# ORGANIC AND BIOLOGICAL CHEMISTRY

Macro Rings. XXV. Fate of Carbonium Ions Held in π-Clouds of Benzene Rings[1]

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The fate of carbonium ions has been examined when generated at different distances from, and over several positions in, the face of a benzene ring. The rates and products of acetolysis of systems I and II have been found to vary in an interesting manner with changes in values of m and n. Both phenyl and hydrogen become involved as neighboring groups, in one case probably at the same time. Acetolysis of I ($m = 3$, $n = 5$) to give the corresponding acetate occurs with retention of configuration.

The research described here involves a combination of two phenomena which have separately received a great deal of attention in recent years, transannular effects and phenyl or hydrogen participation in carbonium ion formation. Two general systems, I and II, were selected for investigation. These classes of compounds provide a means for systematic variation of molecular structure, and allow study of the attendant electronic effects.
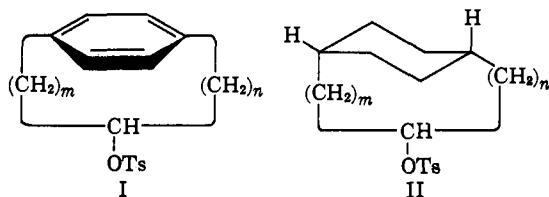
Starting Materials.—The compounds needed for this study were synthesized by the schemes outlined in Chart I. The general approach was developed in previous investigations,[2] which provided some of the substances required for solvolysis studies. Thus alcohol XXXIV had been prepared,[2a] as had the two isomeric alcohols XXV and XXXIII, although the structures of the latter compounds had not been differentiated.

At the outset, a plan was devised which would resolve the structural ambiguity that arises from the fact that the acyloin ring-closure provides two isomeric ketols, and ultimately two isomeric alcohols and their tosylates. Five isomers are possible which possess the general formula I in which $m + n = 8$: $m = 8$, $n = 0$; $m = 7$, $n = 1$; $m = 6$, $n = 2$; $m = 5$, $n = 3$ and $m = n = 4$. Of these, each but the first and last could in principle be obtained from *two different esters* as an ultimate starting material. Production of each of two of the tosylates (I with $m = 2$, $n = 6$, and with $m = 3$, $n = 5$) by two different routes would allow structural assignments to be made to all five tosylates. In practice the scheme failed due to the failure of esters XII and XVI to undergo any ring-closing acyloin reaction. Only polymer and starting materials were obtained. However, tosylates I with $m = n = 4$, $m = 5$ and $n = 3$, $m = 6$ and $n = 2$, and $m = 7$ and $n = 1$ were identified as follows.

Ring closure of ester XIII gave in 35% yield a mixture of two acyloins (XXII), one of which was obtained free of the other. Reduction of the pure isomer with propanedithiol gave a mixture of ketones XXIV and XXXI, the former predominating. Clearly the acyloins equilibrated at least partially under the reaction conditions. A reduction of the acyloin mixture with zinc and acetic acid gave predominantly ketone

XXXI. The corresponding alcohols XXV and XXXIII were assigned structures making use of their differences in symmetry properties. Thus the brucine salt of the acid phthalate of XXV provided optically active XXV, whereas the corresponding salt derived from XXXIII failed to resolve.

Since diesters such as XI which contain a methylene group activated by both a phenyl and ester group do not undergo direct acyloin ring closure,[3] XI was reduced to XV which gave a 75% yield of acyloin mixture XVII. The final mixture of alcohols XXVII and XXVIII) could not be induced to crystallize, nor could the derived tosylate mixture. The acetolysis rate of this mixture was measured (see kinetic section), and the resulting drifting rate was disected into two good first-order rates. The calculated rate constants indicated 6% of a tosylate with a fast solvolysis rate and 94% with a slow rate. The assignment of structure to each isomer in the mixture was made on the following basis. The ketonic mixture from which the tosylate mixture was derived exhibited an ultraviolet spectrum with a shoulder at 286 mμ with $\epsilon = 123$. These values are in good agreement with the spectra of α-phenyl ketones, which absorb in the region of 284–300 mμ with $\epsilon = 130$–330.[4] Had the ketone responsible for this absorption been present only to the extent of 6%, the pure ketone would have had $\epsilon = 2050$, which is highly unlikely. This structural assignment is also compatible with the pattern of solvolysis rate constant relationships (see kinetic section).

Preparation of the other desired alcohols and their tosylates followed conventional paths, and are outlined in Chart I.

Kinetics.—Kinetic measurements on the six pure tosylates and the one mixture were made in the usual manner[5] in dry glacial acetic acid. The tosylates of alcohols XXV, XXVI, XXXIII, XXXIV, XXXV and XXXVI exhibited good first-order kinetics through 90% reaction, and the integrated rate constants are recorded in Table I. The mixture of tosylates of alcohols XXVII and XXVIII gave an apparent downward drifting rate. When a point, taken after 15% reaction, was arbitrarily presumed to be the zero point, and the integrated rate constant was calculated for each subsequent point, a good rate constant for the tosylate of XXVII (the 2-isomer) was obtained. To obtain the rate constant for the tosylate of XXVIII (the 3-isomer) many points were taken during the first 20% of reaction of the tosylate mixture. The calculated titer due to the reaction of the 2-isomer was subtracted from the experimental titer. The titer due to reaction of the 3-isomer, thus calculated, eventually became constant. This constant value was taken as the infinity titer for the calculation of the rate constant for the tosylate of
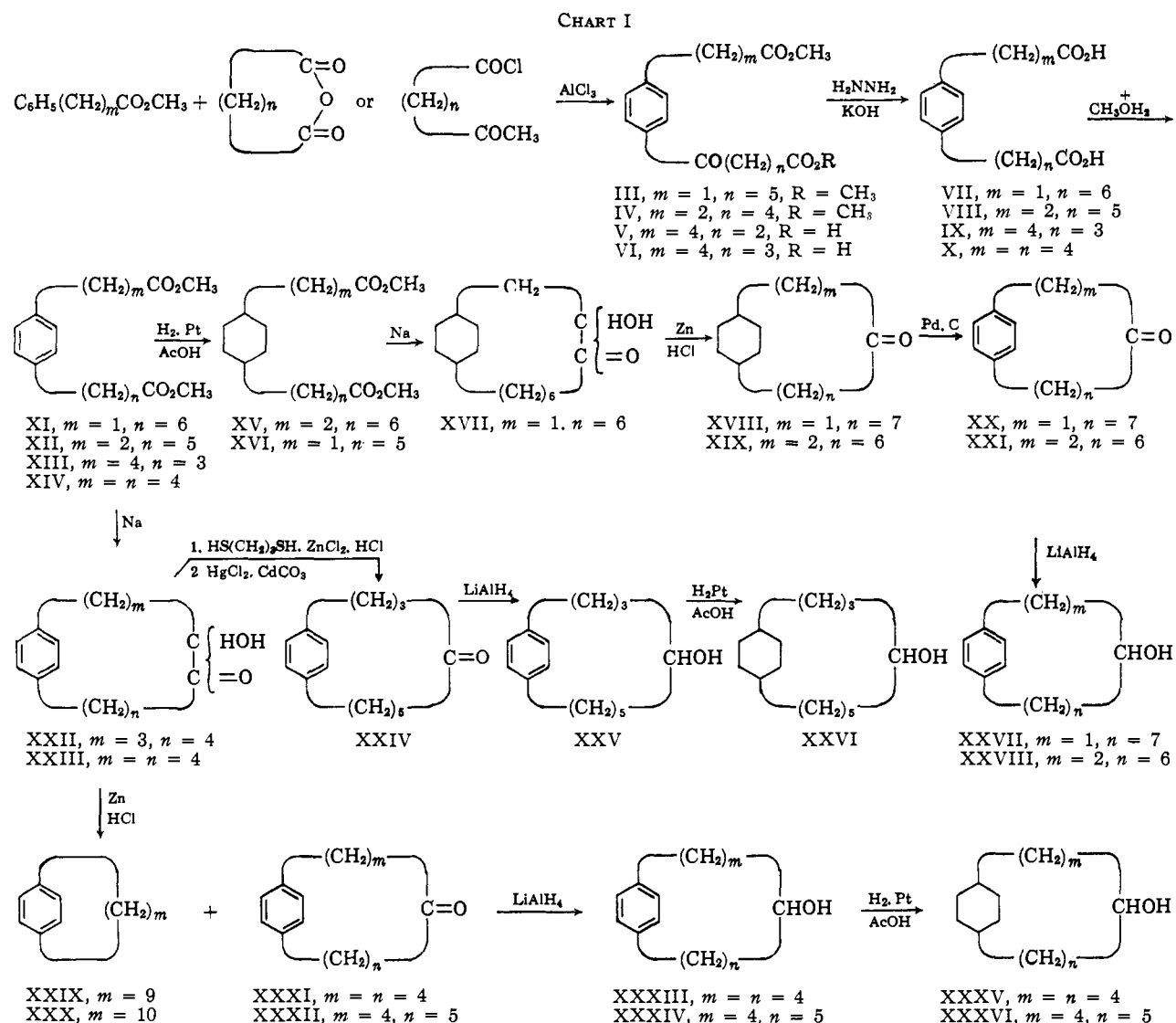
(1) This work was supported by the U. S. Army Research Office (Durham).

(2) (a) D. J. Cram and M. Cordon. *J. Am. Chem. Soc.*, **77**, 4090 (1955); (b) D. J. Cram and M. F. Antar. *ibid.*, **80**, 3109 (1958); (c) **80**, 3103 (1958).

(3) D. J. Cram and H. Steinberg, *ibid.*, **73**, 5691 (1951).

(4) D. Biquard. *Bull. soc. chim. France.* [5], **8**, 55 (1941).

(5) S. Winstein, E. Grunwald and L. L. Ingraham. *J. Am. Chem. Soc.*, **70**, 826 (1948).

CHART I

$C_6H_5(CH_2)_mCO_2CH_3$ + (CH_2)_n $\begin{matrix} C=O \\ O \\ C=O \end{matrix}$ or (CH_2)_n $\begin{matrix} COCl \\ COCH_3 \end{matrix}$ $\xrightarrow{AlCl_3}$ [ring with $(CH_2)_mCO_2CH_3$ and $CO(CH_2)_nCO_2R$] $\xrightarrow[KOH]{H_2NNH_2}$ [ring with $(CH_2)_mCO_2H$ and $(CH_2)_nCO_2H$] $\xrightarrow{CH_3OH_2^+}$

III, $m = 1, n = 5, R = CH_3$
IV, $m = 2, n = 4, R = CH_3$
V, $m = 4, n = 2, R = H$
VI, $m = 4, n = 3, R = H$

VII, $m = 1, n = 6$
VIII, $m = 2, n = 5$
IX, $m = 4, n = 3$
X, $m = n = 4$

[ring with $(CH_2)_mCO_2CH_3$ and $(CH_2)_nCO_2CH_3$] $\xrightarrow[AcOH]{H_2, Pt}$ [ring with $(CH_2)_mCO_2CH_3$ and $(CH_2)_nCO_2CH_3$] $\xrightarrow{Na}$ [ring with CH_2 and $(CH_2)_6$ and $C{-}C=O$] $\begin{matrix}HOH\end{matrix}$ $\xrightarrow[HCl]{Zn}$ [ring with $(CH_2)_m$ and $(CH_2)_n$ and C=O] $\xrightarrow{Pd. C}$ [ring with $(CH_2)_m$ and $(CH_2)_n$ and C=O]

XI, $m = 1, n = 6$
XII, $m = 2, n = 5$
XIII, $m = 4, n = 3$
XIV, $m = n = 4$

XV, $m = 2, n = 6$
XVI, $m = 1, n = 5$

XVII, $m = 1. n = 6$

XVIII, $m = 1, n = 7$
XIX, $m = 2, n = 6$

XX, $m = 1, n = 7$
XXI, $m = 2, n = 6$

↓ Na

1. HS(CH_2)_3SH. ZnCl_2. HCl
2 HgCl_2. CdCO_3

↓ LiAlH_4

[ring with $(CH_2)_m$ and $(CH_2)_n$ and $C{-}C=O$, HOH] $\xrightarrow{}$ [ring with $(CH_2)_3$ and $(CH_2)_5$ and C=O] $\xrightarrow{LiAlH_4}$ [ring with $(CH_2)_3$ and $(CH_2)_5$ and CHOH] $\xrightarrow[AcOH]{H_2Pt}$ [ring with $(CH_2)_3$ and $(CH_2)_5$ and CHOH] [ring with $(CH_2)_m$ and $(CH_2)_n$ and CHOH]

XXII, $m = 3, n = 4$
XXIII, $m = n = 4$

XXIV

XXV

XXVI

XXVII, $m = 1, n = 7$
XXVIII, $m = 2, n = 6$

↓ Zn HCl

[ring with $(CH_2)_m$] + [ring with $(CH_2)_m$ and $(CH_2)_n$ and C=O] $\xrightarrow{LiAlH_4}$ [ring with $(CH_2)_m$ and $(CH_2)_n$ and CHOH] $\xrightarrow[AcOH]{H_2. Pt}$ [ring with $(CH_2)_m$ and $(CH_2)_n$ and CHOH]

XXIX, $m = 9$
XXX, $m = 10$

XXXI, $m = n = 4$
XXXII, $m = 4, n = 5$

XXXIII, $m = n = 4$
XXXIV, $m = 4, n = 5$

XXXV, $m = n = 4$
XXXVI, $m = 4, n = 5$

XXVIII, and it established the percentage of XXVIII in the original alcohol mixture. In all cases the rates were determined at two temperatures, and the calculated thermodynamic parameters are recorded in Table I.

Solvolysis Products.—The acetolysis products of tosylates XXXVII and XXXVIII were examined, and the products are indicated in Chart II. The product studies were made in dry acetic acid solutions 0.02 M in substrate and 0.022 M in sodium acetate, whereas no acetate was added to the kinetic runs. The balance of the four products proved to be essentially the same in the absence and presence of the added base, a fact that suggests the products were kinetically controlled in both the kinetic and product runs. Alcohols were separated from hydrocarbons by chromatography on alumina, whereas the olefinic hydrocarbons were separated from the tricyclic hydrocarbon by gas chromatography.

Repetition of the isolation procedure with synthetic mixtures of alcohols XXV and XXXIII indicated that as little as 2% of the symmetrical 5-isomer could have been detected in the alcohol fraction.

In order to obtain larger amounts of the hydrocarbon products than were available through acetolysis, tosylate XXXVIII was treated with a 0.1 M solution of

lithium perchlorate in ether.[6] A precipitate of lithium perchlorate rapidly appeared, and the hydrocarbon product was immediately isolated.

Tricyclic hycrocarbon XLI was identified by elemental analysis, by the fact that it absorbed three moles of hydrogen to give a saturated hydrocarbon (XLIV), and exhibited an ultraviolet absorption spectrum (see later section) distinctly different from [9]paracyclophane but similar to that of tetracyclic hydrocarbon XLV.[7] Thus tricyclic hydrocarbon XLI appears to contain a much more distorted benzene ring than [9]paracyclophane itself.

The mixture of olefins from solvolysis was not separated into its components, but the structures and compositions were determined as follows. The infrared spectrum of the mixture contained a very intense band at 10.5 μ, characteristic of trans-disubstituted alkenes. Molecular models of olefins XLII and XLIII indicate that the trans configuration is much less strained than the cis. Catalytic reduction of the mixture gave [9]-paracyclophane identical in all respects with authentic material obtained by reduction of acyloin XXII with zinc and acetic acid.

Oxidation of the olefin mixture[8] obtained from the lithium perchlorate treatment of tosylate XXXVIII (see above) gave a mixture of diacids, VIII and IX,

(6) S. Winstein. S. Smith and D. Darwish. *J. Am. Chem. Soc.*, **81**, 5511 (1959).

(7) H. Rapoport and G. Smolinsky. *ibid.*, **82**, 1171 (1960).

(8) E. von Rudloff. *Can. J. Chem.*, **33**, 1741 (1955).

<div align="center">

Table I

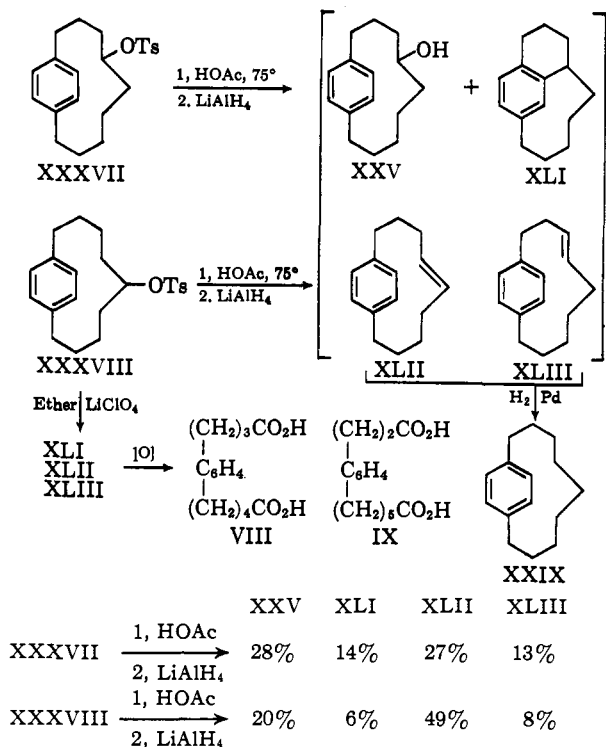Kinetics of Acetolysis of 0.02 M Solutions of Tosylates

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Run	Tosylate	No. corres. alcohol	T. °C.	k, sec.$^{-1a}$	$\Delta H^{\ddagger}$, kcal./mole	$\Delta S^{\ddagger}$, e.u.^{b,c}
1	[9]Paracyclophane-2-	XXVII	50	5.54 ± 0.16 × 10^{-6d}	26.9 ± 0.4	+0.5
2	[9]Paracyclophane-2-	XXVII	75	1.20 ± .02 × 10^{-4d}		
3	[9]Paracyclophane-3-	XXVIII	25	4.6 ± .3 × 10$^{-6d,e}$	24.0 ± .6	-2.4
4	[9]Paracyclophane-3-	XXVIII	50	1.14 ± .02 × 10$^{-4d,f}$		
5	[9]Paracyclophane-4-	XXV	25	1.54 ± .03 × 10^{-4}	23.1 ± .6	+1.8
6	[9]Paracyclophane-4-	XXV	50	3.4 ± .2 × 10^{-3g}		
7	[9]Paracyclophane-5-	XXXIII	25	1.12 ± .02 × 10^{-5}	25.2 ± .2	+3.3
8	[9]Paracyclophane-5-	XXXIII	50	3.23 ± .04 × 10^{-4}		
9	[10]Paracyclophane-5-	XXXIV	50	2.86 ± .02 × 10^{-5g}	25.7 ± .1	-0.1
10	[10]Paracyclophane-5-	XXXIV	75	5.39 ± .06 × 10^{-5g}		
11	Hexahydro[9]paracyclophane-4-	XXVI	50	1.06 ± .03 × 10^{-5}	26.5 ± .4	+0.6
12		XXVI	75	2.21 ± .04 × 10^{-4}		
13	Hexahydro[9]paracyclophane-5-	XXXV	50	9.47 ± .08 × 10^{-6}	27.3 ± .2	+2.9
14		XXXV	75	2.15 ± .03 × 10^{-4h}		
15	Hexahydro[10]paracyclophane-5-	XXXVI	50	3.50 ± .03 × 10^{-6}	27.4 ± .2	+1.3
16		XXXVI	75	8.05 ± .07 × 10^{-5}		

^{a} Average value of integrated rate constant for 7 points unless otherwise specified. ^{b} For 50°. ^{c} ±2 e.u. ^{d} Five-point rate. ^{e} Concentration 0.002 M. ^{f} Concentration 0.001 M. ^{g} Six point rate. ^{h} Extrapolated from $k_{38.2} = 8.4 \pm 0.2 \times 10^{-4}$, four-point rate.

identified by mixture melting point experiments with appropriate mixtures of authentic acids. The ratio of VIII to IX (estimated by comparison of the melting point of the mixture and the phase diagram) suggested

<div align="center">Chart II</div>

the starting olefinic mixture to be 70% XLII and 30% XLIII. A second approximate measure of the relative amounts of the two olefins was obtained by a synthetic symmetrical peak treatment of the gas chromatograms of the mixture (the two peaks overlapped), and indicated 75% of XLII and 25% of XLIII was present. Similar gas chromatography of the olefin mixture obtained from solvolysis of XXXVII and XXXVIII gave estimates of the amounts of each olefin in the mixture. The actual yields of the four products of the acetolysis are set forth in Chart II.

A number of experiments were conducted to see if the olefins and the tricyclic hydrocarbon were interconvertible. In treatment of tosylate XXXVIII with
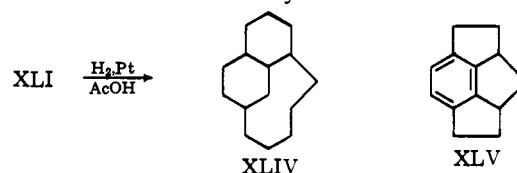
refluxing ether–lithium perchlorate, the ratio of olefin to tricyclic hydrocarbon produced after 5 minutes was 5:1. After several days at reflux, the ratio was about 1:1. When the same tosylate dissolved in 0.1 M

lithium perchlorate in ether was held in a sealed tube at 75° for several days, the ratio was 1:3 (olefin to tricyclic hydrocarbon). However, when tricyclic hydrocarbon and an equivalent amount of p-toluenesulfonic acid were dissolved in 0.1 M lithium perchlorate–ether solution and the solution was refluxed for 5 days, no olefin was produced. This experiment demonstrates that although olefin in acid produces tricyclic hydrocarbon, the opposite reaction was not realized.

Acetolysis of optically active tosylate XXXVII gave acetate with 98 ± 2% retention of configuration. The tricyclic hydrocarbon XLI which was formed was also optically active, but its optical purity could not be determined since optically pure material was not available for comparison.

The products of acetolysis of the other tosylates were less thoroughly studied. Solvolysis of the tosylate mixture derived from the alcohol mixture of XXVII (94%) and XXVIII (6%) at 75° gave after lithium aluminum hydride reduction an alcohol fraction, an olefin fraction and tricyclic hydrocarbon XLI. The alcohol fraction contained less than 5% (limits of detection) of rearranged alcohol XXV, and appeared to be mainly XXVII. The olefin fraction contained at least three components (vapor phase chromatography), at least one of which is a cis-olefin, and at least one trans. The tricyclic hydrocarbon XLI produced probably arose from the tosylate of XXVIII, and accounts for a sizable fraction of that starting material.
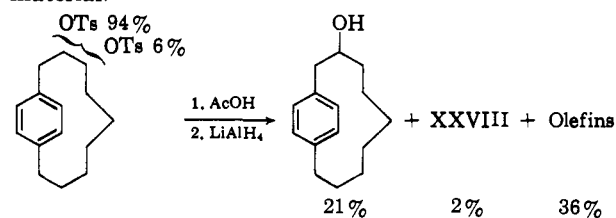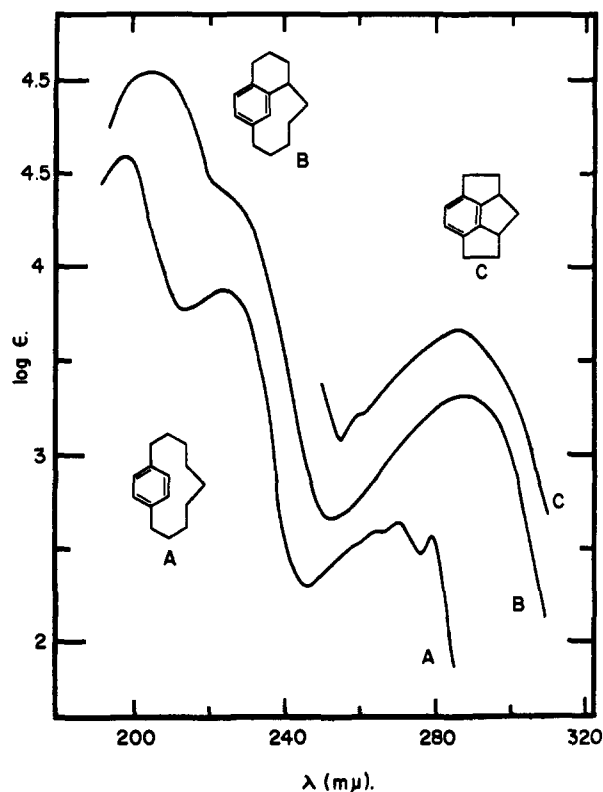
Fig. 1.—Ultraviolet absorption spectra in 95% ethanol. Except for bottom curve, the spectra are all displaced upward on the ordinate axis by 0.5 log ε unit increments from the curve immediately below.

Spectra.—The ultraviolet absorption spectra of [9]-paracyclophane, of tricyclic hydrocarbon XLI and of tetracyclic hydrocarbon XLV are recorded in Fig. 1. Some of the fine structure of 1,4-dialkylbenzenes[9] is absent in the spectrum of [9]paracyclophane, and the bands in the 250 to 280 mμ region are moved to slightly longer wave lengths compared to [10]paracyclophane, but not to the extent observed for either the tricyclic or tetracyclic hydrocarbons. The spectra of the two latter compounds possess bands at much longer wave lengths, as does [8]paracyclophane.[10] Examination of molecular models of the last three substances suggests that the benzene rings in all three compounds are warped, and in somewhat different ways since the constraints imposed on the benzene ring by the carbon bridges are different in each compound.

Figure 2 compares the ultraviolet spectra of the three keto [9]paracyclophanes with that of [9]paracyclophane itself. The only notable difference in spectra in the four compounds is found in that of 2-keto[9]paracyclophane, in which the benzene ring is α to the carbonyl group. Molecular models indicate the carbonyl groups of the 4- and 5-keto compounds are further from the π-electrons of the benzene ring than in the 2-derivative, and transannular effects are not operative.

Figures 3, 4 and 5 record the nuclear magnetic resonance spectra of the important hydrocarbons, ketones and alcohols of this investigation. Earlier studies demonstrated that a hydrogen in the proximity of the π-electron cloud of an aromatic ring absorbs in the n.m.r. at higher field than otherwise.[11] The spectrum of [10]paracyclophane in Fig. 3 confirms that reported by Waugh, and a comparison of its spectrum with that of [9]paracyclophane is informative. The methylene

(9) D. J. Cram and N. L. Allinger, *J. Am. Chem. Soc.*, **76**, 6132 (1954).

(10) D. J. Cram and G. R. Knox, *ibid.*, **83**, 2205 (1961).

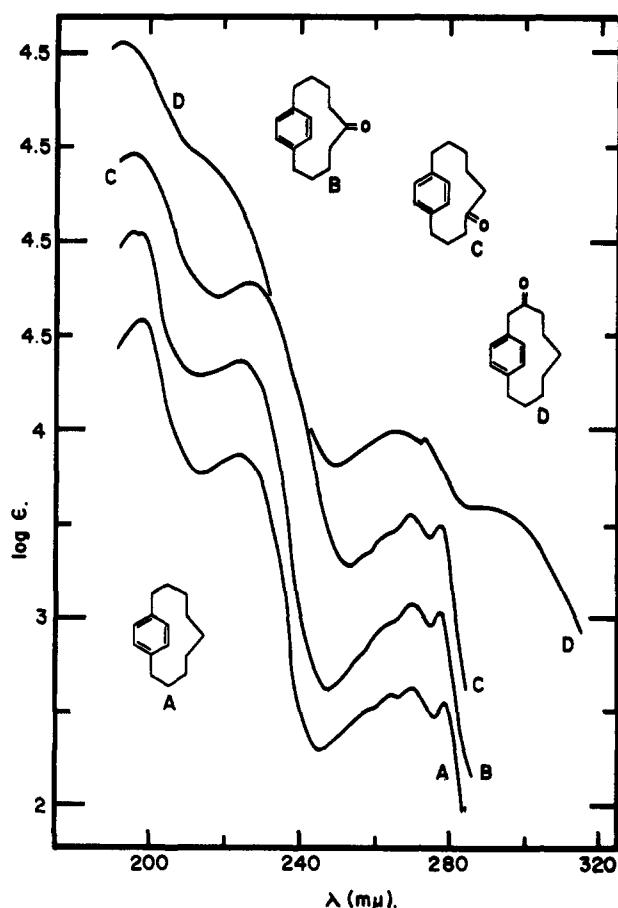(11) J. S. Waugh and R. W. Fessenden, *ibid.*, **79**, 846 (1957).

Fig. 2.—Ultraviolet absorption spectra in 95% ethanol. Except for bottom curve, the spectra are all displaced upward on the ordinate axis by 0.5 log ε unit increments from the curve immediately below.

hydrogens that absorb at highest field in [9]paracyclophane appear to be four in number and absorb at a higher field (τ 9.6) than those which absorb at highest field in [10]paracyclophane (τ 9.3). Thus the hydrogens in [9]paracyclophane exhibit a more pronounced transannular effect than in its larger homolog, as is predicted by theory.

The shift to higher fields of the aromatic hydrogens of the tricyclic hydrocarbon XLI is attributed to inhibition of the flow of π-electrons by a slight warping of the benzene ring.

In the spectrum of the mixture of two [9]paracyclophenes the olefinic hydrogens absorb at τ 5.8 and τ 5.4. Since the two hydrogens of olefin XLII are closer to the center of the benzene ring than those of XLIII, the absorption at 5.8 is probably associated with olefin XLII. This conclusion is in harmony with the greater intensity of absorption at 5.8, which is expected since the mixture was richer in XLII than XLIII. Clearly, the shift to higher fields of these bands is attributable to transannular effects of ring current on the vinyl hydrogens Interestingly, the aromatic hydrogens are also shifted to higher fields (τ 3.2).

Figure 4 records the n.m.r. spectra of 2-, 4-, and 5-keto [9]paracyclophane, and of 5-keto[10]paracyclophane. In only the 2-keto isomer is there absorption above τ = 8.8, probably because the carbonyl group when more centrally located in the methylene belt cancels the benzene ring current effect by virtue of its electron-withdrawing ability. As might be expected, the most symmetrical ketone (5-keto[9]paracyclophane)possesses the most simple pattern of methylene absorptions.
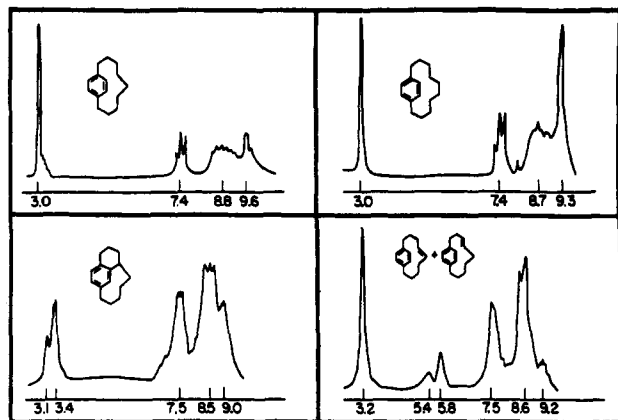
Fig. 3.—Nuclear magnetic resonance spectra, peak positions reported in τ-values.

In the spectra of the four alcohols (Fig. 5) derived from the above ketones, the closer the hydroxyl group is to the center of the benzene ring, the higher the field at which the hydroxyl hydrogen absorption occurs. In 2-hydroxy[9]paracyclophane, this hydrogen gives a sharp peak at τ 6.4. In the spectrum of 5-hydroxy-[10]paracyclophane, the sharp peak at τ 7.2 is probably the hydroxyl hydrogen absorbing at the same field strength as the benzyl hydrogens, the same being true of 4-hydroxy[9]paracyclophane. In the 5-hydroxy isomer the absorption has probably moved to τ 8.4, where it adds to the absorptions of the non-benzyl hydrogens of the methylene bridge in the 3-position.

Reaction Mechanisms.—In Table II the relative rates of the systems of this study along with other cyclic systems are listed. Cyclohexyl tosylate is used as a
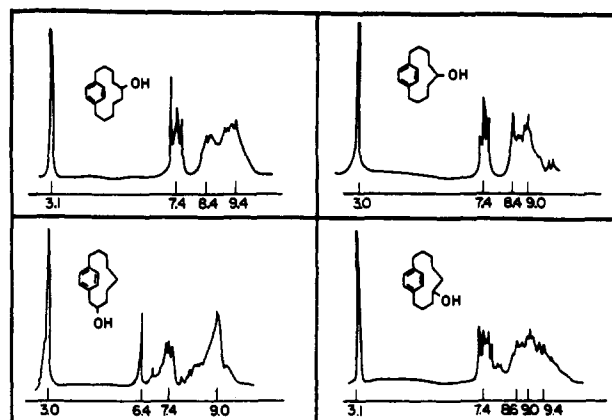
TABLE II
RELATIVE RATES OF ACETOLYSIS AT 50°

Tosylate	Rel. rate	$\Delta H^{\ddagger}$ kcal./mole	$\Delta S^{\ddagger}$ e.u.	Ref.
Cyclohexyl	1	27.3	−0.6	a
Cycloheptyl	31	33.5	−5.4	a
Cycloöctyl	285	22.5	−4.1	a
Cyclononyl	266	23.9	+0.1	a
Cyclodecyl	539	23.0	−1.1	a
Cycloundecyl	67	24.7	−0.2	a
Cyclododecyl	3.1	27.9	+3.8	a
Cyclotridecyl	3.5	26.2	−1.3	b
Cyclotetradecyl	1.3	27.8	+1.7	b
cis-5-Cyclodecenyl	3770	..	...	c

Tosylates
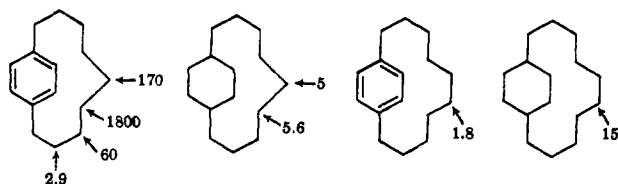
a Ref. 12.   b H. C. Brown and G. Ham, *J. Am. Chem. Soc.*, **78**, 2735 (1956).   c Ref. 13.

standard for comparison. Of the simple cycloalkanyl systems, the maximum acceleration of rate (factor of 539) is reached with cyclodecyl tosylate.[12] This effect was attributed to relief of strain associated with non-bonded interactions in going to the carbonium ion. The rate factor of 3770 for cis-5-cyclodecenyl tosylate was attributed to transannular π-electron involvement in ionization.[13]

(12) R. Heck and V. Prelog, *Helv. Chim. Acta*, **38**, 1541 (1955).

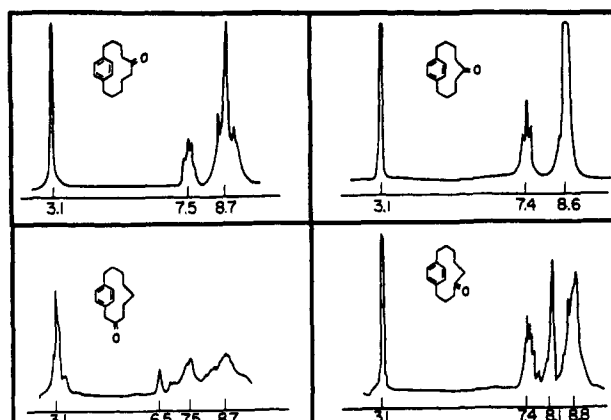(13) H. L. Goering, H. H. Espy and W. D. Closson, *J. Am. Chem. Soc.*, **81**, 329 (1959).

Fig. 4.—Nuclear magnetic resonance spectra, peak positions reported in τ-values.

Fig. 5.—Nuclear magnetic resonance spectra, peak positions reported in τ-values.

In the present study, the three hexahydroparacyclophanyl systems showed a rate increase by factors that range between 5 and 15, the system with the bigger methylene bridge exhibiting the larger factor. Clearly some release of strain is evident in these small factors. In a sense, these systems act as models for the paracyclophanes themselves. Fisher–Taylor–Hirschfelder molecular models suggest that hexahydro[9]paracyclophane is more strained than [9]paracyclophane, and that the same relationship exists between [10]paracyclophane and its hexahydro derivative. Substantiation of this idea is found in the fact that the hexahydro[10]paracyclophanyl tosylate solvolyzes 8 times as fast as the corresponding benzenoid system. Likewise, the two hexahydro[9]paracyclophanyl tosylates solvolyze faster than [9]paracyclophanyl-2-tosylate.

As the tosyl group, and therefore the incipient carbonium ion, is moved over the face of the benzene ring, the rate is accelerated by factors that range from 60 to 1800. Clearly, the π-electron cloud of the benzene is providing this acceleration by becoming involved in the rate-determining transition state.

An attempt was made to estimate the distances between the different carbons of the methylene belt and the carbon atoms of the benzene ring through use of molecular models. First a replica of [9]paracyclophane was constructed from Fisher–Taylor–Hirschfelder models to establish the conformation of the methylene bridge which would suffer the least hydrogen–hydrogen and hydrogen–benzene repulsions. Next the model was duplicated with Dreiding stereomodels, and the methylene-to-benzene distances were measured. The models were disassembled and reassembled several

times, and the average values obtained. The bond angles in the Dreiding stereomodels are only slightly flexible and the bonds are rigid, so the values listed in Table III for these distances do not take into consideration the distortion of the benzene ring and the bridge bond angles.

The shortest distance listed in Table III would involve a 1,3-interaction between carbons 2 and 13. The lack of acceleration for the 2-tosylate (rate factor was only 1.9) probably arises from the fact that the ethylene phenonium ion that would be formed by phenyl participation would not only involve the strain of the three-membered ring, but would tighten the methylene belt to the point where the benzene ring would have to become seriously deformed, as in [8]paracyclophane.[10] A 1,6-distance between carbons 4 and 12 is the next shortest (2.7 Å.) in Table III. The corresponding tosylate provided the greatest acceleration of the paracyclophanes, a factor of 1800 faster than cyclohexyl tosylate.

<center>TABLE III</center>
<center>TRANSANNULAR CARBON–CARBON DISTANCES</center>

C-m	to	C-n	Distance, Å.
2		13	2.4
3		13	2.8
4		13	3.2
4		12	2.7
5		14	3.0
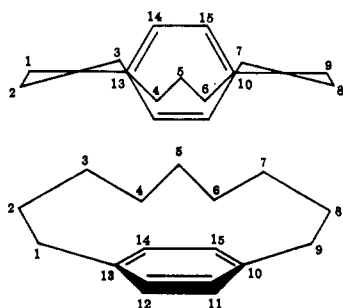
The products as well as the rates provide ample evidence for phenyl participation in carbonium ion formation during solvolysis of the 4-tosylate. The acetate was formed from optically active tosylate with complete retention of configuration, and optically active tricyclic hydrocarbon was produced. Both results indicate that ion A was formed directly from starting material. In formation of A, carbon-4 was inverted, and when the benzene ring acted as a leaving group for solvent attack
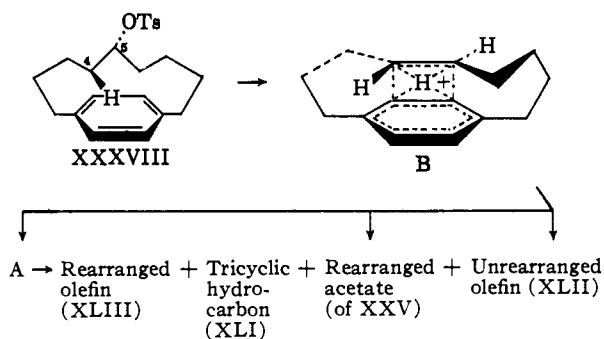

<center>A</center>
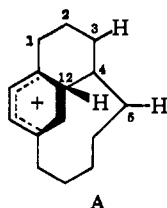
on carbon-4, a second inversion occurred to give acetate with over-all retention. Loss of a proton from C-12 led to optically active tricyclic hydrocarbon, whereas loss of a proton from either C-3 or C-5 would provide the two observed olefins. Molecular models of A indicate that the phenyl and one of the two hydrogens on C-3 or on C-5 are *trans* to one another, and are in a good position to drop off to form *trans*-olefin.

The next smallest distance of Table III (2.8 Å.) involves a 1,4-interaction between C-3 and C-13. Considerable acceleration is evident from the factor of 60

by which the rate of the 3-tosylate exceeds that of cyclohexyl tosylate. Unfortunately this tosylate was never isolated in a pure state, and therefore its solvolysis products could not be examined carefully. It is clear, however, that a small amount of tricyclic hydrocarbon XLI was formed from the mixture of 2- and 3-tosylates. This material undoubtedly came from the 3-tosylate as a product of a hydrogen migration from carbon-4.

Considerable acceleration of rate is evident in the rate factor of 170 for acetolysis of the 5-tosylate, although three of the four products involve hydrogen migration. No unrearranged acetate was produced. Thus the acceleration would appear to be associated with neighboring hydrogen participation in ionization. Since hydrogen attached to secondary carbon is not usually a rate-enhancing neighboring group, and since the benzene ring ultimately becomes attached to C-3 in the tricyclic hydrocarbon produced, the rate enhancement could well be due to *simultaneous involvement of hydrogen and the benzene ring in ionization*. Molecular models indicate that one of the hydrogens at C-4 and one at C-6 are pressed into the π-electron cloud of the benzene ring. Much of the resulting strain would be released in going to an non-classical bridged ion whose structure can best be envisioned as a *trans* double bond pressed against the face of a benzene ring with a proton embedded in the π-clouds of both the double bond and the benzene ring (see formula B). The presence of a positive charge in the π-cloud should greatly reduce the π–π-repulsions between the two unsaturated systems.

<center>XXXVIII   B</center>

A → Rearranged + Tricyclic + Rearranged + Unrearranged
    olefin   hydro-   acetate   olefin (XLII)
    (XLIII)   carbon   (of XXV)
             (XLI)

In principle, all four products could arise directly from B. In practice, at least a portion of each of the four compounds probably involved A also as an intermediate. Since the ratio of rearranged olefin to tricyclic hydrocarbon is the same from both tosylates (see Chart II), all of each of the two substances must have involved a common intermediate, probably A. Since the ratio of the two olefins produced from the 5-tosylate is different from that from the 4-tosylate; some unrearranged olefin must have come by a path not involving A. Thus about half of the unrearranged olefin probably arose directly from B, and the other half involved both A and B as intermediates. Simple loss of the proton from bridged ion B would produce unrearranged olefin. Since the ratio of rearranged acetate to tricyclic hydrocarbon is different for the two tosylates, about 40% of the rearranged acetate from the 5-tosylate must have not involved A as an intermediate. Rearranged acetate could be formed by simple reaction of solvent at C-4, simultaneously to the bridged hydrogen becoming fully bonded to C-5. A similar interpretation can be given to the production of the tricyclic hydrocarbon XLI from the 3-tosylate (tosylate of XXVIII). Some evidence for existence of a hydrogen bridge as a discrete intermediate[14] and

(14) D. J. Cram and J. Tadanier, *J. Am. Chem. Soc.*, **81**, 2737 (1959).

for neighboring hydrogen participation in ionization[15] has been obtained in earlier work.

The $\Delta S^{\ddagger}$ values for the systems of this study (Table I) and those of the simple cycloalkyl systems (Table II) are comparable and in an apparently random manner range from −5.4 to +3.8 e.u., with most values lying within experimental error of zero. Thus the entropies of activation cannot be used as a criterion for neighboring group involvement in ionization. On the other hand, $\Delta H^{\ddagger}$ values reflect in a simple manner rate enhancement due to neighboring groups. In a study of open-chain phenylalkyl tosylates,[16] a correlation was made which associated an increase in entropy with neighboring group involvement in ionization. Thus entropies of −11 e.u. were observed for phenyl involvement and −17 e.u. for lack of phenyl assistance in ionization. Apparently the rigidity of the ring systems and the flexibility of the open-chain compounds are associated with these differences in entropy.

Experimental

All melting points are corrected, and all boiling points are uncorrected. Most of the syntheses were repeated several times, and a typical procedure is described here.

Spectra.—Ultraviolet spectra were recorded on a Cary model 11PMS or model 14M spectrophotometer, in 95% ethanol which had been distilled from sodium hydroxide. Infrared spectra were recorded on either a Perkin–Elmer model 21 or a Beckman model IR5 spectrophotometer, using either chloroform of carbon tetrachloride solutions or a liquid film.

The proton magnetic resonance spectra were run on a Varian V-4310A high resolution spectrometer operating at 40 megacycles. Carbon disulfide solutions were used with 1% tetramethylsilane as internal standard. Frequency measurements were made by the side-band technique.

Gas Chromatography.—Analytical gas chromatography was done on a Perkin–Elmer model 154C vapor fractometer. The carrier gas used was Airco helium. The following columns were used. All are 0.25 in. diameter except column D: column A, length 1.5 meters, packing 30% silicone grease on firebrick; column B, length 30 in., packing 30% γ-methyl-γ-nitropimelonitrile on firebrick; column C, length 1 meter, packing, same as column B; column D, length 1 meter, diameter ³/₈ in., packing same as column B.

Kinetics.—Rate runs 1, 2, 4 and 7–16 were conducted by the sealed ampoule technique which has been amply described by Winstein and co-workers.[5] A zero time point was withdrawn from the bath soon after temperature equilibrium had been reached. Seven additional points were taken during the first 3 reaction half-lives, and an infinity point was pulled after 10 reaction half-lives. Quenching of the reaction in the 50 and 75° runs was accomplished by shaking the ampoule in an ice–water slush for 30 seconds. The time was recorded at the beginning of the quench. In the 25° runs the ampoule was opened and an aliquot taken and titrated as quickly as possible, and the time was recorded at the titration end-point.

Runs 3, 5 and 6 were carried out in ground glass stoppered volumetric flasks from which aliquots were pipetted at appropriate times. In run 3 the time was recorded at the titration endpoint. In runs 5 and 6 the aliquots were pipetted into 25 ml. of cold dioxane to quench the reaction, and the time was recorded at the beginning of draining of the automatic pipet.

The developing p-toluenesulfonic acid was followed by titration with standard sodium acetate in acetic acid, using 7 drops (per 5.00-ml. aliquot) of saturated brom phenol blue in acetic acid as indicator. Table VI provides a typical set of data for a given run. Tables IV and V record the data which involve use of a mixture tosylates as starting material.

Solvents.—Acetic acid containing 0.01 M acetic anhydride[17] and dioxane[16] were previously described.

Standard Solution.—Standard sodium acetate in glacial acetic acid was prepared by accurately weighing the desired amount of Baker analyzed reagent grade anhydrous sodium carbonate from a freshly opened bottle.

Methyl ω-(4-Methyl acetate)-benzoylcaproate (III).—A Friedel–Crafts acylation was carried out according to the procedure described previously.[2b] From 158 g. (0.82 mole) of ω-carbo-

(15) S. Winstein, B. K. Morse, E. Grunwald, H. W. Jones, J. Corse, D. Trifan and H. Marshall, *J. Am. Chem. Soc.,* **74,** 1127 (1952).

(16) R. Heck and S. Winstein, *ibid.,* **79,** 3105 (1957).

(17) A. H. Fainberg and S. Winstein, *ibid.,* **78,** 2770 (1956).

(18) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Boston, Mass., 3rd ed., 1955, p. 292.

TABLE IV
ACETOLYSIS OF [9]PARACYCLOPHAN-3-TOSYLATE PRESENT AS A 6% IMPURITY IN [9]PARACYCLOPHAN-2-TOSYLATE AT 50°. TOTAL CONCN. 0.02 M (RUN 4)

Time, sec.	Ml.ᵃ 0.02 M NaOAc			Reaction, %ᵇ		$10^4 k$,
	x	y	$x - y$	Tot.	[9]-3-	sec.⁻¹
000	0.04	0.00	0.04	0.8	13	
600	.08	.02	.06	1.6	10	0.88ᵈ
1,800	.14	.05	.09	2.9	29	1.14
3,120	.20	.08	.12	4.1	39	1.12
4,560	.27	.12	.15	5.5	48	1.14
6,600	.35	.17	.18	7.2	58	1.10
10,260	.51	.26	.25	10.5	81	1.46ᵈ
16,140	.68	.41	.27	21.6	87	1.18
32,700	1.10	.79	.31	22.6	(100)ᶜ	..
	4.82	..	..	99.9	..	..
				Av.	1.14 ± 0.02	

ᵃ Per 5.00-ml. aliquot; x is experimental value, y is calculated titer due to [9]paracyclophan-2-tos, calculated from its rate constant. ᵇ Tot. $= \dfrac{100x}{4.86}$ [9]-3- $= \dfrac{100(x - y)}{0.31}$; 4.86 = theor. at $t = \infty$. ᶜ Subsequent points give $x - y = 0.31$. ᵈ Not included in average.

TABLE V
ACETOLYSIS OF 0.02 M [9]PARACYCLOPHAN-2-TOSYLATEᵃ AT 50° (RUN 1)

Time, sec.	Reaction, %	Ml.ᵇ 0.02 M NaOAc	$10^6 k$, sec.
000ᶜ	16	0.78	..
14,400	22	1.06	5.80
47,220	33	1.60	5.67
74,120	40	1.96	5.57
144,120	55	2.69	5.50
324,000	74	3.62	5.18
∞	88ᵈ	4.27	..
		Av. 5.54 ± 0.16	

ᵃ Contains 6% [9]paracyclophane-3-tosylate. ᵇ Per 5.00-ml. aliquot. ᶜ Eight hours after mixing to allow for complete reaction of the 3-isomer. ᵈ This sample of p-toluenesulfonate was contaminated with pyridine.

TABLE VI
ACETOLYSIS OF 0.02 M [9]PARACYCLOPHAN-5-TOSYLATE AT 25° (RUN 7)

Time, sec.	Reaction, %	Ml.ᵃ 0.02 M NaOAc	$10^6 k$, sec.⁻¹
000	09	0.43	..
4,320	13	0.64	1.08
12,180	21	1.02	1.11
21,540	28	1.41	1.10
33,300	38	1.88	1.13
49,500	49	2.43	1.14
96,780	71	3.53	1.14
167,820	88	4.42	1.17
∞	101	5.06	
		Av. 1.12 ± 0.02	

ᵃ Per 5.00-ml. aliquot.

methoxycaproyl chloride,[19] 125 g. (0.82 mole) of methyl phenylacetate and 450 g. (3.38 moles) of aluminum chloride in 1000 ml. of tetrachloroethane was obtained 121 g. (45%) of a pale yellow liquid, b.p. 210–216° (2 mm.). A small sample was redistilled through a 1-meter Podbielniak column; b.p. 214–215° (3 mm.), n^{26}D 1.5519.

Anal. Calcd. for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.42; H, 7.00.

ω-(4-Acetic acid)-phenylheptanoic Acid (VII).—A Wolff–Kishner reduction[2c] with 121 g. (0.4 mole) of keto-diester III, 112 g. (2 moles) of potassium hydroxide and 50 ml. (1.3 moles) of 85% hydrazine hydrate in 50 ml. of diethylene glycol gave around 90 g. of crude product as a red oil. A small sample was distilled through a short Vigreux column. The light yellow distillate solidified on standing. Several recrystallizations from benzene yielded a white solid, m.p. 124.6–125.6°.

(19) F. C. Pennington, W. D. Celmer, W. M. McLamore, V. V. Bogert and I. A. Solomons, *J. Am. Chem. Soc.,* **75,** 109 (1953).

Anal. Calcd. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.05; H, 7.50.

Methyl ω-(4-Methyl acetate)-phenylheptanoate XI.—Crude diacid VII (90 g.) was dissolved in 800 ml. of anhydrous methanol, and after the addition of 5 ml. of concentrated sulfuric acid, the solution was heated under reflux for 5 hours. The solution was then poured into 6 liters of a mixture of ice and water and extracted with three 500-ml. portions of ether. The combined ether extracts were washed with water, 5% sodium bicarbonate solution and again with water. The ether solution was dried over anhydrous magnesium sulfate, and the drying agent was removed by filtration. A red oil remained upon evaporation of the ether. Distillation of this material through a short Vigreux column yielded 89 g. of a light yellow liquid, b.p. 179–189° (2 mm.). A small sample was redistilled through a 1-meter Podbielniak column; b.p. 191° (4 mm.), $n^{25}D$ 1.4953.

Anal. Calcd. for $C_{17}H_{24}O_4$: C, 69.84; H, 8.27. Found: C, 69.59; H, 8.13.

Methyl ω-(4-Methyl acetate)-cyclohexylheptanoate (XV).—A solution of 87 g. of diester XI in 400 ml. of glacial acetic acid was shaken with 1 g. of platinum oxide under 30 p.s.i. hydrogen pressure for 4 hr. The solution was filtered free of catalyst and the solvent was distilled at reduced pressure. The yellow residual oil was first distilled through a short Vigreux column and then through a 1-meter Podbielniak column. In the second distillation, after a very small fore-run, 64.2 g. (70%) of a colorless liquid was collected, b.p. 171–173° (4 mm.), $n^{25}D$ 1.4612. The ultraviolet spectrum indicated the absence of a benzene nucleus.

Anal. Calcd. for $C_{17}H_{30}O_4$: C, 68.42; H, 10.13. Found: C, 68.12; H, 10.43.

Acyloin XVII.—A detailed description of the apparatus and procedure for the high dilution acyloin cyclization has been given.[20] A solution of 20 g. (0.07 mole) of diester XV in 1 liter of pure, dry toluene was added over a period of 48 hours to 6.9 g. (0.30 mole) of sodium stirred at high speed in 2 l. of boiling toluene. The reaction product was purified by distillation in an atmosphere of dry nitrogen to yield 9.5 g. (75%) of a very viscous yellow oil, b.p. 150–160° (2 mm.). This material had bands in the infrared for hydroxyl and carbonyl functions (3.0 and 5.9 μ) and gave a positive acyloin test with bismuth trioxide. No attempt was made to further purify this crude isomeric mixture.

Anal. Calcd. for $C_{15}H_{26}O_2$: C, 75.58; H, 11.00. Found: C, 74.37; H, 11.07.

2-Ketohexahydro[9]paracyclophane (XVIII).—The procedure of Cope[21] was followed with the following modification.

Reagent grade zinc dust was activated by swirling for several minutes in 1:1 concentrated hydrochloric acid–glacial acetic acid. The zinc was then washed with water, acetone and pentane.

From 4.1 g. of acyloin XVII was obtained 3 g. of a light yellow oil, b.p. 151–165°. The oil was dissolved in a small amount of pentane and adsorbed on 200 g. of neutral, active alumina. Elution with several hundred ml. of pentane yielded 0.07 g. of an oil having no carbonyl absorption in the infrared. This material was assumed to be completely reduced hydrocarbon (2% yield). Elution with several hundred ml. of 15% ether in pentane gave 1.84 g. of an oil which had an infrared absorption at 5.9 μ. This material (XVIII), when distilled through a 1-meter Podbielniak column, yielded 1.80 g. (48%) of a colorless liquid, b.p. 155° (10 mm.), $n^{25}D$ 1.5021.

Anal. Calcd. for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 80.76; H, 11.48.

The pot residue from the distillation of the crude reaction product yielded, upon further distillation at reduced pressure, 0.48 g. (12%) of starting material.

2-Hydroxy[9]paracyclophane (XXVII).—A mixture of 0.5 g. of ketone XVIII and 0.05 g. of 10% palladium-on-charcoal was heated to 310° over a period of 1.5 hours. During that time 87% of the theoretical amount of hydrogen had been collected, and further heating at that temperature had no observable effect. After the mixture was cooled, methanol was added and the catalyst was removed by filtration. The methanol was distilled through a short column at water aspirator pressure, and the residual oil was distilled at 2.5 mm. and a pot temperature of 170°. The distillate was 0.30 g. (62%) of a colorless liquid, $n^{25}D$ 1.5307. This ketonic material (XX) was treated with lithium aluminum hydride in the usual manner to yield 0.5 g. (71%) of a colorless glass. Attempts to crystallize this material from a variety of solvents were uniformly unsuccessful, so it was distilled through a short Vigreux column at a pot temperature of 190° (1 mm.).

(20) D. J. Cram and H. Steinberg, *J. Am. Chem. Soc.*, **73**, 5702 (1951).

(21) A. C. Cope, J. W. Barthel and R. D. Smith, *Org. Syntheses*, **36**, 14 (1956).

Anal. Calcd. for $C_{15}H_{22}O$: C, 82.51; H, 10.16. Found: C, 82.57; H, 10.05.

p-Nitrobenzoate of 2-Hydroxy[9]paracyclophane (XXVII).—A solution of 0.69 g. (0.003 mole) of alcohol XXVII and 1.7 g. (0.009 mole) of p-nitrobenzoyl chloride in 3 ml. of pyridine was heated on the steam-bath for 0.5 hour. After cooling to room temperature the pyridine solution was poured into 30 ml. of 3 N sulfuric acid, and the resulting mixture was extracted with 30 ml. of ether. The ether solution was washed with water, 5% sodium bicarbonate solution and again with water. The ether solution was dried over anhydrous magnesium sulfate, and after filtering to remove the drying agent, the ether was evaporated. The 0.73 g. of yellow oil which remained crystallized from ether–pentane solution, and after 4 recrystallizations from methanol the first crop was 0.1 g. (9%) of a white powder, m.p. 63.5–66.5°.

Anal. Calcd. for $C_{22}H_{25}NO_4$: C, 71.91; H, 6.86. Found: C, 72.08; H, 6.90.

A second crop of 74 mg. (7%) of yellow plates, m.p. 60–69°, was obtained from the mother liquors.

Methyl δ-(4-β-Methyl propionate)-benzoylvalerate (IV).—A Friedel–Crafts acylation was carried out in tetrachloroethane, as previously described, with 164 g. (1 mole) of methyl hydrocinnamate, 208 g. (1.1 moles) of ω-carbomethoxyvaleryl chloride and 456 g. (3.4 moles) of aluminum chloride. The product was 192 g. (58%) of a white solid, m.p. 46.6–48.0°, after several recrystallizations from benzene–Skelly B.

Anal. Calcd. for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.54; H, 7.47.

δ-(4-β-Propionic acid)-phenylcaproic Acid (VIII).—A Wolff–Kishner reduction was performed using 190 g. (0.62 mole) of keto-diester IV, 129 g. (2.3 moles) of potassium hydroxide and 66 ml. (1.7 moles) of 85% hydrazine hydrate in 600 ml. of diethylene glycol. The crude, dried reaction product was used directly in the next step.

A small sample was recrystallized once from chloroform–carbon tetrachloride to give a white solid, m.p. 123.4–124.8°.

Anal. Calcd. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.24; H, 7.57.

Methyl δ-(4-β-Methyl propionate)-phenylcaproate (XII).—A solution of 181 g. of a crude mixture of diacid VIII and potassium chloride and 9 ml. of concentrated sulfuric acid was heated under reflux overnight. The diester was isolated in the usual manner and was distilled through a 1-meter Podbielniak column. The fraction with b.p. 160–162° (2 mm.) and $n^{25}D$ 1.4960 weighed 128 g. (73% for two steps).

Anal. Calcd. for $C_{17}H_{24}O_4$: C, 69.83; H, 8.27. Found: C, 69.90; H, 8.27.

Methyl δ-(4-β-Methyl propionate)-cyclohexylcaproate (XVI).—In a 2-l. stainless steel bomb fitted with a motor driven stirrer, 4 g. of platinum oxide was added to 334 g. of diester XII in 700 ml. of glacial acetic acid. The mixture was stirred for 12 hours at 70° under 1000 p.s.i. of hydrogen pressure. After filtration to remove catalyst, the acetic acid was distilled at reduced pressure. Distillation of the residual oil yielded 322 g. (95%) of a colorless liquid, b.p. 155–159° (1 mm.), $n^{25}D$ 1.4638. The ultraviolet spectrum indicated the absence of a benzene nucleus.

Anal. Calcd. for $C_{17}H_{30}O_4$: C, 68.42; H, 10.13. Found: C, 68.61; H, 10.05.

Attempts to Ring Close Diesters XII and XVI.—One attempt to form the cyclic acyloin from XII in toluene, using 128.5 g. (0.44 mole) of diester and 42.6 g. (1.85 moles) of sodium, yielded only 89 g. (70%) of starting material.

Two runs were made in xylene using about 0.2 mole of diester and 1 mole of sodium. Starting material was recovered in 52 and 63% yields. In each of the three attempts to cyclize XII, there was formed some of the presumably low molecular weight polymer which appears as a very viscous pot residue in the distillation of product. There was found, however, none of the spongy polymer, of presumably high molecular weight, which is usually formed to some extent in a successful acyloin cyclization.

Two attempts to ring close diester XVI gave similar results. In xylene, from 75 g. (0.25 mole) of diester and 26.5 g. (1.15 moles) of sodium there was recovered 50 g. (67%) of starting material, 8 g. (11%) of low molecular weight polymer and 14.5 g. (19%) of spongy polymer.

Methyl δ-Phenylvalerate.—The procedure described for the preparation of ethyl δ-phenylvalerate[2c] was followed, except for the substitution of methanol for ethanol in the esterification step.

From 2345 ml. of benzene, 1340 g. (10 moles) of aluminum chloride and 520 g. (4.55 moles) of glutaric anhydride was obtained 810 g. (90%) of crude γ-benzoylbutyric acid. The 810 g. of keto-acid, when treated with 600 g. (10.7 moles) of potassium hydroxide and 520 ml. (13.5 moles) of 85% hydrazine hydrate in 4.5 l. of diethylene glycol, yielded 737 g. (95%) of color-

less liquid, b.p. 108–116° (3 mm.). The reported[22] boiling point for methyl δ-phenylvalerate is 173° (35 mm.).

β-(4-δ-Methyl valyrate)-benzoylpropionic Acid (V).—A well stirred slurry of 530 g. (4 moles) of aluminum chloride in 1.0 liter of dichloromethane was cooled to 10°, and 125 g. (1.25 moles) of succinic anhydride was added. The mixture was cooled to 5°, and while that temperature was maintained, 250 g. (1.25 moles) of methyl-δ-phenylvalerate in 100 ml. of dichloromethane was added dropwise. The addition took 1 hour. The mixture was stirred at 5° for 1 hour, and was then heated under reflux for 1 hour. At the end of this time the reaction mixture was cooled to about 10°, and was poured over a mixture of 3 kg. of ice and 500 ml. of concentrated hydrochloric acid. The resulting layers were separated, and the aqueous layer was washed once with dichloromethane. The combined organic layers were washed three times with dilute hydrochloric acid and three times with saturated sodium chloride solution. The cloudy organic phase became clear on standing over anhydrous magnesium sulfate overnight. The solution was filtered and the solvent was evaporated to yield 328 g. (88%) of a white solid.

A small sample of this material was recrystallized 3 times from benzene–Skelly B to yield white plates, m.p. 98.2–100.8°.

Anal. Calcd. for $C_{16}H_{20}O_5$: C, 65.73; H, 6.89. Found: C, 65.70; H, 6.91.

Methyl δ-(4-γ-Methyl butyrate)-phenylvalerate (IX).—Crude half-ester V was subjected to the previously described Wolff–Kishner reduction followed by methyl esterification. From 328 g. (1.1 moles) of V, 185 g. (3.3 moles) of potassium hydroxide and 125 ml. (3.3 moles) of 85% hydrazine hydrate in 1.5 liters of diethylene glycol, a green solid (IX) was obtained. From this crude material, 1.5 liters of methanol and 20 ml. of concentrated sulfuric acid was obtained 237 g. (76% for two steps) of colorless oil, b.p. 166–171° (0.5 mm.), n^{25}D 1.4952. Cram and Antar report for methyl δ-(4-γ-methyl butyrate)-phenyl-valerate, b.p. 165–166° (0.2 mm.) and n^{25}D 1.4952.

Acyloin XXII.—The acyloin condensation was carried out as previously described. Diester IX (79 g., 0.27 mole) in 1 liter of pure xylene was added to 28 g. (1.2 moles) of clean molten sodium in 2 liters of refluxing xylene during 45 hours. An excess of acetic acid was added, and the sodium acetate was collected and washed with pure xylene. The filtrate and washings were combined, and the solvent was removed by distillation at 25 mm. under nitrogen. The remaining yellow oil was distilled through a short Vigreux column to yield 23 g. (36%) of a viscous yellow oil, b.p. 144–147° (0.3 mm.). This material gave a positive acyloin test with bismuth trioxide and absorbed in the infrared at 3.0 and 5.9 μ (hydroxyl and carbonyl). Cram and Antar[2b] report that this compound distils at a pot temperature of 157–160° (0.2 mm.).

Acetate of Acyloin XXII.—A solution of 64 g. (0.275 mole) of acyloin XXII and 100 g. (1 mole) of acetic anhydride in 75 ml. of pyridine was heated at 40° for several minutes. The solution after standing at room temperature for 20 hours was poured into 600 ml. of cold 2 N sulfuric acid, and the resulting solution was extracted with two 150-ml. portions of ether. The ether extracts were washed with water, 5% sodium bicarbonate solution and again with water. The ether layer was dried over anhydrous magnesium sulfate and was filtered. The yellow oil remaining after evaporation of the ether was distilled through a short Vigreux column to yield 69 g. (92%) of a viscous, yellow oil, b.p. 159–162° (0.1 mm.). This crude isomeric mixture was used without further purification in the reductions described in the next two procedures.

On one occasion, after standing for a month in the refrigerator, a 20-g. sample of acyloin acetate partially crystallized. The partially crystalline mass was transferred to a Buchner funnel and was washed with pentane to yield 8 g. of white solid, m.p. 54–57°. After three recrystallizations from pentane the yield was 5 g. of prisms, m.p. 65.5–66.5°. The infrared spectra of carbon tetrachloride solutions of the oil and the crystalline acetates were identical.

Anal. Calcd. for $C_{17}H_{12}O_3$: C, 74.41; H, 8.08. Found: C, 74.49; H, 8.11.

5-Keto[9]paracyclophane (XXXI).—The use of acyloin or acyloin acetate in this reaction gave comparable results, so acyloin was usually used. Subjection of 2 g. of crude acyloin XXII, 1.5 g. of zinc dust, 4 ml. of glacial acetic acid and three 3.2-ml. of portions of concentrated hydrochloric acid to the conditions previously described yielded 1.7 g. of a pale yellow oil. This material crystallized from pentane, and 4 recrystallizations from methanol yielded 0.31 g. (17%) of white plates, m.p. 47.8–52.5°, reported[2b] m.p. 51.5–52.8°. The residue from evaporation of the mother liquors was combined with like material from several large-scale runs and was chromatographed on alumina. A column of 1250 g. of neutral active alumina was prepared with pentane, and 40 g. of crude ketone residues in a

little pentane was adsorbed on the column. Elution with 5 liters of pentane gave 2.4 g. of oil (fract. 1). Elution with 10 liters of 2% ether and 1.5 liters of 40% ether gave 12 g. of oil (fract. 2). The next 4 liters of 40% ether gave 17 g. of a soft, white solid (fract. 3). Fraction 1 was distilled at 0.2 mm. and 145° pot temperature to yield 2.2 g. of a colorless oil. The infrared spectrum of this material in carbon tetrachloride solution was identical with that of [9]paracyclophane prepared previously.[2b] Gas chromatography on column A, at 220° and 15 lb. pressure, gave a retention time of 8.5 min. for the major peak from each material. A minor component, retention time 4 min., was present in the current material; and a minor component, retention time 9 min., was present in the reference sample. From a 2 m. × ⁵/₈ in. column of the same packing at 200° and 5 lb. pressure, the major component was collected. From 2 g. of fract. 1 was obtained 0.5 g. (after distillation at 0.1 mm.) of a colorless oil, n^{25}D 1.5312. This material gave one peak in a subsequent gas chromatogram.

Fraction 2 gave a precipitate with 2,4-dinitrophenylhydrazine reagent and had an infrared spectrum (chloroform solution) similar to those of authentic samples of 4- and 5-keto[9]para-cyclophane. This material, when combined with the mother liquors from fract. 3 and adsorbed on 300 g. of alumina, yielded on elution with 7% ether in pentane, 1.5 g. of ketone XXIV, m.p. 68–72°, 6 g. of an oil (mixture of ketones) and 2.5 g. of ketone XXXI, m.p. 45–51° (after 2 recrystallizations from pentane). Fraction 3 was recrystallized once from pentane and once from methanol to yield 12.6 g. of ketone XXXI as white plates, m.p. 47.5–55.5°.

4-Keto[9]paracyclophane (XXIV).—The procedure described previously[23] for the conversion of acyloins to ketones was followed. The zinc chloride used in the reaction was not fused but was dried in the following manner. A 100-ml. round-bottom flask was half filled with zinc chloride from a freshly opened bottle, and thionyl chloride was added to the three-quarter mark. The flask was closed with a Drierite filled drying tube and was heated gently on the steam-bath for several hours. The excess thionyl chloride was distilled at reduced pressure, and the flask was three-quarters filled with benzene. The benzene was distilled at reduced pressure, leaving anhydrous zinc chloride as a finely divided, dry, white powder.

From 20 g. of acyloin XXII (acetate was used in some runs with comparable results), 20 g. of zinc chloride and 34 ml. of propanedithiol in 600 ml. of benzene was obtained a yellow oil. Treatment of this oil with 34 g. of mercuric chloride, 35 g. of cadmium carbonate and 30 ml. of water in 150 ml. of acetone yielded 10 g. of a pale yellow oil. This material was adsorbed on 300 g. of neutral, active alumina. Elution with 2 l. of pentane yielded, after distillation, 0.6 g. (3.5%) of an oil. The infrared spectrum of this material was almost identical with that of [9]paracyclophane. Gas chromatography on column C at 150° and 15 lb. pressure gave several small peaks of short retention time and a large peak at 8.7 min.; [9]paracyclophane has a retention time of 8.7 min. under these conditions.

Elution with 4 l. of 3% ether gave 3.6 g. of a soft white solid. Three recrystallizations of this material from Skelly B yielded 2.6 g. (14%) of ketone XXIV as white plates, m.p. 67–71.5°; reported[2b] m.p. 68–69.5°.

Elution with 1.5 l. of 20% and 1.5 l. of 50% ether yielded 2 g. of a partially solid material which gave, after 2 recrystallizations from Skelly B, 1.0 g. (5.5%) of ketone XXXI, m.p. 52–56.5°.

4-Keto[9]paracyclophane Propylenethiolketal.—On one occasion, upon chromatography of the crude product of the above procedure, only an oil was obtained. This material (35 g.) was distilled at 5 mm., and 21 g. was collected, b.p. 115.5–118°. The distillate solidified on standing, and subsequent chromatography proved it to be a mixture of ketones XXIV and XXXI.

The pot residue, a glass, was covered with a layer of pentane, and on standing crystals formed at the interface. When the crystalline layer was scraped away as it formed, the entire mass crystallized. Three recrystallizations from Skelly B yielded 12.4 g. of large white prisms, m.p. 114.9–116.6°. Infrared analysis of a carbon tetrachloride solution of this material indicated the absence of hydroxyl or carbonyl functions. A sodium fusion and elemental analysis indicated the presence of sulfur.

Anal. Calcd. for $C_{18}H_{26}S_2$: C, 70.56; H, 8.55. Found: C, 70.76; H, 8.31.

This material gave on hydrolysis 7.7 g. (85%) of ketone XXIV, m.p. 67–71.5°.

5-Hydroxy[9]paracyclophane (XXXIII).—A mixture of 1 g. of lithium aluminum hydride in 100 ml. of ether was stirred with a magnetic stirrer and bar in an erlenmeyer flask. A solution of 8 g. of ketone XXXI in 50 ml. of ether was added dropwise, as rapidly as possible without excessive foaming. After the addition was complete (about 10 minutes) the mixture was stirred for 1 hour. Saturated potassium carbonate solution

(22) I. M. Heilbron and O. O. Bunbury, "Dictionary of Organic Compounds," Vol. IV, Eyre and Spottiswoode, London, 1953, p. 186.

(23) D. J. Cram and M. Cordon, *J. Am. Chem. Soc.*, **77**, 1810 (1955).

was added dropwise to decompose the excess hydride, and the mixture was filtered. The clear ether solution was evaporated to a colorless oil which crystallized on standing. One recrystallization from Skelly B yielded 7.8 g. (97%) of long, white needles, m.p. 111–115°, reported[2b] m.p. 110–111.5°.

Derivatives of Alcohol XXXIII. *p*-Nitrobenzoate.—A solution of 170 mg. (0.78 mmole) of alcohol XXXIII and 200 mg. (1.1 mmoles) of *p*-nitrobenzoyl chloride in 3 ml. of pyridine was heated for several minutes on the steam-bath, and was allowed to stand at room temperature for 24 hours. The usual work-up yielded 195 mg. (68%) of yellow needles, m.p. 110–116°. One recrystallization from benzene–Skelly B gave pale yellow needles, m.p. 114–117.4°.

Anal. Calcd. for $C_{22}H_{25}NO_4$: C, 71.91; H, 6.86. Found: C, 71.94; H, 6.90.

3,5-Dinitrobenzoate.—From 195 mg. (0.89 mmole) of alcohol XXXIII and 250 mg. (1.1 mmoles) of 3,5-dinitrobenzoyl chloride in 3 ml. of pyridine, treated as in the above procedure, was obtained 304 mg. (92%) of yellow plates, m.p. 142–146°. One recrystallization from benzene–Skelly B gave pale yellow prisms, m.p. 143.8–147°.

Anal. Calcd. for $C_{22}H_{24}N_2O_6$: C, 64.25; H, 5.83. Found: C, 64.04; H, 6.09.

Acid Phthalate.—A solid mixture of 9.11 g. (0.042 mole) of alcohol XXXIII and 6.22 g. (0.042 mole) of phthalic anhydride was heated to 115°. The resulting melt was heated at that temperature overnight. The melt was cooled to room temperature, and the resulting glass was dissolved in 110 ml. of carbon tetrachloride. This solution was evaporated to half its volume. On standing in the refrigerator for several hours the solution deposited chunky white crystals. Five recrystallizations from benzene–Skelly B yielded 10.8 g. (71%) of chunky white crystals, m.p. 131–135.5°. A small sample was recrystallized once from methanol and carefully dried; m.p. 139.5–141°.

Anal. Calcd. for $C_{23}H_{26}O_4$: C, 75.37; H, 7.15. Found: C, 75.52; H, 7.11.

Brucine Salt of Acid Phthalate.—A solution of 1.0 g. (2.74 mmoles) of the acid phthalate of alcohol XXXIII in 3 ml. of acetone was added to a solution of 1.08 g. (2.74 mmoles) of brucine in 2 ml. of acetone. The solution was condensed to about 3 ml. and was cooled. An oil precipitated but would not crystallize. Most of the acetone was evaporated, and the residue was taken up in 4 ml. of methanol. Water (2 ml.) was added, and on cooling a white solid precipitated. Two recrystallizations from wet methanol gave 1.5 g. of white rosettes, m.p. 110–117°. Six more recrystallizations yielded 0.5 g. of the salt which was hydrolyzed to yield 0.19 g. of acid phthalate, m.p. 129–134° (after one recrystallization from methanol), $[\alpha]^{27}D$ 0.0° (c 15, CHCl₃).

4-Hydroxy[9]paracyclophane (XXV).—A solution of 7.7 g. of ketone XXIV in 75 ml. of ether was added to 1.5 g. of lithium aluminum hydride in 75 ml. of ether. The procedure used was the same as previously described. The product after one recrystallization from Skelly B was 6.2 g. (80%) of chunky white crystals, m.p. 59–62°, reported[2b] m.p. 57.5–58°.

Derivatives of Alcohol XXV. *p*-Nitrobenzoate.—From a solution of 100 mg. (0.46 mmole) of alcohol XXV and 100 mg. (0.54 mmole) of *p*-nitrobenzoyl chloride in 3 ml. of pyridine, by the previously described procedure, was obtained 119 mg. (70%) of yellow crystals, m.p. 95–98°. One recrystallization of this material from Skelly B yielded clusters of yellow needles, m.p. 95.8–99.3°.

Anal. Calcd. for $C_{22}H_{25}NO_4$: C, 71.91; H, 6.86. Found: C, 72.09; H, 6.80.

3,5-Dinitrobenzoate.—From 130 mg. (0.60 mmole) of alcohol XXV and 200 mg. (0.87 mmole) of 3,5-dinitrobenzoyl chloride in 3 ml. of pyridine was obtained 234 mg. (95%) of yellow crystals, m.p. 134–138°. One recrystallization from benzene–Skelly B yielded pale yellow rosettes, m.p. 134–137.2°.

Anal. Calcd. for $C_{22}H_{24}N_2O_6$: C, 64.25; H, 5.83. Found: C, 64.50; H, 5.75.

Acid Phthalate.—A mixture of 3.24 g. (0.015 mole) of alcohol XXV and 2.27 g. (0.015 mole) of phthalic anhydride was heated overnight at 115°. Attempts to crystallize the resulting oil failed. This oil was dissolved in 1:1 methanol–5% sodium bicarbonate solution, and the resulting solution was washed with 1:1 ether–pentane. The aqueous phase was acidified and extracted with ether. The ether extracts were washed once with water and once with saturated sodium chloride solution. The ether phase was dried over anhydrous magnesium sulfate, and the drying agent was filtered. Evaporation of the ether yielded an oil, which solidified on standing under ether–pentane for several days in the refrigerator. One recrystallization of this solid from benzene–Skelly B yielded 4.2 g. (76%) of white rosettes, m.p. 109–115°.

Anal. Calcd. for $C_{23}H_{26}O_4$: C, 75.37; H, 7.15. Found: C, 75.44; H, 7.19.

Resolution of 4-Hydroxy[9]paracyclophane.—Brucine (4.55 g., 0.115 mole) was added to a solution of 4.2 g. (0.115 mole) of acid phthalate of alcohol XXV in 15 ml. of acetone, and the mixture was gently heated. When cooled, the solution deposited an oil. The mother liquor was decanted, and the oil was dissolved in 15 ml. of methanol. Water was added until a thin film of oil was deposited on the bottom of the flask. On standing at room temperature for several hours, the oil solidified. By adding several drops of water every hour for several days in this manner, 3.7 g. of a soft white solid was obtained. This material was recrystallized by the above method 8 times to yield 0.2 g. of a white powder, m.p. 111–116°. From hydrolysis of 60 mg. of this salt, 20 mg. of the crude acid phthalate was obtained, $[\alpha]^{27}D$ +45°, $[\alpha]^{27}_{546}$ +54° (c 2.0, CHCl₃).

In another, larger scale experiment, 30.1 g. (0.082 mole) of the acid phthalate in 150 ml. of methanol was added to 32.4 g. (0.082 mole) of brucine in 350 ml. of methanol. Upon adding 100 ml. of water and cooling the solution, an oil precipitated. The crystalline salt could not be obtained, even by seeding with crystals from the small scale experiment. Finally the mother liquor was decanted, and the oil was again dissolved in methanol–water and was reprecipitated. One more reprecipitation from methanol–water yielded 14 g. of oil. Hydrolysis of a small sample gave crude acid phthalate, $[\alpha]^{25}_{546}$ +3° (c 7.5, CHCl₃). The mother liquor of the original salt formation was concentrated, and an oil precipitated. This material was reprecipitated twice from methanol–water to yield 20 g. of oil. A small sample was hydrolyzed to give crude acid phthalate, $[\alpha]^{25}_{546}$ −3.5° (c 7.5, CHCl₃).

When the 14 g. of crude brucine salt of (+)-acid phthalate was dissolved in 100 ml. of 2-butanone, and the solution was diluted with 50 ml. of Skelly B, crystals deposited on cooling. One recrystallization from the same solvent pair gave 5 g. of crystalline salt. Hydrolysis of a small sample gave crude acid phthalate, $[\alpha]^{25}_{546}$ −11° (c 7.5, CHCl₃).

The 20 g. of crude brucine salt of (−)-acid phthalate yielded, after 2 recrystallizations from 2-butanone–Skelly B, 10 g. of crystalline salt. Hydrolysis of a small sample gave crude acid phthalate, $[\alpha]^{25}_{546}$ −7° (c 7.5, CHCl₃).

Additional crops were brought up from the mother liquors, and after several recrystallizations 17.2 g. of brucine salt (acid phthalate $[\alpha]^{25}_{546}$ −10° (c 7.5, CHCl₃)) was obtained.

The 17.2 g. of crystalline brucine salt was shaken with excess 2 N hydrochloric acid and ether. The ether layer was washed once with 2 N hydrochloric acid and twice with water. The ether layer was dried over anhydrous magnesium sulfate, filtered and evaporated. The 9 g. of crude acid phthalate thus obtained was treated with lithium aluminum hydride. The clear ether solution obtained from the previously described basic work-up was washed several times with water to remove phthalyl alcohol. Upon evaporation of the dried ether solution, 5.4 g. of an oil was obtained. This material crystallized from Skelly B to give 4 g. of soft, white crystals, $[\alpha]^{25}_{546}$ −3.6° (c 14.1, CHCl₃). Three more recrystallizations from Skelly B yielded 1.9 g. of (−)-4-hydroxy[9]paracyclophane, m.p. 61–67°, $[\alpha]^{27}_{546}$ −8.6° (c 13.7, CHCl₃). A second crop of 1 g. of white crystals, $[\alpha]^{27}_{546}$ −6.5° (c 10, CHCl₃) was obtained from the mother liquors.

From evaporation of the mother liquors of the brucine salt, followed by hydrolysis of the residue and lithium aluminum hydride treatment of the hydrolysate, was obtained 6 g. of white crystals, m.p. 58–64°, $[\alpha]^{25}_{546}$ +4° (c 10, CHCl₃). This material was recrystallized twice from Skelly B to yield 4.9 g. of (+)-4-hydroxy[9]paracyclophane, m.p. 56–63°, $[\alpha]^{27}_{546}$ +8.5° (c 14, CHCl₃).

5-Hydroxyhexahydro[9]paracyclophane (XXXV).—A solution of 2 g. of ketone XXXI in 50 ml. of glacial acetic acid was shaken with 0.1 g. of platinum oxide catalyst overnight, under 40 p.s.i. hydrogen. The catalyst was removed by filtration, and the solvent was distilled at reduced pressure. The residual oil crystallized from Skelly B. Four recrystallizations from Skelly B yielded 1.0 g. (50%) of white needles, m.p. 105–108°. The infrared spectrum of a concentrated carbon tetrachloride solution of this material had bands at 3.0 and 2.8 μ (hydroxyl) and none at 5.9 or 6.7 μ (carbonyl and benzene).

Anal. Calcd. for $C_{15}H_{26}O$: C, 80.28; H, 12.57. Found: C, 80.48; H, 12.39.

4-Hydroxyhexahydro[9]paracyclophane (XXVI).—A solution of 2.0 g. of ketone XXIV in 15 ml. of acetic acid was shaken overnight with 0.1 g. of platinum oxide catalyst under 38 p.s.i. hydrogen. The catalyst was removed by filtration, and the solvent was evaporated at reduced pressure. The residual oil was dissolved in 1:1 ether–pentane and the solution was washed, first with 5% sodium bicarbonate solution, then with water. The organic phase was dried over anhydrous magnesium sulfate. The drying agent was filtered and the solvent was evaporated from the filtrate. The 1.0 g. (50%) of colorless oil which remained would not crystallize. It was converted directly to *p*-toluenesulfonate, the properties of which are given in Table VII.

TABLE VII

PROPERTIES AND ANALYSES OF ALCOHOL TOSYLATES

Compound[a]	M.p., °C.	Yield, %	Recrystn. solvent	Carbon, %		Hydrogen, %	
				Calcd.	Found	Calcd.	Found
[9]PC-2-Ts	Oil	68	Ether–pentane[b]	70.94	70.99	7.58	7.32
[9]PC-3[c]-Ts	…	..	…	…	…	…	…
[9]PC-4-Ts	59.5 dec.	76	Ether–pentane	70.94	71.19	7.58	7.52
[9]PC-5-Ts	79.7 dec.	80	Benzene–Skelly B	70.94	70.84	7.58	7.82
[10]PC-5-Ts	65.3–67.3	85	Ether–pentane	71.47	71.48	7.82	7.78
H₆[9]PC-4-Ts	52.8–55.2	66	Skelly B	69.80	69.64	9.05	8.75
H₆[9]PC-5-Ts	103.0–106.0	66	Benzene–Skelly B	69.80	69.69	9.05	9.00
H₆[10]PC-5-Ts	82.5–85.5	63	Ether–Skelly B	70.36	70.22	9.24	9.19

[a] Abbreviations: PC = paracyclophan, H₆ = hexahydro, Ts = tosylate. [b] Oil dissolved, solution cooled and mother liquor decanted from precipitated oil. [c] Present as 6% impurity in [9]PC-2-.

In another experiment, 2.0 g. of (+)-4-hydroxy[9]paracyclophane ([α]²⁷₅₄₆ +8.5°) was hydrogenated, and the product was distilled at 0.5 mm. (pot temp. 175°). The yield was 1.4 g. (70%) of an oil, 4-hydroxyhexahydro[9]paracyclophane, [α]²⁷₅₄₆ +5.4° (c 9.8, CHCl₃).

Anal. Calcd. for C₁₅H₂₂O: C, 80.28; H, 12.57. Found: C, 80.16; H, 12.67.

γ-(4-δ-Methyl valerate)-benzoylbutyric Acid (VI).—The previously described procedure for a Friedel–Crafts acylation in methylene chloride was applied. From 100 g. (0.5 mole) of methyl δ-phenylvalerate, 57 g. (0.5 mole) of glutaric anhydride and 237 g. (1.8 moles) of aluminum chloride was obtained 130 g. (83%) of a pale green solid. This material was used without further purification in the next procedure. A small sample was recrystallized 3 times from benzene–Skelly B to yield white plates, m.p. 96.8–99.3°.

Anal. Calcd. for C₁₇H₂₂O₅: C, 66.65; H, 7.24. Found: C, 66.82; H, 7.26.

Dimethyl p-Phenylene-bis-(δ-valerate) (XIV).—The Wolff–Kishner reduction was applied to 130 g. of VI, and the crude product X was esterified in the usual manner to yield 113 g. (87%) of XIV as a colorless oil, b.p. 180–187° (0.5 mm.), reported²⁴ b.p. 182–184° (0.4 mm.).

5-Hydroxy-6-keto[10]paracyclophane (XXIII).—The acyloin condensation was carried out as previously described. From 113 g. (0.37 mole) of diester XIV in 1 liter of xylene and 41 g. (1.8 moles) of sodium in 2 l. of xylene was obtained 63 g. (70%) of acyloin, b.p. 149–152° (0.3 mm.), reported²⁴ b.p. 158–161° (0.4 mm.).

5-Hydroxy[10]paracyclophane (XXXIV).—Acyloin XXIII (30 g.) in 60 ml. of glacial acetic acid was treated with 20 g. of zinc dust and 150 ml. of concentrated hydrochloric acid, as previously described. The yield, 29.6 g. of a yellow oil, was chromatographed on 1 kg. of neutral, active alumina. Elution with 3 l. of pentane yielded 5.2 g. of an oil which gave no precipitate with 2,4-dinitrophenylhydrazine reagent. Elution with 4 l. of 40% ether yielded 21 g. of an oil which gave a precipitate with 2,4-dinitrophenylhydrazine reagent. This oil XXXII was treated with lithium aluminum hydride to yield 20 g. of an oil which crystallized from pentane. The white, crystalline solid, m.p. 41–45°, weighed 15.5 g. (55% for 2 steps); reported²ᵇ for alcohol XXXIV, m.p. 43–47°.

5-Hydroxyhexahydro[10]paracyclophane (XXXVI).—A solution of 3 g. of alcohol XXXIV in 75 ml. of glacial acetic acid was shaken with 0.15 g. of platinum oxide catalyst overnight under 38 p.s.i. of hydrogen. The catalyst was filtered, and the solvent was evaporated at reduced pressure. The residual oil crystallized from Skelly B, and after 3 recrystallizations the yield was 1.1 g. (33%) of white crystals, m.p. 80.0–81.0°.

Anal. Calcd. for C₁₆H₃₀O: C, 80.60; H, 12.69. Found: C, 80.65; H, 12.59.

Preparation of Tosylates.—All of the tosylates used in this work were prepared in the following manner. The alcohol, 1–2 g., was dissolved in 2–3 ml. of pyridine. Two molar equivalents of p-toluenesulfonyl chloride was added and dissolved with swirling. The resulting solution was kept in the refrigerator overnight. At the end of that time there was in every case a precipitate of large needles of pyridinium hydrochloride. Several chunks of ice were added and the mixture was swirled for 2 minutes; then 20–30 ml. of cold water was added. The resulting mixture was extracted with 2 portions of ether (about 40 ml. each). The combined ether extracts were washed with water, 2 N sulfuric acid, water, 5% sodium bicarbonate solution and again with water. The ether phase was dried over anhydrous magnesium sulfate. The drying agent was filtered and the solvent was evaporated to a small volume (about 5 ml.). Two or three volumes of pentane were added, and the solution was allowed to stand at 0°. Usually, after several hours the tosylate

crystallized. In those cases where the product oiled out of solution, the mother liquor was decanted, and the oil was redissolved. Cooling of the new solution gave crystalline material in every case except one. Table VII records the yields and physical properties of the tosylates.

General Procedure for Isolation of Solvolysis Products.—The acetic acid solution was added to 5 volumes of water. The resulting solution was extracted with 3 portions of 1:1 ether–pentane (total volume about equal to that of aqueous solution). The combined organic extracts were washed with water, 5% sodium bicarbonate solution and again with water. The organic phase was dried over anhydrous magnesium sulfate. The drying agent was filtered and the solvent was evaporated from the filtrate. The resulting oil was taken up in ether and treated with lithium aluminum hydride. The product of this treatment was adsorbed on neutral, inactive alumina. Elution with pentane yielded the hydrocarbon products, and elution with ether gave the product alcohol.

Acetolysis of [9]Paracyclophane-5-tosylate (XXXVIII).—A solution of 2.14 g. (5.75 mmoles) of XXXVIII in 300 ml. of acetic acid, containing 0.02 M sodium acetate, was allowed to stand at room temperature for 4 days. Isolation and treatment of the products, as previously described, yielded 0.6 g. (52%) of hydrocarbon and 0.4 g. (32%) of alcohol.

The alcohol fraction was recrystallized once from Skelly B to yield 0.22 g. (55%) of alcohol XXV, m.p. 61–63°, mixture m.p. 60–63° with XXV of m.p. 59–62°.

The hydrocarbon fraction was an oil which had a strong band at 10.5 μ (trans-olefin) in the infrared. Gas chromatography on column A at 220° and 15 lb. pressure gave 2 peaks, one at 8 min. and one at 10 min. The relative areas were 8:1, the first peak (XLII+XLIII) being the larger. The relative amounts of these two olefins in the mixture were estimated by a synthetic symmetrical peak treatment of this unsymmetrical peak. The retention times on column B at 150° and 8 lb. pressure were 11 min. and 17 min. Using column D, samples of each component were collected. (The hydrocarbon mixture separated by preparative gas chromatography was actually mixed with some prepared by the LiClO₄ in ether treatment described in the next procedure.) The collected fractions were dissolved in pentane and filtered through a short plug of neutral active alumina. After vacuum distillation, each was a colorless oil.

The major component (olefin XLII) had a strong band at 10.5 μ in the infrared. The three components XLI, XLII and XLIII were present in the original hydrocarbon mixture in ratios of 1:8.2:1.33, respectively.

Anal. Calcd. for C₁₅H₂₀: C, 89.94; H, 10.06. Found: C, 89.74; H, 9.96.

Hydrogenation of 35 mg. of a mixture of XLII and XLIII in 5 ml. of 95% ethanol, with 10 mg. of 10% palladium-on-carbon as catalyst, gave 20 mg. of an oil. This product and [9]paracyclophane had identical infrared and ultraviolet (Fig. 1) spectra and identical retention times on various gas chromatography columns. The infrared spectra had intense bands at 6.87, 6.92 and 12.2 μ; medium bands at 6.63, 9.01, 12.5, 12.6 and 14.2 μ; weak bands at 6.25, 7.07, 7.93, 8.03, 10.1, 10.7, 11.3, 11.5, 11.8 and 13.7 μ. The gas chromatography retention times were: 9.5 min. on col. C at 150°, 15 lb.; 8.5 min. on col. A at 220°, 15 lb.

The minor component (hydrocarbon XLI) had no band at 10.5 μ in the infrared, and had an ultraviolet spectrum suggestive of a very distorted benzene ring (see Fig. 1).

Anal. Calcd. for C₁₅H₂₀: C, 89.94; H, 10.06. Found: C, 90.05; H, 9.86.

Hydrogenation of 24 mg. of this material in 5 ml. of 95% ethanol, with 10 mg. of palladium-on-carbon, yielded 11 mg. of an oil which gave 4 peaks of comparable area on gas chromatography. This experiment was repeated, using platinum oxide catalyst, and from 49 mg. of hydrocarbon XLI was obtained 30 mg. of an oil. This material had no infrared absorptions at-

(24) D. J. Cram and H. U. Daeniker. J. Am. Chem. Soc., 76, 2743 (1954).

tributable to benzene and did not absorb in the ultraviolet. Gas chromatography on column C at 150° and 15 lb. gave a single peak (XLIV) with retention time 7 min. Under these conditions [9]paracyclophane has retention time 9.5 min., and its hexahydro derivative has retention time 4.5 min.

Anal. Calcd. for $C_{16}H_{26}$: C, 87.30; H, 12.70. Found: C, 87.51; H, 12.47.

Reaction of [9]Paracyclophan-5-tosylate in 0.1 *M* Lithium Perchlorate in Ether.—A solution of 1.075 g. of the tosylate and 1.6 g. of anhydrous lithium perchlorate[25] in 150 ml. of ether (freshly distilled from calcium hydride) was heated under reflux. A precipitate of lithium *p*-toluenesulfonate began to form almost immediately, and after about 30 minutes the amount of precipitate seemed to remain constant. A 2-ml. aliquot was taken after about an hour, and it was diluted with 5 ml. of pentane. The resulting mixture was filtered through a short plug of basic alumina. The solution was evaporated to about 20 ml. and was run on the vapor fractometer. Two peaks were observed with retention times of 11 and 17 min. on column B at 150° and 8 lb. pressure. The areas were in the ratio of 5:1, the first peak predominating. The aliquots were taken at intervals of about 8 hours and analyzed by gas chromatography. The product ratio gradually changed to 1:1 after 4 days. By this time the rate of change was very small. The reaction mixture was filtered through a plug of basic alumina, and the solvent was evaporated from the filtrate. The residue was 400 mg. (77%) of an oil. This material was combined with the hydrocarbon mixture from acetolysis of the *p*-toluenesulfonate, and was separated by gas chromatography by the procedure of the preceding section.

Treatment of Hydrocarbon XLI with Lithium Perchlorate in Ether.—A 0.1 *M* solution of anhydrous *p*-toluenesulfonic acid in ether (1 ml.) was added to a solution of 2 mg. of hydrocarbon XLI and 50 mg. of anhydrous lithium perchlorate in 5 ml. of ether (distilled from calcium hydride). The solution was heated under reflux for 55 hours. The reaction mixture was filtered through a plug of basic alumina, and the solvent was evaporated. Gas chromatographic analysis of the residual oil (2 ml.) showed 100% hydrocarbon XLI.

Products of Solvolysis of [9]Paracyclophan-4-tosylate (XXXVII).—The 600 ml. of dioxane–acetic acid solution from the 2 kinetic runs on the tosylate was added to 3 l. of water. The resulting solution was treated as previously described to yield 0.19 g. (53%) of hydrocarbon fraction and 0.18 g. (46%) of alcohol fraction.

The alcohol fraction was recrystallized once from Skelly B to yield 0.1 g. (56%) of alcohol XXV, m.p. 54.5–61°, mixture m.p. with authentic material 55–61° (pure XXV has m.p. 59–62°).

Gas chromatographic analysis of the hydrocarbon fraction indicated the presence of two components with retention times equal to those of hydrocarbon XLI, olefins XLII and XLIII in ratios of 1:1.93:0.93, respectively.

Acetolysis of Tosylates XXVII, XXV and XXXIII at 75°.—A solution of 600 mg. of XXVII in 75 ml. of 0.024 *M* sodium acetate in acetic acid was sealed in an ampoule and heated at 75° for 12.5 hours. The solution was worked up, as previously described, to yield 125 mg. (38%) of hydrocarbon fraction and 70 mg. (21%) of alcohol fraction. The alcohol could not be crystallized.

A solution of 600 mg. of tosylate XXXVIII in 90 ml. of acetic acid, 0.024 *M* in sodium acetate, was heated at 75° in a ground glass stoppered flask for 13 min. The usual work-up yielded 160 mg. (60%) of hydrocarbon fraction and 50 mg. (20%) of alcohol fraction. The alcohol fraction, m.p. 53–57°, yielded, on one recrystallization from Skelly B, 38 mg. (76%) of alcohol XXV, m.p. 59.5–61.6°. To set a limit on the amount of alcohol XXXIII which could have been in the alcohol fraction before recrystallization, mixtures of XXV with 10% XXXIII (A), 5% XXXIII (B) and 2% XXXIII (C) were prepared. Each mixture was recrystallized from Skelly B with the following results: A, 50 mg., gave 27 mg. (54%), m.p. 53–76°; B, 100 mg., gave 78 mg. (78%), m.p. 60.5–69°; C, 223 mg., gave 180 mg. (81%), m.p. 59.5–64°.

A solution of 120 mg. of XXXVII in 15 ml. of 0.024 *M* sodium acetate in acetic acid was heated at 75° in a stoppered flask for 1.1 min. The usual work-up yielded 34 mg. (50%) of hydrocarbon fraction and 19 mg. (28%) of alcohol fraction. The al-

cohol fraction was recrystallized from Skelly B to give 13 mg. (69%) of alcohol XXV, m.p. 61.5–64.5°.

The hydrocarbon fractions of the three solvolyses were analyzed on gas chromatography column B at 150° and 8 lb. pressure. From tosylate XXXVII, peaks at 11.0 and 17 min., ratio 2.6:1; from tosylate XXXVIII, peaks at 11.2 and 17 min., ratio 9.75:1; from tosylate of XXVII, peaks at 11.6 (shoulder on each side) and 16.6 min., ratio 14:1. The infrared spectrum of this material has a band at 10.3 μ (*trans*-olefin), but is quite dissimilar to that of the other olefins (XLII or XLIII).

Oxidative Cleavage of Olefin Mixture (XLII and XLIII).—Olefin mixture XLII and XLIII (100 mg.) from the reaction of XXXVIII in lithium perchlorate–ether solution was dissolved in 40 ml. of dioxane. Water was added to make the total volume 100 ml. The cloudy solution was stirred with a magnetic stirring bar and motor, and 138 mg. of potassium carbonate was added. A solution of 0.834 g. of sodium metaperiodate and 15 mg. of potassium permanganate in 100 ml. of water was added, and the cloudy, violet colored solution was stirred for 20 hours. During that time the cloudiness disappeared and the color changed, first to red, then to amber. The solution was cooled in an ice–water-bath, and 10 ml. of 10% sulfuric acid was added. Powdered sodium bisulfite was added in small portions until the solution was colorless. The aqueous solution was washed once with pentane, and the pentane layer was discarded. The aqueous phase was extracted with three 75-ml. portions of benzene. The combined benzene extracts were washed once with water and once with saturated sodium chloride solution. The benzene phase was dried over anhydrous magnesium sulfate. After filtration, the benzene was evaporated at reduced pressure. The yellow residue was recrystallized from benzene–Skelly B to yield 51 mg. (39%) of white powder, m.p. 103–112.5°.

Anal. Calcd. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.14; H, 7.70.

Mixtures of pure ω-(4-β-propionic acid)-phenylcaproic acid (VIII) and δ-(4-γ-butyric acid)-phenylvaleric acid (IX) were prepared as follows. A stock solution of 10 mg. of diacid in 7 ml. of benzene was made up for each isomer. By mixing together appropriate amounts of each stock solution, and evaporating the solvent, the following mixtures of the two acids were obtained: pure VIII, m.p. 123–126°; 83% VIII, m.p. 114.6–121.5°; 67% VIII, m.p. 104.5–111.4°; 50% VIII, m.p. 102.6–108°; 33% VIII, m.p. 104.8–112.8°; 17% VIII, m.p. 113.4–118°; pure IX, m.p. 120–123°. A mixture composed of 2 mg. of oxidation product and 0.9 mg. of VIII gave m.p. 99.4–106°. A mixture of 5.3 mg. of oxidation product with 1.5 mg. of IX gave m.p. 110–115.8°.

Acetolysis of Tosylate of (−)-XXV.—Alcohol XXV (1.8 g.), $[\alpha]^{25}_{546}$ −8.6° (*c* 13.7, CHCl₃), was treated with 3.0 g. of *p*-toluenesulfonyl chloride in 10 ml. of pyridine according to the usual procedure. The product was not crystallized, but was dissolved directly in 500 ml. of acetic acid containing 0.02 *M* sodium acetate. After standing at room temperature for 14 hours, the solvolysis solution was worked up as previously described to yield 0.76 g. (46%) of hydrocarbon fraction and 0.79 g. (44%) of alcohol fraction.

The alcohol fraction was crystallized but was freed of solvent, dissolved in 5.0 ml. of chloroform, and the optical rotation was measured in a 1-dec. polarimeter tube: $[\alpha]^{27}_{546}$ −8.4° (*c* 15.7, CHCl₃).

The hydrocarbon fraction was analyzed on gas chromatographic column 5 at 150° and 8 lb. pressure. The chromatogram indicated the presence of 68% olefin mixture (XLII and XLIII), retention time 11 min., and 32% hydrocarbon XLI, retention time 17 min.

With a custom built preparative vapor fractometer with a 2 m. × ⁵/₈ in. column of 30% γ-methyl-γ-nitropimelonitrile on firebrick at 150°, the olefin and tricyclic hydrocarbon fractions were separated and collected. Each component was dissolved in pentane, and the resulting solution was filtered through a plug of active alumina. In each case, the solvent was evaporated and the residue distilled. There was obtained 0.373 g. of olefin mixture, which in a 0.25-dec. polarimeter tube had $[\alpha]^{27}_{546}$ 0.0°. With hydrocarbon XLI in a 0.25-dec. tube, the observed $[\alpha]^{27}_{546}$ was +0.02 ± 0.005°. With a Rudolph spectropolarimeter model S-80 equipped with a xenon arc, the rotation was measured at shorter wave lengths. In a 0.25-dec. tube with quartz end-plates, the following values were obtained; $[\alpha]^{25}_{obs}$ +0.5° at 450 mμ, +1.4° at 400 mμ, and +4.0° at 350 mμ.

(25) S. Winstein and R. Adams, *J. Am. Chem. Soc.*, **70**, 838 (1948).