.6-4.5 mm, 0.7 g.

Fraction II, b.p. 119-118°/4.5 mm, 3.2 g.

Fraction III, b.p. 118-119°/4.5 mm, 4.9 g.

Fraction IV, b.p. 118-119°/4.5 mm, 1.4 g.

Fraction V, b.p. 119°/4.5 mm, 1.6 g.

Fractions II, III, IV, and V were combined to give ester that was determined to be 95.5% trans and 4.5% cis by gas chromatography.

Cis-1,2-cycloheptanedicarboxylic Acid

2-Carbethoxycycloheptanone. Potassium amide (1.2 moles) was prepared by addition of potassium (46.0 g, 1.2 moles) to excess ammonia, with ether (100 ml) added as a cosolvent. Ferric nitrate (0.2 g) was added as a catalyst to convert the metal to potassium amide, the ammonia was allowed to evaporate, and the volume of ether increased to 600 ml. Cycloheptanone (98.0 g, 0.9 mole) in ether (100 ml) was added dropwise to the cooled solution, over a period of thirty minutes. The solution was refluxed for two hours, cooled and then ethyl carbonate

(202 g, 1.71 moles) was added. After two more hours reflux, the solution was allowed to stand overnight. The solution was acidified with dilute hydrochloric acid and extracted twice with ether (500 ml). The combined ethereal phases were washed twice with water (100 ml), and dried over anhydrous sodium sulfate. After filtration, the ether was removed by distillation. The residual oil was fractionated, to give Fraction I, b.p. 25-28°/1.25 mm, $n_D^{27}$ 1.3829, 5.0 g, recovered ethyl carbonate, Fraction II, b.p. 29-40°/1.0 mm, $n_D^{27}$ 1.4576, 9.7 g, recovered cycloheptanone, and Fraction III, b.p. 66-80°/1.0 mm, 81.6 g (50.5%), $n_D$1.4724. (Almost all product collected at 80°). Fraction III was shown to be the desired beta-ketoester. The infrared spectrum showed absorptions at: 1735 (ester carbonyl), 1705 (cycloheptanone carbonyl), and 1640 $cm^{-1}$ (enolic band).

Cyanohydrin of 2-carbethoxycycloheptanone. 2-Carbethoxycycloheptanone (81.6 g, 0.44 mole) was added to liquid hydrogen cyanide (150 ml) and ethanol (200 ml) to which about 2 ml of saturated potassium cyanide solution had been added. The solution was kept at 0° for twelve hours, and then allowed to stand at room temperature for twenty-four hours. The solution was neutralized with saturated oxalic acid solution and filtered. After the filtrate had been evaporated under vacuum, the residual oil was taken up in ether, and dried over anhydrous sodium sulfate. After removal of the solid material by filtration, the ether was distilled under vacuum to yield 83.9 g (90.5%) of a red brown oil. This material had infrared absorptions at 3350-3450 $cm^{-1}$, 2210 $cm^{-1}$, 1705 and 1735 $cm^{-1}$, corresponding to those expected for this product (contaminated with some starting material).

Attempts to dehydrate this compound with phosphorus oxychloride and pyridine were not successful, and only 2-carbethoxycycloheptanone was obtained on workup.

### Cis-1,2-cycloheptanedicarboxylic Anhydride

1,2-Cyclohept-2-enedicarboxylic anhydride (8.8 g, 0.05 moles) was refluxed with excess acetic anhydride (60 ml) for 48 hours. The acetic anhydride was removed by distillation and the residual oil distilled b.p. 109-112°/0.5 mm. The distillate was hydrogenated with Adams catalyst (1 g) in dioxane (60 ml). After absorption ceased (0.057 moles) the mixture was filtered to remove the catalyst. The residual oil was then distilled to yield an oil (4.5 g, 50.8%), with b.p. 106-110°/0.35 mm., (lit.[45], b.p. 126-127°/10.5 mm).

### Cis-1,2-cycloheptanedicarboxylic Acid

The cis anhydride was heated with water for one hour. The acid was extracted three times with ether (50 ml) and the ethereal solution dried over anhydrous magnesium sulfate. The drying agent was removed by filtration and the ether by distillation. The acid (2.8 g, 51.0%) was recrystallized from acetone-hexane to give m.p. 129-135° (lit.[45] 133-135°).

### Dimethyl cis-1,2-cycloheptanedicarboxylate

Dimethyl cis-1,2-cycloheptanedicarboxylate was prepared from the cis acid by treatment with diazomethane. The data for this synthesis is listed in Table 12. This ester was a mixture of 89% cis and 11% trans epimer.

## Preparation of Samples for Kinetic Determinations

### Standard Ester Solutions

Solutions of the esters were prepared 0.25 M, by weighing the required amount of ester into a previously tared volumetric flask (100 ml). The solution was made to volume with methanol. All methanol used in the kinetic studies was specially dried by reaction with magnesium followed by distillation, and was stored over Molecular Sieve (III-A) under a drying tube.

### Standard Base Solutions

Sodium methoxide solutions were prepared approximately 0.25 M by dissolving hexane washed sodium metal in methanol treated as above in a dried volumetric flask (250 ml). The solution was made to volume by addition of methanol. Each solution was standardized by titration of weighed portions of potassium acid phthalate dissolved in water, using phenolphthalein as indicator. These stock solutions were prepared several times in the course of the work to avoid the use of sodium methoxide samples contaminated with sodium hydroxide.

### Epimerization of Esters

Aliquots of the standard ester and base solutions necessary to prepare the desired concentrations were pipetted into dried volumetric flasks (25 ml). These flasks were filled to volume with methanol, and a septum placed in the neck of the flask. The solution was agitated and placed in a constant temperature bath. In cases where the reaction was reasonably fast, the ester solution and methanol

were added, and the mixture was allowed to reach temperature equilibrium. The base solution was then added and the solution quickly agitated.

Duplicate kinetic samples were run in each case and equilibrium was approached with both cis and trans samples. Constant temperature baths were operated at 50± 0.02° (mineral oil), 35± 0.05° (mineral oil) and 25 ± 0.05° (water).

## Removal of Samples and Workup from Kinetic Runs

Samples (1 ml) were removed in the course of the kinetic runs with a syringe and quenched with 0.1 N hydrochloric acid. The acid used was prepared by dilution of constant boiling hydrochloric acid. Saturated sodium chloride solution (1 ml) and ether (1 ml) were added to the quenched sample in a three inch test tube. The tube was shaken and the phases were allowed to separate. The ethereal phase was removed and dried over a small amount of anhydrous magnesium sulfate. Samples prepared in this manner were used for gas chromatography without further preparation. Each sample was analyzed three times, and the average of these three values of relative percentages was used for subsequent calculations. The relative percentages of known ester samples worked up in the above manner showed no significant deviations from the known values.

## Treatment of Data and Results

The kinetics of a first order reversible reaction of the type $A \underset{k_t}{\overset{k_c}{\rightleftharpoons}} B$, where $K = k_c/k_t$, may be expressed as:[66]

$$\ln(AK-B) = \ln(A_0K-B_0) - (k_t + k_c)\, t, \qquad (1)$$

where $A_0$ and $B_0$ are the initial concentrations of A and B. The kinetics of the base catalyzed epimerization reactions of cis and trans-1,2-cycloalkanedicarboxylates was observed to obey this equation and to have pseudo-first order, reversible kinetics.

The necessary values of the equilibrium constants, K, were measured from analysis of the equilibrium concentrations, except those for dimethyl 1,2-cyclopropanedicarboxylate. The values for this ester have been reported by Shiengthong.[38]

The concentrations of the esters, A and B, were calculated from their relative percentages a and b, which were measured by gas chromatography and the initial concentration, $A_0$, by the relations:

$$A = aA_0(0.01)$$

$$B = bA_0(0.01).$$

Equation 1 is linear, therefore plots of $\ln(AK-B) = Yi$, versus t (time) have a slope of $-(k_t + k_c)$ and a y intercept of $\ln(A_0K-B_0)$. Several representative plots of this type follow.

The least squares equation for the slope, S, and the y intercept are as follows:

$$S = -(k_c + k_t) = \frac{N\sum t_iY_i - \sum t_i \sum Y_i}{N\sum t_i^2 - (\sum t_i)^2}$$

and

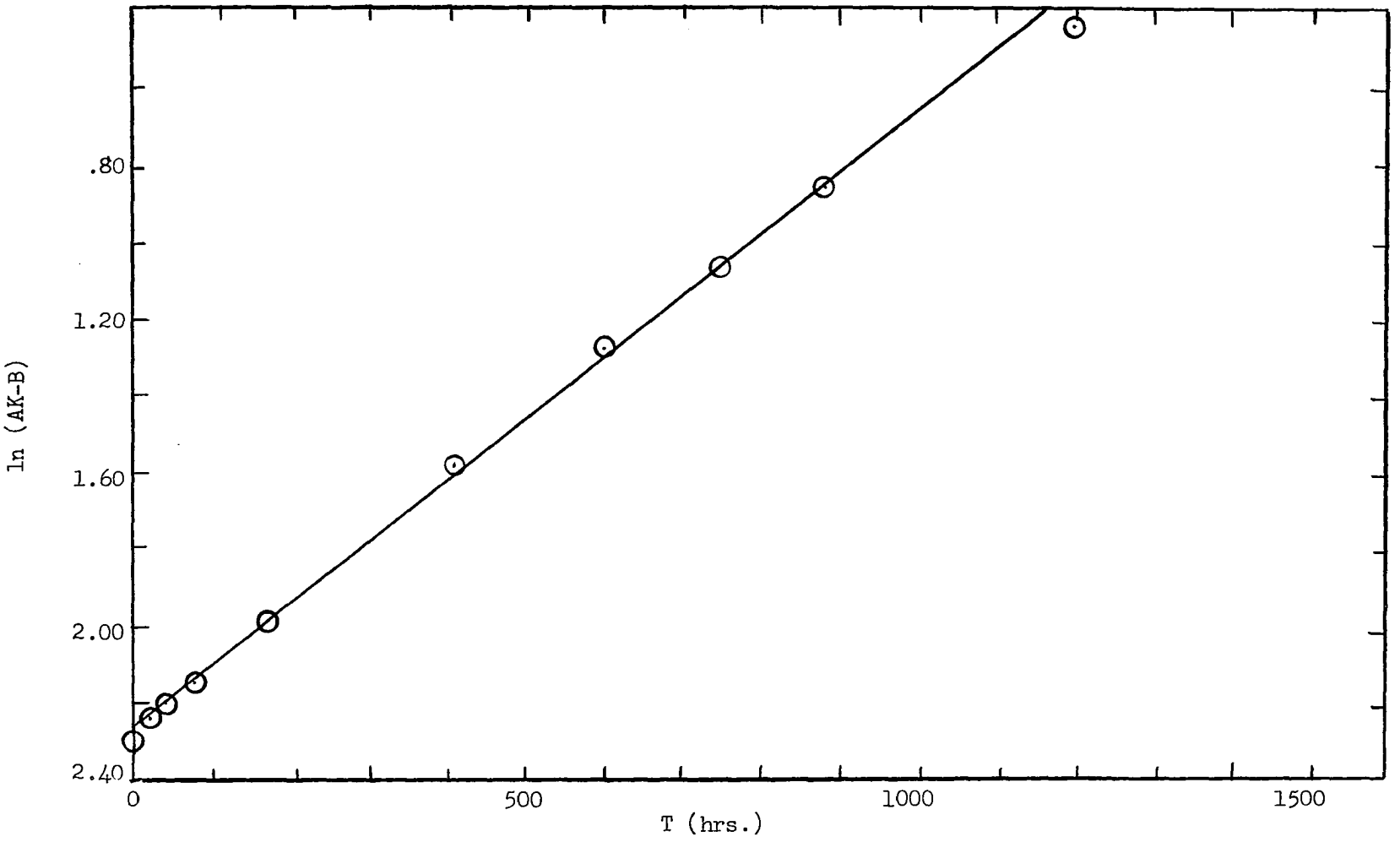



Figure 18. Plot of ln(AK-B) versus T for the Epimerization of 0.10 M Dimethyl cis-1,2-cyclopropanedicarboxylate at 50°.

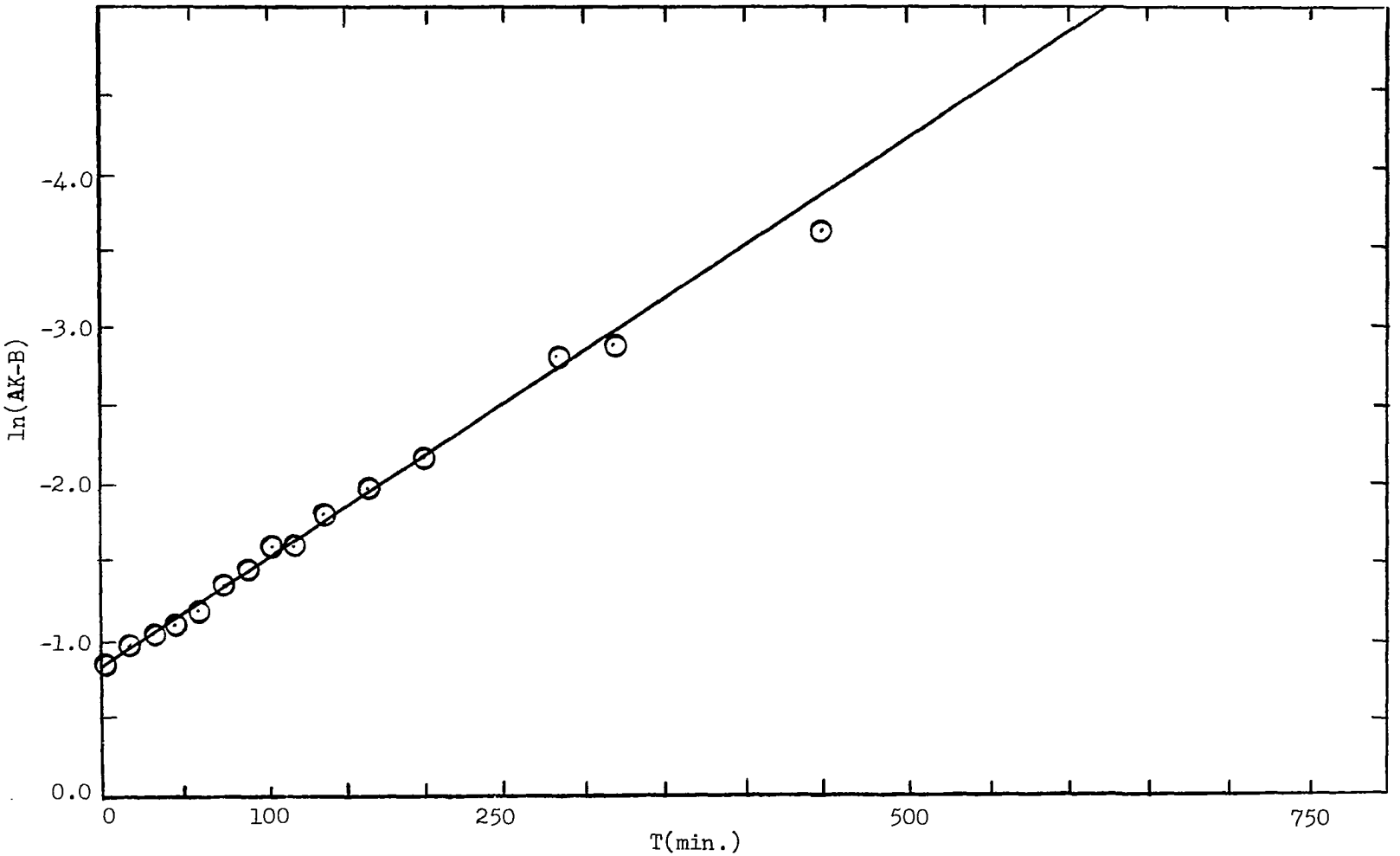



Figure 19. Plot of ln(AK-B) versus T for the Epimerization of .05 M Dimethyl cis-1,2-cyclobutanedicarboxylate at 50°.

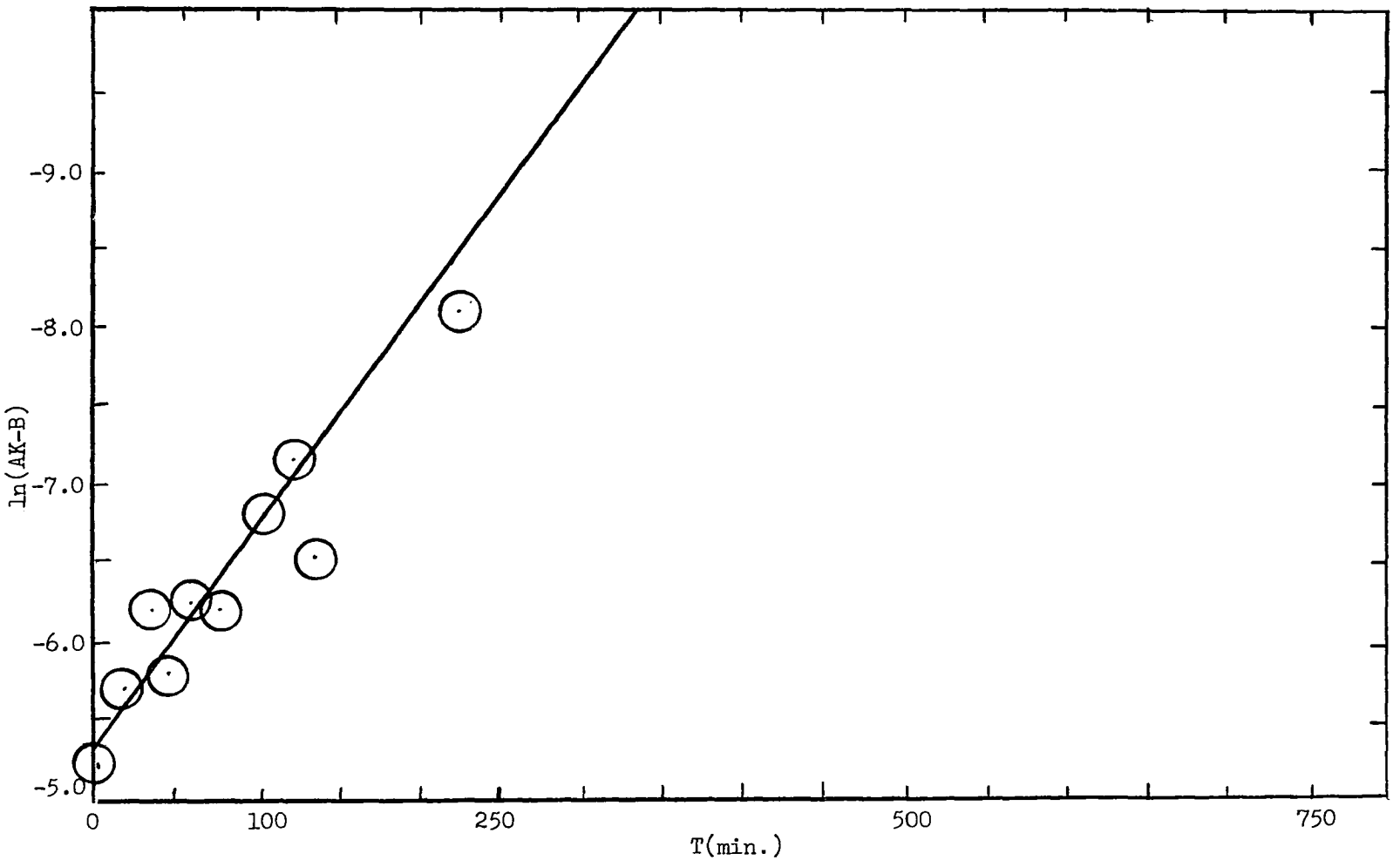



Figure 20. Plot of ln(AK-B) versus T for the Epimerization of .05 M Dimethyl trans-1,2-cyclobutanedicarboxylate at 50°.

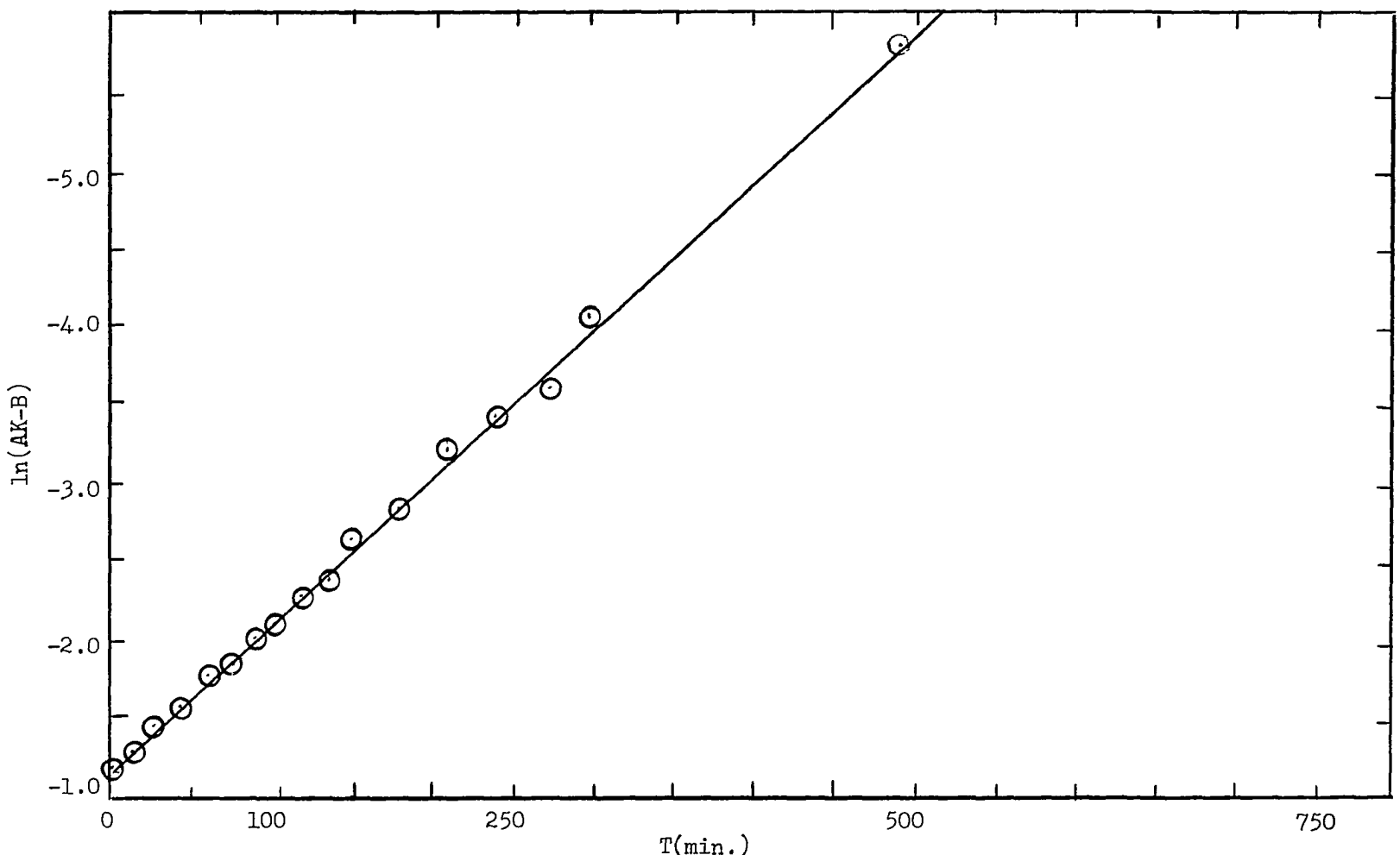



Figure 21. Plot of ln(AK-B) versus T for the Epimerization of .05 M Dimethyl cis-1,2-cyclopentanedicarboxylate at 50°.

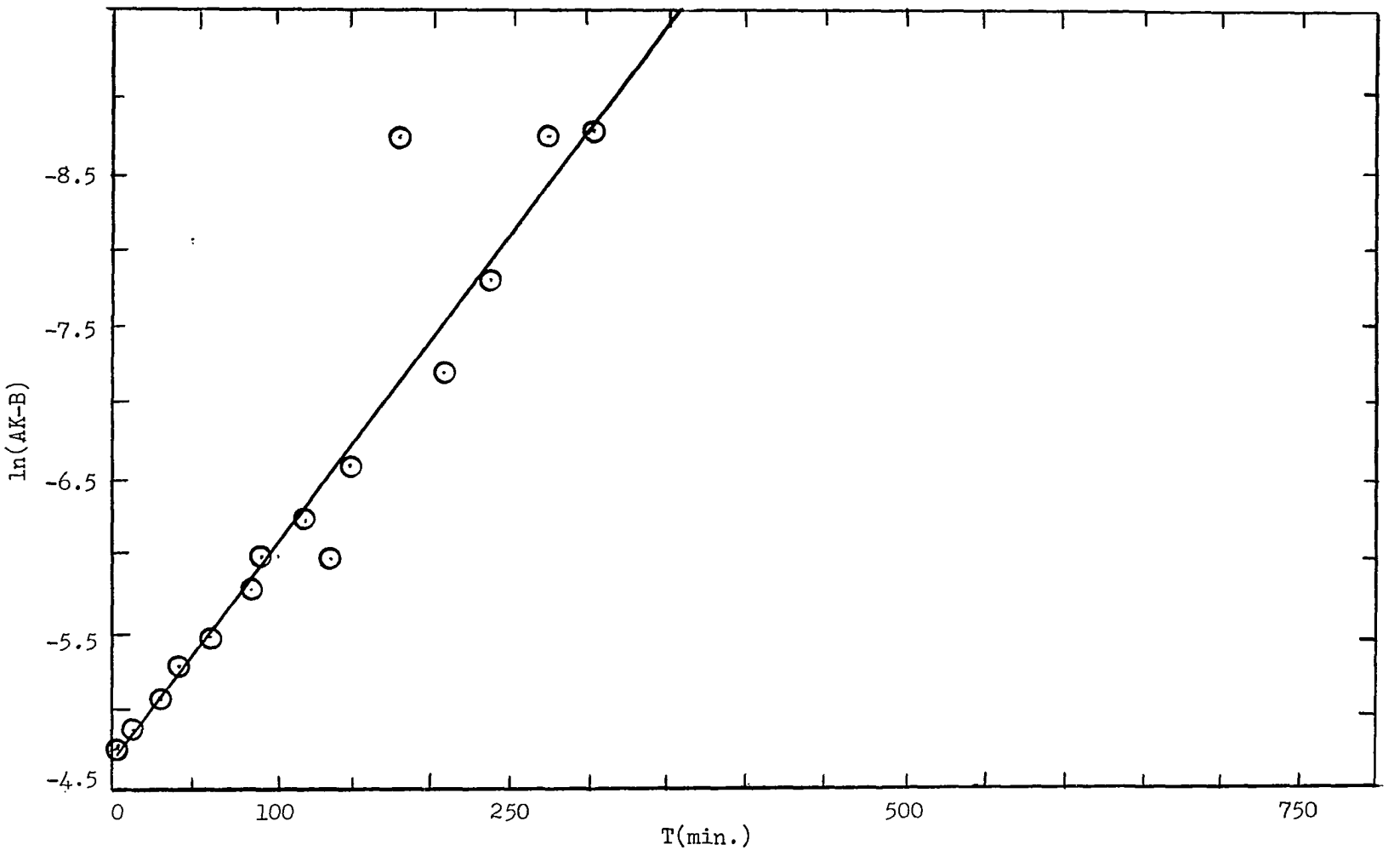



Figure 22. Plot of ln(AK-B) versus T for the Epimerization of .05 M Dimethyl trans-1,2-cyclopentanedicarboxylate at 50°.

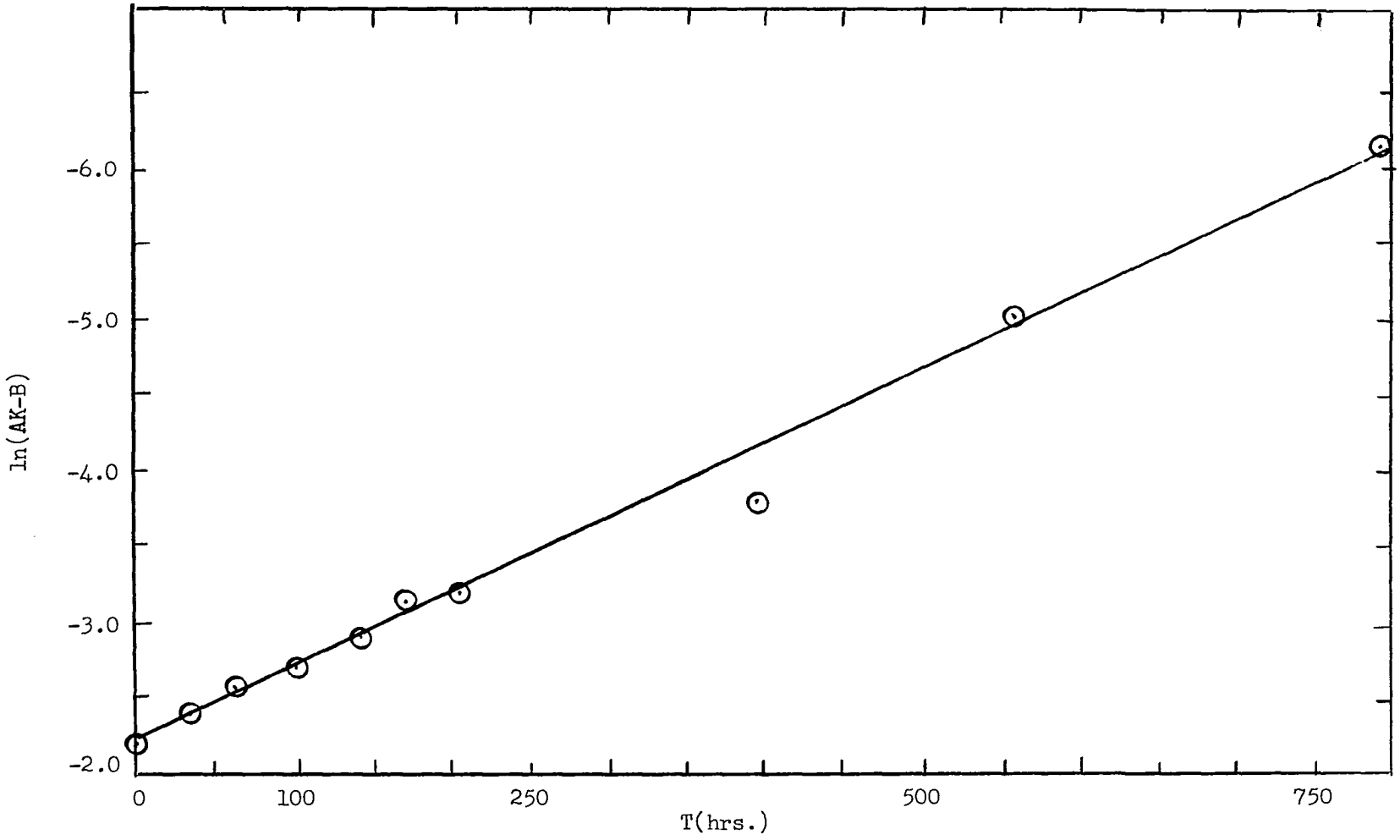



Figure 23. Plot of ln(AK-B) versus T for the Epimerization of .01 M Dimethyl cis-1,2-cyclohexanedicarboxylate at 50°.

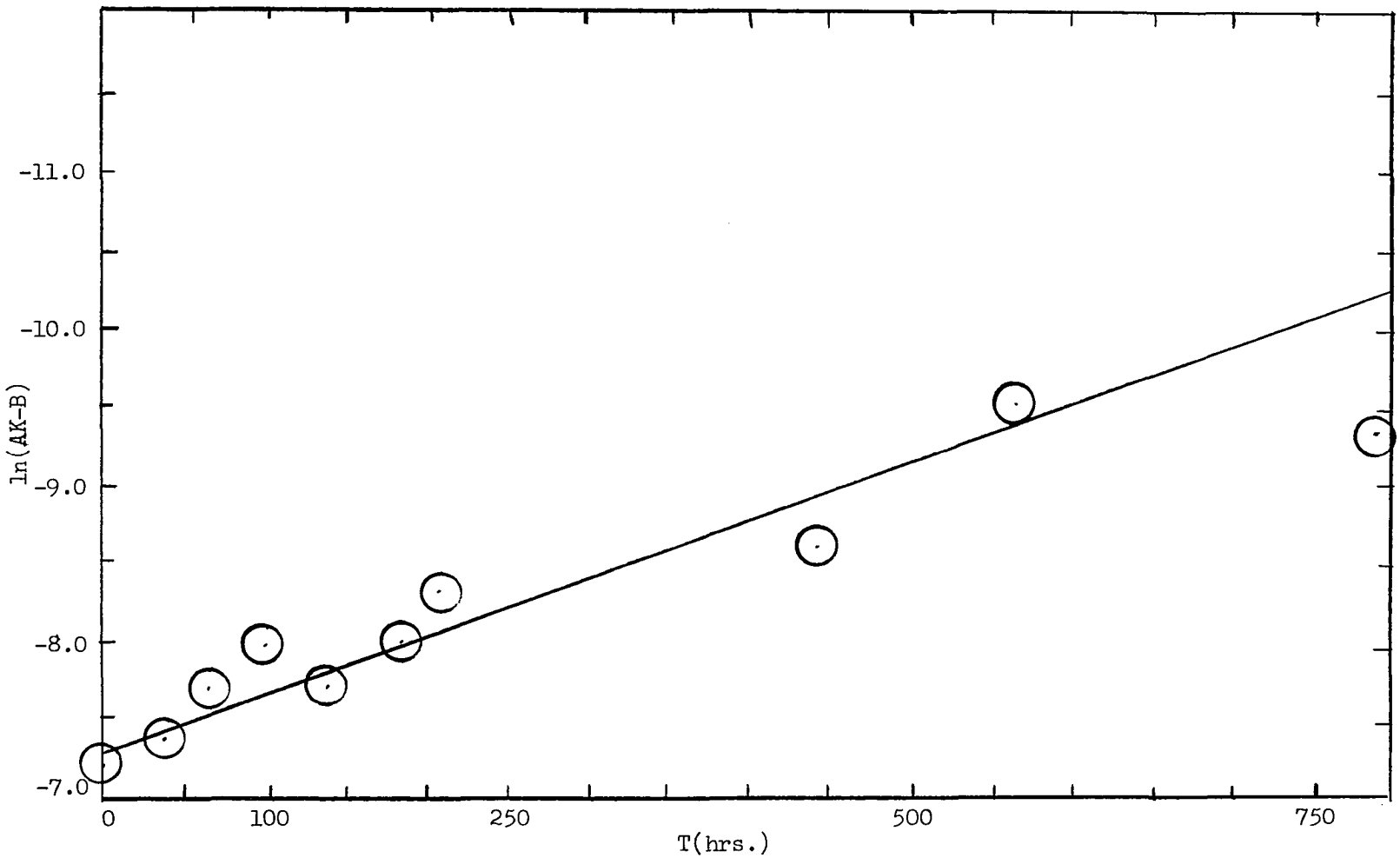



Figure 24. Plot of ln(AK-B) versus T for the Epimerization of .01 M Dimethyl <u>trans</u>-1,2-cyclohexanedicarboxylate at 50°.

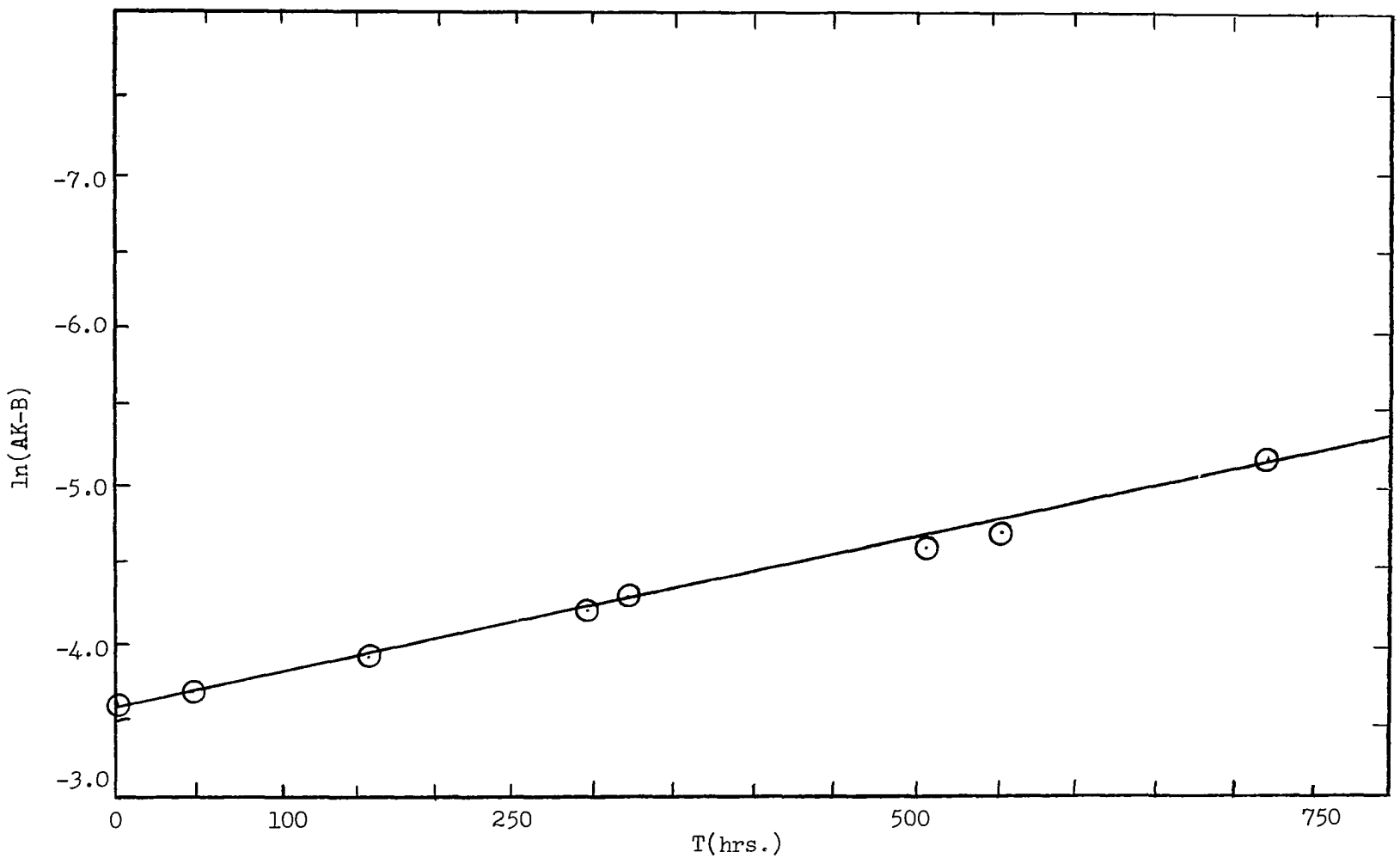



Figure 25. Plot of ln(AK-B) versus T for the Epimerization of .01 M Dimethyl cis-1,2-cyclohex-4-enedicarboxylate at 25°.

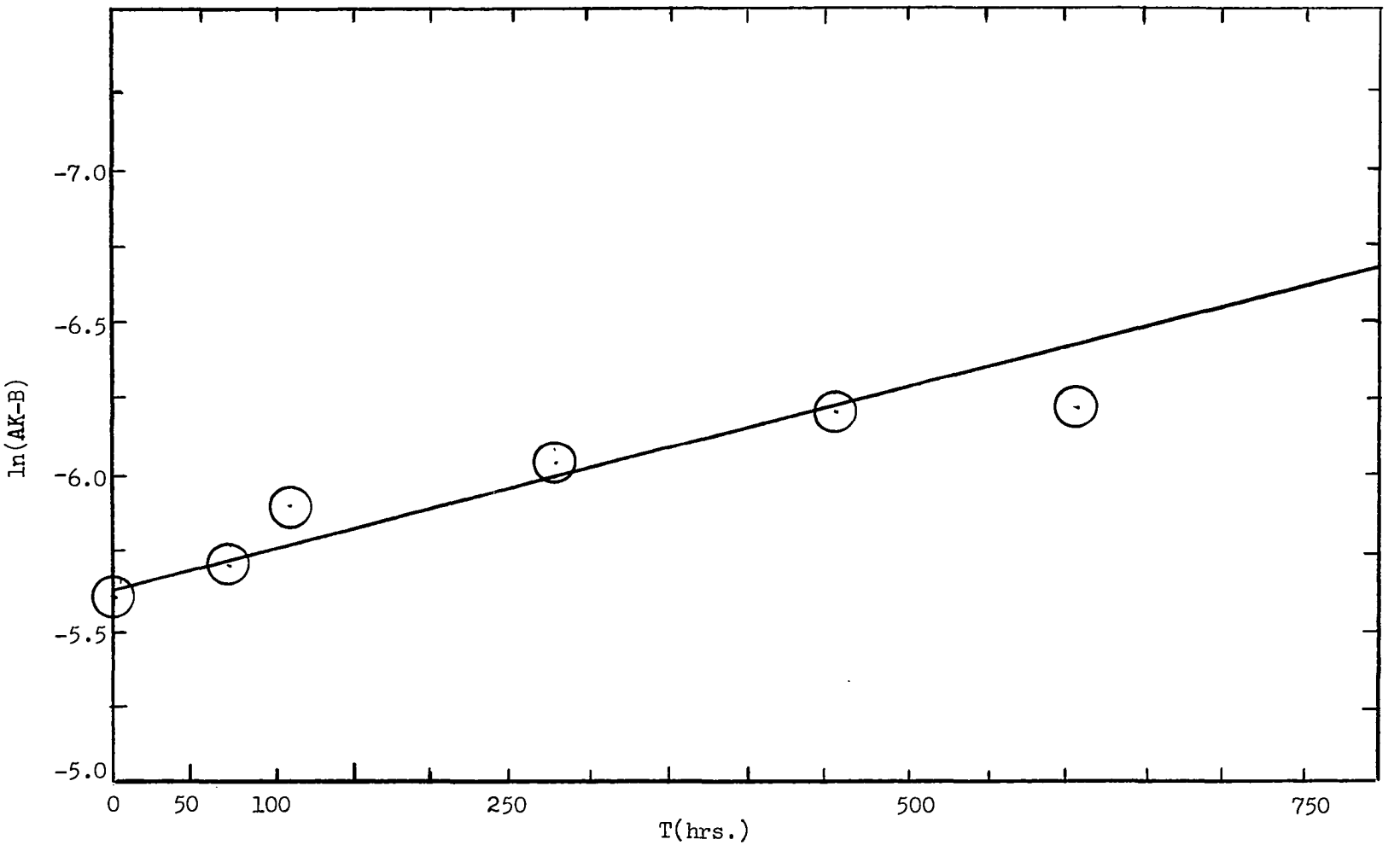



Figure 26. Plot of ln(AK-B) versus T for the Epimerization of .01 M Dimethyl trans-1,2-cyclohex-4-enedicarboxylate at 25°.

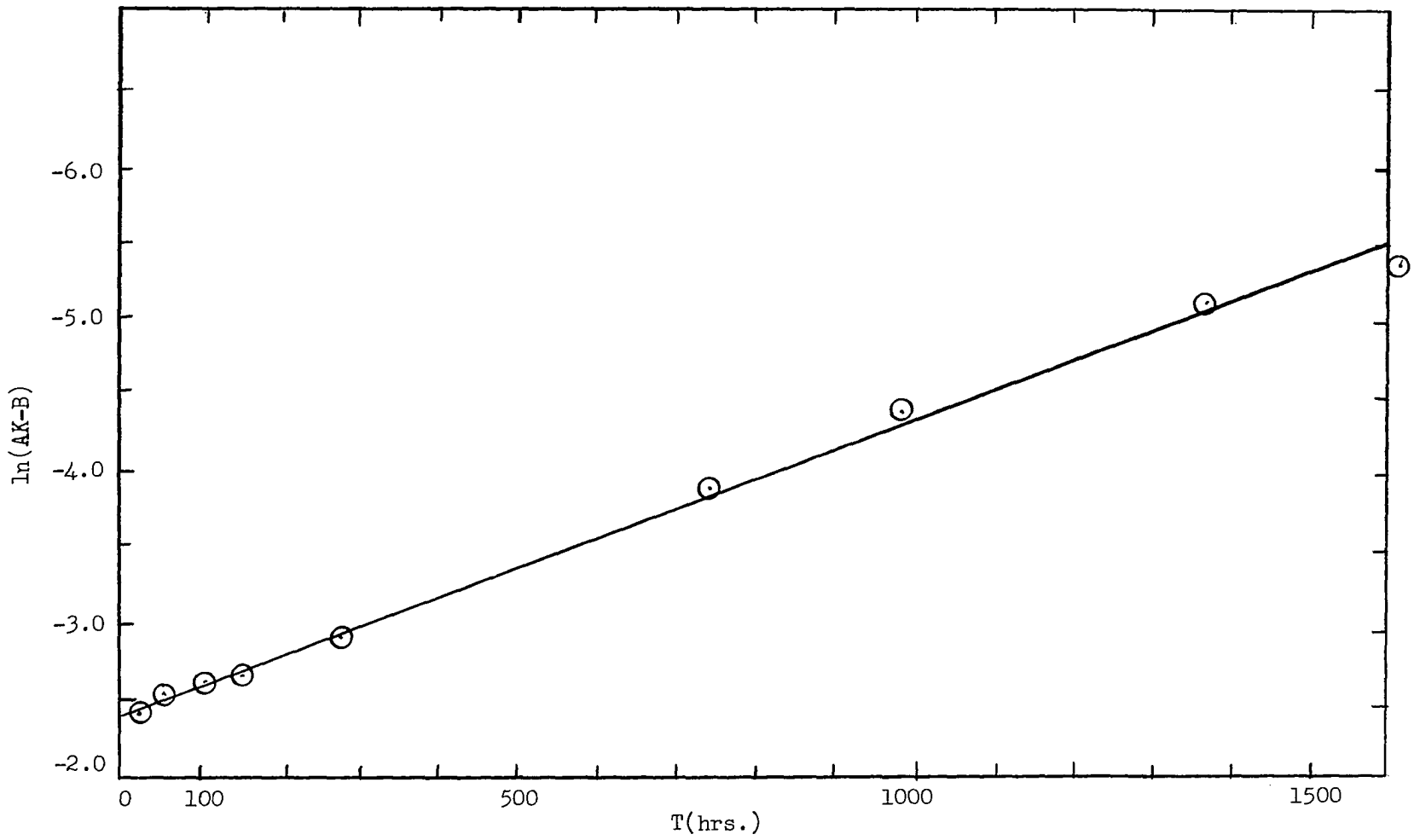



Figure 27. Plot of ln(AK-B) versus T for the Epimerization of .05 M Dimethyl cis-1-methyl-1,2-cyclohexanedicarboxylate at 50°.

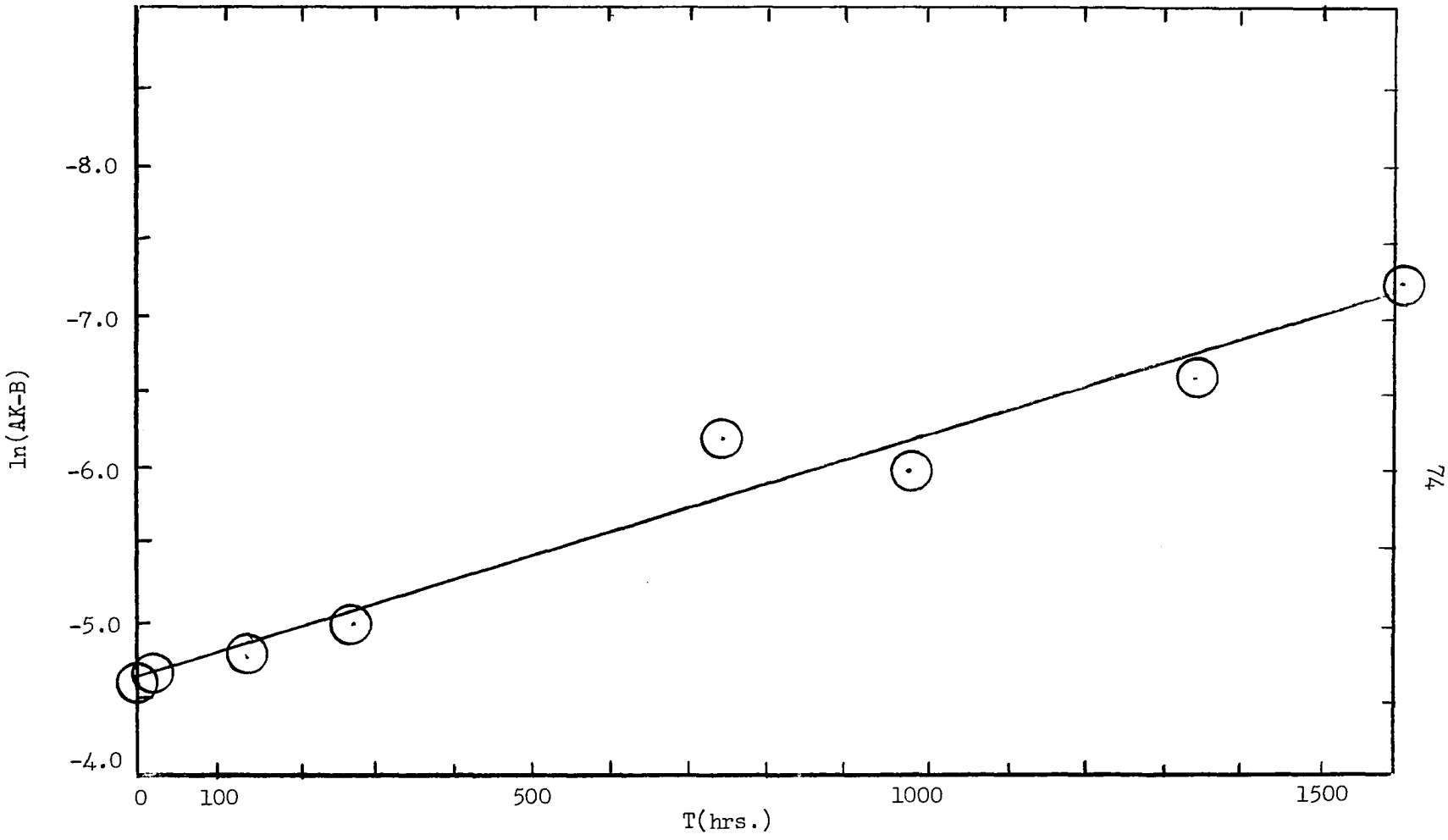



Figure 28. Plot of ln(AK-B) versus T for the Epimerization of Dimethyl <u>trans</u>-1-methyl-1,2-cyclohexanedicarboxylate (.05 M) at 50°.

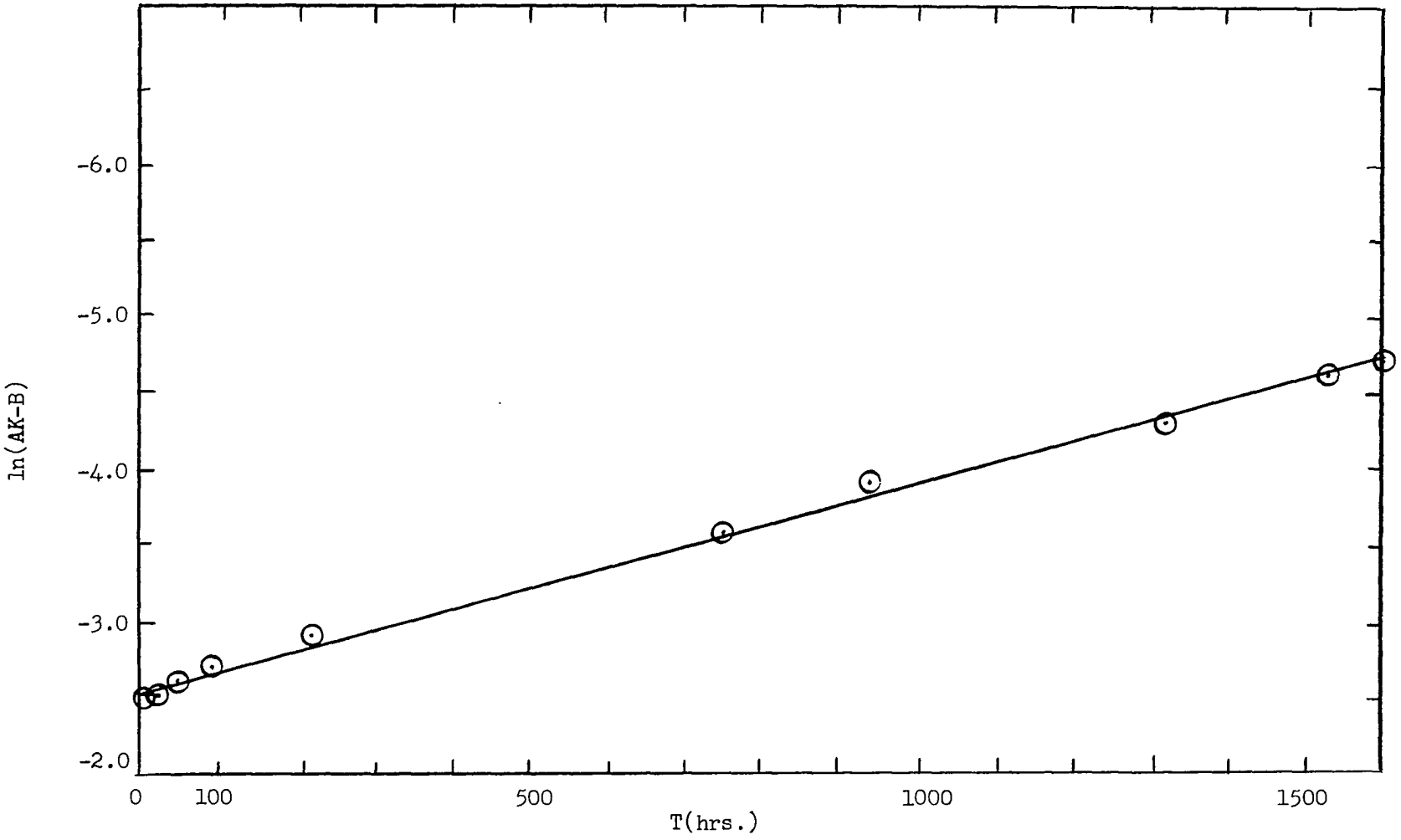



Figure 29. Plot of ln(AK-B) versus T for the Epimerization of .05 M Dimethyl cis-1-methyl-1,2-cyclohex-4-enedicarboxylate at 35°.

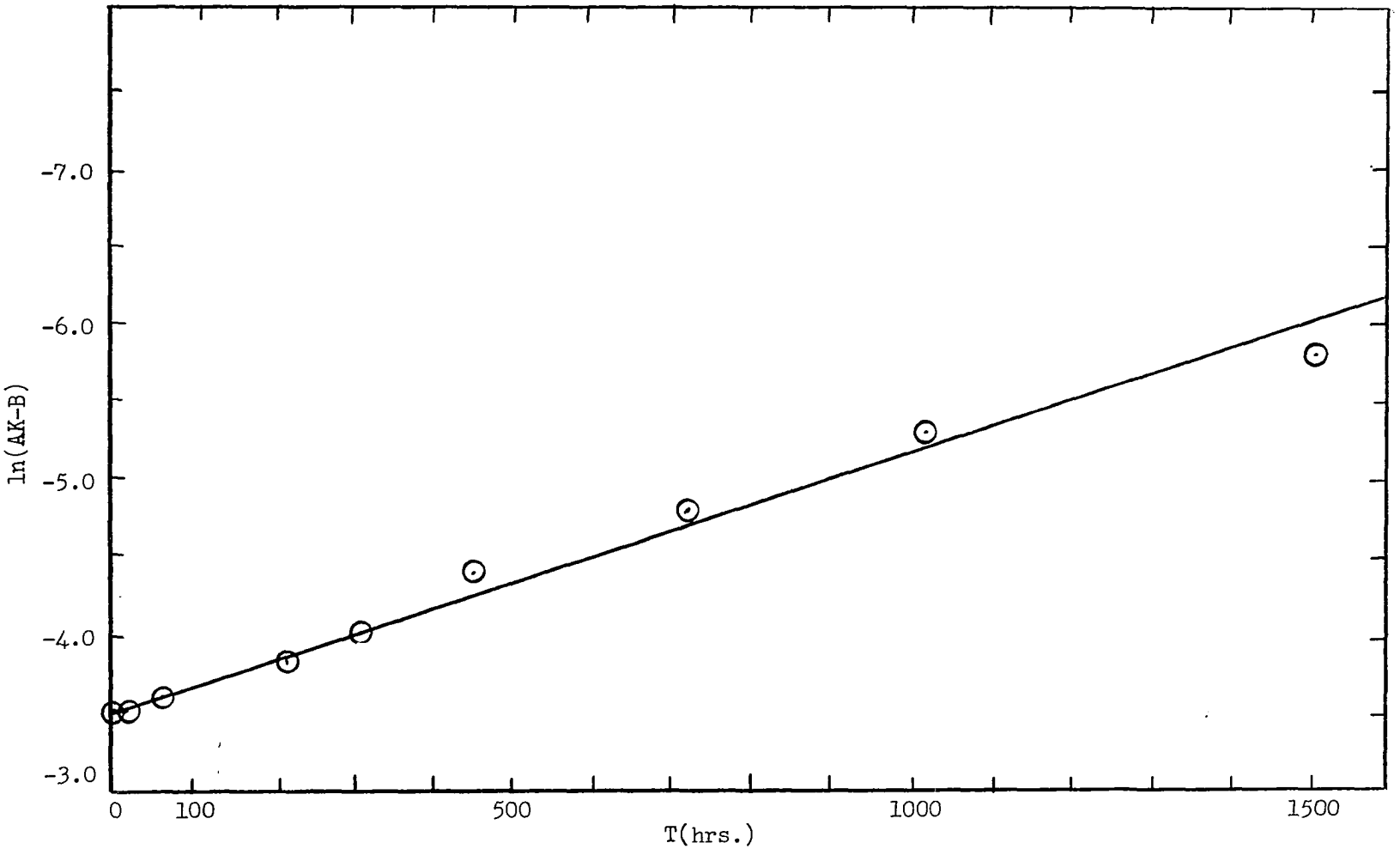



Figure 30. Plot of ln(AK-B) versus T for the Epimerization of .05 M Dimethyl trans-1-methyl-1,2-cyclohex-4-enedicarboxylate at 35°.

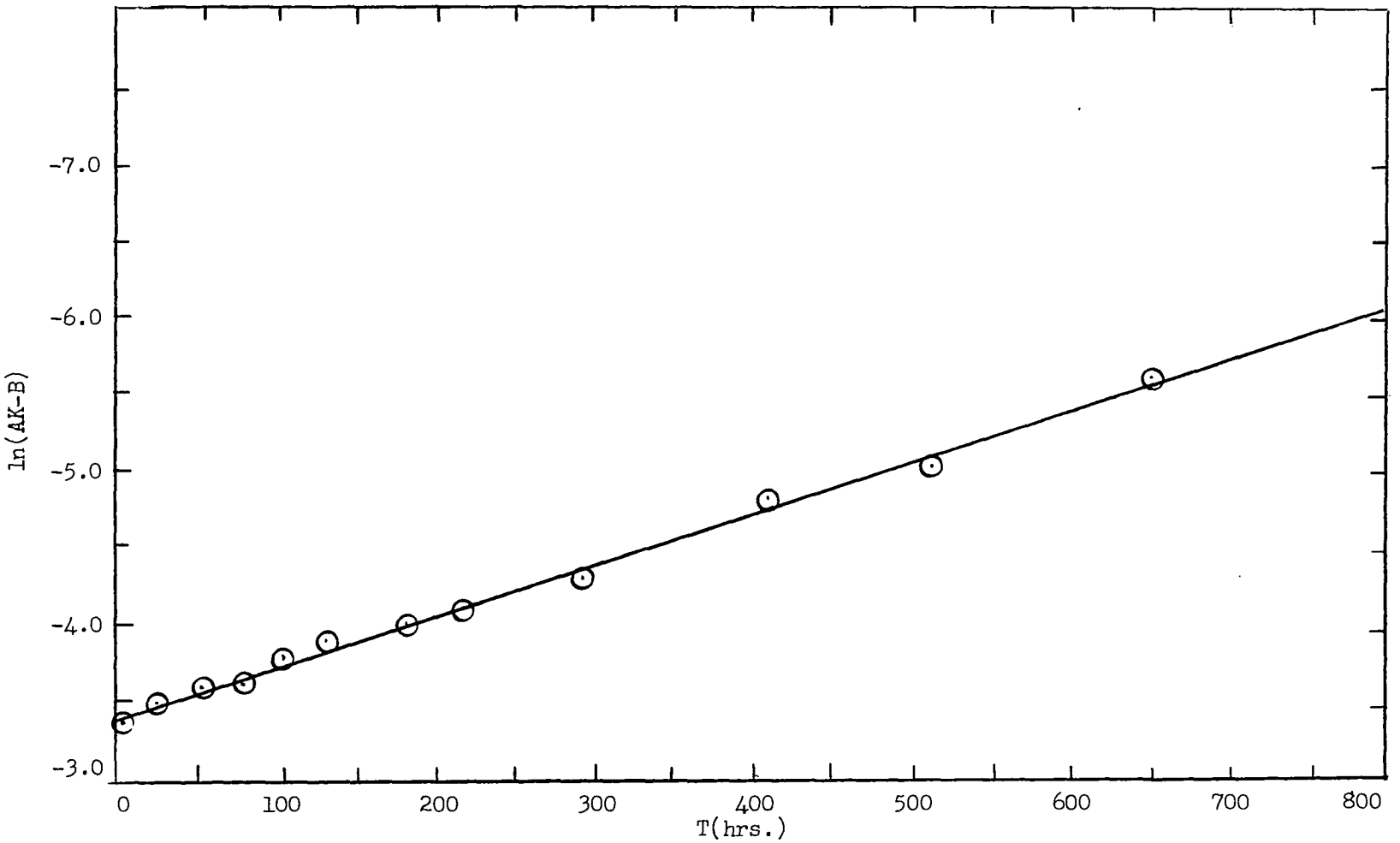



Figure 31. Plot of ln(AK-B) versus T for the Epimerization of .01 M Dimethyl cis-1,2-cycloheptanedicarboxylate at 25°.

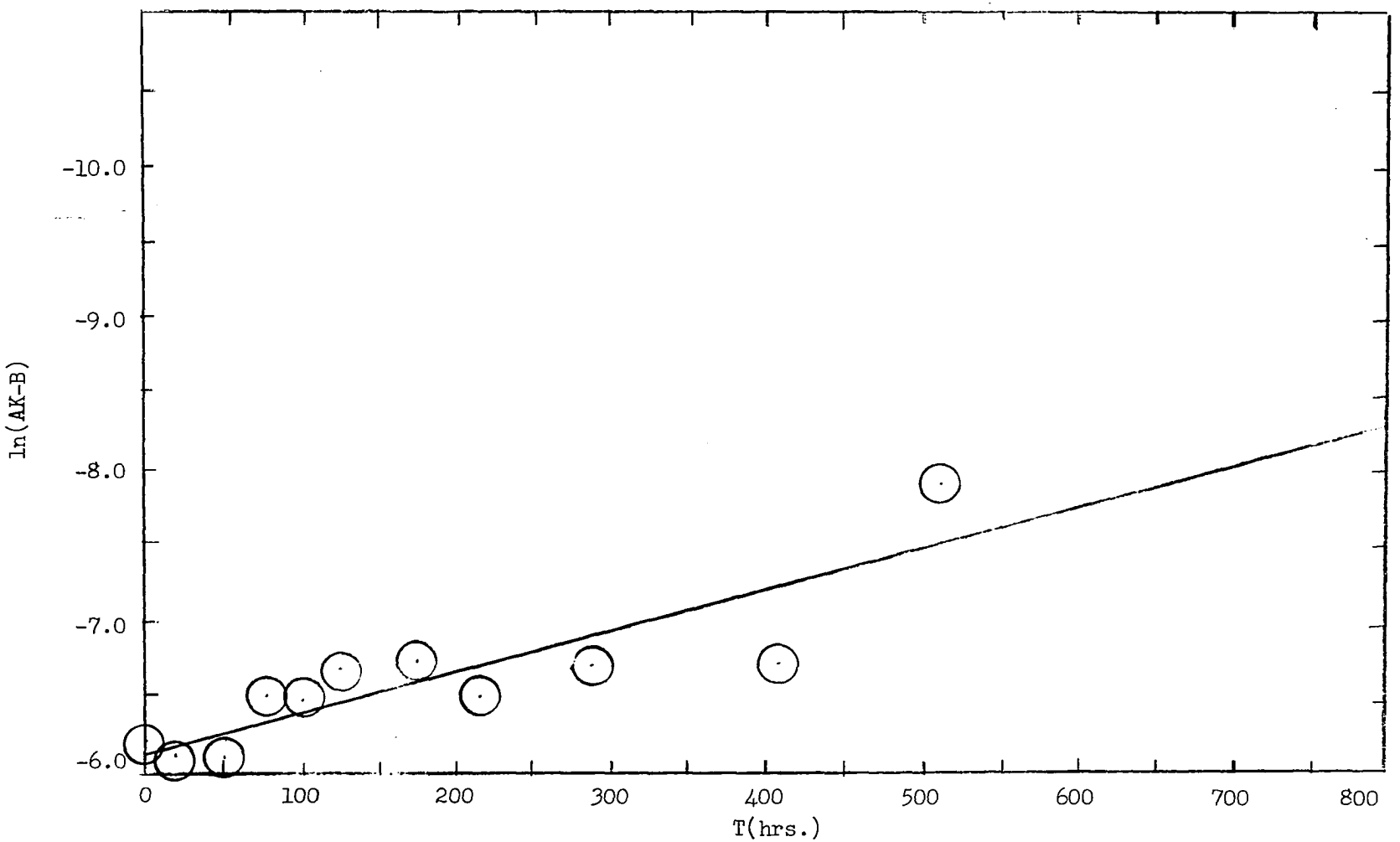



Figure 32. Plot of ln(AK-B) versus T for the Epimerization of .01 M Dimethyl trans-1,2-cycloheptanedicarboxylate at 25°.

$$\ln(A_0K-B_0) = \frac{\sum t_i^2 \sum Y_i - \sum t_i \sum t_iY_i}{N\sum t_i^2 - (\sum t_i)^2} \quad .$$

Since the reliability of the data decreases as equilibrium is approached, the equations above were modified so a weighted least squares treatment could be used to calculate the rate constant. The data was weighted in the following manner: The deviation of each value of Y, (ln(AK-B)), was calculated from the least squares line by the equation

$$DY = [K(DA) - KB] \; / \; AK - B$$

where DA and DB are the errors in A and B respectively. The error in A is assumed to be the same for all values with a corresponding relative percentage greater than 97.0% and for B with a value less than 3.0%.

The weighting factors, $w_i$, were calculated by the following, arbitrary, relation,

$$w_i = 1.0/|DY| .$$

The factors were then normalized so that $\sum w_i = 1.0$. With the inclusion of weighting factors the least squares equations become:[67]

$$S = \frac{\sum w_it_iY_i - \sum w_it_i \sum w_iY_i}{\sum (w_it_i)^2 - (\sum w_it_i)^2}$$

and

$$\ln (A_0K - B_0) = \frac{\sum w_iY_i \sum (w_it_i)^2 - \sum w_it_iY_i \sum w_it_i}{\sum (w_it_i)^2 - (\sum w_it_i)^2}$$

The standard deviation of the data is estimated by the relation,

$$\sigma_{data} = \sqrt{1/N\sum[t_i + \ln (A_0K-B_0) - Y_i]^2}$$

From the above information one can calculate the standard deviation of the slope.

$$\sigma_s^2 = \frac{N\sigma_{data}^2}{N\sum t_i^2 - (\sum t_i)^2}$$

The standard deviations of the rate constants $k_c$ and $k_t$, are calculated from the equations,[68]

$$\sigma_{k_t} = k_t\sqrt{\frac{[\sigma_s^2 / s^2] + \sigma_K^2}{(1.0 + K)^2}}$$

and

$$\sigma_{k_c} = k_c\sqrt{\frac{K\ k_t^2 + \sigma_{k_t}\ K^2}{K^2k_t^2}}\ .$$

The value for the standard deviation of the equilibrium constant, $\sigma_K$, is calculated from a separate statistical analysis. The values for the equilibrium constant and the standard deviation of the equilibrium constant of certain kinetic runs were assumed to be the same as those of similar runs which were proceeding too slowly to reach equilibrium in a reasonable period of time.

The values for A, B, Y, and t are tabulated on the following pages. Following these, are the tables of the values of the standard deviations of the data, equilibrium constants, $k_c$, $k_t$, and the slope. The pseudo-first order rate constants obtained were corrected for base concentration by the relation:

$$k_c = k_c \text{ (pseudo)} \; / \; \text{base concentration.}$$

All rate constants are expressed in the units l $sec^{-1}$ $moles^{-1}$. Values of $k_c$, $k_t$, K, and T are found in Tables 98 to 105. Values of $\sigma_K$, $\sigma k_c$, $\sigma k_t$, $\sigma_{data}$ and $\sigma_S$(slope) are found in Tables 106 to 113.

Table 14

Kinetic Data for the Epimerization of 0.05 M Dimethyl cis-1,2-cyclopropanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(days) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | 1.599 |
| .05000 | .00000 | 0.9 | 1.599 |
| .04900 | .00100 | 3.0 | 1.579 |
| .04900 | .00100 | 7.1 | 1.579 |
| .04875 | .00125 | 18.0 | 1.574 |
| .04840 | .00160 | 46.3 | 1.567 |
| .04650 | .00350 | 96.0 | 1.526 |
| .04770 | .00230 | 131.0 | 1.552 |
| .04785 | .00216 | 149.0 | 1.555 |

Table 15

Kinetic Data for the Epimerization of 0.10 M Dimethyl *cis*-1,2-cyclopropanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,*cis* | conc.,*trans* | time(hrs) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | 1.599 |
| .05000 | .00000 | 168.0 | 1.599 |
| .04950 | .00050 | 521.7 | 1.589 |
| .04740 | .00260 | 1215.8 | 1.545 |
| .04725 | .00275 | 1897.5 | 1.542 |

Table 16

Kinetic Data for the Epimerization of 0.05 M Dimethyl *cis*-1,2-cyclopropanedicarboxylate With Sodium Methoxide at 35°.

Concentrations are expressed in moles/liter.

| conc.,*cis* | conc.,*trans* | time(hrs) | ln(AK-B) |
|---|---|---|---|
| .04915 | .00085 | 0.0 | 1.582 |
| .04695 | .00305 | 614.9 | 1.536 |
| .04550 | .00450 | 908.4 | 1.504 |
| .04290 | .00710 | 1204.7 | 1.445 |
| .04460 | .00540 | 1562.4 | 1.484 |
| .04510 | .00490 | 1876.7 | 1.495 |
| .04460 | .00540 | 2338.9 | 1.484 |

Table 17

Kinetic Data for the Epimerization of 0.01 M Dimethyl *cis*-1,2-cyclopropanedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc.,*cis* | conc.,*trans* | time(hrs) | ln(AK-B) |
|---|---|---|---|
| .01000 | .00000 | 0.0 | $-1.005 \times 10^{-2}$ |
| .01000 | .00000 | 17.8 | $-1.005 \times 10^{-2}$ |
| .01000 | .00000 | 217.6 | $-1.005 \times 10^{-2}$ |
| .00906 | .00094 | 665.4 | $-1.098 \times 10^{-1}$ |
| .00852 | .00148 | 1241.5 | $-1.720 \times 10^{-1}$ |
| .00774 | .00226 | 1915.3 | $-2.692 \times 10^{-1}$ |

Table 18

Kinetic Data for the Epimerization of 0.05 M Dimethyl cis-1,2-cyclopropanedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(hrs) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | 1.599 |
| .04975 | .00025 | 0.7 | 1.594 |
| .04950 | .00050 | 5.0 | 1.589 |
| .04800 | .00200 | 18.2 | 1.558 |
| .04640 | .00360 | 43.5 | 1.524 |
| .04535 | .00465 | 94.3 | 1.501 |
| .04475 | .00525 | 143.3 | 1.487 |
| .04000 | .01000 | 309.7 | 1.374 |
| .03500 | .01500 | 717.4 | 1.238 |
| .03415 | .01585 | 1134.0 | 1.213 |

Table 19

Kinetic Data for the Epimerization of 0.10 M Dimethyl cis-1,2-cyclopropanedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .10000 | .00000 | 0.0 | 2.293 |
| .09670 | .00330 | 14.6 | 2.259 |
| .09180 | .00810 | 37.4 | 2.206 |
| .08710 | .01290 | 88.4 | 2.153 |
| .07270 | .01730 | 168.5 | 1.971 |
| .05000 | .05000 | 405.8 | 1.589 |
| .03680 | .06320 | 601.6 | 1.275 |
| .03010 | .06990 | 752.3 | 1.068 |
| .02470 | .07530 | 885.2 | $8.629 \times 10^{-1}$ |
| .01650 | .08350 | 1201.7 | $4.383 \times 10^{-1}$ |
| .01280 | .08720 | 1535.5 | $1.655 \times 10^{-1}$ |
| .01000 | .09000 | 1851.5 | $-1.054 \times 10^{-1}$ |
| .00830 | .09170 | 2305.0 | $-3.147 \times 10^{-1}$ |
| .00550 | .09450 | 2762.5 | $-7.985 \times 10^{-1}$ |

Table 20

Kinetic Data for the Epimerization of 0.01 M Dimethyl cis-1,2-cyclobutanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .00995 | .00005 | 0.0 | -2.408 |
| .00929 | .00071 | 0.7 | -2.485 |
| .00930 | .00070 | 11.3 | -2.483 |
| .00830 | .00170 | 39.3 | -2.612 |
| .00598 | .00402 | 116.2 | -2.994 |
| .00403 | .00597 | 218.9 | -3.490 |
| .00223 | .00777 | 380.0 | -4.389 |
| .00180 | .00820 | 542.7 | -4.817 |
| .00146 | .00834 | 715.3 | -5.324 |
| .00124 | .00876 | 881.7 | -6.007 |

Table 21

Kinetic Data for the Epimerization of 0.01 M dimethyl trans-1,2-cyclobutanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,trans | conc.,cis | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .00995 | .00005 | 0.0 | -6.836 |
| .00965 | .00035 | 1.2 | -7.208 |
| .00961 | .00039 | 2.2 | -7.270 |
| .00965 | .00035 | 3.6 | -7.208 |
| .00956 | .00044 | 11.3 | -7.354 |
| .00956 | .00044 | 39.3 | -7.354 |
| .00938 | .00062 | 116.2 | -7.729 |
| .00901 | .00099 | 218.9 | -10.480 |
| .00897 | .00103 | 380.0 | -11.020 |
| .00904 | .00096 | 542.7 | -9.696 |
| .00902 | .00098 | 715.3 | -10.145 |
| .00892 | .00108 | 881.7 | -9.538 |

Table 22

Kinetic Data for the Epimerization of 0.05 M Dimethyl *cis*-1,2-cyclobutanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,*cis* | conc.,*trans* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .04950 | .00000 | 0.0 | $-8.776 \times 10^{-1}$ |
| .04795 | .00205 | 1.0 | $-9.145 \times 10^{-1}$ |
| .04620 | .00380 | 2.0 | $-9.564 \times 10^{-1}$ |
| .04445 | .00555 | 3.5 | -1.000 |
| .03810 | .01190 | 11.6 | -1.177 |
| .02180 | .02820 | 35.6 | -1.865 |
| .00920 | .04080 | 87.1 | -3.311 |
| .00540 | .04460 | 218.8 | -7.182 |

Table 23

Kinetic Data for the Epimerization of 0.05 M Dimethyl trans-1,2-cyclobutanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,trans | conc.,cis | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .04950 | .00050 | 0.0 | -5.214 |
| .04815 | .00185 | 0.5 | -5.540 |
| .04840 | .00160 | 2.0 | -5.471 |
| .04760 | .00240 | 3.5 | -5.710 |
| .04670 | .00330 | 11.6 | -6.073 |
| .04505 | .00495 | 35.6 | -7.693 |
| .04430 | .00570 | 87.1 | -7.865 |
| .04485 | .00515 | 218.8 | -8.369 |

Table 24

Kinetic Data for the Epimerization of 0.10 M Dimethyl cis-1,2-cyclobutanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| Conc.,cis | conc.,trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .09770 | .00230 | 0.0 | $-4.424 \times 10^{-1}$ |
| .09450 | .00550 | 0.3 | $-4.809 \times 10^{-1}$ |
| .09250 | .00750 | 0.6 | $-5.058 \times 10^{-1}$ |
| .08970 | .01030 | 1.1 | $-5.418 \times 10^{-1}$ |
| .08920 | .01080 | 1.6 | $-5.483 \times 10^{-1}$ |
| .07970 | .02030 | 3.3 | $-6.818 \times 10^{-1}$ |
| .07630 | .02370 | 6.0 | $-7.342 \times 10^{-1}$ |
| .06540 | .03460 | 8.3 | $-9.237 \times 10^{-1}$ |
| .05450 | .04550 | 12.5 | -1.158 |
| .04310 | .05690 | 16.4 | -1.480 |
| .03980 | .06020 | 20.4 | -1.597 |
| .03020 | .06980 | 28.3 | -2.044 |
| .02010 | .07990 | 32.8 | -2.942 |
| .01530 | .08470 | 97.5 | -4.118 |
| .01220 | .08780 | 165.8 | -4.923 |

Table 25

Kinetic Data for the Epimerization of 0.10 M Dimethyl *trans*-1,2-cyclobutanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .10000 | .00000 | 0.0 | -4.160 |
| .09760 | .00240 | 0.6 | -4.356 |
| .09550 | .00450 | 1.1 | -4.566 |
| .09500 | .00500 | 1.6 | -4.623 |
| .09440 | .00560 | 3.3 | -4.597 |
| .09330 | .00670 | 6.0 | -4.847 |
| .09360 | .00640 | 8.3 | -4.893 |
| .09120 | .00880 | 12.5 | -5.216 |
| .09010 | .01090 | 16.4 | -5.759 |
| .08890 | .01110 | 20.4 | -5.889 |
| .08920 | .01080 | 28.3 | -5.771 |
| .08540 | .01460 | 32.8 | -6.663 |
| .08710 | .01290 | 97.5 | -7.282 |
| .08640 | .01360 | 165.8 | -9.015 |

Table 26

Kinetic Data for the Epimerization of 0.05 M Dimethyl cis-1,2-cyclobutanedicarboxylate with Sodium Methoxide at 35°.

Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .04875 | .00125 | 0.0 | -1.048 |
| .04565 | .00435 | 0.6 | -1.124 |
| .04470 | .00530 | 1.0 | -1.148 |
| .04285 | .00715 | 2.0 | -1.197 |
| .04025 | .00975 | 3.0 | -1.270 |
| .03775 | .01225 | 4.1 | -1.346 |
| .03525 | .01475 | 5.2 | -1.429 |
| .03180 | .01820 | 6.9 | -1.554 |
| .02745 | .02255 | 9.5 | -1.740 |
| .02490 | .02510 | 11.6 | -1.867 |
| .02165 | .02835 | 15.8 | -2.057 |
| .01695 | .03305 | 20.0 | -2.416 |
| .01445 | .03555 | 25.1 | -2.677 |
| .01325 | .03675 | 29.1 | -2.832 |
| .01075 | .03925 | 39.8 | -3.261 |
| .00840 | .04160 | 46.7 | -3.962 |
| .00760 | .04240 | 71.2 | -4.386 |
| .00645 | .04355 | 99.9 | -5.809 |
| .00610 | .04390 | 122.0 | -8.998 |

Table 27

Kinetic Data for the Epimerization of 0.05 M Dimethyl *trans*-1,2-cyclobutanedicarboxylate with Sodium Methoxide at 35°.

Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .04670 | .00330 | 0.0 | -5.808 |
| .04775 | .00225 | 0.6 | -5.474 |
| .04740 | .00260 | 1.0 | -5.573 |
| .04670 | .00330 | 2.0 | -5.808 |
| .04610 | .00390 | 3.0 | -6.065 |
| .04620 | .00380 | 4.1 | -6.017 |
| .04620 | .00380 | 5.2 | -6.017 |
| .04600 | .00400 | 6.9 | -6.115 |
| .04500 | .00500 | 9.5 | -6.835 |
| .04490 | .00510 | 11.6 | -6.947 |
| .04435 | .00565 | 15.8 | -7.995 |
| .04455 | .00545 | 20.0 | -7.480 |
| .04385 | .00615 | 25.1 | -8.376 |
| .04365 | .00635 | 29.1 | -7.690 |
| .04365 | .00635 | 39.8 | -7.690 |
| .04405 | .00595 | 46.7 | -12.637 |
| .04490 | .00510 | 71.2 | -6.947 |
| .04365 | .00635 | 99.9 | -7.690 |

Table 28

Kinetic Data for the Epimerization of 0.05 Dimethyl *cis*-1,2-cyclobutanedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc.,*cis* | conc.,*trans* | time(min.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | $-8.463 \times 10^{-1}$ |
| .04530 | .00470 | 15.0 | $-9.572 \times 10^{-1}$ |
| .04215 | .00785 | 30.0 | -1.039 |
| .03700 | .01300 | 45.0 | -1.189 |
| .03550 | .01450 | 60.0 | -1.238 |
| .03225 | .01775 | 75.0 | -1.351 |
| .02945 | .02055 | 90.0 | -1.460 |
| .02620 | .02380 | 105.0 | -1.604 |
| .02615 | .02385 | 120.0 | -1.607 |
| .02210 | .02790 | 135.0 | -1.822 |
| .01985 | .03015 | 165.0 | -1.965 |
| .01725 | .03275 | 225.0 | -2.161 |
| .01165 | .03835 | 280.0 | -2.787 |
| .01120 | .03980 | 320.0 | -2.877 |
| .00810 | .04190 | 450.0 | -3.590 |
| .00680 | .04320 | 1100.0 | -4.190 |
| .00550 | .04450 | 1385.0 | -5.918 |

Table 29

Kinetic Data for the Epimerization of 0.05 M Dimethyl trans-1,2-cyclobutanedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc.,trans | conc.,cis | time(min.) | ln(AK-B) |
|---|---|---|---|
| .04950 | .00050 | 0.0 | -5.232 |
| .04770 | .00230 | 15.0 | -5.705 |
| .04655 | .00345 | 30.0 | -6.193 |
| .04750 | .00250 | 45.0 | -5.775 |
| .04640 | .00360 | 60.0 | -6.279 |
| .04650 | .00350 | 75.0 | -6.221 |
| .04570 | .00430 | 105.0 | -6.819 |
| .04540 | .00460 | 120.0 | -7.186 |
| .04605 | .00395 | 135.0 | -6.513 |
| .04500 | .00500 | 225.0 | -8.079 |
| .04475 | .00525 | 1385.0 | -10.398 |

Table 30

Kinetic Data for the Epimerization of 0.01 M Dimethyl *cis*-1,2-cyclopentanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,*cis* | conc.,*trans* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .00970 | .00030 | 0.0 | -2.358 |
| .00949 | .00051 | 1.1 | -2.383 |
| .00926 | .00074 | 4.0 | -2.410 |
| .00917 | .00083 | 8.5 | -2.421 |
| .00740 | .00260 | 32.2 | -2.663 |
| .00723 | .00277 | 81.4 | -2.689 |
| .00534 | .00466 | 93.0 | -3.046 |
| .00368 | .00632 | 146.5 | -3.518 |
| .00235 | .00765 | 283.5 | -4.178 |
| .00102 | .00898 | 787.5 | -6.912 |

Table 31

Kinetic Data for the Epimerization of 0.01 M Dimethyl *trans*-1,2-cyclopentanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .01000 | .00000 | 0.0 | -6.869 |
| .00995 | .00005 | 0.5 | -6.923 |
| .00974 | .00026 | 1.1 | -7.191 |
| .00981 | .00019 | 1.5 | -7.094 |
| .00980 | .00020 | 2.0 | -7.107 |
| .00980 | .00020 | 4.0 | -7.107 |
| .00990 | .00010 | 8.5 | -6.981 |
| .00965 | .00035 | 19.0 | -7.333 |
| .00952 | .00048 | 81.4 | -7.581 |
| .00916 | .00084 | 146.5 | -9.091 |
| .00886 | .00114 | 283.5 | -8.428 |
| .00914 | .00086 | 787.5 | -9.309 |

Table 32

Kinetic Data for the Epimerization of 0.05 M Dimethyl cis-1,2-cyclopentanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .04720 | .00280 | 0.0 | $-8.052 \times 10^{-1}$ |
| .04595 | .00405 | 0.5 | $-8.350 \times 10^{-1}$ |
| .04450 | .00550 | 1.7 | $-8.709 \times 10^{-1}$ |
| .04075 | .00925 | 5.3 | $-9.700 \times 10^{-1}$ |
| .03555 | .01445 | 8.5 | -1.126 |
| .03120 | .01880 | 10.3 | -1.278 |
| .02390 | .02610 | 19.0 | -1.601 |
| .02165 | .02835 | 24.0 | -1.726 |
| .01555 | .03445 | 32.3 | -2.174 |
| .01135 | .03865 | 72.0 | -2.666 |
| .00475 | .04575 | 170.5 | -7.637 |

Table 33

Kinetic Data for the Epimerization of 0.05 M Dimethyl *trans*-1,2-cyclopentanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | -5.150 |
| .04975 | .00025 | 1.2 | -5.199 |
| .04950 | .00050 | 1.7 | -5.251 |
| .04895 | .00105 | 4.0 | -5.376 |
| .04755 | .00245 | 5.3 | -5.787 |
| .04775 | .00225 | 10.3 | -5.717 |
| .04695 | .00305 | 19.0 | -6.034 |
| .04630 | .00370 | 24.0 | -6.394 |
| .04615 | .00385 | 32.3 | -6.500 |
| .04510 | .00490 | 72.0 | -8.012 |
| .04495 | .00505 | 170.5 | -8.714 |

Table 34

Kinetic data for the Epimerization of 0.10 M Dimethyl *cis*-1,2-cyclopentanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,*cis* | conc.,*trans* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .09630 | .00370 | 0.0 | $-2.532 \times 10^{-1}$ |
| .09130 | .00870 | 0.3 | $-3.136 \times 10^{-1}$ |
| .08550 | .01450 | 0.6 | $-3.885 \times 10^{-1}$ |
| .08520 | .01480 | 1.2 | $-3.926 \times 10^{-1}$ |
| .07630 | .02370 | 1.5 | $-5.203 \times 10^{-1}$ |
| .08130 | .01870 | 1.8 | $-4.466 \times 10^{-1}$ |
| .07910 | .02090 | 2.0 | $-4.783 \times 10^{-1}$ |
| .07550 | .02450 | 2.3 | $-5.326 \times 10^{-1}$ |
| .07350 | .02650 | 2.7 | $-5.641 \times 10^{-1}$ |
| .07210 | .02790 | 3.5 | $-5.868 \times 10^{-1}$ |
| .05840 | .04160 | 5.7 | $-8.406 \times 10^{-1}$ |
| .05340 | .04660 | 7.2 | $-9.521 \times 10^{-1}$ |
| .03550 | .06450 | 11.5 | -1.500 |
| .02600 | .07400 | 17.0 | -1.991 |
| .01910 | .08090 | 21.0 | -2.606 |
| .01180 | .08820 | 36.5 | -4.909 |
| .01070 | .08930 | 207.0 | -5.941 |

Table 35

Kinetic Data for the Epimerization of 0.10 M Dimethyl *trans*-1,2-cyclopentanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc., *trans* | conc., *cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .10000 | .00000 | 0.3 | -4.398 |
| .09950 | .00050 | 0.6 | -4.445 |
| .09670 | .00330 | 0.8 | -4.757 |
| .09510 | .00490 | 1.5 | -4.991 |
| .09790 | .00210 | 1.8 | -4.611 |
| .09580 | .00420 | 2.0 | -4.882 |
| .09620 | .00380 | 2.7 | -4.824 |
| .09390 | .00610 | 3.5 | -5.212 |
| .09290 | .00710 | 7.2 | -5.443 |
| .08950 | .01050 | 17.0 | -7.584 |
| .08930 | .01070 | 36.5 | -8.167 |
| .08930 | .01070 | 207.0 | -8.167 |

Table 36

Kinetic Data for the Epimerization of 0.05 M Dimethyl cis-1,2-cyclopentanedicarboxylate with Sodium Methoxide at 35°.

Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(min.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | $-9.943 \times 10^{-1}$ |
| .04630 | .00370 | 17.0 | -1.082 |
| .03965 | .01035 | 95.0 | -1.262 |
| .03420 | .01580 | 155.0 | -1.439 |
| .03135 | .01865 | 210.0 | -1.545 |
| .02700 | .02300 | 330.0 | -1.733 |
| .02270 | .02730 | 450.0 | -1.961 |
| .01645 | .03355 | 590.0 | -2.428 |
| .01515 | .03485 | 785.0 | -2.561 |
| .01000 | .04000 | 1195.0 | -3.381 |
| .00595 | .04405 | 1495.0 | -10.820 |
| .00645 | .04355 | 1830.0 | -5.477 |
| .00690 | .04310 | 2970.0 | -4.833 |

Table 37

Kinetic Data for the Epimerization of 0.05 M Dimethyl *trans*-1,2-cyclopentanedicarboxylate with Sodium Methoxide at 35°.

Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(min.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | -4.969 |
| .05000 | .00000 | 17.0 | -4.969 |
| .04890 | .00110 | 95.0 | -5.168 |
| .04760 | .00240 | 155.0 | -5.469 |
| .04675 | .00325 | 210.0 | -5.730 |
| .04615 | .00385 | 330.0 | -5.966 |
| .04590 | .00410 | 450.0 | -6.084 |
| .04460 | .00540 | 490.0 | -7.132 |
| .04425 | .00575 | 785.0 | -7.822 |
| .04375 | .00625 | 1195.0 | -8.688 |
| .04465 | .00535 | 1495.0 | -7.063 |
| .04420 | .00580 | 1830.0 | -7.975 |
| .04405 | .00595 | 2970.0 | -8.663 |

Table 38

Kinetic Data for the Epimerization of 0.05 M Dimethyl cis-1,2-cyclopentanedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(min.) | ln(AK-B) |
|---|---|---|---|
| .04850 | .00150 | 0.0 | -1.227 |
| .04550 | .00450 | 13.0 | -1.302 |
| .04000 | .01000 | 27.0 | -1.457 |
| .03650 | .01350 | 42.0 | -1.569 |
| .03150 | .01850 | 61.0 | -1.755 |
| .02900 | .02100 | 75.0 | -1.863 |
| .02650 | .02350 | 91.0 | -1.984 |
| .02400 | .02600 | 105.0 | -2.122 |
| .02150 | .02850 | 120.0 | -2.282 |
| .02000 | .03000 | 135.0 | -2.391 |
| .01800 | .03200 | 150.0 | -2.559 |
| .01550 | .03450 | 183.0 | -2.819 |
| .01300 | .03700 | 210.0 | -3.171 |
| .01150 | .03850 | 240.0 | -3.462 |
| .01100 | .03900 | 275.0 | -3.582 |
| .00950 | .04050 | 305.0 | -4.062 |
| .00750 | .04250 | 490.0 | -5.789 |
| .00700 | .04300 | 1165.0 | -7.652 |

Table 39

Kinetic Data for the Epimerization of 0.05 M Dimethyl *trans*-1,2-cyclopentanedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(min.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | -4.788 |
| .04950 | .00050 | 13.0 | -4.861 |
| .04800 | .00200 | 27.0 | -5.117 |
| .04700 | .00300 | 42.0 | -5.334 |
| .04650 | .00350 | 61.0 | -5.463 |
| .04550 | .00450 | 75.0 | -5.784 |
| .04500 | .00500 | 91.0 | -5.994 |
| .04500 | .00500 | 105.0 | -5.994 |
| .04450 | .00550 | 120.0 | -6.261 |
| .04500 | .00500 | 135.0 | -5.994 |
| .04400 | .00600 | 150.0 | -6.626 |
| .04300 | .00700 | 180.0 | -8.743 |
| .04350 | .00650 | 210.0 | -7.205 |
| .04250 | .00750 | 240.0 | -7.766 |
| .04300 | .00700 | 275.0 | -8.743 |
| .04300 | .00700 | 305.0 | -8.743 |
| .04350 | .00650 | 490.0 | -7.205 |
| .04300 | .00700 | 1165.0 | -8.743 |

Table 40

Kinetic Data for the Epimerization of 0.01 M Dimethyl *cis*-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 35°.

Concentrations are expressed in moles/liter.

| conc.,*cis* | conc.,*trans* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .01000 | .00000 | 0.0 | -2.332 |
| .00976 | .00024 | 25.0 | -2.359 |
| .00964 | .00036 | 52.5 | -2.373 |
| .00936 | .00064 | 72.5 | -2.405 |
| .00920 | .00080 | 98.3 | -2.424 |
| .00907 | .00093 | 125.8 | -2.440 |
| .00887 | .00113 | 146.0 | -2.465 |
| .00803 | .00197 | 208.5 | -2.577 |
| .00711 | .00289 | 330.5 | -2.716 |
| .00633 | .00367 | 555.5 | -2.851 |
| .00577 | .00423 | 723.0 | -2.960 |
| .00463 | .00537 | 916.0 | -3.229 |
| .00415 | .00585 | 1038.5 | -3.368 |
| .00395 | .00605 | 1196.5 | -3.433 |
| .00365 | .00635 | 1446.4 | -3.537 |
| .00317 | .00683 | 1714.0 | -3.732 |
| .00306 | .00694 | 1904.0 | -3.782 |

Table 41

Kinetic Data for the Epimerization of 0.01 M Dimethyl *trans*-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 35°.

Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .00995 | .00005 | 0.0 | -6.954 |
| .00990 | .00010 | 25.0 | -7.013 |
| .00990 | .00010 | 52.5 | -7.013 |
| .00985 | .00015 | 72.5 | -7.076 |
| .00985 | .00015 | 98.3 | -7.076 |
| .00985 | .00015 | 125.8 | -7.076 |
| .00980 | .00020 | 146.0 | -7.144 |
| .00975 | .00025 | 208.5 | -7.216 |
| .00970 | .00030 | 330.5 | -7.294 |
| .00965 | .00035 | 555.5 | -7.378 |
| .00970 | .00030 | 723.0 | -7.294 |
| .00955 | .00045 | 916.0 | -7.572 |
| .00950 | .00050 | 1038.5 | -7.685 |
| .00950 | .00050 | 1196.5 | -7.685 |
| .00945 | .00055 | 1446.4 | -7.813 |
| .00940 | .00060 | 1714.0 | -7.959 |
| .00940 | .00060 | 1904.0 | -7.959 |

Table 42

Kinetic Data for the Epimerization of 0.05 M Dimethyl cis-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 35°.

Concentrations are expressed in moles/liter.

| conc., cis | conc., trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | $-7.226 \times 10^{-1}$ |
| .04365 | .00635 | 25.0 | $-8.735 \times 10^{-1}$ |
| .03890 | .01110 | 52.5 | -1.003 |
| .03715 | .01285 | 72.5 | -1.056 |
| .02875 | .02125 | 98.3 | -1.355 |
| .02800 | .02200 | 125.8 | -1.387 |
| .02615 | .02365 | 146.0 | -1.469 |
| .02050 | .02950 | 208.5 | -1.775 |
| .01625 | .03375 | 330.5 | -2.087 |
| .00550 | .04450 | 555.5 | -4.721 |
| .00450 | .04550 | 723.0 | -6.317 |
| .00550 | .04450 | 916.0 | -4.721 |
| .00500 | .04500 | 1038.5 | -5.641 |
| .00500 | .04500 | 1196.5 | -5.641 |
| .00450 | .04550 | 1446.4 | -6.317 |

Table 43

Kinetic Data for the Epimerization of 0.05 M Dimethyl trans-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 35°.

Concentrations are expressed in moles/liter.

| conc.,trans | conc.,cis | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | -5.288 |
| .04950 | .00050 | 25.0 | -5.404 |
| .04850 | .00150 | 52.5 | -5.684 |
| .04650 | .00350 | 72.5 | -6.728 |
| .04750 | .00250 | 98.3 | -6.076 |
| .04700 | .00300 | 125.8 | -6.350 |
| .04700 | .00300 | 146.0 | -6.350 |
| .04600 | .00400 | 208.5 | -7.345 |
| .04600 | .00400 | 330.5 | -7.345 |
| .04500 | .00500 | 555.5 | -7.695 |
| .04450 | .00550 | 723.0 | -6.902 |
| .04475 | .00525 | 916.0 | -7.222 |
| .04550 | .00450 | 1038.5 | -9.256 |
| .04525 | .00475 | 1196.5 | -8.624 |
| .04500 | .00500 | 1446.4 | -7.695 |

Table 44

Kinetic Data for the Epimerization of 0.10 M Dimethyl *cis*-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 35°.

Concentrations are expressed in moles/liter.

| conc.,*cis* | conc.,*trans* | time(min.) | ln(AK-B) |
|---|---|---|---|
| .10000 | .00000 | 0.0 | $8.618 \times 10^{-2}$ |
| .10000 | .00000 | 35.0 | $8.618 \times 10^{-2}$ |
| .09590 | .00410 | 145.0 | $4.038 \times 10^{-2}$ |
| .09350 | .00650 | 360.0 | $1.257 \times 10^{-2}$ |
| .08850 | .01150 | 535.0 | $-4.798 \times 10^{-2}$ |
| .07940 | .02060 | 1080.0 | $-1.686 \times 10^{-1}$ |
| .06010 | .03090 | 2870.0 | $-4.173 \times 10^{-1}$ |
| .04040 | .05960 | 5470.0 | $-9.656 \times 10^{-1}$ |
| .02400 | .07600 | 9970.0 | -1.684 |
| .02120 | .07880 | 11350.0 | -1.882 |
| .01590 | .08410 | 15400.0 | -2.417 |
| .00760 | .09240 | 20050.0 | -4.650 |

Table 45

Kinetic Data for the Epimerization of 0.10 M Dimethyl *trans*-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 35°.

Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(min.) | ln(AK-B) |
|---|---|---|---|
| .10000 | .00000 | 0.0 | -4.711 |
| .09850 | .00150 | 35.0 | -4.911 |
| .09720 | .00280 | 145.0 | -5.125 |
| .09750 | .00250 | 360.0 | -5.071 |
| .09440 | .00560 | 535.0 | -5.844 |
| .09670 | .00330 | 1080.0 | -5.221 |
| .09380 | .00620 | 2870.0 | -6.100 |
| .09320 | .00680 | 5470.0 | -6.445 |
| .09120 | .00880 | 9970.0 | -7.432 |
| .08920 | .01080 | 15400.0 | -5.888 |
| .09240 | .00760 | 20050.0 | -7.242 |

Table 46

Kinetic Data for the Epimerization of 0.01 M Dimethyl cis-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc., cis | conc., trans | time(days) | ln(AK-B) |
|---|---|---|---|
| .01000 | .00000 | 0.8 | -1.966 |
| .00962 | .00038 | 4.5 | -2.008 |
| .00799 | .00201 | 11.6 | -2.209 |
| .00819 | .00181 | 22.0 | -2.182 |
| .00789 | .00211 | 33.2 | -2.222 |
| .00703 | .00297 | 41.0 | -2.349 |
| .00676 | .00324 | 57.0 | -2.393 |
| .00602 | .00398 | 87.8 | -2.522 |
| .00554 | .00446 | 102.2 | -2.616 |
| .00533 | .00467 | 120.0 | -2.660 |
| .00447 | .00553 | 152.0 | -2.864 |

Table 47

Kinetic Data for the Epimerization of 0.01 M Dimethyl *trans*-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(days) | ln(AK-B) |
|---|---|---|---|
| .00995 | .00005 | 0.8 | -7.228 |
| .00990 | .00010 | 4.5 | -7.305 |
| .00975 | .00025 | 22.0 | -7.580 |
| .00965 | .00035 | 33.2 | -7.817 |
| .00965 | .00035 | 41.0 | -7.817 |
| .00955 | .00045 | 57.0 | -8.129 |
| .00960 | .00040 | 87.8 | -7.961 |
| .00960 | .00040 | 120.0 | -7.961 |
| .00965 | .00035 | 152.0 | -7.817 |

Table 48

Kinetic Data for the Epimerization of 0.05 M Dimethyl *cis*-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,*cis* | conc.,*trans* | time(days) | ln(AK-B) |
|---|---|---|---|
| .04810 | .00190 | 0.8 | $-3.982 \times 10^{-1}$ |
| .04075 | .00975 | 4.5 | $-5.785 \times 10^{-1}$ |
| .03265 | .01735 | 11.6 | $-8.125 \times 10^{-1}$ |
| .02545 | .02455 | 22.0 | -1.103 |
| .01960 | .03040 | 33.2 | -1.411 |
| .01590 | .03410 | 41.0 | -1.669 |
| .01160 | .03840 | 57.0 | -2.087 |
| .00575 | .04425 | 87.8 | -3.317 |
| .00550 | .04450 | 102.2 | -3.427 |
| .00400 | .04600 | 120.0 | -4.605 |

Table 49

Kinetic Data for the Epimerization of 0.05 Dimethyl trans-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,trans | conc.,cis | time(days) | ln(AK-B) |
|---|---|---|---|
| .04975 | .00025 | 0.8 | -5.618 |
| .04950 | .00050 | 4.5 | -5.696 |
| .04900 | .00100 | 11.6 | -5.870 |
| .04850 | .00150 | 22.0 | -6.082 |
| .04750 | .00250 | 33.2 | -6.721 |
| .04750 | .00250 | 41.0 | -6.721 |
| .04675 | .00325 | 57.0 | -7.833 |
| .04675 | .00325 | 87.8 | -7.833 |
| .04650 | .00350 | 102.2 | -8.971 |
| .04650 | .00350 | 120.0 | -8.971 |

Table 50

Kinetic Data for the Epimerization of 0.10 M Dimethyl cis-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .10000 | .00000 | 0.0 | $1.989 \times 10^{-1}$ |
| .09800 | .00200 | 1.0 | $1.770 \times 10^{-1}$ |
| .09560 | .00440 | 2.8 | $1.501 \times 10^{-1}$ |
| .09500 | .00500 | 5.0 | $1.432 \times 10^{-1}$ |
| .09660 | .00340 | 6.5 | $1.614 \times 10^{-1}$ |
| .09320 | .00680 | 10.7 | $1.224 \times 10^{-1}$ |
| .09150 | .00850 | 20.3 | $1.024 \times 10^{-1}$ |
| .08650 | .01350 | 35.8 | $4.095 \times 10^{-2}$ |
| .06990 | .03010 | 106.7 | $-1.952 \times 10^{-1}$ |
| .05280 | .04720 | 182.3 | $-5.159 \times 10^{-1}$ |
| .03080 | .06970 | 472.3 | -1.204 |
| .01100 | .08900 | 815.8 | -3.097 |
| .01000 | .09000 | 1209.3 | -3.442 |

Table 51

Kinetic Data for the Epimerization of 0.10 M Dimethyl *trans*-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .10000 | .00000 | 0.0 | -4.791 |
| .09900 | .00100 | 1.0 | -4.931 |
| .09900 | .00100 | 2.8 | -4.931 |
| .09900 | .00100 | 5.0 | -4.931 |
| .09900 | .00100 | 6.5 | -4.931 |
| .09900 | .00100 | 10.7 | -4.931 |
| .09800 | .00200 | 20.3 | -5.094 |
| .09750 | .00250 | 35.8 | -5.186 |
| .09600 | .00400 | 106.7 | -5.529 |
| .09600 | .00400 | 182.3 | -5.529 |
| .09350 | .00650 | 472.3 | -6.676 |
| .09300 | .00700 | 815.8 | -7.238 |
| .09200 | .00800 | 1209.3 | -7.918 |

Table 52

Kinetic Data for the Epimerization of 0.01 M Dimethyl cis-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .01000 | .00000 | 0.0 | -2.180 |
| .00810 | .00190 | 35.3 | -2.412 |
| .00699 | .00301 | 61.9 | -2.577 |
| .00629 | .00315 | 101.9 | -2.689 |
| .00538 | .00462 | 140.5 | -2.879 |
| .00430 | .00570 | 171.5 | -3.149 |
| .00416 | .00584 | 205.8 | -3.190 |
| .00269 | .00731 | 395.3 | -3.768 |
| .00135 | .00865 | 558.5 | -5.020 |
| .00100 | .00900 | 786.3 | -6.075 |
| .00085 | .00915 | 1007.3 | -7.695 |

Table 53

Kinetic Data for the Epimerization of 0.01 M Dimethyl *trans*-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .01000 | .00000 | 0.0 | -7.024 |
| .00975 | .00025 | 35.3 | -7.389 |
| .00960 | .00040 | 61.9 | -7.697 |
| .00950 | .00050 | 101.9 | -7.971 |
| .00960 | .00040 | 140.5 | -7.697 |
| .00950 | .00050 | 171.5 | -7.971 |
| .00940 | .00060 | 205.8 | -8.349 |
| .00935 | .00065 | 395.3 | -8.611 |
| .00925 | .00075 | 558.5 | -9.522 |
| .00910 | .00090 | 786.3 | -9.315 |
| .00920 | .00080 | 1007.3 | -10.882 |

Table 54

Kinetic Data for the Epimerization of 0.05 M Dimethyl cis-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc., cis | conc., trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | $-5.533 \times 10^{-1}$ |
| .04800 | .00200 | 0.5 | $-5.977 \times 10^{-1}$ |
| .04775 | .00225 | 1.0 | $-6.034 \times 10^{-1}$ |
| .04565 | .00490 | 2.0 | $-6.537 \times 10^{-1}$ |
| .04535 | .00465 | 3.0 | $-6.599 \times 10^{-1}$ |
| .04415 | .00585 | 4.0 | $-6.893 \times 10^{-1}$ |
| .04625 | .00735 | 5.0 | $-7.274 \times 10^{-1}$ |
| .04175 | .00825 | 6.0 | $-7.510 \times 10^{-1}$ |
| .03925 | .01075 | 7.0 | $-8.195 \times 10^{-1}$ |
| .03845 | .01155 | 8.0 | $-8.424 \times 10^{-1}$ |
| .03475 | .01525 | 10.0 | $-9.560 \times 10^{-1}$ |
| .02750 | .02250 | 14.0 | -1.225 |
| .02560 | .02440 | 24.0 | -1.309 |
| .02250 | .02750 | 27.5 | -1.464 |
| .01975 | .03025 | 33.5 | -1.625 |
| .01775 | .03225 | 52.0 | -1.761 |
| .01205 | .03795 | 78.0 | -2.296 |
| .00550 | .04450 | 87.5 | -3.976 |
| .00525 | .04475 | 127.3 | -4.159 |
| .00500 | .04500 | 148.0 | -4.381 |
| .00475 | .04525 | 172.5 | -4.669 |

Table 55

Kinetic Data for the Epimerization of 0.05 M Dimethyl *trans*-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc.*trans* | conc.,*cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | -5.438 |
| .04950 | .00050 | 0.5 | -5.571 |
| .04950 | .00050 | 1.0 | -5.571 |
| .04900 | .00100 | 2.0 | -5.725 |
| .04925 | .00075 | 3.0 | -5.645 |
| .04850 | .00150 | 4.0 | -5.907 |
| .04850 | .00150 | 5.0 | -5.907 |
| .04825 | .00175 | 6.0 | -6.013 |
| .04800 | .00200 | 7.0 | -6.130 |
| .04825 | .00175 | 8.0 | -6.013 |
| .04825 | .00175 | 10.0 | -6.013 |
| .04775 | .00225 | 14.0 | -6.264 |
| .04700 | .00300 | 24.00 | -6.822 |
| .04700 | .00300 | 27.5 | -6.822 |
| .04725 | .00275 | 33.5 | -6.600 |
| .04700 | .00300 | 52.0 | -6.822 |
| .04675 | .00425 | 78.0 | -8.607 |
| .04675 | .00325 | 87.5 | -7.110 |
| .04600 | .00400 | 127.3 | -13.122 |
| .04625 | .00375 | 148.0 | -8.203 |
| .04650 | .00350 | 172.5 | -7.514 |
| .04600 | .00400 | 204.5 | -13.122 |

Table 56

Kinetic Data for the Epimerization of 0.10 M Dimethyl cis-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .09850 | .00150 | 0.0 | $3.195 \times 10^{-3}$ |
| .09540 | .00460 | 0.7 | $-3.203 \times 10^{-2}$ |
| .09000 | .01000 | 1.5 | $-9.651 \times 10^{-2}$ |
| .08400 | .01600 | 2.5 | $-1.734 \times 10^{-1}$ |
| .07850 | .02150 | 3.5 | $-2.495 \times 10^{-1}$ |
| .07580 | .02420 | 4.5 | $-2.891 \times 10^{-1}$ |
| .06690 | .03310 | 6.8 | $-4.319 \times 10^{-1}$ |
| .06320 | .03680 | 8.0 | $-4.978 \times 10^{-1}$ |
| .04780 | .05220 | 12.5 | $-8.316 \times 10^{-1}$ |
| .03990 | .06010 | 17.8 | -1.059 |
| .01550 | .08450 | 37.5 | -2.609 |
| .01000 | .09000 | 108.1 | -4.423 |
| .01000 | .09000 | 183.9 | -4.423 |

Table 57

Kinetic Data for the Epimerization of 0.10 M Dimethyl *trans*-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .10000 | .00000 | 0.0 | -4.615 |
| .10000 | .00000 | 0.7 | -4.615 |
| .09900 | .00100 | 1.5 | -4.733 |
| .09900 | .00100 | 2.5 | -4.733 |
| .09750 | .00250 | 3.5 | -4.940 |
| .09700 | .00300 | 4.5 | -5.020 |
| .09600 | .00400 | 6.8 | -5.202 |
| .09600 | .00400 | 8.0 | -5.202 |
| .09550 | .00450 | 12.5 | -5.307 |
| .09500 | .00500 | 17.8 | -5.425 |
| .09150 | .00850 | 37.5 | -7.490 |
| .09050 | .00950 | 108.1 | -7.523 |
| .09000 | .01000 | 183.9 | -6.822 |

Table 58

Kinetic Data for the Epimerization of 0.05 M Dimethyl *cis*-1-methyl-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,*cis* | conc.,*trans* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | -2.386 |
| .05000 | .00000 | 168.8 | -2.386 |
| .04670 | .00330 | 560.1 | -2.493 |
| .04595 | .00405 | 774.0 | -2.520 |
| .04595 | .00405 | 967.6 | -2.520 |
| .04525 | .00475 | 1320.4 | -2.545 |
| .04295 | .00705 | 1806.9 | -2.631 |
| .04405 | .00595 | 1990.8 | -2.589 |
| .04155 | .00845 | 2660.7 | -2.688 |
| .03870 | .01130 | 3246.7 | -2.815 |

Table 59

Kinetic data for the Epimerization of 0.05 M Dimethyl *trans*-1-methyl-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 25°. Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .03965 | .01035 | 0.0 | -4.483 |
| .03965 | .01035 | 168.8 | -4.483 |
| .04000 | .01000 | 560.1 | -4.436 |
| .03875 | .01125 | 774.0 | -4.614 |
| .03940 | .01060 | 967.6 | -4.518 |
| .03940 | .01060 | 1320.4 | -4.518 |
| .03950 | .01050 | 1806.9 | -4.504 |
| .03810 | .01190 | 1990.8 | -4.721 |
| .03815 | .01185 | 2660.7 | -4.713 |
| .03850 | .01150 | 3246.7 | -4.654 |

Table 60

Kinetics of Epimerization of 0.05 M Dimethyl cis-1-methyl-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 35°.

Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | -2.386 |
| .05000 | .00000 | 15.9 | -2.386 |
| .05000 | .00000 | 30.8 | -2.386 |
| .05000 | .00000 | 53.4 | -2.386 |
| .05000 | .00000 | 70.3 | -2.386 |
| .04975 | .00025 | 102.1 | -2.394 |
| .04815 | .00185 | 146.3 | -2.445 |
| .04345 | .00665 | 601.9 | -2.613 |
| .03755 | .01245 | 1297.4 | -2.871 |
| .03430 | .01585 | 1905.4 | -3.052 |

Table 61

Kinetic Data for the Epimerization of 0.05 M Dimethyl trans-1-methyl-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 35°. Concentrations are expressed in moles/liter.

| conc.,trans | conc.,cis | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .04000 | .01000 | 0.0 | -4.436 |
| .03965 | .01035 | 15.9 | -4.483 |
| .04000 | .01000 | 30.8 | -4.436 |
| .03985 | .01015 | 53.4 | -4.456 |
| .03900 | .01100 | 70.3 | -4.576 |
| .04000 | .01000 | 102.1 | -4.436 |
| .03955 | .01045 | 146.3 | -4.497 |
| .03910 | .01090 | 601.9 | -4.561 |
| .03660 | .01340 | 1297.4 | -5.023 |
| .03640 | .01360 | 1905.4 | -5.071 |

Table 62

*Kinetic Data for the Epimerization of 0.01 Dimethyl cis-1-methyl-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 50°. Concentrations are expressed in moles/liter.*

| conc.,cis | conc.,trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .01000 | .00000 | 0.0 | -3.995 |
| .00955 | .00045 | 144.0 | -4.067 |
| .00815 | .00185 | 591.7 | -4.332 |
| .00758 | .00242 | 900.6 | -4.463 |
| .00756 | .00244 | 1168.3 | -4.468 |
| .00666 | .00334 | 1514.5 | -4.720 |
| .00656 | .00344 | 1841.6 | -4.752 |
| .00604 | .00396 | 2393.7 | -4.940 |

Table 63

Kinetic Data for the Epimerization of 0.01 M Dimethyl *trans*-1-methyl-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .00792 | .00208 | 0.0 | -6.099 |
| .00781 | .00219 | 144.0 | -6.178 |
| .00748 | .00252 | 591.7 | -6.460 |
| .00742 | .00258 | 900.6 | -6.522 |
| .00737 | .00263 | 1168.3 | -6.576 |
| .00752 | .00248 | 1514.5 | -6.422 |
| .00720 | .00280 | 1841.6 | -6.784 |
| .00708 | .00292 | 2393.7 | -6.964 |

Table 64

Kinetic Data for the Epimerization of 0.05 Dimethyl *cis*-1-methyl-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc., *cis* | conc., *trans* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | -2.386 |
| .05000 | .00000 | 0.3 | -2.386 |
| .05000 | .00000 | 0.5 | -2.386 |
| .04915 | .00085 | 0.9 | -2.413 |
| .04830 | .00170 | 12.5 | -2.440 |
| .04500 | .00500 | 46.6 | -2.554 |
| .04305 | .00695 | 106.1 | -2.627 |
| .04225 | .00775 | 144.5 | -2.659 |
| .03665 | .01335 | 278.5 | -2.917 |
| .02495 | .02505 | 742.9 | -3.870 |
| .02215 | .02785 | 984.3 | -4.350 |
| .01980 | .03020 | 1365.3 | -5.078 |
| .01930 | .03070 | 1613.9 | -5.337 |
| .01350 | .03150 | 1813.5 | -5.976 |
| .01800 | .03200 | 2099.9 | -6.794 |
| .01810 | .03190 | 2164.0 | -6.568 |

Table 65

Kinetic Data for the Epimerization of 0.05 M *trans*-1-methyl-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .03875 | .01125 | 0.0 | -4.611 |
| .03870 | .01130 | 0.5 | -4.618 |
| .03840 | .01160 | 12.5 | -4.667 |
| .03745 | .01255 | 144.5 | -4.836 |
| .03670 | .01330 | 278.5 | -4.995 |
| .03360 | .01640 | 742.9 | -6.225 |
| .03395 | .01605 | 984.4 | -5.983 |
| .03320 | .01680 | 1365.3 | -6.600 |
| .03185 | .01815 | 1613.9 | -7.225 |
| .03280 | .01720 | 1813.5 | -7.207 |
| .03375 | .01625 | 2099.9 | -6.114 |
| .03240 | .01760 | 2164.0 | -9.005 |

Table 66

Kinetic Data for the Epimerization of 0.10 M Dimethyl cis-1-methyl-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc., cis | conc., trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .10000 | .00000 | 0.0 | -1.741 |
| .10000 | .00000 | 3.2 | -1.741 |
| .10000 | .00000 | 4.8 | -1.741 |
| .09900 | .00100 | 8.5 | -1.757 |
| .09380 | .00620 | 11.9 | -1.843 |
| .09270 | .00730 | 18.8 | -1.862 |
| .08850 | .01150 | 24.7 | -1.940 |
| .08670 | .01330 | 48.1 | -1.975 |
| .08380 | .01620 | 72.1 | -2.034 |
| .06960 | .03040 | 122.1 | -2.389 |
| .06050 | .03950 | 202.1 | -2.709 |
| .04080 | .05920 | 649.8 | -4.393 |
| .03750 | .06250 | 818.8 | -5.721 |
| .03680 | .06320 | 940.3 | -6.610 |
| .03600 | .06400 | 1066.0 | -7.063 |

Table 67

Kinetic Data for the Epimerization of 0.10 M Dimethyl trans-1-methyl-1,2-cyclohexanedicarboxylate with Sodium Methoxide at 50°. Concentrations are expressed in moles/liter.

| conc.,trans | conc.,cis | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .07850 | .02150 | 0.0 | -3.779 |
| .07920 | .02080 | 3.2 | -3.732 |
| .07910 | .02090 | 4.8 | -3.738 |
| .07760 | .02240 | 8.5 | -3.842 |
| .07900 | .02100 | 11.9 | -3.745 |
| .07670 | .02330 | 18.8 | -3.910 |
| .07690 | .02310 | 24.7 | -3.895 |
| .07590 | .02410 | 48.1 | -3.975 |
| .07440 | .02560 | 72.1 | -5.108 |
| .07300 | .02700 | 122.1 | -4.351 |
| .06920 | .03080 | 202.1 | -4.792 |
| .06350 | .03650 | 649.8 | -7.382 |
| .06460 | .03540 | 818.8 | -6.813 |
| .06410 | .03590 | 940.3 | -8.058 |
| .06400 | .03600 | 1066.0 | -8.740 |

Table 68

Kinetic Data for the Epimerization of 0.01 M Dimethyl cis-1,2-cyclohex-4-enedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .01000 | .00000 | 0.0 | -3.565 |
| .00925 | .00075 | 47.8 | -3.672 |
| .00768 | .00232 | 155.0 | -3.942 |
| .00644 | .00355 | 288.5 | -4.222 |
| .00620 | .00380 | 338.0 | -4.287 |
| .00515 | .00485 | 504.5 | -4.633 |
| .00496 | .00504 | 552.8 | -4.711 |
| .00411 | .00589 | 719.8 | -5.160 |
| .00363 | .00637 | 893.9 | -5.546 |
| .00326 | .00674 | 1056.5 | -5.997 |
| .00307 | .00693 | 1229.1 | -6.344 |
| .00263 | .00737 | 1395.5 | -9.526 |

Table 69

Kinetic Data for the Epimerization of 0.01 M Dimethyl *trans*-1,2-cyclohex-4-enedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .01000 | .00000 | 0.0 | -5.632 |
| .00980 | .00020 | 74.8 | -5.711 |
| .00945 | .00055 | 118.9 | -5.866 |
| .00914 | .00086 | 281.5 | -6.027 |
| .00886 | .00114 | 454.1 | -6.199 |
| .00884 | .00116 | 620.5 | -6.212 |
| .00858 | .00162 | 884.0 | -6.535 |
| .00818 | .00182 | 1028.4 | -6.805 |
| .00812 | .00188 | 1426.0 | -6.881 |
| .00805 | .00195 | 1820.0 | -6.978 |

Table 70

Kinetic Data for the Epimerization of 0.05 M Dimethyl *cis*-1,2-cyclohex-4-enedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,*cis* | conc.,*trans* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .04975 | .00025 | 0.0 | -2.017 |
| .04030 | .00970 | 48.0 | -2.320 |
| .02750 | .02250 | 154.5 | -2.972 |
| .01990 | .03010 | 288.0 | -3.762 |
| .01875 | .03125 | 237.5 | -3.963 |
| .01510 | .03490 | 504.0 | -5.191 |
| .01465 | .03535 | 552.5 | -5.544 |
| .01295 | .03705 | 720.3 | -6.056 |

Table 71

Kinetic Data for the Epimerization of 0.05 M Dimethyl *trans*-1,2-cyclohex-4-enedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | -3.966 |
| .04465 | .00535 | 75.0 | -4.459 |
| .04325 | .00675 | 119.0 | -4.642 |
| .04020 | .00980 | 281.5 | -5.215 |
| .03855 | .01145 | 454.2 | -5.757 |
| .03740 | .01260 | 620.5 | -6.454 |

Table 72

Kinetic Data for the Epimerization of 0.10 M Dimethyl cis-1,2-cyclohex-4-enedicarboxylate with Sodium Methoxide at 25°. Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(min.) | ln(AK-B) |
|---|---|---|---|
| .10000 | .00000 | 0.0 | -1.096 |
| .09900 | .00100 | 25.0 | -1.110 |
| .09740 | .00260 | 55.0 | -1.131 |
| .09540 | .00460 | 260.0 | -1.158 |
| .08890 | .01110 | 515.0 | -1.252 |
| .08660 | .01340 | 750.0 | -1.288 |
| .08270 | .01730 | 1000.0 | -1.351 |
| .06830 | .03170 | 2455.0 | -1.627 |
| .05490 | .04510 | 4175.0 | -1.979 |
| .03840 | .06160 | 8275.0 | -2.708 |
| .02620 | .07380 | 16935.0 | -4.290 |
| .02420 | .07580 | 42000.0 | -5.293 |
| .02140 | .07860 | 66035.0 | -4.944 |

Table 73

Kinetic Data for the Epimerization of 0.10 M Dimethyl trans-1,2-cyclohex-4-enedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,trans | conc.,cis | time(min.) | ln(AK-B) |
|---|---|---|---|
| .10000 | .00000 | 0.0 | -3.497 |
| .09950 | .00050 | 25.0 | -3.518 |
| .09730 | .00270 | 55.0 | -3.620 |
| .04930 | .00570 | 515.0 | -3.778 |
| .09390 | .00610 | 750.0 | -3.801 |
| .09360 | .00640 | 1000.0 | -3.818 |
| .08590 | .01410 | 2455.0 | -4.429 |
| .08360 | .01640 | 4175.0 | -4.718 |
| .07910 | .02090 | 8275.0 | -5.787 |
| .07500 | .02500 | 16935.0 | -6.086 |
| .07720 | .02280 | 42000.0 | -7.433 |
| .07790 | .02210 | 66035.0 | -6.500 |

Table 74

Kinetic Data for the Epimerization of 0.05 M Dimethyl cis-1,2-cyclohex-4-enedicarboxylate with Sodium Methoxide at 35°. Concentrations are expressed in moles/liter.

| Conc.,cis | conc.,trans | time(min.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | -1.836 |
| .04800 | .00200 | 235.0 | -1.890 |
| .04645 | .00355 | 320.0 | -1.934 |
| .04315 | .00685 | 535.0 | -2.034 |
| .04335 | .00665 | 750.0 | -2.028 |
| .03950 | .01050 | 1230.0 | -2.159 |
| .03695 | .01305 | 1535.0 | -2.256 |
| .03355 | .01645 | 2200.0 | -2.402 |
| .03035 | .01965 | 2945.0 | -2.562 |
| .02485 | .02515 | 4435.0 | -2.917 |
| .01965 | .03035 | 7295.0 | -3.432 |
| .01435 | .03565 | 12245.0 | -4.594 |
| .01175 | .03825 | 34785.0 | -7.157 |

Table 75

Kinetic Data for the Epimerization of 0.05 M Dimethyl *trans*-1,2-cyclohex-4-enedicarboxylate with Sodium Methoxide at 35°.

Concentrations are expressed in moles/liter.

| Conc.,*trans* | conc.,*cis* | time(min.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | -4.145 |
| .05000 | .00000 | 235.0 | -4.145 |
| .05000 | .00000 | 320.0 | -4.145 |
| .04935 | .00065 | 535.0 | -4.200 |
| .04900 | .00100 | 750.0 | -4.231 |
| .04785 | .00215 | 1230.0 | -4.341 |
| .04775 | .00225 | 1535.0 | -4.352 |
| .04440 | .00560 | 2200.0 | -4.771 |
| .03995 | .01005 | 2945.0 | -5.947 |
| .03910 | .01090 | 4435.0 | -6.506 |
| .03840 | .01160 | 12245.0 | -7.465 |
| .03785 | .01215 | 34785.0 | -8.795 |

Table 76

Kinetic Data for the Epimerization of 0.05 M Dimethyl cis-1,2-cyclohex-4-enedicarboxylate with Sodium Methoxide at 50°. Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(min.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | -1.959 |
| .04875 | .00125 | 13.0 | -1.993 |
| .04815 | .00185 | 28.0 | -2.010 |
| .04630 | .00370 | 43.0 | -2.065 |
| .04400 | .00600 | 103.0 | -2.136 |
| .04080 | .00920 | 163.0 | -2.246 |
| .03915 | .01085 | 223.0 | -2.307 |
| .02965 | .02035 | 503.0 | -2.760 |
| .02235 | .02765 | 1548.0 | -3.342 |
| .01375 | .03625 | 2188.0 | -5.982 |
| .01320 | .03680 | 5023.0 | -7.766 |

Table 77

Kinetic Data for the Epimerization of 0.05 Dimethyl trans-1,2-cyclohex-4-enedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc.,trans | conc.,cis | time(min.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | -4.017 |
| .05000 | .00000 | 13.0 | -4.017 |
| .04750 | .00250 | 43.0 | -4.227 |
| .04685 | .00315 | 103.0 | -4.289 |
| .04455 | .00545 | 163.0 | -4.548 |
| .04475 | .00525 | 223.0 | -4.523 |
| .04135 | .00865 | 503.0 | -5.077 |
| .04155 | .00845 | 1548.0 | -5.035 |
| .03720 | .01280 | 2188.0 | -7.432 |
| .03675 | .01325 | 5023.0 | -10.820 |

Table 78

Kinetic Data for the Epimerization of 0.05 M Dimethyl cis-1-methyl-1,2-cyclohex-4-enedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .04860 | .00140 | 0.0 | -2.570 |
| .04550 | .00450 | 166.9 | -2.681 |
| .04230 | .00770 | 568.3 | -2.811 |
| .04030 | .00970 | 765.9 | -2.901 |
| .03865 | .01135 | 781.5 | -2.983 |
| .03875 | .01125 | 935.6 | -2.978 |
| .03800 | .01200 | 1288.3 | -3.017 |
| .03280 | .01720 | 1798.9 | -3.341 |
| .03295 | .01705 | 1982.6 | -3.330 |
| .02925 | .02075 | 2652.6 | -3.643 |
| .02665 | .02335 | 3288.8 | -3.943 |

Table 79

Kinetic Data for the Epimerization of 0.05 M Dimethyl trans-1-methyl-1,2-cyclohex-4-enedicarboxylate with Sodium Methoxide at 25°. Concentrations are expressed in moles/liter.

| conc.,trans | conc.,cis | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | -3.456 |
| .05000 | .00000 | 38.9 | -3.456 |
| .05000 | .00000 | 54.5 | -3.456 |
| .04190 | .00090 | 208.6 | -3.504 |
| .04750 | .00250 | 561.3 | -3.595 |
| .04320 | .00680 | 1071.8 | -3.889 |
| .04240 | .00760 | 1255.6 | -3.955 |
| .03980 | .01020 | 1925.6 | -4.205 |
| .03770 | .01220 | 2561.8 | -4.458 |

Table 80

Kinetic Data for the Epimerization of 0.05 Dimethyl cis-1-methyl-1,2-cyclohex-4-enedicarboxylate with Sodium Methoxide at 35°. Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | -2.523 |
| .04775 | .00225 | 1.3 | -2.599 |
| .04750 | .00250 | 1.8 | -2.608 |
| .04680 | .00320 | 2.8 | -2.633 |
| .04690 | .00310 | 16.3 | -2.629 |
| .04650 | .00350 | 40.6 | -2.644 |
| .04545 | .00455 | 89.9 | -2.683 |
| .04055 | .00945 | 208.6 | -2.890 |
| .03000 | .02000 | 759.4 | -3.571 |
| .02735 | .02265 | 938.7 | -3.853 |
| .02450 | .02550 | 1320.3 | -4.283 |
| .02295 | .02705 | 1530.8 | -4.629 |
| .02270 | .02730 | 1600.3 | -4.698 |
| .02225 | .02775 | 1776.3 | -4.836 |
| .02110 | .02890 | 2086.8 | -5.309 |
| .02140 | .02860 | 2226.3 | -5.163 |
| .02030 | .02970 | 2509.7 | -5.857 |
| .02000 | .03000 | 2814.1 | -6.175 |
| .01980 | .03020 | 3171.1 | -6.464 |

Table 81

*Kinetic Data for the Epimerization of 0.05 M Dimethyl* trans*-1-methyl-1,2-cyclohex-4-endicarboxylate with Sodium Methoxide at 35°. Concentrations are expressed in moles/liter.*

| conc.,*trans* | conc.,*cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | -3.456 |
| .05000 | .00000 | 17.3 | -3.456 |
| .04785 | .00215 | 62.7 | -3.574 |
| .04510 | .00490 | 216.7 | -3.748 |
| .04040 | .00960 | 309.3 | -4.142 |
| .03790 | .01210 | 448.7 | -4.438 |
| .03585 | .01415 | 718.1 | -4.771 |
| .03385 | .01615 | 1024.5 | -5.257 |
| .03260 | .01740 | 1505.3 | -5.754 |
| .03180 | .01820 | 1720.5 | -6.284 |
| .03145 | .01855 | 2349.0 | -6.649 |

Table 82

Kinetic Data for the Epimerization of 0.01 M Dimethyl cis-1-methyl-1,2-cyclohex-4-enedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .00992 | .00008 | 0.0 | -4.089 |
| .00790 | .00210 | 144.0 | -4.482 |
| .00650 | .00350 | 591.4 | -4.888 |
| .00592 | .00408 | 880.6 | -5.121 |
| .00484 | .00516 | 1168.0 | -5.790 |
| .00456 | .00544 | 1541.5 | -6.074 |
| .00441 | .00559 | 1841.8 | -6.267 |
| .00399 | .00601 | 2652.0 | -7.176 |

Table 83

Kinetic Data for the Epimerization of 0.01 M Dimethyl trans-1-methyl-1,2-cyclohex-4-enedicarboxylate with Sodium Methoxide at 50°. Concentrations are expressed in moles/liter.

| conc.,trans | conc.,cis | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .01000 | .00000 | 0.0 | -5.128 |
| .00920 | .00080 | 144.0 | -5.370 |
| .00804 | .00196 | 591.4 | -5.875 |
| .00760 | .00240 | 880.6 | -6.163 |
| .00716 | .00284 | 1168.0 | -6.567 |
| .00665 | .00335 | 1541.5 | -7.430 |
| .00643 | .00357 | 1841.8 | -8.322 |
| .00643 | .00357 | 2652.0 | -8.322 |

Table 84

Kinetic Data for the Epimerization of 0.05 M Dimethyl cis-1-methyl-1, 2-cyclohex-4-enedicarboxylate with Sodium Methoxide at 50°. Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | -2.466 |
| .04900 | .00100 | 4.4 | -2.499 |
| .04850 | .00150 | 7.5 | -2.515 |
| .04405 | .00595 | 16.0 | -2.676 |
| .04390 | .00610 | 19.6 | -2.682 |
| .04180 | .00820 | 30.9 | -2.768 |
| .03915 | .01085 | 42.4 | -2.889 |
| .03795 | .01205 | 53.5 | -2.949 |
| .03595 | .01405 | 70.3 | -3.058 |
| .03245 | .01805 | 102.2 | -3.295 |
| .02970 | .02030 | 146.4 | -3.502 |
| .02205 | .02795 | 310.3 | -4.657 |
| .01780 | .03220 | 597.7 | -6.227 |
| .01965 | .03035 | 918.9 | -5.804 |

Table 85

Kinetic Data for the Epimerization of 0.05 M Dimethyl trans-1-methyl-1,2-cyclohex-4-enedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc.,trans | conc.,cis | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .05000 | .00000 | 0.0 | -3.518 |
| .05000 | .00000 | 4.4 | -3.518 |
| .05000 | .00000 | 7.5 | -3.518 |
| .04680 | .00320 | 16.0 | -3.707 |
| .04625 | .00375 | 19.6 | -3.743 |
| .04550 | .00450 | 30.9 | -3.795 |
| .04420 | .00580 | 42.4 | -3.892 |
| .04325 | .00675 | 53.5 | -3.969 |
| .04200 | .00800 | 70.3 | -4.080 |
| .03710 | .01290 | 102.2 | -4.699 |
| .03740 | .01260 | 146.4 | -4.648 |
| .03660 | .01340 | 310.3 | -4.791 |
| .03675 | .01325 | 597.7 | -4.763 |
| .03040 | .01960 | 918.9 | -6.455 |

Table 86

Kinetic Data for the Epimerization of 0.10 M Dimethyl *cis*-1-methyl-1,2-cyclohex-4-enedicarboxylate with Sodium Methoxide at 50°. Concentrations are expressed in moles/liter.

| conc.,*cis* | conc.,*trans* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .10000 | .00000 | 0.0 | -1.857 |
| .09850 | .00150 | 0.8 | -1.882 |
| .09100 | .00900 | 4.2 | -2.016 |
| .08670 | .01330 | 7.8 | -2.103 |
| .07890 | .02110 | 9.0 | -2.281 |
| .07140 | .02860 | 32.0 | -2.490 |
| .06430 | .03570 | 48.5 | -2.737 |
| .05200 | .04800 | 56.3 | -3.404 |
| .04400 | .05600 | 124.2 | -4.364 |
| .03860 | .06140 | 310.4 | -6.806 |
| .03950 | .06050 | 600.0 | -6.726 |
| .03930 | .06070 | 920.4 | -7.284 |

Table 87

Kinetic Data for the Epimerization of 0.10 M Dimethyl *trans*-1-methyl-1,2-cyclohex-4-enedicarboxylate with Sodium Methoxide at 50°. Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .10000 | .00000 | 0.0 | -2.740 |
| .09860 | .00140 | 0.8 | -2.776 |
| .09590 | .00410 | 4.2 | -2.850 |
| .09340 | .00660 | 7.8 | -2.924 |
| .08960 | .01040 | 9.0 | -3.047 |
| .08000 | .02000 | 32.0 | -3.452 |
| .07190 | .02810 | 48.5 | -3.998 |
| .07080 | .02920 | 56.3 | -4.102 |
| .06630 | .03370 | 124.2 | -4.696 |
| .06440 | .03560 | 310.4 | -5.116 |
| .05150 | .03850 | 600.0 | -6.702 |
| .06160 | .03840 | 920.4 | -6.576 |

Table 88

Kinetic Data for the Epimerization of 0.01 M Dimethyl cis-1,2-cycloheptanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .00884 | .00116 | 0.0 | -3.405 |
| .00812 | .00188 | 22.9 | -3.517 |
| .00789 | .00211 | 48.8 | -3.555 |
| .00756 | .00244 | 76.5 | -3.613 |
| .00676 | .00324 | 100.2 | -3.770 |
| .00623 | .00377 | 127.4 | -3.889 |
| .00582 | .00418 | 178.4 | -3.992 |
| .00541 | .00459 | 215.4 | -4.107 |
| .00471 | .00530 | 293.1 | -4.344 |
| .00373 | .00627 | 411.5 | -4.799 |
| .00340 | .00660 | 513.7 | -5.017 |
| .00280 | .00720 | 648.8 | -5.602 |
| .00214 | .00786 | 1105.0 | -7.679 |

Table 89

Kinetic Data for the Epimerization of 0.01 M Dimethyl *trans*-1,2-cycloheptanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .00867 | .00033 | 0.0 | -6.235 |
| .00960 | .00040 | 22.9 | -6.150 |
| .00962 | .00038 | 48.8 | -6.138 |
| .00913 | .00087 | 76.5 | -6.476 |
| .00912 | .00088 | 100.2 | -6.484 |
| .00885 | .00115 | 127.4 | -6.737 |
| .00894 | .00106 | 178.4 | -6.645 |
| .00905 | .00095 | 215.4 | -6.544 |
| .00890 | .00110 | 293.1 | -6.685 |
| .00891 | .00109 | 411.5 | -6.675 |
| .00822 | .00178 | 513.7 | -7.849 |
| .00786 | .00214 | 648.8 | -9.642 |
| .00801 | .00199 | 1105.0 | -8.990 |

Table 90

Kinetic data for the Epimerization of 0.05 M Dimethyl cis-1,2-cycloheptanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .04255 | .00745 | 0.5 | -1.885 |
| .04160 | .00840 | 1.4 | -1.915 |
| .04375 | .00625 | 2.2 | -1.848 |
| .03955 | .01045 | 5.4 | -1.983 |
| .04055 | .00945 | 6.8 | -1.949 |
| .03935 | .01065 | 9.4 | -1.990 |
| .03640 | .01360 | 13.1 | -2.098 |
| .03065 | .01935 | 23.8 | -2.349 |
| .02725 | .02275 | 35.4 | -2.535 |
| .02115 | .02885 | 61.4 | -2.989 |
| .01435 | .03565 | 98.4 | -4.012 |
| .01250 | .03750 | 174.8 | -4.676 |
| .01180 | .03820 | 293.5 | -5.117 |
| .00995 | .04005 | 395.7 | -5.883 |

Table 91

Kinetic Data for the Epimerization of 0.05 M Dimethyl *trans*-1,2-cycloheptanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .04775 | .00225 | 0.5 | -4.516 |
| .04750 | .00250 | 1.4 | -4.546 |
| .04665 | .00335 | 2.2 | -4.654 |
| .04625 | .00375 | 5.4 | -4.709 |
| .04570 | .00430 | 6.8 | -4.790 |
| .04710 | .00290 | 9.4 | -4.595 |
| .04735 | .00265 | 13.1 | -4.564 |
| .04700 | .00300 | 23.8 | -4.608 |
| .04615 | .00385 | 35.4 | -4.723 |
| .04165 | .00835 | 61.4 | -5.762 |
| .03960 | .01040 | 98.4 | -7.543 |
| .04175 | .00825 | 174.8 | -5.722 |
| .03990 | .01010 | 293.5 | -6.999 |
| .03860 | .01140 | 395.7 | -7.200 |

Table 92

Kinetic Data for the Epimerization of 0.10 M Dimethyl cis-1,2-cycloheptanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .08690 | .01310 | 0.0 | -1.096 |
| .08870 | .01130 | 0.3 | -1.069 |
| .08460 | .01540 | 0.6 | -1.131 |
| .08390 | .01610 | 1.3 | -1.142 |
| .08150 | .01850 | 1.8 | -1.180 |
| .07980 | .02020 | 2.7 | -1.208 |
| .07660 | .02340 | 4.9 | -1.263 |
| .07080 | .02920 | 6.8 | -1.371 |
| .06800 | .03200 | 8.5 | -1.428 |
| .05910 | .03090 | 15.7 | -1.633 |
| .05060 | .04940 | 34.7 | -1.878 |
| .02770 | .07230 | 48.7 | -3.259 |
| .02070 | .07930 | 76.7 | -5.667 |
| .01980 | .08020 | 100.0 | -6.869 |
| .02440 | .07560 | 117.4 | -3.819 |

Table 93

Kinetic Data for the Epimerization of 0.10 M Dimethyl *trans*-1,2-cycloheptanedicarboxylate with Sodium Methoxide at 25°.

Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .09500 | .00500 | 0.0 | -3.956 |
| .09470 | .00530 | 0.3 | -3.976 |
| .09500 | .00500 | 0.6 | -3.956 |
| .09460 | .00540 | 1.3 | -3.983 |
| .09450 | .00550 | 1.8 | -3.990 |
| .09400 | .00600 | 2.7 | -4.024 |
| .09470 | .00530 | 4.9 | -3.976 |
| .09400 | .00600 | 6.8 | -4.024 |
| .09280 | .00720 | 8.5 | -4.112 |
| .09250 | .00750 | 15.7 | -4.135 |
| .09040 | .00960 | 22.8 | -4.315 |
| .08730 | .01270 | 34.7 | -4.659 |
| .08390 | .01610 | 48.7 | -5.257 |
| .08130 | .01870 | 100.0 | -6.240 |
| .07880 | .02120 | 117.4 | -6.738 |

Table 94

Kinetic Data for the Epimerization of 0.05 M Dimethyl cis-1,2-cycloheptanedicarboxylate with Sodium Methoxide at 35°.

Concentrations are expressed in moles/liter.

| conc., cis | conc., trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .04345 | .00655 | 0.0 | -1.664 |
| .04420 | .00580 | 0.6 | -1.642 |
| .04220 | .00780 | 1.0 | -1.701 |
| .04175 | .00825 | 1.6 | -1.715 |
| .04200 | .00800 | 2.7 | -1.707 |
| .03775 | .01225 | 3.8 | -1.845 |
| .03660 | .01340 | 6.5 | -1.886 |
| .03385 | .01615 | 8.1 | -1.992 |
| .02860 | .02140 | 10.2 | -2.230 |
| .02680 | .02320 | 14.4 | -2.326 |
| .02255 | .02745 | 19.7 | -2.601 |
| .02005 | .02995 | 23.6 | -2.806 |
| .01720 | .03180 | 27.7 | -3.084 |
| .01575 | .03425 | 48.3 | -3.303 |
| .01175 | .03825 | 45.5 | -4.218 |
| .01035 | .03965 | 82.0 | -4.959 |
| .00900 | .04100 | 99.0 | -7.778 |
| .00930 | .04070 | 120.6 | -6.698 |

Table 95

Kinetic Data for the Epimerication of 0.05 M Dimethyl *trans*-1,2-cycloheptanedicarboxylate with Sodium Methoxide at 35°.

Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .04835 | .00165 | 0.0 | -4.670 |
| .04790 | .00210 | 0.6 | -4.731 |
| .04725 | .00275 | 1.0 | -4.825 |
| .04725 | .00275 | 1.6 | -4.825 |
| .04685 | .00315 | 2.7 | -4.889 |
| .04705 | .00295 | 3.8 | -4.857 |
| .04695 | .00305 | 6.5 | -4.872 |
| .04535 | .00465 | 8.1 | -5.169 |
| .04455 | .00545 | 10.2 | -5.359 |
| .04385 | .00615 | 14.4 | -5.560 |
| .04460 | .00540 | 19.7 | -5.346 |
| .04060 | .00940 | 23.6 | -8.851 |
| .04135 | .00865 | 27.7 | -7.159 |
| .04090 | .00910 | 38.4 | -8.399 |
| .04140 | .00860 | 45.4 | -7.083 |
| .04035 | .00965 | 82.0 | -7.706 |
| .04030 | .00920 | 99.0 | -11.365 |
| .04165 | .00835 | 120.6 | -6.771 |

Table 96

Kinetic Data for the Epimerization of 0.05 M Dimethyl cis-1,2-cycloheptanedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc.,cis | conc.,trans | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .04460 | .00540 | 0.0 | -1.781 |
| .04300 | .00700 | 0.3 | -1.828 |
| .04060 | .00940 | 0.7 | -1.904 |
| .03815 | .01185 | 1.1 | -1.988 |
| .03285 | .01715 | 2.0 | -2.199 |
| .03090 | .01910 | 2.4 | -2.289 |
| .02800 | .02200 | 3.2 | -2.440 |
| .02370 | .02630 | 4.4 | -2.716 |
| .02145 | .02855 | 5.2 | -2.899 |
| .01900 | .03100 | 6.2 | -3.144 |
| .01750 | .03250 | 7.3 | -3.331 |
| .01330 | .03670 | 13.0 | -4.188 |
| .01065 | .04435 | 20.3 | -5.873 |
| .01000 | .04000 | 39.2 | -6.908 |

Table 97

Kinetic Data for the Epimerization of 0.05 M Dimethyl *trans*-1,2-cycloheptanedicarboxylate with Sodium Methoxide at 50°.

Concentrations are expressed in moles/liter.

| conc.,*trans* | conc.,*cis* | time(hrs.) | ln(AK-B) |
|---|---|---|---|
| .04760 | .00240 | 0.0 | -4.617 |
| .04735 | .00265 | 0.3 | -4.650 |
| .04750 | .00250 | 0.7 | -4.630 |
| .04750 | .00250 | 1.1 | -4.630 |
| .04700 | .00300 | 2.0 | -4.697 |
| .04595 | .00405 | 2.4 | -4.853 |
| .04670 | .00330 | 3.2 | -4.739 |
| .04630 | .00370 | 4.4 | -4.798 |
| .04155 | .00845 | 5.2 | -6.088 |
| .04150 | .00850 | 6.2 | -6.116 |
| .04125 | .00875 | 7.3 | -6.270 |
| .04040 | .00960 | 13.0 | -7.102 |
| .03965 | .01035 | 20.3 | -9.026 |
| .03985 | .01015 | 39.2 | -8.938 |

Table 98

Kinetic Data for Epimerization of Dimethyl 1,2-cyclopropanedicarboxylate

| conc. (M/l) | T (°) | K (t/c) | $k_c$(pseudo) (1 $sec^{-1}mole^{-1}$) | $k_t$(pseudo) (1 $sec^{-1}mole^{-1}$) | $k_c$(corr.) (1 $sec^{-1}mole^{-1}$) | $k_c$(corr.) (1 $sec^{-1}mole^{-1}$) |
|---|---|---|---|---|---|---|
| 0.05 | 25 | 99.0[a] | $3.53 \times 10^{-9}$ | $3.56 \times 10^{-11}$ | $7.06 \times 10^{-8}$ | $7.11 \times 10^{-10}$ |
| 0.10 | 25 | 99.0[a] | $9.69 \times 10^{-9}$ | $9.78 \times 10^{-11}$ | $9.69 \times 10^{-8}$ | $9.78 \times 10^{-10}$ |
| 0.05 | 35 | 99.0[a] | $1.21 \times 10^{-8}$ | $1.22 \times 10^{-10}$ | $2.42 \times 10^{-7}$ | $2.44 \times 10^{-9}$ |
| 0.01 | 50 | 99.0[a] | $3.83 \times 10^{-8}$ | $3.86 \times 10^{-10}$ | $3.83 \times 10^{-6}$ | $3.86 \times 10^{-8}$ |
| 0.05 | 50 | 99.0[a] | $1.05 \times 10^{-7}$ | $1.06 \times 10^{-9}$ | $2.09 \times 10^{-6}$ | $2.12 \times 10^{-8}$ |
| 0.10 | 50 | 99.0[a] | $4.08 \times 10^{-7}$ | $4.14 \times 10^{-9}$ | $4.08 \times 10^{-6}$ | $4.14 \times 10^{-8}$ |

[a]Value taken from Shiengthong.[38]

Table 99

Kinetic Data for Epimerization of Dimethyl 1,2-cyclobutanedicarboxylate

| Conc. (M/l) | T (°) | K (t/c) | $k_c$(pseudo) (l $sec^{-1}mole^{-1}$) | $k_t$(pseudo) (l $sec^{-1}mole^{-1}$) | $k_c$(corr.) (l $sec^{-1}mole^{-1}$) | $k_t$(corr.) (l $sec^{-1}mole^{-1}$) |
|---|---|---|---|---|---|---|
| 0.01 | 25 | 9.05 | $1.13 \times 10^{-5}$<br>$9.00 \times 10^{-7}$[a] | $1.24 \times 10^{-7}$<br>$1.01 \times 10^{-7}$[a] | $1.13 \times 10^{-3}$<br>$9.00 \times 10^{-5}$[a] | $1.24 \times 10^{-5}$<br>$1.01 \times 10^{-5}$[a] |
| 0.05 | 25 | 8.40 | $6.61 \times 10^{-6}$<br>$4.28 \times 10^{-6}$[a] | $7.86 \times 10^{-7}$<br>$5.11 \times 10^{-7}$[a] | $1.32 \times 10^{-4}$<br>$8.56 \times 10^{-5}$[a] | $1.57 \times 10^{-5}$<br>$1.02 \times 10^{-5}$[a] |
| 0.10 | 25 | 6.60 | $1.22 \times 10^{-5}$<br>$8.78 \times 10^{-6}$[a] | $1.85 \times 10^{-6}$<br>$1.37 \times 10^{-6}$[a] | $1.22 \times 10^{-4}$<br>$8.78 \times 10^{-5}$[a] | $1.85 \times 10^{-5}$<br>$1.37 \times 10^{-5}$[a] |
| 0.05 | 35 | 7.67 | $1.50 \times 10^{-5}$<br>$5.58 \times 10^{-6}$[a] | $1.96 \times 10^{-6}$<br>$7.53 \times 10^{-7}$[a] | $3.00 \times 10^{-4}$<br>$1.12 \times 10^{-4}$[a] | $3.92 \times 10^{-5}$<br>$1.51 \times 10^{-5}$[a] |
| 0.05 | 50 | 8.58 | $8.53 \times 10^{-5}$<br>$8.81 \times 10^{-5}$[a] | $9.92 \times 10^{-6}$<br>$1.03 \times 10^{-5}$[a] | $1.71 \times 10^{-3}$<br>$1.76 \times 10^{-3}$[a] | $2.42 \times 10^{-4}$<br>$2.07 \times 10^{-4}$[a] |

[a]Calculated from the trans runs.

Table 100

Kinetic Data for Epimerization of Dimethyl 1,2-cyclopentanedicarboxylate

| Conc. (M/l) | T (°) | K (t/c) | $k_c$(pseudo) (l $sec^{-1}mole^{-1}$) | $k_t$(pseudo) (l $sec^{-1}mole^{-1}$) | $k_c$(corr.) (l $sec^{-1}mole^{-1}$) | $k_t$(corr.) (l $sec^{-1}mole^{-1}$) |
|---|---|---|---|---|---|---|
| 0.01 | 25 | 9.78 | $1.53 \times 10^{-6}$<br>$9.11 \times 10^{-7}$[a] | $1.56 \times 10^{-7}$<br>$9.47 \times 10^{-8}$[a] | $1.53 \times 10^{-4}$<br>$9.11 \times 10^{-5}$[a] | $1.56 \times 10^{-5}$<br>$9.47 \times 10^{-5}$[a] |
| 0.05 | 25 | 9.53 | $8.78 \times 10^{-6}$<br>$6.83 \times 10^{-6}$[a] | $9.22 \times 10^{-7}$<br>$7.28 \times 10^{-7}$[a] | $1.76 \times 10^{-4}$<br>$1.65 \times 10^{-4}$[a] | $1.84 \times 10^{-5}$<br>$1.51 \times 10^{-5}$[a] |
| 0.10 | 25 | 8.46 | $2.09 \times 10^{-5}$[a]<br>$5.14 \times 10^{-6}$[a] | $2.42 \times 10^{-6}$<br>$6.11 \times 10^{-7}$[a] | $2.09 \times 10^{-4}$<br>$5.14 \times 10^{-5}$[a] | $2.42 \times 10^{-5}$<br>$6.11 \times 10^{-5}$[a] |
| 0.05 | 35 | 7.37 | $2.86 \times 10^{-5}$<br>$6.00 \times 10^{-6}$[a] | $3.89 \times 10^{-6}$<br>$2.86 \times 10^{-6}$[a] | $5.72 \times 10^{-4}$<br>$4.56 \times 10^{-4}$[a] | $7.78 \times 10^{-5}$<br>$5.72 \times 10^{-5}$[a] |
| 0.05 | 50 | 6.08 | $1.27 \times 10^{-4}$<br>$7.19 \times 10^{-5}$[a] | $2.08 \times 10^{-5}$<br>$1.20 \times 10^{-5}$[a] | $2.55 \times 10^{-3}$<br>$1.44 \times 10^{-3}$ | $4.17 \times 10^{-4}$<br>$2.39 \times 10^{-4}$[a] |

[a]Calculated from trans runs.

Table 101

Kinetic Data for Epimerization of Dimethyl 1,2-cyclohexanedicarboxylate

| Conc. (M/1) | T (°) | K (t/c) | $k_c$(pseudo) (1 $sec^{-1}mole^{-1}$) | $k_t$(pseudo) (1 $sec^{-1}mole^{-1}$) | $k_c$(corr.) (1 $sec^{-1}mole^{-1}$ | $k_t$(corr.) (1 $sec^{-1}$ $mole^{-1}$) |
|---|---|---|---|---|---|---|
| 0.01 | 25 | 14.0 | $6.06 \times 10^{-8}$<br>$4.58 \times 10^{-8a}$ | $4.33 \times 10^{-9}$<br>$3.56 \times 10^{-9a}$ | $6.06 \times 10^{-6}$<br>$4.58 \times 10^{-6a}$ | $4.33 \times 10^{-7}$<br>$3.56 \times 10^{-7a}$ |
| 0.05 | 25 | 13.5 | $3.36 \times 10^{-6}$<br>$3.22 \times 10^{-7a}$ | $2.48 \times 10^{-8}$<br>$2.42 \times 10^{-8a}$ | $6.72 \times 10^{-6}$<br>$6.44 \times 10^{-6a}$ | $4.97 \times 10^{-7}$<br>$4.83 \times 10^{-7a}$ |
| 0.10 | 25 | 12.2 | $8.36 \times 10^{-7}$<br>$7.33 \times 10^{-7a}$ | $6.81 \times 10^{-8}$<br>$6.14 \times 10^{-8a}$ | $8.36 \times 10^{-6}$<br>$7.33 \times 10^{-6a}$ | $6.81 \times 10^{-7}$<br>$6.14 \times 10^{-7a}$ |
| 0.01 | 35 | 9.72 | $2.23 \times 10^{-7}$<br>$1.35 \times 10^{-7a}$ | $2.29 \times 10^{-8}$<br>$1.41 \times 10^{-8a}$ | $2.23 \times 10^{-5}$<br>$1.35 \times 10^{-5a}$ | $2.29 \times 10^{-6}$<br>$1.41 \times 10^{-6a}$ |
| 0.05 | 35 | 9.71 | $1.18 \times 10^{-6}$<br>$4.36 \times 10^{-7a}$ | $1.21 \times 10^{-7}$<br>$4.39 \times 10^{-8a}$ | $2.36 \times 10^{-5}$<br>$8.72 \times 10^{-6a}$ | $2.43 \times 10^{-6}$<br>$8.78 \times 10^{-7a}$ |
| 0.10 | 35 | 10.9 | $2.75 \times 10^{-6}$<br>$1.14 \times 10^{-6a}$ | $2.50 \times 10^{-7}$<br>$1.08 \times 10^{-7a}$ | $2.75 \times 10^{-5}$<br>$1.15 \times 10^{-5a}$ | $2.50 \times 10^{-6}$<br>$1.08 \times 10^{-6a}$ |
| 0.01 | 50 | 11.3 | $1.17 \times 10^{-6}$<br>$8.06 \times 10^{-8a}$ | $1.03 \times 10^{-7}$<br>$7.17 \times 10^{-8a}$ | $1.17 \times 10^{-4}$<br>$8.06 \times 10^{-5a}$ | $1.03 \times 10^{-5}$<br>$7.17 \times 10^{-6a}$ |

Table 101--Continued

| Conc. (M/l) | T (°) | K (k/c) | $k_c$(pseudo) (l $sec^{-1}mole^{-1}$) | $k_t$(pseudo) (l $sec^{-1}mole^{-1}$) | $k_c$(corr.) (l $sec^{-1}mole^{-1}$) | $k_t$(corr.) (l $sec^{-1}mole^{-1}$) |
|---|---|---|---|---|---|---|
| 0.05 | 50 | 11.7 | $7.03 \times 10^{-6}$<br>$3.86 \times 10^{-6}$[a] | $6.00 \times 10^{-7}$<br>$3.39 \times 10^{-7}$[a] | $1.41 \times 10^{-4}$<br>$7.72 \times 10^{-5}$[a] | $1.20 \times 10^{-5}$<br>$6.78 \times 10^{-6}$[a] |
| 0.10 | 50 | 9.83 | $1.31 \times 10^{-5}$<br>$3.44 \times 10^{-7}$[a] | $1.34 \times 10^{-6}$<br>$3.42 \times 10^{-7}$[a] | $1.31 \times 10^{-4}$<br>$3.44 \times 10^{-5}$[a] | $1.34 \times 10^{-5}$<br>$3.42 \times 10^{-6}$[a] |

[a]Calculated from the trans runs.

Table 102

Kinetic Data for Epimerization of Dimethyl 1-methyl-1,2-cyclohexanedicarboxylate

| Conc. (M/l) | T (°) | K (t/c) | $k_c$(pseudo) (l $sec^{-1}mole^{-1}$) | $k_t$(pseudo) (l $sec^{-1}mole^{-1}$) | $k_c$(corr.) (l $sec^{-1}mole^{-1}$) | $k_t$(corr.) (l $sec^{-1}mole^{-1}$) |
|---|---|---|---|---|---|---|
| 0.05 | 25 | 1.84 | $2.21 \times 10^{-8}$<br>$1.28 \times 10^{-8}$[a] | $1.20 \times 10^{-7}$<br>$7.00 \times 10^{-9}$[a] | $4.42 \times 10^{-7}$<br>$2.56 \times 10^{-7}$[a] | $2.41 \times 10^{-7}$<br>$1.40 \times 10^{-7}$[a] |
| 0.05 | 35 | 1.84 | $6.28 \times 10^{-8}$<br>$6.31 \times 10^{-8}$[a] | $3.42 \times 10^{-8}$<br>$3.44 \times 10^{-8}$[a] | $1.26 \times 10^{-6}$<br>$1.26 \times 10^{-6}$[a] | $6.83 \times 10^{-7}$<br>$6.83 \times 10^{-7}$[a] |
| 0.01 | 50 | 1.84 | $5.94 \times 10^{-8}$<br>$5.72 \times 10^{-8}$[a] | $3.22 \times 10^{-8}$<br>$3.14 \times 10^{-8}$[a] | $5.94 \times 10^{-6}$<br>$5.72 \times 10^{-6}$[a] | $3.22 \times 10^{-6}$<br>$3.14 \times 10^{-6}$[a] |
| 0.05 | 50 | 1.84 | $3.50 \times 10^{-7}$<br>$2.01 \times 10^{-7}$[a] | $1.90 \times 10^{-7}$<br>$1.11 \times 10^{-7}$[a] | $7.00 \times 10^{-6}$<br>$4.03 \times 10^{-6}$[a] | $3.81 \times 10^{-6}$<br>$2.21 \times 10^{-6}$[a] |
| 0.10 | 50 | 1.75 | $8.00 \times 10^{-7}$<br>$7.86 \times 10^{-7}$[a] | $4.56 \times 10^{-7}$<br>$4.44 \times 10^{-7}$[a] | $8.00 \times 10^{-6}$<br>$7.86 \times 10^{-6}$[a] | $4.56 \times 10^{-6}$<br>$4.44 \times 10^{-6}$[a] |

[a]Calculated from trans runs.

Table 103

Kinetic Data for Epimerization of Dimethyl 1,2-cyclohex-4-endicarboxylate

| Conc. (M/l) | T (°) | K (t/c) | $k_c$(pseudo) (l $sec^{-1}mole^{-1}$) | $k_t$(pseudo) (l $sec^{-1}mole^{-1}$) | $k_c$(corr.) (l $sec^{-1}mole^{-1}$) | $k_t$(corr.) (l $sec^{-1}mole^{-1}$) |
|---|---|---|---|---|---|---|
| 0.01 | 25 | 2.83 | $4.39 \times 10^{-7}$<br>$1.53 \times 10^{-7}$[a] | $1.55 \times 10^{-5}$<br>$5.47 \times 10^{-6}$[a] | $4.39 \times 10^{-5}$<br>$1.53 \times 10^{-5}$[a] | $1.55 \times 10^{-5}$<br>$5.47 \times 10^{-6}$[a] |
| 0.05 | 25 | 2.68 | $1.21 \times 10^{-6}$<br>$7.44 \times 10^{-7}$[a] | $4.53 \times 10^{-6}$<br>$2.83 \times 10^{-7}$[a] | $2.42 \times 10^{-7}$<br>$1.49 \times 10^{-5}$[a] | $9.06 \times 10^{-6}$<br>$5.62 \times 10^{-6}$[a] |
| 0.10 | 25 | 3.34 | $1.36 \times 10^{-6}$<br>$7.11 \times 10^{-7}$[a] | $4.11 \times 10^{-7}$<br>$2.15 \times 10^{-7}$[a] | $1.36 \times 10^{-5}$<br>$7.11 \times 10^{-6}$[a] | $4.11 \times 10^{-6}$<br>$2.15 \times 10^{-6}$[a] |
| 0.05 | 35 | 3.19 | $2.75 \times 10^{-6}$<br>$2.63 \times 10^{-6}$[a] | $8.61 \times 10^{-7}$<br>$8.25 \times 10^{-7}$[a] | $5.50 \times 10^{-5}$<br>$5.25 \times 10^{-5}$[a] | $1.72 \times 10^{-5}$<br>$1.65 \times 10^{-5}$[a] |
| 0.05 | 50 | 2.82 | $1.23 \times 10^{-5}$<br>$9.78 \times 10^{-6}$[a] | $4.39 \times 10^{-6}$<br>$3.53 \times 10^{-6}$[a] | $2.47 \times 10^{-4}$<br>$1.96 \times 10^{-4}$[a] | $8.78 \times 10^{-5}$<br>$7.06 \times 10^{-5}$[a] |

[a]Calculated from trans runs.

Table 104

Kinetic Data for Epimerization of Dimethyl 1-methyl-1,2-cyclohex-4-enedicarboxylate

| Conc. (M/1) | T (°) | k (t/c) | $k_c$(pseudo) (1 $sec^{-1}mole^{-1}$) | $k_t$(pseudo) (1 $sec^{-1}mole^{-1}$) | $k_c$(corr.) (1 $sec^{-1}mole^{-1}$) | $k_t$(corr.) (1 $sec^{-1}mole^{-1}$) |
|---|---|---|---|---|---|---|
| 0.05 | 25 | 1.60 | $6.75 \times 10^{-8}$<br>$6.83 \times 10^{-8}$[a] | $4.22 \times 10^{-8}$<br>$4.31 \times 10^{-8}$[a] | $1.35 \times 10^{-6}$<br>$1.32 \times 10^{-6}$[a] | $8.44 \times 10^{-7}$<br>$8.61 \times 10^{-7}$[a] |
| 0.05 | 35 | 1.60 | $2.19 \times 10^{-7}$<br>$2.49 \times 10^{-7}$[a] | $1.38 \times 10^{-6}$<br>$1.57 \times 10^{-7}$[a] | $4.33 \times 10^{-6}$<br>$5.00 \times 10^{-6}$[a] | $2.71 \times 10^{-6}$<br>$3.14 \times 10^{-6}$[a] |
| 0.01 | 50 | 1.70 | $1.93 \times 10^{-7}$<br>$2.38 \times 10^{-7}$[a] | $1.14 \times 10^{-7}$<br>$1.41 \times 10^{-7}$[a] | $1.93 \times 10^{-6}$<br>$2.38 \times 10^{-5}$[a] | $1.14 \times 10^{-5}$<br>$1.43 \times 10^{-5}$[a] |
| 0.05 | 50 | 1.70 | $8.78 \times 10^{-7}$<br>$4.03 \times 10^{-7}$[a] | $5.17 \times 10^{-7}$<br>$2.39 \times 10^{-7}$[a] | $1.76 \times 10^{-5}$<br>$8.06 \times 10^{-6}$[a] | $1.03 \times 10^{-5}$<br>$4.78 \times 10^{-6}$[a] |
| 0.10 | 50 | 1.56 | $1.72 \times 10^{-6}$<br>$8.17 \times 10^{-7}$[a] | $1.10 \times 10^{-6}$<br>$5.28 \times 10^{-7}$[a] | $1.72 \times 10^{-5}$<br>$8.17 \times 10^{-6}$[a] | $1.10 \times 10^{-5}$<br>$5.28 \times 10^{-6}$[a] |

[a]Calculated from trans runs.

Table 105

Kinetic Data for the Epimerization of Dimethyl 1,2-cycloheptanedicarboxylate

| Conc. (M/l) | T (°) | K (t/c) | $k_c$(pseudo) (l $sec^{-1}mole^{-1}$) | $k_t$(pseudo) (l $sec^{-1}mole^{-1}$) | $k_c$(corr.) (l $sec^{-1}mole^{-1}$) | $k_t$(corr.) (l $sec^{-1}mole^{-1}$) |
|---|---|---|---|---|---|---|
| 0.01 | 25 | 3.89 | $7.17 \times 10^{-7}$<br>$5.53 \times 10^{-7a}$ | $1.84 \times 10^{-7}$<br>$1.46 \times 10^{-7a}$ | $7.17 \times 10^{-5}$<br>$5.53 \times 10^{-5a}$ | $1.84 \times 10^{-5}$<br>$1.46 \times 10^{-5a}$ |
| 0.05 | 25 | 3.74 | $3.03 \times 10^{-6}$<br>$1.61 \times 10^{-6a}$ | $8.06 \times 10^{-7}$<br>$4.44 \times 10^{-7a}$ | $6.06 \times 10^{-5}$<br>$3.22 \times 10^{-5a}$ | $1.61 \times 10^{-5}$<br>$8.89 \times 10^{-6a}$ |
| 0.10 | 25 | 4.03 | $6.19 \times 10^{-6}$<br>$5.25 \times 10^{-6a}$ | $1.53 \times 10^{-6}$<br>$1.33 \times 10^{-6a}$ | $6.19 \times 10^{-5}$<br>$5.25 \times 10^{-5a}$ | $1.54 \times 10^{-5}$<br>$1.33 \times 10^{-5a}$ |
| 0.05 | 35 | 4.51 | $1.08 \times 10^{-5}$<br>$5.44 \times 10^{-6a}$ | $2.39 \times 10^{-6}$<br>$1.24 \times 10^{-6a}$ | $2.02 \times 10^{-4}$<br>$1.09 \times 10^{-4a}$ | $4.78 \times 10^{-5}$<br>$2.48 \times 10^{-5a}$ |
| 0.05 | 50 | 3.90 | $4.56 \times 10^{-5}$<br>$3.83 \times 10^{-5a}$ | $1.44 \times 10^{-5}$<br>$9.89 \times 10^{-6a}$ | $9.11 \times 10^{-4}$<br>$7.42 \times 10^{-4a}$ | $2.33 \times 10^{-5}$<br>$1.98 \times 10^{-5a}$ |

[a]Calculated from trans runs.

Table 106

Standard Deviations of Data for Epimerization of Dimethyl 1,2-cyclopropanedicarboxylate

| Conc. (M/1) | Temp. (°) | $\sigma_K$ | $\sigma_{k_c}$ | $\sigma_{k_t}$ | $\sigma_{data}$ | $\sigma_S$ |
|---|---|---|---|---|---|---|
| .05 | 25 | 5.00 | $9.58 \times 10^{-10}$ | $9.50 \times 10^{-12}$ | $1.37 \times 10^{-2}$ | $8.0 \times 10^{-5}$ |
| .10 | 25 | 5.00 | $1.49 \times 10^{-9}$ | $1.39 \times 10^{-11}$ | $7.59 \times 10^{-3}$ | $1.0 \times 10^{-5}$ |
| .05 | 35 | 5.00 | $4.17 \times 10^{-9}$ | $3.89 \times 10^{-11}$ | $2.87 \times 10^{-2}$ | $1.0 \times 10^{-5}$ |
| .01 | 50 | 5.00 | $3.30 \times 10^{-9}$ | $2.50 \times 10^{-11}$ | $1.18 \times 10^{-2}$ | $1.0 \times 10^{-5}$ |
| .05 | 50 | 5.00 | $7.50 \times 10^{-9}$ | $6.94 \times 10^{-11}$ | $2.48 \times 10^{-2}$ | $2.0 \times 10^{-5}$ |
| .10 | 50 | 5.00 | $4.33 \times 10^{-8}$ | $3.81 \times 10^{-10}$ | $3.80 \times 10^{-1}$ | $1.10 \times 10^{-4}$ |

Table 107

Standard Deviations of Data for Epimerization of Dimethyl 1,2-cyclobutanedicarboxylate

| Conc. (M/l) | T (°) | $\sigma_k$ | $\sigma_{k_c}$ | $\sigma_{k_t}$ | $\sigma_{data}$ | $\sigma_s$ |
|---|---|---|---|---|---|---|
| .01 | 25 | 1.17 | $2.01 \times 10^{-7}$<br>$2.52 \times 10^{-7}$[a] | $1.54 \times 10^{-8}$<br>$3.14 \times 10^{-9}$[a] | 1.90<br>1.051[a] | $1.9 \times 10^{-4}$<br>$1.00 \times 10^{-3}$[a] |
| .05 | 25 | .794 | $8.61 \times 10^{-7}$<br>$8.67 \times 10^{-7}$[a] | $7.06 \times 10^{-8}$<br>$1.14 \times 10^{-7}$[a] | .163<br>.705[a] | $8.0 \times 10^{-4}$<br>$3.49 \times 10^{-3}$[a] |
| .10 | 25 | 1.06 | $3.03 \times 10^{-6}$<br>$8.92 \times 10^{-7}$[a] | $3.42 \times 10^{-7}$<br>$2.78 \times 10^{-9}$[a] | 1.091<br>.611[a] | $6.35 \times 10^{-3}$<br>$3.60 \times 10^{-3}$[a] |
| .05 | 35 | 1.32 | $3.53 \times 10^{-6}$<br>$3.31 \times 10^{-6}$[a] | $3.11 \times 10^{-7}$<br>$4.56 \times 10^{-7}$[a] | .417<br>1.526[a] | $2.79 \times 10^{-3}$<br>$1.35 \times 10^{-2}$[a] |
| .05 | 50 | .727 | $1.37 \times 10^{-5}$<br>$1.37 \times 10^{-4}$[a] | $1.87 \times 10^{-5}$<br>$1.36 \times 10^{-6}$[a] | 1.009<br>1.155[a] | $6.5 \times 10^{-4}$<br>$9.1 \times 10^{-4}$[a] |

[a]Calculated from trans runs.

Table 108

Standard Deviation of Data for Epimerization of Dimethyl 1,2-cyclopentanedicarboxylate

| Conc. (M/l) | T (°) | $\sigma_K$ | $\sigma_{k_c}$ | $\sigma_{k_t}$ | $\sigma_{data}$ | $\sigma_S$ |
|---|---|---|---|---|---|---|
| .01 | 25 | 1.34 | $2.89 \times 10^{-7}$<br>$1.67 \times 10^{-7}$[a] | $2.01 \times 10^{-8}$<br>$2.05 \times 10^{-8}$[a] | .135<br>.480[a] | $1.8 \times 10^{-4}$<br>$6.2 \times 10^{-4}$[a] |
| .05 | 25 | 1.11 | $1.59 \times 10^{-6}$<br>$7.64 \times 10^{-7}$[a] | $1.12 \times 10^{-7}$<br>$1.26 \times 10^{-7}$[a] | .339<br>.488[a] | $2.11 \times 10^{-3}$<br>$3.03 \times 10^{-3}$[a] |
| .10 | 25 | .954 | $4.80 \times 10^{-6}$<br>$1.38 \times 10^{-6}$[a] | $4.94 \times 10^{-7}$<br>$1.75 \times 10^{-7}$[a] | 2.884<br>1.079[a] | $1.46 \times 10^{-2}$<br>$5.53 \times 10^{-3}$[a] |
| .05 | 35 | 1.23 | $1.15 \times 10^{-5}$<br>$3.58 \times 10^{-6}$[a] | $1.45 \times 10^{-6}$<br>$7.03 \times 10^{-7}$[a] | 1.989<br>.745[a] | $6.5 \times 10^{-4}$<br>$2.4 \times 10^{-4}$[a] |
| .05 | 50 | .577 | $1.98 \times 10^{-5}$<br>$1.48 \times 10^{-7}$[a] | $2.60 \times 10^{-6}$<br>$2.75 \times 10^{-6}$[a] | .926<br>1.148[a] | $8.3 \times 10^{-4}$<br>$1.03 \times 10^{-3}$[a] |

[a]Calculated from trans runs.

Table 109

Standard Deviation of Data for Epimerization of Dimethyl 1,2-cyclohexanedicarboxylate

| Conc. (M/l) | T (°) | $\sigma K$ | $\sigma k_c$ | $\sigma k_t$ | $\sigma_{data}$ | $\sigma_S$ |
|---|---|---|---|---|---|---|
| .01 | 25 | 1.83 | $1.14 \times 10^{-8}$<br>$1.62 \times 10^{-8a}$ | $5.89 \times 10^{-9}$<br>$1.52 \times 10^{-9a}$ | $5.38 \times 10^{-2}$<br>$.223^a$ | $3.3 \times 10^{-4}$<br>$1.50 \times 10^{-3a}$ |
| .05 | 25 | 1.83 | $6.33 \times 10^{-8}$<br>$2.19 \times 10^{-8a}$ | $3.28 \times 10^{-9}$<br>$4.11 \times 10^{-9a}$ | .168<br>$.256^a$ | $1.31 \times 10^{-4}$<br>$2.0 \times 10^{-3a}$ |
| .10 | 25 | 2.01 | $1.90 \times 10^{-7}$<br>$4.00 \times 10^{-8a}$ | $1.08 \times 10^{-8}$<br>$1.16 \times 10^{-8a}$ | .199<br>$.200^a$ | $1.4 \times 10^{-4}$<br>$1.5 \times 10^{-4a}$ |
| .01 | 35 | 1.25 | $3.97 \times 10^{-8}$<br>$6.19 \times 10^{-9a}$ | $2.81 \times 10^{-9}$<br>$1.91 \times 10^{-8a}$ | $8.09 \times 10^{-2}$<br>$6.06 \times 10^{-2a}$ | $3.0 \times 10^{-5}$<br>$2.0 \times 10^{-5a}$ |
| .05 | 35 | .396 | $1.24 \times 10^{-7}$<br>$9.89 \times 10^{-7a}$ | $1.18 \times 10^{-8}$<br>$1.16 \times 10^{-7a}$ | .763<br>$.708^a$ | $4.2 \times 10^{-4}$<br>$3.9 \times 10^{-4a}$ |
| .10 | 35 | 2.19 | $7.78 \times 10^{-7}$<br>$4.44 \times 10^{-7a}$ | $5.03 \times 10^{-8}$<br>$4.86 \times 10^{-8a}$ | .333<br>$.647^a$ | $1.0 \times 10^{-5}$<br>$2.0 \times 10^{-5a}$ |

Table 109--Continued

| Conc. (M/l) | T (°) | $\sigma_K$ | $\sigma_{k_c}$ | $\sigma_{k_t}$ | $\sigma_{data}$ | $\sigma_S$ |
|---|---|---|---|---|---|---|
| .01 | 50 | 1.05 | $1.63 \times 10^{-7}$<br>$6.97 \times 10^{-6}$[a] | $1.08 \times 10^{-8}$<br>$9.56 \times 10^{-8}$[a] | .291<br>.288[a] | $2.7 \times 10^{-4}$<br>$2.7 \times 10^{-4}$[a] |
| .05 | 50 | 2.21 | $2.18 \times 10^{-6}$<br>$1.36 \times 10^{-6}$[a] | $1.47 \times 10^{-7}$<br>$1.34 \times 10^{-7}$[a] | 1.358<br>1.526[a] | $4.73 \times 10^{-3}$<br>$5.32 \times 10^{-3}$[a] |
| .10 | 50 | 2.30 | $4.58 \times 10^{-6}$<br>$9.33 \times 10^{7}$[a] | $3.47 \times 10^{-7}$<br>$1.00 \times 10^{-7}$[a] | 1.494<br>.700[a] | $7.87 \times 10^{-3}$<br>$3.69 \times 10^{-3}$[a] |

[a]Calculated from trans runs.

Table 110

Standard Deviations of Data for Epimerization of Dimethyl 1-methyl-1,2-cyclohexanedicarboxylate

| Conc. (M/1) | T (°) | $\sigma_K$ | $\sigma_{k_c}$ | $\sigma_{k_t}$ | $\sigma_{data}$ | $\sigma_S$ |
|---|---|---|---|---|---|---|
| .05 | 25 | 1.42 | $2.53 \times 10^{-9}$<br>$3.67 \times 10^{-9}$[a] | $1.01 \times 10^{-9}$<br>$2.064 \times 10^{-9}$[a] | $2.68 \times 10^{-2}$<br>$6.50 \times 10^{-2}$[a] | $1.0 \times 10^{-5}$<br>$2.0 \times 10^{-5}$[a] |
| .05 | 35 | .142 | $6.08 \times 10^{-9}$<br>$6.00 \times 10^{-9}$[a] | $1.99 \times 10^{-9}$<br>$4.14 \times 10^{-9}$[a] | $2.07 \times 10^{-2}$<br>$6.37 \times 10^{-2}$[a] | $1.0 \times 10^{-5}$<br>$3.0 \times 10^{-5}$[a] |
| .01 | 50 | .142 | $8.86 \times 10^{-9}$<br>$8.14 \times 10^{-9}$[a] | $4.11 \times 10^{-9}$<br>$5.00 \times 10^{-9}$[a] | $8.48 \times 10^{-2}$<br>$9.78 \times 10^{-2}$[a] | $3.0 \times 10^{-5}$<br>$4.0 \times 10^{-5}$[a] |
| .05 | 50 | .142 | $3.28 \times 10^{-8}$<br>$3.22 \times 10^{-8}$[a] | $1.00 \times 10^{-8}$<br>$2.56 \times 10^{-8}$[a] | $9.71 \times 10^{-2}$<br>.695[a] | $3.0 \times 10^{-5}$<br>$2.4 \times 10^{-4}$[a] |
| .10 | 50 | .124 | $7.22 \times 10^{-8}$<br>$3.53 \times 10^{-8}$[a] | $2.56 \times 10^{-8}$<br>$3.22 \times 10^{-8}$[a] | .220<br>.257[a] | $1.15 \times 10^{-4}$<br>$1.7 \times 10^{-4}$[a] |

[a]Calculated from trans runs.

Table 111

Standard Deviation of Data for Epimerization of Dimethyl 1,2-cyclohex-4-enedicarboxylate

| Conc. (M/1) | T (°) | $\sigma_K$ | $\sigma_{k_c}$ | $\sigma_{k_t}$ | $\sigma_{data}$ | $\sigma_S$ |
|---|---|---|---|---|---|---|
| .01 | 25 | .325 | $1.29 \times 10^{-7}$<br>$1.44 \times 10^{-8}$[a] | $4.22 \times 10^{-8}$<br>$8.17 \times 10^{-9}$[a] | .852<br>.123[a] | $5.5 \times 10^{-4}$<br>$6.0 \times 10^{-5}$[a] |
| .05 | 25 | .343 | $1.96 \times 10^{-7}$<br>$3.97 \times 10^{-8}$[a] | $4.50 \times 10^{-8}$<br>$3.67 \times 10^{-8}$[a] | .138<br>.084[a] | $2.0 \times 10^{-4}$<br>$1.5 \times 10^{-4}$[a] |
| .10 | 25 | .414 | $2.81 \times 10^{-7}$<br>$1.39 \times 10^{-7}$[a] | $6.75 \times 10^{-8}$<br>$4.83 \times 10^{-8}$[a] | 1.012<br>.748[a] | $1.0 \times 10^{-5}$<br>$1.0 \times 10^{-5}$[a] |
| .05 | 35 | .288 | $3.97 \times 10^{-7}$<br>$3.69 \times 10^{-7}$[a] | $9.72 \times 10^{-8}$<br>$3.69 \times 10^{-7}$[a] | .640<br>.948[a] | $1.0 \times 10^{-5}$<br>$2.0 \times 10^{-5}$[a] |
| .05 | 50 | .324 | $2.27 \times 10^{-6}$<br>$2.42 \times 10^{-6}$[a] | $6.25 \times 10^{-7}$<br>$9.58 \times 10^{-7}$[a] | .563<br>.945[a] | $1.10 \times 10^{-4}$<br>$1.9 \times 10^{-4}$[a] |

[a]Calculated from trans runs.

Table 112

Standard Deviation of Data for Epimerization of Dimethyl 1-methyl-1,2-cyclohex-4-enedicarboxylate

| Conc. (M/1) | T (°) | $\sigma_K$ | $\sigma_{k_c}$ | $\sigma_{k_t}$ | $\sigma_{data}$ | $\sigma_S$ |
|---|---|---|---|---|---|---|
| .05 | 25 | 1.87 | $9.56 \times 10^{-9}$<br>$3.17 \times 10^{-9}$[a] | $3.36 \times 10^{-9}$<br>$4.83 \times 10^{-9}$[a] | $4.37 \times 10^{-2}$<br>$2.57 \times 10^{-3}$[a] | $1.0 \times 10^{-5}$<br>$1.0 \times 10^{-5}$[a] |
| .05 | 35 | 1.87 | $3.00 \times 10^{-8}$<br>$1.60 \times 10^{-8}$[a] | $1.89 \times 10^{-8}$<br>$2.56 \times 10^{-8}$[a] | .187<br>.220[a] | $7.0 \times 10^{-5}$<br>$1.5 \times 10^{-4}$[a] |
| .01 | 50 | 1.54 | $2.27 \times 10^{-8}$<br>$2.43 \times 10^{-8}$[a] | $8.50 \times 10^{-9}$<br>$1.97 \times 10^{-8}$[a] | .126<br>.309[a] | $5.0 \times 10^{-5}$<br>$1.3 \times 10^{-4}$[a] |
| .05 | 50 | .154 | $1.26 \times 10^{-7}$<br>$5.11 \times 10^{-8}$[a] | $5.72 \times 10^{-8}$<br>$4.28 \times 10^{-8}$[a] | .467<br>.333[a] | $4.7 \times 10^{-4}$<br>$3.40 \times 10^{-4}$ |
| .10 | 50 | .136 | $3.06 \times 10^{-7}$<br>$1.07 \times 10^{-7}$[a] | $1.70 \times 10^{-7}$<br>$8.81 \times 10^{-8}$[a] | 1.434<br>.591[a] | $1.46 \times 10^{-3}$<br>$6.0 \times 10^{-4}$[a] |

[a]Calculated from trans runs.

Table 113

Standard Deviations of Data for Epimerization of Dimethyl 1,2-cycloheptanedicarboxylate

| Conc. (M/l) | T (°) | $\sigma_K$ | $\sigma_{k_c}$ | $\sigma_{k_t}$ | $\sigma_{data}$ | $\sigma_S$ |
|---|---|---|---|---|---|---|
| .01 | 25 | .679 | $1.65 \times 10^{-7}$<br>$1.14 \times 10^{-7}$[a] | $2.75 \times 10^{-8}$<br>$3.89 \times 10^{-8}$[a] | .194<br>.559[a] | $1.7 \times 10^{-4}$<br>$5.1 \times 10^{-4}$[a] |
| .05 | 25 | .522 | $5.92 \times 10^{-7}$<br>$3.11 \times 10^{-7}$[a] | $1.11 \times 10^{-7}$<br>$1.08 \times 10^{-7}$[a] | .510<br>.629[a] | $1.14 \times 10^{-3}$<br>$1.40 \times 10^{-3}$[a] |
| .10 | 25 | .629 | $1.97 \times 10^{-6}$<br>$2.09 \times 10^{-6}$[a] | $4.25 \times 10^{-7}$<br>$2.09 \times 10^{-6}$[a] | 1.015<br>$8.35 \times 10^{-2}$[a] | $6.86 \times 10^{-3}$<br>$6.0 \times 10^{-4}$[a] |
| .05 | 35 | .792 | $2.53 \times 10^{-6}$<br>$2.23 \times 10^{-6}$[a] | $3.72 \times 10^{-7}$<br>$5.39 \times 10^{-7}$[a] | .415<br>1.475[a] | $2.76 \times 10^{-3}$<br>$9.81 \times 10^{-3}$[a] |
| .05 | 50 | .278 | $6.14 \times 10^{-6}$<br>$4.42 \times 10^{-6}$[a] | $1.33 \times 10^{-6}$<br>$1.36 \times 10^{-6}$[a] | .787<br>.762[a] | $2.04 \times 10^{-2}$<br>$1.98 \times 10^{-2}$[a] |

[a]Calculated from trans runs.

The free energy of each reaction was calculated by the relation,

$$\Delta F^\circ = - RT \ln K$$

These values accompanied by their estimated errors are listed in Table 114. The errors were calculated by the relation:

$$\Delta(\Delta F^\circ) = - RT\Delta K/ K$$

This relation incorporates the assumption that all errors are in the values of the equilibrium constant.

Table 114

Free Energy Values for Epimerization of cis- and trans-1,2-cycloalkanedicarboxylates at 50°C.

| Ester | K (t/c) | $\Delta F^\circ$ (kcal/mole) | $\Delta(\Delta F^\circ)$ | log K |
|---|---|---|---|---|
| Dimethyl 1,2-cyclopropane-dicarboxylate | 99.0 ± 5.0 | -2.62 | ± 0.03 | 1.996 |
| Dimethyl 1,2-cyclobutane-dicarboxylate | 8.58 ± .73 | -1.27 | ± 0.06 | 0.934 |
| Dimethyl 1,2-cyclopentane-dicarboxylate | 6.08 ± .58 | -1.06 | ± 0.07 | 1.784 |
| Dimethyl 1,2-cyclohexane-dicarboxylate | 11.7 ± 2.2 | -1.45 | ± 0.12 | 1.069 |
| Dimethyl 1-methyl-1,2-cyclo-hexanedicarboxylate | 1.84 ± .14 | -0.36 | ± 0.05 | 0.265 |
| Dimethyl 1,2-cyclohex-4-enedicarboxylate | 2.82 ± .32 | -0.61 | ± 0.07 | 0.450 |
| Dimethyl 1-methyl-1,2-cyclo-hex-4-enedicarboxylate | 3.90 ± .28 | -0.80 | ± 0.05 | 0.591 |
| Dimethyl 1,2-cycloheptane-dicarboxylate | 3.99 ± .27 | -0.82 | ± 0.06 | 0.602 |

The energy of activation, Ea, is calculated by the relation,

$$\frac{d \ln k}{d (1/T)} = -E_a/R$$

The slope of the line from a plot of ln k versus 1/T is $-E_a/R$. The activation energy can be calculated from the relation

$$E_a = - (\text{slope}) R.$$

The values for the slope were calculated with a least squares treatment. Several plots of this type are shown in Figure 33.

The standard deviation of the slope was calculated from the equations used previously for the calculation of standard deviations of rate constants. The values of the activation energies and their standard deviations are given in the following table, Table 115.

The enthalpy, $\Delta H^{\pm}$, free energy, $\Delta F^{\pm}$, and the entropy $\Delta S^{\pm}$, of activation were calculated by the following relations,

$$\Delta H^{\pm} = E_a - RT$$

$$\Delta F^{\pm} = RT \ln k_r + RT \ln (h/ k T)$$

and

$$\Delta S^{\pm} = (\Delta H^{\pm} - \Delta F^{\pm}) / T$$

where h is Plancks constant, ($6.6 \times 10^{-27}$ erg-seconds), and k is Boltzmann's constant ($1.38 \times 10^{-16}$ erg $deg^{-1}$ $molecule^{-1}$). These values are listed in Table 116.

Table 115

Activation Energy and Standard Deviation of Activation Energy for Epimerization of 1,2-Cycloalkanedicarboxylates.

| Ester | $E_a$ (kcal/mole) | $\sigma_{E_a}$ |
|---|---|---|
| Dimethyl 1,2-cyclopropane-dicarboxylate | 20.8 | ± .2 |
| Dimethyl 1,2-cyclobutane-dicarboxylate | 19.2 | ± .2 |
| Dimethyl 1,2-cyclopentane-dicarboxylate | 19.9 | ± .3 |
| Dimethyl 1,2-cyclohexane-dicarboxylate | 22.2 | ± .3 |
| Dimethyl 1-methyl-1,2-cyclohexane-dicarboxylate | 20.7 | ± .2 |
| Dimethyl 1,2-cyclohex-4-enedi-carboxylate | 19.8 | ± .2 |
| Dimethyl 1-methyl-1,2-cyclohex-4-enedicarboxylate | 24.2 | ± .2 |
| Dimethyl 1,2-cycloheptane-dicarboxylate | 20.3 | ± .2 |

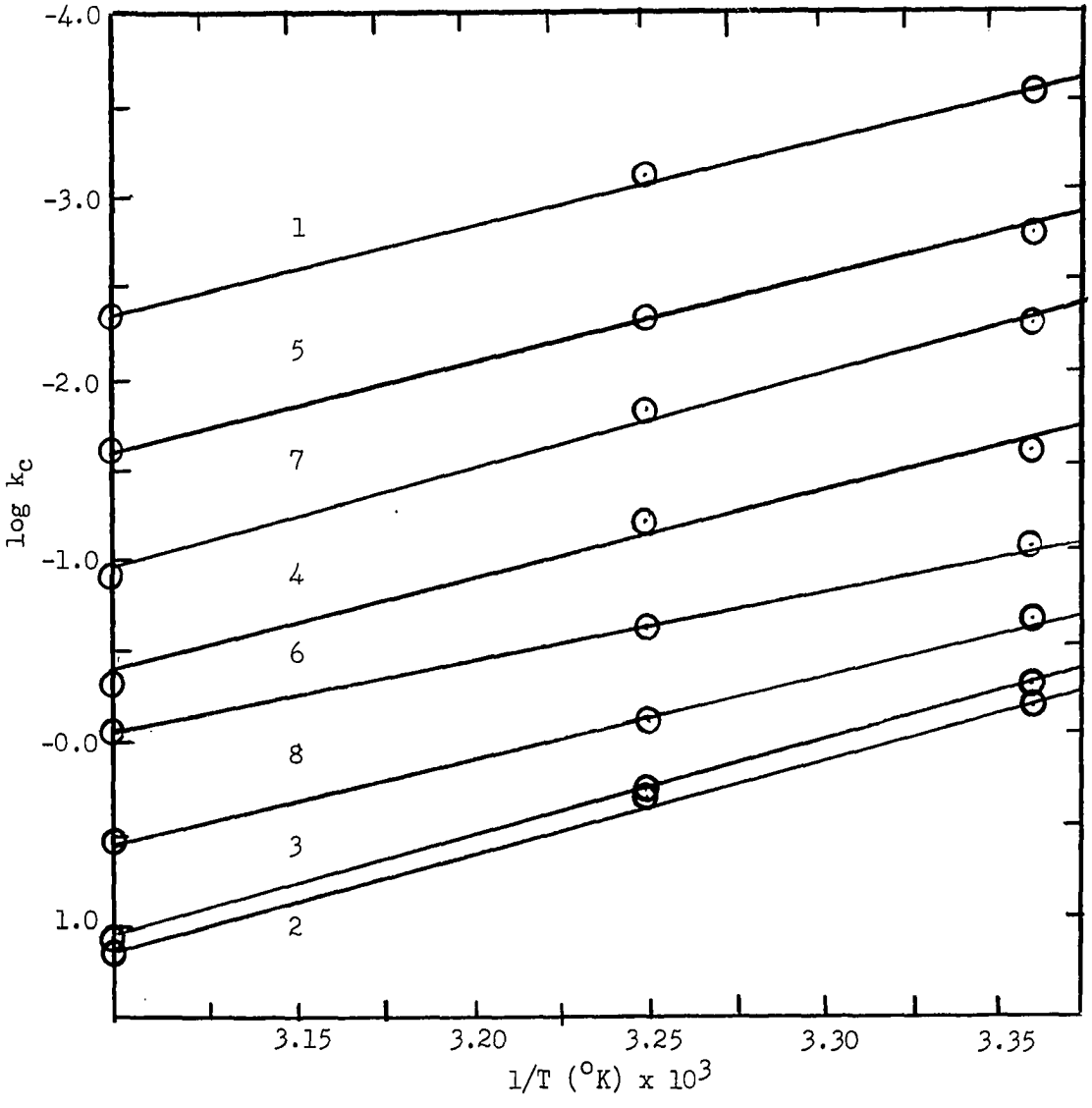
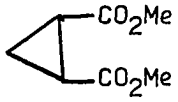
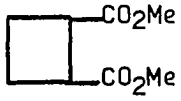
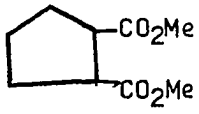
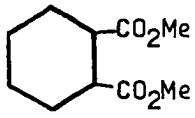
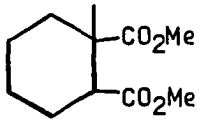
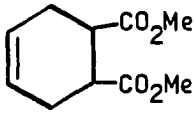
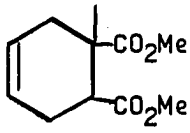
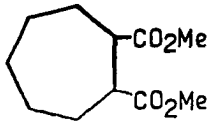



Figure 33: Plot of log $k_c$ versus (1/T) for:

1. Dimethyl 1,2-cyclopropanedicarboxylate
2. Dimethyl 1,2-cyclobutanedicarboxylate
3. Dimethyl 1,2-cyclopentanedicarboxylate
4. Dimethyl 1,2-cyclohexanedicarboxylate
5. Dimethyl 1-methyl-1,2-cyclohexanedicarboxylate
6. Dimethyl 1,2-cyclohex-4-enedicarboxylate
7. Dimethyl 1-methyl-1,2-cyclohex-4-enedicarboxylate
8. Dimethyl 1,2-cycloheptanedicarboxylate

Table 116

Enthalpy ($\Delta H^{\pm}$), Free Energy ($\Delta F^{\pm}$) and Entropy ($\Delta S^{\pm}$) of Activation for Epimerization of 1,2-Cycloalkanedicarboxylates

| Ester | $\Delta H^{\pm}$ (kcal/mole) | $\Delta(\Delta H^{\pm})$ | $\Delta F^{\pm}$ (kcal/mole) | $\Delta(\Delta F^{\pm})$ | $\Delta S^{\pm}$ (e.u.) | $\Delta(\Delta S^{\pm})$ |
|---|---|---|---|---|---|---|
|  | 20.2 | ± .2 | 27.1 | ± .1 | -23. | ± 1 |
|  | 18.7 | ± .2 | 22.7 | ± .1 | -10. | ± 1 |
|  | 19.4 | ± .3 | 22.5 | ± .1 | -10. | ± 1 |
|  | 21.7 | ± .3 | 28.6 | ± .1 | -23. | ± 1 |
|  | 20.2 | ± .2 | 26.0 | ± .1 | -20. | ± 1 |
|  | 19.3 | ± .2 | 23.7 | ± .1 | -15. | ± 1 |
|  | 23.7 | ± .2 | 25.4 | ± .1 | - 6. | ± 1 |
|  | 19.8 | ± .2 | 23.1 | ± .1 | -11. | ± 1 |

The errors in $\Delta H^{\pm}$, $\Delta F^{\pm}$, and $\Delta S^{\pm}$ are estimated by the following equations:

$$\Delta(\Delta F^{\pm}) = -(RT / k_r)\Delta k_r$$

$$\Delta(\Delta S^{\pm}) = \frac{\Delta(\Delta H^{\pm})}{T} \quad \frac{\Delta(\Delta F^{\pm})}{T}$$

The maximum error $\Delta(\Delta H^{\pm})$ in $\Delta H^{\pm}$ is assumed to be approximately the standard deviation of $E_a$.

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## APPENDIX

Most of the calculations described in the "Treatment of Data and Results" section were made with a Fortran II computer language program, which was executed on an IBM 1410 computer. This program calculates the least squares slope, the rate constants and their associated errors, as well as a statistical analysis of the equilibrium constant values. The data necessary for operation of the program are: the relative percentages of the cis and trans esters, the estimated error of the relative percentages, the elapsed times, the number of points to be calculated, the average equilibrium constant, the number of values of the equilibrium constant to be considered in the statistical treatment, and the values of the equilibrium constants.

### Program

```
    DIMENSION A(25), B(25), X(25), Y(25), DY(25), W(25), WW(25),
   1XKEQ(50),DDELA(25),DDELB(25)
  1 READ 100,N,JJB,CI,EQK,P,XBAR
100 FORMAT (213,4F10.5)
  2 PRINT 102
102 FORMAT (//,12H N JJB      CI,6X,4H EQK,7X,2H P,6X,5H XBAR)
    PRINT 103, N, JJB, CI, EQK,P, XBAR
103 FORMAT (1X,I2,1X,I2,4F10.5)
```

```
      IF (N)200,200,559
  559 CONTINUE
      SY=0.0
      SX=0.0
      XY=0.0
      XX=0.0
      SUMW=0.0
      READ 600,(XKEQ(I),I=1,JJB)
  600 FORMAT (8F10.2)
      DO 3 I=1,N
      READ 101,A(I),B(I),X(I)
      IF (97.0-A(I))314,313,313
  314 DDELA(I)=CI*0.01*P/97.0
      GO TO 315

  313 CONTINUE
      DDELA(I)=CI*0.01*P/A(I)
  316 CONTINUE
      IF (B(I)-3.0)317,316,316
  317 DDELB(I)=CI*0.01*P/3.0
      GO TO 318
  316 CONTINUE
      DDELB(I)=CI*0.01*P/B(I)
  318 CONTINUE
      A(I)=A(I)*CI*0.01
      B(I)=B(I)*CI*0.01
```

```
      Y(I)=LOG(ABS(A)*EQK-B(I)))
      SY=SY+Y(I)
      SX=SX+X(I)
      XX=XX+X(I)*X(I)
      XY=XY+X(I)*Y(I)
      IF(A(I)*EQK-B(I))401,402,401
  401 DY(I)=(EQK*DDELA(I)-DDELB(I))/(A(I)*EQK-B(I))
      W(I)=1.0/ABS(DY (I))
      SUMW=SUMW+W(I)
  101 FORMAT (2F10.5,F10.2)
      IF(A(I)*EQK-B(I))405,502,405
  402 DY(I)=.9999E30
  405 PRINT 104,I,I,I,I,I
  104 FORMAT (//,4X,3H A(,I2,2H ),5X,3H B(,I2,2H ),4X,3H X(,I2,2H),
     1 8X,3H Y(,I2,2H ),10X,4H DY(,I2,2H ))
      PRINT 105, A(I),B(I), X(I), Y(I), DY(I)
  105 FORMAT (//,2F10.5,F10.2,2(6X,E14.8))
    3 CONTINUE
      Z=SX*SX
      EN=N
      IF(EN*XX-Z)407,408,407
  407 S=(EN*XY-SX*SY)/(EN*XX-Z)
      YINT=(XX*SY-SX*XY)/(EN*XX-Z)
      PRINT 106,S,YINT
  106 FORMAT (///,3X,3H S=,E14.8/6H YINT=,E14.8)
  408 CONTINUE
```

```
409 C=1.0/SUMW
    WWXY=0.0
    WWX=0.0
    WWY=0.0
    WWXX=0.0
  4 DO 5 I=1,N
411 CONTINUE
    WW(I)=W(I)*C
    WWXY=X(I)*Y(I)*WW(I)+WWXY
    WWX=X(I)*WW(I)+WWX
    WWY=Y(I)*WW(I)+WWY
    WWXX=WW(I)*X(I)*X(I)+WWXX
  5 CONTINUE
    PRINT 108
108 FORMAT (///,6H WW(I))
    PRINT 109,(WW(I),I=1,N)
109 FORMAT (//,7E15.8)
    ZZ=WWX*WWX
    IF(WWXX-ZZ)412,200,412
412 CONTINUE
    SW= (WWXY-WWX*WWY)/(WWXX-ZZ)
    YINTW=(WWY*WWXX-WWXY*WWX)/(WWXX-ZZ)
    PRINT 110, SW, YINTW
110 FORMAT (///,3X,4H SW=,E14.8/7H YINTW=,E14.8,///)
    BIRD=0.0
  6 DO 7 I=1,N
```

```
      SXKEQ=0.0
    7 CONTINUE
    8 DO9 I=1,JJB
      BIRD=BIRD+(XKEQ(I)-XBAR)*(XKEQ(I)-XBAR)
      SXKEQ=SXKEQ+XKEQ(I)
    9 CONTINUE
      XJJB=JJB
      IF (XJJB-1.0) 150,151,150
  151 CONTINUE
      EQKVAR=0.0
      GO TO 153
  150 CONTINUE
      EQKVAR=(1.0/(XJJB-1.0))*BIRD
  153 CONTINUE
      IF(EQKVAR)503,504,503
  504 READ 505,EQKVAR
  505 FORMAT(F10.5)
  503 CONTINUE
      EQKSD=SQRT(EQKVAR)
      AVKEQ= SXKEQ/XJJB
      RK2=-SW/(1.0+AVKEQ)
      RK1=RK2*AVKEQ
      FINK=0.0
      PRINT 111,EQKVAR,EQKSD,AVKEQ,RK2,RK1
  111 FORMAT (1X,8H EQKVAR=,E14.8,2X,7H EQKSD=,E14.8,2X,7H AVKEQ=,
     1 E14.8/1X,5H RK2=,E14.8,10X,5H RK1=,E14.8)
```

```
 10 DO 11 I=1,N
    FINK =FINK+(SW*X(I)+YINTW-Y(I)*(SW*X(I)YINTW-Y(I))
 11 CINTINUE
    DVAR+(1.0/EN)*FINK
    DSD=SQRT(DVAR)
    YVAR=DVAR*XX/(EN*XX-Z)
    SVAR=EN*DVAR/(EN*XX-Z)
    SSD=SQRT (SVAR)
    YSD=SQRT(YVAR)
    RK2VAR=RK2*(SVAR/(SW*SW)+EQKVAR/(( 1.0+AVKEQ)*(1.0+AVKEQ)))*RK2
    RK1VAR=RK1*((EQKVAR*RK2*RK2VAR*AVKEQ*AVKEQ)/(AVKEQ*AVKEQ*RK2*R
   1K2))*RK1
    RK2SD= SQRT(RK2VAR)
    RK1SD=SQRT(RK1VAR)
    PRINT 112, DSD, YSD, SSD, RK2SD, RK1SD
112 FORMAT (1X,5H DSD=,F10.5,2X,5H YSD=,F10.5,2X,5H SSD=,F10.5/
   11X,7H RK2SD=,F10.8,2X,7H RK1SD=,F10.8)
    IF(N)200,200,1
200 STOP
```

# A STUDY OF THE PHYTOCHEMISTRY OF THE GENUS *CNIDOSCOLUS*

## CHAPTER I

## INTRODUCTION

The genus *Cnidoscolus* has long been known as a group of undesirable range plants. In the Southeast area of the United States the principal species is *Cnidoscolus stimulosus* (Michx.) Gray; in the Southcentral area *Cnidoscolus texanus* (Muell. Arg.) Small; and in the Southwest area *Cnidoscolus angustidens* Torr. Other closely related species are found in the Southwest and south into tropical America.

These species are much branched stout-stemmed plants having large leaves, and are noticeably covered with large clusters of fragrant, waxy, white flowers. The plants are all called stinging nettles or bull nettles, (not to be confused with certain members of the *Solanaceae*, namely *Solanum rostratum* and *Solanum carolinense*.) *Cnidoscolus angustidens* is commonly known as the *mala mujer*, the bad woman. Schultz considers *Cnidoscolus texanus* to be the best naturally protected plant except for the cacti.[1]

Small describes *Cnidoscolus stimulosus* (*Bivonea stimulosa* (Michx.) Raf.) as follows:

> Plant 1-12 dm tall; leaf blades 8-30cm broad, coarsely or finely lobed; staminate calyx with a cylindrical tube, and lobes about equal in length; capsule 10-16 cm (mm?) long, bristly. Dry woods, sandy hammocks, pinelands, and sand-dunes, coastal plain and adjacent provinces, Florida to Texas and Virginia.[2]

More recent reports indicate that Cnidoscolus stimulosus has not been collected west of the Mississippi River.[3,4]

Cnidoscolus texanus is described by Shinners as follows:[6]

> Perennial up to 80 cm tall from a deep, branching root forming loose patches. Stems densely and leaves more sparsely hispid with pale stinging hairs. Leaves alternate, long petioled; blades cordate, palmately deeply lobed, the lobes corsely toothed or again lobed, stipules inconspicuous narrow toothed. Flowers in terminal, determinate corymbs slightly shorter to slightly longer than the leaves. Perianth large, white, showy, sweet-scented, with subcylindrical tube slightly longer than the 4-5 subrotate lobes. Sandy open woods, fields, and roadsides; common, locally abundant. April to July, less freely to September.

Hopkins[5] describes the range of Cnidoscolus texanus as Texas, Arkansas and Oklahoma.

Cnidoscolus angustidens is described by Kearney and Peebles in the following manner:[7]

> Perennial herb; leaves long-petioled, the lobes attenuate and slenderly toothed; stipules thin, lacerate; cymes terminal on the stems and branches; staminate calyx white, petaloid, 5-lobed, the stamens 10, the staminoda 3, filiform, the filiments united into a column with a ring of hairs at base, the anthers in whorls of 5, the glands united with the androphore just beneath the ring of hairs; pistillate calyx white, petaloid, 5-merous, the sepals distinct, caducous, the ovary 3-celled, the ovules solitary, the styles three, connate below, twice bifid above; seeds large carunculate. Cochise, Santa Cruz and Pima counties, Arizona, 2300 to 4000 feet, rocky slopes.

Hopkins compares Cnidoscolus stimulosus and texanus in the following way:

> Cnidoscolus texanus has larger flowers, a more heavily armed staminate calyx, and more numerous spines on the stems and leaves,

Cnidoscolus stimulosus has smaller flowers, more nearly glabrate staminate calyx, and fewer spines on the leaves and stems.

Several other members of the genus Cnidoscolus are recognized in Mexico and Central and South America.

The brazilian stinging nut (Cnidoscolus neglectus Pohl.), because of its stinging hairs is one of the most poisonous plants known.[8,9]

The closely related species Cnidoscolus urens is also very poisonous. This plant is listed by Blohm as a common poisonous plant in Venezuela,[10] and is described by Lutz as being common in Panama.[11]

The distinction between the genera Cnidoscolus and Jatropha was poorly defined until, in 1944, McVaugh suggested the currently accepted separation.[12] Jatropha is a genus containing many tropical plants; e.g., sweet and bitter cassava (the source of tapioca), and the Cuban Physic nut, Jatropha curcas, commonly used as a purgative in tropical America.

No medical uses of Cnidoscolus texanus are reported in the literature but Cnidoscolus stimulosus is reported to have been used by natives of central and South America for some time in the treatment of paralysis, rheumatism, and various other ailments.[13] Standley reports that the thick fleshy roots were employed locally for the treatment of venereal and other diseases.[14] However, no mention is made of the effectiveness of such treatment. There is some question as to the exact identity of the plant of Standley's[14] and Roig y Mesa's[13] studies. It is likely that the plant to which they refer is presently known as Cnidoscolus urens.

## Hairs

The stems and leaves of the bull nettle are covered with stinging hairs. The hairs (of Cnidoscolus urens) show the same structure as those of the common nettle. The poison is produced by a cell of the epidermis, which swells during growth, forming a goblet-shaped bulb set into the surrounding tissue. The hair is a long tube, the walls of which have incrustations of silicic acid in the upper part and are calcified in the lower parts so that they are very brittle and break at the lightest touch. Near the top of the cell is a slight expansion with very thin walls which, when touched, breaks in an oblique direction, forming the point of a cannula, which enters the skin. At the same time the poisonous liquid is discharged into the wound. When in contact with the skin these hairs produce a lasting and painful irritation. In immunological tests all persons tested show sensitivity to the hairs of Cnidoscolus texanus.[15]

The reaction of at least one individual to the hairs of Cnidoscolus urens (Jatropha urens), is described by Lutz:[11]

> . . . the writer became acquainted with Jatropha urens by unavoidable contact with a single specimen of the plant. All at once he felt an intense burning on the left hand, where about 10 of the stinging hairs had entered pretty deep into the skin. The inflammation produced by this touch was very similar to that produced by nettles, but the pain soon increased, the whole hand began to swell and inside of half an hour had assumed a monstrous shape. Then the arm commenced to swell also, the right hand and arm, without having been inoculated, yet showed the same abnormal symptoms, and a very strong itching sensation was felt all over the upper part of the body. At about the same time parts of the face, around the eyes and nose, swelled considerably. The itching sensation rapidly spread over the abdomen and the lower extremities and red pimples appeared everywhere. In less than an hour the poison had extended over the whole surface of the body, and its

> entrance into the blood current was indicated by the corresponding physiological reaction of the interior organs. The palpitation of the heart became extremely accelerated and the mind was soon overcome by an agonizing depression. The respiration seemed to be delayed as if under a great pressure, cold sweat broke out, and the patient gave way altogether, remaining unconscious for more than an hour, except for feverish dreams. After coming back to his senses, he had several fits of copious vomiting, from which it may be surmised that the poison was slowly eliminated from the organism. The weakness, however, remained for several days.
>
> A case of such extreme effects . . . has never been recorded, as far as the literature on the subject shows. Undoubtedly the intensity of the intoxication was due to the rather strong contact with the plant, which caused a considerable amount of poison to be introduced into the blood circulation.

The toxic principle of the hairs in many true nettles are acetylcholine and histamine, and a third substance apparently of lesser physiological activity is thought to be present.[16] It has been suggested that the toxic principle of Cnidoscolus texanus hairs is formic acid, but this seems untenable in the face of available evidence.

By analogy to true nettles the toxic principles are most likely to be acetylcholine and histamine.

## Seeds

The seed of the bull nettle (often referred to as a nut) is edible and may have some possibility as a source of edible oils.[17,18] It is enclosed in a hull which upon ripening dehisces explosively, throwing seeds several feet. The hull is covered with stinging hairs.

Analysis of the protein fraction of the seed indicates that it contains a large amount of histidine.[18]

Cnidoscolus phyllacanthus seeds contain a protein fraction (35-37%) which contains two unidentified amino acids.[19]

The seeds of many Euphorbiaceae are poisonous. In at least two examples of this toxicity it is because of a toxic protein. The seeds of Ricinus communis, the Castor bean, contain the phytotoxin ricin. Pure ricin is one of the most toxic compounds known.[20] The seed of the bull nettle so closely resembles the Castor bean in physical appearance that it is difficult to distinguish the two.

The seeds of Jatropha curcas contain the toxic protein curcin. This principle has similar effects to those of ricin, but they are somewhat milder. This protein is rendered nontoxic by roasting.[20]

Toxins of this type must be absent from the seeds of Cnidoscolus as they are edible and nonpoisonous.

The composition of the fatty acid components of oils from selected Euphorbiaceae species are listed in Table 1.[21,22]

Euphorbiaceae seed oils are listed as members of Group II by Hilditch (Oleic, linoleic, linolenic acids as main constituents).

The seed oils of many of the Euphorbiaceae are used as cathartics. The oil of the genus Croton is a powerful purgative. Only a few drops of the pure oil are lethal to animals.[23] The oil of Jatropha curcas is intermediate in purgative effect, lying between that of Croton oil and Castor oil.[20]

Analyses of the seed oils of Cnidoscolus texanus have been performed by Menaul[18] and by Cushing and Cirino.[17] Menaul's materials were collected in Oklahoma, and Cushing's material in Texas. As Cnidoscolus stimulosus is restricted to an area east of the Mississippi, it is apparent they both worked with Cnidoscolus texanus.

Table 1

The Percentage Composition of the Oils of Selected *Euphorbiaceae*

| Acid | Castor Oil (*Ricinus communis*) | *Cephalocroton cordofanus* | Tung Oil (*Aleurites cordata*) | Conophor Oil (*Tetracarpidium conophorum*) | Physic Nut Oil (*Jatropha curcas*) | Croton Oil (*Croton tiglium*) |
|---|---|---|---|---|---|---|
| Myristic | --- | --- | --- | --- | 0.1 | 11.3 |
| Palmitic | --- | 3.9 | --- | 4.0 | 11.9 | 1.3 |
| Stearic | 0.3 | 2.8 | 7.0 (Palm.-stearic) | 3.0 | 5.1 | 0.5 |
| Oleic | 8.0 | 9.8 | --- | 13.0 | 63.4 | 56.0 |
| Linoleic | 3.6 | 17.1 | 19 | 17.0 | 18.8 | 29.0 |
| Linolenic | --- | --- | --- | 63.0 | --- | --- |
| Arachidic | --- | 0.7 | --- | --- | 0.4 | 2.3 |
| Ricinoleic (D(+)-12-hydroxy-octadec-*cis*-9-enoic acid) | 87.8 | --- | --- | --- | --- | --- |
| Dihydroxyoleic | --- | 3.7 | --- | --- | --- | --- |
| α-Elaeosteric(*cis*-9-*trans*-11-*trans*-13-trienoic acid) | --- | --- | 74.0 | --- | --- | traces of lower unsaturated acids |
| Vernolic (*cis*-12, 13-epoxyoctadec-*cis*-9-enoic acid) | --- | 62.0 | --- | --- | --- | --- |

Cushing and Cirino found the pentane extracted oil contained 82.8% unsaturated and 12.4% saturated acids. These values were determined by a spectrophotometric method.

## Roots

The root of Cnidoscolus texanus is about five inches in diameter and often penetrates the soil to a depth of five feet. Those of Cnidoscolus stimulosus and angustidens are somewhat smaller. These roots are similar to those of cassava in appearance. The roots of Cnidoscolus texanus have been studied by Rouse.[4] They are succulent (80.2% water) and contain large amounts of carbohydrates which consist largely of glucose, fructose and starch.

There has been only one previous report of the toxicity of Cnidoscolus species (excepting the toxicity of the stinging hairs); Cnidoscolus angustidens is reported by Pammel to contain a cyanogenetic compound.[8]

The roots of several other Euphorbiaceae are toxic. The roots of Jatropha manihot, cassava, contain a cyanogenetic glycoside and an enzyme capable of liberating hydrocyanic acid.[10] (Most authorities now place this plant in a separate genus. A more correct scientific name is Manihot esculenta Crantz.) The concentration of the poisonous principle ranges from 0.03-0.001% by weight,[24] and varies greatly with environmental conditions. The concentration of the glycoside is not the same in all parts of the plant, the peeling of the root containing about 60% of the compound.[25] The roots become edible if the sap is expressed, indicating the toxic principle is contained therein. If the roots are roasted the toxic compound is inactivated.[26]

The toxic principle of cassava has been identified as acetone cyanohydrin-beta-glucoside.[27] This compound is found in the seeds of Hevea braziliensis (the source of natural rubber), another of the Euphorbiaceae.[31] The Castor bean has been reported as a cyanophoric species, however, the structure of the cyanogenetic principle has not been elucidated.[8]

## Systematic Investigation of the Genus Cnidoscolus

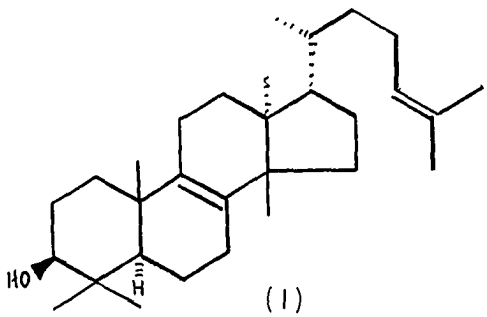
Little systematic investigation of the constituents of the non-toxic compounds of the plants of the Euphorbiaceae has been made. The resins of several species have been investigated and found to contain triterpenoid materials. Euphol (1) was first isolated by Newbold and Spring from euphorbia resin (Euphorbia resinifera).[28] Since that time it has been isolated from other Euphorbia species. The structure determination of euphol is discussed by de Mayo and Fieser.[29,30]

Haines and Warren isolated another triterpenoid, tirucallol (2) from the resin of Euphorbia tirucalli. Tirucallol was established to be identical in structure to euphol except that it is the $C_{20}$ epimer.[32]

Euphorbol (3), with 31 carbon atoms, was also isolated from the resin of Euphorbia resinifera. The structure was shown to differ from tirucallol only in the $C_{24}$ position.[33,34]

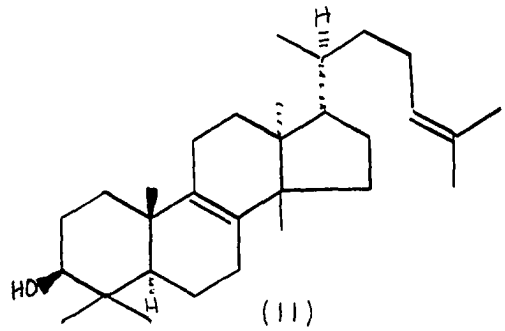
A triterpenoid compound which contains a cyclopropane ring, cycloartenol (4) has been found in Euphorbia handiensis.[35,36]

Phyllanthol (5) which also contains a cyclopropane ring has been isolated from Phyllanthus engleri resin. This compound is hexacyclic and a member of the alpha-amyrin group of triterpenoids.[29] It is the only member of the alpha-amyrins known to contain a cyclopropane



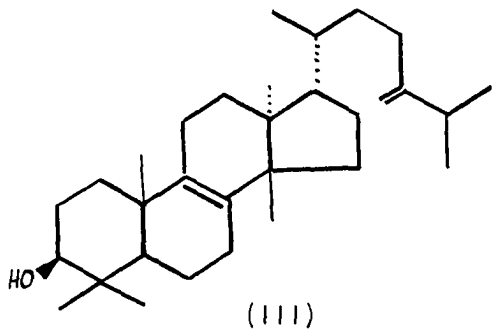

(I)

Euphol



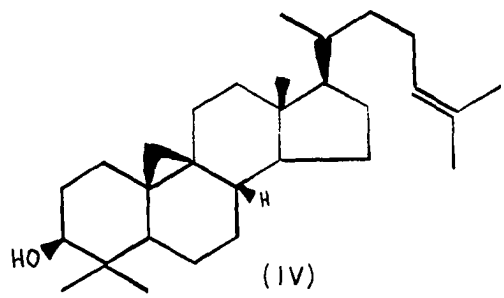

(II)

Tirucallol



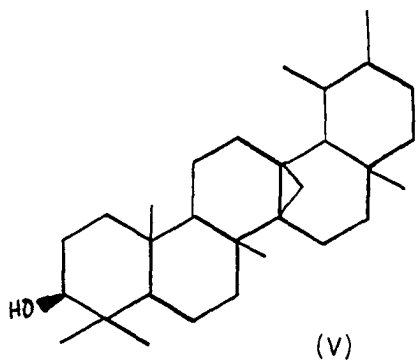

(III)

Euphorbol




(IV)

Cycloartenol



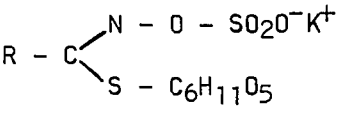

(V)

Phyllanthol

ring. The final structure was established by Barton, Page, and Warnhoff.[37]

The flower wax of many species consists almost entirely of n-alkanes. The surface waxes of many plants are also largely alkanes, for example commercial "Candelilla" wax which is derived from Pedilanthus paronis (Euphorbiaceae), consists of over 50% alkane fractions. The waxes of several species of Euphorbia have been studied by Englinton, but the species studied showed little similarity.[38] Various combinations of odd numbered carbon chains were observed ranging from $C_{25}$ to $C_{33}$.

Thioglucosides have been observed in the latexes of Putranjiva ruxburghii and Jatropha multifida.[39,40] Glucotropaeolin (1) was reported by Freise, although Kjaer questions the identification of this compound. Kjaer and Friis found Putranjiva roxburghii contained glucoputranjivin (2), glucocochlearin (3), glucojiaputin (4) and glucocleomin (5).



(1) R = $\phi$ $-CH_2-$ benzyl

(2) R = $CH_3-\underset{|}{CH}-CH_3$ 2-propyl

(3) R = $CH_3-CH_2-\underset{|}{CH}-CH_3$ 2-butyl

(4) R = $CH_3-CH_2-\underset{|}{\underset{CH_3}{CH}}-CH_2-$ 2-methylbutyl

(5) R = $(CH_3CH_2)(CH_3)C(OH)-CH_2-$ 2-methyl-2-hydroxybutyl

Kjaer states unpublished evidence from his laboratory indicates the occurrence of thioglucosides in the Euphorbiaceae is very sporadic.

## CHAPTER II

## DISCUSSION

Virtually all species of the family Euphorbiaceae are poisonous. The toxic principles vary in structure, and few have been completely characterized. The genus Cnidoscolus is unusual as it contains two separate systems of toxic principles, that of the stinging hairs and a cyanogenetic glycoside.

The seeds of the genus Cnidoscolus, in contrast to those of other related genera, are edible and contain an oil similar to linseed oil in composition.

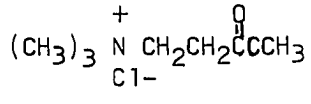
The phytochemical study of the genus Cnidoscolus described here was undertaken to determine the structure of the toxic principles of Cnidoscolus texanus, stimulosus, and angustidens, and to characterize any terpenoid and alkaloid materials encountered.

The presence of a cyanogenetic glycoside in Cnidoxcolus texanus was first suspected because of the strong odor of hydrocyanic acid from freshly procured roots. Its presence was confirmed by a color test with picrate impregnated paper.[20]

Alkaloids have been reported in Jatropha gossipifolia L. var. elegans Muell. The alkaloid jatrophine occurs in small quantities (0.04% of the dry weight.)[41] The absence of alkaloids in Cnidoscolus

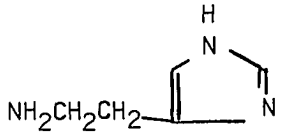
texanus leaf and stem material was established by a series of screening tests.[42,43]

The toxic principles of Urtica (true nettles) species are acetylcholine and histamine, and a third (unidentified) substance of lesser activity.[16] The physiological actions of Urtica and Cnidoscolus species are similar, and by analogy the toxic principles are probably acetylcholine and histimine.



(I)

Acetylcholine Chloride



(II)

Histamine

The toxic principles of the hairs are not removed by steeping overnight in water, but are removed by a prior pentane treatment followed by aqueous extraction. The activity is reduced by extraction with methanol, but is not reduced by pentane or ether extraction.

The presence of histamine in Cnidoscolus texanus hairs has been confirmed by a color test involving diazotization with the diazonium salt of sulfanilic acid.[44] A quantitative determination of histamine has not been made.

The qualitative presence of choline in Cnidoscolus texanus hairs was established by precipitation as the reinecke salt. This procedure was followed by thin layer chromatography and comparison with

known choline.[45] Acetylcholine is ordinarily found in small quantities in the presence of choline; also acetylcholine may have been hydrolyzed during the isolation procedure (as this occurred to some extent with known acetylcholine). Thus, the presence of acetylcholine is not rigorously established, but is indicated by the above procedure.

The methanolic extract of Cnidoscolus texanus hairs contains flavanoid materials with absorptions in the ultraviolet spectrum at 315 and 285 mμ. Preliminary tests indicate these compounds have little physiological activity (under conditions similar to those where the hairs are active). Spectral information and various color tests indicate the compounds are probably flavanols or flavones.[46]

The seed oils of Cnidoscolus texanus are edible and have a pleasant flavor. Both the seed and its oil are nontoxic and non-cathartic.[47] The seeds of Cnidoscolus stimulosus are much smaller than those of Cnidoscolus texanus but are also edible.

The seeds of Cnidoscolus texanus and stimulosus were extracted with pentane. The oil removed in this manner was light yellow and darkened slightly upon standing. Cnidoscolus texanus seeds contain 18% oil; those of stimulosus 31%.

The oil was transesterified in a manner known to induce little isomerization.[48] The methyl esters of the glycoside fatty acids were determined gas chromatographically, and identified by peak enhancement techniques and relative retention times. All components of Cnidoscolus texanus oil were identified, but in Cnidoscolus stimulosus oil, a small amount (1.3%) of an unidentified ester was observed, as a shoulder of

the methyl palmitate peak. The data for the composition of the seed oils is tabulated below.* The seed oils of Cnidoscolus texanus and

Table 2

Percentage Composition of Fatty Acids of Cnidoscolus Seed Oils

| Acid | Cnidoscolus texanus | Cnidoscolus stimulosus |
|---|---|---|
| Saturated | | |
| Palmitic | 10.0 | 12.3[b] |
| Stearic | 3.0 | 2.8 |
| Lauric | trace[a] | 0.0 |
| Myristic | trace[a] | 0.2 |
| Unsaturated | | |
| Linoleic | 71.0 | 64.8 |
| Oleic | 15.5 | 18.9 |
| Linolenic | 0.5 | trace[a] |

[a](0.05-0.1%)

[b]One unknown component is present in small amounts (1.3%).

stimulosus fall in the same category (Group II) of Hilditchs classification scheme as do other Euphorbiaceae.[22]

The toxic principle of Cnidoscolus texanus roots was isolated by cutting the roots into small pieces, followed by extraction with

*The Data for Cnidoscolus texanus seed oil has been published: D. S. Seigler and J. J. Bloomfield, Phytochemistry, 6, 451 (1967).

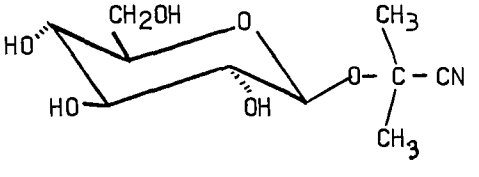
ethyl acetate. Upon concentration and subsequent workup the glycoside was isolated as a partially crystallized syrup (0.02% yield). This percentage corresponds rather closely to that observed in races of cassava that are considered quite toxic. This syrup was established to be a pure compound by thin layer chromatography. The nmr spectrum of the compound in deuterium oxide showed a sharp singlet at 1.62 $\delta$ (acetone cyanohydrin 1.62 $\delta$) and complex multiplet from 3.3-3.8 $\delta$ and a sharp singlet at 4.61 $\delta$ (HDO).

The glycoside is readily hydrolyzed by base, but slowly hydrolyzed by acid. A sample of the glycoside was hydrolyzed under basic conditions for one hour and the nmr spectrum was determined. The singlet at 1.62 $\delta$ decreased and a singlet appeared at 2.17 $\delta$ (acetone 2.17 $\delta$).

A sample of the glycoside was hydrolyzed with dilute base and made neutral. The 2,4-dinitrophenylhydrazone was prepared and shown, by comparison, to be identical with acetone 2,4-dinitrophenylhydrazone.

Another sample was hydrolyzed with dilute acid and the sugar was shown to be glucose.

The glycoside was identified by its hydrolysis products, spectra, and physical properties as acetone cyanohydrin-beta-glucoside (3).



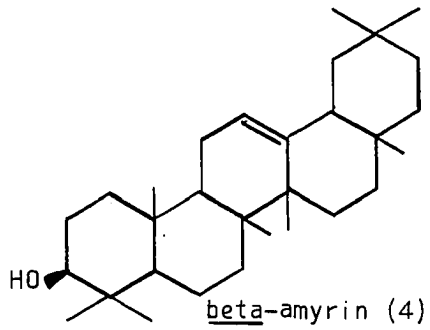

(3)

A systematic investigation of the phytochemistry of the genus Cnidoscolus is currently in progress. Ground air-dried leaf and stem materials from Cnidoscolus texanus and stimulosus were extracted with a series of solvents of increasing polarity. The concentrated fractions from this procedure were then chromatographed to separate pigments and glycerides from terpenes and other materials of interest to this study. The fractions obtained by this procedure are further chromatographed to separate the individual components.

This work is largely in the preliminary stages and few fractions have actually been treated in this manner.

The nmr spectra, infrared spectra, melting points, solubilities, analyses, and other properties of the compounds isolated thus far, indicate these compounds are triterpenoid in nature. These are likely similar to the type compounds isolated from other Euphorbiaceae (see introduction section).

Beta-amyrin (4) and beta-amyryl acetate were isolated from chromatographed fractions of the first pentane extractions, (CTLS-I-A, $alpha_5$ and $alpha_6^0$ respectively.)




beta-amyrin (4)

These compounds were identified by comparison of their physical properties and spectra with known beta-amyrin and beta-amyryl acetate.

Beta-amyryl acetate was prepared from beta-amyrin by treatment with acetic anhydride.

# CHAPTER III

## CONCLUSIONS

The phytochemistry of the genus Cnidoscolus appears to be similar in many respects to that of other genera of the Euphorbiaceae. The stinging hairs are almost unique in the family, (except for the genus Tragia), whereas the presence of a cyanogenetic glycoside is found in several related genera. The structure of the glycoside is shown to be acetone cyanohydrin-beta-glucoside.

The seed oil is a fast drying oil similar to that of a few other Euphorbiaceae, but does not contain any unusual acids, as vernolic or ricinoleic, which are found in other related genera. The seeds of the genus Cnidoscolus are nontoxic and edible.

The principal components of the dried leaves and stems appear to be triterpenoid in nature, likely similar to those isolated from resins produced by other genera, especially the genus Euphorbia.

# CHAPTER IV

## EXPERIMENTAL

All melting points are uncorrected. Optical rotations were obtained with a Gaertner L-320 polarimeter. Thin layer chromatograms were obtained on glass plates (5 x 20 cm) coated with a 0.25 mm layer of silica gel H (E. Merck AG Darmstadt), except where noted otherwise. Iodine vapor was used to visualize the plates.

Column chromatographies were performed utilizing either 100 mesh silicic acid (Mallinckrodt Chemical Company) or 100-200 mesh Florisil (Floridin Company) unless noted otherwise.

Hexane and benzene were distilled before use in chromatographic separations.

Elemental analyses were conducted by A. Bernhardt, Microanalytical Laboratories, Mülheim (Ruhr) Germany.

Nmr spectra were obtained with a Varian A-60 instrument with tetramethylsilane as internal standard. Chemical shifts are reported in δ-values (p.p.m. from TMS).

Infrared spectra were recorded on a Beckman IR-8 spectrophotometer. Mass spectra were run by courtesy of Monsanto Company, St. Louis, Missouri.

Cnidoscolus stimulosus material was collected the last week

of August, 1966, ten miles west of Bogalusa, Louisiana, in Washington Parish. These plants were collected on the grounds of the Louisiana State University, School of Forestry and on land of Crown Zellerbach Corporation in the vicinity. Seeds, leaf and stem material and roots were collected.

Cnidoscolus texanus material has been collected on several occasions in fields on the south-west outskirts of Norman, Cleveland County, Oklahoma, where it grows abundantly.

Cnidoscolus angustidens material was collected the first week of June, 1967, near Ruby, Arivaca, and Patagonia, Santa Cruz County, Arizona, on the grounds of the Coronado National Forest. Seed material was not available at the time of collection.

Specimens of Cnidoscolus angustidens and stimulosus have been deposited in the Bebb Herbarium of the University of Oklahoma.

## Tests for Alkaloids on Cnidoscolus texanus Material

Tests for alkaloids were performed by the procedure of Lüning and that of Abisch and Reichstein.[42] The results of these tests are summarized in the tables below. No alkaloids were found in any Cnidoscolus texanus material. All the reagents gave a positive test with a dilute solution of brucine. Directions for preparing the necessary reagents and the details of the procedure are found in Paech and Tracey.[49]

Table 3

Summary of Alkaloid Tests on *Cnidoscolus texanus* Material

| Test | Result of Test |
|---|---|
| Mayer's Test | Negative |
| Silicotungstic Acid | Negative |
| Hager's Test | Negative |
| Sonnenschein's Test | Negative |
| Wagner's Test | Negative |

## Isolation of the Seed Oil

Seeds of *Cnidoscolus texanus* (Muell. Arg.) Small (250 g) were ground with a blendor, covered with pentane and allowed to stand several hours. The pentane solution was then filtered through a bed of diatomaceous earth. This procedure was repeated three times, the solutions were combined and the pentane was removed by distillation. The product, a light yellow, slightly viscous oil, darkened upon exposure to air (45 g, 18%).

Seeds of *Cnidoscolus stimulosus* (Michx.) Gray (74.2 g) were extracted in the same manner to yield a yellow oil (22.7 g , 31%).

## Transesterification of Oil Glycerides

The seed oils from both *Cnidoscolus texanus* and *stimulosus* were transesterified using a method similar to that of Haller and Youssoufian.[48]

## Determination of the Methyl Esters of the Glyceride Fatty Acids

The methyl esters were determined, in ether solution using a MicroTek GC-1600 gas chromatograph fitted with a ten foot, 1/8 inch, stainless steel column, packed with 20% Carbowax 20M on Anakrom ABS at 170°, through a flame ionization detector. The peaks were identified by peak enhancement techniques, using known samples of esters, and by relative retention times. A prior determination indicated no volatile components were present in the original oil.

## Quantitative Determination of the Fatty Acids

The percentage of each component was evaluated by multiplying the height by the width at half height.[50] The error was estimated to be ±0.5%. In the oil of Cnidoscolus texanus, all esters present in greater than trace amounts were identified, but in Cnidoscolus stimulosus a small amount (1.3%) of an unidentified ester was observed as a shoulder of the palmitic acid peak. (See Table 4.)

## Isolation of Acetone Cyanhohydrin-beta-glucoside from Cnidoscolus texanus Roots

Six freshly dug roots (10 kg) were chopped and boiled 20 minutes with ethyl acetate. The total volume of solution was twenty liters. This solution gave a positive test for hydrocyanic acid with the picric acid test, when heated with acetic acid.[20] The solution was dried over anhydrous magnesium sulfate and then filtered. The ethyl acetate solution was concentrated to a volume of 200 ml under

vacuum on a rotary evaporator with hot water (60-70°). The precipitate gave a strong hydrocyanic acid test with dilute sodium hydroxide but a weak test with acetic acid. The supernatant liquid gave only a faint positive hydrocyanic acid test.

Table 4

Percentage Composition of the Fatty Acid Components of Cnidoscolus Seed Oils.

| Acid | Cnidoscolus texanus | Cnidoscolus stimulosus |
|---|---|---|
| Saturated | | |
| Palmitic | 10.0 | 12.3[b] |
| Stearic | 3.0 | 2.8 |
| Lauric | trace[a] | 0.0 |
| Myristic | trace[a] | 0.2 |
| Unsaturated | | |
| Linoleic | 71.0 | 64.8 |
| Oleic | 15.5 | 18.9 |
| Linolenic | 0.5 | trace[a] |

[a](0.05-0.1%)

[b]One unknown component is present in small amounts (1.3%).

The hydrocyanic acid test is done in the following manner. Filter paper strips are dipped in an aqueous solution containing 5% sodium carbonate and 0.5% picric acid, and almost allowed to dry. They are suspended over a sample to which has been added a few drops of chloroform or dilute acetic acid, and then incubated at 30-35°.

A positive test is indicated by a color change from yellow to red or maroon.

The roots of Cnidoscolus stimulosus and angustidens also give a positive test for hydrocyanic acid, but the glycoside was not isolated from these species. Thin layer chromatography (on 0.25 mm silicic acid) of the precipitate dissolved in ethyl acetate showed five components were present, with Rf values a) 0.0, b) 0.22, c) 0.44, d) 0.55 and e) 0.72. A mixture of n-propanol, water, and ethanol (7:2:1) was used as the eluant, and the plate was developed in an iodine tank.

The slurry produced by concentration of the ethyl acetate solution was evaporated to a thick syrup (with conditions as above) and treated with distilled water (200 ml). This mixture was filtered and the filtrate again concentrated to a thick syrup. The residue gave an intense test for hydrocycanic acid. Thin layer chromatography carried out as above showed six components with Rf values: a) 0.0, b) 0.15, c) 0.44, d) 0.56, e) 0.64 and f) 0.72. The thin layer plates (after they had been developed with iodine) were sprayed with sodium hydroxide solution (10%) until damp. The plates were first covered with a wire gauze, then a strip of filter paper impregnated with sodium picrate solution, and finally covered with a glass plate. When incubated at 60° for ten minutes, a positive test for hydrocyanic acid was observed, which corresponded to the component with the Rf value of 0.72.

The syrup (approximately 10 g) from the aqueous solution was chromatographed on a silica gel column (250 g) with 95% ethanol. Ten fractions of fifty ml were collected. The glycoside was readily eluted

from the column (Fractions 4 and 5) and all other fractions contained only traces of unidentified materials. After concentration under vacuum and standing several days the partially crystallized glycoside weighed 2.4 g, (0.02%). Thin layer chromatography showed this partially crystallized syrup to consist of one component with an Rf value of 0.72. Crystallization was facilitated by dissolving the sample in a small amount of alcohol, adding benzene and then distilling off most of the liquid phase under vacuum. Recrystallization from absolute ethanol yielded yellow crystals, m.p.136.5-138° (lit.[51] m.p. 140-141°). A small sample recrystallized from tetrahydrofuran-ether had m.p. 141-142°.

The optical rotation of the glycoside (m.p. 136.5-138° ) was determined in 95% ethanol $[\alpha]_D^{27°} = -34.8°$ (on 19 mg material). (lit.[52] $[\alpha]_D^{18°} = -29.06°$).

The infrared spectrum showed absorptions at 3000-2900 $cm^{-1}$ (carbon-hydrogen) 3400-3100 $cm^{-1}$ (hydroxyl) and 2215 $cm^{-1}$ (nitrile). Other broad absorptions were located at 1700-1600 $cm^{-1}$ and 1450-1000 $cm^{-1}$. The nmr spectrum of the glycoside was run in deuterium oxide, and the values reported are relative to HDO at 4.61$\delta$ . A singlet observed at 1.62$\delta$ was attributed to the acetone methyl groups (acetone cyanohydrin 1.62$\delta$ [53]). A broad new multiplet was observed at 3.3-3.8$\delta$ which corresponds in chemical shift to the protons of glucose. Peaks of ethanol and a small amount of impurity (1.70 $\delta$ ) were also observed in the spectrum.

## Hydrolysis of Acetone Cyanohydrin-beta-glucoside

A sample of the glycoside dissolved in deuterium oxide in an nmr tube was treated with two drops of 5% hydrochloric acid. After heating at 50° for one hour the nmr spectrum was unchanged. The solution was neutralized, and two drops of 5% sodium hydroxide were added. After one hour, the amplitude of the singlet at 1.62 $\delta$ was decreased and another singlet appeared at 2.17 $\delta$ (acetone 2.17 $\delta$ ).[53]

## Determination of Sugar of Glycoside

Crude glycoside (10mg) was heated for 24 hours with 3% hydrochloric acid solution (5 ml). The solution was then passed over a basic ion exchange resin, and eluted with water (50 ml). The resulting solution was concentrated and the residue taken up in water (3 x 5 ml). This solution was concentrated in a conical flask and taken up in water (1 ml).

The solution was thin layer chromatographed on silicic acid with n-propanol, ethyl acetate, and water (7:2:1) and the sugar was shown by comparison to be identical with glucose.

## 2,4-Dinitrophenylhydrazone of Ketone from Aglycone

A small sample of the glycoside (approximately 50 mg) was allowed to stand with 5 drops of 10% sodium hydroxide solution for one hour and then was neutralized. The 2,4-dinitrophenylhydrazone derivative was prepared using Shine's reagent.[54] After recrystallization from ethanol the red-yellow crystals had m.p. 120-123° (lit. 125°). Thin layer chromatography of the derivative on silica gel with ethyl

acetate showed it to be identical with known acetone 2,4-dinitrophenylhydrazone.

## Hairs

### Aqueous Extraction of Cnidoscolus texanus Hairs

Sieved Cnidoscolus texanus hairs were steeped in water (200 ml) at room temperature for twenty-four hours. The extract was removed by filtration, and the hairs were air dried. The dried hairs retained their physiological activity. Bull nettle hairs were incubated overnight in water at 50°. The activity was not reduced. This treatment was followed by extraction with pentane for twelve hours, without subsequent loss of activity. After this treatment, the hairs were again incubated for twelve hours. A substantial decrease in activity was observed.

### Determination of Physiological Activity of Cnidoscolus texanus Hairs

Several hairs were chosen randomly from the extracted mass and from air dried material. Then the forearm of the author was pricked slightly with several hairs from each group. The hairs produced a slight irritation and swelling in the immediate area of the injection in each case.

### Extraction of Cnidoscolus texanus Hairs with a Series of Solvents of Increasing Polarity

The hairs of Cnidoscolus texanus from the above aqueous extraction were placed in a Soxhlet extractor and extracted with a series of solvents

in order of increasing polarity. The data for this extraction is tabulated below.

Table 5

Data for Extraction of Cnidoscolus texanus Hairs

| Fraction | Solvent | Weight | Physiological Activity at End of Extraction |
|---|---|---|---|
| CTH-I | Water | -- | Positive |
| CTH-II | Pentane | 0.51 | Positive |
| CTH-II | Ether | 0.04 | Positive (?) |
| CTH-II | Acetone | 0.11 | Negative (?) |
| CTH-II | Methanol | 0.87 | Negative |

Test for Presence of Histamine in Methanol Extract

The methanolic extract (1 ml) was mixed with water (1 ml). To the aqueous methanolic solution was added saturated sodium carbonate solution (1 ml) and a solution of sodium nitrite (1 ml) and sulfanilic acid (1 ml).[44] The solutions were prepared by adding sulfanilic acid (0.9 g) to water (100 ml) which contained concentrated hydrochloric acid (9 ml); and by adding sodium nitrite (7 g) to water, (100 ml), The sulfanilic acid solution (1 ml) and sodium nitrite solution (1 ml) were mixed and allowed to stand briefly before addition to the basic solution. The test solution gave a strong positive test (a deep cherry red color) for histamine. This test is positive only for histamine and

histidine. It is unlikely that free histidine is present in large quantities in the plant material.

### Test for Presence of Choline in Methanolic Extract[45]

The aqueous methanolic solution was adjusted to pH 10 with dilute sodium bicarbonate solution. To this solution was added 4% ammonium reineckate solution (2 ml) and the mixture was allowed to stand in the cold. The precipitate formed was removed by centrifugation, and washed three times with n-propyl alcohol (2 ml). The liquor was removed each time with a pipette. The precipitate was dissolved in acetone (2 ml) and centrifuged to remove insoluble materials. The solution was decanted.

### Thin Layer Chromatography of Acetone Solution

The solution was found to contain choline reineckate by thin layer chromatography. The solution was compared to a solution of known acetylcholine reineckate which showed two spots, the second (with smaller Rf value) corresponding to choline reineckate. The solutions were chromatographed on glass plates (5 x 20 cm) coated with a 0.25 mm layer of MN-cellulose powder with approximately 10% calcium sulfate (Macherey, Nagel & Company, Düren). The materials were spotted and 0.1 N silver nitrate solution (1 drop) was added to free the choline and acetylcholine from the complex. The plates were eluted with a mixture of chloroform (75%), methanol (22%), and water (3%). The plates were visualized with iodine vapor. In each case a yellow spot of silver iodide was observed at the origin.

## Tests Indicating Presence of Flavanoid Components in Hairs of Cnidoscolus texanus

A methanolic extract of Cnidoscolus texanus hairs was shown to contain flavanoid materials by the following tests.[46]

Table 6

Tests for Flavanoid Materials in Cnidoscolus texanus Hairs

| Test | Result of Test | Structure Indicated |
|---|---|---|
| Concentrated hydrochloric acid and magnesium | Color change from yellow to red-orange | Flavone or flavonol |
| Lead acetate | Yellow precipitate | Flavones |
| Conc. sulfuric acid | Intense yellow coloration | Flavone |
| Ferric Chloride solution | No color produced (slight brown discoloration) | --- |

## Thin Layer Chromatography of Methanolic Extract of Cnidoscolus texanus Hairs

The methanolic extract (5 ml) was treated with excess sodium carbonate, solids were removed by filtration and the solution was then reacidified. This solution was compared to the untreated solution by thin layer chromatography. The solution was shown to be unchanged by the above treatment.

Thin layer chromatographies were performed on glass plates (5 x 20 cm) coated with a 0.25 mm layer of Polyamide support. The plates were eluted with a mixture of 50% nitromethane in methanol, and were visualized with a 1% solution of aluminum chloride in methanol spray under ultraviolet light. The methanolic solution contained four components (based on number of spots), with approximate Rf values of 0.8, 0.5, 0.2, and 0.1.

## Ultraviolet Spectra of Methanolic Solution

The ultraviolet spectra were measured on a Beckman DK-1 recording spectrophotometer.

Table 7

Data for Ultraviolet Spectra of *Cnidoscolus texanus* Hair Extract

| Solution | max. (mμ) |
|---|---|
| Methanolic extract | 285, 315, shoulder 225 |
| Methanolic extract, made basic then reacidified | 285, 315, shoulder 225 |
| Methanolic extract + 2 drops 1% aluminum chloride solution | 307, 280, shoulder 225 |
| Methanolic extract + 1 drop 0.25M sodium methoxide solution | 370, 280, shoulder 235 |
| Methanolic extract + pinch anhydrous sodium acetate | 315, 285 |

## Tests Indicating Presence of Flavanoid Components in Cnidoscolus texanus Flowers

In the presence of ammonia fumes, Cnidoscolus texanus flowers immediately change from a white to a yellow color.[46] An ethanolic solution was treated with magnesium and concentrated hydrochloric acid. A color change from yellow to orange red was observed. This test is indicative of the presence of a flavone or flavonol.[46] The ethanolic extract showed absorptions at 315, 267, and a shoulder at 295 mμ.

## Systematic Investigation of Leaves and Stems

Dried Cnidoscolus texanus leaves and stems (1465.7 g) were ground in a Waring blendor. This plant material was placed in a modified Ciereszko type extractor.[55] The material was extracted with solvents in increasing order of polarity. (See Table 8.)

Most of the work described in this section is still in the preliminary stage of investigation. The composition of most extracts is not known.

The solvent was removed from all fractions under vacuum, the concentrate placed in a tared bottle and stored at -5°.

## Extraction of Cnidoscolus stimulosus Leaves and Stems

Dried Cnidoscolus stimulosus leaves and stems (1482.0 g) were ground in a blendor and extracted in the same manner as the Cnidoscolus texanus materials described above. After extraction, the crude extracts were concentrated and stored as the Cnidoscolus texanus material. (See Table 9.)

Table 8

Crude Fractions from Extraction of Cnidoscolus texanus Leaf and Stem Material

| Extract | Solvent | Grams |
|---|---|---|
| CTLS-I-A | Pentane | 20.0 |
| B | | 15.6 |
| C | | 10.0 |
| CTLS-II-A | Benzene | 14.0 |
| B | | 5.3 |
| CTLS-III-A | Ether | 0.8 |
| B | | 2.8 |
| C | | 4.9 |
| D | | 0.8 |
| CTLS-IV-A | Acetone | 10.4 |
| B | | 15.7 |
| C | | 4.1 |
| D | | 7.3 |
| E | | 10.0 |
| F | | 6.4 |
| CTLS-V-A | Methanol | 25.5 |
| B | | 28.0 |
| C | | 120.6 |
| D | | 29.6 |
| E | | 5.7 |
| F | | |

Table 9

Crude Fractions from Extraction of Cnidoscolus stimulosus Leaf and Stem Material

| Extract | Solvent | Grams |
|---|---|---|
| CSLS-I-A | Pentane | 100.0 |
| B | | 26.0 |
| C | | 7.8 |
| CSLS-II-A | Benzene | 12.3 |
| B | | 3.7 |
| C | | 4.0 |
| CSLS-III-A | Ether | 1.3 |
| B | | 13.5 |
| C | | 1.6 |
| CSLS-IV-A | Acetone | 8.3 |
| B | | 8.8 |
| C | | 17.1 |
| D | | 11.4 |
| E | | 11.4 |
| CSLS-V-A | Methanol | 100.7 |
| B | | 63.5 |

Chromatography of Fraction CTLS-I-A

The concentrated extract of fraction CTLS-I-A (20.0g) was dissolved in hexane and placed on a column containing one pound of Florisil support, which was packed in a hexane slurry. Fractions of 100 ml were collected.

Table 10

Chromatography of Fraction CTLS-I-A

| Fractions | Solvent | Weight (g) |
|---|---|---|
| 1-30 | Hexane | 3.93 |
| 31-42 | 10% Benzene in hexane | 1.68 |
| 43-49 | 25% Benzene in hexane | -- |
| 50-65 | Benzene | 6.72 |
| 66-80 | 6% Ethyl acetate in benzene | 3.39 |
| 81-99 | Ethyl acetate | 1.95 |
| 100-111 | 10% Methanol in ethyl acetate | .27 |
| 112-125 | Methanol | 2.18 |

The total material recovered from the column was 20.0 g.

Thin layer chromatographic separations (on silicic acid) of the fractions from the chromatography of CTLS-I-A were made. (See Table 11.)

Table 11

Thin Layer Chromatography of Chromatographic Fractions of CTLS-1-A

| Fractions | Eluant | Composition (Based on number of spots) |
|---|---|---|
| 6-12 | Benzene | 1 major component and 1 trace component |
| 13-44 | Benzene | 2 major components, 1 trace component (14-28) |
| 45-51 | Benzene | 2 major, 3 trace components |
| 52-56 | Benzene | 2 major, 1-3 trace components |
| 57-62 | Benzene | 2 major components |
| 63-73 | 50:50 Benzene ethyl acetate | 4 major, 1 trace (70-73) components |
| 74-84 | 50:50 Benzene ethyl acetate | 3 major, 2 trace components<br>1 major component (74-76) |
| 85-92 | 50:50 Benzene ethyl acetate | 5 major, 2 trace components |
| 93-106 | 50:50 Benzene ethyl acetate | 2 major components |
| 107-119 | 50:50 Benzene ethyl acetate | 1 major component large spot at origin |

Rf values were not calculated because of the large numbers of fractions and the necessity of further chromatographic separations to simplify the complex mixtures obtained.

Chromatography of Fraction CTLS-I-B

This fraction (15.6 g) was chromatographed on a Florisil column (1 pound) in the same manner as fraction CTLS-I-A. The material recovered from the column weighed 13.6 g.

Table 12

Chromatography of Fraction CTLS-I-B

| Fractions | Solvent | Weight (g) |
|---|---|---|
| 1-92 | Hexane to benzene | -- |
| 93-150 | Benzene | 4.21 |
| 151-168 | 5% Ethyl acetate in benzene | 1.81 |
| 169-199 | 25% Ethyl acetate in benzene | 2.18 |
| 200-230 | 50% Ethyl acetate in benzene | .83 |
| 231-253 | Ethyl acetate | .32 |
| 254-285 | 10% Methanol in ethyl acetate | .58 |
| 286-309 | Methanol | 3.71 |

Thin layer chromatographies were performed in a manner similar to those of CTLS-I-A.

Table 13

Thin Layer Chromatography of Chromatographic Fractions of CTLS-I-B

| Fractions | Eluant | Composition (Based on number of spots) |
|---|---|---|
| 93-142 | Benzene | 1 major, 5 minor components |
| 145-176 | Benzene | 1 major, 1 minor component |
| 191-217 | 50:50 Ethyl acetate benzene | 1 major component |

Chromatography of Fraction CTLS-I-C

Fraction CTLS-I-C (10.0 g) was chromatographed on a column packed with Florisil (350 g) in a manner similar to CTLS-I-A. The fractions collected in this chromatography had a volume of 200 ml.

Table 14

Chromatography of Fraction CTLS-I-C

| Fractions | Solvent | Weight (g) |
|---|---|---|
| 1-27 | Hexane-benzene | - |
| 28-50 | Benzene | 2.04 |
| 51-66 | 10% Ethyl acetate in benzene | 1.29 |
| 67-79 | 37% Ethyl acetate in benzene | .78 |
| 80-99 | Ethyl acetate | .87 |
| 100-105 | 10% Methanol in ethyl acetate | .25 |
| 106-123 | 20% Methanol in ethyl acetate | .67 |
| 124-129 | 50% Methanol in ethyl acetate | 1.10 |
| 130-132 | Methanol | 2.19 |

The quantity of material recovered from the column was 9.19 g.

Thin layer chromatographic separations were performed in a manner similar to those of CTLS-I-A.

Table 15

Thin Layer Chromatographic Separation of Chromatography Fractions of CTLS-I-C

| Fractions | Eluant | Composition (Based on Number of Spots) |
|---|---|---|
| 28-38 | 40% Hexane in benzene | 5 major components |
| 39-43 | 40% Hexane in benzene | 2 major, 1 trace components (39-40) |
| 44-53 | Benzene | 4 major components |
| 54-58 | Benzene | 2 major components |
| 59-74 | 50% Ethyl acetate in benzene | 2 major components, streaking from origin (70-74) |
| 75-79 | 50% Ethyl acetate in benzene | 3 major components |
| 90-105 | Ethyl acetate | 1 major component, 2 trace components (103-104) |
| 106-121 | Ethyl acetate | 3 major components |

Chromatography of Fraction CSLS-I-A

Fraction CSLS-I-A (100 g) was chromatographed in a manner similar to that of CTLS-I-A, on a column packed with Florisil. Fractions collected were 100 ml. The large amount of material chromatographed

precluded good separation but the quality of the material was improved greatly.

Table 16

Chromatography of Fraction CSLS-I-A

| Fraction | Solvent | Weight (g) |
|---|---|---|
| 1-34 | Hexane | 54.39 |
| 35-51 | 10% Benzene in hexane | 3.49 |
| 52-90 | 33% Benzene in hexane | 14.15 |
| 91-108 | Benzene | 1.87 |
| 109-139 | 10% Ethyl acetate in benzene | 7.88 |
| 140-158 | 29% Ethyl acetate in benzene | .21 |
| 163-184 | Ethyl acetate | 2.96 |
| 185-209 | 10% Methanol in ethyl acetate | 2.63 |
| 210-218 | 30% Methanol in ethyl acetate | 1.40 |
| 219-227 | Methanol | 4.27 |

The total amount of material recovered from the column weighed 93.6 g.

Thin layer chromatographic separations were performed in a manner similar to those of CTLS-I-A. (See Table 17.)

Chromatography of Fraction CSLS-I-B

Fraction CSLS-I-B (26.0 g) was chromatographed in a manner similar to CTLS-I-A on a column packed with Florisil (400 g). (See Table 18.)

Table 17

Thin Layer Chromatography of the Chromatographic Fractions of CSLS-I-A

| Fractions | Eluant | Composition (Based on Number of Spots) |
|---|---|---|
| 6-21 | Benzene | 6 major components |
| 23-44 | Benzene | 6 major, 3 trace components |
| 50-71 | Benzene | 5 major components |
| 84-99 | 50% Ethyl acetate in benzene | 4 major, 2 trace components |
| 100-115 | 50% Ethyl acetate in benzene | 4 major components, bad streaking |
| 116-130 | 50% Ethyl acetate in benzene | 3 major components, 1 vanishes at 127, streaking from origin 122 |
| 148-163 | 50% Ethyl acetate in benzene | 2 major components, 1 disappears at 156-158, 1 trace component |

Table 18

Chromatography of CSLS-I-B

| Fraction | Solvent | Volume of Fraction (ml) | Weight (g) |
|---|---|---|---|
| 1-21 | Hexane-13% benzene in hexane | 200 | -- |
| 22-32 | 13% Benzene in hexane | 200 | 1.42 |
| 33-58 | 20% Benzene in hexane | 200 | 1.48 |
| 59-76 | 34% Benzene in hexane | 100 | .41 |
| 77-105 | Benzene | 100 | 1.51 |
| 106-131 | 5% Ethyl acetate in benzene | 106-121, 200<br>122-131, 100 | 2.09 |
| 132-153 | 9% Ethyl acetate in benzene | 100 | .43 |
| 154-185 | 18% Ethyl acetate in benzene | 154-177, 100<br>178-185, 200 | .82 |
| 186-199 | 36% Ethyl acetate in benzene | 186-192, 200<br>193-199, 100 | .48 |
| 200-218 | Ethyl acetate | 100 | 1.17 |
| 219-235 | 5% Methanol in ethyl acetate | 100<br>232,233,234 200ml | .73 |
| 236-247 | 10% Methanol in ethyl acetate | 200<br>245,246,247, 100ml | .61 |
| 248-267 | 50% Methanol in ethyl acetate | 100 | 4.26 |
| 268-275 | Methanol | 100 | 2.68 |

Thin layer chromatographic separations were performed in a manner similar to those of CTLS-I-A.

Table 19

Thin Layer Chromatography of Chromatographic Fractions of CSLS-I-B

| Fractions | Eluant | Composition (Based on Number of Spots) |
|---|---|---|
| 0 to 9-20 (combined) | 50% Benzene in hexane | 3 major, 2-3 trace components |
| 21-39 | 50% Benzene in hexane | 4-5 major components |
| 40-93 | Ethyl acetate | 3 major components, trace begins at 88 |
| 94-109 | Ethyl acetate | 4 major components |
| 110-130 | Ethyl acetate | 1 major, 2 trace components |
| 169-218 | Ethyl acetate | 1 major component, streaked badly to origin |
| 248-253 | Methanol | 2 major components |
| 254-260 | Methanol | 2 major components, 1 major 254, 255 origin large spot |
| 261-266 | Methanol | 1 major component, 1 major at origin, 1 major component 263-266 |
| 267-272 | Methanol | 1 major component at origin |

Chromatography of Fraction CSLS-I-C

Fraction CSLS-I-C (7.8 g) was dissolved in a benzene-hexane mixture and chromatographed in a manner similar to CTLS-I-A on a

column packed with Florisil (200 g). The data for this separation is listed below.

Table 20

Chromatography of Fraction CSLS-I-C

| Fraction | Solvent | Volume of Fractions (ml) | Weight (g) |
|---|---|---|---|
| 1-10 | 25% Benzene in hexane | 200 | .12 |
| 11-30 | 68% Benzene in hexane | 100 | .96 |
| 31-44 | Benzene | 100 | .09 |
| 45-58 | 5% Ethyl acetate in benzene | 100 | .78 |
| 59-85 | 10% Ethyl acetate in benzene | 100 | .53 |
| 86-129 | 25% Ethyl acetate in benzene | 100 | .65 |
| 130-149 | 50% Ethyl acetate in benzene | 100 | .25 |
| 150-192 | Ethyl acetate | 100 | .56 |
| 193-204 | 5% Methanol in ethyl acetate | 100 | .43 |
| 205-216 | 10% Methanol in ethyl acetate | 100 | .27 |
| 217-223 | 30% Methanol in ethyl acetate | 100 | 1.72 |
| 224-229 | 50% Methanol in ethyl acetate | 100 | 1.49 |
| 230-232 | Methanol | 100 | .65 |

Thin layer chromatographic separations were performed in a manner similar to those of CTLS-I-A and are shown in Table 21.

Table 21

Thin Layer Chromatography of Chromatographic Fractions of CSLS-I-C

| Fraction | Eluant | Composition (Based on Number of Spots) |
|---|---|---|
| 1-13 | Benzene | 1-2 major components |
| 14-25 | Benzene | 5 major components |
| 26-37 | 50% Ethyl acetate in benzene | 3 major components |
| 42-57 | 50% Ethyl acetate in benzene | 2 major components |
| 58-71 | 50% Ethyl acetate in benzene | 2 major components, traces in 63-71, streaked 67-71 |
| 140-150 | Ethyl acetate | 4 major components |
| 151-158 | Ethyl acetate | 6 major components |
| 159-190 | 50% Methanol in ethyl acetate | 2 major components |
| 191-195 | 50% Methanol in ethyl acetate | 2 major components |
| 210-230 | 50% Methanol in ethyl acetate | 4 major components |
| 231-232 | 50% Methanol in ethyl acetate | 5 major components |

Chromatographic Separation of CTLS-I-A, Fractions 6-55*

Fractions 6-55 (7.9 g) from the chromatography of CTLS-I-A were combined and chromatographed on a column packed with neutral alumina (300 g). (Alpha chromatography.)

Table 22

Chromatography of Fractions 6-55 of Fraction CTLS-I-A

| Fraction | Solvent | Volume of Fraction (ml) | Weight (g) |
|---|---|---|---|
| 1-37 | Hexane | 50 | 1.60 |
| 38-49 | 2.5% Benzene in hexane | 50 | 0.07 |
| 50-67 | 8% Benzene in hexane | 50 | 0.0 |
| 68-72 | 15% Benzene in hexane | 50 | 0.0 |
| 73-78 | 25% Benzene in hexane | 50 | 0.0 |
| 79-88 | 47% Benzene in hexane | 50 | 0.0 |
| 89-111 | Benzene | 50 | 6.29 |
| 112-166 | 4% Ethyl acetate in benzene | 194-203, 100 ml | 1.02 |

The fractions from the above chromatography were chromatographed by the thin layer method as described previously.

*The following experimental work was performed by A. Yankie.

Table 23

Thin Layer Chromatography of Fractions from (alpha) Chromatography of CTLS-I-A Fractions 6-55

| Fraction | Eluant | Composition (Based on Number of Spots) |
|---|---|---|
| 6-12 | Hexane | 1 major component |
| 13-23 | Hexane | 1 major component, 1 trace (6-12) |
| 118-128 | Benzene | 1 major, 1-3 minor components 1 major component (118-122) |
| 129-151 | Benzene | 3 major, 2 trace components |
| 171-173 | Benzene | 1 major, 1 trace component |
| 174-197 | Benzene | 1 major component |

Several fractions with similar thin layer patterns were combined to make four fractions.

| | | |
|---|---|---|
| $alpha_1$ | 6-23 | .20 g |
| $alpha_3$ | 135-169 | .95 g |
| $alpha_5$ | 187-197 | .61 g |
| $alpha_0$ | 118-123 | 2.68 g |

Fractions $alpha_3$ and $alpha_5$ were combined and chromatographed.

Chromatography of Fraction $alpha_0$ from CTLS-I-A

Fraction $alpha_0$ (2.86 g) was chromatographed on a column packed with silicic acid (150 g).

Table 24

Chromatography of Fraction $alpha_0$ from CTLS-I-A

| Fraction | Solvent | Weight (g) |
|---|---|---|
| 1-40 | Hexane-15% benzene in hexane | -- |
| 41-112 | 15% Benzene in hexane | 1.28 |

Thin layer chromatographic separations indicate fractions 89-99 consist of one component, Rf= 0.4, 87-85 of two components, Rf = 0.4, 0.6, 72-79 of one component with Rf = .6, 38-52 one component, Rf = 0.3, 53-71 one component, Rf = 0.6, and 101-111, two components, Rf = 0.2, 0.3. The thin layer chromatograms were eluted with a mixture of 40% hexane in benzene. Several of the fractions were recombined to produce the fractions listed below:

| | | |
|---|---|---|
| $alpha_0^1$ | .15 g | 89-99 |
| $alpha_0^2$ | .81 g | 53-77 |
| $alpha_0^6$ | .50 g | 101-111 |

After recrystallization of $alpha_0^6$ from hexane, the thin layer chromatogram showed only one component Rf = 0.4. Fraction $alpha_0^1$ showed two components Rf = 0.4, 0.3. Both fractions were eluted with benzene. Fraction $alpha_0^6$ was recrystallized from hexane to yield a white solid,

m.p. 215-235°. Upon recrystallization of the solid from ethanol it had m.p. 227-234°. The thin layer of this compound showed two components to be present. Anal. Calcd. (beta-amyryl acetate) C,81.99; H, 11.1; O, 6.83. Found: C, 82.44; H, 10.62; O, 6.74.

## Acetylation of Fraction $alpha_5$

This fraction was suspected to be beta-amyrin and $alpha_0^6$ was thought to be beta-amyryl acetate.

Fraction $alpha_5$ (50 mg) was dissolved in benzene (3 ml) and acetic anhydride (1 ml) was added. The mixture was refluxed for four hours. Water (3 ml) was added and the mixture evaporated to dryness under vacuum. A thin layer chromatogram eluted with benzene showed this compound to be identical to $alpha_0^6$, thought to be beta-amyryl acetate.

## Hydrolysis of Fraction $alpha_0^6$ with Potassium Hydroxide

Fraction $alpha_0^6$ (m.p. above 110°) (170 mg) was refluxed with excess alcoholic potassium hydroxide solution for six hours. The solution was acidified, ether was added (2 ml) and the solution was washed twice with water (1 ml). The results of thin layer chromatography (eluted with benzene) showed two components, one identical with starting material and the other coincided with ($alpha_5$) beta-amyrin.

The acetate prepared from known beta-amyrin (L. Light Co.) was established to be identical to the acetate of $alpha_5$ by thin layer chromatography.

The nmr spectrum of $alpha_5$ is identical to that of beta-amyrin except that it contains peaks which correspond to a small percentage of beta-amyryl acetate.

The infrared spectrum of $alpha_0^6$ (beta-amyryl acetate) is identical to that of known beta-amyryl acetate in all respects. Absorptions are observed at 2850-2950 $cm^{-1}$ (carbon-hydrogen), 1735 $cm^{-1}$ (acetate carbonyl), 1450 $cm^{-1}$ and 1460 $cm^{-1}$ (methyl group), 1365 $cm^{-1}$ (acetate methyl), 1240 $cm^{-1}$ (ether absorption) 1020 and 975 $cm^{-1}$.

## Chromatography of Fraction CTLS-I-B

All fractions of CTLS-I-B (13.6 g) were recombined and chromatographed on a column packed with silicic acid (about 200 g). (beta-chromatography.)

Table 25

Chromatography of Fractions of CTLS-I-B

| Fraction | Solvent | Weight (g) |
|---|---|---|
| 1-27 | Hexane | 1.34 |
| 28-40 | 4.5% Benzene in hexane | 0.0 |
| 41-54 | 20% Benzene in hexane | 0.0 |
| 55-90 | 50% Benzene in hexane | .61 |
| 91-119 | Benzene | 3.27 |
| 120-140 | 2% Ethyl acetate in benzene | 0.0 |
| 141-154 | 12% Ethyl acetate in benzene | 4.00 |
| 155-158 | 60% Ethyl acetate in benzene | 0.00 |

The material recovered from the column weighed 9.2 g.

Fractions of the beta-chromatography of CTLS-I-B were chromatographed by the thin layer method in a manner similar to the fractions of CTLS-I-A.

Table 26

Thin Layer Chromatography of Fraction of Beta Chromatography of CTLS-I-B

| Fraction | Eluant | Composition (Based on Number of Spots) |
|---|---|---|
| 4-8 | Benzene | 1 major component |
| 9-18 | Benzene | 1 major, 3 trace components |
| 22-39 | Benzene | 1 major, 1 trace component |
| 40-53 | Benzene | 2 major, 3 colored trace components |
| 54-97 | Benzene | 2 major components |
| 98-100 | Benzene | 1 major component |
| 101-105 | Benzene | 2 major components |
| 106-117 | Benzene | 2 major components |
| 118-134 | 20% Ethyl acetate in benzene | 3 major components |
| 138-154 | 20% Ethyl acetate in benzene | 2 major, 1 trace component |
| 155-158 | 20% Ethyl acetate in benzene | 1 major component, badly streaked from origin |

Several groups of fractions with similar thin layers were combined to form new fractions:

| | | |
|---|---|---|
| $beta_0$ | 54–100 | 4.9 g |
| $beta_1$ | 155–158 | 1.1 g |
| $beta_2$ | 138–154 | 2.1 g |
| $beta_3$ | 101–134 | 2.0 g |
| $beta_4$ | 4–8 | .2 g |
| $beta_5$ | 10–20 | .7 g |

Purification of Fraction $beta_0$ from CTLS-I-B

Fraction $beta_0$ was an orange liquid which crystallizes slowly at room temperature. This fraction was recrystallized from hexane to yield a white crystalline solid, m.p. 97–101°. After successive recrystallization from acetone, white crystals are obtained, m.p. 109–110°.

This compound decolorized bromine in carbon tetrachloride solution. The infrared spectrum shows absorptions at 2920 and 2850 $cm^{-1}$ (carbon-hydrogen) 1705 $cm^{-1}$ (carbonyl), 1460 $cm^{-1}$, 1360 and 1375 $cm^{-1}$. The nmr spectrum shows a tall singlet at 1.25$\delta$. A complex multiplet is observed between 0.80 and 1.10$\delta$. By use of a Varian Company 1024 Time Averaging Computer certain low intensity peaks were observed. A multiplet lies at 2.2–2.4$\delta$, a much split triplet at 4.5–4.7$\delta$ and a multiplet at 5.1–5.3$\delta$.

Anal. Found: C, 81.98; H, 11.77; O, 6.23

Purification of Fraction $beta_3$ from CTLS-I-B

Fraction $beta_3$ was recrystallized from hexane to yield a white waxy solid. This solid was recrystallized from 80% ethanol, and then from acetone to yield a white solid (m.p. 140.5-144.5°). The solid was dried under vacuum, m.p. 138.5-140.5°.

The infrared spectrum has absorptions at 3450 $cm^{-1}$ (broad, hydroxyl) 2930 and 2960 $cm^{-1}$ (carbon-hydrogen), 1460, 1350, and 1050 $cm^{-1}$.

The nmr spectrum shows a broad multiplet from 0.8-2.3 $\delta$, and a multiplet at 5.2-5.4 $\delta$.

Anal. Found: C,83.68; H, 11.55; O,4.54.

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# X-RAY CRYSTAL STRUCTURE OF TRANS-1,3-CYCLOBUTANEDICARBOXYLIC ACID

## CHAPTER I

## INTRODUCTION

Studies related to the synthesis and structure determination of cis and trans-1,3-cyclobutanedicarboxylic acid have been endowed with numerous interesting problems.

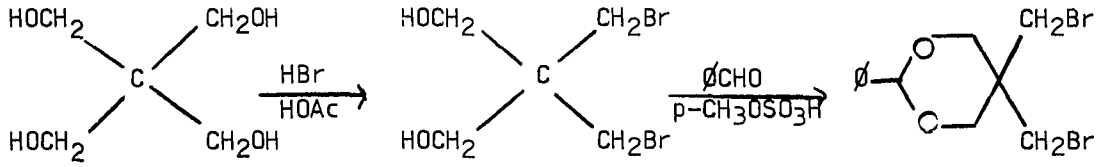
The synthesis of this pair of acids was first reported by Markownikoff and Krestownikoff in 1881.[1] In 1898, Haworth and Perkin reported a new and different synthesis.[2]

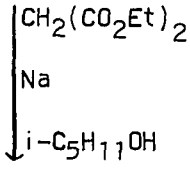
In the years that followed many confusing pieces of data were added to the literature. Deutsch and Buchman reported the physical constants for the cis and trans acids but not the details of the synthesis.[3]

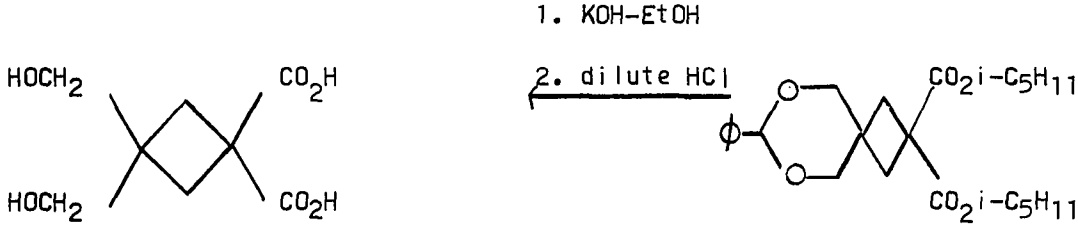
The Deutsch and Buchman synthesis was finally published in 1965 by Allinger and Tushaus.[4]

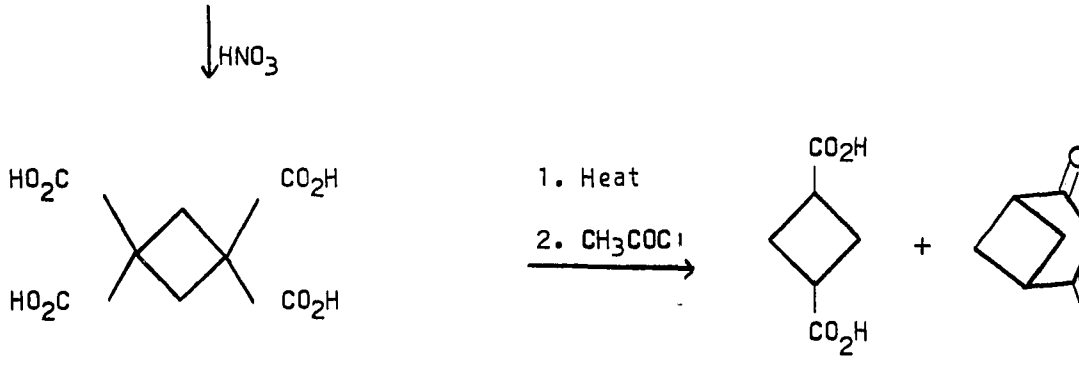
The synthesis of Perkin was shown to produce methyleneglutaric acid, that of Markownikoff to produce 1-methyl-1,2-cyclopropanedicarboxylic acid. It should be noted that nearly all the data concerning the 1,3-acids in the literature is in error.

The Deutsch and Buchman synthesis of cis and trans-1,3-cyclobutanedicarboxylic acid is outlined below:



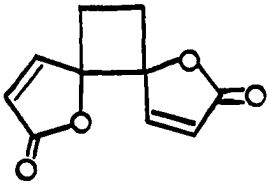

Cis-1,3-cyclobutanedicarboxylic acid m.p. 135-136°[5]

Trans-1,3-cyclobutanedicarboxylic acid m.p. 190-101°[5]

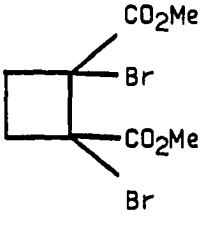
The cyclobutane ring has been shown to exist in two conformations: a planar form and a bent or puckered form. The planar form is found in many cyclobutanes which are part of condensed polycyclic or aromatic systems. Four examples which do not involve aromatic systems have been reported. These are tetracyanocyclobutane,[6] tetraphenylcyclobutane,[7] octahydroxycyclobutane[9] and trans1,3-cyclobutanedicarboxylic acid.[8]

All of these compounds crystallize in the space group $P_{2_1/c}$. Octahydroxycyclobutane was reported in $P_{2_1/n}$, but this can be transformed to $P_{2_1/c}$ by a simple transformation of axes.

The x-ray crystal structures of octachlorocyclobutane,[10] anemonin[12](I), and (both) cis and trans-1,2-dibromo-1,2-dicarbomethoxy-cyclobutane[11] (II), provide examples of puckered cyclobutane rings. In general, the deviation from planarity of the puckered cyclobutane ring is on the order of 20-30°.



(I)




(II)

Other examples of puckered cyclobutane rings have been established by methods such as electron diffraction techniques,[13] nmr splitting patterns,[16] equilibrium studies,[17] and infrared and Raman spectroscopy.[18]

Cyclobutane has been shown to exist in a puckered form.[13,18] The following potential energy curve was proposed, based on entropy data and the results of infrared and Raman spectroscopy.

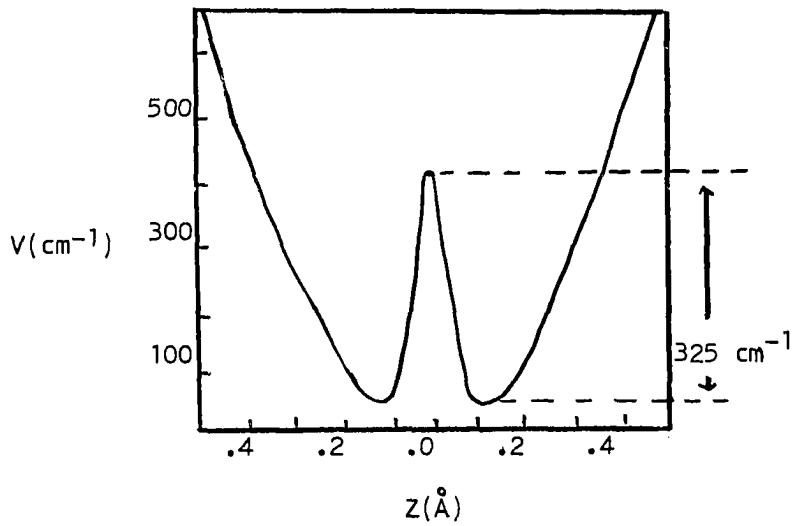



Figure 1. Potential Energy for the Out of Plane Bending Motion.

The molecule has $D_{2d}$ symmetry but the energy barrier is low enough that an appreciable number of molecules obey $D_{4h}$ selection rules.

The presence of somewhat lengthened carbon-carbon bonds in cyclobutanes has provided another interesting problem. Values as high as 1.60 Å have been reported, (compared to a normal value of 1.53 to 1.54 Å) but some of these values are likely not of the greatest precision. This effect is attributed to nonbonded carbon-carbon repulsion.[13] Another explanation is the larger p contribution in the hybridized orbitals of the carbon-carbon bonds.

Difficulty in refining data from cyclobutane systems is observed, and most workers have resorted to anisotropic temperature

parameters (which are quite large in some cases) to reduce the residual to an acceptable level.[8,9,12,14,15]

Results of studies of aliphatic dicarboxylic acids ($C_6$-$C_{10}$) indicate the oxygens of the carboxyl groups have intermediate value temperature factors perpendicular to the plane of the hydrogen bonded acid groups. There also appears to be a significant degree of freedom perpendicular to the chain of these molecules which produces anisotropic temperature movement of the entire chain.[19-22]

Similar phenomena have been observed in studies of the corresponding amides.[23,24] Both the nitrogen and oxygen atoms have rather large movements, which are accompanied by a lesser anisotropic movement of the entire chain.

As previously mentioned, trans-1,3-cyclobutanedicarboxylic acid contains a planar cyclobutane ring. The structure of this compound has been determined by Margulis with the symbolic addition method, using film data.[34] Scintillation counter data was used for final refinement of the structure.

The acid crystallizes in space group $P2_1/c$, and has two molecules per unit cell. Consequently, each molecule must be centrosymmetric such that the center of symmetry corresponds with the center of symmetry of the unit cell.

The trial structure of the present work was determined from a plot of the Patterson function, before publication of the study of Margulis and Fischer. Our refined structure is based on a larger amount of data, and is therefore more accurate. We further wished to examine the large anisotropic movement of the cyclobutane system

and, if possible, relate this effect to the structure. For these reasons we continued our study.

## CHAPTER II

## EXPERIMENTAL

A sample of trans-1,3-cyclobutanedicarboxylic acid, m.p. 190-191°, was obtained from Dr. J. J. Bloomfield. A small crystal (0.3 and 0.05 mm as the largest and smallest dimension) was used for the intensity measurements. A larger crystal was later used to remeasure certain unobserved or low intensity reflections.

A General Electric XRD-5 X-ray diffraction unit fitted with an SPG spectrogoniometer and a single crystal orienter was used for the experimental work. The radiation used for these measurements was copper $K_{alpha}$ (1.5418 Å).

The space group was determined to be $P_{2_1/c}$ by the systematic absence of the following types of reflections: hOl, $l \neq 2n$; OkO, $k \neq 2n$.[25]

The crystal has the following cell dimensions:

$a^* = .19228 \pm .00006$ Å$^{-1}$

$b^* = .12785 \pm .00005$ Å$^{-1}$

$c^* = .12879 \pm .00004$ Å$^{-1}$

$\beta^* = 72.56 \pm 0.02°$

$a = 5.452 \pm .002$ Å

$b = 7.822 \pm .003$ Å

$c = 8.139 \pm .003$ Å

$\beta^* = 107.44 \pm .02°$

The density of the acid was determined by the flotation method to be 1.438 g/ml. If the number of molecules in the unit cell is assumed to be 2, the calculated density is 1.441 g/ml.

A total of 630 reflections were measured using a theta-2 theta scan.* All reflections with 2 theta value less than 145° were observed.

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*A total of 650 reflections were included for the final refinement steps using the program of Ahmed and workers.[35] (See Appendix B)

## CHAPTER III

## TREATMENT OF DATA

The data was put on the same relative scale. No correction for absorption was made because of the absence of heavy atoms and the small size of the crystal. Lorentz-polarization corrections were applied directly to the intensity data. These corrections were made with the following relations:

$$L.P. = \frac{1 + \cos^2 2\theta}{2 \sin 2\theta} \qquad (1)$$

and

$$|F_{hkl}|^2 = (1/L.P.)\ I_{hkl}. \qquad (2)$$

$I_{hkl}$ is the observed intensity value for each reflection.

The multiplicity was then assigned for all reflections. Reflections of the type hkl,0kl, and hk0 have multiplicity of 4, h0l 2, and 0k0, 00l, or h00 2.

Scattering factors were calculated at this stage for later use.

Squaring the amplitude values broadens the peaks (in a Patterson synthesis) and a sharpening factor must be introduced to sharpen the peaks without introducing large secondary maxima. The Patterson function was sharpened by the following relation:

$$|F_{hkl}|^2 = (Z/\sum n_i f_i)^2 \quad \exp \frac{P \sin^2 \theta}{\lambda^2} \qquad (3)$$

where Z is the total number of electrons, $f_i$ is the scattering factor for each atom, and $n_i$ is the number of each atom. P is an adjustable parameter assigned a value of zero in this case. Thus the sharpening factor reduces to:

$$|F_{jkl}|^2 = (Z/\sum n_i f_i)^2 \qquad (4)$$

The Patterson synthesis may be expressed in general form as:

$$P(u\ v\ w) = 1/V^2 \sum_h \sum_k \sum_l |F_{hkl}|^2 \cos 2\pi(hu+kv+lw) \qquad (5)$$

This form readily shows the relation necessary to calculate the Patterson synthesis but must be changed to a product form to reduce the time necessary for computer calculation. For a monoclinic space group, equation (5) may be written as a sum of two terms with $|F_{hkl}|^2$ and $|F_{hk\bar{l}}|^2$.

$$P(u\ v\ w) = 4/V \sum_h \sum_k \sum_l \left\{ |F_{hkl}|^2 \cos 2\pi(hu+lw) + |F_{hk\bar{l}}|^2 \cos 2\pi(-hu+lw) \right\} \cos kv \qquad (6)$$

This further expanded to:

$$P(u\ v\ w) = 4/V \sum_h \sum_k \sum_l \left\{ |F_{hk\bar{l}}|^2 + |F_{hkl}|^2 \right\} \cos 2\pi hu \cos 2\pi kv \cos 2\pi lw + \left\{ |F_{hk\bar{l}}|^2 - |F_{hkl}|^2 \right\} \sin 2\pi hu \cos 2\pi kv \sin 2\pi lw. \qquad (7)$$

The three dimensional Patterson synthesis was calculated for u from 0.00-1.00, for v from 0.00-0.50 and for w from 0.00-0.50 with intervals respectively of 0.04, 0.02 and 0.02. This comprised the asymmetric unit.

## Interpretation of the Patterson Synthesis

The symmetry of the Patterson synthesis is $P_{2/m}$. The space group for trans-1,3-cyclobutanedicarboxylic acid has been determined $P_{2_1/c}$, a space group with four equivalent positions. The number of molecules in the unit cell has been calculated to be two. Thus, the center of symmetry of the molecule must coincide with the center of symmetry of the space group. Therefore, only two oxygen and three carbon atoms must be located, as the other five atoms are related by a center of symmetry. The four equivalent positions in $P_{2_1/c}$ are:

$$x,y,z;\ \bar{x},\bar{y},\bar{z};\ \bar{x},1/2+y,\ 1/2-z;\ \text{and}\ x,\ 1/2-y,\ 1/2+z. \qquad (8)$$

The symmetry peaks for each atom arising from (8) are:[26]

| | u | v | w | |
|---|---|---|---|---|
| (9) | 2x | 2y | 2z | center of symmetry |
| (10) | 2x | 1/2 | 1/2+2z | two fold screw axis (Harker section) |
| (11) | 0 | 1/2 + 2y | 1/2 | c-glide plane (Harker line) |

Thus a plot of the vector density versus v at w = 0.5 and u = 0 shows maxima from which one may calculate the value of y. This line is called the Harker line.

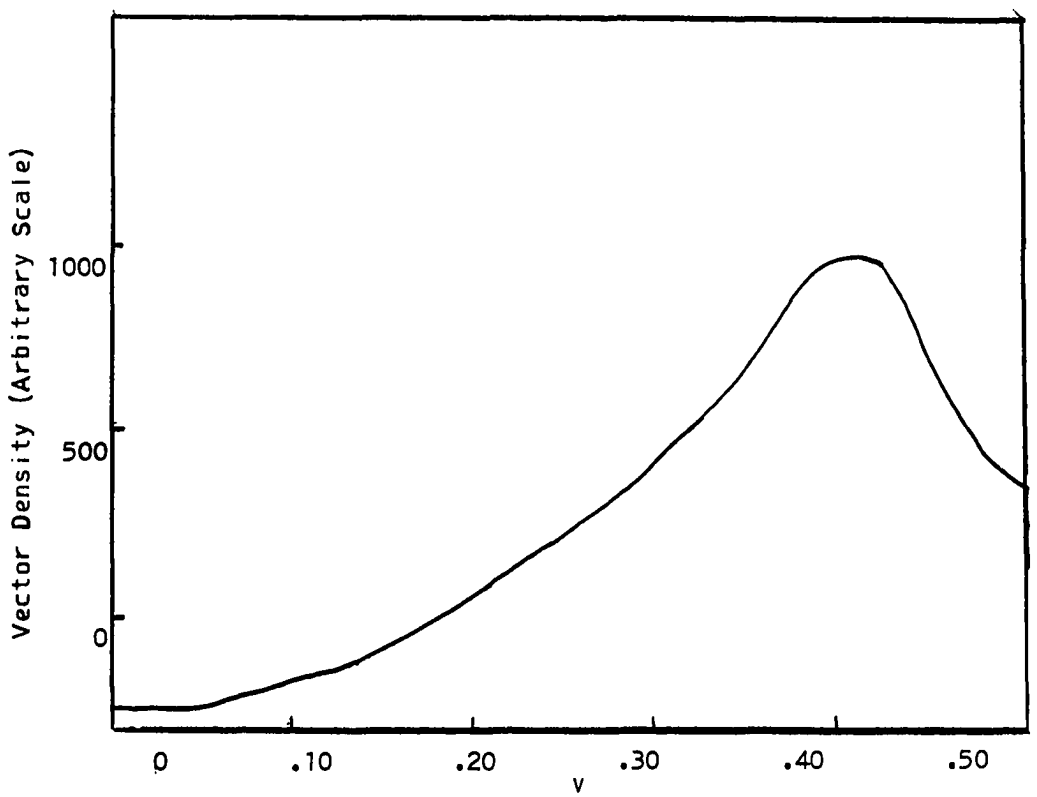



Figure 2. Plot of Vector Density versus v. (Harker line)

For the present structure this plot provided a broad maximum at v = 0.40. By formula (10) the value of y is 0.05. The value of y and the type plot observed above indicate the molecule largely lies near the y = 0 plane.

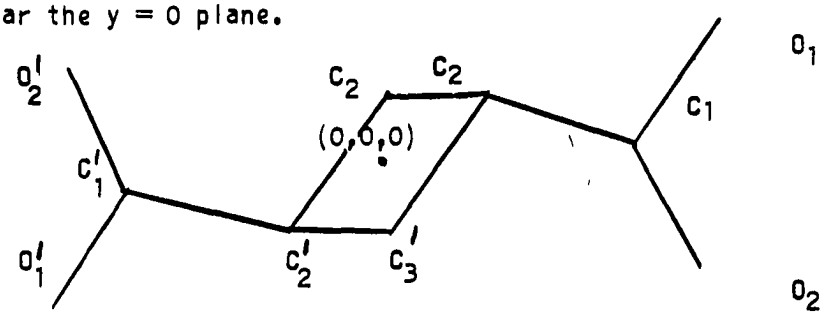



Figure 3. Model Chosen from the Patterson Synthesis.

The Patterson was interpreted by looking for the following features: A vector of 2.65 Å between $O_1$ and $O_2'$ (This indicates that it is related to $O_2$ by a center of symmetry) and $O_2$-$O_1'$ are expected as the result of two hydrogen bonded acid groups around a center of symmetry. Furthermore, a set of vectors lying in one plane and with angles of approximately 120° is expected as a result of the carboxyl group itself. $O_1$-$C_2$ and $O_2$-$C_2$ (2.35-2.40 Å) and $O_1$-$O_2$ (2.25 Å). The last three vectors may be seen in Figures 5 and 6 as maxima at u, v, w coordinates: (a) 0.36, 0.08, 0.20; (b) 0.03, 0.04, 0.28; and (c) 0.67, 0.12, 0.08. These determine the relative orientation of the molecule. The assignment of peak d, (0.25, 0.02, 0.34), in Figure 5 as the $O_1$-$O_2'$ and $O_2$-$O_1'$ peak determines the location of the three atoms. For example:

$$.36 = XO_1\text{-}XC_2 \tag{12}$$

$$.03 = XO_2\text{-}XC_2 \tag{13}$$

$$.33 = XO_1\text{-}XO_2 \tag{14}$$

$$.25 = (1\text{-}XO_2) - XO_1 \tag{15}$$

Formula (14) and (15) yield $XO_2 = .21$ and $XO_1 = .54$. Inserting these values in (12) and (13) gives $XC_2 = .18$. The y and z coordinates of these three atoms can be calculated in a similar manner. The location of three atoms automatically determines the location of $C_1$, which is confirmed by peak e (0.14, 0.00, 0.18) in Figure 5. The x, y and z values of these four atoms are listed in Table 1. All 36 vectors which can be calculated from these locations were observed in the Patterson synthesis.

Table 1

Coordinates of Atoms Determined from Patterson Synthesis

| Atom | x | y | z |
|---|---|---|---|
| $O_1$ | .54 | .95 | .29 |
| $O_2$ | .21 | .07 | .37 |
| $C_1$ | .32 | .03 | .27 |
| $C_2$ | .18 | .03 | .09 |
| $C_3$ | .06 | .86 | .99 |

The location of $C_3$ was more difficult. By considerations of its probable location from the model, the position was obtained. The vectors for this atom were weak but were present.

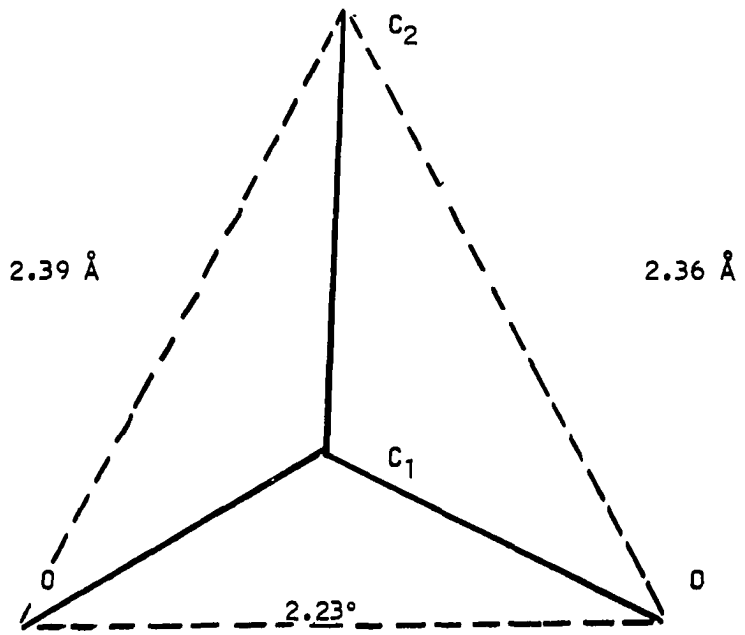



Figure 4. Model Used for Calculation of Vectors for Patterson Synthesis

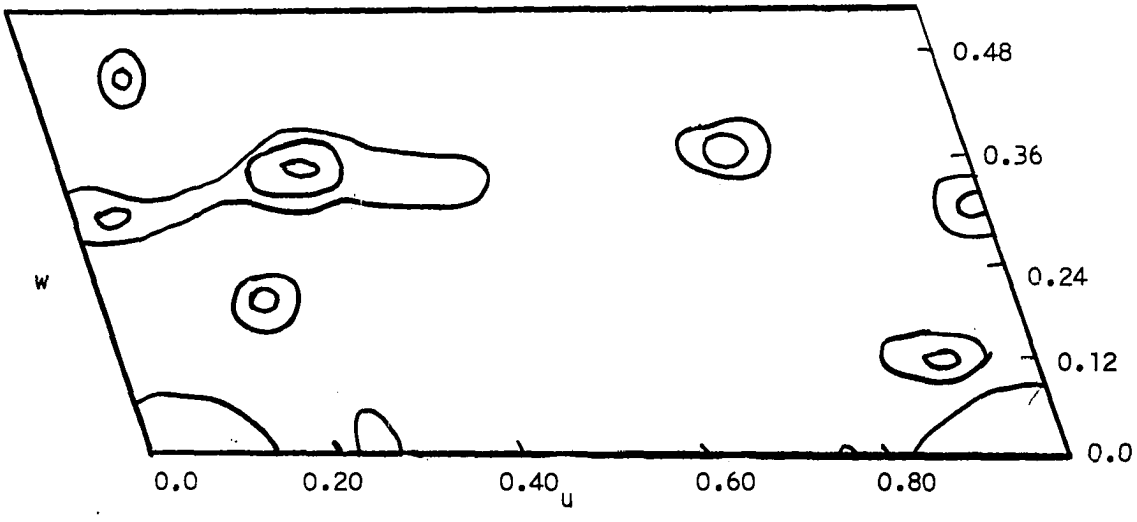



Figure 5. Patterson Synthesis. Arbitrary scale. v=0.02. Contours on 200, except at the origin.

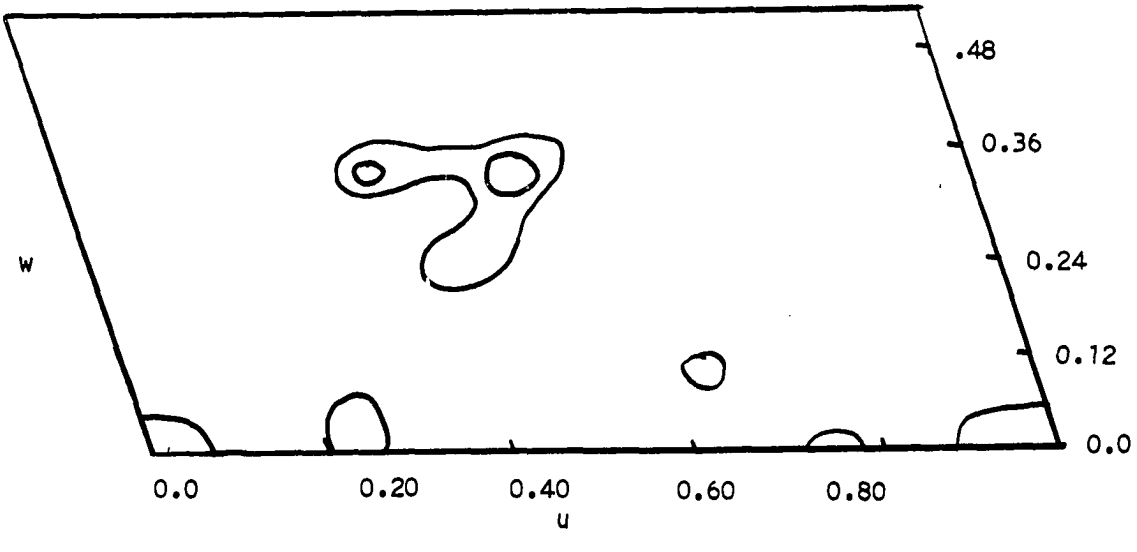



Figure 6. Patterson Synthesis. Arbitrary scale. v=0.08. Contours on 200, except at the origin.

Table 2

Vectors Calculated for Patterson Synthesis

| Vectors | u | v | w |
|---|---|---|---|
| $O_1$-$O_1$ | .92 | .10 | .42 |
| | .08 | .50 | .08 |
| | .00 | .40 | .50 |
| $O_1$-$O_2$ | .67 | .12 | .08 |
| | .25 | .02 | .34 |
| | .75 | .38 | .16 |
| | .33 | .48 | .42 |
| $O_2$-$O_2$ | .58 | .14 | .26 |
| | .42 | .50 | .24 |
| | .00 | .36 | .50 |
| $O_1$-$C_1$ | .22 | .08 | .02 |
| | .14 | .02 | .44 |
| | .86 | .42 | .48 |
| | .78 | .48 | .48 |
| $O_1$-$C_2$ | .36 | .08 | .20 |
| | .72 | .02 | .38 |
| | .28 | .42 | .12 |
| | .64 | .48 | .30 |

Table 2--(Continued)

| Vectors | u | v | w |
|---|---|---|---|
| $O_2$-$C_1$ | .89 | .04 | .10 |
| | .47 | .10 | .36 |
| | .53 | .46 | .14 |
| | .11 | .40 | .40 |
| $O_2$-$C_2$ | .03 | .04 | .28 |
| | .39 | .10 | .46 |
| | .61 | .46 | .04 |
| | .97 | .40 | .22 |
| $O_1$-$C_3$ | .48 | .09 | .30 |
| | .60 | .19 | .28 |
| | .40 | .41 | .22 |
| | .52 | .31 | .20 |
| $O_2$-$C_3$ | .15 | .21 | .38 |
| | .27 | .07 | .36 |
| | .73 | .29 | .14 |
| | .85 | .43 | .12 |
| $C_1$-$C_1$ | .36 | .06 | .46 |
| | .64 | .50 | .04 |
| | -.00 | .44 | .50 |

Table 2--(Continued)

| Vectors | u | v | w |
|---|---|---|---|
| $C_1$-$C_2$ | .14 | .00 | .18 |
| | .50 | .06 | .36 |
| | .50 | .50 | .14 |
| | .86 | .44 | .32 |
| $C_1$-$C_3$ | .26 | .17 | .28 |
| | .38 | .11 | .26 |
| | .62 | .33 | .24 |
| | .74 | .39 | .22 |
| $C_2$-$C_2$ | .36 | .06 | .18 |
| | .64 | .50 | .32 |
| | .00 | .44 | .50 |
| $C_2$-$C_3$ | .12 | .17 | .10 |
| | .24 | .11 | .08 |
| | .76 | .33 | .42 |
| | .88 | .39 | .40 |
| $C_3$-$C_3$ | .88 | .28 | .02 |
| | .12 | .50 | .48 |
| | .00 | .22 | .50 |

## Calculation of Structure Factors

Structure factors may be calculated by a relation such as (16), which has been written as two exponential factors, a geometric and a temperature movement portion. The scattering factors, $f_j$, have been previously calculated, and tabulated.[22]

$$F_{hkl} = \sum_j f_j \exp 2\pi i (hx_j+ky_j+lz_j) \exp - B_j \sin^2\theta/\lambda \qquad (16)$$

The values of h, k, l , and $x_j, y_j$, and $z_j$ are from the Patterson synthesis known for each atom. The initial values for $B_j$, the isotropic temperature parameter for each atom was assumed to be 1.700.

For a centrosymmetric space group, (16) reduces to:

$$F_{hkl} = \sum_{j=1}^{J/2} f_j \cos 2\pi(hx_j+ky_j+lz_j) \exp - B_j \sin^2\theta/\lambda \qquad (17)$$

The check of the coordinates determined from the trial structure was made by the calculation of structure factors and the residual, R:

$$R = \sum |F_o - F_c| \; / \sum |F_o| = 0.44 \qquad (18)$$

where the $F_o$ are the observed and $F_c$ the calculated amplitudes.

In practice these calculations were made by the procedure of van der Helm,[28] which closely paralleled the work of Cruickshank.[29]

A least squares refinement was used to obtain the coordinate and temperature parameter shifts. This procedure has been described by Lipson and Cochran.[30]

Early refinements were made on the five carbon and oxygen atoms with isotropic temperature parameters. After five refinements the R value had stabilized at about 0.34. The logical routine of the program was changed to include reflections with lower $F_o$ values, and after eight more refinements the R value had decreased to approximately 0.24, and stabilized.

At this point anisotropic temperature factors were introduced. With nine additional refinements the R value was reduced to 0.16. Three hydrogen atoms were put into the structure at this point.

Table 3

Coordinates of Hydrogen Atoms*

| Atom | x | y | z |
|---|---|---|---|
| $H_1$ | .3130 | .1230 | .0210 |
| $H_2$ | .8470 | .1520 | .1210 |
| $H_3$ | .8900 | .2290 | .9430 |

*The positions for the hydrogen atoms were taken from Margulis and Fischer: T. N. Margulis and M. S. Fischer, J. Am. Chem. Soc., 89, 223 (1967).

Following a complete check of the data, several values for the structure factor input were corrected and a few duplicate values were removed. After four refinements the R value fell to 0.084.

A total of twenty-eight refinement steps were conducted.

## The Fourier Synthesis

By use of the phases from the calculated $F_c$'s one may calculate the electron density at any point in the unit cell with a Fourier synthesis.

k+l = even

$$\rho(x\ y\ z) = 4/V \sum_{h=0}^{\infty} \sum_{k=0}^{\infty} \sum_{l=0}^{\infty} F_{hkl} \cos 2\pi(hx + lz) \cos 2\pi ky - F_{hk\bar{l}} \cos 2\pi(lz-hx) \cos 2\pi ky \tag{19}$$

k+ l = odd

$$\rho(x\ y\ z) = 4/V \sum_{h=0}^{\infty} \sum_{k=0}^{\infty} \sum_{l=0}^{\infty} - F_{hkl} \sin 2\pi(hx + lz) \sin 2\pi ky + F_{hk\bar{l}} \sin 2\pi(lz-hx) \sin 2\pi ky \tag{20}$$

As in the Patterson function, these equations are put into the product form, which is more suitable for calculation on a computer.

By using the differences in the $F_c$ and $F_o$ values one can calculate a difference Fourier synthesis, which shows any errors or omissions in the model used to calculate the set of $F_c$'s.

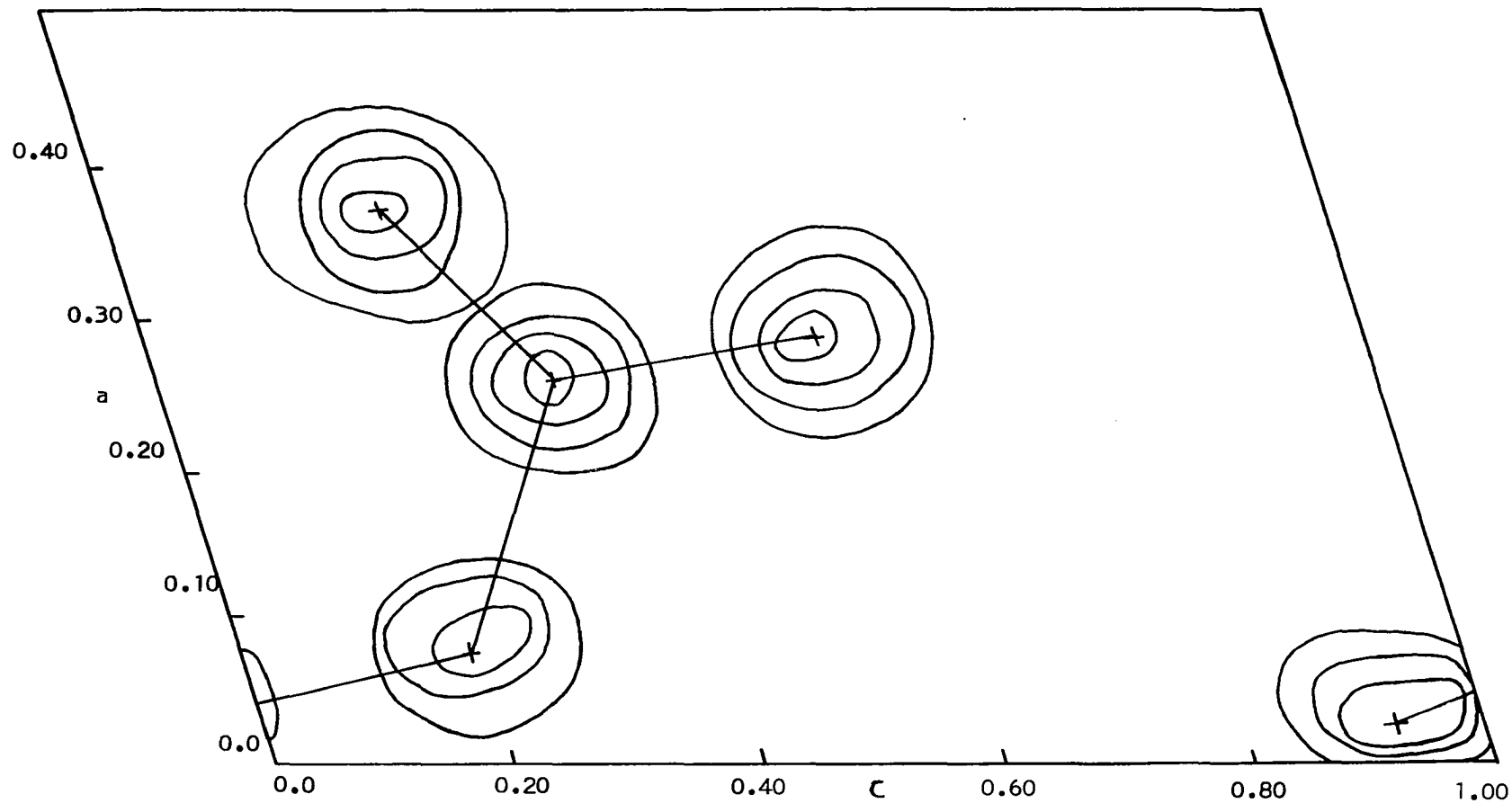



Figure 7. Composite drawing of Fourier Synthesis
Contours on 2.0 electrons per $\AA^3$.

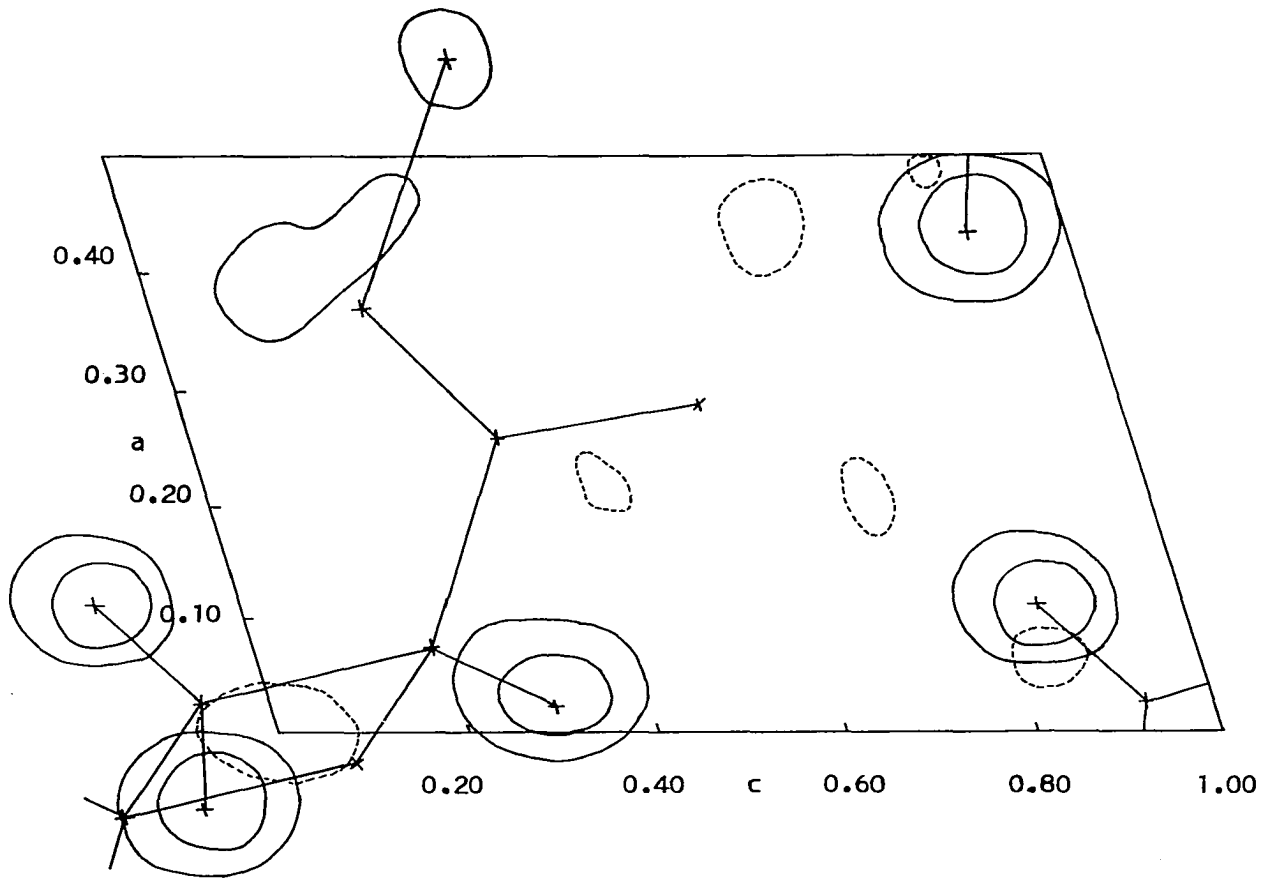



Figure 8. Composite drawing of difference Fourier Synthesis. Contours on 0.25 electrons per $Å^3$. Dotted lines represent negative values.

The three dimensional Fourier and difference Fourier syntheses were calculated for x from 0.00-1.00, for y from 0.00-0.50, and for z from 0.00-0.50 with intervals respectively of 0.04, 0.02, and 0.02. This comprised the asymmetric unit.

The difference Fourier synthesis was calculated for the three hydrogen atoms already included in the structure, as well as the fourth hydrogen atom, which was previously not located. The three hydrogens were found to be in the correct location and had electron densities of 0.6-0.7 electrons $\mathring{A}^3$, at their respective maxima. The coordinates of the carboxyl hydrogen (as determined from the difference Fourier synthesis are ( .38, .06, .58). The electron density at its maximum was slightly less than that for the other three atoms, possibly because of the large anisotropic temperature factor associated with this atom.

The Fourier synthesis was performed for the five carbon and oxygen atoms. All atoms were shown to be in the proper location.

Composite drawings of the difference Fourier and Fourier syntheses are found in Figures 7 and 8.

## Programs

Most of the computations necessary for this work were done on IBM 1620, 1410, and 360 computers, largely with programs provided by Dr. D. van der Helm and his research group. The following programs were used:

A goniostat setting program used the values for the cell parameters and space group data to calculate numerical values of 2 theta, chi and phi for each set of h k l values. This program, similar to that of Johnson,[31] was written by P. Schapiro, and was run on an IBM 1410 computer.

The L. P. program required data from the intensity measurements and made Lorentz-polarization corrections. It then assigned multiplicities, calculated scattering factors and provided output which was used for a Patterson synthesis and for structure factor calculations.

The structure factors and least squares treatments were calculated by the program of van der Helm.[28]

This method calculates the contributions of the atoms in the asymmetric unit of the unit cell with the basic structure equation of $P_1$, while each group of symmetry related atoms is simulated with a set of equivalent indices, by means of a matrix and in the case of a screw axis or glide plane with an additional translation vector. Each set of indices is substituted in the basic formula and the contributions are added to give the structure factor for the entire unit cell.

This program provides the phases from which one may make a Fourier synthesis.

The program used for the Fourier and Patterson syntheses was written by D. van der Helm[32] and modified by G. S. D. King[33] for card input and output.

Because of the limited storage of the IBM 1620 computer, the program makes the necessary summations in sections. Calculations are made for one section, and the data must be reintroduced for subsequent sections. The first sum is calculated over $h$ for each set of $kl$ values, for a particular value of $x$ for each section. These values are used in the second summation made over $k$ for the required values of $y$. The third sum is for the values of $z$ for the section and is

over l. The summation sequence can be interchanged by an appropriate change in the input cards.

A program for the calculation of accurate cell parameters and their estimated standard deviation was run on the IBM 360 computer.

The important planes of the molecule were calculated with a least squares program which minimizes the sums of the deviations of points from a plane. The above two programs were written and provided by T. Willoughby.

Intramolecular distances and angles were calculated by means of a program written by W. Franks. Intermolecular distances were calculated by a program written by G. Shepherd. These programs were both adopted for and run on an IBM 360 computer.

The values of B for each axis of the ellipsoids, the unit vectors and the direction cosines were calculated from the cell parameters and the anisotropic temperature parameters, with a program written by W. Franks. This program was run on an IBM 360 computer.

Further refinement of the data was accomplished with a program written by Ahmed and workers for the I B M 360 computer.[35] Several additional structure factor and least squares cycles were performed and the Fourier and difference Fourier syntheses were run.

## CHAPTER IV

## DISCUSSION

Trans-1,3-cyclobutanedicarboxylic acid crystallizes in the monoclinic space group $P_{2_1/c}$, with two molecules per unit cell. As mentioned previously, each molecule must be centrosymmetric such that the centers of symmetry corresponds with the centers of symmetry of the unit cell.

The crystal consists of long chains of molecules linked by hydrogen bonded carboxyl groups around centers of symmetry.

The final parameters of the atoms in the asymmetric unit (1/4 of the unit cell) are given in the following tables.

Table 4

Coordinates of Atoms of Asymmetric Unit

| Atom | x | y | z |
|---|---|---|---|
| $O_1$ | .5534 | .9616 | .2923 |
| $O_2$ | .2286 | .0682 | .3706 |
| $C_1$ | .3223 | .0298 | .2596 |
| $C_2$ | .1901 | .0490 | .0702 |
| $C_3$ | .0831 | .8780 | .9799 |

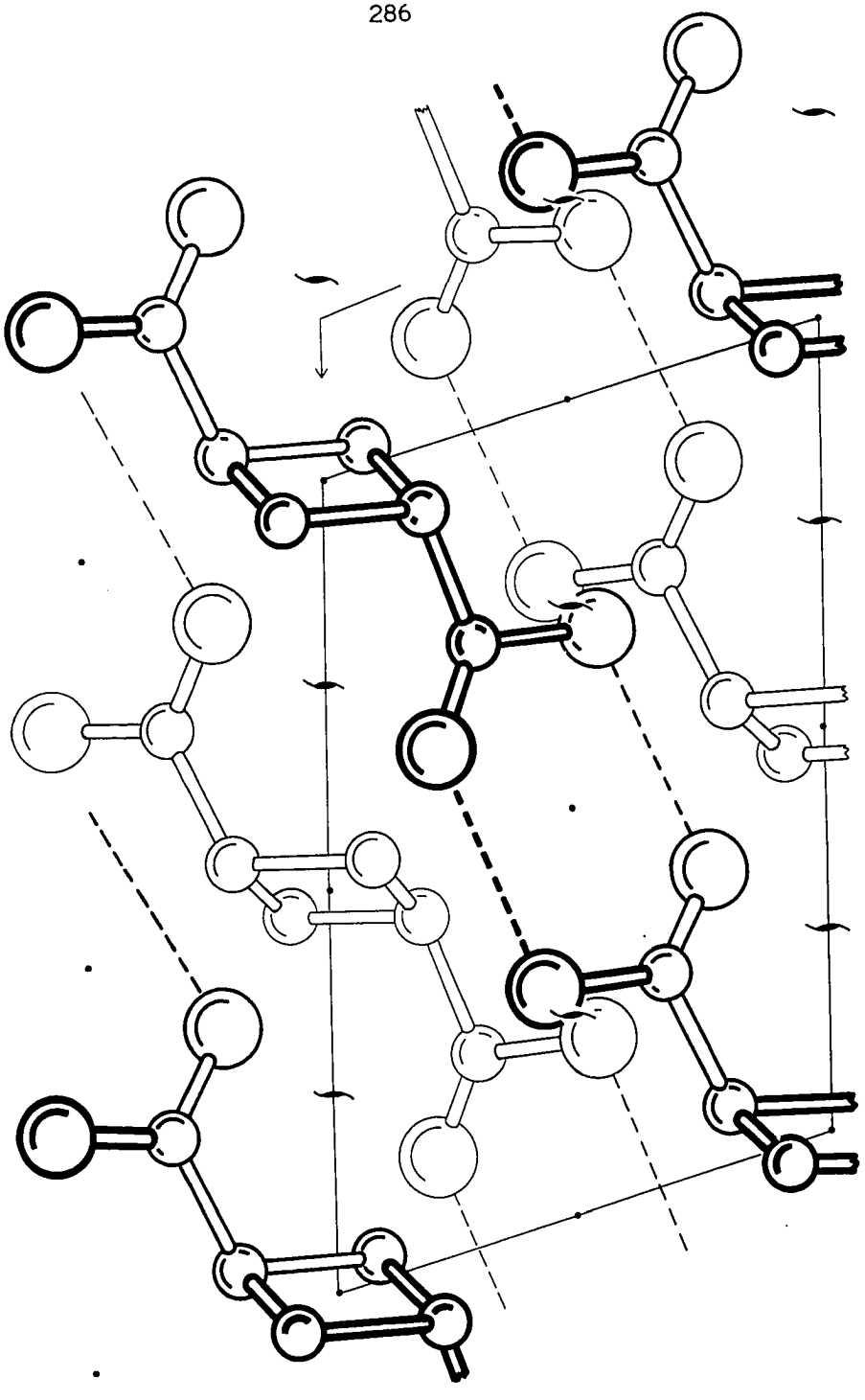


Figure 9. The Chain Structure of Trans-1,3-cyclobutane-dicarboxylic Acid viewed along $[\bar{1}\,0\,\bar{1}]$. The chain of molecules lies along $[1\,0\,1]$.

Table 5

Standard Deviations of Coordinates of Atoms ($X10^4$)

| Atom | x | y | z |
|---|---|---|---|
| $O_1$ | 6 | 5 | 4 |
| $O_2$ | 6 | 4 | 3 |
| $C_1$ | 7 | 4 | 4 |
| $C_2$ | 7 | 4 | 4 |
| $C_3$ | 7 | 5 | 5 |

The significant angles of the asymmetric unit were calculated. The results are listed in Table 6.

The bond lengths in many cyclobutanes are slightly longer than the values for these bonds in acyclic compounds. Margulis has reported those of trans-1,3-cyclobutanedicarboxylic acid are somewhat lengthened (average 1.555 $\pm$ 0.005). The values of the present study (average 1.542 $\pm$ 0.004 Å) do not show a significant lengthening. These values are compared to the average C=C bond length of 1.537 Å. given by Sutton.[15]

The values for the length of the cyclobutane C-C bonds can be corrected for thermal motion resulting in an increase of 0.005 Å.

Table 6

Angles of Molecule for Trans-1,3-cyclobutanedicarboxylic Acid

| Angle | Degrees |
|---|---|
| $O_1$-$C_1$-$O_2$ | 123.15 |
| $O_1$-$C_1$-$C_2$ | 112.34 |
| $O_2$-$C_1$-$C_2$ | 124.50 |
| $C_1$-$C_2$-$C_3$ | 113.28 |
| $C_3$-$C_2$-$C_3'$ | 89.99 |
| $C_2$-$C_3$-$C_2'$ | 90.01 |
| $C_1$-$C_2$-$C_3'$ | 115.92 |
| $C_1$-$C_2$-$H_1$ | 106.48 |
| $C_2$-$C_3$-$H_3$ | 116.64 |
| $H_1$-$C_2$-$C_3'$ | 111.96 |
| $C_2$-$C_3$-$H_2$ | 113.35 |
| $H_1$-$C_2$-$C_3$ | 119.02 |
| $H_2$-$C_3$-$H_3$ | 106.35 |

Table 7

Bond Lengths*

| Bond | Length (Å) |
|---|---|
| $O_1$-$C_1$ | 1.319 |
| $O_2$-$C_1$ | 1.203 |
| $C_1$-$C_2$ | 1.498 |
| $C_2$-$C_3$ | 1.552 |
| $C_2$-$C_3'$ | 1.531 |
| $H_1$-$C_2$ | 1.052 |
| $H_2$-$C_3$ | 1.030 |
| $H_3$-$C_3$ | 1.030 |

*The standard deviation of all C-C and O-O bonds is ± 0.004 Å (uncorrected).

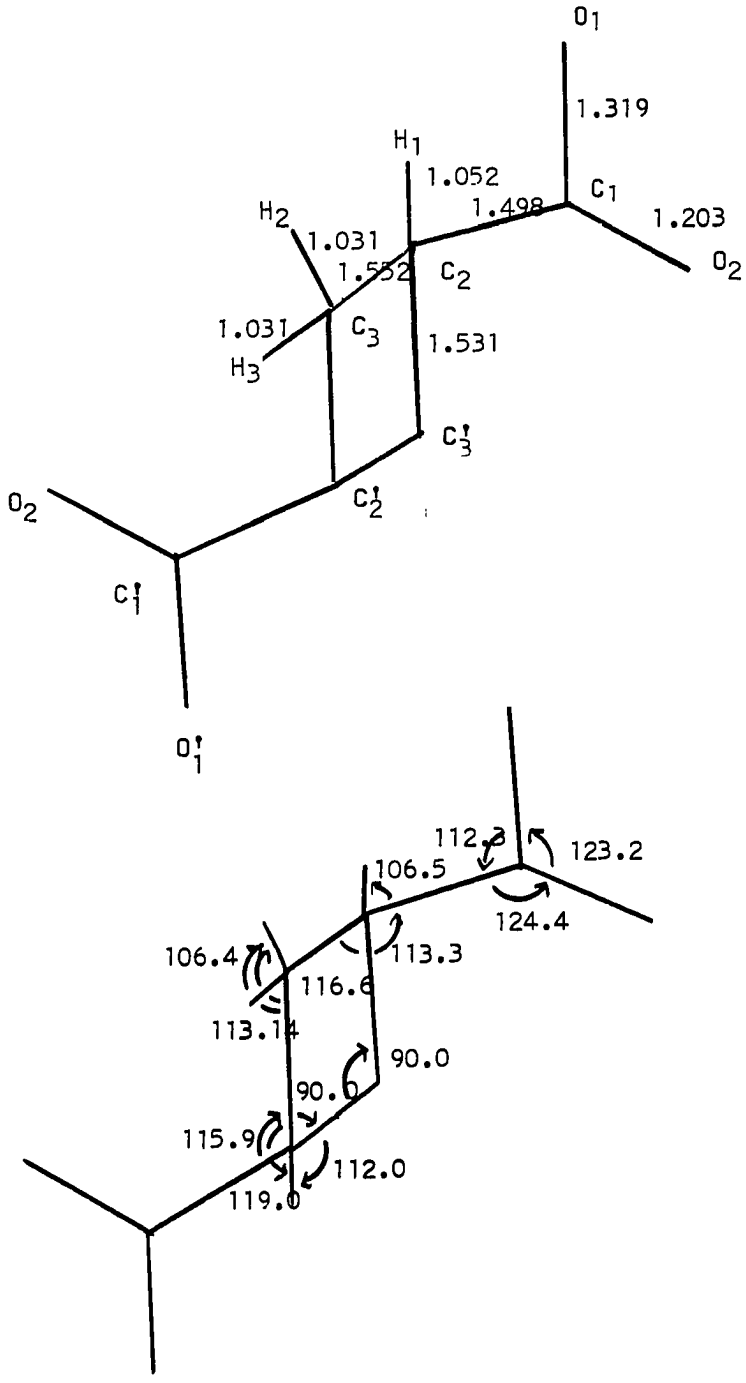



Figure 10. Bond Lengths and Angles of <u>trans</u>-1,3-cyclobutanedicarboxylic Acid.

Table 8

Selected Intramolecular Distances

| Atoms | Distance (Å) |
|---|---|
| $O_2$-$C_2$ | 2.392 |
| $O_1$-$O_2$ | 2.218 |
| $O_1$-$C_2$ | 2.341 |
| $O_1$-$H_1$ | 2.537 |
| $C_1$-$C_3$ | 2.546 |
| $H_1$-$H_2$ | 2.784 |
| $C_3$-$H_1$ | 2.257 |
| $O_2$-$C_3'$ | 2.874 |
| $C_1$-$C_1'$ | 4.624 |
| $C_3$-$C_3'$ | 2.180 |
| $C_2$-$C_2'$ | 2.180 |
| $C_1$-$H_2'$ | 2.670 |

The equations for planes will be given in the following form:

$$m_1x + m_2y + m_3z = d \qquad (21)$$

where d is the distance in Angstroms from the origin and x, y, and z are fractional coordinates.**

The equation for the plane of the cyclobutane ring is:

$$2.109\ x + 2.687\ y - 7.588\ z = 0 \qquad (22)$$

and the equation for the plane of the carboxyl group is:

$$2.179\ x + 7.177\ y - 0.741\ z = 0.716 \qquad (23)$$

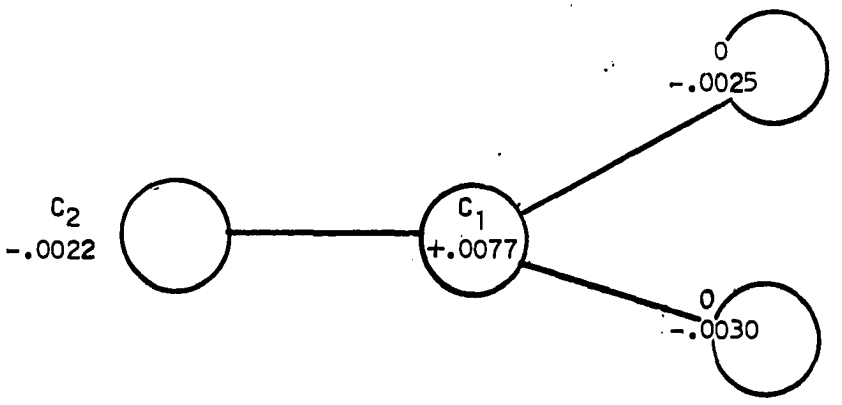



Figure 11. The Deviations of Atoms from plane of Carboxyl Group.

The atom $C_3$ (0.0831, 0.1220, 0.0201) is about 0.04 Å out of the plane of the acid group.

The equation of the plane of two carboxyl groups hydrogen bonded around a center of symmetry is:

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**Calculations made by Dr. Dick van der Helm.

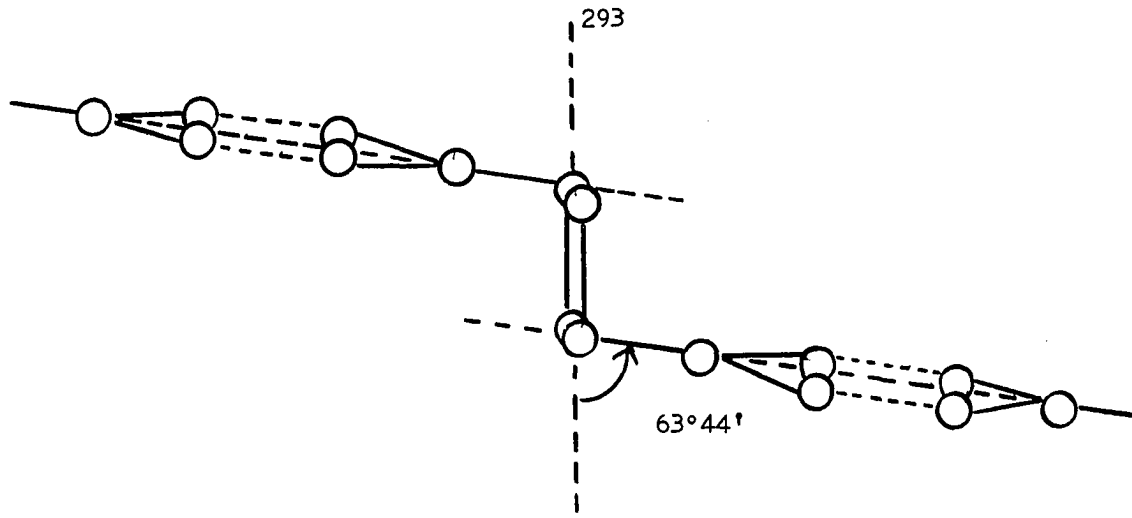



Figure 12. Angle between Planes of Carboxyl and Cyclobutane Rings.

$$2.177\ x + 7.178\ y - 0.750\ z = 0.714 \qquad (24)$$

The deviations of the eight atoms are also slight in this case, which indicates planarity of the ring formed by the two acid groups.

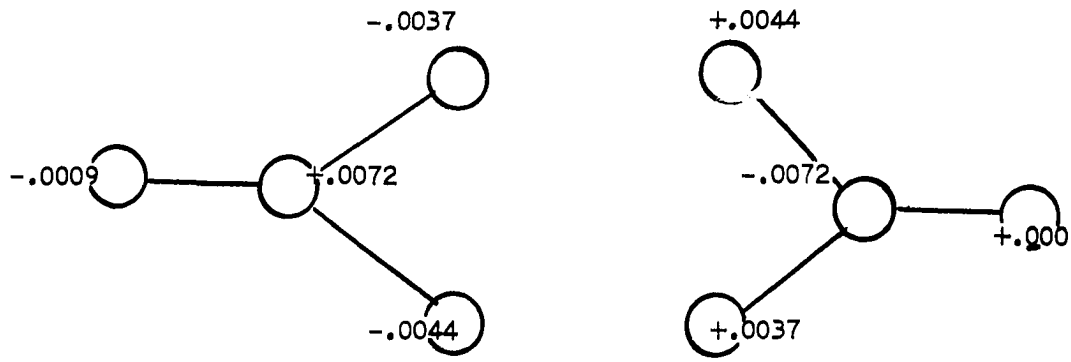



Figure 13. Deviations from Plane of Ring Formed by Hydrogen Bonded Acid Group.

Table 9

Important Intermolecular Distances

| From Atom | To Atom | Distance (Å) | Related By |
|---|---|---|---|
| $O_1$ | $O_2'$ | 2.649 | (a) (1/2,0,1/2) |
| $O_1$ | $C_1'$ | 3.502 | (a) (1/2,0,1/2) |
| $O_1$ | $O_1'$ | 3.983 | (b) (1/2,0,1/4) |
| $O_1$ | $C_2'$ | 3.560 | (b) (1/2,0,1/4) |
| $O_1$ | $C_1'$ | 3.495 | (b) (1/2,0,1/4) |
| $O_1$ | $O_2'$ | 3.687 | (b) (1/2,0,1/4) |
| $O_2$ | $O_1'$ | 2.649 | (a) (1/2,0,1/2) |
| $O_2$ | $O_2'$ | 4.728 | (b) (1/2,0,1/4) |
| $O_2$ | $C_1'$ | 4.661 | (b) (1/2,0,1/4) |
| $O_2$ | $C_2'$ | 4.847 | (b) (1/2,0,1/4) |
| $O_2$ | $C_3'$ | 3.390 | (c) |
| $O_2$ | $C_2'$ | 3.443 | (c) |
| $C_1$ | $C_2'$ | 3.292 | (a) (0,0,0) |
| $C_1$ | $O_1'$ | 4.394 | (b) (1/2,0,1/4) |
| $C_1$ | $C_1'$ | 4.414 | (b) (1/2,0,1/4) |
| $C_2$ | $O_2'$ | 4.750 | (b) (1/2,0,1/4) |
| $C_2$ | $C_3'$ | 4.144 | (d) |

(a) Center of symmetry
(b) Two fold screw axis
(c) Glide plane parallel to c axis
(d) Translation along a axis

Note: Only the closest distances are listed.

Table 9--(Continued)

| From Atom | To Atom | Distance (Å) | Related By |
|---|---|---|---|
| $C_3$ | $O_2'$ | 3.745 | (c) |
| $C_3$ | $C_1'$ | 4.319 | (d) |
| $C_3$ | $C_1''$ | 4.063 | (c) |
| $C_3$ | $C_3''$ | 3.831 | (d) |

(a) Center of symmetry

(b) Two fold screw axis

(c) Glide plane parallel to c axis

(d) Translation along a axis.

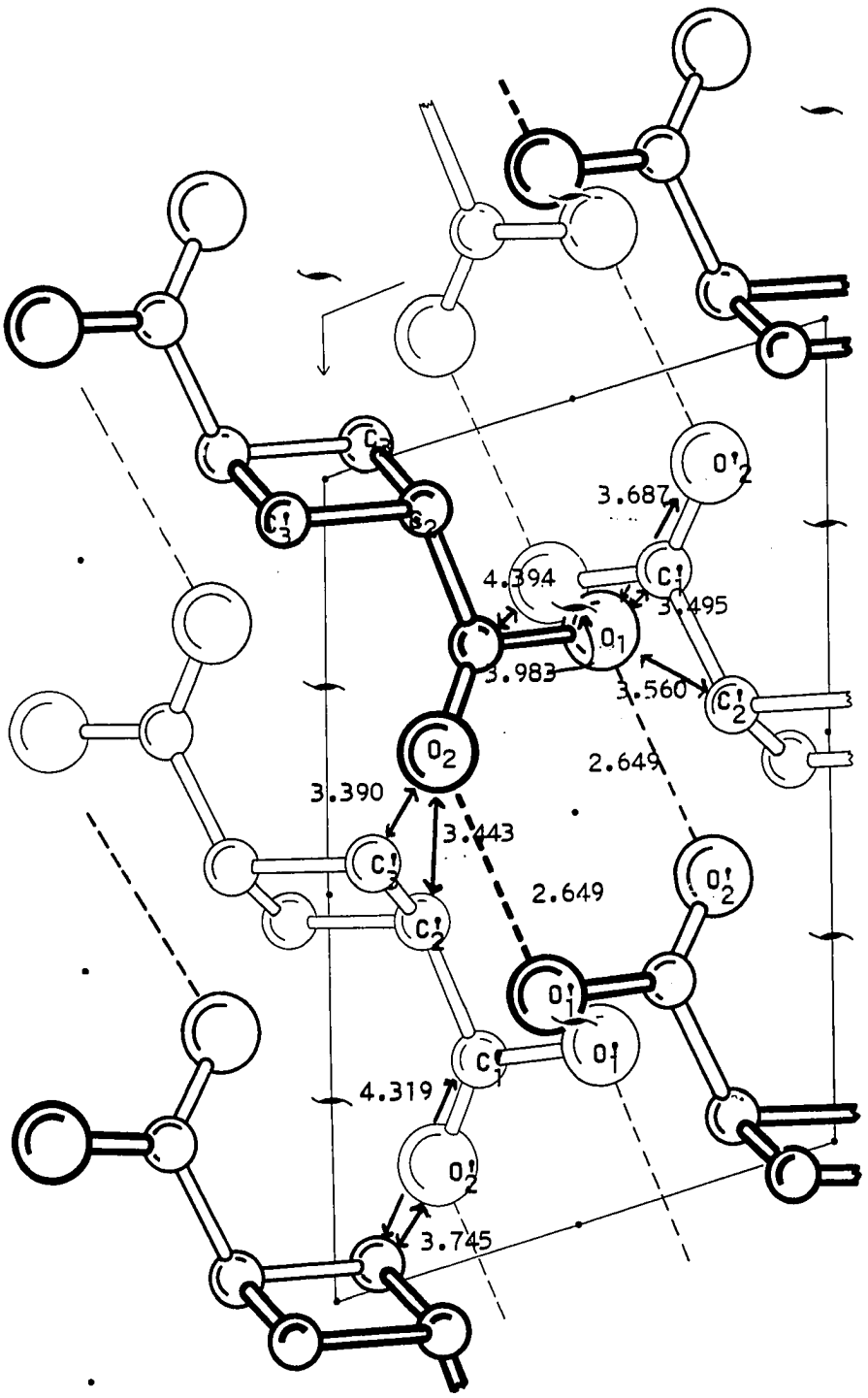



Figure 14. Intermolecular Distances in Unit Cell of <u>trans</u>-1,3-cyclobutanedicarboxylic acid

The atoms of trans-1,3-cyclobutanedicarboxylic acid have a rather large anisotropic temperature movement. Part of the purpose of this study was to determine the nature and magnitude of this effect. The anisotropic temperature factors and their standard deviations are listed below.

Table 10

Anisotropic Temperature Parameters

| Atom | $\beta_{11}$ | $\beta_{12}$ | $\beta_{13}$ | $\beta_{22}$ | $\beta_{23}$ | $\beta_{33}$ |
|---|---|---|---|---|---|---|
| $O_1$ | .0334 | .0243 | .0026 | .0353 | -.0028 | .0118 |
| $O_2$ | .0385 | .0171 | .0001 | .0280 | .0003 | .0100 |
| $C_1$ | .0277 | .0016 | .0033 | .0150 | -.0021 | .0107 |
| $C_2$ | .0315 | -.0026 | .0047 | .0147 | .0017 | .0097 |
| $C_3$ | .0370 | .0102 | .0014 | .0145 | -.0028 | .0110 |

Table 11

Standard Deviations of Anisotropic Temperature Parameters ($\times 10^4$)

| Atom | $\beta_{11}$ | $\beta_{22}$ | $\beta_{33}$ | $\beta_{23}$ | $\beta_{13}$ | $\beta_{12}$ |
|---|---|---|---|---|---|---|
| $O_1$ | 9 | 6 | 4 | 7 | 8 | 11 |
| $O_2$ | 9 | 5 | 3 | 6 | 8 | 10 |
| $C_1$ | 9 | 4 | 4 | 7 | 10 | 10 |
| $C_2$ | 10 | 4 | 4 | 6 | 9 | 10 |
| $C_3$ | 11 | 4 | 4 | 7 | 10 | 11 |

The six anisotropic temperature factors for each atom allow the temperature movement for each atom to be described by an ellipsoid. It is possible to determine the three main axes of these ellipsoids and these are given for each atom in the table below. In addition, the components of the unit vector of each axis are given with respect to the real axes of the crystal system. The values listed for each B are the values $n_i$ in the equation:

$$\vec{n} = n_1 \vec{a} + n_2 \vec{b} + n_3 \vec{c}, \qquad (25)$$

where $|n|\,|n| = 1$.

The question of planarity versus puckering for cyclobutane systems has been the subject of many studies. In at least one case involving a non-planar cyclobutane the question has been raised as to whether the nonplanarity is "static" or "dynamic." The above study was done on cyclobutane in the gas phase, and the "dynamic" hypothesis appears to have some possibility.[18,13]

In the case of the chloroiron derivative of tetraphenylporphine an unusually large temperature movement was explained by locating half iron atoms and two sets of half oxygen atoms on both sides of the plane rather than in the plane.[14]

The possibility of a puckered cyclobutane ring in <u>trans</u>-1,3-cyclobutanedicarboxylic acid such that the puckering was equally likely in two directions was considered.

It is readily shown with models that only one puckering is possible. Moving atoms 3 and 3′ has an identical effect to moving 2 and 2′.

Table 12

Values of B and Unit Vectors (Real)

| Atom | B | Unit Vectors | | |
|---|---|---|---|---|
| $O_1$ | 9.596 | .064 | .117 | -.011 |
| | 3.562 | -.106 | .046 | .070 |
| | 2.487 | .145 | -.018 | .107 |
| $O_2$ | 7.560 | .077 | .115 | -.001 |
| | 3.848 | .154 | -.054 | -.020 |
| | 2.374 | .083 | -.007 | .127 |
| $C_1$ | 3.992 | .085 | .093 | -.045 |
| | 3.366 | -.113 | .085 | .032 |
| | 2.305 | .128 | .013 | .116 |
| $C_2$ | 4.082 | .126 | -.077 | -.028 |
| | 3.354 | .110 | .100 | -.004 |
| | 2.251 | .091 | -.013 | .125 |
| $C_3$ | 5.421 | -.135 | -.062 | .035 |
| | 2.978 | -.079 | .111 | .016 |
| | 2.422 | .110 | .003 | .122 |

Table 13

Direction Cosines for Anisotropic Temperature Movements

| Atom | Direction Cosine | | |
|---|---|---|---|
| $O_1$ | .379 | .921 | -.194 |
| | -.752 | .362 | .745 |
| | .535 | -.143 | .635 |
| $O_2$ | .429 | .902 | -.113 |
| | .889 | -.426 | -.414 |
| | .149 | -.055 | .897 |
| $C_1$ | .576 | .735 | -.509 |
| | -.697 | .669 | .445 |
| | .421 | .103 | .734 |
| $C_2$ | .961 | -.607 | -.437 |
| | .615 | .786 | -.216 |
| | .196 | -.109 | .877 |
| $C_3$ | -.825 | -.489 | .508 |
| | -.472 | .871 | .262 |
| | .304 | .025 | .818 |

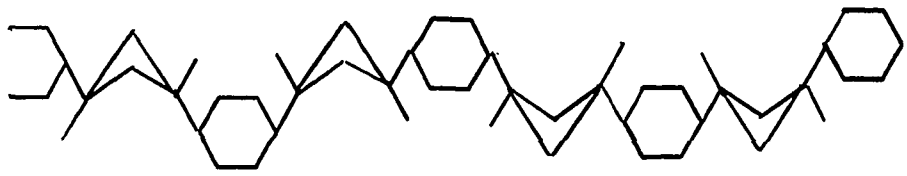


Figure 15. Random Distribution of Two Possible Puckered Forms of trans-1,3-cyclobutane-dicarboxylic Acid

Preliminary calculations indicate that the anisotropic movement is largely perpendicular to the plane of the carboxyl groups, essentially excluding any contributions from puckered structures.

Table 14

Angles Formed Between Main B Axis and Perpendicular to Plane of Carboxyl Group*

| Acid | Angle | At Carboxyl Atom |
|---|---|---|
| Trans-1,3-cyclobutanedicarboxylic acid | 9° 43' | $O_1$ |
| | 0° | $O_2$ |
| Cis-1,2-cyclobutanedicarboxylic acid | 17° 40' | $O_1$ |
| | 13° 35' | $O_2$ |
| | 13° 55' | $O_9$ |
| | 22° 30' | $O_{10}$ |

*The structure of the cis-1,2-diacid has been determined by J. Sims and D. van der Helm.

In cis-1,2-cyclobutanedicarboxylic acid the main axes for the oxygen atoms are: 6.147, 8.673, 9.580, and 8.045 $Å^2$.

In this compound the movement is also essentially perpendicular to the plane of the carboxyl group. The anisotropic movement of terephthalic acid (which must be planar) is not as large as that in the cyclobutanedicarboxylic acids above. The principle axes are: 5.785 and 4.901.

The data of the present study agrees largely with that of Margulis. The cell dimensions and angles are within two standard deviations of Margulis' values.

The values of the fractional coordinates (x, y, and z) as well as almost all those from the anisotropic temperature parameters (a few are as great as five standard deviations different), fall within three standard deviations.

Most bond lengths and angles agree within three standard deviations (as calculated by Margulis). Moreover, the standard deviation of Margulis' values (0.005-0.006Å) are somewhat larger than those of this study (0.004 Å). The long bonds reported by Margulis almost fall within three standard deviations of the "average" value, and the larger difference in length observed is probably not significant.

# CHAPTER V

## SUMMARY

Trans-1,3-cyclobutanedicarboxylic acid crystallizes in the monoclinic space group $P_{2_1/c}$; with two molecules per unit cell. The molecule must be centrosymmetric such that the center of symmetry of the molecule corresponds to the center of symmetry of the unit cell, and the cyclobutane ring is planar.

The structure was determined from a Patterson synthesis. The positions of the atoms were refined by the least squares method of van der Helm, and the residual was reduced to a value of 0.084.

The rather large temperature movements perpendicular to the plane of the caryboxyl groups are larger than those of other dicarboxylic acids, e.g., terephthalic acid, but are apparently similar in origin.

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## APPENDIX A

The structure factors for the determination of trans-1,3-cyclobutanedicarboxylic acid are listed in the following appendix. An asterisk indicates an unobserved reflection.

| h | k | l | $F_o$ | $F_c$ |
|---|---|---|---|---|
| 0 | 0 | 4 | 065 | 077 |
| 0 | 0 | 6 | 048 | -044 |
| 0 | 1 | 1 | 071 | 105 |
| 0 | 0 | 8 | 037 | 038 |
| *0 | 1 | 2 | 005 | -003 |
| 0 | 1 | 4 | 036 | -031 |
| 0 | 1 | 5 | 055 | -059 |
| 0 | 1 | 6 | 074 | -076 |
| *0 | 1 | 7 | 008 | 001 |
| *0 | 1 | 8 | 002 | -005 |
| 0 | 1 | 9 | 066 | -058 |
| 0 | 2 | 0 | 617 | 065 |
| 0 | 2 | 1 | 172 | 169 |
| 0 | 2 | 2 | 186 | 225 |
| 0 | 2 | 3 | 223 | -207 |
| 0 | 2 | 4 | 037 | 035 |
| 0 | 2 | 5 | 017 | -021 |
| 0 | 2 | 6 | 069 | -067 |
| 0 | 2 | 7 | 011 | 014 |
| 0 | 2 | 8 | 011 | 011 |
| 0 | 2 | 9 | 049 | -049 |
| 0 | 3 | 1 | 108 | -115 |
| *0 | 3 | 2 | 011 | 000 |
| 0 | 3 | 3 | 055 | 061 |
| 0 | 3 | 4 | 058 | -054 |
| 0 | 3 | 5 | 095 | -099 |
| 0 | 3 | 6 | 124 | -124 |
| 0 | 3 | 9 | 047 | -044 |
| 0 | 4 | 0 | 038 | 039 |
| 0 | 4 | 1 | 095 | -097 |
| 0 | 4 | 2 | 169 | -166 |
| 0 | 4 | 3 | 122 | -122 |

| h | k | l | $F_o$ | $F_c$ |
|---|---|---|---|---|
| 0 | 4 | 4 | 021 | 018 |
| 0 | 4 | 5 | 017 | -019 |
| 0 | 4 | 6 | 066 | -067 |
| 0 | 4 | 7 | 042 | 041 |
| 0 | 4 | 8 | 017 | -017 |
| 0 | 5 | 1 | 027 | -028 |
| 0 | 5 | 2 | 006 | 008 |
| 0 | 5 | 3 | 046 | -043 |
| 0 | 5 | 4 | 004 | -008 |
| 0 | 5 | 5 | 062 | -055 |
| 0 | 5 | 6 | 046 | -044 |
| 0 | 5 | 7 | 015 | 013 |
| 0 | 5 | 8 | 029 | 028 |
| 0 | 6 | 0 | 036 | -032 |
| 0 | 6 | 1 | 034 | -036 |
| 0 | 6 | 2 | 033 | -033 |
| 0 | 6 | 3 | 012 | -015 |
| 0 | 6 | 4 | 041 | 041 |
| 0 | 6 | 5 | 015 | -015 |
| 0 | 6 | 6 | 007 | -007 |
| 0 | 6 | 7 | 045 | 042 |
| 0 | 7 | 1 | 021 | 022 |
| 0 | 7 | -2 | 017 | 016 |
| 0 | 7 | 2 | 014 | -016 |
| *0 | 7 | 3 | 006 | -002 |
| 0 | 7 | 4 | 006 | -006 |
| 0 | 7 | 5 | 010 | 010 |
| *0 | 7 | 6 | 003 | -001 |
| 0 | 8 | 0 | 012 | -008 |
| 0 | 8 | 1 | 023 | -020 |
| 0 | 8 | 2 | 014 | 015 |
| 0 | 8 | 3 | 008 | 006 |
| 0 | 8 | 4 | 031 | 034 |
| 0 | 8 | 5 | 025 | -024 |
| 0 | 9 | 1 | 006 | 005 |
| 0 | 9 | 2 | 012 | -012 |
| 0 | 9 | 3 | 005 | 005 |
| 1 | 0 | 0 | 056 | -039 |
| 1 | 0 | -2 | 287 | 339 |
| 1 | 0 | 2 | 493 | 509 |
| 1 | 0 | 4 | 120 | -121 |
| *1 | 0 | -4 | 004 | -003 |
| 1 | 0 | 6 | 054 | -056 |
| 1 | 0 | -8 | 019 | -017 |
| 1 | 0 | 8 | 043 | 043 |
| 1 | 1 | 0 | 134 | -125 |
| 1 | 1 | -1 | 501 | 527 |
| 1 | 1 | 1 | 055 | -082 |
| 1 | 1 | 2 | 054 | 057 |
| 1 | 1 | -2 | 018 | 063 |

| h | k | l | $F_o$ | $F_c$ |
|---|---|---|---|---|
| 1 | 1 | -3 | 088 | 100 |
| 1 | 1 | 3 | 141 | -176 |
| 1 | 1 | 4 | 006 | 005 |
| 1 | 1 | -5 | 128 | 142 |
| 1 | 1 | 5 | 093 | 099 |
| 1 | 1 | -6 | 027 | 030 |
| 1 | 1 | 6 | 015 | 017 |
| 1 | 1 | -7 | 141 | -141 |
| 1 | 1 | 7 | 008 | 013 |
| 1 | 1 | -8 | 013 | 011 |
| 1 | 1 | 8 | 026 | -024 |
| 1 | 1 | -9 | 052 | 049 |
| 1 | 2 | -1 | 262 | 233 |
| *1 | 2 | 1 | 003 | 002 |
| 1 | 2 | 3 | 103 | -107 |
| 1 | 2 | 4 | 122 | -126 |
| 1 | 2 | -4 | 049 | -053 |
| 1 | 2 | -5 | 037 | 037 |
| 1 | 2 | 5 | 022 | -016 |
| 1 | 2 | -6 | 079 | 076 |
| 1 | 2 | 6 | 046 | -049 |
| 1 | 2 | -7 | 089 | 094 |
| 1 | 2 | 7 | 020 | 018 |
| 1 | 2 | -8 | 016 | -015 |
| 1 | 2 | 8 | 009 | 010 |
| 1 | 2 | -9 | 034 | 035 |
| 1 | 3 | 0 | 312 | -292 |
| 1 | 3 | -1 | 074 | 082 |
| 1 | 3 | 1 | 120 | -134 |
| 1 | 3 | -2 | 041 | 039 |
| 1 | 3 | 3 | 107 | -114 |
| 1 | 3 | 4 | 017 | -012 |
| 1 | 3 | -4 | 169 | 185 |
| 1 | 3 | 5 | 026 | -023 |
| 1 | 3 | -5 | 077 | 075 |
| 1 | 3 | -6 | 056 | 054 |
| 1 | 3 | 6 | 042 | 042 |
| 1 | 3 | 7 | 029 | -028 |
| 1 | 3 | -7 | 084 | -083 |
| 1 | 3 | 8 | 028 | -034 |
| 1 | 3 | -8 | 008 | 007 |
| 1 | 3 | -9 | 028 | 025 |
| 1 | 4 | 0 | 121 | -129 |
| 1 | 4 | -1 | 091 | 089 |
| 1 | 4 | 1 | 062 | -056 |
| 1 | 4 | 2 | 040 | -037 |
| 1 | 4 | -3 | 077 | -082 |
| 1 | 4 | 3 | 099 | -094 |

| h | k | l | $F_o$ | $F_c$ |
|---|---|---|---|---|
| 1 | 4 | 4 | 087 | -092 |
| 1 | 4 | -5 | 016 | 018 |
| 1 | 4 | 5 | 005 | 007 |
| 1 | 4 | 6 | 021 | -023 |
| *1 | 4 | -6 | 004 | -003 |
| 1 | 4 | -7 | 059 | 063 |
| 1 | 4 | 7 | 026 | 024 |
| 1 | 4 | 8 | 027 | -026 |
| 1 | 4 | -8 | 006 | -005 |
| 1 | 5 | 0 | 181 | -189 |
| 1 | 5 | -1 | 032 | -034 |
| 1 | 5 | 1 | 026 | -024 |
| 1 | 5 | -2 | 029 | -017 |
| 1 | 5 | 2 | 041 | 038 |
| 1 | 5 | -3 | 070 | -069 |
| 1 | 5 | 3 | 007 | -010 |
| 1 | 5 | 4 | 026 | -026 |
| 1 | 5 | -4 | 038 | 039 |
| 1 | 5 | -5 | 041 | 039 |
| 1 | 5 | 5 | 048 | -046 |
| 1 | 5 | 6 | 057 | 050 |
| 1 | 5 | -6 | 023 | 018 |
| 1 | 5 | 7 | 021 | -022 |
| 1 | 5 | -7 | 016 | -014 |
| 1 | 5 | -8 | 019 | -018 |
| 1 | 6 | 0 | 018 | -021 |
| 1 | 6 | -1 | 014 | -016 |
| 1 | 6 | 1 | 050 | -050 |
| 1 | 6 | -2 | 028 | 026 |
| 1 | 6 | 2 | 019 | -018 |
| 1 | 6 | -3 | 041 | -048 |
| 1 | 6 | 3 | 040 | -045 |
| 1 | 6 | -4 | 016 | -016 |
| *1 | 6 | 4 | 009 | 001 |
| 1 | 6 | 5 | 027 | 025 |
| 1 | 6 | -5 | 008 | -007 |
| 1 | 6 | -6 | 012 | -010 |
| 1 | 6 | 6 | 025 | 025 |
| 1 | 6 | -7 | 004 | 008 |
| 1 | 7 | 0 | 071 | -076 |
| 1 | 7 | 1 | 032 | 033 |
| 1 | 7 | -1 | 009 | -010 |
| 1 | 7 | 2 | 014 | 010 |
| *1 | 7 | -2 | 004 | -003 |
| 1 | 7 | -3 | 028 | -025 |
| 1 | 7 | 3 | 052 | 046 |
| 1 | 7 | -4 | 021 | -020 |

| h | k | l | $F_o$ | $F_c$ |
|---|---|---|---|---|
| 1 | 7 | 4 | 033 | -033 |
| 1 | 7 | -5 | 017 | 018 |
| 1 | 7 | 5 | 007 | 007 |
| 1 | 7 | -6 | 018 | -014 |
| 1 | 7 | 6 | 036 | 032 |
| 1 | 8 | 0 | 015 | 015 |
| 1 | 8 | -1 | 019 | -017 |
| 1 | 8 | 1 | 016 | -017 |
| 1 | 8 | 2 | 019 | 017 |
| 1 | 8 | -2 | 007 | 009 |
| 1 | 8 | 3 | 017 | -018 |
| *1 | 8 | -3 | 003 | -001 |
| 1 | 8 | 4 | 034 | 035 |
| *1 | 8 | -4 | 002 | 001 |
| 1 | 8 | -5 | 010 | 007 |
| 1 | 9 | 0 | 013 | -014 |
| 1 | 9 | 1 | 020 | 020 |
| 1 | 9 | -1 | 005 | -006 |
| 1 | 9 | -2 | 022 | 018 |
| 1 | 9 | 2 | 012 | 013 |
| 1 | 9 | -3 | 009 | -008 |
| 2 | 0 | 0 | 152 | -163 |
| 2 | 0 | -2 | 131 | -120 |
| 2 | 0 | 2 | 012 | 013 |
| 2 | 0 | -4 | 234 | 267 |
| 2 | 0 | 4 | 066 | 061 |
| 2 | 0 | -6 | 047 | 050 |
| 2 | 0 | -8 | 070 | -072 |
| 2 | 0 | 8 | 012 | -011 |
| 2 | 1 | -1 | 100 | 101 |
| 2 | 1 | 1 | 041 | -032 |
| 2 | 1 | -3 | 064 | 048 |
| 2 | 1 | 3 | 067 | -064 |
| 2 | 1 | -4 | 027 | 030 |
| 2 | 1 | 4 | 075 | 080 |
| 2 | 1 | -5 | 110 | -113 |
| 2 | 1 | 5 | 016 | -012 |
| 2 | 1 | -6 | 012 | 012 |
| 2 | 1 | 6 | 024 | 021 |
| 2 | 1 | -7 | 117 | 118 |
| 2 | 1 | 7 | 069 | 067 |
| 2 | 1 | -8 | 023 | 021 |
| 2 | 1 | 8 | 007 | 006 |
| 2 | 1 | -9 | 029 | -024 |
| 2 | 2 | 0 | 117 | -122 |
| 2 | 2 | 1 | 258 | 241 |
| 2 | 2 | -2 | 103 | -097 |
| 2 | 2 | 2 | 026 | -027 |

| h | k | l | $F_o$ | $F_c$ |
|---|---|---|---|---|
| 2 | 2 | -3 | 035 | 036 |
| 2 | 2 | 3 | 072 | 078 |
| 2 | 2 | -4 | 142 | 143 |
| 2 | 2 | 4 | 006 | -008 |
| *2 | 2 | 5 | 001 | 001 |
| 2 | 2 | -6 | 042 | 040 |
| 2 | 2 | 6 | 030 | 034 |
| 2 | 2 | -7 | 086 | 090 |
| 2 | 2 | 7 | 017 | 017 |
| 2 | 2 | -8 | 037 | -037 |
| 2 | 2 | 8 | 021 | -020 |
| 2 | 2 | -9 | 012 | 013 |
| 2 | 3 | 0 | 058 | 054 |
| 2 | 3 | -1 | 005 | -007 |
| 2 | 3 | -2 | 070 | 072 |
| 2 | 3 | 2 | 119 | -129 |
| 2 | 3 | 3 | 071 | -072 |
| 2 | 3 | -3 | 016 | 045 |
| 2 | 3 | 4 | 139 | 135 |
| 2 | 3 | -4 | 020 | 018 |
| 2 | 3 | 5 | 027 | -024 |
| 2 | 3 | -5 | 042 | -038 |
| 2 | 3 | 6 | 029 | 031 |
| *2 | 3 | -6 | 003 | 003 |
| 2 | 3 | 7 | 011 | -009 |
| 2 | 3 | -7 | 062 | 062 |
| 2 | 3 | -8 | 025 | 026 |
| 2 | 3 | -9 | 004 | -006 |
| 2 | 4 | 0 | 031 | -030 |
| 2 | 4 | -1 | 210 | -192 |
| 2 | 4 | 1 | 117 | 117 |
| 2 | 4 | -2 | 022 | -016 |
| 2 | 4 | 2 | 034 | -037 |
| 2 | 4 | -3 | 020 | -020 |
| 2 | 4 | 3 | 026 | 026 |
| 2 | 4 | 4 | 074 | -073 |
| 2 | 4 | -4 | 015 | 012 |
| 2 | 4 | -5 | 017 | -019 |
| *2 | 4 | 5 | 003 | 001 |
| 2 | 4 | 6 | 010 | -010 |
| 2 | 4 | -6 | 033 | 031 |
| 2 | 4 | -7 | 073 | 066 |
| 2 | 4 | 7 | 021 | 019 |
| 2 | 4 | -8 | 010 | 010 |
| 2 | 5 | 0 | 018 | -022 |
| 2 | 5 | -1 | 036 | -036 |
| 2 | 5 | 1 | 037 | -035 |
| 2 | 5 | -2 | 063 | -060 |
| 2 | 5 | 2 | 111 | -111 |

| h | k | l | $F_o$ | $F_c$ |
|---|---|---|---|---|
| 2 | 5 | -3 | 037 | 030 |
| 2 | 5 | 3 | 018 | -015 |
| 2 | 5 | -4 | 024 | -031 |
| 2 | 5 | 4 | 089 | 084 |
| 2 | 5 | -5 | 010 | 013 |
| *2 | 5 | 5 | 001 | -002 |
| 2 | 5 | -6 | 029 | -031 |
| *2 | 5 | 6 | 005 | 003 |
| 2 | 5 | -7 | 013 | 011 |
| *2 | 5 | -8 | 004 | -002 |
| 2 | 6 | -1 | 120 | -121 |
| 2 | 6 | 1 | 015 | 013 |
| 2 | 6 | 0 | 023 | 024 |
| 2 | 6 | -2 | 013 | 011 |
| 2 | 6 | 2 | 018 | 018 |
| 2 | 6 | -3 | 030 | -032 |
| 2 | 6 | 3 | 014 | -017 |
| 2 | 6 | -4 | 033 | -034 |
| 2 | 6 | 4 | 026 | -023 |
| 2 | 6 | -5 | 064 | -062 |
| *2 | 6 | 5 | 007 | 005 |
| *2 | 6 | -6 | 003 | 005 |
| 2 | 6 | 6 | 005 | 004 |
| 2 | 6 | -7 | 030 | 022 |
| 2 | 7 | 0 | 009 | -012 |
| 2 | 7 | 1 | 025 | 022 |
| 2 | 7 | -1 | 009 | -007 |
| 2 | 7 | -2 | 070 | -068 |
| 2 | 7 | 2 | 049 | -050 |
| *2 | 7 | -3 | 011 | 004 |
| 2 | 7 | 3 | 035 | 033 |
| 2 | 7 | -4 | 036 | -018 |
| 2 | 7 | 4 | 040 | 038 |
| 2 | 7 | 5 | 027 | 024 |
| 2 | 7 | -5 | 005 | 004 |
| 2 | 7 | -6 | 014 | -015 |
| 2 | 8 | 0 | 028 | 028 |
| 2 | 8 | -1 | 033 | -034 |
| 2 | 8 | 1 | 005 | 006 |
| 2 | 8 | -2 | 016 | 012 |
| 2 | 8 | 2 | 030 | 029 |
| 2 | 8 | -3 | 008 | 006 |
| 2 | 8 | 3 | 008 | -010 |
| 2 | 8 | -4 | 025 | -025 |
| 2 | 8 | -5 | 028 | -028 |
| 2 | 9 | 0 | 020 | 020 |
| 2 | 9 | 1 | 023 | 019 |
| 2 | 9 | -1 | 005 | 006 |
| 2 | 9 | -2 | 016 | -015 |

| h | k | l | $F_o$ | $F_c$ |
|---|---|---|---|---|
| 2 | 9 | -3 | 009 | -010 |
| 3 | 0 | 0 | 110 | -111 |
| 3 | 0 | -2 | 065 | 068 |
| 3 | 0 | 2 | 136 | -141 |
| 3 | 0 | -4 | 036 | -037 |
| 3 | 0 | 4 | 149 | 153 |
| 3 | 0 | -6 | 044 | -042 |
| 3 | 0 | 6 | 021 | 019 |
| 3 | 0 | -8 | 011 | 010 |
| 3 | 1 | 0 | 099 | 100 |
| 3 | 1 | -1 | 242 | -228 |
| 3 | 1 | 1 | 154 | 166 |
| 3 | 1 | -2 | 051 | 056 |
| 3 | 1 | 2 | 068 | 071 |
| 3 | 1 | -3 | 098 | -093 |
| 3 | 1 | 3 | 026 | -028 |
| *3 | 1 | -4 | 002 | -004 |
| *3 | 1 | 4 | 005 | -002 |
| 3 | 1 | -5 | 033 | 024 |
| 3 | 1 | 5 | 036 | 036 |
| 3 | 1 | 6 | 028 | 026 |
| *3 | 1 | -6 | 010 | -005 |
| 3 | 1 | 7 | 031 | 030 |
| 3 | 1 | -7 | 038 | 039 |
| 3 | 1 | -8 | 036 | 037 |
| *3 | 1 | -9 | 005 | 001 |
| 3 | 2 | 0 | 058 | -059 |
| 3 | 2 | -1 | 071 | 070 |
| 3 | 2 | 1 | 022 | 018 |
| 3 | 2 | -2 | 025 | 018 |
| 3 | 2 | 2 | 102 | -106 |
| 3 | 2 | 3 | 131 | 132 |
| *3 | 2 | -3 | 002 | -004 |
| 3 | 2 | 4 | 100 | 103 |
| 3 | 2 | -4 | 014 | -025 |
| 3 | 2 | -5 | 085 | 094 |
| 3 | 2 | 5 | 041 | 042 |
| 3 | 2 | -6 | 011 | -013 |
| 3 | 2 | 6 | 013 | -012 |
| 3 | 2 | -7 | 022 | -024 |
| 3 | 2 | 7 | 013 | -012 |
| 3 | 2 | -8 | 020 | 019 |
| *3 | 2 | -9 | 005 | 003 |
| 3 | 3 | 0 | 095 | 097 |
| 3 | 3 | -1 | 092 | -096 |
| 3 | 3 | 1 | 058 | 057 |
| 3 | 3 | -2 | 038 | 039 |

| h | k | l | $F_o$ | $F_c$ |
|---|---|---|---|---|
| 3 | 3 | 2 | 079 | 085 |
| *3 | 3 | -3 | 006 | -003 |
| 3 | 3 | 3 | 048 | -049 |
| 3 | 3 | 4 | 017 | -016 |
| 3 | 3 | -4 | 042 | -048 |
| *3 | 3 | -5 | 009 | -004 |
| 3 | 3 | 5 | 005 | 004 |
| 3 | 3 | -6 | 039 | -043 |
| 3 | 3 | 6 | 045 | 042 |
| 3 | 3 | -7 | 039 | 039 |
| 3 | 3 | -8 | 054 | 058 |
| 3 | 3 | -9 | 026 | 022 |
| 3 | 4 | 0 | 004 | 005 |
| 3 | 4 | -1 | 018 | 020 |
| 3 | 4 | 1 | 032 | -034 |
| 3 | 4 | -2 | 027 | -030 |
| 3 | 4 | 2 | 047 | -047 |
| 3 | 4 | -3 | 083 | -079 |
| 3 | 4 | 3 | 104 | 097 |
| 3 | 4 | -4 | 022 | 017 |
| 3 | 4 | 4 | 030 | 029 |
| 3 | 4 | -5 | 053 | 048 |
| 3 | 4 | 5 | 013 | 014 |
| 3 | 4 | -6 | 030 | 030 |
| 3 | 4 | 6 | 044 | -043 |
| 3 | 4 | -7 | 050 | -052 |
| 3 | 4 | -8 | 022 | 022 |
| *3 | 5 | 0 | 003 | 002 |
| *3 | 5 | 1 | 004 | -001 |
| *3 | 5 | -1 | 007 | -005 |
| 3 | 5 | -2 | 015 | -018 |
| 3 | 5 | 2 | 017 | 020 |
| 3 | 5 | -3 | 047 | 048 |
| 3 | 5 | 3 | 030 | -026 |
| 3 | 5 | -4 | 064 | -061 |
| 3 | 5 | 4 | 029 | -027 |
| 3 | 5 | -5 | 013 | -016 |
| *3 | 5 | 5 | 004 | -001 |
| 3 | 5 | -6 | 068 | -068 |
| 3 | 5 | -7 | 014 | 015 |
| 3 | 5 | -8 | 028 | 023 |
| 3 | 6 | 0 | 035 | 036 |
| 3 | 6 | 1 | 035 | -039 |
| *3 | 6 | -1 | 002 | 001 |
| 3 | 6 | -2 | 028 | -024 |
| *3 | 6 | 2 | 002 | 006 |
| 3 | 6 | -3 | 090 | -089 |

| h | k | l | $F_o$ | $F_c$ |
|---|---|---|---|---|
| 3 | 6 | 3 | 031 | 032 |
| 3 | 6 | -4 | 008 | 011 |
| 3 | 6 | 4 | 008 | 009 |
| *3 | 6 | -5 | 008 | 003 |
| 3 | 6 | -6 | 012 | 013 |
| 3 | 6 | -7 | 039 | -043 |
| 3 | 7 | 0 | 017 | -017 |
| 3 | 7 | -1 | 015 | 017 |
| *3 | 7 | 1 | 014 | 002 |
| 3 | 7 | -2 | 016 | -021 |
| 3 | 7 | 2 | 004 | 004 |
| 3 | 7 | -3 | 029 | 030 |
| 3 | 7 | 3 | 006 | 005 |
| 3 | 7 | -4 | 025 | -023 |
| 3 | 7 | -5 | 022 | -023 |
| 3 | 7 | -6 | 036 | -036 |
| 3 | 8 | 0 | 026 | 024 |
| 3 | 8 | -1 | 019 | 021 |
| 3 | 8 | 1 | 005 | -008 |
| 3 | 8 | 2 | 011 | 011 |
| *3 | 8 | -2 | 006 | -004 |
| 3 | 8 | -3 | 036 | -036 |
| 3 | 8 | -4 | 006 | -005 |
| 4 | 0 | 0 | 033 | 036 |
| 4 | 0 | -2 | 085 | -078 |
| 4 | 0 | 2 | 017 | 022 |
| 4 | 0 | -4 | 070 | -066 |
| 4 | 0 | 4 | 045 | -045 |
| 4 | 0 | -6 | 098 | -101 |
| 4 | 0 | -8 | 040 | 041 |
| 4 | 1 | 0 | 049 | 053 |
| 4 | 1 | -1 | 016 | 015 |
| 4 | 1 | 1 | 107 | -108 |
| 4 | 1 | 2 | 045 | 043 |
| 4 | 1 | -2 | 005 | 004 |
| 4 | 1 | -3 | 128 | -125 |
| 4 | 1 | 3 | 136 | 137 |
| *4 | 1 | -4 | 006 | -002 |
| 4 | 1 | 4 | 014 | 013 |
| 4 | 1 | -5 | 029 | 033 |
| 4 | 1 | 5 | 016 | -014 |
| 4 | 1 | -6 | 032 | 029 |
| 4 | 1 | -7 | 042 | -044 |
| 4 | 1 | -8 | 015 | -014 |
| 4 | 1 | -9 | 013 | -013 |
| 4 | 2 | 0 | 028 | 029 |
| 4 | 2 | -1 | 042 | 040 |

| h | k | l | $F_o$ | $F_c$ |
|---|---|---|---|---|
| 4 | 2 | 1 | 027 | 029 |
| 4 | 2 | -2 | 035 | -033 |
| 4 | 2 | 2 | 032 | 034 |
| 4 | 2 | -3 | 087 | 096 |
| 4 | 2 | 3 | 025 | 026 |
| 4 | 2 | 4 | 029 | -031 |
| 4 | 2 | -4 | 023 | -023 |
| 4 | 2 | -5 | 033 | -036 |
| 4 | 2 | 5 | 031 | 028 |
| 4 | 2 | -6 | 062 | -064 |
| 4 | 2 | -7 | 025 | -025 |
| 4 | 2 | -8 | 041 | 039 |
| *4 | 2 | -9 | 003 | 000 |
| 4 | 3 | 0 | 073 | 077 |
| 4 | 3 | -1 | 061 | 062 |
| 4 | 3 | 1 | 035 | -038 |
| 4 | 3 | 2 | 062 | 059 |
| *4 | 3 | -2 | 003 | -005 |
| 4 | 3 | -3 | 075 | -073 |
| 4 | 3 | 3 | 075 | 072 |
| 4 | 3 | -4 | 035 | -035 |
| *4 | 3 | 4 | 005 | 003 |
| 4 | 3 | 5 | 019 | -019 |
| 5 | 3 | -5 | 044 | 043 |
| 4 | 3 | -6 | 035 | 037 |
| 4 | 3 | -7 | 006 | -005 |
| 4 | 3 | -8 | 032 | -034 |
| 4 | 4 | 0 | 004 | -004 |
| 4 | 4 | -1 | 012 | 011 |
| *4 | 4 | 1 | 002 | 007 |
| 4 | 4 | -2 | 015 | 014 |
| 4 | 4 | 2 | 032 | 032 |
| 4 | 4 | -3 | 071 | 069 |
| *4 | 4 | 3 | 003 | 002 |
| 4 | 4 | -4 | 032 | 033 |
| 4 | 4 | 4 | 009 | -009 |
| 4 | 4 | -5 | 050 | -053 |
| 4 | 4 | -6 | 010 | -009 |
| 4 | 4 | 7 | 036 | -034 |
| 4 | 4 | -8 | 026 | 025 |
| 4 | 5 | 0 | 029 | 028 |
| 4 | 5 | -1 | 057 | 059 |
| 4 | 5 | 1 | 004 | -004 |
| 4 | 5 | 2 | 012 | 012 |
| *4 | 5 | -2 | 006 | -001 |

| h | k | l | $F_o$ | $F_c$ |
|---|---|---|---|---|
| 4 | 5 | -3 | 031 | -025 |
| 4 | 5 | 3 | 011 | 010 |
| 4 | 5 | -4 | 049 | -045 |
| 4 | 5 | 4 | 036 | -032 |
| 4 | 5 | -5 | 028 | 028 |
| 4 | 5 | -6 | 011 | 012 |
| 4 | 5 | -7 | 005 | 004 |
| 4 | 6 | 0 | 022 | -018 |
| 4 | 6 | -1 | 011 | -010 |
| *4 | 6 | 1 | 008 | -003 |
| 4 | 6 | -2 | 010 | 014 |
| 4 | 6 | 2 | 015 | 015 |
| 4 | 6 | -3 | 024 | 023 |
| 4 | 6 | 3 | 012 | -013 |
| 4 | 6 | -4 | 023 | 026 |
| 4 | 6 | -5 | 029 | -027 |
| *4 | 6 | -6 | 001 | -001 |
| *4 | 7 | 0 | 005 | 002 |
| 4 | 7 | -1 | 019 | 021 |
| *4 | 7 | 1 | 016 | -005 |
| 4 | 7 | -2 | 014 | 015 |
| *4 | 7 | -3 | 030 | -008 |
| 4 | 7 | 3 | 005 | -015 |
| 4 | 7 | -4 | 026 | -022 |
| *4 | 7 | -5 | 002 | 000 |
| 5 | 0 | 0 | 004 | 004 |
| 5 | 0 | 2 | 025 | 024 |
| *5 | 0 | -2 | 005 | -002 |
| 5 | 0 | -4 | 124 | -117 |
| 5 | 0 | 4 | 017 | -014 |
| 5 | 0 | -6 | 028 | 031 |
| 5 | 0 | -8 | 053 | -050 |
| 5 | 1 | 0 | 006 | -007 |
| 5 | 1 | -1 | 055 | -054 |
| 5 | 1 | 1 | 033 | 036 |
| 5 | 1 | -2 | 010 | 013 |
| 5 | 1 | 2 | 016 | 018 |
| 5 | 1 | -3 | 060 | 058 |
| 5 | 1 | 3 | 037 | -036 |
| 5 | 1 | -4 | 022 | 028 |
| 5 | 1 | 4 | 013 | 012 |
| 5 | 1 | -5 | 067 | -065 |
| *5 | 1 | -6 | 003 | -001 |
| 5 | 1 | -7 | 049 | -048 |
| 5 | 1 | -8 | 011 | -011 |
| 5 | 2 | 0 | 028 | 023 |
| 5 | 2 | -1 | 041 | 048 |

| h | k | l | $F_o$ | $F_c$ |
|---|---|---|---|---|
| 5 | 2 | 1 | 023 | 025 |
| 5 | 2 | -2 | 027 | 028 |
| 3 | 2 | 2 | 028 | 026 |
| 5 | 2 | 3 | 022 | -023 |
| 5 | 2 | -3 | 007 | 006 |
| 5 | 2 | -4 | 076 | -070 |
| 5 | 2 | -5 | 012 | -007 |
| 5 | 2 | -6 | 034 | 035 |
| 5 | 2 | -7 | 005 | -004 |
| 5 | 2 | -8 | 033 | -033 |
| 5 | 3 | 0 | 017 | -018 |
| 5 | 3 | -1 | 018 | -018 |
| 5 | 3 | 1 | 054 | 052 |
| 5 | 3 | 2 | 019 | 022 |
| 5 | 3 | -2 | 011 | 014 |
| 5 | 3 | -3 | 062 | 056 |
| *5 | 3 | 3 | 006 | -003 |
| 5 | 3 | -4 | 038 | 040 |
| 5 | 3 | -5 | 014 | -011 |
| *5 | 3 | -6 | 003 | -005 |
| *5 | 3 | -7 | 004 | -001 |
| 5 | 4 | 0 | 031 | 024 |
| 5 | 4 | -1 | 030 | 031 |
| 5 | 4 | 1 | 009 | 010 |
| 5 | 4 | -2 | 042 | 043 |
| 5 | 4 | 2 | 013 | 012 |
| 5 | 4 | -3 | 017 | 010 |
| 5 | 4 | -4 | 013 | -008 |
| 5 | 4 | -5 | 011 | -010 |
| 5 | 4 | -6 | 026 | 027 |
| *5 | 4 | -7 | 007 | -004 |
| 5 | 5 | 0 | 014 | -015 |
| 5 | 5 | 1 | 032 | 031 |
| *5 | 5 | -1 | 010 | -006 |
| *5 | 5 | -2 | 006 | 004 |
| 5 | 5 | -3 | 026 | 023 |
| 5 | 5 | -4 | 026 | 024 |
| 5 | 5 | -5 | 005 | 007 |
| *5 | 5 | -6 | 008 | 003 |
| *5 | 6 | 0 | 004 | -002 |
| *5 | 6 | -1 | 002 | 002 |
| 5 | 6 | -2 | 012 | 015 |
| 5 | 6 | -3 | 025 | 021 |
| 5 | 6 | -4 | 004 | 005 |
| *6 | 0 | 0 | 010 | -006 |
| 6 | 0 | -2 | 032 | -032 |

| h | k | l | $F_o$ | $F_c$ |
|---|---|---|---|---|
| *6 | 0 | 2 | 035 | -007 |
| 6 | 0 | -4 | 046 | 043 |
| 6 | 0 | -6 | 032 | -030 |
| *6 | 1 | 0 | 004 | -001 |
| 6 | 1 | -1 | 039 | 037 |
| 6 | 1 | 1 | 018 | -016 |
| *6 | 1 | -2 | 003 | 000 |
| *6 | 1 | -3 | 011 | -002 |
| 6 | 1 | -4 | 008 | 011 |
| 6 | 1 | -5 | 018 | -020 |
| 6 | 1 | -6 | 009 | -007 |
| 6 | 2 | 0 | 011 | 010 |
| *6 | 2 | 1 | 007 | -005 |
| *6 | 2 | -1 | 006 | -004 |
| 6 | 2 | -2 | 010 | -010 |
| 6 | 2 | -3 | 017 | -010 |
| 6 | 2 | -4 | 043 | 033 |
| *6 | 2 | -5 | 003 | 003 |
| 6 | 2 | -6 | 017 | 015 |
| *6 | 3 | 0 | 009 | -004 |
| 6 | 3 | -1 | 034 | 028 |
| 6 | 3 | -2 | 009 | -007 |
| 6 | 3 | -3 | 020 | 019 |
| 6 | 3 | -4 | 026 | 025 |
| 6 | 3 | -5 | 007 | 008 |
| *6 | 4 | -1 | 004 | 000 |
| 6 | 4 | -2 | 010 | 009 |
| 6 | 4 | -3 | 013 | -012 |
| 6 | 4 | -4 | 021 | 018 |

## APPENDIX B

The data was further refined using the program of Ahmed and workers,[35] after twenty reflections were included which were omitted in the initial work. These reflections were: $12\bar{2}$, $13\bar{3}$, 132, 038, $14\bar{4}$, $14\bar{2}$, $22\bar{1}$, 013, 210, 212, 231, $11\bar{4}$, 002, $21\bar{2}$, 037, $22\bar{5}$, $12\bar{3}$, 120, 122, and 206.

The final R value was 0.063, and the coordinates of the atoms are listed below.

| | x | y | z |
|---|---|---|---|
| $O_1$ | .5523 | -.0386 | .2919 |
| $O_2$ | .2282 | .0679 | .3708 |
| $C_1$ | .3232 | .0294 | .2590 |
| $C_2$ | .1902 | .0486 | .0709 |
| $C_3$ | .0843 | -.1220 | -.0209 |
| $H_1$ | .2985 | .1013 | .0122 |
| H2 | .8458 | .1437 | .1136 |
| $H_3$ | .8864 | .2223 | .9418 |
| $H_4$ | .3764 | .4518 | .0757 |

The B values for the hydrogen atoms were:

| | |
|---|---|
| $H_1$ | 3.930 |
| $H_2$ | 3.664 |

$H_3$ 4.352

$H_4$ 8.164

The anisotropic temperature parameters were:

| | $B_{11}$ | $B_{22}$ | $B_{33}$ | $B_{23}$ | $B_{13}$ | $B_{12}$ |
|---|---|---|---|---|---|---|
| $O_1$ | .0318 | .0334 | .0105 | -.0013 | .0029 | .0235 |
| $O_2$ | .0363 | .0264 | .0092 | -.0009 | .0050 | .0199 |
| $C_1$ | .0251 | .0133 | .0092 | -.0012 | .0018 | -.0001 |
| $C_2$ | .0275 | .0136 | .0080 | .0019 | .0032 | -.0003 |
| $C_3$ | .0300 | .0135 | .0103 | -.0020 | .0003 | .0058 |