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Anodic Oxidations of Medium Ring Cycloalkanecarboxylic Acids.

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ANODIC OXIDATIONS OF MEDIUM RING
CYCLOALKANECARBOXYLIC ACIDS

A Dissertation

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in

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by
John S. Dehn
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ABSTRACT

Product distribution data have been obtained for the anodic oxidation (with a graphite anode) of the seven- to ten-membered ring cycloalkanecarboxylic acids. The energetic cycloalkyl cations produced eliminate protons (to an extent roughly proportional to the strain associated with the ring moiety) or react with solvent or carboxylate to form alcohols or esters. From 6 to 21% of the elimination reaction are transannular 1,3- or 1,5-elimination reactions giving the corresponding cis-bicyclo[X.1.0]- and -[X.3.0]alkanes. The amount of cis-cycloalkene varies inversely with ring size and trans olefin formation competes favorably with transannular eliminations for the two larger rings, the cyclooctane ring system giving the largest amount of transannular products.

These elimination products are compared with other medium ring elimination reactions involving cations, carbenes and carbanions. It appears that the cation produced by anodic oxidation is sparingly solvated and is similar to cations produced by deaminations even though considerable selectivity is demonstrated in the extent and type of subsequent elimination.

The NMR spectra of cis-bicyclo[X.1.0]alkanes indicate the cyclopropane syn-hydrogen shielding is affected by the size of the second ring; in the medium ring region the signal is upfield from tetramethylsilane.

CHAPTER I

INTRODUCTION

The electrolysis of carboxylic acids dates back to M. Faraday.¹ Several theories have been proposed² for the coupling reaction known as the Kolbe electrolysis^{3,4} but the free radical mechanism was accepted soon after its presentation.⁵ The reaction at the anode was depicted as follows:

Detailed studies have been made on the variables, concentration, current density, temperature and acetate/acid ratio for the optimum conditions for the formation of ethane from acetates.⁶ These variables have been shown to be applicable to many other acids for the Kolbe reaction. In Kolbe's original work,⁷ traces of ethylene and methyl acetate were detected. It was later found that alcohols could be obtained⁸ in good conversions by suppressing the Kolbe reaction. Factors favoring alcohol formation (the Hofer-Moest reaction)⁸ were alkaline conditions and the addition of inorganic salts, particularly perchlorates, sulfates and bicarbonates.

The Kolbe coupling reaction is not general. Aromatic acids are not oxidized⁹ at all at the anode, and other acids, especially alpha-substituted carboxylic acids,¹⁰ give abnormal products such as olefins, alcohols, ethers and esters, products more typical of carbonium ion reactions. Some specific examples are the formation of di- and tri-

phenylmethyl ethers and acetates by electrolysis of di- and triphenylacetic acids in methanol or acetic acid¹¹ and of N-methoxymethyl amides by electrolysis of acylaminoacetic acids in methanol with platinum electrodes.¹¹

It has been shown¹² that some acids undergo anodic oxidation involving cationic intermediates. High voltage and structures favoring relatively stable carbonium ions are most favorable for the reaction; for example:

Bicyclo[2.2.1]heptane and bicyclo[2.2.1]hept-7-ene derivatives have been shown repeatedly¹³ to easily give stable cations which rearranged to give exo-norbornyl derivatives and tricyclene derivatives, respectively, as illustrated above. The electrolysis of cyclobutanecarboxylic acid¹² in water (20 volts, 100°) affords mainly cyclobutanol and cyclopropylmethanol (ratio 1.1 to 1) and a small amount of 3-buten-1-ol, a mixture identical with that resulting from the deamination of cyclobutylamine.¹⁴

The most convenient method developed so far for the attainment of abnormal products via anodic oxidation was reported by Koehl.¹⁵ He electrolysed simple aliphatic acids with a graphite anode at low current density. Although these acids normally give the radical-coupling products with platinum electrodes, Koehl obtained almost exclusively the

abnormal products with the graphite electrode. The product distribution data were very similar to those obtained from carbonium ion reactions such as deaminations^{16,17} and deoxidations.¹⁸

Thus it appears that anodic oxidation of carboxylic acids via carbon electrodes can be a convenient route to carbonium ions. The entry to carbonium ion chemistry made available by such a tool should provide valuable information pertinent to reaction mechanisms.

An efficient approach to the understanding of this electrochemical process as a mechanistic tool is perhaps the utilization of medium ring cycloalkanecarboxylic acids as reactants. To justify this statement the properties of medium rings must be considered.

Medium rings are those with eight to eleven carbon atoms in the ring. Several chemical characteristics¹⁹ set apart medium rings from other compounds so the classification is not arbitrary. These special properties arise from the type of strain inherent in the closed ring structure. Pitzer strain (lateral repulsion between vicinal groups) and Bayer strain (bond angle deformation) are present to some extent in medium ring compounds, but the end-on interaction of hydrogen atoms attached to opposite sides of the molecule (transannular strain) is a major source of strain. X-ray studies²⁰ have shown the hydrogen-hydrogen atomic distance (across the ring) to be less than van der Waals radii and the heats of combustion of the medium ring hydrocarbons clearly verify²¹ the presence of strain which is maximum in the ten-membered ring.

The most remarkable chemical characteristic of medium rings is that some reactions do not take place on the classically activated sites but involve atoms located on opposite sides of the ring. The observation of these transannular reactions were reported almost simul-

taneously from the laboratories of Prelog and Cope in 1952^{22,23} for peroxyformic acid oxidations of cyclooctenes and cyclodecenes.

In addition to these transannular hydride shifts, transannular hydrogen atoms migrate in free radical processes^{24,25}, carbenes transannularly insert to give bicycloalkanes^{26,27}, and medium ring cations eliminate transannular protons to form bicycloalkanes^{26,28}. These reactions are usually stereo-selective due to the fixed steric requirements of the atoms involved in the medium ring compound. Cope²⁹ suggests the term "proximity effect" to include these and other nonvicinal interactions of atoms or groups that are fixed in the proximity of each other by steric requirements.

These characteristics make medium ring compounds particularly attractive in the study of reaction mechanisms. Small changes in the intermediates (or transition states) can lead to gross changes in the ultimate products obtained^{30,31}.

CHAPTER II

RESULTS AND DISCUSSION

The seven through ten membered medium ring cycloalkanecarboxylic acids were electrolyzed at a graphite anode and the product distribution data were obtained. The results are certainly in accord with Koehl's view that the carboxylate anion loses two electrons at the anode in a two-step electrode process to form a carbonium ion:

The resultant carbonium ion can then react in a variety of ways, for example, elimination, rearrangement and combination with solvent.

A typical example of the complete anodic oxidation reaction of a medium ring acid is shown below for the electrolysis of cyclooctanecarboxylic acid. The resulting cyclooctyl cation can undergo solvent capture to yield alcohol or react with carboxylate ion to give ester. Approximately 75% does react this way. Only 25% of the cations suffer elimination, but we have chosen this part of the reaction for study since it is these products that allow us to capitalize on the sensitivity of the medium ring intermediate to mechanistic subtleties which help toward an over-all understanding of the mechanism. The intermediates are particularly sensitive to conformation and proximity effects which characterize other reactions of medium ring compounds. As shown below, 21% of the hydrocarbon products from cyclooctanecarboxylic acid resulted from transannular elimination.

A. The Electrolysis Cell

A diagram of the cell is shown in Figure 1. The design of the cell was based upon materials at hand and a desire for simplicity. Fortunately, the design was successful enough to obtain the data with a reasonable efficiency. This aspect will be explained later in Section E.

The cell consisted of a 250 ml. electrolytic beaker with a tight fitting rubber stopper. Four holes were drilled to tightly fit a graphite cylindrical bar (0.55 in. diameter), a copper bar of the same diameter, a thermometer and a Dry Ice, cold finger condenser. The source of the electrical current was two 12-volt batteries in series. The graphite anode was connected to the (+) post of the battery while the copper cathode was connected through the variable resistor and the ammeter to the (-) post of the battery.

A standard apparent current density (c.d.) was used for all electrolyses. The c.d. chosen was $0.045 \text{ amp. cm}^{-2}$. For 100 ml. of carboxylate solution, the electrode dimensions demanded a total current of 0.8 amp. This reading was maintained throughout each experiment. The total current was estimated ebullimetrically. The anode reactions were:

Figure 1
Electrolytic Cell

The cathode reaction was:

The amount of gas produced at the anode per Faraday of electricity passed depended on the reaction. However, this factor was ignored and a current efficiency was defined as the number of moles of acid consumed divided by twice the number of moles of gas produced. This definition is correct only at 100% efficiency.

The products obtained could be readily separated into three groups according to the reaction path. The simplest fraction was the unreacted acid which was extracted with excess dilute alkali. This procedure along with those following are described in detail in the experimental section.

The next two fractions were separated according to the ultimate fate of the intermediate cycloalkyl cation produced. The hydrocarbon fraction, formed by elimination of a proton from the intermediate, contained cyclic olefins (conventional eliminations) and cis-bicycloalkanes (transannular elimination). The solvolysis fraction, formed by capture of the intermediate by solvent or carboxylate, contained cycloalkanol and ester, respectively. This fraction was separated into the two components when convenient.

The total material balance was the molar sum of each fraction divided by the moles of starting material. The elimination fraction was the moles of hydrocarbon fraction divided by the moles of acid consumed.

B. Electrolysis

A brief summary of the data is shown in Table 1. The increase

Table 1

Data from the electrolysis of cyclo-
alkanecarboxylic acids.^(a)

	<u>Expt. No.</u>	<u>Temp. °C</u>	<u>Material balance, %</u>	<u>Current eff., %</u>	<u>Elim. Fraction</u>
1	44	82.5	113	0.05
2	40	86.5	120	0.20
	3	45	87.5	130	0.23
4	44	84	80	0.25
	5	54	91	80	0.21
6	58	100	51	0.55
	(b) 7	61	93	42	0.31
	(c) 8	67	98.6	7.2	0.24
	(d) 9	66	99.5	7.3	0.15

(a) Electrolysed with cell described in text unless otherwise specified.

(b) Circular copper cathode.

(c) Circular copper cathode and platinum anode.

(d) Copper bar cathode and bar platinum anode

in elimination reaction, shown in the last column, as the size of the ring increases is roughly proportional to the strain associated with the ring portion of the cycloalkanecarboxylic acid. This dependence on ring size clearly shows that the intermediate cycloalkane cation discriminates between the solvolytic and the elimination processes.

The current efficiency indicates that an increase in ring size requires a higher potential for the anodic oxidative process. A potential of 1.7 volts should give hydrogen and oxygen at one atmosphere of pressure at their respective electrode. However, depending on the electrode composition, environment, past history and other variables, a higher potential is required to break down water electrolytically. This excess potential is called overvoltage. Since these experiments were conducted at constant current and the current efficiency decreased as ring size increased, it appears that only for the nine and ten membered ring acids was there sufficient potential for the electrolysis of water to compete with or exceed the electrolysis of the carboxylate anion.

The high temperatures for the nine and ten membered ring acids were required to break up a viscous jell that formed when the solutions were made up. Foaming and poor stirring resulted at lower temperatures.

The electrolysis of cycloheptanecarboxylic acid resulted mainly in oxygenated products, alcohol and ester. The hydrocarbon fraction was 0.052; that is, 5.2% of the acid consumed gave elimination products (Table 1). The hydrocarbon fraction contained 87% cis-cycloheptene and 12% cis-bicyclo[4.1.0]heptane (norcarane) (Table 2).

Other elimination reactions associated with the cycloheptyl moiety are listed in Table 2. The p-toluenesulfonylhydrazone

Table 2
Electrolysis of Cycloheptanecarboxylic Acid
Compared to Other Elimination Reactions

	<u>Hydrocarbon Fraction, Mole % Composition</u>
	-COOH	12	87
=N-NHTos (DG)	10	90
" (ETG)	18	81

(tosylhydrazone) of cycloheptanone, when pyrolysed in the presence of sodium methoxide in diglyme (diethyleneglycol dimethyl ether, DG), gives the diazocycloalkane which eliminates nitrogen to form a carbene^{26,27}. The carbene gives bicycloalkanes via a transannular insertion reaction or olefin via hydrogen rearrangement. The same tosylhydrazone pyrolyzed in sodium methoxide in ethylene glycol or sodium ethylene glycolate in the same solvent (ETG) proceeds through a diazonium cation which eliminates nitrogen to give, in this case the cycloalkyl cation²⁶. Olefins are formed by α -elimination of a proton and bicycloalkanes are formed via a transannular proton elimination. In both transannular reactions above, cis-bicycloalkanes are formed due to the restraint imposed on the transition state by the ring (a proximity effect²⁹). In the case of the carbene mechanism (DG), the cycloheptyl ring gave 10% transannular products while the cation process (ETG) gave 18%. The seven membered ring is the only ring studied in the present investigation for which the carbene process gives less transannular products than does the cation process.

The fact that only elimination products, alcohol and ester, were obtained and no bicycloheptyl or cycloheptane (less than 1% cycloheptane can readily be detected), indicates a carbonium ion mechanism.

The extent of the solvolysis reaction (approximately 7 : 1 in isolated products over elimination) indicates a distinct preference for that reaction with the seven-membered ring. Less preference for solvolytic product formation is exhibited by the product proportions obtained from the medium ring acids.

The electrolysis of cyclooctanecarboxylic acid produced the greatest portion of transannular elimination products of the acids studied (Table 3). By vapor phase chromatography (v.p.c.) comparison with

Table 3
Electrolysis of Cyclooctanecarboxylic Acid
Compared to Other Elimination Reactions

	Hydrocarbon Fraction, Mole % Composition				
	<u>bicycloalkane</u>		<u>cycloalkene</u>		<u>Other</u>
	<u>3.3.0</u>	<u>5.1.0</u>	<u>trans</u>	<u>cis</u>
<chem>C1CCC2CCCC2C1C(=O)O</chem>	8 8.5	13 11.3		75 76	4 ^a 4.2 ^a
<chem>C1CCC2CCCC2C1=N-NHTos(DG)</chem>	46	9		45	
(ETG)	6	10		83
<chem>C1CCC2CCCC2C1=CC(Br)C2</chem>				100
<chem>C1CCC2CCCC2C1=CC(MgCl)C2</chem>	2			55	43 ^b

a Unidentified volatile hydrocarbon.

b Cyclooctane.

authentic samples, the unidentified product listed was shown not to be bicyclo[4.2.0]octane or 1-methylcycloheptene. The product ratios for the eight membered ring derivatives are similar to those from anodic oxidation and tosylhydrazone decomposition in ethylene glycol. On the other hand, a decided contrast in product ratio is shown in Table 3 for the carbenic process, tosylhydrazone pyrolysis in DG, compared to the above cationic processes.

The solvolysis of cyclooctyl bromide in 67% aqueous tetrahydrofuran gave only cis-cyclooctene; this difference in products clearly signals a difference in the intermediate cation. Solvolysis of the same bromide in the presence of silver acetate gives little more than detectable amounts of 1-methylcycloheptene and transannular products²⁶.

Extensive side products were obtained in the preparation of cyclooctanecarboxylic acid via carbonation of the Grignard reagent. Considerable amounts of bicyclooctyl (15%) were formed as well as elimination products. Table 3 shows the composition of the hydrocarbon portion less the coupling product: 43% cyclooctane, 55% cis-cyclooctene and 2% cis-bicyclo[3.3.0]octane.

The electrolysis of cyclononanecarboxylic acid produced a hydrocarbon fraction containing 27% trans-cyclononene (Table 4). The extent of transannular elimination was less than 10%. The cationic tosylhydrazone decomposition showed similar results; the hydrocarbon portion contained 4% transannular elimination products and 12% of the fraction was trans-cyclononene. The carbenic tosylhydrazone process resulted in vastly different product distribution data: 53% transannular products and no trans olefin.

Also listed in Table 4 are data for the solvolysis of cyclononyl P-toluenesulfonate³¹. The significance of the ratio of trans- to cis-

Table 4
Electrolysis of Cyclodecanecarboxylic Acid
Compared to Other Elimination Reactions

Hydrocarbon Fraction, Mole % Composition				
	Bicycloalkane		Cycloalkene	
	<u>[4.3.0]</u>	<u>[6.1.0]</u>	<u>trans</u>	<u>cis</u>
-COOH	5.8 4.3	3.8 1.5	27.9 27.3	60.4 66.5
-N ₂ HTos (DG)	42	11		47
" (ETG)	2	2	12	84
-OTos (a)			33	67

(a) See reference 31

cyclononenes will be discussed later.

The hydrocarbon portion obtained from the electrolysis of cyclodecanecarboxylic acid contained 55% trans-cyclodecene. The trans-annular elimination products identified amounted to only 6% of the hydrocarbon portion, but another 5% of this fraction was an unidentified hydrocarbon which may have resulted from a transannular reaction, Table 5. The decomposition of cyclodecanone tosylhydrazone in ethylene glycol (cationic process) gave very little transannular products²⁶ and the trans to cis ratio of cyclodecenes was 0.43 to 1. The trans to cis ratio of the cyclic olefins for the electrolysis reaction was 1.6 to 1. The solvolysis of cyclodecyl tosylate gave the ratio, 5.6 : 1. The thermodynamic ratio³² is 0.08 : 1, so the high trans to cis ratios are the result of kinetic control. The conformation of the cyclodecyl cation favors the formation of the trans olefin^{31,33}. Formation of the trans olefin from the cyclodecyl cation may take place with little movement of atomic centers in the preferred conformation for the solvolysis of cyclodecyl tosylates. The cyclodecene formed by acetolysis of cyclodecyl tosylate was a mixture of 5 trans : 1 cis-cyclodecene; when the cyclodecyl tosylate was labeled with ¹⁴C and with D, transannular hydride shifts (to the extent of 12 - 16%) preceding olefin formation were detected.^{31,34}

Kinetic control was perhaps of even more significance for the cyclononanecarboxylic acid electrolysis, in which a trans to cis ratio of 0.5 : 1 was obtained. The equilibrium ratio is 0.004 : 1.³²

The carbenic cyclodecanone tosylhydrazone process gave 80% trans-annular products. For all the rings studied so far only the ten-membered ring has produced a trans-cyclene (6%, Table 5).

The carbanion process, carbonation of cyclodecylmagnesium

Table 5
Electrolysis of Cyclodecanecarboxylic Acid
Compared to Other Elimination Reactions

Hydrocarbon Fraction, Mole % Composition					
	Bicycloalkane			Cycloalkene	
	<u>[4.4.0]</u>	<u>[5.3.0]</u>	<u>[7.1.0]</u>	<u>trans</u>	<u>cis</u>
-COOH		6		55	34
-NH ₂ TOS (DG)	18	62		6	14
(ETG)	0.05	0.2		30	70 (a)
-OTOS	trace			85	15 (b)
-MgCl	<u>cis</u> 8	2		20	20 (c)
	<u>trans</u> 4				

(a) Reference 23

(b) Reference 31

(c) Cyclodecane 46% also formed

chloride, produced a hydrocarbon fraction containing 14% transannular products. Most notable was the appearance of 4% trans-bicyclo[4.4.0]-decane (decalin) along with 8% cis-decalin and 2% cis-bicyclo[5.3.0]-decane. Carbonation of cyclodecylmagnesium bromide is reported to give 4% of trans-decalin as the only transannular product.²⁶ Perhaps the chlorine containing Grignard reagent exhibits more ionic character which could account for the increase in transannular reaction variety. The mechanism could be an S_N2 type displacement of hydride:

Transition state for
cis-decalin

Transition state for
trans-decalin

Carbanions are isoelectronic with amines and very little energy of activation should be required to invert their configuration. Geometrically stable carbanions have been detected only with a few rigid systems.³⁵

From an examination of models,³⁶ it appears that the closest approach of the orbital of the carbanion leads to the cis product. However, considerable hydrogen-hydrogen repulsion would occur at carbons 2 and 7, as shown:

cis-insertion trans-insertion

Table 6 shows the hydrocarbon fraction obtained from the electrolysis of each cycloalkanecarboxylic acid. The extent of transannular reaction obtained from the seven- to ten-membered ring acids was 12, 21, 10 and 6% respectively; if the unidentified portion is included, the amounts are modified to 13, 25, 12 and 11%, respectively. The total extent of cycloalkene formation was about constant for the series of acids, but there is a definite correlation between ring strain and cis-cycloalkene formation; 87, 75, 60 and 34% was obtained for the seven- to ten-membered rings, respectively. The less stable trans olefins appear only with the nine and ten membered rings, which yielded hydrocarbon fractions containing 28 and 55% trans-cycloalkenes, respectively. This result indicates that, with these larger rings, the transition state leading to trans-cycloalkene competes favorably with the one leading to transannular elimination.

Transannular elimination
transition state α -elimination transition
state (trans-product)

All the bicyclic hydrocarbons identified in these reactions can

Table 6
Product Distribution Data of the Hydrocarbon
Fraction Produced by Anodic Oxidation

	<u>Hydrocarbon Fraction, Mole % Composition</u>				
	<u>Bicycloalkane</u>		<u>Cycloalkene</u>		<u>Uniden- tified</u>
	<u>[X.1.0]</u>	<u>[X.3.0]</u>	<u>trans</u>	<u>cis</u>
12			87	1
8	13		75	4
4	6	28	60	2
6	55	34	5

be accommodated by transannular 1,3-eliminations giving cis-bicyclo-[X.1.0]alkanes and 1,5-eliminations giving the cis-bicyclo[X.3.0]alkanes.

The seven-membered ring acid gave exclusively 1,3-elimination products. The eight-membered ring acid gave 62% 1,3-elimination and 38% 1,5-elimination, virtually a complete reversal of proportions as the 1,3- and 1,5- hydride shifts (39 and 61%, respectively) reported²⁹ for the formolysis of deuterated cyclooctene oxide.

For another product of the same reaction, 3-cyclooctene-1-ol, the same workers found 94% 1,5-hydride and only 6% 1,3-hydride shifts.

The appearance of the three-membered ring derivatives decreases as the size of the parent ring increases. The hydrocarbon fractions obtained for the seven- to ten membered ring acids contained 12, 8, 4 and 0%, respectively, of cyclopropane derivatives. The formation of bicyclo-[X.1.0]alkanes necessarily requires the concurrent formation of two rings in the bicyclic system. As the size of the parent ring increases, the larger of the two rings in the bicycloalkane produced enters into the medium ring region (1,3-transannular elimination of nine- and ten-membered cyclic cations must create eight- and nine-membered ring derivatives) and perhaps the energy requirements become prohibitive for their

formation. The formation of cyclopentane derivatives, shown in Table 6, was 0, 8, 6 and 6%, respectively, for the same acids above. The absence of 1,4-elimination in the seven-membered ring acid electrolysis is perhaps justified since it requires the concurrent formation of a cyclobutane derivative; apparently this size ring formation is energetically unfavorable.

All of the transannular products may be accounted for by 1,3- and 1,5-eliminations. No products of 1,4-eliminations were formed, perhaps because of the unfavorable energy requirements as mentioned above. In spite of the seemingly favorable 1,6-elimination for cyclo-decyl cation, products of 1,6-elimination were also absent from the mixtures. Even the carbene process, decalin (formed by a 1,6-insertion reaction) constituted only 18% of the hydrocarbon products. It is interesting to note that the bicycloalkanes formed in highest proportion by the anodic oxidation process were bicyclo[5.1.0]octane and bicyclo[4.1.0]heptane, having a three- and seven-membered ring and a three- and six-membered ring, respectively.

As the size of the ring was increased, the cationic tosylhydrazine decomposition gave less transannular products, while the anodic process showed no orderly change. This difference could be accounted for by the solvent. The fate of carbonium ions are assumed to be dependent upon their mode of formation and environment. Cationic species are more "reactive" when formed by diazotization of amines in protic solvents than by solvolysis.³⁷ Diazotizations of amines in aprotic solvents give cations different from those in protic solvents.³⁸ Minimum skeletal rearrangements and double bond migrations are observed, and cyclopropane formation and reaction with solvent (e.g., alkylation of benzene) increase.

With the above factors considered, the cycloalkyl cation produced by anodic oxidation appears more "reactive" and, hence, less solvated than the cation produced by tosylhydrazone decomposition in ethylene glycol or by deamination of cyclodecylamine with nitrous acid.²⁶ Deamination of cyclodecylamine was reported to give mainly cis-cyclodecene,²⁶ but unpublished investigations of this reaction in these laboratories show similar results to those of anodic oxidation obtained above.³⁹ The ten-fold increase in proportion of elimination reaction obtained from the cycloheptane- to cyclodecanecarboxylic acids and the fact that most of the reaction products were solvolytic ones suggest only a moderately energetic cationic intermediate, despite the slightly higher "reactivity" of the anodic oxidation intermediates compared to the cycloalkanone tosylhydrazone cationic decomposition intermediates.

In summary, it can be concluded that the reaction mechanism of the anodic oxidation of the medium ring cycloalkanecarboxylic acids with graphite electrodes involves an energetic cycloalkyl cation intermediate, which shows considerable selectivity as to the extent and type of elimination reaction.

This selectivity is illustrated by the increase of elimination products as the acid ring-size is increased (Table 1).

The selectivity among types of elimination is shown in several ways: (a) the cyclopropane derivatives decreased as the size of the ring increased (Table 6), (b) there was an absence of cyclobutane derivatives (Table 6) and (c) the ten- and nine-membered ring acid gave a high ratio of trans- : cis-oléfin.

C. Synthetic Work.

The synthetic work reported in this section are new synthesis

methods or those in which conditions were improved.

1. Synthesis of Medium Ring Acids.

Carbonations of medium ring cycloalkylmagnesium bromides were reported to give 0 to 18% yields of the corresponding acids.⁴⁰ The use of ultra-pure magnesium metal and a 3.8 molar ratio of ether to bromide resulted in major side reactions.²⁹ The use of ordinary magnesium turnings and a high molar ratio of ether to bromide improved the yield.²⁹ Cycloalkyl chlorides and magnesium turnings in anhydrous ether with a molar ratio of ether to chloride of 20 to 33 were shown in these investigations to give yields up to 68%.

The preparation of cycloalkyl chlorides is much easier since the pure cycloalkenes and cycloalkanes have become commercially available.⁴¹ A procedure modified after a British patent⁴² was chosen; anhydrous hydrogen chloride was slowly added to an olefin-benzene solution with anhydrous zinc chloride catalyst. Addition was complete to cyclooctene in 5 hours but cyclodecene took considerably longer. The yields obtained were 92 and 88%, respectively, from cyclooctene and cyclodecene.

Another source of cyclodecyl chloride that appears promising is the direct chlorination of cyclodecane. On a small scale, a 35% yield of the monochloride was obtained in one hour at room temperature by passing dry chlorine through the pure, dry cyclodecane. The unreacted cyclodecane was recovered and very small amounts of dichloride (less than 10%) was obtained.

The medium ring acids containing an odd number of ring-carbons were prepared from even numbered cycloalkenes. The first step involved hydroboration of the olefin to the alcohol.⁴³ Oxidation to the ketone, halogenation and Favorskii rearrangement of the 2-haloketone gave the

acid.⁴⁴ Conversions of cycloalkanols to ketones were accomplished in highest yields (85-95%) by the use of stoichiometric amounts of sodium dichromate dihydrate and alcohol with about 0.9 equivalent of sulfuric acid.

Nitration of cyclodecane followed by the Nef reaction to ketone proved dissappointing. Overall yield of the ketone from the cycloalkane was only 20%.

Halogenation of the cyclic ketones presented a different problem. N-bromosuccinimide,⁴⁴ cupric bromide⁴⁵ and elemental bromide⁴⁶ all gave good yields of the corresponding 2-bromocycloalkanone. Reaction of N-bromosuccinimide was hard to control⁴⁷ and the cupric bromide reaction involved more time and expense than direct bromination with bromine. For direct bromination, the bromine color acted as an indicator to tell the extent of the reaction and a high yield of acid was obtained without purification of the intermediate bromoketone. The mixed solvent system (carbon tetrachloride and enough water to make 3*N* hydrogen bromide) resolved any inconvenience of hydrogen bromide evolution nicely. The over all yield of acid from the olefin was better than 50%.

2. Cyclononadiene Synthesis

The reduction of 9,9-dibromobicyclo[6.1.0]nonane⁴⁸ proceeds readily to 1,2-cyclononadiene⁴⁹ with methyllithium or magnesium under Grignard conditions. The allene can then be hydrogenated to cis-cyclononene.⁵⁰ Cyclononanone can be made by hydroboration followed by oxidation with sodium dichromate. The magnesium reduction was preferred by the author since it required less time and chemicals to complete the reaction. A side product that was not mentioned in the above reference was obtained in 8 to 10% yield in each preparation by the author. The identity proved to be bicyclo[6.1.0]nonane.

Two reaction paths were postulated for its presence: a) two atoms of magnesium react to give a di-Grignard reagent.

or b) an active hydrogen donor could attack the mono-Grignard reagent before elimination of magnesium bromide and subsequent rearrangement.

Di-Grignard reagents from 1,2- and 1,3-dihalides are unstable and eliminate and form cyclopropanes respectively.⁵¹ Di-Grignard reagents from 1,1-dihalides have never been prepared so the first scheme above is unlikely. However, carbonation prior to hydrolysis could distinguish between the two proposed paths. The first path would give a dicarboxylic acid and the latter giving a monocarboxylic acid. Carbonation of the Grignard reagent did give a small amount of acid (3%). Attempts to purify the acid by recrystallization proved fruitless. It appeared that the acid was a pair of geometric isomers, quite possibly the syn- and anti-bicyclo[6.1.0]nonane-9-carboxylic acids. Carbon-hydrogen analysis of the solid acid "mixture" showed results in good agreement for the mono-carboxylic acid. The apparent failure to obtain

a pure crystalline material is attributed to the presence of a pair of geometrical isomers.

D. Identification of Hydrocarbon Products

The material balance of each run was determined by the separation of the reaction products into four fractions: (a) recovered acid, (b) hydrocarbon fraction, (c) alcohol fraction and (d) ester fraction. The total number of moles of the above products divided by the moles of starting materials was the total material balance.

The hydrocarbon fraction was analysed by vapor phase chromatography (v.p.c.). The identity of each component was established by the introduction of an authentic sample and noting the enlargement of that peak on the chromatogram.

For example, the hydrocarbon fraction from the electrolysis of cycloheptanecarboxylic acid contained 12% norcarane and 87% cycloheptene. A small sample of the hydrocarbon mixture, about 10 μ l., was placed in a melting point tube by the use of a chromatographic syringe. The addition of 1 μ l. of norcarane, followed by mixing (loading and ejection of syringe), would give a chromatogram showing approximately 20% norcarane. This same solution would be analysed in another column or at a different temperature to establish the fact that the unknown component and the authentic sample were not separable and therefore probably the same compound.

The preparation of authentic samples of the olefins was simple. Dehydration of cycloheptanol with 80% phosphoric acid readily produced cycloheptene in a good yield. Cyclooctene and a mixture of cis- and trans-cyclodecene were commercially available. Gardner's method⁴⁸ was used to prepare cis-cyclononene from cyclooctene. Trans-cyclononene

was identified by the infrared spectrum of the hydrocarbon fraction from the nine-membered ring acid.

The bicyclo[X.1.0]alkanes were prepared by methylenation of the corresponding cis-cycloalkenes with methylene iodide and zinc-copper couple in ether.⁵²

The other bicycloalkanes were prepared by the decomposition of the tosylhydrazones in diglyme²⁴ or ethylene glycol²³. The mixtures obtained were not separated into the pure components but were used as obtained. Published identifications were accepted.

Cis- and trans-decalin were separated, via a preparative gas chromatograph,⁵³ from a commercial sample of decahydronaphthalene.

Bicyclo[4.2.0]octane was prepared by the photo-isomerization of 1,3-cyclooctadiene in a Rayonette photochemical reactor with 2537 Å source.⁵⁴ The resulting bicyclo[4.2.0]oct-7-ene was hydrogenated to the bicycloalkane in a low pressure Paar hydrogenator utilizing 5% platinum on carbon catalyst.

E. Electrode Studies

An examination of Table 1 shows that reasonable current efficiencies were encountered in the electrolysis of the medium ring acids with a graphite anode. The expected carbonium ion was indeed obtained as evidenced by other data above. Two changes in the electrolytic cell were tried. The first was the use of a 1.25 inch circular copper cathode to provide for a uniform field and therefore a uniform current density. The second change was substitution of a platinum anode for the graphite anode with the intent of establishing if any mechanistic changes were associated with the electrode composition (catalytic activity).

The change in electrode rearrangement produced very little

product and efficiency changes (Expts. 6, 7, 8 and 9; Table 1). The similar results obtained by the two different electrode arrangements should perhaps have been expected based on the following information. The current density was shown⁵⁵ to affect the ethane efficiency in the electrolysis of 20% potassium acetate with platinum electrodes. For example, a current density of 0.04, 0.3 and 4 gave ethane efficiencies of 28, 81 and 88%, respectively. Acetate-acetic acid ratio had little effect on the electrolysis. Ratios from pure acetic acid to pure acetate gave⁵⁶ ethane efficiencies from 67 to 77%. Therefore the variation in current density caused by a non-uniform field would not be expected to give much different results.

The substitution of a platinum anode for graphite resulted in a sharp decrease in the current efficiency and elimination fraction. For the ten-membered ring acid the current efficiency (51 and 42% with a carbon anode and the two different copper cathodes) dropped to 7% with a platinum anode. The hydrocarbon fraction remained the same but the elimination fraction decreased from 0.55 and 0.31 with carbon anodes to 0.15 and 0.24 with platinum anodes.

F. Nuclear Magnetic Resonance Spectra of cis-Bicyclo[X.1.0]alkanes

The nuclear magnetic resonance (n.m.r.) spectra of some cis-bicyclo[X.1.0]alkanes ($X = 2$ to 8 and 10, Table 7) show some interesting chemical shift positions for the cyclopropane CH_2 protons as the size of the larger ring increases (Table 7). It appears that the syn-proton (H_a) experiences a decided shielding effect causing the chemical shift position to appear at higher field positions as the size of the larger ring increases. The normal chemical shift (tetramethylsilane = 0 p.p.m.) position for cyclopropane derivatives is about -0.2 p.p.m.⁵⁷ Table 7

shows the chemical shift position up-field as far as 0.5 p.p.m. for the ten-membered ring derivative. The anti-proton is deshielded from the regular cyclopropane position to approximately the same degree although the exact position is difficult to specify because the signal is mixed with those of the bridgehead and other hydrogens.

This shielding-deshielding effect could be the result of an aliphatic ring current. This reasoning prompted the synthesis of the cyclopentane derivative to assess the importance of ring planarity for shielding effect and the aliphatic ring current. The results indicate that relative planarity is not important since bicyclo[3.1.0]hexane gave a chemical shift position for H_a at the normal cyclopropane position. Bicyclo[2.1.0]pentane (Table 7) showed methylene absorption the farthest down-field.⁵⁸

Perhaps the syn-proton is shielded by proximal methylene groups, and the proximity is a function of ring size. This explanation however does not account for the deshielding of the anti-proton.

A very interesting problem pertinent to these considerations was reported⁶⁰ concerning the electronic structure of the homotropylium cation, prepared by protonation of cyclooctatetraene.⁶¹

The n.m.r. spectrum of the cation displays absorptions at -8.6, -6.6, -5.2 and 0.6 p.p.m. (areas 5:2:1:1) which can be assigned to the five protons on C_2 to C_6 ,

Table 7

NMR Chemical Shift Position of Cyclopropane

Protons in cis-bicyclo[X.1.0]alkanes.

Bicyclo- alkane	Chemical Shift, ^a	
	H _a	H _b
2.1.0 ^b	-0.4	-0.7
3.1.0 ^c	-0.02	-0.21
4.1.0 ^d	-0.02	(-0.4)
5.1.0	(0-0.1) ^e	--
6.1.0	0.3	(-0.4)
7.1.0	0.4	(-0.4)
8.1.0	0.5	(-0.5)
10.1.0	0.37	(-0.4)

(a) Center of signal, in ppm, relative to internal tetramethylsilane.

Figures in parentheses are estimates of maximum upfield positions of signals. (b) Reference 58. (c) Apparent coupling constants:

J_{AB} 4.5-5.0, J_{AC} 4.5, J_{BC} 7.5. (d) Apparent coupling constants:

J_{AB} 3.5, J_{AC} 4.5. (e) Maximum upfield signal (in ppm) is -0.1 for

bicyclo[5.1.0]oct-3-ene, 0.0 for bicyclo[5.1.0]oct-2-ene and for cis-

and trans-tricyclo[6.1.0.0^{3,5}]nonane, and +0.1 for tricyclo[6.1.0.0^{2,4}]nonane; See Reference 59.

the two equivalent protons H_1 and H_7 , and protons H_b and H_a , respectively. The authors suggest and give evidence for the presence of a ring current in the molecule which is primarily responsible for the extraordinarily large difference in chemical shifts (5.8 p.p.m.) between the two protons H_a and H_b , the largest chemical shift difference reported for two protons attached to the same proton.

Thus it appears that an aliphatic ring current may be operating for the larger rings and, apparently, the size of the ring is more important for an aliphatic ring current than planarity of the ring.

CHAPTER III
EXPERIMENTAL

A. Preparation of Cycloheptane- and Cyclononanecarboxylic Acids

1. Preparation of Cyclononanecarboxylic Acid⁴⁴

a. Preparation of Cyclodecanol

Hydroboration⁴³ of cis-cyclodecene⁶² was performed by the dropwise addition of 35.5 g. (0.25 mole) of boron trifluoride etherate to a solution of 69 g. (0.5 mole) of cyclodecene and 7.0 g. (0.188 mole) of sodium borohydride in 1 l. of diglyme at 0°. The mixture was stirred for 0.5 hour and then oxidized by the addition of 50 ml. of 3M sodium hydroxide (0.15 mole) and 68 g. (0.6 mole) of 30% hydrogen peroxide at 25° with stirring and cooling. The mixture was extracted four times with 100 ml. portions of petroleum ether, and the combined extracts were washed with five 100 ml. portions of water. The solvent was removed by rotary evaporation, and the residue was distilled at reduced pressure to give 40.9 g. (69%) of cyclodecanol; b.p. 87° (1.2 mm.) (lit.⁶³ b.p. 125 (12 mm.)).

b. Preparation of Cyclodecanone

This oxidation was carried out by the addition, all at once, of 40.9 g. (0.262 mole) of cyclodecanol in 100 ml. of 50% aqueous acetone to a solution of 26.0 g. (0.088 mole) of sodium dichromate dihydrate and 35 g. (0.35 mole) of concentrated sulfuric acid in 150 ml. of water. The temperature was controlled at 50 to 55° by the addition of ice and the mixture was stirred for an additional hour at the same temperature.

The mixture was diluted with 150 ml. of water and extracted three times with 100 ml. portions of petroleum ether, and the combined extracts were washed with water. After the solution had been dried with anhydrous magnesium sulfate, the solvent was removed by a rotary evaporator to leave 32.6 g. (81%) of cyclodecanone. The ketone was used without further purification.

c. Bromination of Cyclodecanone⁴⁶

A mixture of 25.6 g. (0.166 mole) of cyclodecanone, 60 ml. of carbon tetrachloride, and 90 ml. of water was brought to reflux in a 500 ml., 3-necked flash. A solution of 26.5 g. (0.166 mole) of bromine in 30 ml. of carbon tetrachloride was added to keep a constant reflux while the reaction mixture was irradiated with a 150-watt light bulb. The bromine color dissipated step-wise, apparently via a free radical mechanism since bromination of cyclooctanone in the presence of benzoyl peroxide gave similar step-wise bromine consumption. The mixture was diluted with 100 ml. of solvent and washed with water until neutral. The solution was dried and the solvent was removed at reduced pressure to leave 39 g. of 2-bromocyclodecanone (approximately 100%); infrared absorption, 1712 cm^{-1} (lit.⁶⁴ 1712 cm^{-1}). The bromoketone was used directly in the next step without further purification.

d. Cyclononanecarboxylic Acid Via Favorskii Reaction

A solution of 39 g. (0.166 mole) of 2-bromocyclodecanone was added in one hour to a solution of 12 g. (0.52 g. atom) of sodium in 200 ml. of methanol at -20° . The solution was stirred at -20° for one-half hour, allowed to warm to room temperature in two hours, and finally heated to reflux for one hour. After the addition of a solution of 30 g. of potassium hydroxide in 75 ml. of water, the mixture was refluxed

for three hours. The alkaline solution was washed with petroleum ether, acidified with concentrated hydrochloric acid and extracted with five 75 ml. portions of petroleum ether. The combined extracts were dried, concentrated by rotary evaporation, and finally distilled at reduced pressure to give 19.5 g. (69%) of cyclononanecarboxylic acid; b.p. 118° (0.15 mm.). (lit.⁴⁴ b.p. 114 - 115 (0.1 mm.)).

2. Preparation of Cycloheptanecarboxylic Acid

a. Preparation of Cyclooctanone

A solution of 40 g. (0.13 mole) of sodium dichromate dihydrate and 20 ml. (0.35 mole) of sulfuric acid in 200 ml. of water was added to 50 g. (0.391 mole) of cyclooctanol⁶² in 75 ml. of water at once with good stirring. The temperature was controlled at 50 to 55° by the addition of small amounts of ice, and the solution was stirred at the same temperature for one hour, diluted with 300 ml. of water, and extracted with three 125-ml. portions of petroleum ether. The combined extracts were washed with water until neutral, concentrated by rotary evaporation, and distilled at reduced pressure to give 45.7 g. (93%) of cyclooctanone; b.p. 68 (48 mm.). (lit.⁶⁵ b.p. 115 (60 mm.)). In other preparations yields as low as 77% were obtained.

b. 2-bromocyclooctanone

A solution of 20.2 g. (0.16 mole) of cyclooctanone in 25 ml. of chloroform was slowly added to a refluxing slurry of 75 g. (0.32 mole) of cupric bromide in 100 ml. of chloroform and 125 ml. of ethyl acetate.⁴⁵ After a 20 min. induction period, the black cupric bromide turned green and hydrogen bromide began to evolve. The mixture was stirred for two hours, the white cuprous bromide was filtered off, and the solvent was removed with a rotary evaporator. There was obtained 33 g. (approx. 100%) of crude 2-bromocyclooctanone, which was used

without further purification in the next step.

Bromination of the above ketone with N-bromosuccinimide was hard to control; e.g., in one experiment a sudden exotherm blew the condenser to the roof of the hood.

Good success was obtained by direct bromine addition with or without benzoyl peroxide in water-carbon tetrachloride suspensions and irradiation of the mixture with an ordinary 150-watt light bulb. Direct chlorination was sluggish and lacked the color of the bromine to indicate the extent of the reaction.

The color-indicator properties of the bromine reagent along with the ease of manipulation make direct bromination the preferred method for 2-halocycloalkanone preparation.

c. Preparation of Cycloheptanecarboxylic Acid

A solution of 73.6 g. (0.358 mole) of 2-bromocyclooctane in 50 ml. methanol was added to a solution of 15 g. (0.65 g. atom) of metallic sodium in 300 ml. of anhydrous methanol in one-half hour at -20° . The mixture was stirred for an additional hour at the same temperature, allowed to warm to room temperature over night, and finally brought to reflux for one hour. A solution of 40 g. of potassium hydroxide in 100 ml. of water was added, and the mixture was refluxed three hours and then diluted with 400 ml. of water. The neutral portion was extracted four times with petroleum ether and the organic phase was discarded. The aqueous phase was acidified with concentrated hydrochloric acid and extracted five times with 125 ml. portions of petroleum ether. The solvent was removed from the combined organic solution, and the residue was distilled to give 20.7 g. (40%) of cycloheptanecarboxylic acid; b.p. 88° (0.25 mm.), (lit.⁴⁰ b.p. $130-2^{\circ}$ (15 mm.)).

B. Preparation of Cyclooctane- and Cyclodecanecarboxylic Acid

1. Preparation of Cyclooctanecarboxylic Acid⁴⁰

a. Cyclooctyl Chloride⁴²

To a solution of 55.0 g. (0.5 mole) of cis-cyclooctene and 5.0 g. of zinc chloride in 200 ml. of benzene, one mole of dry hydrogen chloride was added at room temperature with stirring; protection from atmospheric moisture was provided by a calcium chloride drying tube. The hydrogen chloride addition was complete in five hours. The mixture was decanted from the zinc chloride, washed five times with water, and concentrated by rotary evaporation. Distillation at reduced pressure gave 67.8 g. (92% of cyclooctyl chloride; b.p. 60° (5 mm.)), (lit.⁴² b.p. 87-90° (19 mm.)). Anal. (S).⁶⁶ Calcd. for $C_8H_{15}Cl$: C, 64.4; H, 10.2. Found: C, 64.2; H, 10.3.

b. Cyclooctanecarboxylic Acid

A 2 l. 3-necked flask equipped with a stirrer, ice-water condenser, and nitrogen atmosphere was charged with 12.0 g. (0.5 g. atom) of magnesium turnings and 300 ml. of ether. A solution of 56.5 g. (0.38 mole) of cyclooctyl chloride in 1200 ml. of ether was added in 5 hours. The resulting Grignard reagent was forced, under nitrogen pressure, through a filter stick into a large erlenmeyer flask containing excess solid carbon dioxide. The transfer was completed in about 20 minutes. After the mixture had been stirred well and allowed to warm up over night, it was acidified with hydrochloric acid. The layers were separated and the aqueous layer was extracted twice with ether. The combined extracts were treated with excess 5% potassium hydroxide solution. The resulting ether solution was set aside for analytical determination of its constituents. After ether washing, the potassium carboxylate solution was acidified and extracted with petroleum ether. The solvent was removed,

and the crude cyclooctanecarboxylic acid was distilled at reduced pressure. There was obtained 26.3 g. (44%) of cyclooctanecarboxylic acid; b.p. 108 (0.12 mm.). (lit.⁶⁷ b.p. 150 (19 mm.) and⁴⁰ 142-5° (11 mm.))

The neutral portion of this reaction was found by v. p. c. analysis to contain cyclooctane (12%), cyclooctene (12%), a trace of bicyclo-[3.3.0]octane and bicyclooctyl (15%). Preparations of authentic samples for the above analysis are described in later sections.

2. Preparation of Cyclodecanecarboxylic Acid

a. Cyclodecyl Chloride

A mixture of 70.1 g. (0.508 mole) of cyclodecene,⁶² 200 g. of benzene and 5-6 g. of anhydrous zinc chloride was placed in a 500 ml., 3-necked flask equipped with a stirrer, condenser and gas bubbler. Dry hydrogen chloride was generated by dropping concentrated hydrochloric acid into 98% sulfuric acid and scrubbing out the residual moisture with a sulfuric acid trap. The dry hydrogen chloride was passed through the bubbler tube into the reaction flask. The flask was protected from atmospheric moisture by a calcium chloride drying tube. The only indication of reaction at room temperature was that the solid (zinc chloride) began to turn brown. After 30 minutes of slow addition of gas, the reaction temperature was 35°. The contents of the flask were stirred and left under a hydrogen chloride atmosphere over the weekend.

The mixture was diluted with 200 ml. of petroleum ether and washed several times with water to get rid of traces of zinc chloride and acid. After the organic layer had been dried over magnesium sulfate, the solvent was removed. Distillation at reduced pressure gave about 3 g. of cyclodecene and 78.8 g. (88%) of chlorocyclodecane; b.p. 58-58.5 (0.12 mm.); n_D^{25} 1.4900.

b. Cyclodecyl Chloride from Cyclodecane

For one hour, dry chlorine gas was bubbled through 20.0 g. (0.143 mole) of cyclodecane irradiated with a 150-watt light bulb. The mixture was diluted with 100 ml. petroleum ether and washed with water until neutral. Distillation after solvent removal gave 8.8 g. (35%) of chlorocyclodecane; b.p. 82° (2.0 mm.), n_D^{25} 1.4900. Anal. (S). Calcd. for $C_{10}H_{19}Cl$: C, 68.74; H, 10.96. Found: C, 68.75; H, 10.97.

The yield of dichlorocyclodecane was estimated by v.p.c. to be less than 10%.

3. Preparation of Cyclodecanecarboxylic Acid

A small iodine crystal and 1 ml. of methyl iodide was used to activate 12.2 g. (0.5 g. atom) of magnesium turnings in 100 ml. of anhydrous ether in a 2 l., 3-necked flask protected with a nitrogen atmosphere and calcium chloride-filled drying tube. A solution of 78.5 g. (0.43 mole) of cyclodecyl chloride in 1500 ml. of ether was added in 5 hours. The contents of the flask were forced backwards, by means of nitrogen pressure, through the bubbler tube into a 4 l. erlenmeyer flask containing excess solid carbon dioxide. The acid was worked up as in the previous section. Distillation at reduced pressure gave 52.3 g. (66.5%) of cyclodecanecarboxylic acid; b.p. 122 to 123° (0.11 mm.). The acid slowly crystallized on standing at room temperature; m.p. 53° , lit.⁴⁰ m.p. 53° . The infrared spectrum was that expected for such an acid. Standard tests for unsaturation were negative. The methyl ester made by dissolving the acid in methanol and adding a drop of boron trifluoride etherate gave a single v.p.c. peak.

C. Preparation of cis-Bicyclo[X.1.0]alkanes

1. Preparation of cis-Bicyclo[4.1.0]heptane⁵²

The preparation of norcarane⁵² is described in Organic Syntheses and this procedure was used for the synthesis of the bicycloalkanes in this section.

A mixture of 16.4 g. (0.26 mole) of zinc-copper couple⁵² and 200 ml. of anhydrous ether was placed in a 500 ml. flask previously flushed with nitrogen. Several crystals of iodine were added to activate the catalyst. After the iodine color dissipated, a solution of 20 g. (0.244 mole) of cyclohexene and 67 g. (0.25 mole) of methylene iodide was added all at once. The mixture was stirred and refluxed over night.

The product was worked up by adding 75 ml. of petroleum ether and washing out the zinc iodide with saturated ammonium chloride or 3% hydrochloric acid. Hydrochloric acid appeared to have the preferred distribution coefficient. The organic phase was washed twice with potassium carbonate or 5% sodium hydroxide and twice with water. The solvent was removed by rotary evaporation and the residue was distilled to give 10 g. (43%) of cis-bicyclo[4.1.0]heptane; b.p. 115°, n_D^{25} 1.4549. lit.⁵², b.p. 116 to 117°, n_D^{25} 1.4546. Anal. (G).⁶⁶ Calcd. for C_7H_{12} : C, 87.42; H, 12.53. Found: C, 87.50; H, 12.70. The infrared spectrum showed C-H absorption at 3.2μ , which is characteristic of cyclopropanes.⁶⁸

The n.m.r. spectrum could be divided into 4 areas: 0.02 p.p.m. (1 proton) split triplet; -0.3 to -1.05 p.p.m. (3 protons) unresolved multiplet, -1.2 p.p.m. (4 protons) "triplet-like" multiplet and -1.5 to -2.2 p.p.m. (4 protons) unresolved multiplet. It appears that the last two peaks (4 protons each) are the equatorial and axial protons of the cyclohexane ring. The 3-proton absorption peak represents the bridge-head hydrogens plus the anti-hydrogen, and the 1-proton peak is caused by the syn-hydrogen of the cyclopropane ring. The assignment of the syn- and anti-hydrogens is based on the assumption that the ring is causing some

kind of shielding effect. In this compound the geminal coupling constant, J_{AB} , is 3.7 cps. (unexpectedly small) and the coupling with the bridgehead hydrogens, H_c , gave the constant $J = 4.5$ cps.

2. Preparation of Bicyclo[3.1.0]hexane

The preparation of this bicyclohexane was conducted in a manner similar to the above preparation. A solution of 31.0 g. (0.544 mole) of cyclopentene and 134 g. (0.5 mole) of methylene iodide in 100 ml. of ether was added at once to 35 g. (0.55 mole) of zinc-copper couple in 150 ml. of ether after activation with iodine crystals. The product was worked up and distilled to obtain 25 g. of crude material. This product was carefully fractionated to give a center cut of 8.0 g. of about 95% bicyclo[3.1.0]hexane, b.p. 79° . Lit.⁵² b.p. $81-82^\circ$. Anal. (G). Calcd. for C_6H_{10} : C, 87.74; H, 12.27. Found: C, 87.57; H, 12.13. The infrared spectrum showed C-H absorption at 3.28, 3.32, 3.35, 3.40 and 3.51 microns.

The n.m.r. spectrum of bicyclo[3.1.0]hexane is very complex and without decoupling experiments the complete understanding of the spectrum is impossible. However, the cyclopropane geminal hydrogen absorptions can be assigned and coupling constants between the bridgehead hydrogens and the two geminal hydrogens have been tentatively assigned (Figure 2).

Four general peaks were observed: -0.1 p.p.m. (2 protons on cyclopropane geminal positions) two split triplets, -1.0 to -1.5 p.p.m. (4 protons) unresolved multiplet, -1.6 p.p.m. (2 protons) "singlet-like" multiplet, and -1.7 p.p.m. (2 protons) unresolved multiplet.

The two cyclopropane hydrogens should couple with each other to give two doublet signals of different chemical shift. The two identical bridgehead protons should split each peak of the doublet into a

Figure 2
 Analysis of AB Portion of the NMR
 Spectrum of Bicyclo[3.1.0]hexane

Observed Spectrum

J_{AC} 4.5 cps, J_{BC} 7.5 cps, J_{AB} 4.5 cps

triplet. This gives a total of 12 peaks but only 9 could be distinguished. However, by a trial and error process, it was shown that the observed peaks can accommodate this multiplicity (Figure 2).

The integrated area of the right-hand four peaks was equivalent to exactly one proton and the other five to an area for exactly one proton which strengthens this argument.

The chemical shift of the bridgehead hydrogens (H_c) cannot be assigned without further work. Protons H_c would couple with the other protons H_d and H_d^1 (anti to cyclopropane ring) as well as H_a and H_b to give a broad complex multiplet. The multiplicity of the signals at -1.7 and -1.6 p.p.m. are not that complex. The only signal left is at -1.0 to -1.5 p.p.m., up field from the ring hydrogens, where about eleven sawtooth peaks are shown.

3. Preparation of Bicyclo[8.1.0]undecane

The procedure was essentially the same that was used for norcamrane.⁵² The starting materials were 26.2 g. (0.4 mole) of zinc-copper couple, 69 g. (0.26 mole) of methylene iodide and 34.5 g. (0.25 mole) of 78% cis-cyclodecene (the remainder was 2.2% trans-cyclodecene and cyclodecadienes). After the product was worked up, a v.p.c. analysis indicated the reaction had proceeded to about 60% with considerable amounts of tricyclododecanes resulting from the addition of 2 moles of methylene iodide to the diene contaminants in the cyclodecene sample. However, careful fractionation provided a 5 g. center cut of 85% bicyclo[8.1.0]undecane; b.p. 76 to 77° (5.5 mm.) n_D^{25} 1.4786. Anal. (G). Calcd. for $C_{11}H_{20}$: C, 86.76; H, 13.24. Found: C, 86.84; H, 13.17.

The infrared spectrum showed C-H absorption at 3.25, 3.35, 3.42 and 3.48 microns. The n.m.r. spectrum showed 4 absorption peaks: 0.5 p.p.m. (1 proton) broad unresolved multiplet; -0.6 p.p.m. (3.4 protons)

singlet; -1.3 to -1.7 p.p.m. (12.6 protons) unresolved multiplet; and -1.9 p.p.m. (3 protons) unresolved multiplet.

4. Preparation of Bicyclo[7.1.0]decane

The reaction was carried out in a 500 ml. flask in the same way as that previously described. The starting materials consisted of 10.0 g. (0.081 mole) of cis-cyclononene, 22.8 g. (0.085 mole) of methylene iodide and 5.9 g. (0.09 mole) of zinc-copper couple in 100 ml. of ethyl ether. Distillation of the crude product at reduced pressure gave 6.0 g. (54%) of bicyclo[7.1.0]decane, b.p. 83 to 84° (16 mm.) n_D^{24} 1.4740. Anal. (G). Calcd. for $C_{10}H_{18}$: C, 86.90; H, 13.10. Found: C, 87.05; H, 13.00.

The infrared spectrum indicated the presence of the bridgehead hydrogens by an absorption peak at 3.25, 3.35, 3.42 and 3.48 microns. The n.m.r. spectrum contained 4 peaks: 0.4 p.p.m. (1 proton) unresolved multiplet, -0.6 p.p.m. (4.4 protons) unresolved quartet, -1.6 p.p.m. (12.6 protons) a sharp singlet superimposed on a broad multiplet, and -1.8 to -2.2 (2 protons) broad multiplet.

5. Preparation of Bicyclo[6.1.0]nonane²⁷

The reaction was carried out in a manner previously described. The starting materials were 33 g. (0.3 mole) of cis-cyclooctene, 99 g. (0.32 mole) of methylene iodide and 23 g. (0.35 mole) of zinc-copper couple in 400 ml. of ethyl ether. Distillation of the crude product at reduced pressure gave 26 g. (70%) of bicyclo[6.1.0]nonane; b.p. 71 to 71.5° (26 mm.) n_D^{25} 1.4682; lit.²⁷; b.p. 43° (8 mm.), n_D^{25} 1.4622. Anal. (G). Calcd. for C_9H_{16} : C, 87.06; H, 12.94. Found: C, 86.81; H, 13.22.

The infrared spectrum showed C-H absorption at 3.28, 3.36, 3.44 and 3.52 μ . The n.m.r. spectrum contained 5 peaks: 0.32 p.p.m. (1

proton) a "triplet-like" multiplet; -0.58 p.p.m. (4 protons) unresolved multiplet; -0.98 p.p.m. (1 proton) unresolved multiplet; -1.5 p.p.m. (8 protons) unresolved multiplet; -1.9 p.p.m. (1.3 protons) unresolved multiplet and -2.1 p.p.m. (0.7 proton) unresolved multiplet.

6. Preparation of Bicyclo[10.1.0]tridecane

The reaction was carried out in a manner described in the previous sections. The starting materials consisted of 20 g. (0.12 mole) of a mixture of 59% trans- and 41% cis-cyclododecene, 35 g. (0.13 mole) of methylene iodide and 8.5 g. (0.13 mole) of zinc-copper couple in 75-100 ml. of anhydrous ether. The induction period took two days of refluxing but the reaction was finally started by the addition of more iodine crystals. Distillation of the crude product gave 6 g. (28%) of a mixture of 65% trans- and 35% cis- bicyclo[10.1.0]tridecane; b.p. 102 - 106° (4.5 mm.), n_D^{25} 1.4817. Anal. (S). Calcd. for $C_{13}H_{24}$: C, 86.58; H, 13.42. Found: C, 86.27; H, 13.34. The last ml. of this fraction was collected separately (106° at 4.5 mm.) and analysis by v.p.c. showed equal portions of the cis- and trans-isomers.

The infrared spectrum showed C-H absorption at 3.28, 3.36, 3.44 and 3.51 microns. The n.m.r. spectrum of the 65/35 sample consisted of 4 regions: -1.14 p.p.m. (19 + protons) unresolved multiplet with broad base 1.4 p.p.m. wide; -0.5 p.p.m. (3.3 protons) broad unresolved multiplet, -0.2 p.p.m. (1.4 protons) unresolved multiplet, and 0.36 p.p.m. (0.3 proton) unresolved multiplet.

Although only 19 protons appear in the large peak (-1.4 p.p.m.) the 20th proton appears to be mixed with the bridgehead protons at -0.5 p.p.m. The one-third proton at 0.36 p.p.m. could be the syn-proton of the cis isomer and the anti-proton might be at the -0.5 p.p.m. with the bridgehead protons. The methylene hydrogens for the trans-isomer could be located

at -0.2 p.p.m.; the normal chemical shift for cyclopropane hydrogens.

D. The Preparation of Cyclononanone

1. Dibromomethylene Addition⁴⁸ to cis-cyclooctene

A solution of 180 g. (1.60 mole) of potassium tert-butoxide in 1500 ml. of tert-butyl alcohol was prepared in a 3 liter, 3-necked flask equipped with a stirrer, condenser, dropping funnel and a nitrogen atmosphere. The contents were cooled to 5° by an ice slurry. A solution of 495 g. (3.0 mole) of cyclooctene and 399.5 g. (1.5 mole) of bromoform was added in 5 hours at 5 - 10°. The ice bath was removed and the solution stirred for 2 hours at room temperature. The solution was diluted with 1500 ml. water and the organic layer was removed. The aqueous layer was extracted 4 times with 200 ml. portions of petroleum ether. The extracts were combined with the original organic phase, and the alcohol was removed by extracting 4 times with 500 ml. portions of water. After the solvent had been removed by rotary evaporation, the residue was distilled at reduced pressure to give 410 g. of cyclooctene and 227.4 g. (80.5%) of 9,9-dibromobicyclo[6.1.0]nonane, b.p. 89° (0.3 mm.), n_D^{25} 1.5508; (lit.⁶⁹ b.p. 92-93° (0.9 mm.)),

2. Reduction of 9,9-dibromobicyclo[6.1.0]nonane

a. Preparation of 1,2-cyclononadiene

The reduction reaction can be carried out successfully utilizing methyllithium or magnesium metal under Grignard conditions. The latter method gave slightly lower yields and contained some bicyclo[6.1.0]nonane but the preparation was considerably simpler and was preferred over the former.

A 1000 ml., 3-necked flask equipped for stirring and cooling was charged with 30.0 g. (1.24 g. atom) of magnesium metal and 500 ml.

of ether. The reaction was started with methyl iodide and iodine crystals under a nitrogen atmosphere. A solution of 120 g. (0.425 mole) of 9,9-dibromobicyclo[6.1.0]nonane and 100 ml. of ethyl ether was added in 2 hours. A magnesium bromide etherate layer began to separate in about 30 minutes. The mixture was stirred 30 minutes after the addition was complete and hydrolysed with saturated ammonium chloride. After 200 ml. of pentane had been added, the magnesium bromide was removed by water washing. The solvent was removed from the organic solution and the residue was distilled at reduced pressure to give a mixture (b.p. 68 to 72° (18 mm.); lit.⁶⁹ 83-84.5 (36 mm.)) shown by v.p.c. analysis to be 23.3 g. (46%) of 1,2-cyclononadiene and 4.8 (9%) of bicyclo[6.1.0]nonane. The retention time of the bicyclononane was identical to that obtained from the reaction of cis-cyclooctene and methylene iodide in ethyl ether with zinc-copper couple (temperatures of v.p.c., 60 and 75°; v.p.c. conducted with a 100 ft. capillary column coated with GE-96 silicone).

b. Preparation of Bicyclo[6.1.0]nonane-9-carboxylic acid

Another reduction of 9,9-dibromobicyclo[6.1.0]nonane was performed (utilizing 0.355 mole of dibromide) in which, prior to hydrolysis with saturated ammonium chloride solution, the mixture was cooled to 2° and bone dry carbon dioxide was added slowly over the surface of the solution. The temperature rose to 5-6° and remained steady for 20 minutes, then dropped to 2° again. No precipitate was observed but a carbon dioxide atmosphere was maintained for an hour. The mixture was hydrolyzed with 5% hydrochloric acid and 200 ml. of pentane was added. The aqueous layer was extracted with 100 ml. pentane, and the combined organic phases were washed once with 200 ml. of water and then with 100 ml. of 5% sodium hydroxide solution. The organic layer was worked up,

and a mixture of 21.1 g. of 1,2-cyclononadiene and a small amount of bicyclo[6.1.0]nonane was obtained similar to that above. The aqueous layer was acidified with concentrated hydrochloric acid and extracted 3 times with 75 ml. portions of petroleum ether. The extracts were combined and the solvent removed to give 3.2 g. (5.5%) of a solid acid; m.p. 38 to 45°. The wide melting point range despite 3 recrystallizations indicates a mixture of perhaps syn- and anti-bicyclo[6.1.0]nonane-9-carboxylic acid. The infrared spectrum showed the definite presence of the carboxylic acid functional group. Elemental analysis supported this conclusion. Anal. (S) Calcd. for $C_{10}H_{16}O_2$: C, 71.50; H, 9.58. Found: C, 71.60; H, 9.29.

3. Hydrogenation of 1,2-cyclononadiene

A solution of 30 g. (0.246 mole) of the cyclononadiene (not free of bicyclo[6.1.0]nonane) in 180 ml. of methanol and a pinch of 5% palladium on carbon were placed in a low pressure Paar hydrogenator. After 2 hours, the rate of pressure drop indicated the diene had been consumed (i.e., the rate of hydrogenation of cis-cyclononene is slow compared to that of the diene). The mixture was diluted with 100 ml. of petroleum ether, and the methanol was removed by extracting the organic phase 5 times with 100 ml. portions of water. The solvent was removed, and the residue was distilled at reduced pressure to give 28.3 g. (93%) of cis-cyclononene; b.p. 69-71° (23 mm.) (lit.⁶⁹ b.p. 86-87° (50 mm.)).

4. Preparation of Cyclononanol

A solution of 40.0 g. (0.322 mole) of cis-cyclononene and 4.72 g. (0.121 mole) of sodium borohydride in 100 ml. of diglyme was cooled to 10° in a 500 ml. flask. A solution of 22.9 g. (0.161 mole) of boron trifluoride-etherate in 50 ml. of diglyme was added in one-half hour. More solvent was required as the alkylborane produced was a solid and

stirring became difficult. After the addition was complete, the mixture was stirred for an additional hour. The excess borohydride was destroyed by water. A solution of 70 ml. (0.6 mole) of 30% of hydrogen peroxide in 35 ml. of 10% sodium hydroxide was added at 25°. The mixture was stirred for one-half hour, diluted with 300 ml. of water and extracted 5 times with 50 ml. of petroleum ether. The diglyme was removed from the combined petroleum ether solution by 5 water washes of 50 ml. each. The solvent was removed by rotary evaporation and the residue distilled at reduced pressure to give 32.2 g. (71%) of cyclononanol, b.p. 70° (0.6 mm.) (lit.⁶³ b.p. 115° (17 mm.)).

5. Preparation of cyclononanone

A solution of 12.6 g. (0.042 mole) of sodium dichromate dihydrate and 16.8 g. (0.168 mole) of sulfuric acid in 100 ml. of water was stirred in a 600 ml. beaker by a magnetic stirrer. A slurry of 18.3 g. (0.129 mole) of cyclononanol in 50 ml. of water was added at once and stirring was continued rapidly. The temperature was controlled at 55° by the addition of ice as needed. The remainder of the alcohol was washed into the beaker with 50 ml. acetone. Stirring was continued for one hour. The mixture was extracted with five 75 ml. portions of petroleum ether. The combined extracts were washed twice with water, dried over magnesium sulfate and concentrated to give 18.0 g. (99%) of crude cyclononanone.

E. Preparation of Medium Ring Tosylhydrazones

1. Preparation of p-Toluenesulfonylhydrazide⁷⁰

Exactly 135 ml. of 85% (2.22 moles) of hydrazine hydrate was diluted with water (30 ml.) to 50% hydrazine by weight and added, in 20 to 25 minutes at 10°, to a solution of 200 g. (1.05 moles) of p-toluene-

sulfonyl chloride in 304 ml. of tetrahydrofuran (THF) in a 1000 ml. flask cooled by an ice-water bath. The mixture was stirred for 15 minutes, and the water layer was drawn off from a separatory funnel. The THF layer was washed twice with 60 ml. portions of saturated sodium chloride solution and dried over magnesium sulfate. The solution was filtered into a 2 l. flask. An equal volume of petroleum ether was added to the solution with vigorous stirring. The hydrazide immediately started to precipitate, and the slurry was cooled over night in a refrigerator. The crystals were filtered by suction, washed with petroleum ether and air dried. The hydrazide was recrystallized from 50% methanol to give 164 g. (86%) of *p*-toluenesulfonylhydrazide (tosylhydrazide), m.p. 104 to 107° (lit.⁷⁰ m.p. 101-104°)

2. Preparation of Cycloalkanone Tosylhydrazones²⁷

Equal molar quantities of cycloalkanone and tosylhydrazide were refluxed for 15 minutes in methanol (approximately 400 ml. per 0.1 mole of ketone). A quantity of water equal to 80% of the alcohol was added while the solution was hot. The solution was set aside to cool, and the tosylhydrazone was allowed to precipitate overnight. The crystals were filtered by suction, washed with water and air-dried. They were stored in a vacuum desicator for 24 hours over phosphorus pentoxide prior to use. For all cyclic ketones, the reaction was found to be essentially quantitative.

The following melting points were obtained:

	tosylhydrazone, m.p.	Lit. ²⁷ , m.p.
cycloheptanone	143 - 145°	144 - 146°
cyclooctanone	139 - 141°	140 - 141°
cyclononanone	133 - 134°	135 - 136°
cyclodecanone	125 - 128°	137 - 138°

F. Decomposition of p-toluenesulfonylhydrazones

1. Decomposition in Diglyme (Carbene Intermediate)²⁷

The decomposition of the medium ring tosylhydrazones were carried out in aprotic medium (diglyme) by a procedure adapted from Freidman and Shechter.²⁷

In a 200 ml. round bottom flask, 1.2 equivalents of metallic sodium were dissolved in excess anhydrous methanol. The excess methanol was removed via a Buchi rotary solvent evaporatory. The tosylhydrazone and solvent diglyme were added to the solid sodium methoxide and refluxed 8 to 12 hours under a nitrogen atmosphere at 150 to 175° while the mixture was stirred magnetically. The mixture was diluted with 1.5 times its volume of water and extracted three times with small amounts of pentane. The solvent was removed and the bicycloalkane and olefin fraction was collected by distillation at reduced pressure. The hydrocarbon mixture was analyzed by v.p.c. on a Barber-Coleman chromatograph with a 100' capillary column coated with GE-96 silicone. The results are tabulated below:

Decomposition in Diglyme

<u>tosylhydrazone</u>	<u>bicycloalkane, %</u>			<u>olefin, %</u>	
	<u>[X.1.0]</u>	<u>[X.3.0]</u>	<u>[X.4.0]</u>	<u>trans-</u>	<u>cis-</u>
cycloheptanone	10				90
cyclooctanone	9	46			45
cyclononanone	11	42			47
cyclodecanone		62	18	6	4

2. Decomposition in Ethylene Glycol (Cation Intermediate)²⁶

These reactions were carried out in exactly the same way as in the previous section except that ethylene glycol was utilized as solvent. This proton containing solvent promotes the formation of a diazonium

cation which eliminates nitrogen to form the cycloalkyl cations.²⁶ The results are tabulated below:

Decomposition in Ethylene Glycol

<u>tosylhydrazone</u>	<u>bicycloalkane, %</u>			<u>olefin, %</u>	
	<u>[X.1.0]</u>	<u>[X.3.0]</u>	<u>[X.4.0]</u>	<u>trans.</u>	<u>cis.</u>
cycloheptanone	18				81
cyclooctanone	10	6			83
cyclononanone	2	2		12	84
(cyclodecanone ²⁶		0.2	0.05	30	70)

G. Separation of Cis- and Trans-decalin

The two components of a commercial⁷¹ sample of decahydronaphthalene were separated by preparative gas chromatography on an Aerograph Autoprep Model A-700 with a 10 ft. x 3/8 in. column packed with carbowax on chromsorb P at 135°.

The less volatile component, cis-bicyclo[4.4.0]decane, as obtained was found to contain only 3% of the trans isomer by v.p.c. analysis. The n.m.r. spectrum showed two absorption peaks: -1.60 p.p.m. (2 protons) a tall unresolved multiplet and -1.44 p.p.m. (16 protons) a tall unresolved multiplet.

The less volatile component, trans-bicyclo[4.4.0]decane, was obtained in essentially the pure form as analyzed by v.p.c. methods. The n.m.r. spectrum showed a broad absorption from -0.7 to -1.9 p.p.m. with 5 maxima. The preferred conformation at the union of the two cyclohexane rings is e,e (equatorial, equatorial) and a conversion to the a, a (axial, axial) conformer is energetically not feasible.⁷² On the other hand, the two conformers of the cis-isomer are of equal energy (e, a vs a, e) and a rapid change of conformation at room temperature cannot be resolved.⁷³ Therefore, the n.m.r. shows only average values for each

proton which results in a much simpler spectrum for the cis-isomer.

H. Preparation of Bicyclo[4.2.0]octane

1. Preparation of Bicyclo[4.2.0]oct-7-ene⁵⁴

A 110 g. (1.02 moles) sample of cis-cis-1,3-cyclooctadiene in a 300 ml. quartz flask was irradiated for eight days in a Rayonet Photochemical Reactor with 24 tubes giving 2537 Å light. Samples were taken daily, and the increase to an indicated 17.2% conversion to bicyclooctene was practically linear over that period. Ethyl ether was added and a polymer precipitated. The eight-carbon fraction was separated from the solvent and high boiling residue by distillation at reduced pressure and this distillate was carefully fractionated in a 12 in. packed column at 35 mm. pressure to obtain 3 fractions. The first fraction (17 g., b.p. 52.5 to 55°) contained 27% of the cyclobutene derivative. The other fractions boiled at 57° and contained 18 and 7% cyclobutene for an overall yield of 10%.

The first two cuts were combined and the cyclobutene derivative was separated from the diene by preparative chromatography (10 ft. x 3/8 in. column packed with carbowax on chromosorp P at 125°). There was obtained 2.5 g. of the bicyclo[4.2.0]oct-7-ene in essentially the pure state.

In another experiment, no product was formed in 3 days of irradiation in the same photochemical reactor with 3500 Å source lamps. In a 2 to 1 benzene solution and under a nitrogen atmosphere, the best conversion was obtained at 11.9%. However, the extent of polymer formation was essentially the same.

The infrared spectrum showed strong "vinyl type" absorption at 3.2 microns. No carbon-carbon multiple bonding was indicated in the 6

micron region. This agrees with theory; cis-double bond vibrations do not result in dipole moment changes and therefore do not absorb. The n.m.r. spectrum was obtained from a neat sample with TMS (tetramethylsilane) and chloroform as dual internal references. Three peaks were indicated: -1.60 p.p.m. (8.2 cyclohexane protons) unresolved multiplet, -2.88 p.p.m. (2.0 bridgehead protons) smeared quintet and -6.18 p.p.m. (2 vinyl protons) sharp singlet. The chemical shift positions did not agree with those reported by Chappell and Clark, but their integrated areas were 8.5/2/2.8 at -1.42, -2.58 and -5.48 p.p.m., respectively. It appears that their instrument had a faulty sweep width adjustment since these values are roughly proportional to those above.

2. Preparation of Bicyclo[4.2.0]octane

The first attempt to prepare this compound was made by hydrogenation of a solution that analyzed 5.6 g. (0.052 mole) of bicyclo[4.2.0]oct-7-ene and 26.2 g. (0.242 mole) of cis-cis-1,3-cyclooctadiene. The solution was dissolved in 160 ml. of anhydrous methanol, and 0.1 g. of 5% palladium on carbon was added as catalyst. The hydrogenation was started with 36.2 psi in the Paar low pressure hydrogenator, and the hydrogenation was stopped 15 minutes later at 31.6 psi (0.049 mole of hydrogen consumed) to see if there was a preference to saturate the cyclobutene derivative over the diene. Chromatographic analysis of the mixture showed that a new peak was formed (of intermediate volatility compared to the two starting materials) but that the total area of the unreacted cyclobutene and the hydrogenated species decreased decidedly with respect to the diene. It was found that cis-cyclooctene and the 1,3-diene have identical retention time in the GE-96 silicone capillary column. It appeared that maybe the palladium catalyst was rearranging the cyclobutene to the 1,3-diene or the cyclobutane derivative to cyclooctene.

For the second attempt, 2.2 g. of cyclobutene derivative which had been separated by the Autoprep was quantitatively hydrogenated with 5% platinum on carbon (platinum has less tendency to isomerize olefins)⁷⁴ at 30 psi in 2 hours. The product hydrocarbon had an identical v.p.c. retention time as the new peak noted above. The saturated derivative was isolated by distillation and subjected to spectroscopic analysis. The n.m.r. spectrum showed roughly 3 peaks: -1.47 p.p.m. (7.75 protons from the cyclohexane ring) a tall rounded unresolved multiplet, -1.82 p.p.m. (4.2 protons from cyclobutane ring) a quartet with smaller side bands, and -2.32 p.p.m. (2.02 protons for the bridgehead positions) a rounded unresolved multiplet showing considerable width (about 0.5 p.p.m.).

I. Electrolysis of Cycloalkanecarboxylic Acids

1. Description of Cells

The apparatus (Figure 1) consisted of a 250 ml. electrolytic beaker fitted with a large rubber stopper into which a thermometer, a condenser, and a 0.55 in. diameter copper cathode and graphite anode was inserted. Provision for stirring was supplied by a magnetic stirrer. The current source was two 85 amp., 12 volt batteries in series. The current density (c.d.) of 0.045 amp. x cm.⁻² was maintained for all experiments. This c.d. amounted to 0.8 amp. with these electrodes and 100 ml. total solution; the current was adjusted by a variable resistor and monitored by an indicating ammeter. The current was also checked by a gas ebullometer during the electrolysis. This allowed the estimation of the total quantity of electricity passed through the cell. Water breaks down under a potential of 1.7 volts to produce hydrogen and oxygen at one atmosphere pressure. This reaction took place along with the electrolysis. The reactions were:

For the calculation of the current efficiency the simplifying assumption was made that a mole of gas was produced as one Faraday passed from the cathode to the anode. For the electrolysis of water there would be 0.75 mole of gas produced, however.

The current efficiency was defined as the amount of acid consumed divided by the moles of electrons passing through the cell as determined by the volume of gas produced.

The elimination fraction is the amount of olefin plus bicycloalkane produced (the hydrocarbon portion) divided by the amount of acid consumed.

The hydrolysis portion of the reaction was composed of alcohol and ester, which were formed as a result of solvent or carboxylate attack on the resulting cycloalkyl cation.

Two cell modifications were used to determine the effect of electrode composition on the reaction. The first modification was the incorporation of a circular copper cathode of 1.25 in. diameter, perforated to facilitate stirring. This allowed a uniform field around the anode and a uniform current density.

The other modification was the incorporation of a platinum anode to determine if there is actually catalytic activity involved with a graphite electrode.

2. Electrolysis of Cycloheptanecarboxylic Acid

An aqueous solution of 28.4 g. (0.2 mole) of cycloheptanecarboxylic acid and 3.0 g. (0.075 mole) of sodium hydroxide (100 ml. total) was placed in the cell, and the current was adjusted to 0.8 amp. (0.045

c.d.). Stirring was maintained and Dry Ice was kept in the condenser while the gas evolved. After 5 hours, the current dropped to 0.6 amp. and electrolysis was stopped 2.5 hours later at 0.2 amp. The mixture was made alkaline with sodium hydroxide and filtered to remove most of the graphite which crumbled off the electrode. The mixture was extracted 3 times with 75 ml. portions of petroleum ether, and the aqueous layer was set aside for recovery of the unreacted acid. The organic solvent was removed by rotary evaporation, and the product mixture was distilled at reduced pressure to give 0.3 g. (0.0031 mole) of hydrocarbon; b.p. 56° (96 mm.); 0.3 g. (0.0025 mole) of cycloheptanol, b.p. 65° (6 mm.), n_D^{24} 1.4700; and 2.0 g. (0.0171 mole) of cycloheptyl cycloheptanecarboxylate. Cycloheptanecarboxylic acid (19.9 g., 0.14 mole) was recovered from the aqueous solution by acidification with hydrochloric acid, extraction in pentane and distillation at reduced pressure. Total material balance was 82.5%.

The gas collected was 2600 ml. (0.106 eq.) for a current efficiency of 113%. The elimination fraction based on acid consumed was 0.052.

The hydrocarbon fraction was analyzed by v.p.c. and found to contain 87% of cycloheptene and 12% bicyclo[4.1.0]heptane. The retention times for the two components were identical to those of products obtained from the tosylhydrazone decompositions.

3. Electrolysis of Cyclooctanecarboxylic Acid

An aqueous solution of 31.2 g. (0.2 mole) of cyclooctanecarboxylic acid and 3 g. sodium hydroxide (0.075 mole) (100 ml. total) was prepared; the mixture required heating to 30° to affect dissolution. The apparatus was the same as that used for the previous acid. The current was adjusted to 0.8 amp. (0.045 c.d.), and the temperature was maintained at 39 to 40° during the electrolysis. After 6 hours of steady evolution

of gas (2.35 l. or 0.0955 eq.), the electrolysis was stopped, and the products were isolated as before.

The hydrocarbon fraction contained 1.4 g. (0.012 mole) and the cyclooctanol and ester fractions contained 0.2 g. (0.0016 mole) and 2.5 g. (0.0189 mole), respectively. There was recovered 21.9 g. (0.14 mole) acid for a total material balance of 86.5%. The elimination fraction was 0.20.

Analysis by v.p.c. revealed that the hydrocarbon fraction contained 75% cis-cyclooctene, 11.3% bicyclo[5.1.0]octane, 8.5% bicyclo[3.3.0]octane and 4.2% of a slightly more volatile hydrocarbon.

A second run was made in which 2.1 g. (0.019 mole) of hydrocarbon, 0.9 g. (0.007 mole) of cyclooctanol, 4.5 g. (0.034 mole) of ester and 15.7 g. (0.10 mole) of recovered acid were obtained from a similar electrolysis of 28.5 g. (0.183 mole) of acid at 40°. The total material balance was 87.5%. The total gas collected was 3150 ml. (0.128 eq.).

The hydrocarbon fraction contained 75% cis-cyclooctene, 13% bicyclo[5.1.0]octane, 8% bicyclo[3.3.0]octane and 4% of the most volatile component.

The current efficiency for the two runs was 120 and 126%, respectively, while the elimination fraction was 0.20 and 0.23, respectively.

4. Electrolysis of Cyclononanecarboxylic Acid

An aqueous solution (100 ml.) of cyclononanecarboxylic acid (19.4 g., 0.108 mole) and sodium hydroxide (3.0 g., 0.075 mole) was placed in the cell and electrolyzed. The current was adjusted to 0.8 amp. and the temperature was allowed to reach 44° to facilitate stirring. At lower temperatures, foaming occurred and danger of losing product to the

condenser was apparent. After 6 hours, the total gas collected was 3,325 ml. (0.133 eq.). The products were worked up as before. The hydrocarbon fraction weighed 1.8 g. (0.0145 mole). The oxygenated products were 1.0 g. (0.007 mole) of alcohol and 2.9 g. (0.0191 mole) of ester. There was 9.1 g. (0.05 mole) of recovered acid for a total material balance of 84%. The elimination fraction based on acid consumed was 0.25 and the current efficiency obtained was 80%.

The hydrocarbon fraction contained 60.4% cis-cyclononene, 27.9% trans-cyclononene, 3.8% bicyclo[6.1.0]nonane, 5.8% bicyclo[4.3.0]nonane and 2% of a more volatile component.

The second run was conducted at 51 to 54° and a total of 3,300 ml. (0.133 eq.) of gas was collected in 6 hours and 20 minutes. From 23.0 g. (0.135 mole) of acid, 2.0 g. (0.016 mole) of hydrocarbon fraction and 4.4 g. (0.03 mole) of alcohol plus ester were produced. The recovered acid amounted to 13.1 g. (0.077 mole) for a total material balance of 91%. The elimination fraction based on acid consumed was 0.21. The current efficiency was again 80%.

The hydrocarbon fraction contained 66.5% cis-cyclononene, 27.3% trans-cyclononene, 1.5% bicyclo[6.1.0]nonane, 4.3% bicyclo[4.3.0]nonane and 0.7% of the more volatile component.

The hydrocarbons produced in both these runs exhibited identical retention times as those produced by the cyclononanone p-toluenesulfonylhydrazone decompositions. The bicyclo[6.1.0]nonane made from cyclooctene and methylene iodide provided further evidence to help in the establishment of the identity of this species in the above mixture. Its retention time was identical to the peak so designated in each sample above.

5. Electrolysis of Cyclodecanecarboxylic Acid

An aqueous mixture (100 ml.) of 27.8 g. (0.151 mole) of cyclo-

decanecarboxylic acid and 3.0 g. (0.075 mole) of sodium hydroxide was prepared. Instead of a true solution being formed, the mixture resulted in a viscous jell that could not be stirred. However, when the temperature was raised to 55° and more water (25 ml.) was added, the jell was broken and a uniform solution was obtained. Electrolysis was started at 0.8 amp. and the temperature was maintained at 55 to 60°. After 6 hours of electrolysis, the total gas collected was 3,030 ml. (0.123 eq.). The acid recovered amounted to 22.9 g. (0.125 mole) or 0.0315 mole of acid consumed. This made a current efficiency of only 51%. After working up the electrolysis products, the hydrocarbon fraction was found to contain 2.4 g. (0.0174 mole) and the oxygenated fraction 1.5 g. (0.009 mole) for a total material balance of approximately 100%. The hydrolysis fraction had the characteristic odor of cyclodecanone. Evidently at this low current efficiency, some of the alcohol was oxidized by the oxygen produced at the anode. The elimination fraction based on acid consumed was 0.55, the highest of any of the medium ring acids.

The cyclodecene fraction was composed of 34.3% cis-cyclodecene, 55% trans-cyclodecene, and 10.7% of a mixture of approximately 60% bicyclo[5.3.0]decane and an unidentified hydrocarbon. The bicyclo[5.3.0]decane had a retention time identical to that obtained by the decomposition of the cyclodecanone tosylhydrazone. The unidentified component was not trans-bicyclo[4.4.0]decane, cis-bicyclo[8.1.0]decane or 1-methylcyclodecene. A sample of bicyclo[6.2.0]decane was not available for comparison.

The apparatus for the second electrolysis of cyclodecanecarboxylic acid was that described previously, except that the circular copper cathode and the graphite centrally located anode was used to produce a homogeneous field and a correspondingly uniform current density.

An aqueous solution (100 ml.) of 21.1 g. (0.15 mole) of the acid and 3.0 g. (0.075 mole) of sodium hydroxide was charged to the above cell and electrolyzed at 0.045 c.d. A total of 2425 ml. (0.099 eq.) of gas was evolved. After work up, 17.3 g. (0.094 mole) of acid was recovered. This acid consumption made for a current efficiency of 42%. The hydrocarbon fraction was 0.9 g. (0.0065 mole) and the hydrolysis fraction contained 1.0 g. (0.0062 mole). The over all material balance was 93% and the elimination fraction was 0.31.

The hydrocarbon fraction contained 35.8% cis-cyclodecene, 51.9% trans-cyclodecene and 12.2% of a mixture of approximately 60% bicyclo-[5.3.0]decane and the remainder was the unidentified hydrocarbon.

The third electrolysis utilized the circular cathode and a smooth platinum anode of the same diameter as the previously used graphite electrode. An aqueous solution (100 ml.) of 24.0 g. (0.13 mole) of cyclodecanecarboxylic acid and 3.0 g. (0.075 mole) of sodium hydroxide was placed in the cell, the electrolysis was started at 0.045 c.d., and the temperature was allowed to reach 67° to prevent foaming which occurred at lower temperatures. The total gas collected was 3415 ml. (0.139 eq.). The hydrocarbon portion contained 0.18 g. (0.0013 mole), the hydrolysis fraction was 0.32 g. (0.002 mole) and the recovered acid was 23.0 g. (0.125 mole). The total material balance was 98.6% and the elimination fraction was 0.24. The current efficiency was only 7.2% and the alcohol-ester fraction possessed the odor of cyclodecanone. This was partially verified by comparison of the retention time obtained by v.p.c. to a chromatogram of cyclodecanone obtained several months prior to the experiment. No authentic sample was available at the time. The integrated area ratio of the cyclodecanone to the hydrocarbon fraction was 4 to 10.

The hydrocarbon fraction contained 42.3% cis-cyclodecene, 50.5% trans-cyclodecene and 7.2% of the partially resolved (by v.p.c.) mixture of bicyclo[5.3.0]decane and the unidentified hydrocarbon.

The neutral portions (hydrocarbon and hydrolysis fraction) had infrared spectra almost identical to the corresponding product fractions from the two prior reactions. No evidence of Kolbe coupling products were noted in the last run. A v.p.c. of the neutral portion showed only hydrocarbon and cyclodecanone up to 36 minutes at 130° and 30 psi in a 100 ft. capillary column coated with GE-96 silicone.

The fourth electrolysis of cyclodecanecarboxylic acid was performed with a 0.55 in. diameter platinum anode and a copper cathode of the same size. An aqueous solution (100 ml.) of 24.1 g. (0.131 mole) of acid and 3.0 g. (0.075 mole) of sodium hydroxide was electrolyzed in 5.5 hours at about 65° and 0.045 amp. x cm⁻² c.d. A total of 3,340 ml. (0.136 eq.) of gas was produced. The recovered acid amounted to 23.2 g. (0.126 mole) while the neutral portions contained a total of only 0.7 g. An analysis by v.p.c., using cyclooctene as an internal standard, showed 0.1 g. (0.00073 mole) of hydrocarbon and 0.6 g. (0.0038 mole) of alcohol-ester. The hydrocarbon showed the same analysis as the third run of this acid. The material balance was 99.5%, the current efficiency was 7.3% and the elimination fraction was 0.15. The neutral portion again contained considerable cyclodecanone, presumably from oxidation of the cyclic alcohol by the evolved oxygen.

J. Solvolysis of Cyclooctyl Bromide

A solution of 7.3 g. (0.038 mole) of cyclooctyl bromide in 150 ml. of 67% aqueous tetrahydrofuran was refluxed over the week-end (90 hours). The solution was diluted with 200 ml. of water and the aqueous

portion extracted 3 times with 75 ml. portions of petroleum ether. The combined extracts were washed 5 times with water to remove the tetrahydrofuran. The solution was dried over magnesium sulfate, concentrated by a rotary evaporator and distilled at reduced pressure to give 0.8 g. (19%) of cis-cyclooctene and 1.0 g. of cyclooctanol. Test experiments indicated that bicyclooctanes are not lost preferentially from mixtures of hydrocarbons during rotary evaporation of solvent. No evidence for the presence of any bicyclooctanes could be found by v.p.c. analysis of the apparently pure cis-cyclooctene fraction.

APPENDIX

A. Attempts to Prepare 2-hydroxycyclooctanecarboxylic Acid

1. Introduction

In these laboratories, considerable attention has been directed to the chemistry of the 2-hydroxycycloalkyl cation. Acid-catalysed rearrangement of cyclooctene glycols⁶⁹ and cyclooctene oxides,^{22,23} deamination of 2-hydroxycyclooctyl amine,⁷⁵ and solvolysis of trans-2-chloro- and trans-2-bromocyclooctanol⁷⁶ give product mixtures containing unequal amounts of both transannular and nontransannular products. Competing mechanisms involving different kinds of cationic intermediates have been proposed.^{75,76}

Perhaps the electrolysis of 2-hydroxycyclooctanecarboxylic acid, generating a 2-hydroxycyclooctyl cation, could provide additional data relevant to reaction mechanisms. An endeavor to obtain this acid is described in this section. Some of the methods used in the attempts to prepare 2-hydroxycyclooctanecarboxylic acid merit only a description of the scheme employed, while others merit considerable attention due to the synthesis of some interesting and valuable compounds.

2. Addition of Acetylchloride to cis-Cyclooctene

The method used was adopted from a procedure⁷⁷ to prepare 2-chlorocyclohexyl methyl ketone:

The product was then to be oxidized to the unsaturated acid via sodium hypochlorite, esterified, hydroborated to the hydroxy ester and hydrolysed to the acid. The first step resulted in mostly polymer. The 2-acetylcyclooctyl cation apparently adds to cyclooctene to give polymer rather than eliminate to olefin.

3. Attempted Preparation of 1-acetylcyclooctene

This method was adopted from a procedure⁷⁸ for the preparation of 1-acetylcyclohexane:

Extensive tar and polymer were obtained from this reaction.

4. Addition of Hydrogen Cyanide to cis-cyclooctene Oxide

The following scheme was attempted:

Very little reaction took place but acid hydrolysis of the mixture was tried. About 0.5 g. of an acid was made based on 43 g. (0.34 mole) of cyclooctene oxide in excess aqueous hydrogen cyanide solution.

5. Addition of Carbon Tetrabromide to cis-cyclooctene

There was obtained a fair yield of a compound of comparable volatility to that expected for 1-bromo-2-tribromomethylcyclooctane (extrapolated from the volatility of 1-bromo-2-trichloromethylcyclooctane²⁴) but

hydrolysis gave only 0.25 g. of an acid, the infrared spectrum of which was similar to that obtained in section 4 above.

6. Addition of Benzoyl Chloride to Cyclooctene Oxide

The following scheme was attempted:

The first step was unsuccessful with several solvents with and without Lewis Acid catalysts (AlCl_3 , BF_3 and ZnCl_2). Probably the equilibrium favors the reverse reaction as no reaction could be detected and starting materials were recovered.

7. Reaction of trans-2-chlorocyclooctanol with Sodium Cyanide

The following scheme was attempted:

The chlorohydrin lost hydrogen chloride immediately to form cis-cyclooctene oxide in an exothermic reaction.

8. Preparation of 1-cyclooctenyllithium

The following scheme was attempted:

This reaction took place so sluggishly that it appeared the alkyllithium reacted with solvent as fast as it was formed. Upon subsequent carbonation no acid was obtained.

9. α -Pyranyl Ether Protective Group Approach

a. 2,3-Dihydropyran⁷⁹

Tetrahydrofurfuryl alcohol was distilled into an 8 in. x 10 mm. tube packed with 200 mesh alumina which was heated to 200 to 250° by a tube furnace. A slight positive pressure of nitrogen moved the vapors through the catalyst into a condenser at 0°, and a volatile, black liquid was collected in a flask. The escaping vapors were directed to a hood since powerfully lachramatory components were produced as side products. From 200 ml. of tetrahydrofurfuryl alcohol, about 50 ml. of the black liquid was collected. This crude product was distilled to give 16 g. of 2,3-dihydropyran; b.p. 84° (760 mm.); (lit.⁷⁹ b.p. 85-86° (760 mm.)). The forecut contained an extremely powerful lachramator.

b. 2-Bromocyclooctyl α -Pyranyl Ether⁸⁰

A sample of cis-cyclooctene oxide⁸¹ (b.p. 67° (8.5 mm.); lit.⁶⁹ b.p. 69.5 (40 mm.)) was prepared in 69% yield. The oxide was converted to trans-2-bromocyclooctanol⁸² (b.p. 74 - 76° (0.2 mm.)) by anhydrous hydrogen bromide in carbon tetrachloride for an 80% yield.

In a 500 ml. erlymeyer flask with a magnetic teflon stirring bar were mixed 15 g. (0.179 mole) of 2,3-dihydropyran and 34.2 g. (0.166 mole) of trans-2-bromocyclooctanol. The mixture immediately warmed to 45°, and stirring was maintained for 30 minutes. A v.p.c. analysis showed the quantitative removal of 2,3-dihydropyran. Woods and Karmer⁸⁰ used concentrated hydrochloric acid as a catalyst and few of their alcohols gave such high conversions. The infrared spectrum contained an

ether absorption at 9.6μ but no O-H, vinyl C-H, or C=C absorptions. The n.m.r. spectrum showed 4 signals: -1.6 p.p.m. (12 protons: 8 from cyclooctane ring and 4 from pyran ring), large unresolved multiplet; -1.8 p.p.m. (2 protons: CH_2 at carbon-3 on pyran ring), shoulder to 12 proton peak; -1.9 to -2.3 p.p.m. (4 protons: CH_2 at carbon-3 and carbon-8 of cyclooctane ring), broad unresolved multiplet; -3.0 to -4.4 p.p.m. (4 protons; CH_2 at carbon-5 on pyran, -CHO- and -CHBr- on cyclooctane), broad sawtooth type multiplet and -4.75 p.p.m. (1 proton: -OCH-O- on pyran ring) broad singlet-like multiplet.

c. Attempts to Prepare Grignard Reagent

The addition of 2-bromocyclooctyl α -pyranyl ether to magnesium metal turnings in ether resulted in no reaction. In another experiment the reaction was started using 5 g. of methyl iodide and the addition of the above ether resulted in a slight exothermic reaction but the reaction ceased as soon as the methylmagnesium iodide was used up. Further addition of methyl iodide indicated that the solution still contained Grignard activity; the methyl iodide reacted vigorously. Cyclooctene was produced as a side product of the reaction. The acetal oxygen on the pyran ring could attack the magnesium intramolecularly to give the following:

The aldehyde formed could quickly react with any remaining Grignard reagent. Isolation of the aldehyde product was unfortunately not attempted, but the infrared spectrum showed hydroxyl as well as carbonyl absorption.

The reaction of the pyranyl ether with lithium metal in ether gave similar results. The infrared spectrum showed hydroxyl and carbonyl absorption and cyclooctene was indicated by v.p.c. analysis. It was reported⁸³ that attempts to prepare the Grignard reagent of 2-bromoethyl α -pyranyl ether with an equimolar amount of methyl iodide (no reaction when ether was used alone) gave ethylene and no evidence of any Grignard reagent upon carbonation.

10. Reaction of 2-Bromocyclooctyl α -Pyranyl Ether with Sodium Cyanide

A solution of 21.3 g. (0.072 mole) of the α -pyranyl ether in 100 ml. of dimethyl sulfoxide was heated to 80°, a slurry of 3.6 g. (0.075 mole) of sodium cyanide in DMSO was added, and the mixture was stirred for several hours. Petroleum ether was added and the salt and solvent DMSO were washed out by 6 water extractions. The solvent was removed by a rotary evaporator to obtain an oil. The infrared spectrum of the oil showed only starting material.

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EXAMINATION AND THESIS REPORT

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Major Field: Chemistry

Title of Thesis: Anodic Oxidations of Medium Ring Cycloalkanecarboxylic Acids

Approved:

James G. Traynham
Major Professor and Chairman

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Date of Examination:

April 18, 1966