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Solvolysis of *cis*-Pinocarvyl
p-Bromobenzenesulfonate and Related Esters

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SOLVOLYSIS OF cis-PINOCARVYL p-BROMOBENZENESULFONATE
AND RELATED ESTERS

A thesis submitted by

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SUMMARY

The solvolysis of cis-pinocarvyl p-bromobenzenesulfonate (brosylate) and related esters was investigated. The reaction products were identified by infrared and gas chromatographic comparison with known compounds. The product proportions and yields were determined by gas chromatography. Several new derivatives of cis-pinocarveol and related alcohols were prepared. Stable sulfonate esters of trans-pinocarveol and myrtenol could not be isolated.

Methanolysis of cis-pinocarvyl brosylate yielded trans-pinocarvyl methyl ether (65%) and myrtenyl methyl ether (35%). Reaction of the brosylate with 0.1M methanolic sodium methoxide gave the same proportion of trans-pinocarvyl and myrtenyl methyl ethers. Reaction of 2-methylenecyclohexyl brosylate with 0.1M methanolic sodium methoxide yielded 2-methylenecyclohexyl methyl ether (44%) and 1-cyclohexenemethyl methyl ether (56%).

Reaction of cis-pinocarvyl brosylate with 0.1M methanolic sodium methoxide in the presence of 0.5M lithium perchlorate yielded an increased amount of rearranged product, myrtenyl methyl ether (50%). Hydrolysis of the brosylate in 55% aqueous acetone gave trans-pinocarveol (50%) and myrtenol (50%). Hydrolysis of 2-methylenecyclohexyl brosylate gave 2-methylenecyclohexanol (42%) and 1-cyclohexenemethanol (58%).

The products of solvolysis of cis-pinocarvyl brosylate and 2-methylenecyclohexyl brosylate did not isomerize at the reaction conditions employed. Solvolysis of cis-pinocarvyl brosylate yielded no derivatives of cis-pinocarveol. Apparently, steric hindrance by the isopropylidene bridge prevented their formation.

Pseudo-first-order rate constants were determined for the methanolysis of cis-pinocarvyl brosylate ($9.6 \times 10^{-4} \text{ sec.}^{-1}$) and 2-methylenecyclohexyl brosylate

(9.7×10^{-4} sec.⁻¹) at 5°. The isopropylidene bridge has no effect on the rate of methanolysis of cis-pinocarvyl brosylate. Addition of 0.02M sodium methoxide causes no increase in the rate of methanolysis for the two brosylates. Addition of 0.5M lithium perchlorate causes a twofold increase in the rate of alkaline methanolysis of cis-pinocarvyl brosylate.

Based on the product analyses and kinetic studies, unimolecular mechanisms are proposed for the solvolysis of cis-pinocarvyl brosylate. Methanolysis and alkaline methanolysis proceeds through an unsymmetrical ion-pair mechanism. The brosylate leaving group is forced by the isopropylidene bridge to assume a position close to the exocyclic carbon atom. Hydrolysis and alkaline methanolysis in the presence of 0.5M lithium perchlorate proceed through a free allylic carbonium ion.

Alkaline methanolysis of cis-pinocarvyl brosylate and 2-methylenecyclohexyl brosylate did not yield elimination products. Alkaline methanolysis of similar saturated compounds (isopinocampyl and trans-2-methylcyclohexyl brosylate) yielded a large proportion of elimination products. The unsaturated compounds are not susceptible to elimination because of excessive ring strain introduced by diene formation.

Reaction of cis-pinocarvyl, trans-pinocarvyl and 2-methylenecyclohexyl p-nitrobenzoate with 0.1M methanolic sodium methoxide in the absence of oxygen yielded only the parent alcohols. The formation of alcohol products implies that the acyl carbon-oxygen bond is cleaved. Alkaline methanolysis of cis-pinocarvyl and 2-methylenecyclohexyl brosylate involves carbon-oxygen bond cleavage. The alkyl carbon-oxygen bond in the p-nitrobenzoates is relatively strong. As expected, the brosylate group is a more effective leaving group than the p-nitrobenzoate group.

In the presence of oxygen, alkaline methanolysis of cis-pinocarvyl p-nitrobenzoate yields cis-pinocarveol and a carbonyl compound, suspected to be pinocarvone, in a 3:1 ratio. Reaction of trans-pinocarvyl and 2-methylenecyclohexyl p-nitrobenzoate at the above conditions yields only the parent alcohols.

INTRODUCTION

The purpose of this work is to contribute to the chemistry of pinocarveol derivatives. cis- and trans-Pinocarveol are derivatives of β -pinene which is a major component of the turpentine produced in the pulping of pinewood.

The principal objective in this study is to gain a better understanding of the solvolysis* reactions of cis-pinocarvyl esters. The cis-pinocarvyl structure is unique, since it has an allyl group and a strained bicyclic ring (Fig. 1). The solvolysis of allylic compounds and of bicyclic compounds have been extensively studied. However, the solvolysis of allylic, bicyclic compounds has not been studied. It is of interest to determine the effects of the pinocarvyl structural features on the course of solvolysis reactions. For example, elimination may be an important reaction pathway as it is in the case of other cyclic esters. Substitution may or may not involve allylic rearrangement.

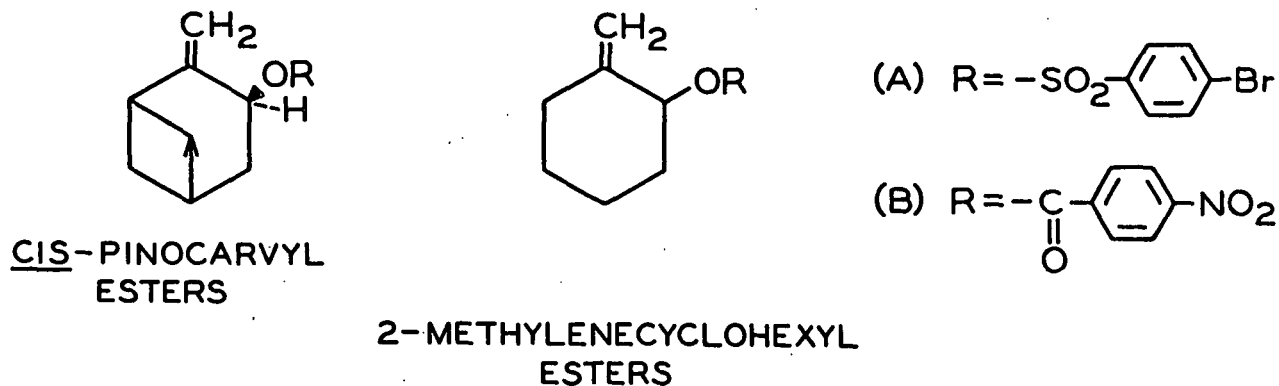


Figure 1. Unsaturated Esters

The solvolysis of compounds similar to the cis-pinocarvyl esters should be investigated, in order to better understand the effect of the pinocarvyl structural features on the solvolysis reactions. 2-Methylenecyclohexyl esters

*Solvolysis refers to a nucleophilic substitution reaction in which the attacking nucleophile is the solvent.

(Fig. 1) are allylic compounds, but they are monocyclic. Isopinocampyl esters are bicyclic compounds, but they are nonallylic. trans-2-Methylcyclohexyl esters are neither bicyclic nor allylic. Solvolysis of these comparison compounds should be informative in assessing the effects of the pinocarvyl allylic group and bicyclic bridge on the solvolysis mechanisms.

Solvolysis of sulfonate esters (brosylates or tosylates) is preferred, since the sulfonate group is an exceptionally good leaving group. Carboxylate esters may solvolyze with either alkyl- or acyl-oxygen cleavage. Therefore, the solvolyses of cis-pinocarvyl brosylate (Fig. 1A) and p-nitrobenzoate (Fig. 1B) may involve different mechanisms due to the difference in leaving groups.

SOLVOLYSIS REACTION MECHANISMS

The solvolysis of acyclic and alicyclic sulfonate esters belong to the class of reactions known as nucleophilic substitutions. The nucleophilic solvent, N, forms a new bond to the carbon atom under attack, and the sulfonate ester group, L, departs with the pair of electrons that comprised the broken bond (Fig. 2). In addition to substitution, solvolysis reactions may involve elimination of hydrogen from a carbon atom which is β to the carbon containing the ester group (Fig. 3).



Figure 2. Nucleophilic Substitution

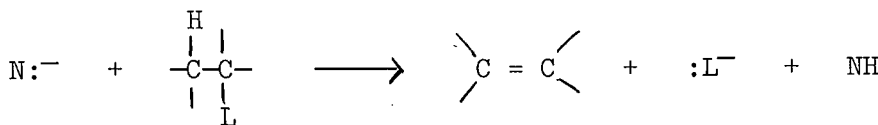


Figure 3. Elimination

The reaction of acyclic and alicyclic carboxylate esters in basic solution (such as methanolic sodium methoxide) may involve nucleophilic substitution at an acyl carbon or alkyl carbon (Fig. 4).

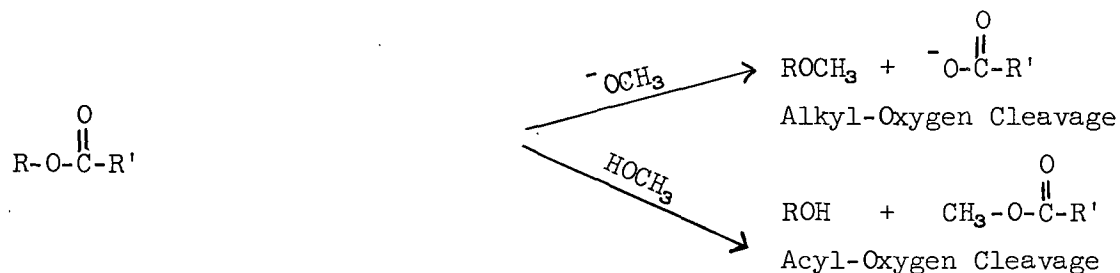


Figure 4. Carboxylate Ester Cleavage

A brief discussion of the various solvolysis reaction mechanisms, with emphasis on allylic esters, follows. More detailed discussions of these mechanisms are available in several sources (1-4).

UNIMOLECULAR NUCLEOPHILIC SUBSTITUTION WITH ALKYL CLEAVAGE (S_N1)

In the S_N1 mechanism, the bond to the leaving group is broken before the new bond is formed (Fig. 5). The reaction proceeds through an intermediate carbonium ion. The initial, bond-breaking step is normally the rate-determining step.

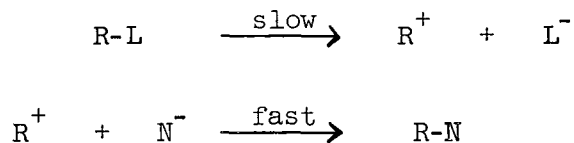


Figure 5. General S_N1 Mechanism

In the case of allylic esters, the carbonium ion intermediate may be represented as a resonance hybrid (Fig. 6). The positive charge is distributed over the entire π -electron system. The incoming nucleophile may attack either the α - or the γ -carbon. If the attack occurs at the α -carbon a normal substitution

product results, but if the attack occurs at the γ -carbon an allylic rearrangement product results.

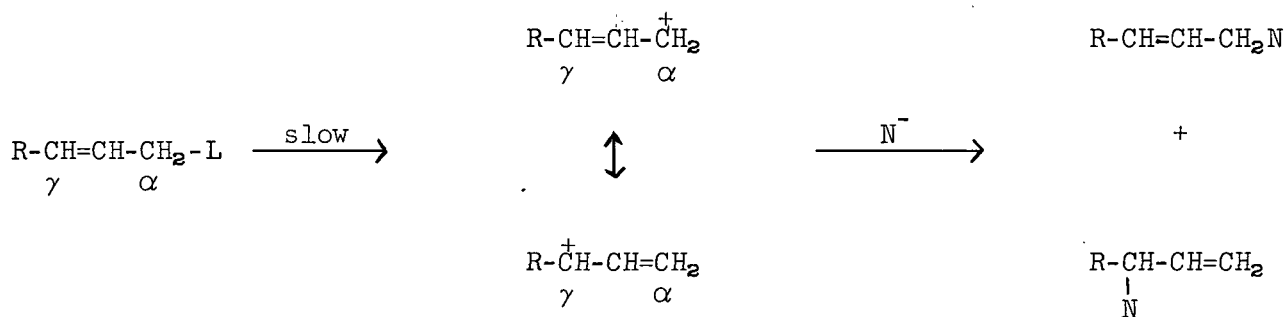


Figure 6. Allylic S_N1 Mechanism

Reactions of the S_N1 type exhibit first-order kinetics. The rate of reaction is dependent only on the concentration of the compound forming the carbonium ion. The rate of reaction is independent of the nucleophilicity* of the attacking group. An increase in the polarity of the reaction medium results in an increase in the rate of S_N1 reactions.

BIMOLECULAR NUCLEOPHILIC SUBSTITUTION WITH ALKYL CLEAVAGE (S_N2)

In the S_N2 mechanism, the breaking of the bond between the carbon atom and the leaving group is simultaneous with the formation of the bond between the attacking nucleophile and the carbon atom. Figure 7 illustrates the possible S_N2 mechanism for allylic esters. In the transition state the incoming nucleophile and the leaving group are both partially bonded to the carbon atom.

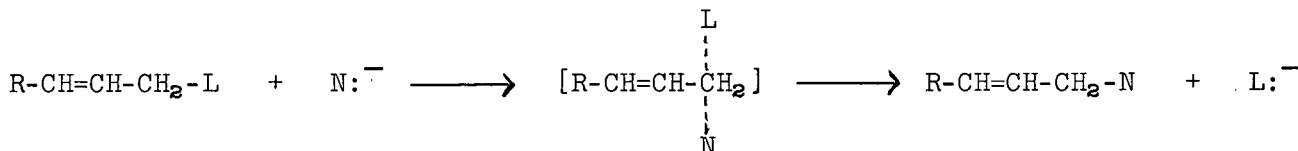


Figure 7. Allylic S_N2 Mechanism

*Nucleophilicity is defined as the availability of the nucleophiles' valence electrons for co-ordination. The strongest bases or most polarizable ions are generally the most reactive nucleophiles (1,2).

An S_N2 reaction results in complete inversion of configuration. For instance, a reactant in which the ester group was cis to a neighboring group would be converted to a trans product.

Reactions of the S_N2 type exhibit second-order kinetics. The rate of reaction is dependent on the concentrations of the attacking nucleophile and the compound experiencing substitution. The rate of reaction increases with an increase in nucleophilicity of the attacking group.

ABNORMAL BIMOLECULAR NUCLEOPHILIC SUBSTITUTION (S_N2')

The formation of a rearranged product is not sufficient evidence to conclude that solvolysis of an allylic ester has occurred by an S_N1 mechanism. Rearrangement could occur as a result of the S_N2' mechanism (Fig. 8). The incoming nucleophile attacks the γ -carbon, pushing π -electron density from the β - γ bond to the α - β bond as the leaving group is pulled off by the solvent. Only rearranged product is formed by this mechanism. The S_N2' mechanism has been found to occur only for allylic compounds which sterically hinder the occurrence of a normal S_N2 mechanism (5).

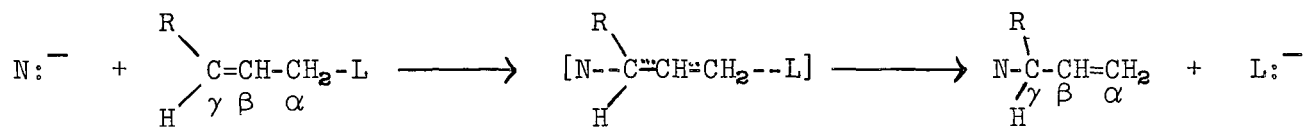


Figure 8. S_N2' Mechanism

Reactions of the S_N2' type exhibit second-order kinetics. The rate of reaction increases with an increase in nucleophilicity of the attacking group.

ION-PAIRS

The ion-pair mechanism lies between the extremes designated as S_N1 and S_N2 (or S_N2'). In the intermediate the bond between the carbon atom and the leaving

group is not completely broken. In the case of an allylic ester, a bridged ion-pair is the result (Fig. 9). The leaving group is partially bonded to both the γ - and α -carbons. The incoming nucleophile can attack either the γ - or α -carbon. The rate-determining step is formation of the ion-pair.

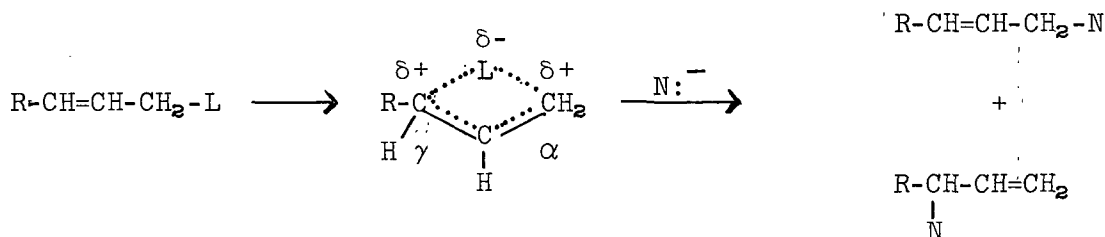


Figure 9. Ion-Pair Mechanism

If the stability of the intermediate is increased or decreased, such as by a change in the ionizing power of the solvent, the reaction may approach the limiting mechanisms S_N1 and S_N2 , respectively.

Reactions of this type exhibit first-order kinetics and show no marked rate dependence on the nucleophilic strength of the nucleophile.

BIMOLECULAR NUCLEOPHILIC SUBSTITUTION WITH ACYL CLEAVAGE ($B_{AC}2$)

Sulfonate esters commonly undergo solvolysis reactions in which the relatively weak carbon-oxygen bond is broken. Carbosylate esters, on the other hand, may undergo solvolysis reaction in which either the acyl- or alkyl-oxygen bond is broken. If the alkyl-oxygen bond is broken, the reaction mechanism is of a type already discussed (such as S_N1 or S_N2). If the acyl-oxygen bond is broken in a basic medium, the reaction mechanism is referred to as bimolecular nucleophilic substitution with acyl cleavage ($B_{AC}2$). Figure 10 illustrates the $B_{AC}2$ mechanism for the reaction of an allylic carboxylate ester with methanolic sodium methoxide (transesterification).

DETERMINATION OF SOLVOLYSIS REACTION MECHANISMS

The mechanism of a reaction is usually determined by considering all the mechanisms that may be devised in agreement with known data on reaction mechanisms in general and comparing their requirements with the experimental observation on the given reaction. Product analyses and kinetic studies are tools that have been used extensively in the study of solvolysis reaction mechanisms.

PRODUCT ANALYSIS

Identification of the reaction products is an essential step in the determination of a reaction mechanism. Product identification may show whether a nucleophilic substitution reaction involves acyl- or alkyl-oxygen cleavage. For example, an alcoholysis reaction would yield ethers if alkyl cleavage was involved and alcohols if acyl cleavage was involved. In the case of solvolysis of allylic esters, product identification will show whether or not allylic rearrangement is involved. For instance, if only a normal, inverted product is formed, the indicated mechanism is S_N2 . If normal and rearranged products are formed, more information is needed in order to determine the reaction mechanism.

Identification of the products will show whether or not elimination products are formed, in addition to substitution products.

Quantitative analysis of the reaction products is important for the following reasons: (1) The extent of reaction can be determined, (2) the yield and relative amounts of reaction products can be determined, and (3) the relative amounts of elimination and substitution can be determined. It should be noted that the relative amounts of substitution products, in the case of solvolysis of allylic esters, may be important in the determination of the solvolysis reaction mechanism. A change in the product ratios at various reaction conditions may indicate a change in the reaction mechanism.

KINETIC STUDIES

Under solvolysis conditions reactions occurring by any of the previously discussed substitution mechanisms would exhibit first-order kinetics. Since the nucleophile is in large excess, first-order dependence only on the compound undergoing substitution would be evident. Therefore, reaction characteristics other than kinetic order must be used to ascertain the mechanism.

Reactions of the bimolecular type (S_N2 or S_N2') should show an increased rate in the presence of stronger nucleophiles. The rate of reactions of the unimolecular type (S_N1 or ion pair) are not dependent on nucleophilicity. The addition of sodium methoxide to methanol should increase the rate of an S_N2 reaction relative to the rate in methanol.

An increase in solvent polarity should increase the rate of a unimolecular solvolysis reaction since the activation process requires a separation of unlike charges. In contrast, the rate of a bimolecular solvolysis reaction should be decreased with an increase in solvent polarity since the activation process requires slight dispersal of a negative charge. Therefore, an increase in the dielectric strength of the solvent or the addition of a salt (such as lithium perchlorate) to the solvent should increase the rate of an S_N1 (or ion-pair) reaction.

SOLVOLYSIS OF ALLYLIC COMPOUNDS: LITERATURE SURVEY

Studies of the solvolysis of allylic compounds have involved almost exclusively the acyclic halides (5-7). In the solvolysis of allylic halides, allylic rearrangement is the rule rather than the exception. Allylic rearrangement becomes more prominent as the ionizing power of the solvent is increased. Allylic halides, in general, undergo solvolysis reactions at a faster rate than similar

saturated compounds. For example, allyl chloride reacts with ethanolic sodium ethoxide 37 times faster than *n*-propyl chloride at 44.6° (8).

The S_N2' reaction mechanism has been observed in the solvolysis of various allylic compounds in which normal substitution is hindered by neighboring bulky groups (5,6,9,10). Young, *et al.* (10) found that the solvolysis of α-methylallyl chloride in diethylamine yielded only rearranged product. When the reaction was run in the presence of benzene, second-order kinetics were observed. The rearrangement was not due to preliminary isomerization of the starting chloride or isomerization of the normal reaction product.

Solvolysis of several noncyclic allylic compounds in alcoholic alkoxides have been found to yield elimination and substitution products (5).

Goering, *et al.* (11,12) found that *cis*- and *trans*-5-methyl-2-cyclohexenyl *p*-nitrobenzoates undergo solvolysis and internal return when reacted with 80% aqueous acetone. The reactions proceed through a symmetric bridged ion-pair (Fig. 12). Dilute alkaline alcoholysis and hydrolysis of several aliphatic allyl carboxylate esters has been shown to involve carbonium ion intermediates (13,14).

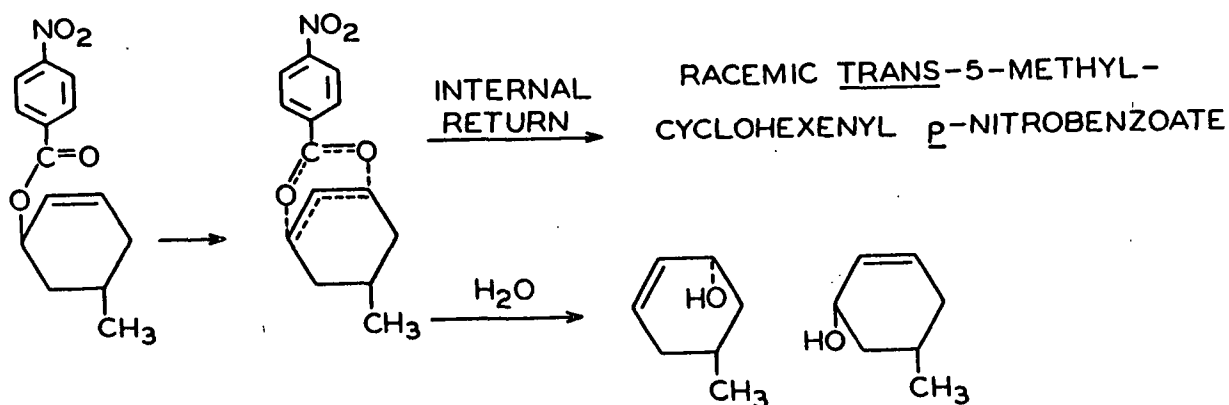


Figure 12. Solvolysis of 5-Methyl-2-cyclohexenyl *p*-Nitrobenzoate

The effect of lyate ion (such as hydroxide or methoxide) on the rate of solvolysis of allylic halides has been used as evidence for a particular solvolysis mechanism (15-19). For example, allyl chloride is solvolyzed almost 25 times faster in alkaline (0.17M potassium hydroxide) 50% ethanol than in 50% ethanol at 44.6° (17). In contrast, there is no appreciable difference in the rate of solvolysis of crotyl chloride in 50% ethanol and alkaline (0.05M sodium hydroxide) 50% ethanol at 25° (19). The former is characteristic of S_N2 reactions, and the latter is characteristic of S_N1 reactions.

SOLVOLYSIS OF BICYCLIC AND MONOCYCLIC SATURATED
COMPOUNDS: LITERATURE SURVEY

The solvolyses of saturated cyclic *p*-toluenesulfonate (tosylate) and brosylate esters have been extensively studied (1,20). Elimination competes very favorably with substitution in the solvolysis of saturated, cyclic sulfonate esters. Alkaline methanolysis of trans-2-methylcyclohexyl tosylate (Fig. 13) yields an elimination to substitution product ratio of 75%:25% (21).

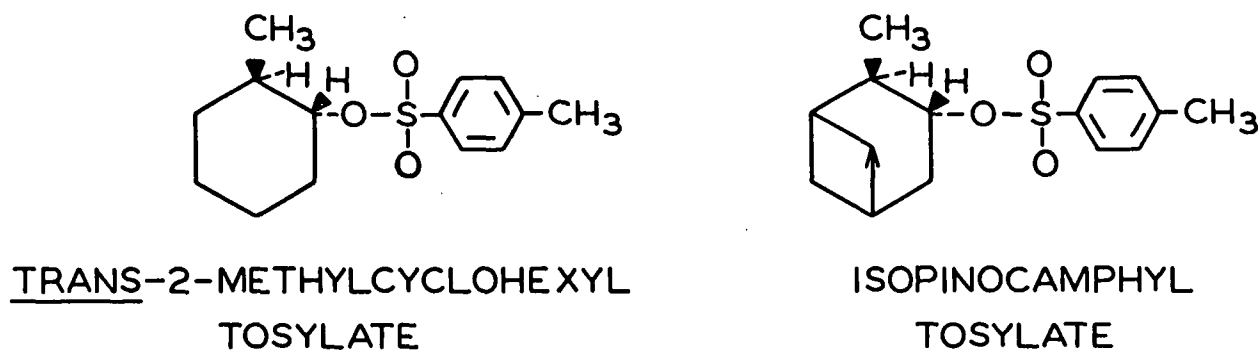


Figure 13. Saturated Tosylate Esters

The elimination to substitution product ratio for the alkaline ethanolysis of isopinocamphyl tosylate (Fig. 13) is 80%:20% (22).

EXPERIMENTAL PROCEDURES AND RESULTS

GENERAL METHODS

REAGENT AND SOLVENT PURIFICATION

Commercial β -pinene (K & K Laboratories, 76% pure) was purified by distillation through a 24-in. spinning band column. A 300-ml. charge was used. The first 100 ml. of distillate were discarded (reflux ratio 23:1). β -Pinene (95-98% pure, b.p. 44° at 10 mm., reflux ratio 15:1 to 23:1) was collected in the next 140 ml. of distillate. Purity was determined by gas chromatographic analysis on didecyl phthalate.

Lead tetraacetate (K & K) was freed from acetic acid by suction filtration with a rubber dam and stored overnight in a vacuum desiccator over potassium hydroxide.

All other reagents were reagent grade, unless stated otherwise. Magnesium sulfate was used as a drying agent.

Methanol and isopropanol were purified by the procedure reported by Lund and Bjerrum (23). Magnesium turnings (5 g.), iodine (0.5 g.), and reagent-grade alcohol (50 ml.) were placed in a 2-liter flask. The mixture was warmed until the iodine color disappeared. An additional 900 ml. of alcohol were added, and the mixture was refluxed for two hours. The mixture was distilled, with the exclusion of moisture, through a 40-cm. Vigreux column. Only the middle distillate fraction was retained.

Diglyme was purified by the procedure reported by Brown, *et al.* (24). Practical-grade diglyme (250 ml.) was distilled from calcium hydride (2.5 g.) through a 40-cm. Vigreux column. The middle distillate fraction (200 ml., b.p. 160°) was redistilled,

with the exclusion of moisture, from lithium aluminum hydride (1.0 g.). The middle distillate fraction (b.p. 75° at 35 mm.) was retained.

Pyridine was purified by a modification of the procedure reported by Tipson (25). Reagent-grade pyridine (800 ml.) was refluxed for one-half hour over barium oxide (5 g.) and then distilled, with the exclusion of moisture, through a 40-cm. Vigreux column. The middle distillation fraction (700 ml., b.p. 115°) was retained.

MELTING POINTS AND INFRARED SPECTRA

All uncorrected melting points of known compounds were run on a calibrated Thomas-Hoover "Uni-melt," capillary melting point apparatus. Corrected melting points of new compounds were run in a modified Thiele tube with thermometers calibrated by the National Bureau of Standards.

Infrared spectra were run on a Perkin-Elmer Model 21 recording infrared spectrophotometer. Solid samples were run as potassium bromide pellets, unless stated otherwise. Liquid samples were run neat between salt plates.

ELEMENTAL ANALYSES

All carbon, hydrogen, and nitrogen analyses on new compounds were run by Geller Laboratories, Charleston, West Virginia. Bromine and sulfur quantitative analysis procedures are shown in Appendix I.

PREPARATION OF COMPOUNDS

ALCOHOLS

trans-Pinocarveol and Myrtenol

trans-Pinocarveol and myrtenol were prepared by lead tetraacetate oxidation of β -pinene and subsequent transesterification of the monoacetate fraction (26).

β -Pinene (33.0 g., 0.242 mole) in reagent-grade benzene (300 ml.) was added to a stirred suspension of lead tetraacetate (106.0 g., 0.239 mole) in benzene (450 ml.) over a 30-min. period at room temperature. The reaction was carried out in the absence of direct light. After stirring for an additional hour, the lead diacetate precipitate was filtered. The filtrate was washed with three 600-ml. portions of water and dried over magnesium sulfate. The benzene was distilled from the dried solution and the product mixture was fractionally distilled through an 18-in. spinning band column.

Unreacted β -pinene (7.6 g., 0.056 mole) was recovered by distillation at 8 mm. Continued distillation gave several fractions totalling 22.6 g. (0.116 mole, 62% yield based on unrecovered β -pinene) of monoacetate, b.p. 47-55° at 0.30 mm. Gas chromatography of the several monoacetate fractions showed two major products: trans-pinocarvyl acetate (46.0% yield) and myrtenyl acetate (12.6% yield).

Monoacetate fractions which contained a relatively large amount of trans-pinocarvyl acetate (88%) were combined. A solution of this mixture (13.8 g., 0.071 mole) and sodium (0.2 g.) in methanol (200 ml.) was heated to its boiling point. Methanol and methyl acetate formed in the transesterification were distilled from the solution, over a 4-hour period, until a negative ester test was observed with ferric hydroxamate reagent (27). The remaining solution was poured into water (200 ml.), and that mixture was extracted with three 75-ml. portions of ether. The combined ether extracts were dried over magnesium sulfate.

The ether was removed, and the mixture of alcohols was distilled in vacuo through an 18-in. spinning band column. A total of 9.6 g. (0.063 mole, 89% yield) of alcohols was obtained in five fractions. Fractions 2-4 were 99% pure trans-pinocarveol (8.7 g., 81% yield), b.p. 39° at 0.40 mm. The infrared spectrum showed O-H absorption at 3370 cm.⁻¹ and disubstituted alkene absorption at 1650

and 893 cm.^{-1} . The p-nitrobenzoate* derivative was recrystallized twice from hot methanol to give white platelets, m.p. 93-94°, lit. m.p. 91-92° (28), 93.5-94.5° (29).

Several alcohol fractions (from similar transesterifications) which contained a relatively large amount of myrtenol (65% based on gas chromatographic analysis) were combined. The mixture was distilled in vacuo through an 18-in. spinning band column. Myrtenol of 98% purity was obtained, b.p. 53° at 0.35 mm. The infrared spectrum showed O-H absorption at 3330 cm.^{-1} and trisubstituted alkene absorption at 1661 and 800 cm.^{-1} .

cis-Pinocarveol

cis-Pinocarveol was prepared by selenium dioxide oxidation of β -pinene in pyridine (30) and subsequent aluminum isopropoxide reduction of pinocarpone (31).

The selenium dioxide oxidation of β -pinene gave a combined yield of pinocarpone and myrtenal of 40%, literature yield 34% (30). Gas chromatographic analysis showed that the product consisted of 85% pinocarpone and 15% myrtenal. The two products were separated after formation of their sodium bisulfite addition compounds. Myrtenal was steam distilled from the sodium bisulfite solution. Pure pinocarpone was steam distilled after the addition of 25% sodium hydroxide solution. The infrared spectrum of pinocarpone showed the expected bands for ketone carbonyl (1715 cm.^{-1}) and alkene (1633 cm.^{-1}).

The product of the reaction of pinocarpone with aluminum isopropoxide was distilled in vacuo through an 18-in. spinning band column. cis-Pinocarveol was obtained in 56% yield, b.p. 51° at 0.35 mm., m.p. 45-46°, literature m.p. 50-51°

*All p-nitrobenzoate derivatives were prepared by the method of Schenck, et al. (29).

(31). The p-nitrobenzoate derivative was recrystallized twice from hot methanol to give white needles, m.p. 103.5-104.5°, literature m.p. 104° (28). The infrared spectrum of cis-pinocarveol showed O-H absorption at 3378 cm.^{-1} and typical disubstituted alkene absorption at 1655 and 888 cm.^{-1} . The infrared spectrum and gas chromatographic retention times differed considerably from those of trans-pinocarveol.

2-Methylenecyclohexanol and 1-Cyclohexenemethanol

2-Methylenecyclohexanol and 1-cyclohexenemethanol were prepared by lithium aluminum hydride reduction of 2-carbethoxycyclohexanone (32). The reaction product was distilled in vacuo through an 18-in. spinning band column. 2-Methylenecyclohexanol, b.p. 79.5° at 18 mm., was recovered in 54% yield, literature yield 52% (32). The p-nitrobenzoate derivative was recrystallized twice from hot methanol to give white platelets, m.p. 63.5-64.5°, literature m.p. 61-62.5° (32). The infrared spectrum of 2-methylenecyclohexanol showed the expected bands for O-H absorption at 3360 cm.^{-1} and disubstituted alkene absorption at 1662 and 896 cm.^{-1} .

Continued distillation of the reaction product gave 1-cyclohexenemethanol, b.p. 95-96.5° at 18 mm., in 17% yield, literature yield 21% (32). The infrared spectrum showed O-H absorption at 3320 cm.^{-1} and trisubstituted alkene absorption at 1675 and 800 cm.^{-1} . The p-nitrobenzoate derivative was recrystallized twice from hot methanol to give white platelets, m.p. 64.5-65.5°. This compound has not been reported previously. Calculated for $\text{C}_{14}\text{H}_{15}\text{O}_4\text{N}$: C, 64.35; H, 5.78; N, 5.36. Found: C, 64.45; H, 5.59; N, 5.36.

Isopinocampheol

Isopinocampheol was prepared by hydroboration of α -pinene in diglyme and subsequent hydrogen peroxide oxidation of the product (33). The oxidized reaction product was recrystallized twice from petroleum ether (30-60°).

Isopinocampheol, m.p. 53-55°, was obtained in 55% yield. Zweifel and Brown (33) reported a 79% yield of isopinocampheol, m.p. 55-57°. The infrared spectrum showed O-H absorption at 3370 cm.⁻¹. The p-nitrobenzoate derivative was recrystallized twice from hot methanol to give small, white needles, m.p. 90.5-91.5°. This compound has not been reported previously. Calculated for C₁₇H₂₁O₄N: C, 67.31; H, 6.98; N, 4.62. Found: C, 67.24; H, 6.93; N, 4.87.

trans-2-Methylcyclohexanol

trans-2-Methylcyclohexanol was prepared by hydroboration of 1-methylcyclohexene in diglyme and subsequent hydrogen peroxide oxidation of the product (34). The oxidized reaction product was distilled in vacuo through an 18-in. spinning band column, giving trans-2-methylcyclohexanol, b.p. 75° at 16.5 mm. The infrared spectrum was identical with that of authentic trans-2-methylcyclohexanol*. The p-nitrobenzoate derivative was recrystallized twice from hot methanol to give small, white platelets, m.p. 63.5-64.5°, literature m.p. 63.7-64.2° (35).

SULFONATE ESTERS

Esters of trans-Pinocarveol and Myrtenol

The tosylate, methanesulfonate (mesylate), and brosylate derivatives of many bicyclic alcohols have been prepared by the reaction of a sulfonyl chloride with the appropriate alcohol in pyridine (25,36,37). Several attempts were made to prepare sulfonate ester derivatives of trans-pinocarveol. The reaction conditions are shown in Table I. Crystalline products could not be isolated from the reaction mixtures by crystallization, preparative gas chromatography, or distillation.

Extraction of the reaction mixtures resulted in relatively small amounts of product. Apparently, a large amount of the alcohol was converted to a water-soluble

*Sadtler Standard Spectra.

TABLE I

ATTEMPTED PREPARATION OF trans-PINOCARVYL ESTERS

<u>trans</u> -Pinocarveol, moles	Sulfonyl Chloride, moles	Solvent	Reaction Temperature and Time	Work Up Procedure Reference	Method of Isolation and Analysis
0.013	<u>p</u> -Toluene-0.015	Large excess Pyridine	0°, 1 hr.	(25)	Gas Chromatography (GLC)
0.013	<u>p</u> -Toluene-0.015	Excess Pyridine	25°, 12 hr.	(25)	Crystallization, GLC
0.013	<u>p</u> -Toluene-0.013	Pyridine 0.037 mole	0°, 4 days	(37)	Crystallization
0.021	<u>p</u> -Toluene-0.023	Large excess pyridine	0°, 4 days	(25)	Distillation, IR
0.033	<u>p</u> -Toluene-0.033	Pyridine 0.093 mole	25°, 5 hr.	(37)	IR, Crystallization, Distillation, GLC
0.0066	<u>p</u> -Toluene-0.0066	Dimethyl aniline 0.019 mole	25°, 1 $\frac{1}{2}$ hr.	(37)	GLC
0.0066	Methane-0.007	Pyridine 0.082 mole	0°, 6 hr.	(37)	IR, GLC, Distillation
0.033	Methane-0.033	Pyridine 0.050 mole	-40°, 2 hr.	(37)	IR, GLC, Distillation
0.0185	Methane-0.020	Large excess pyridine	3°, 1 day	(36)	Crystallization
0.013	<u>p</u> -Bromobenzene-0.014	Large excess pyridine	-40°, 2 days and 1 week	(36)	IR, Crystallization

derivative, such as a pyridinium salt (25). Infrared analysis of the extracted products indicated the presence of bands characteristic of sulfonate esters (38). Attempts to crystallize the products from petroleum ether (30-60°) or hexane resulted in the formation of viscous, dark oils. Distillation of the products apparently caused decomposition of the esters. The pot residues rapidly darkened as the temperature increased and the infrared spectra of the collected fractions showed no evidence of sulfonate ester bands. Infrared spectra of samples collected by gas chromatography showed no evidence of sulfonate ester bands.

Attempts to prepare the brosylate derivative of myrtenol yielded viscous, dark oils.

Esters of cis-Pinocarveol, 2-Methylenecyclohexanol, Isopinocampheol, and trans-2-Methylcyclohexanol

The brosylate derivatives of the title compounds were prepared by a modification of the procedure reported by Chloupek and Zweifel (36) for the preparation of isopinocampheyl mesylate.

The appropriate alcohol (2.0 g.) was dissolved in pyridine, (20 ml.) and the solution was cooled to -40°. p-Bromobenzenesulfonyl chloride (10% excess) was added. The reactions were run at -40°. The esterification of cis-pinocarveol and 2-methylenecyclohexanol was terminated after two days, while isopinocampheol and trans-2-methylcyclohexanol were allowed to react for three days. The light yellow, partially crystalline reaction mixtures were poured into equal volumes of 6N hydrochloric acid (50 ml.) and ether (50 ml.) in a cold room (3°). The mixtures were shaken, and the ether portions were removed. The aqueous portions were again extracted with ether (25 ml.). The combined ether extracts were washed with 6N hydrochloric acid (10 ml.) and water until neutral. The dried ether extracts were concentrated on a rotary evaporator with ice-water cooling. The products were recrystallized twice from pentane - ether (10:3) at -40°.

cis-Pinocarvyl brosylate decomposed at 42-44° when the capillary melting point procedure was used. The white, crystalline material decomposed to a black tar within two hours when kept in a nitrogen atmosphere in the dark at room temperature. The crystals did not darken when stored under pentane at -40°. The infrared spectrum was run as a Nujol mull at room temperature. The suspension was stable for several hours. The spectrum was indicative of an unsaturated sulfonate ester. Typical disubstituted alkene absorption appeared at 1655 and 870 cm^{-1} . Strong bands characteristic of sulfonate esters (39) appeared at 1182 (S-O) and 827 cm^{-1} (para-disubstituted benzene). The instability of the compound made it impractical to have carbon and hydrogen analyses run. Bromine and sulfur analyses were run (see Appendix I). Calculated for $\text{C}_{16}\text{H}_{19}\text{O}_3\text{SBr}$: Br, 21.53; S, 8.64. Found: Br, 21.74; S, 8.70.

2-Methylenecyclohexyl brosylate rapidly decomposed to a black tar at room temperature. The white, crystalline material could be stored without decomposition at -40° under pentane for three to four weeks. The infrared spectrum was run in 25% carbon tetrachloride solution in a fixed cell (0.0265 mm.) at room temperature. The solution did not discolor while the spectrum was determined. Disubstituted alkene absorption appeared at 1660 and 884 cm^{-1} . Strong bands characteristic of sulfonate esters (39) appeared at 1187 cm^{-1} (S-O) and 822 cm^{-1} (para-disubstituted benzene). Bromine and sulfur analyses were run (see Appendix I). Calculated for $\text{C}_{13}\text{H}_{15}\text{O}_3\text{SBr}$: Br, 24.13; S, 9.67. Found: Br, 24.73; S, 9.67.

Isopinocampyl brosylate decomposed at 53-54°. The white, crystalline material did not darken when stored under pentane at -40°. The infrared spectrum was run as a Nujol mull at room temperature. There were S-O absorption at 1186 cm^{-1} and para-disubstituted benzene absorption at 822 cm^{-1} . Bromine and sulfur analyses were run. Calculated for $\text{C}_{16}\text{H}_{21}\text{O}_3\text{SBr}$: Br, 21.41; S, 8.59. Found: Br, 21.34; S, 8.54.

trans-2-Methylcyclohexyl brosylate had a melting point of 52-53° and was stable at room temperature. The infrared spectrum (run as a Nujol mull) showed S-O absorption at 1183 cm.⁻¹ and para-disubstituted benzene absorption at 823 cm.⁻¹. Calculated for C₁₃H₁₇O₃SBr: C, 46.85; H, 5.14; Br, 23.98; S, 9.62. Found: C, 46.71; H, 4.92; Br, 24.00; S, 9.62.

METHYL ETHERS

The methyl ether derivatives of cis-pinocarveol, trans-pinocarveol, myrtenol, 2-methylenecyclohexanol, and 1-cyclohexenemethanol were prepared by methylation of the sodium salts of the alcohols.

The appropriate alcohol (2.0 g.) was reacted with metallic sodium (50% excess) in ether (20 ml.) for one day at room temperature. Methyl iodide (20% excess) was added to the reaction mixtures and the methylations were run for three days at room temperature. The reaction mixtures were then washed to remove sodium iodide. The dried ether extracts were concentrated by slow distillation of ether. The reaction products were distilled in vacuo through an 18-in. spinning band column. The boiling points of the methyl ethers were as follows: trans-pinocarvyl - 57-60° at 6 mm., cis-pinocarvyl - 70° at 6 mm., myrtenyl - 65° at 7 mm., 2-methylenecyclohexyl - 58-59° at 43 mm., and 1-cyclohexenemethyl - 64-66° at 32 mm.

The methyl ethers were further purified by preparative gas chromatography. The pure compounds were characterized by infrared spectra and elemental analyses. The important infrared frequencies in each of the compounds are shown in Table II. Bellamy (38) reports a range of 2832-2815 cm.⁻¹ for methoxy C-H stretch and 1150-1060 cm.⁻¹ for aliphatic ether C-O stretch. The results of carbon and hydrogen analyses on each of the compounds, except cis-pinocarvyl methyl ether, are shown

in Table III. cis-Pinocarvyl methyl ether became very viscous upon standing for several days at room temperature. Satisfactory carbon and hydrogen analyses were not obtained for this compound.

TABLE II
INFRARED ANALYSIS OF METHYL ETHERS

Band	<u>trans</u> - Pinocarvyl	<u>cis</u> - Pinocarvyl	Myrtenyl	2-Methylene- cyclohexyl	1-Cyclohexene- methyl
Methoxy C-H stretch	2830 cm. ⁻¹	2830 cm. ⁻¹	2830 cm. ⁻¹	2830 cm. ⁻¹	2837 cm. ⁻¹
C=C stretch	1650	1655	1660	1660	1675
Ether C-O stretch	1092	1115	1110 (doublet)	1096	1102 (doublet)
CH ₂ =CHR ₁ R ₂ out-of-plane deformation	896	888		896	
CHR ₁ =CR ₂ R ₃ out-of-plane deformation			800		801

TABLE III
ELEMENTAL ANALYSIS OF METHYL ETHERS

Compound	Calculated		Found	
	C, %	H, %	C, %	H, %
<u>trans</u> -Pinocarvyl	79.45	10.93	79.57	10.86
Myrtenyl	79.45	10.93	79.43	10.95
2-Methylene- cyclohexyl	76.12	11.20	76.00	11.10
1-Cyclohexene- methyl	76.12	11.20	76.40	11.05

GAS CHROMATOGRAPHY

Gas chromatography was employed extensively in the qualitative and quantitative analysis of solvolysis reaction products and in the determination of compound purity. A Wilkens Aerograph A-90-S gas chromatograph with a Sargent SR recorder was used for analysis. A Wilkens Aerograph Autoprep A-700 gas chromatograph with a Brown-Honeywell Elektronik recorder was used for the purification of compounds in relatively large amounts.

Four different columns were used. Column no. 1 (hyprose) contained 20% by weight of hyprose on hexamethyldisilazane (HMDS) treated Chromosorb W (60-80 mesh) packed into a 10-ft. by 0.25-in. stainless steel (ss) column. Column no. 2 (prep hyprose) was identical with Column no. 1 except that the packing was contained in a 10-ft. by 0.375-in. aluminum column. Column no. 3 (ODPN) contained 15% β , β' -oxydipropionitrile on HMDS-treated Chromosorb W (60-80 mesh) packed into a 10-ft. by 0.25-in. ss column. Column no. 4 (didecyl phthalate) contained 25% of didecyl phthalate on HMDS-treated Chromosorb W (60-80 mesh) packed into a 6.5-ft. by 0.25-in. ss column. Carrier gas flow rates were uncorrected.

QUALITATIVE GAS CHROMATOGRAPHY

Retention times (time lapse between sample injection and the appearance of the peak maximum) relative to reference compounds are reported in Tables IV-VI. Comparison of the retention times of the reaction products on two columns with those of known compounds aided in the identification of the reaction products.

The solvolysis reaction products were isolated from the reaction mixtures by gas chromatography. The purified products were collected at the instrument exit port in a glass U-tube (with or without acetone-dry ice cooling). The

TABLE IV

RELATIVE RETENTION TIMES FOR UNSATURATED HYDROCARBONS

Compound	Didecyl Phthalate ^a	ODPN ^b
1-Methylcyclohexene	0.25	-- ^e
α -Pinene	0.70	0.56
Camphene	0.83	0.84
β -Pinene	1.00 ^c	1.00 ^d
Limonene	1.44	1.74

^a110°, 100 ml./min. He flow rate.

^b68°, 50 ml./min. He flow rate.

^cRetention time 15.5 min.

^dRetention time 5.7 min.

^eRetention time 3.2 min. at 68° and 30 ml./min. He flow rate.

Table V

RELATIVE RETENTION TIMES FOR ALCOHOLS AND RELATED COMPOUNDS

Compound	Hyprose ^a	Didecyl Phthalate ^a
<u>trans</u> -2-Methylcyclohexanol	0.37	--
2-Methylenecyclohexanol	0.49	0.30
<u>trans</u> -Pinocarvyl acetate	0.70	--
Pinocarvone	0.70	--
Myrtenyl acetate	0.77	--
Myrtenal	0.82	--
<u>trans</u> -Pinocarveol	0.82	0.83
1-Cyclohexenemethanol	0.94	0.47
Borneol	1.00 ^b	1.00 ^c
Isopinocampheol	1.14	--
<u>cis</u> -Pinocarveol	1.24	1.17
Myrtenol	1.34	1.10

^a145°, 100 ml./min. He flow rate.

^bRetention time 9.9 min.

^cRetention time 24.5 min.

collected materials were submitted to infrared and, in some cases, refractive index analyses. The results of these analyses were compared with those of known compounds.

TABLE VI

RELATIVE RETENTION TIMES FOR METHYL ETHERS

Methyl Ether	ODPN ^a	Prep Hyprose ^b	Didecyl Phthalate ^c
2-Methylenecyclohexyl	0.22	0.42	0.63
1-Cyclohexenemethyl	0.49	0.67	1.19
<u>trans</u> -Pinocarvyl	0.58	1.00 ^e	--
Myrtenyl	0.67	1.11	--
<u>cis</u> -Pinocarvyl	0.77	--	--
Anisole	1.00 ^d	--	1.00 ^f

^a90°, 75 ml./min. He flow rate.

^b130°, 75 ml./min. He flow rate.

^c105°, 100 ml./min. He flow rate.

^dRetention time 22.3 min.

^eRetention time 11.3 min.

^fRetention time 18.6 min.

QUANTITATIVE GAS CHROMATOGRAPHY

The solvolysis reaction product mixtures were analyzed quantitatively on the gas chromatograph by the internal standardization method (40). Peak areas were measured by the method of approximating triangles (40).

Quantitative methods of analysis which do not involve internal standardization require complete volatilization of the sample to be analyzed. Only relative amounts of volatile components can be determined if there are nonvolatile components in the sample. The internal standardization method allows one to determine the absolute amounts of volatile components and the total absolute amount of any nonvolatile components.

The addition of a known amount of internal standard to a solution containing an unknown concentration of another compound enables one to calculate the unknown concentration from the ratio of the peak areas for the internal standard and the unknown. Since the response per unit weight for the internal standard and the unknown may not be the same, a correction factor must be included. The concentration of each unknown component, therefore, can be calculated from the equation.

$$C_u = (A_u/A_i)(F)(V_i/V_u)(C_i) \quad (1)$$

where

C_u = concentration of component analyzed, g./l.

A_u = response for component analyzed, cm.²

A_i = response for internal standard, cm.²

F = weight response ratio for the component analyzed relative to the internal standard

V_i = volume of internal standard used

V_u = volume of reaction solution used

C_i = concentration of internal standard solution, g./l.

If the internal standard is added to the entire reaction product, the volume factor (V_i/V_u) in Equation (1) becomes unity. The amount of each component is then calculated from the equation

$$G_u = (A_u/A_i)(F)(G_i) \quad (2)$$

where

G_u = weight of component analyzed, g.

G_i = weight of internal standard used

The weight response factors, F , were determined by analysis of a methanolic solution of the internal standard and the known reaction product. The factors were determined at gas chromatographic conditions identical to those used for

the quantitative analysis of the reaction products. The factors were calculated from the observed areas and the known amount of each reaction product and the internal standard by the equation

$$F = (a_i/g_i)/(a_u/g_u) \quad (3)$$

where

\underline{a}_i = response for internal standard, cm.²

\underline{g}_i = weight of internal standard, μg .

\underline{a}_u = response for component analyzed, cm.²

\underline{g}_u = weight of component analyzed, μg .

The weight response factors, \underline{F} , are reported in Table VII. The factors were constant over the concentration range* employed. The volume of aliquot to be analyzed was chosen so that the smallest peak height was at least one-fourth of full scale on the recorder chart. The weight response factor calculations for all solvolysis products are reported in Appendix II.

The weight response factors for 2-methylenecyclohexanol (relative to borneol) are different at the two analysis conditions used. The data in Table XVIII and XX (Appendix II) show that response per unit weight for the alcohol on the didecyl phthalate column was approximately twice that on the hyprose column. The response per unit weight for borneol was approximately the same on both columns. The relatively low response on the hyprose column may be due to partial polymerization or column promoted decomposition of 2-methylenecyclohexanol. The difference in the response factors do not affect the product analyses since the response factor determinations and product analyses were run at the same conditions.

*Two or three concentrations of the internal standard relative to the concentration of the reaction product were employed. Three or four analyses were run at each concentration.

TABLE VII

WEIGHT RESPONSE FACTORS FOR SOLVOLYSIS REACTION PRODUCTS

Compound	Weight Response Factor ^a
<u>trans</u> -Pinocarvyl methyl ether	1.49 ± 0.07 ^b
Myrtenyl methyl ether	1.28 ± 0.08 ^b
2-Methylenecyclohexyl methyl ether	1.11 ± 0.03 ^c
1-Cyclohexenemethyl methyl ether	1.15 ± 0.03 ^c
<u>trans</u> -Pinocarveol	1.13 ± 0.02 ^d
Myrtenol	1.17 ± 0.02 ^d
<u>cis</u> -Pinocarveol	1.02 ± 0.01 ^d
2-Methylenecyclohexanol	0.77 ± 0.02 ^e , 1.05 ± 0.04 ^d
1-Cyclohexenemethanol	0.79 ± 0.02 ^e

^aResponse of anisole relative to the methyl ethers and response of borneol relative to the alcohols.

^bFor methanolysis of cis-pinocarvyl brosylate, on ODPN column.

^cFor methanolysis of 2-methylenecyclohexyl brosylate, on didecyl phthalate column.

^dFor hydrolysis of cis-pinocarvyl brosylate and transesterification of the p-nitrobenzoate esters, on hyprose column.

^eFor hydrolysis of 2-methylenecyclohexyl brosylate, on didecyl phthalate column.

The total yield of solvolysis products (per cent of theoretical) was calculated from the known amount of material solvolyzed and the total amount of solvolysis product. The relative product amounts were calculated from the ratio of the amount of each product to the total product. The quantitative analysis calculations for all solvolysis reactions are reported in Appendix III.

The choice of internal standard to be used for a particular solvolysis reaction product was based on: (1) its similarity to the products, (2) its inertness to the products, and (3) its complete resolution from all components. Anisole and borneol were used as internal standards for all methanolysis and hydrolysis reaction

products, respectively. Anisole was purified by distillation in vacuo through a 24-in. spinning band column, b.p. 41° at 6 mm. Borneol was purified by preparative gas chromatography (Aerograph Autoprep A-700, prep hyprose column).

Analyses of the various reaction products were run at the following conditions:

(1) methanolysis of cis-pinocarvyl brosylate - ODPN column at 90° and 75 ml./min. He flow rate, (2) methanolysis of 2-methylenecyclohexyl brosylate - didecyl phthalate column at 105° and 100 ml./min. He flow rate, (3) hydrolysis of cis-pinocarvyl brosylate and alkaline methanolysis of cis-pinocarvyl, trans-pinocarvyl, and 2-methylenecyclohexyl p-nitrobenzoate - hyprose column at 145° and 100 ml./min. He flow rate, and (4) hydrolysis of 2-methylenecyclohexyl brosylate - didecyl phthalate column at 145° and 100 ml./min. He flow rate.

SOLVOLYSIS PROCEDURES

REACTION CONDITIONS

Methanolysis and Alkaline Methanolysis of Brosylate and p-Nitrobenzoate Esters

The brosylate and p-nitrobenzoate derivatives of cis-pinocarveol and related alcohols were reacted with 0.1M methanolic sodium methoxide*. The reaction conditions are reported in Table VIII. The reaction mixtures were neutralized with methanol-concentrated hydrochloric acid (12/1, w/w).

The four neutralized brosylate reaction mixtures (Table VIII) were poured into water (25 ml.) and extracted twice with ether (25 ml.). The ether extracts were dried and the ether was removed by distillation through a short, unpacked column. The reaction products were identified by gas chromatographic, infrared

*Metallic sodium (2.3 g.) was dissolved in one liter of dry methanol.

spectral, and refractive index comparison with known compounds (see p. 38-39, 48-50).

TABLE VIII

REACTION CONDITIONS FOR ALKALINE METHANOLYSIS OF THE BROSYLATE
AND p-NITROBENZOATE DERIVATIVES OF cis-PINOCARVEOL
AND RELATED ALCOHOLS

Ester ^a	Volume of 0.1M Methanolic Sodium Methoxide, ml.	Reaction Time, days	Reaction Temp., °C.
<u>cis</u> -Pinocarvyl brosylate	20	7	3
2-Methylenecyclohexyl brosylate	22.5	7	3
Isopinocampyl brosylate	20	7	25
<u>trans</u> -2-Methylcyclohexyl brosylate	22.5	7	25
<u>cis</u> -Pinocarvyl <u>p</u> -nitrobenzoate ^b	25	1	50
<u>trans</u> -Pinocarvyl <u>p</u> -nitrobenzoate	25	1	50
2-Methylenecyclohexyl <u>p</u> -nitrobenzoate	25	1	50

^a0.50 g. charge.

^bReaction mixture blanketed with nitrogen during reaction.

The products of the reaction of cis-pinocarvyl and 2-methylenecyclohexyl brosylate were quantitatively determined. The reaction conditions were similar to those reported in Table VIII. The neutralized reaction mixtures were partially concentrated by distillation of methanol through a short, unpacked column. Anisole was added and aliquots of the reaction product were analyzed directly by gas chromatography (see p. 39, 41).

The three neutralized p-nitrobenzoate reaction mixtures were concentrated to 3-4 ml. by distillation of methanol. Borneol was added and aliquots of the reaction product were analyzed directly by gas chromatography (see p. 51). Quantitative and qualitative analyses were made on the same reaction product. The products were identified by gas chromatographic and infrared spectral comparison with known compounds (see p. 52).

cis-Pinocarvyl brosylate (0.50 g.) was reacted with dry methanol (20 ml.) at 3° for one week. The reaction mixture was neutralized with methanolic sodium hydroxide (10% by weight). The qualitative and quantitative analyses of the reaction products were run by procedures similar to those reported for the alkaline methanolysis of cis-pinocarvyl brosylate (see p. 41).

cis-Pinocarvyl brosylate (0.50 g.) was reacted with a methanolic solution of 0.1M sodium methoxide and 0.1M lithium perchlorate (20 ml.). The reaction was run for one week at 3°. The reaction mixture was neutralized with methanol-concentrated hydrochloric acid (12/1, w/w). The reaction products were quantitatively determined by the procedure reported for the alkaline methanolysis of the brosylate (see p. 41). The reaction was repeated with 0.5M lithium perchlorate. Direct quantitative analysis of the products was complicated by a large gas chromatographic peak* at a retention time near that of the known products. The reaction mixture was poured into water (25 ml., containing 5% sodium chloride) and extracted twice with ether (25 ml.). The dried, ether extract was concentrated by slow distillation of ether. The reaction product was diluted with dry methanol (4 ml.) and analyzed on the gas chromatograph (see p. 45). The unknown material did not interfere with the analysis.

*A peak of similar size and retention time was obtained when a methanolic solution of p-bromobenzenesulfonic acid in 0.1M sodium methoxide and 0.5M lithium perchlorate was injected. The material may be a decomposition product of p-bromobenzene sulfonic acid or a portion of the column packing.

Hydrolysis of Brosylate Esters

cis-Pinocarvyl brosylate (0.25 g.) was reacted with 55% aqueous acetone (11 ml.)* at 25° for 26 hours. 2-Methylenecyclohexyl brosylate (0.50 g.) was reacted with 55% aqueous acetone (18 ml.) at 3° for one week. Acetone was slowly removed from the neutralized reaction mixtures with a rotary evaporator at room temperature. Sodium chloride (5% by weight of the aqueous mixture) was added and the mixtures were twice extracted with ether (25 ml.). The dried ether extracts were concentrated with a rotary evaporator. The reaction products were diluted with dry methanol (1-5 ml.). Borneol was added and the reaction products were quantitatively analyzed (see p. 45). The reaction products were identified by gas chromatographic and infrared spectral comparison with known compounds (see p. 45).

TITRIMETRIC RATE MEASUREMENTS

All solvolysis kinetic runs were carried out at $5.1 \pm 0.1^\circ$, and all solvents were precooled to this temperature.

cis-Pinocarvyl brosylate is very insoluble in methanol. However, the brosylate stayed in solution when it was dissolved in acetone and then diluted with dry methanol. In order to compare the rate constants, solvolyses of the brosylates were all run in 10% acetone solution (by volume).

Methanolysis of Brosylate Esters

The pseudo-first-order rate constants for the methanolysis of cis-pinocarvyl and 2-methylenecyclohexyl brosylate were determined titrimetrically by a modification of the procedure used for the ethanolysis of allyl benzenesulfonate (41).

*The brosylates were not soluble in solutions which contained more than 45% water, so solutions were 55% acetone (by volume).

The brosylate (0.45 to 0.5 g.), weighed at 3°, was dissolved in acetone (10 ml.) and placed in the bath. A stopwatch was started when methanol was added. The solution was diluted to 100 ml. and thoroughly mixed. Aliquots (10 ml.) were removed at various times and pipetted into cold carbon tetrachloride (20 ml.) to quench the reaction. Cold water (25 ml.) was added to extract the liberated p-bromobenzenesulfonic acid. The mixtures were quickly titrated to the phenolphthalein end point with 0.03875M sodium hydroxide solution*. The initial ester concentration was obtained by titration of an aliquot of the reaction mixture at long reaction time (six hours). Nine or ten titrations were made for each run. Duplicate runs were made with both brosylates.

The rate constants were graphically determined from a form of the integrated rate equation for a first-order reaction (42).

$$\log c = -k_1 t / 2.303 + \text{constant} \quad (4)$$

where

c = brosylate concentration at time t

k₁ = pseudo-first-order rate constant

A plot of $\log \underline{c}$ versus t yields a straight line with a slope of $-\underline{k}_1/2.303$ if the reaction is first-order or pseudo-first-order.

Alkaline Methanolysis of Brosylate Esters

The rates of reaction of cis-pinocarvyl and 2-methylenecyclohexyl brosylate with 0.02M methanolic sodium methoxide were titrimetrically determined by a

*cis-Pinocarvyl brosylate (0.05 g.) was dissolved in cold carbon tetrachloride (20 ml.). Water (25 ml.) was added, and the mixture was thoroughly mixed. The mixture was titrated to the phenolphthalein end point with a 0.03875M sodium hydroxide solution. The amount of alkali used, 0.02 ml., corresponded to the reagent blank. The brosylate did not react with the water present in the time it took to make the titration.

modification of the procedure used for the alkaline ethanolysis of allyl benzene-sulfonate (41).

The brosylate (0.5 to 0.55 g.), weighed at 3°, was dissolved in acetone (10 ml.) and placed in the bath. A stopwatch was started when standard methanolic sodium methoxide was added.* The reaction solution was diluted to 100 ml. with dry methanol and thoroughly mixed. Aliquots (10 ml.) were removed at various times and pipetted into a cold mixture of carbon tetrachloride (20 ml.), excess standard hydrochloric acid (10.0 ml., 0.01993M) and phenolphthalein. The excess hydrochloric acid was quickly titrated with standard sodium hydroxide solution (0.03875M). The initial ester concentration was obtained by titration of an aliquot of the reaction mixture at long reaction time (six hours).

Pseudo-first-order rate constants were determined from a graphical plot of Equation (4).

Alkaline Methanolysis of cis-Pinocarvyl Brosylate with Added Lithium Perchlorate

The pseudo-first-order rate constant for the reaction of cis-pinocarvyl brosylate with 0.5M lithium perchlorate in methanolic sodium methoxide (0.02M) was determined.

The brosylate was dissolved in acetone (10 ml.) and placed in the bath. A stopwatch was started when a methanolic solution of 5.32 g. lithium perchlorate was added. The reaction solution was diluted to 100 ml. with methanolic sodium methoxide (25 ml., 0.08424M) and dry methanol. Aliquots (10 ml.) were titrated by the procedure used for alkaline methanolysis of the brosylates (see above).

*20.0 ml. 0.0993M methanolic sodium methoxide for cis-pinocarvyl brosylate and 25.0 ml. 0.08424M methanolic sodium methoxide for 2-methylenecyclohexyl brosylate.

The pseudo-first-order rate constant was determined from a graphical plot of Equation (4).

The titrimetric rate data for the solvolysis of cis-pinocarvyl and 2-methyl-ene-cyclohexyl brosylate are reported in Appendix IV.

SOLVOLYSIS OF UNSATURATED BROSYLATES

ALKALINE METHANOLYSIS

cis-Pinocarvyl Brosylate

The products of the reaction of cis-pinocarvyl brosylate with 0.1M methanolic sodium methoxide were trans-pinocarvyl methyl ether and myrtenyl methyl ether. The reaction conditions are shown in Table VIII (p. 33). Gas chromatographic analysis of the reaction products gave no indication of elimination products or cis-pinocarvyl methyl ether.

The two products were isolated from the reaction mixture by gas chromatography*. The infrared spectra of the isolated products were identical to those of known trans-pinocarvyl methyl ether and myrtenyl methyl ether. The gas chromatographic retention times of the products were comparable to those of trans-pinocarvyl methyl ether and myrtenyl methyl ether on the ODPN and prep hyprose columns (see Table VI). The refractive index of the product with the shortest retention time ($n_D^{32^\circ} -1.4731$) was similar to that of trans-pinocarvyl methyl ether ($n_D^{32^\circ} -1.4733$). The refractive index of the product with the longest retention time ($n_D^{22^\circ} -1.4711$) was similar to that of myrtenyl methyl ether ($n_D^{22^\circ} -1.4707$).

The two methyl ethers were obtained in 97% yield. The ratio of trans-pinocarvyl methyl ether to myrtenyl methyl ether was 65.4%:34.6%.

*ODPN column at 90° and 75 ml./min. He flow rate.

The reaction of cis-pinocarvyl brosylate with 0.02M methanolic sodium methoxide showed good first-order kinetics to approximately 80% reaction (see Fig. 14). The pseudo-first-order rate constant was $8.51 \times 10^{-4} \text{ sec.}^{-1}$.

2-Methylenecyclohexyl Brosylate

The products of the reaction of 2-methylenecyclohexyl brosylate with 0.1M methanolic sodium methoxide were 2-methylenecyclohexyl methyl ether and 1-cyclohexenemethyl methyl ether. The reaction conditions are shown in Table VIII (p. 33). Gas chromatographic analysis of the reaction product gave no indication of elimination products.

The two products were isolated from the reaction mixture by gas chromatography.* The infrared spectra of the isolated products were identical to those of known 2-methylenecyclohexyl methyl ether and 1-cyclohexenemethyl methyl ether. The gas chromatographic retention times of the products were comparable to those of 2-methylenecyclohexyl methyl ether and 1-cyclohexenemethyl methyl ether on the ODPN, prep hyprose, and didecyl phthalate columns (see Table VI). The refractive index of the product with the shortest retention time ($n_D^{26^\circ} -1.4496$) was similar to that of 2-methylenecyclohexyl methyl ether ($n_D^{26^\circ} -1.4492$). The refractive index of the product with the longest retention time ($n_D^{26^\circ} -1.4548$) was similar to that of 1-cyclohexenemethyl methyl ether ($n_D^{26^\circ} -1.4551$).

The two methyl ethers were obtained in 94% yield. The ratio of 2-methylenecyclohexyl methyl ether to 1-cyclohexenemethyl methyl ether was 43.8%:56.2%.

The pseudo-first-order rate constant for the reaction of 2-methylenecyclohexyl brosylate with 0.02M methanolic sodium methoxide was $9.42 \times 10^{-4} \text{ sec.}^{-1}$.

*ODPN column at 90° and 75 ml./min. He flow rate.

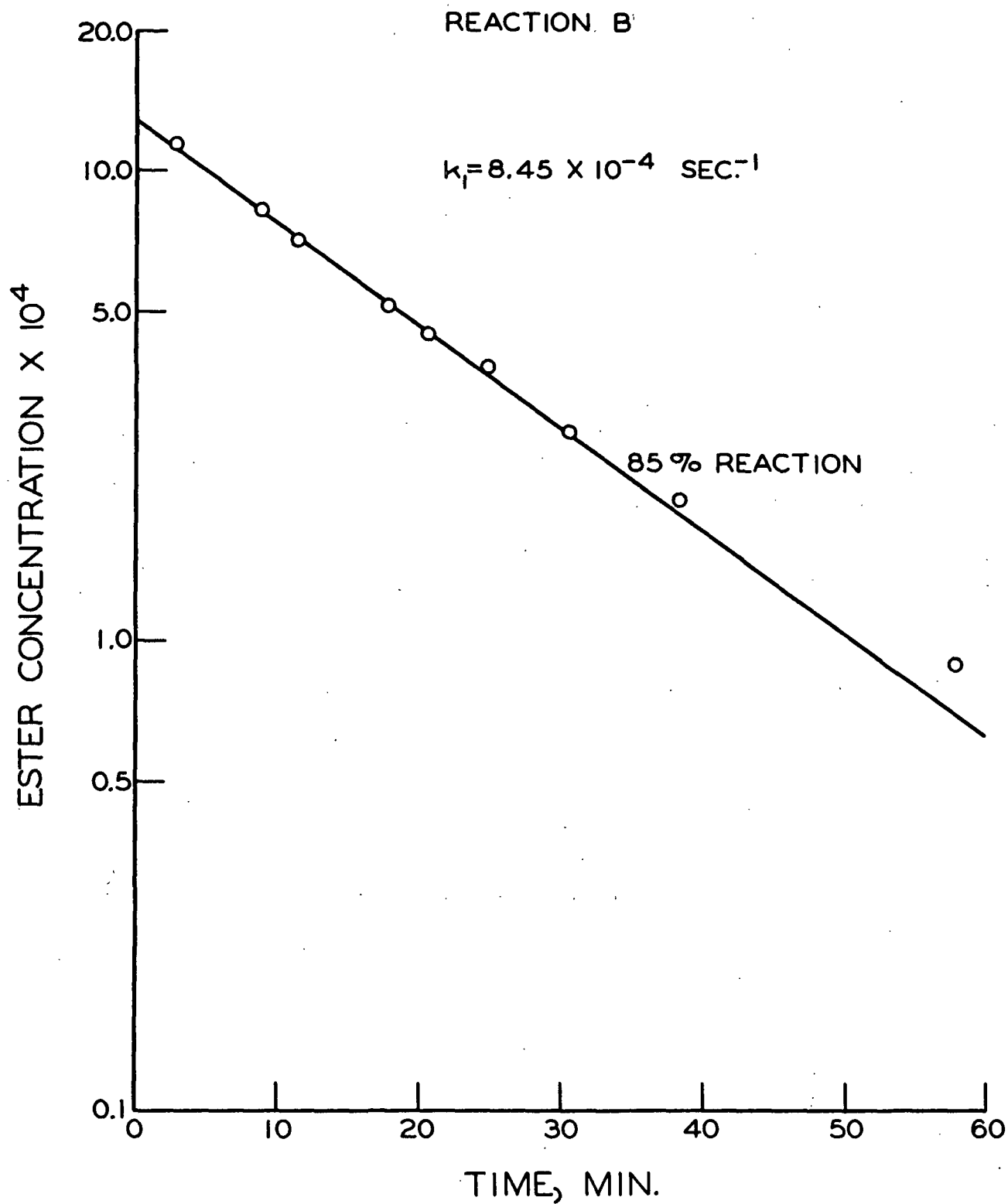


Figure 14. Titrimetric Rate Constant Determination: Alkaline Methanolysis of cis-Pinocarvyl Brosylate at 5.1°

The reaction showed good first-order kinetics to approximately 80% reaction (see Fig. 15).

METHANOLYSIS

cis-Pinocarvyl Brosylate

The products of the reaction of cis-pinocarvyl brosylate with methanol were the same as those found in the alkaline methanolysis of the brosylate. The reaction conditions were reported earlier (p. 34). Addition of known trans-pinocarvyl methyl ether and myrtenyl methyl ether to the reaction product caused an increase in the gas chromatographic peak heights and no new peaks.

The two methyl ethers were obtained in 98% yield. The ratio of trans-pinocarvyl methyl ether to myrtenyl methyl ether was identical to that found in the alkaline methanolysis of the brosylate (65.4%:34.6%).

The methanolysis reaction followed good first-order kinetics to approximately 85% reaction (see Fig. 16). The pseudo-first-order rate constant was 9.6×10^{-4} sec.⁻¹.

2-Methylenecyclohexyl Brosylate

The methanolysis of 2-methylenecyclohexyl brosylate followed good first-order kinetics to approximately 85% reaction (see Fig. 17). The pseudo-first-order rate constant was 9.72×10^{-4} sec.⁻¹. The product ratio was not determined.

ALKALINE METHANOLYSIS OF cis-PINOCARVYL BROSYLATE WITH ADDED LITHIUM PERCHLORATE

The products of the reaction of cis-pinocarvyl brosylate with a methanolic solution of sodium methoxide (0.1M) and lithium perchlorate (0.1M and 0.5M) were identical to those found in the methanolysis and alkaline methanolysis of the

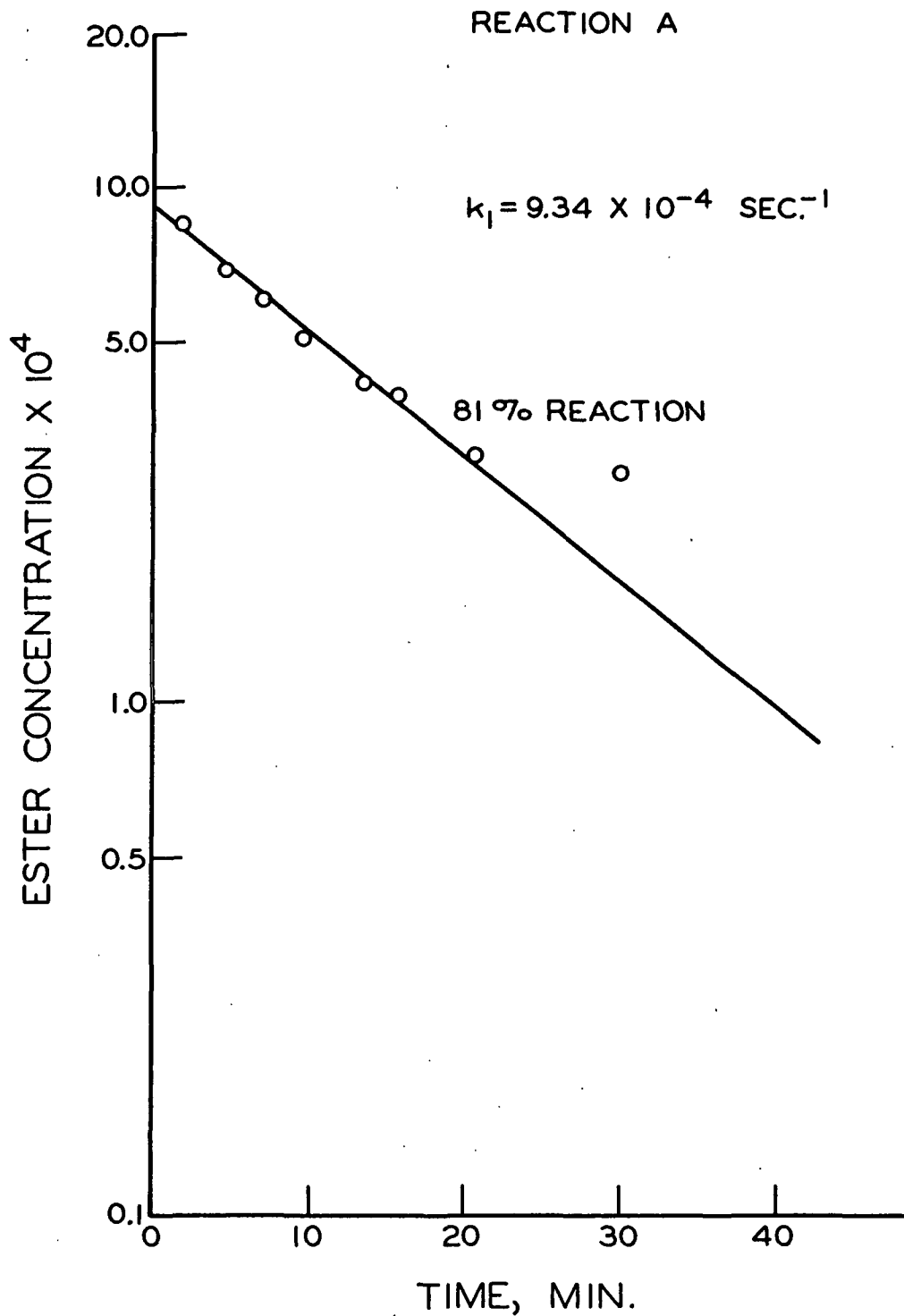


Figure 15. Titrimetric Rate Constant Determination: Alkaline Methanolysis of 2-Methylenecyclohexyl Brosylate at 5.2°

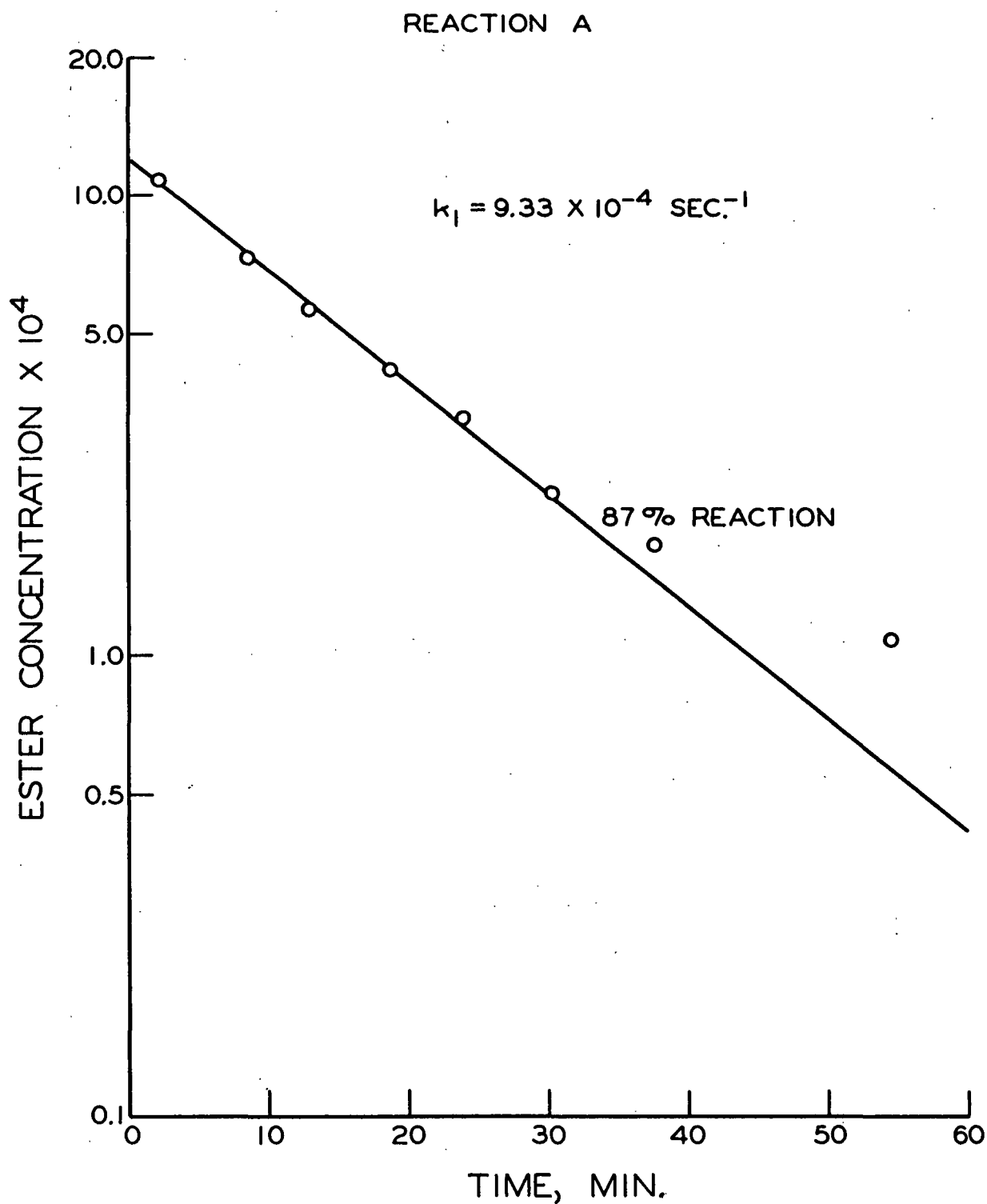


Figure 16. Titrimetric Rate Constant Determination: Methanolysis of cis-Pinocarvyl Brosylate at 5.1°

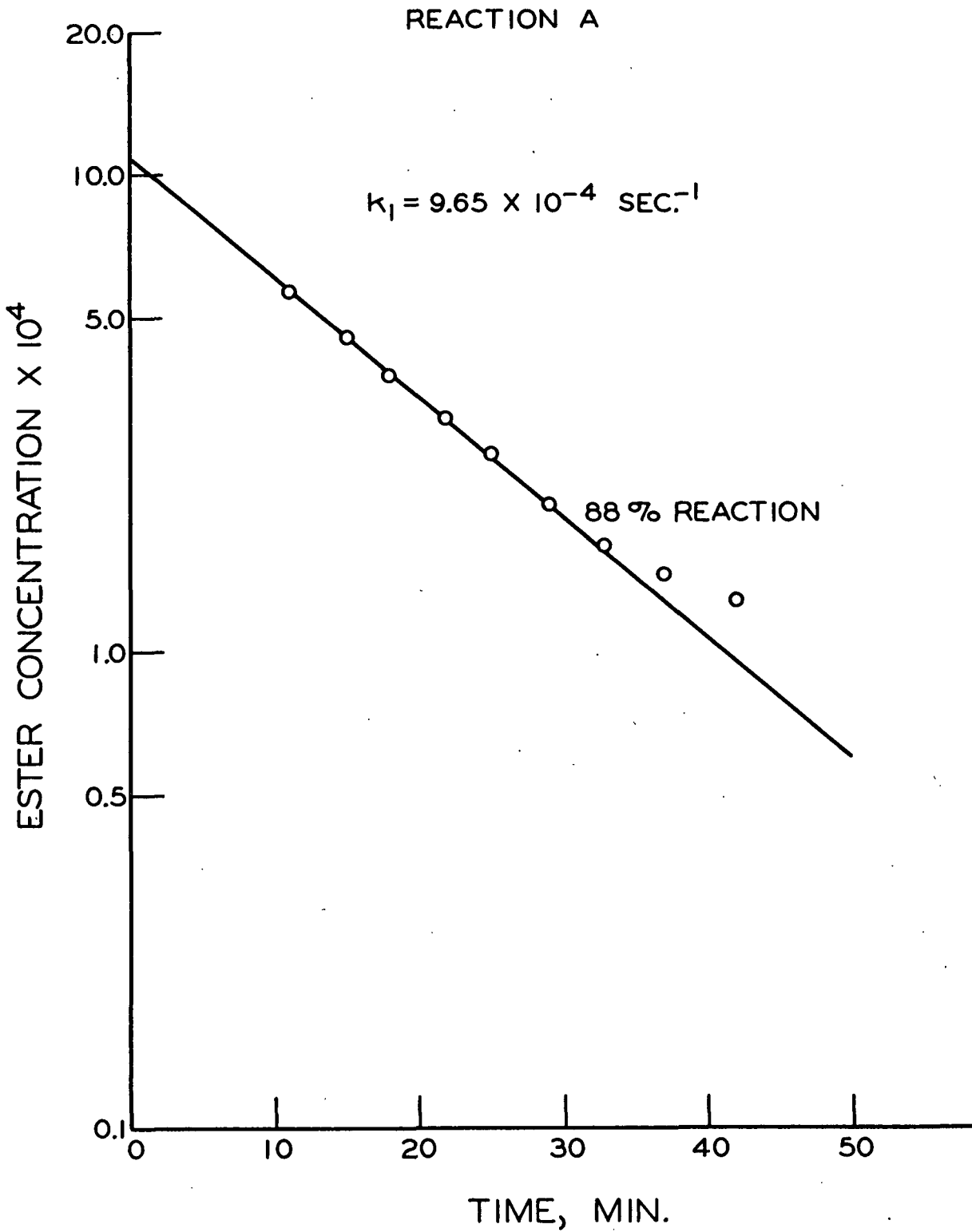


Figure 17. Titrimetric Rate Constant Determination: Methanolysis of 2-Methylenecyclohexyl Brosylate at 5.2°

brosylate. The reaction conditions were reported earlier (p. 34). Gas chromatographic retention times of the two products were identical to those of trans-pinocarvyl and myrtenyl methyl ether.

When 0.1M lithium perchlorate was used, the two methyl ethers were obtained in 99% yield. The ratio of trans-pinocarvyl methyl ether to myrtenyl methyl ether was 62.1%:37.9%. When 0.5M lithium perchlorate was used, the two methyl ethers were obtained in 89% yield. The ratio of trans-pinocarvyl to myrtenyl methyl ether was 49.6%:50.4%.

The reaction of cis-pinocarvyl brosylate with methanolic sodium methoxide (0.02M) and lithium perchlorate (0.5M) followed good first-order kinetics to approximately 85% reaction (see Fig. 18). The pseudo-first-order rate constant was $19.95 \times 10^{-4} \text{ sec.}^{-1}$.

HYDROLYSIS

cis-Pinocarvyl Brosylate

The products of the reaction of cis-pinocarvyl brosylate with 55% aqueous acetone were trans-pinocarveol and myrtenol. The reaction conditions were reported earlier (p. 35). Gas chromatographic analysis of the reaction product gave no indication of elimination products or cis-pinocarveol.

The two products were isolated from the reaction mixture by gas chromatography*. The infrared spectra of the isolated products were identical with those of known trans-pinocarveol and myrtenol. The gas chromatographic retention times of the products were comparable to those of trans-pinocarveol and myrtenol on the hyprose and didecyl phthalate columns (see Table V).

*Hyprose column at 145° and 100 ml./min. He flow rate.

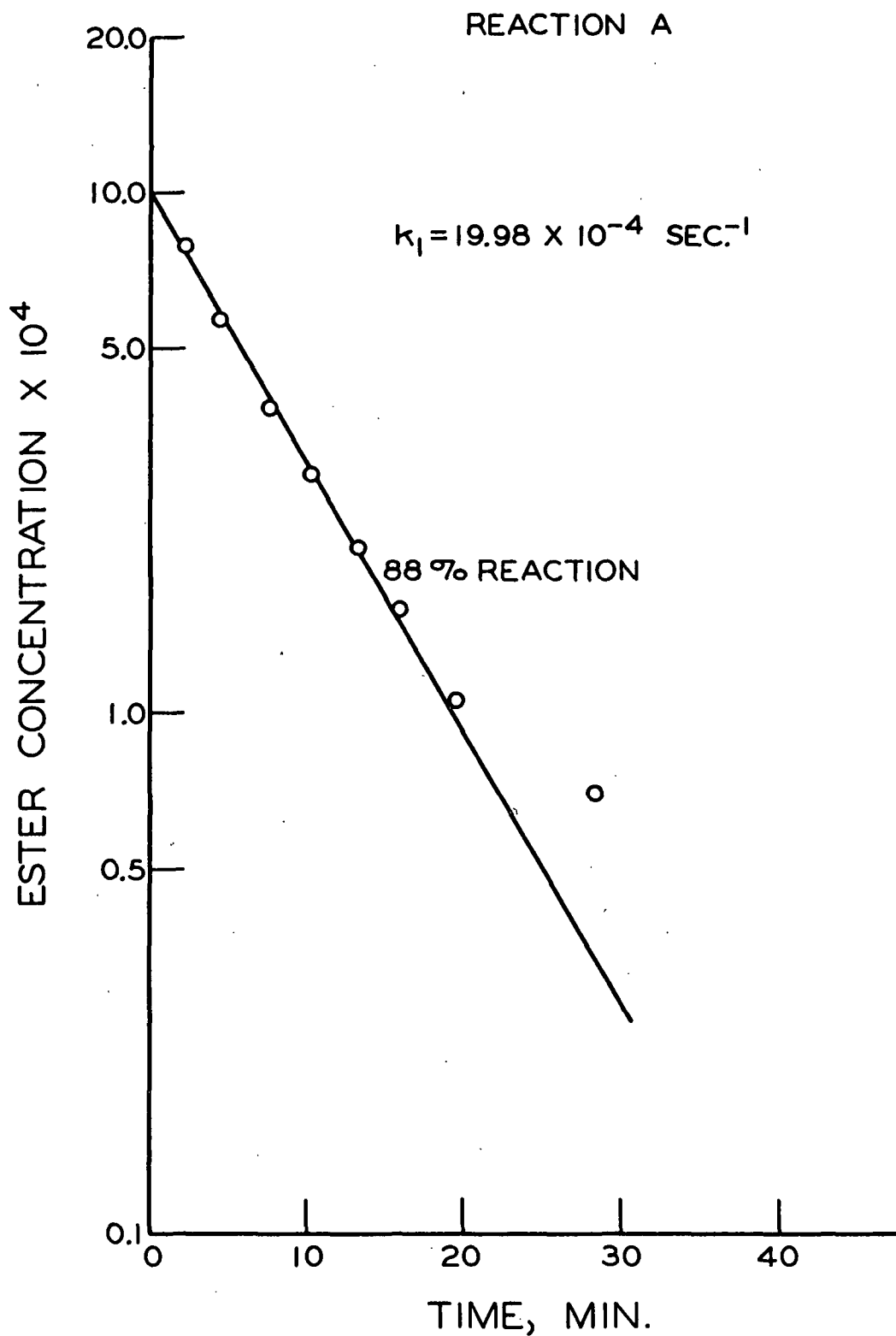


Figure 18. Titrimetric Rate Constant Determination: Alkaline Methanolysis of *cis*-Pinocarvyl Brosylate in the Presence of 0.5M LiClO_4 at 5.1°

The two alcohols were obtained in 94% yield. The ratio of trans-pinocarveol to myrtenol was 49.9%:50.1%.

2-Methylenecyclohexyl Brosylate

The products of the reaction of 2-methylenecyclohexyl brosylate with 55% aqueous acetone were 2-methylenecyclohexanol and 1-cyclohexenemethanol. The reaction conditions were reported earlier (p. 35). Gas chromatographic analysis of the reaction product gave no indication of elimination products.

The two products were isolated from the reaction mixture by gas chromatography¹. The infrared spectra of the isolated products were identical to those of known 2-methylenecyclohexanol and 1-cyclohexenemethanol. The gas chromatographic retention times of the products were comparable to those of 2-methylenecyclohexanol and 1-cyclohexenemethanol on the hyprose and didecyl phthalate columns (see Table V).

The two alcohols were obtained in 91% yield. The ratio of 2-methylenecyclohexanol to 1-cyclohexenemethanol was 42.4%:57.6%.

STABILITY OF SOLVOLYSIS PRODUCTS

The hydrolysis and alkaline methanolysis products were individually carried through the reaction and workup procedures at conditions comparable to those used for the solvolysis product analysis. p-Bromobenzenesulfonic acid², a product of the solvolysis reactions, was dissolved in the reaction mixtures. No new peaks appeared in the gas chromatograph after reaction. The solvolysis reaction conditions (hydrolysis and alkaline methanolysis) caused no isomerization. For example,

¹Didecyl phthalate column at 145° and 100 ml./min. He flow rate.

²Prepared by hydrolysis of p-bromobenzenesulfonyl chloride and recrystallization from benzene.

known trans-pinocarvyl methyl ether showed no peak corresponding to myrtenyl methyl ether after reaction with alkaline methanol.

ACETOLYSIS OF cis-PINOCARVYL BROSYLATE

cis-Pinocarvyl brosylate (0.25 g.) was reacted with dry acetic acid (10 ml.) at 25° for 42 hours. The reaction mixture was poured into water (15 ml.) and extracted twice with pentane (20 ml.). The pentane extract was washed with water until neutral, dried, and concentrated. The light yellow reaction product was analyzed on the hyprose column at 145° and 100 ml./min. He flow rate. Peaks with retention times comparable to trans-pinocarvyl acetate and myrtenyl acetate appeared, in addition to three peaks at longer retention times. The peak areas indicated that a large amount of the product was not volatile.

The acetolysis reaction was not further studied in view of its apparent complex nature. An extensive amount of time would have been needed to complete the product analysis.

SOLVOLYSIS OF SATURATED BROSYLATES

ALKALINE METHANOLYSIS

Isopinocamphyl Brosylate

The reaction of isopinocamphyl brosylate with 0.1M methanolic sodium methoxide yields elimination and substitution products. The reaction conditions are reported in Table VIII (p. 33). Analysis of the reaction product on two columns showed that α -pinene, β -pinene, camphene, and limonene were present (see Table IX). In addition, two other unidentified peaks appeared in the region of hydrocarbon retention time when the ODPN column was employed.

TABLE IX

GAS CHROMATOGRAPHIC ANALYSIS OF THE PRODUCTS OF THE
REACTION OF ISOPINOCAMPHYL AND trans-2-METHYLCYCLOHEXYL
BROSYLATE WITH 0.1M METHANOLIC SODIUM METHOXIDE

Gas Chromatographic Retention Times, min.

Sample Injected	Didecyl Phthalate ^a	ODPN ^b	ODPN ^c	Indicated Compound	Relative Amount, %
1-Methylcyclohexene	3.9		3.2		
α -Pinene	10.9	3.2			
Camphene	12.9	4.8			
β -Pinene	15.5	5.7			
Limonene	22.3	9.9			
Isopinocampyl Brosylate Alkaline Methanolysis Product	10.8	3.2		α -Pinene Unknown Camphene β -Pinene Unknown Limonene	72-76
		4.2			
	13.1	5.0			
	15.8	5.7			
		9.0			
	22.2	10.0			
	26.0	13.4		Methyl Ethers?	24-28
	32.2	16.2			
	37.0	23.4			
<u>trans</u> -2-Methylcyclohexyl Brosylate Alkaline Methanolysis Product	3.9		3.2	1-Methyl- cyclohexene Unknown Unknown	92-95
	4.2		4.0		
	4.9				
			7.0	Methyl Ethers?	5-8
			8.3		

^a 110°, 100 ml./min. He flow rate.

^b 68°, 50 ml./min. He flow rate.

^c 68°, 30 ml./min. He flow rate.

The reaction product showed three peaks at retention times longer than those of the hydrocarbons. These were assumed to be substitution products (methyl ethers).

The ratio of elimination to substitution products was approximately 74%:26%. The peak areas were measured by the method of approximating triangles and were uncorrected.

trans-2-Methylcyclohexyl Brosylate

The reaction of trans-2-methylcyclohexyl brosylate with 0.1M methanolic sodium methoxide was relatively slow. The reaction conditions are shown in Table VIII (p. 33). A mixed melting point showed that crystalline material in the reaction product was unreacted starting material.

The reaction yields a large proportion of elimination products, in addition to substitution products. Analysis of the reaction product on two columns showed that 1-methylcyclohexene was present (see Table IX). Two other unidentified peaks appeared in the hydrocarbon region when the didecyl phthalate column was employed. There were two peaks at retention times longer than those of the hydrocarbons when the ODPN column was employed (one peak on the didecyl phthalate column). These were assumed to be substitution products (methyl ethers).

The ratio of elimination to substitution products was approximately 94%:6%.

SOLVOLYSIS OF UNSATURATED p-NITROBENZOATES

ALKALINE METHANOLYSIS OF cis-PINOCARVYL, trans-PINOCARVYL,
AND 2-METHYLENECYCLOHEXYL p-NITROBENZOATE

Only the parent alcohols were obtained when the title compounds were reacted with 0.1M methanolic sodium methoxide at the conditions reported in Table VIII (p. 33).

The product yields which were obtained by quantitative gas chromatographic analysis are reported in Table X.

The products were isolated from the reaction mixtures by gas chromatography*. The infrared spectra and gas chromatographic retention times (on two columns) of

*Hyprose column at 145° and 100 ml./min. He flow rate.

the products were comparable to those of the known alcohols. For example, the product from the reaction of cis-pinocarvyl p-nitrobenzoate with alkaline methanol compared favorably with known cis-pinocarveol.

TABLE X
QUANTITATIVE ANALYSIS ON THE ALKALINE METHANOLYSIS
OF p-NITROBENZOATE ESTERS

Reactants	Products	Yield, %
<u>cis</u> -Pinocarvyl <u>p</u> -Nitrobenzoate ^a	+ CH ₃ OH $\frac{50^\circ}{\text{NaOCH}_3}$ <u>cis</u> -Pinocarveol	102 ± 2
<u>trans</u> -Pinocarvyl <u>p</u> -Nitrobenzoate	+ CH ₃ OH $\frac{50^\circ}{\text{NaOCH}_3}$ <u>trans</u> -Pinocarveol	96 ± 3
2-Methylene- cyclohexyl <u>p</u> -Nitrobenzoate	+ CH ₃ OH $\frac{50^\circ}{\text{NaOCH}_3}$ 2-Methylenecyclohexanol	101 ± 4

^aReaction mixture blanketed with nitrogen during reaction.

The infrared spectra of the products were contaminated by a small amount of an aromatic carbonyl-containing impurity. A crystalline material was collected from the reaction products by gas chromatography. Its infrared spectrum compared favorably with that of methyl p-nitrobenzoate, a product of the transesterification reactions. All bands not assigned to the alcohols in the spectra of the reaction products were present as the major bands in the crystalline material.

When the cis-pinocarvyl brosylate reaction mixture was not blanketed with nitrogen, two peaks appeared in the gas chromatograph. The retention times on the hyprose and didecyl phthalate columns were comparable to those of cis-pinocarveol and pinocarvone. The reaction product gave a positive carbonyl test (2,4-dinitrophenylhydrazine). A small amount of the material suspected to be pinocarvone was isolated by gas chromatography. The infrared spectrum of this material was very weak (insufficient sample amount). The spectrum indicated that the material could

be impure pinocarvone (contaminated by methyl p-nitrobenzoate). The ratio of cis-pinocarveol to tentatively identified pinocarvone was approximately 3:1.

ATTEMPTED HYDROLYSIS OF cis-PINOCARVYL, trans-PINOCARVYL,
AND 2-METHYLENECYCLOHEXYL p-NITROBENZOATES

The title compounds were reacted with 80% aqueous acetone by the procedure of Goering and Silversmith (11).

The reactions were run in sealed ampoules (20 ml.) that contained 0.05M solutions of the p-nitrobenzoates in 80% (by volume) aqueous acetone. After five days at 100°, the acetone was evaporated with a filtered air stream. The aqueous residue was extracted with ether (50 ml.). The ether extract was washed with 5% sodium bicarbonate (50 ml.) and water until neutral. The dried, ether extract was concentrated on a rotary evaporator. The starting materials, identified by mixed melting points, were recovered in 96-98% yield.

DISCUSSION

cis-PINOCARVYL BROSYLATE SOLVOLYSIS MECHANISMS

CARBON-OXYGEN CLEAVAGE AND ALLYLIC REARRANGEMENT

Methanolysis of cis-pinocarvyl brosylate gives a quantitative yield of trans-pinocarvyl methyl ether and myrtenyl methyl ether (Fig. 19). The formation of ether products is strong evidence for carbon-oxygen bond cleavage. Alcohol products would have resulted if the reaction had involved sulfur-oxygen bond cleavage.

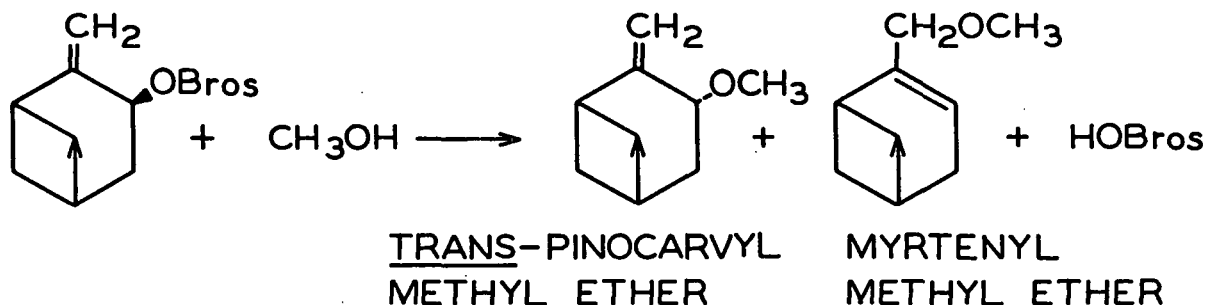


Figure 19. Methanolysis of cis-Pinocarvyl Brosylate

Hydrolysis of cis-pinocarvyl brosylate gives a quantitative yield of trans-pinocarveol and myrtenol (Fig. 20). The formation of normal and rearranged products by methanolysis and hydrolysis implies that carbon-oxygen cleavage is involved. Sulfur-oxygen bond cleavage would yield only normal products. The alcohol and ether products did not isomerize at the reaction conditions employed (p. 47).

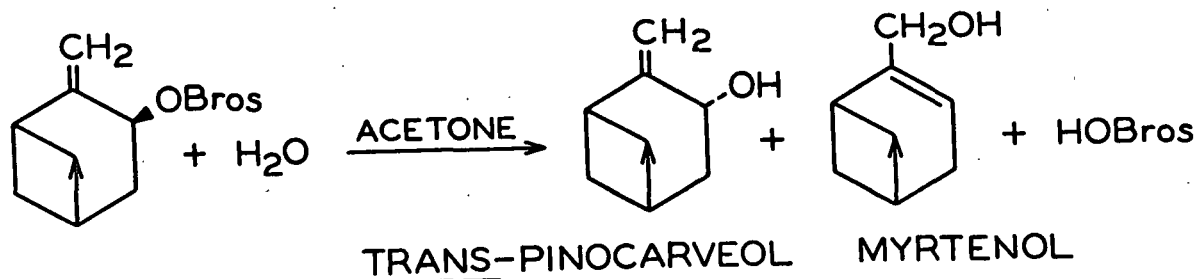


Figure 20. Hydrolysis of cis-Pinocarvyl Brosylate

Analysis of the methanolysis and hydrolysis products showed no evidence of elimination products. The elimination mechanism cannot compete with the substitution process. The significance of this will be discussed later.

LYATE ION EFFECT¹

Methanolysis of cis-pinocarvyl brosylate in the presence of 0.1M sodium methoxide gives a quantitative yield of trans-pinocarvyl methyl ether and myrtenyl methyl ether. Table XI shows that the product proportions are the same for methanolysis and alkaline methanolysis of the brosylate. There is apparently no change in the mechanism of methanolysis when sodium methoxide is present.

The rate of a bimolecular reaction is increased when the nucleophilicity of the attacking group is increased. Such a change would not affect the rate of a unimolecular reaction.² The addition of sodium methoxide, a stronger nucleophile than methanol, should increase the rate of methanolysis of cis-pinocarvyl brosylate if the reaction mechanism is bimolecular. Table XII shows that the pseudo-first-order rate constant for the methanolysis of cis-pinocarvyl brosylate (0.013M) in the presence of 0.02M sodium methoxide is slightly lower (11%) than in pure methanol at 5°.

The effect of lyate ion on the rate of solvolysis reactions has been used extensively as evidence for a particular reaction mechanism (8, 15-19, 41, 43). Bergstrom and Siegel (41) found at least an eightfold increase in the pseudo-first-order rate constant for the bimolecular ethanolysis of allyl benzenesulfonate in the presence of 0.04M sodium ethoxide. Vernon (8) found that the addition of

¹If the solvent is represented as SOH, the corresponding anion is referred to as the lyate ion, SO⁻.

²The rate of reaction increases if the stronger nucleophile causes a significant increase in the ionic strength of the medium.

TABLE XI

QUANTITATIVE ANALYSIS ON THE SOLVOLYSIS OF *cis*-PINOCARVYL
AND 2-METHYLENECYCLOHEXYL BROSYLATE

Reactants		Products and Relative Amounts	Yield, %
<i>cis</i> -Pinocarvyl + CH ₃ OH Brosylate	$\xrightarrow{3^\circ}$	<i>trans</i> -Pinocarvyl + Myrtenyl Methyl Ether 65.4 ± 0.8% 34.6 ± 0.8%	98 ± 2
<i>cis</i> -Pinocarvyl + CH ₃ OH Brosylate	$\xrightarrow[NaOCH_3]{3^\circ}$	<i>trans</i> -Pinocarvyl + Myrtenyl Methyl Ether 65.4 ± 0.6% 34.6 ± 0.6%	97 ± 2
<i>cis</i> -Pinocarvyl + CH ₃ OH Brosylate	$\xrightarrow[NaOCH_3]{3^\circ}$ 0.1M LiClO ₄ (0.5M LiClO ₄)	<i>trans</i> -Pinocarvyl + Myrtenyl Methyl Ether 62.1 ± 0.2% 37.9 ± 0.2% (49.6 ± 0.6%) (50.4 ± 0.6%)	99.0 ± 0.5 (89 ± 2)
<i>cis</i> -Pinocarvyl + H ₂ O Brosylate	$\xrightarrow[acetone]{25^\circ}$	<i>trans</i> -Pinocarveol + Myrtenol 49.9 ± 0.5% 50.1 ± 0.5%	94 ± 1
2-Methylene- cyclohexyl Brosylate	$\xrightarrow[NaOCH_3]{3^\circ}$	2-Methylene- cyclohexyl Methyl Ether 43.8 ± 0.9% + 1-Cyclohexene- methyl Ether 56.2 ± 0.9%	94 ± 3
2-Methylene- cyclohexyl Brosylate	$\xrightarrow[acetone]{3^\circ}$	2-Methylene- cyclohexanol 42.4 ± 0.6% + 1-Cyclohexene- methanol 57.6 ± 0.6%	91 ± 4

0.045M sodium ethoxide gave a pseudo-first-order rate constant for the bimolecular ethanolysis of allyl chloride which was 150 times larger than that in pure ethanol.

TABLE XII

RATE CONSTANTS FOR THE SOLVOLYSIS OF cis-PINOCARVYL
AND 2-METHYLENECYCLOHEXYL BROSYLATE AT 5°

Brosylate	Solvolytic Medium	$k_1 \times 10^4 \text{ sec.}^{-1}$
<u>cis</u> -Pinocarvyl	CH ₃ OH	9.33; 9.76
<u>cis</u> -Pinocarvyl	CH ₃ OH + 0.01986M NaOCH ₃	8.45; 8.57
<u>cis</u> -Pinocarvyl	CH ₃ OH + 0.02106M NaOCH ₃ + 0.5M LiClO ₄	19.98; 19.92
2-Methylenecyclohexyl	CH ₃ OH	9.65; 9.79
2-Methylenecyclohexyl	CH ₃ OH + 0.02106M NaOCH ₃	9.34; 9.50

There is additional evidence that the methanolysis of cis-pinocarvyl brosylate does not proceed by a bimolecular mechanism. Equation (5) gives the kinetic expression for reaction of a sulfonate ester with a hydroxylic solvent and with the lyate ion.

$$dx/dt = k_1(a-x) + k_2(a-x)(b-x) \quad (5)$$

or

$$[1/(a-x)][dx/dt] = k_1 + k_2(b-x) \quad (6)$$

where

a = initial ester concentration

b = initial lyate ion concentration

x = ester concentration reacted at time, t

k₁ = first-order rate constant for reaction with the solvent

k₂ = second-order rate constant for substitution by the lyate ion

The first-order rate constant, k_1 , is a measure of the unimolecular and bimolecular reaction with the solvent.

If a solvolysis reaction follows the rate law shown in Equation (6), a plot of $[1/(a-x)] [dx/dt]$ against $(b-x)$ gives a straight line. The slope is k_2 and the intercept at $(b-x) = 0$ is k_1 .

The titrimetric data for the methanolysis of cis-pinocarvyl brosylate in the presence of 0.02M sodium methoxide did not give a straight line when Equation (6) was plotted. The nonlinearity of the plot is illustrated in Fig. 21. If the term in Equation (6) for reaction with the lyate ion disappears ($k_1 \gg k_2$), the rate law is that of a pseudo-first-order reaction. The titrimetric data fits the integrated form of the equation for a pseudo-first-order reaction (Fig. 14, p. 40).

SALT EFFECT

The presence of a highly ionized salt, lithium perchlorate, results in the formation of a larger relative amount of rearranged product in the alkaline methanolysis of cis-pinocarvyl brosylate. Table XI shows that in the presence of 0.5M lithium perchlorate normal and rearranged products are formed in approximately equal amounts.

The rate of alkaline methanolysis of cis-pinocarvyl brosylate should be increased in the presence of lithium perchlorate if the reaction proceeds by a unimolecular mechanism. The rate of a bimolecular substitution under similar conditions should be unchanged or decreased slightly.*

*A slight decrease in rate may result because the rate-determining step involves a slight dispersal of negative charge which is not favored by increased ionic strength.

REACTION B

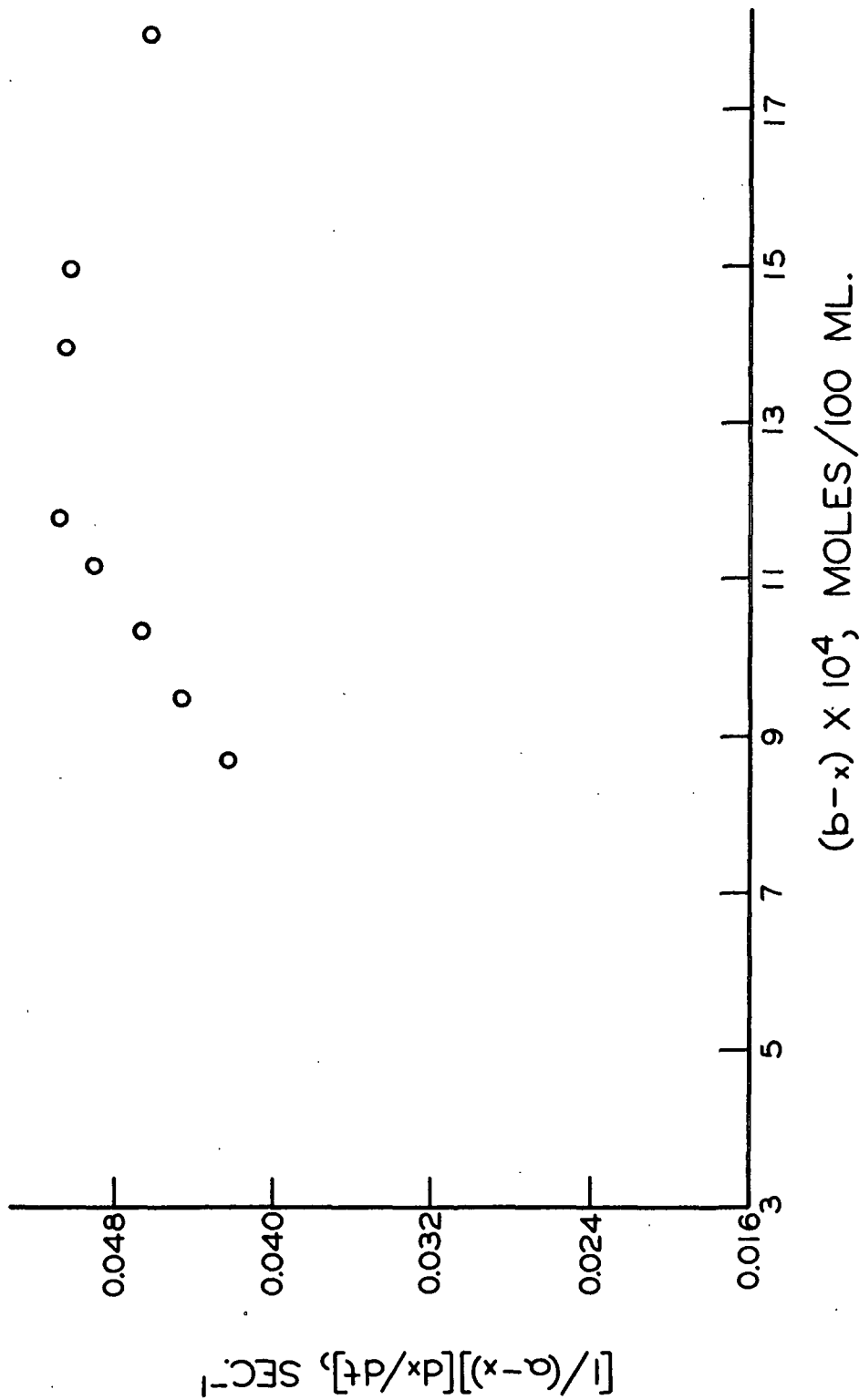


Figure 21. Illustration of Nonlinearity of Plot of Equation (6) for Alkaline Methanolysis of cis-Pinocarvyl Brosylate at 5.1°

Table XII shows that the rate of alkaline methanolysis of cis-pinocarvyl brosylate in the presence of 0.5M lithium perchlorate is more than twice the rate of alkaline methanolysis in the absence of the ionic salt (134% increase in rate). Rate increases of 22 to 107% have been reported for the unimolecular solvolysis of various halides in the presence of 0.1M lithium perchlorate (44-46).

SOLVENT EFFECT

Hydrolysis of cis-pinocarvyl brosylate yields equal amounts of normal and rearranged products (Table XI). Methanolysis of the brosylate yields a larger proportion of normal product (65%).

It is apparent that the change in solvolysis medium from pure methanol to 55% aqueous acetone results in a change in the solvolysis mechanism. On account of its higher dielectric strength, the hydrolysis medium would be expected to promote carbonium ion formation more than methanol does. The formation of a larger relative amount of rearranged product by hydrolysis than by methanolysis is consistent with the increased ability of the solvent to stabilize a carbonium ion intermediate.

Hydrolysis and alkaline methanolysis in the presence of 0.5M lithium perchlorate yield the same relative amount of normal and rearranged product (Table XI). Apparently, the mechanism of solvolysis is the same in these two systems.

PROPOSED SOLVOLYSIS MECHANISMS

The preferred conformation of cis-pinocarvyl brosylate is shown in Fig. 22. The six-member ring which includes the gem-dimethyl carbon assumes a chair conformation. This conformation involves the least interaction between a methyl group and the brosylate group.

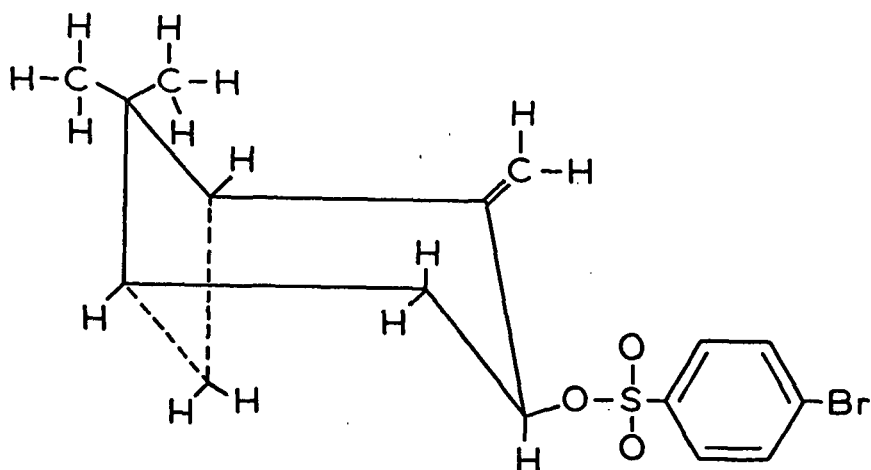


Figure 22. Conformation of cis-Pinocarvyl Brosylate

Product analysis indicates that there is a change in the mechanism of solvolysis of cis-pinocarvyl brosylate when the ionizing power of the solvent is changed. An allylic ion-pair mechanism is proposed for the solvolysis in the relatively poor ionizing solvent, methanol (or alkaline methanol). Two possible forms of the intermediate are shown in Fig. 23. These two extreme forms imply that allylic participation in the intermediate is involved. In Form A the leaving group is close to the carbon to which it was originally bonded. A model* of Form A shows a strong interaction between the leaving group and the nearest methyl group. In Form B the leaving group is close to the exocyclic carbon. There is relatively little interaction in Form B. Therefore, it is likely that the leaving group assumes a position closer to the exocyclic carbon (Form B). The incoming nucleophile is free to attack the cyclic carbon from below the plane of the allyl group (formation of trans-pinocarvyl methyl ether). Nucleophilic attack at the exocyclic carbon is hindered by the proximity of the leaving group. As shown by a model, the formation of cis-pinocarvyl methyl

*Cenco-Peterson Molecular Models, Central Scientific Co., 1700 Irving Park Rd., Chicago, Illinois.

ether is prevented by steric hindrance of the incoming nucleophile by the nearest methyl group. The relatively large amount of normal product (65%) is a result of the shielding effect of the leaving group at the exocyclic carbon in the unsymmetrical ion-pair intermediate.

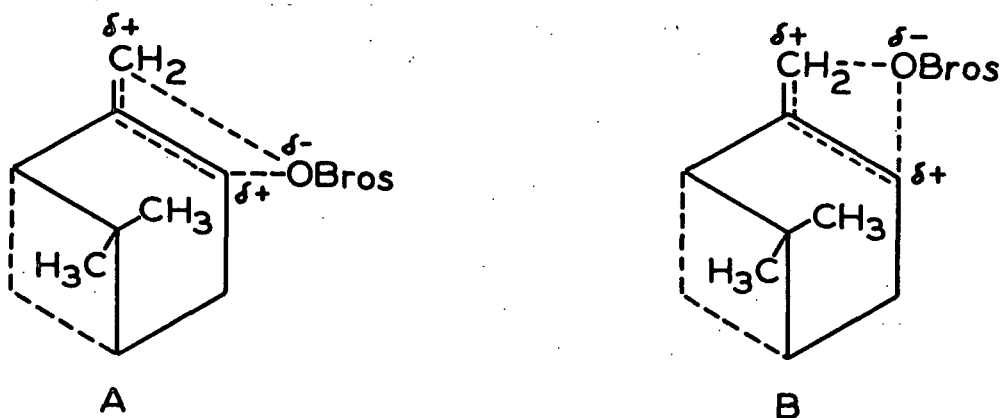


Figure 23. Ion-Pair Intermediates

An allylic carbonium ion mechanism is proposed for the solvolysis of cis-pinocarvyl brosylate in water and in alkaline, 0.5M methanolic lithium perchlorate. The increased ionic strength of the solvolysis medium apparently promotes a change in the methanolysis mechanism. The brosylate leaving group exerts a shielding effect in the ion-pair mechanism of methanolysis. When the solvolysis is carried out in solvents of greater ionizing power, the charge separation is increased to the point that the leaving group exerts no effect on product formation. The formation of a larger relative amount of rearranged product with an increase in the ionizing power of the solvolysis medium is consistent with the fact that carbonium ion formation is favored in a medium of increased ionic or dielectric strength. This proposed free carbonium ion intermediate can be represented as two resonance forms (Fig. 24). The incoming nucleophile can attack with nearly equal freedom at the exocyclic carbon or at the cyclic carbon from below the plane of the allyl group. As in the case of the ion-pair mechanism,

formation of cis-pinocarvyl derivatives is prevented by steric hindrance of the incoming nucleophile. The formation of equal amounts of normal and rearranged product in the stronger ionizing solvents (water and alkaline, 0.5M methanolic lithium perchlorate) is consistent with the carbonium ion mechanism. Apparently, the leaving group also has some shielding effect when the solvolysis is run in 0.1M methanolic lithium perchlorate (62% normal product).

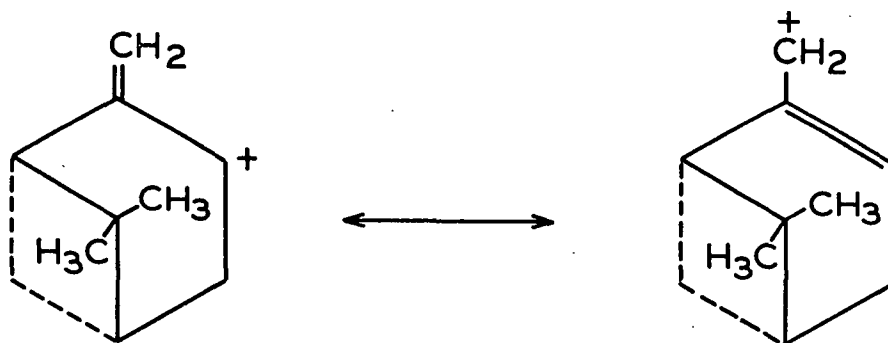


Figure 24. Allylic Carbonium Ion Intermediates

EFFECT OF cis-PINOCARVYL STRUCTURE ON MECHANISM
AND RATE OF BROSYLATE SOLVOLYSIS

EFFECT OF THE ISOPROPYLIDENE BRIDGE

The outstanding effect of the cis-pinocarvyl bicyclic bridge on the mechanism of solvolysis is the steric hindrance produced by the isopropylidene group. The nearest methyl group in the isopropylidene bridge prevents nucleophilic attack from above the plane of the allyl group (Fig. 23 and 24). No cis-pinocarvyl derivatives are found in the reaction products. In addition, the methyl group in the isopropylidene bridge forces the leaving group to assume a position near the exocyclic carbon in the methanolysis ion-pair mechanism (Fig. 23).

The effect of the cis-pinocarvyl bicyclic bridge was further investigated by the study of a similar monocyclic compound, 2-methylenecyclohexyl brosylate (Fig. 1A, p. 4).

Solvolysis of 2-methylenecyclohexyl brosylate in methanolic sodium methoxide gave a 94% yield of 2-methylenecyclohexyl methyl ether and 1-cyclohexenemethyl methyl ether (Fig. 25). Hydrolysis of 2-methylenecyclohexyl brosylate gave a 91% yield of 2-methylenecyclohexanol and 1-cyclohexenemethanol (Fig. 26). Table XI shows that slightly more rearranged product (56-58%) was formed than normal product (42-44%) in both solvent systems. The solvolysis products were shown to be stable at the reaction conditions employed (p. 47). Analysis of the solvolysis products showed no evidence of elimination products.

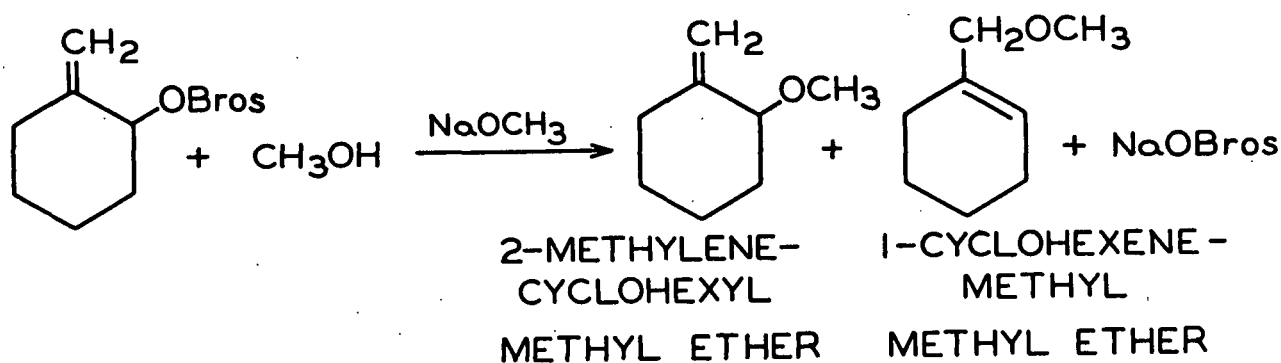


Figure 25. Alkaline Methanolysis of 2-Methylenecyclohexyl Brosylate

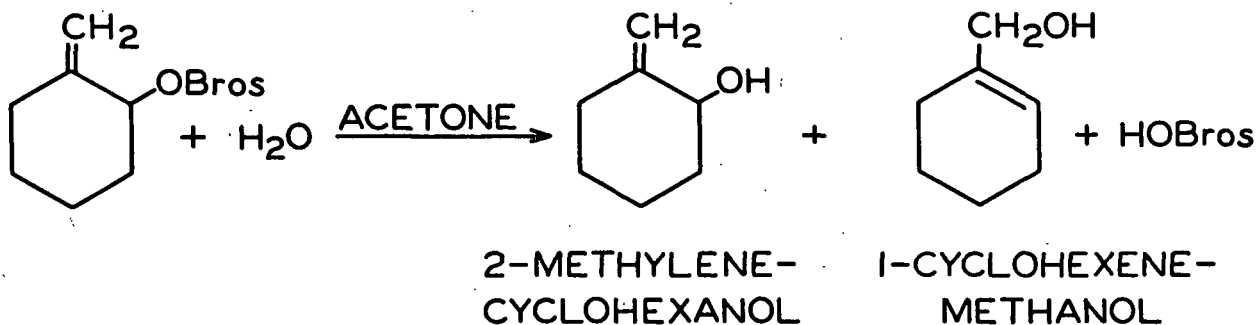


Figure 26. Hydrolysis of 2-Methylenecyclohexyl Brosylate

Pseudo-first-order rate constants were determined for the solvolysis of 2-methylenecyclohexyl brosylate ($0.015M$) in pure methanol and $0.02M$ methanolic sodium methoxide at 5° (Table XII). There is no significant change in rate in the presence of the stronger nucleophile, sodium methoxide. As in the case of cis-pinocarvyl brosylate, the titrimetric rate data did not give a straight line when Equation (6) was plotted.

An allylic ion-pair mechanism is proposed for solvolysis of 2-methylenecyclohexyl brosylate in methanol or alkaline methanol (Fig. 27). The intermediate is similar to that proposed for the methanolysis of cis-pinocarvyl brosylate (Fig. 23).* In the monocyclic compound there is no steric hindrance by a bulky methyl group. It is reasonable to assume that the leaving group has no preference for being close to one or the other of the partially charged carbon atoms. Therefore, a symmetrical ion-pair is proposed. Product analysis shows that only slightly more rearranged product (56%) is formed than normal product.

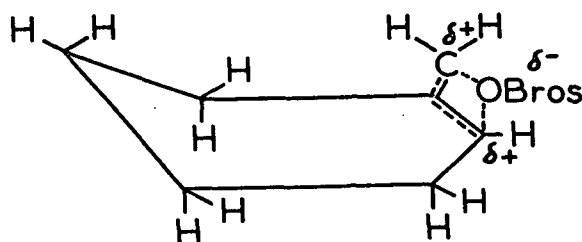


Figure 27. Ion-Pair Intermediate

An allylic carbonium ion mechanism is proposed for the hydrolysis of 2-methylenecyclohexyl brosylate. As in the case of hydrolysis of cis-pinocarvyl brosylate, the intermediate can be represented by two resonance forms (Fig. 28). The formation of a slight excess of rearranged product (58%) may be due to greater stability of the transition state leading to rearrangement because of the

*There is no apparent reason to believe that the monocyclic compound is more easily ionized in methanol than the bicyclic compound.

development of the incipient double bond within the ring. Nonterminal olefins, in general, are more stable than terminal olefins (1,2). Brown, *et al.* (47) reported that 1-methylcyclohexene is more stable than methylenecyclohexane. This has since been verified by other workers (48-50). An endocyclic double bond in the already strained bicyclic cis-pinocarvyl structure probably introduces more strain than an endocyclic double bond in the monocyclic compound. Thus, the hydrolysis of cis-pinocarvyl brosylate gives less rearranged product.

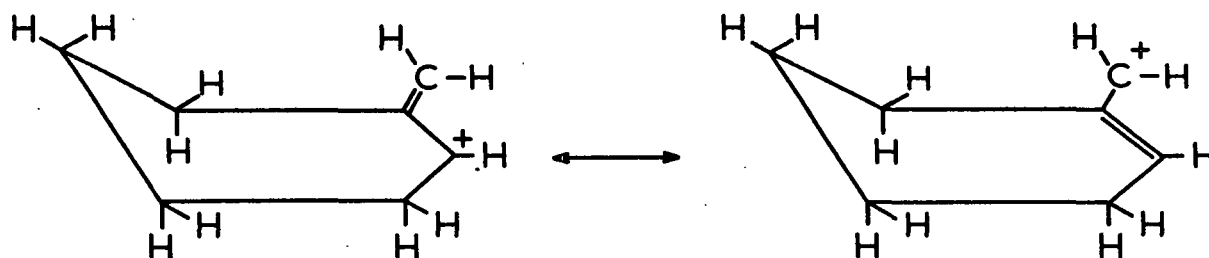


Figure 28. Allylic Carbonium Ion Intermediate

The cis-pinocarvyl bridge does not exert a driving force in the methanolysis of the brosylate. A comparison of the rate constants for the methanolysis of cis-pinocarvyl brosylate ($9.55 \times 10^{-4} \text{ sec.}^{-1}$) and 2-methylenecyclohexyl brosylate ($9.72 \times 10^{-4} \text{ sec.}^{-1}$) shows that there is little difference in the rate of reaction.

At the conditions employed for solvolysis of cis-pinocarvyl brosylate, the isopropylidene bridge has no effect on the extent of elimination in competition with substitution. Solvolysis of cis-pinocarvyl brosylate and 2-methylenecyclohexyl brosylate gave no elimination products.

EFFECT OF UNSATURATION

The effect of the exocyclic double bond in cis-pinocarvyl brosylate on the mechanism of solvolysis was investigated by a study of similar saturated compounds.

The compounds chosen were isopinocampyl brosylate (bicyclic, saturated) and trans-2-methylcyclohexyl brosylate (monocyclic, saturated).

Isopinocampyl brosylate and trans-2-methylcyclohexyl brosylate were reacted with methanolic sodium methoxide (0.1M) at conditions similar to those for cis-pinocarvyl brosylate (Table VIII).* The reaction products, as shown by gas chromatographic analysis, were quite complex (Table IX). Several hydrocarbons were identified in the reaction products.

The isopinocampyl brosylate solvolysis product contained α -pinene, camphene, β -pinene, limonene and two unidentified compounds suspected to be hydrocarbons. These products were identified by gas chromatographic comparison with known compounds. The three longest retention time products are assumed to be methyl ethers. Hückel and Nag (37) identified α -pinene, camphene, and limonene in the reaction product of isopinocampyl tosylate with ethanolic sodium ethoxide. They also found isopinocampyl ethyl ether and other unidentified ethers. The unidentified hydrocarbons may be cis- and trans- δ -pinene. Schmidt (22) found δ -pinene in the hydrocarbon fraction of the reaction product of isopinocampyl tosylate with ethanolic sodium ethoxide.

The trans-2-methylcyclohexyl brosylate solvolysis product contained 1-methylcyclohexene and two unidentified compounds suspected to be hydrocarbons. The two longest retention time products are assumed to be methyl ethers. Hückel, et al. (21) identified 1- and 3-methylcyclohexene in the reaction product of trans-2-methylcyclohexyl tosylate with methanolic sodium methoxide. They also identified three methyl ether products.

*The reactions were run at 25° (rather than 3°) because the saturated brosylates reacted much slower than the unsaturated brosylates.

Gas chromatographic analysis of the isopinocampyl brosylate solvolysis product showed an approximate ratio of 72-76% elimination product to 24-28% substitution product (Table IX). Schmidt (22) found an approximate ratio of elimination to substitution product of 80%:20% for solvolysis of isopinocampyl tosylate in ethanolic sodium ethoxide.

Gas chromatographic analysis of the trans-2-methylcyclohexyl brosylate solvolysis product showed an approximate ratio of 92-95% elimination product to 5-8% substitution product (Table IX). Hückel, *et al.* (21) found a ratio of elimination to substitution product of 75%:25% for solvolysis of trans-2-methylcyclohexyl tosylate in methanolic sodium methoxide. The latter reaction was run at 60° for 18 days.

It is apparent that the cis-pinocarvyl exocyclic double bond is the main controlling factor in the competition between elimination and substitution during solvolysis. Solvolysis of cis-pinocarvyl brosylate and 2-methylenecyclohexyl brosylate yields only substitution products. Solvolysis of the saturated compounds, isopinocampyl brosylate and trans-2-methylcyclohexyl brosylate, yields elimination and substitution products.

A logical explanation of the fact that solvolysis of cis-pinocarvyl brosylate does not yield elimination products is that formation of a diene may cause excessive strain in the bicyclic system. Formation of substitution products does not add strain to the system. In terms of energy requirements for substitution and elimination in the product-determining step (reaction of the carbonium ion or ion-pair intermediate), the formation of substitution products is favored. The ground state energy of the elimination product would be higher than that of the substitution products because of greater ring strain. The elimination mechanism would involve a higher energy maximum (transition-state energy) than the substitution mechanism because of incipient double bond formation.

Similar reasoning can be applied to the solvolysis of 2-methylenecyclohexyl brosylate. Although diene formation in the monocyclic system introduces less ring strain than in the bicyclic system, inspection of the diene model shows considerable ring rigidity and an eclipsed hydrogen interaction.

If ring strain is the reason that elimination does not occur in the solvolysis of cis-pinocarvyl and 2-methylenecyclohexyl brosylate, solvolysis of acyclic allyl compounds should yield elimination products. Reactions of several allylic halides with alcoholic alkoxide have been shown to yield elimination products, in addition to substitution products (51-55). Other workers have reported only substitution products (16,56-60). However, the reported product yields were not quantitative (80% or less). It is quite possible that volatile elimination products, such as butadiene or isoprene, could have been lost in the workup and analysis procedures.

As expected, the allylic sulfonate esters, cis-pinocarvyl and 2-methylenecyclohexyl brosylate, are solvolyzed much faster than similar saturated sulfonate esters. The pseudo-first-order rate constants for ethanolysis of isopinocampyl tosylate (37) at 30° and for methanolysis of trans-2-methylcyclohexyl tosylate (21) at 60° are $1.26 \times 10^{-5} \text{ sec.}^{-1}$ and $4.45 \times 10^{-6} \text{ sec.}^{-1}$, respectively. The pseudo-first-order rate constant for methanolysis of cis-pinocarvyl brosylate at 5° is $9.55 \times 10^{-4} \text{ sec.}^{-1}$ (Table XII). The rate difference would be even greater if the comparison could be made at the same reaction temperature. These large rate differences reflect the importance of the resonance stabilized allylic intermediate formed in the reaction of cis-pinocarvyl brosylate.

EFFECT OF LEAVING GROUP ON MECHANISM OF SOLVOLYSIS OF
cis-PINOCARVYL AND RELATED ESTERS

ALKALINE METHANOLYSIS OF UNSATURATED p-NITROBENZOATES

The p-nitrobenzoate derivatives of cis-pinocarveol, trans-pinocarveol, and 2-methylenecyclohexanol were reacted with methanolic sodium methoxide (0.1M). Gas chromatographic analysis of the reaction products showed that quantitative yields of the parent alcohols were obtained from each p-nitrobenzoate ester (Table X). Methyl p-nitrobenzoate was identified in each of the reaction products. The formation of alcohol products and methyl p-nitrobenzoate indicates that acyl-oxygen cleavage is involved. The three unsaturated p-nitrobenzoates probably react by the common transesterification or $B_{AC}2$ mechanism (Fig. 10, p. 10).

Reaction of cis-pinocarvyl brosylate and 2-methylenecyclohexyl brosylate with methanolic sodium methoxide (0.1M) resulted in cleavage of the carbon-oxygen bond rather than the sulfur-oxygen bond. This difference in type of cleavage between the sulfonate esters and carboxylate esters is attributed to the strength of the carbon-oxygen bond (alkyl-oxygen bond in the p-nitrobenzoate). Sulfonate esters form a relatively weak carbon-oxygen bond and, thus, are effective leaving groups.* Carboxylate esters usually form a strong alkyl-oxygen bond and are cleaved at the acyl-oxygen bond. The results of this work clearly demonstrate the difference in type of cleavage in the solvolysis of the unsaturated brosylate and p-nitrobenzoate esters. There is no report in the literature of a similar comparison for allylic compounds. However, other allylic p-nitrobenzoate (12) and hydrogen phthalate (13,14,61) esters have been shown to react with alkyl-oxygen cleavage in hydroxylic solvents.

*There is a good negative correlation between basicity and effectiveness of leaving groups (1). The less basic the substituent, the more easily it is removed. The brosylate group is less basic than the p-nitrobenzoate group.

Pinocarvone (Fig. 29) was tentatively identified as a product of the reaction of cis-pinocarvyl brosylate with methanolic sodium methoxide in the presence of oxygen. The ratio of cis-pinocarveol to pinocarvone was approximately 3:1. In the absence of oxygen, the only product was cis-pinocarveol. trans-Pinocarvyl p-nitrobenzoate yielded only trans-pinocarveol when reacted with methanolic sodium methoxide in the presence of oxygen. Apparently cis-pinocarveol is more easily air-oxidized in the presence of methanolic sodium methoxide than trans-pinocarveol. A possible explanation of the difference in reactivity of the alcohols is that cis-pinocarveol may have a higher ground state energy due to its conformation.

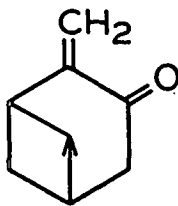


Figure 29. Pinocarvone

HYDROLYSIS OF UNSATURATED p-NITROBENZOATES

As stated earlier, Goering and Silversmith (11) reacted cis- and trans-5-methyl-2-cyclohexenyl p-nitrobenzoate with 80% aqueous acetone. The esters undergo a combination of internal return and hydrolysis. The reaction of both esters proceed through a symmetrical bridged ion-pair (Fig. 12, p. 13).

The p-nitrobenzoate derivatives of cis-pinocarveol, trans-pinocarveol, and 2-methylenecyclohexanol were reacted with 80% aqueous acetone at the conditions reported by Goering and Silversmith (11). In each case, the unreacted starting material was recovered in quantitative amounts (96-98%). The reasons for the difference in reactivity between these compounds and the 5-methyl-2-cyclohexenyl p-nitrobenzoates are not known.

INSTABILITY OF trans-PINOCARVYL AND MYRTENYL
SULFONATE ESTERS

Several attempts to prepare trans-pinocarvyl and myrtenyl sulfonate esters resulted in the recovery of oils which slowly darkened at low temperature (-40°) and rapidly darkened at higher temperatures. As in the case of cis-pinocarvyl brosylate, isolation of the sulfonate esters at room temperature was complicated by their extreme instability. Low-temperature recrystallization (acetone-dry ice bath) resulted in the slow separation of a dark oil. Apparently, the sulfonate esters of trans-pinocarveol and myrtenol are unstable liquids or low-melting solids.

CONCLUSIONS

The solvolysis of cis-pinocarvyl brosylate involves allylic participation in the reaction mechanism. Methanolysis and alkaline methanolysis proceed by an unsymmetrical ion-pair mechanism. In the stronger ionizing solvents, water and alkaline methanolic lithium perchlorate, the reaction proceeds by a free allylic carbonium ion (S_N1).

The cis-pinocarvyl brosylate isopropylidene bridge has little effect on the rate of solvolysis but it does have an effect on product distribution. This steric factor is more important in the product-determining step than in the rate-determining step, formation of the carbonium ion. The isopropylidene bridge has no effect on the extent of elimination in competition with substitution.

The presence of the cis-pinocarvyl brosylate exocyclic double bond makes elimination energetically unfavorable in the product-determining step. The formation of a diene would introduce excessive strain into the ring system. cis-Pinocarvyl brosylate is solvolyzed much faster than similar saturated sulfonate esters because of the resonance stabilization of the allylic intermediate.

The mechanisms for alkaline methanolysis of cis-pinocarvyl sulfonate and carboxylate esters are different. In contrast to the ion-pair mechanism for the brosylate ester, the p-nitrobenzoate ester reacts with acyl-oxygen bond cleavage. The sulfonate group is a more effective leaving group than the carboxylate group.

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APPENDIX I

PROCEDURES FOR QUANTITATIVE ELEMENTAL ANALYSIS

BROMINE

Quantitative bromine analyses were run on the compounds suspected to be cis-pinocarvyl, 2-methylenecyclohexyl, isopinocampyl and trans-2-methylcyclohexyl brosylate. The procedure involved combustion of the brosylate and a Volhard titration on the solution of the absorbed gases (62-64).

A five per cent solution of ammonium carbonate (5 ml.) and distilled water (20 ml.) were put in a Schöniger combustion flask. The flask was purged with oxygen. The brosylate (0.03 to 0.05 g., weighed at 3°) was rolled up in a square piece of filter paper (with a long tab for ignition). The paper and sample were placed in the platinum grid of the combustion flask. The paper was ignited and quickly placed in the flask which was in a horizontal position. After combustion the flask contents were shaken for several minutes and then allowed to stand for one-half hour. Distilled water was poured onto the flared lip of the flask and the stopper was carefully withdrawn. The flask contents and wash water were transferred to a 250-ml. Erlenmeyer flask. Nitric acid (5 ml., 7.5N, previously boiled), standard silver nitrate (10.0 ml., 0.05M), and ferric alum indicator (1 ml., saturated solution) were added. The solution was titrated with standard potassium thiocyanate (0.05N) to the first appearance of a brown color. The reagent blank was negligible.

The percentage of bromine in each compound was calculated from the equation

$$\%Br = 100E(V_1 N_1 - V_2 N_2) / 1000a \quad (7)$$

where

\underline{E} = equivalent weight of bromine, g.

\underline{V}_1 = volume of silver nitrate, ml.

\underline{N}_1 = normality of silver nitrate

\underline{V}_2 = volume of potassium thiocyanate, ml.

\underline{N}_2 = normality of potassium thiocyanate

\underline{a} = weight of brosylate ester, g.

The data for the four brosylate esters are shown in Table XIII. Duplicate analyses were run.

TABLE XIII

QUANTITATIVE BROMINE ANALYSES FOR BROSYLATE ESTERS

Brosylate	0.0500N AgNO ₃ , ml.	0.0506N KSCN, ml.	Sample Wt., g.	Br, Found, %	Br, Theor., %
<u>cis</u> -Pinocarvyl	10.0	7.33	0.0475	21.72	
	10.0	8.37	0.0281	21.75	21.53
2-Methylene- cyclohexyl	10.0	6.80	0.0504	24.71	
	10.0	6.76	0.0510	24.74	24.13
Isopinocamphyl	10.0	7.20	0.0509	21.32	
	10.0	7.43	0.0464	21.36	21.41
<u>trans</u> -2-Methyl- cyclohexyl	10.0	6.92	0.0498	24.08	
	10.0	6.93	0.0498	23.91	23.98

SULFUR

Quantitative sulfur analyses were run on the compounds suspected to be cis-pinocarvyl, 2-methylenecyclohexyl, and isopinocamphyl brosylate. The procedure involved combustion of the brosylate and barium perchlorate titration on the solution of the absorbed gases (63-65).

The combustion procedure was similar to that used for the bromine analyses (see p. 77). The solution used to absorb the gases consisted of hydrogen peroxide (30%, 4 drops) and distilled water. The flask contents and wash water (20 ml.) were transferred to a 100-ml. beaker. Absolute ethanol (40 ml.) was added and the pH of the solution was adjusted to 3.0 with perchloric acid (2.5%). One drop of Thorin indicator was added and the solution was titrated with standard barium perchlorate (0.005M)¹ until a definite pink color appeared. The end point color was compared with that of an indicator blank.² The reagent blank was determined on the paper sample holder.

The percentage of sulfur in each compound was calculated from the equation

$$\% S = 100 T [V - (I + R)] / 1000W \quad (8)$$

where

T = titer of barium perchlorate, mg. S/ml. barium perchlorate

V = ml. of barium perchlorate used for sample

I = ml. of barium perchlorate used for indicator blank

R = ml. of barium perchlorate used for reagent blank, corrected for indicator blank

W = weight of sample, g.

The data for the three brosylate esters are shown in Table XIV. Duplicate analyses were run.

¹Prepared by dissolving 2.0 g. $Ba(ClO_4)_2 \cdot 3H_2O$ in 200 ml. water and adding 800 ml. absolute ethanol. The pH was adjusted to 3.5 with perchloric acid, and the solution was standardized with standard sulfuric acid (0.005M) to the Thorin end point.

²The indicator blank was run on 8 ml. distilled water and 40 ml. absolute ethanol. The pH was adjusted to 3.0 with perchloric acid and the solution was titrated to the Thorin end point with barium perchlorate. A new indicator blank was run for each analysis since the color quickly faded.

TABLE XIV

QUANTITATIVE SULFUR ANALYSES FOR BROSYLATE ESTERS

Brosylate	Ba(ClO ₄) ₂ Titer ^a	Ba(ClO ₄) ₂ Used, ml.	Indicator Blank, ml.	Reagent Blank, ml.	Sample Wt., g.	S Found, %	S Theor., %
cis- Pinocarvyl	0.1101	7.99	0.04	0.04	0.0100	8.71	8.64
	0.1101	7.79	0.03	0.04	0.0098	8.68	
2-Methylene- cyclohexyl	0.1054	9.52	0.07	0.35	0.0100	9.59	9.67
	0.1054	10.44	0.10	0.35	0.0108	9.75	
Isopino- camphyl	0.1101	9.03	0.06	0.03	0.0115	8.56	8.59
	0.1101	7.75	0.06	0.03	0.0099	8.52	

^a mg. S/ml. Ba(ClO₄)₂.

APPENDIX II

DETERMINATION OF WEIGHT RESPONSE FACTORS

This appendix contains the weight response factor data for all solvolysis products (Tables XV-XX). The known products (methyl ethers and alcohols) and the internal standard were diluted to 5 ml. with dry methanol. Aliquots of these solutions were run on the gas chromatograph. Additional internal standard was added to the solutions and aliquots were again run. The weight response factors are an average of all determinations at the various concentrations.

TABLE XV

trans-PINOCARVYL AND MYRTENYL METHYL ETHER
WEIGHT RESPONSE FACTORS^a

0.1002 g. trans-pinocarvyl methyl ether

0.0520 g. myrtenyl methyl ether

0.0693 g. anisole

Sample Size, μ l.	Area/Unit Weight, $\text{cm.}^2/\mu\text{g.}$			Weight Response Factor, \underline{F}	
	<u>trans</u> - Pinocarvyl	Myrtenyl	Anisole	<u>trans</u> - Pinocarvyl	Myrtenyl
40	24.94	28.56	37.79	1.515	1.323
40	23.86	27.50	37.12	1.556	1.350
40	22.33	25.19	36.36	1.628	1.443
0.0967 g. Anisole, Same Amount of Methyl Ethers					
35	25.46	29.78	36.98	1.452	1.242
35	25.20	30.82	37.38	1.483	1.213
35	25.90	29.84	36.35	1.403	1.218
0.1144 g. Anisole, Same Amount of Methyl Ethers					
35	28.00	30.80	42.81	1.529	1.390
35	31.19	37.77	43.81	1.405	1.160
30	31.60	36.15	42.61	1.348	1.179
30	29.77	36.86	46.40	1.559	1.259

^aRun on ODPN column at 90° and 75 ml./min. He flow rate.

TABLE XVI

2-METHYLENOCYCLOHEXYL AND 1-CYCLOHEXENEMETHYL
METHYL ETHER WEIGHT RESPONSE FACTORS^a

0.0870 g. 2-methylenecyclohexyl methyl ether

0.0891 g. 1-cyclohexenemethyl methyl ether

0.0767 g. anisole

Sample Size, μ l	Area/Unit Weight, $\text{cm.}^2/\mu\text{g.}$			Weight Response Factor, \underline{F}	
	2- Methylene- cyclohexyl	1- Cyclohexene- methyl	Anisole	2- Methylene- cyclohexyl	1- Cyclohexene- methyl
25	34.11	32.82	40.18	1.178	1.224
25	35.66	33.04	38.80	1.088	1.174
25	37.38	35.44	40.89	1.094	1.154
0.1173 g. Anisole, Same Amount of Methyl Ethers					
25	35.91	34.12	37.92	1.056	1.111
25	36.30	35.91	41.16	1.134	1.146
25	35.66	34.97	38.79	1.088	1.109

^aRun on didecyl phthalate column at 105° and 100 ml./min. He flow rate.

TABLE XVII

trans-PINOCARVEOL AND MYRTENOL WEIGHT RESPONSE FACTORS^a0.1134 g. trans-pinocarveol

0.0965 g. myrtenol

0.0846 g. borneol

Sample Size, μ l.	Area/Unit Weight, $\text{cm.}^2/\mu\text{g.}$			Weight Response Factor, \underline{F}	
	<u>trans</u> - Pinocarveol	Myrtenol	Borneol	<u>trans</u> - Pinocarveol	Myrtenol
25	25.89	24.81	28.77	1.111	1.160
30	24.88	23.49	27.78	1.117	1.183
35	24.09	22.96	27.56	1.144	1.200
0.1129 g. Borneol, Same Amount of Alcohols					
30	25.93	25.91	28.99	1.118	1.119
30	25.18	24.61	29.29	1.163	1.190
30	25.24	24.28	28.34	1.123	1.167

^aRun on hyprose column at 145° and 100 ml./min. He flow rate.

TABLE XVIII

2-METHYLENECYCLOHEXANOL AND 1-CYCLOHEXENEMETHANOL
WEIGHT RESPONSE FACTORS^a

0.0915 g. 2-methylenecyclohexanol

0.0992 g. 1-cyclohexenemethanol

0.0816 g. borneol

Sample Size, μ l.	Area/Unit Weight, $\text{cm.}^2/\mu\text{g.}$			Weight Response Factor, \bar{F}	
	2- Methylene- cyclohexanol	1- Cyclohexene- methanol	Borneol	2- Methylene- cyclohexanol	1- Cyclohexene- methanol
20	33.83	32.66	24.20	0.715	0.741
25	37.29	35.56	27.94	0.749	0.786
25	33.55	32.36	26.05	0.776	0.805
0.1200 g. Borneol, Same Amount of Alcohols					
25	34.80	33.99	27.07	0.778	0.796
25	35.06	33.17	26.77	0.764	0.807
25	34.01	33.14	27.50	0.809	0.830

^aRun on didecyl phthalate column at 145° and 100 ml./min. He flow rate.

TABLE XIX

cis-PINOCARVEOL WEIGHT RESPONSE FACTOR^a0.1040 g. cis-pinocarveol

0.0876 g. borneol

Sample Size, μ l.	Area/Unit Weight, $\text{cm.}^2/\mu\text{g.}$		Weight Response Factor, <u>F</u>
	<u>cis</u> - Pinocarveol	Borneol	
30	22.07	22.93	1.039
35	22.65	22.99	1.015
35	21.48	22.02	1.025
0.1089 g. Borneol, Same Amount of <u>cis</u> -Pinocarveol			
35	21.28	21.59	1.015
35	21.61	22.35	1.034
35	19.04	19.04	1.000

^aRun on hyprose column at 145° and 100 ml./min. He flow rate.

TABLE XX

2-METHYLENECYCLOHEXANOL WEIGHT RESPONSE FACTOR^a

0.0629 g. 2-methylenecyclohexanol

0.0564 g. borneol

Sample Size, μ l.	Area/Unit Weight, $\text{cm.}^2/\mu\text{g.}$		Weight Response Factor, \underline{F}
	2-Methylene- cyclohexanol	Borneol	
15	16.59	18.17	1.095
15	17.59	18.35	1.043
15	18.03	20.40	1.131
0.0799 g. 2-Methylenecyclohexanol, Same Amount of Borneol			
10	20.04	19.91	0.994
10	20.53	20.72	1.009
10	19.75	20.52	1.039

^aBorneol and 2-methylenecyclohexanol were diluted to one milliliter with dry methanol. Run on hyprose column at 145° and 100 ml./min. He flow rate.

APPENDIX III

QUANTITATIVE ANALYSIS OF SOLVOLYSIS REACTION PRODUCTS

This appendix contains the gas chromatographic quantitative analysis data for all solvolysis reaction products (Tables XXI to XXIX). The internal standard was added to the entire methanolic solution (3 to 8 ml.) of the reaction product. Aliquots (10 to 40 μ l.) of this solution were analyzed. Duplicates were run at each reaction condition and three to four analyses were run on each reaction product. The total yields and relative amounts of reaction products are an average of all analyses.

TABLE XXI

METHANOLYSIS OF cis-PINOCARVYL BROSYLATE^a

Area, cm. ²		Reaction A ^b				Product, g.		Relative Amounts, %	
<u>trans</u> - Pinocarvyl Methyl Ether	Myrtenyl Methyl Ether	Anisole	<u>trans</u> - Pinocarvyl Methyl Ether	Myrtenyl Methyl Ether	Total % Yield	<u>trans</u> - Pinocarvyl Methyl Ether	Myrtenyl Methyl Ether	<u>trans</u> - Pinocarvyl Methyl Ether	Myrtenyl Methyl Ether
30.33	17.79	31.84	0.146	0.073	97.8	66.7	33.3	66.7	33.3
30.15	18.06	32.99	0.140	0.072	94.6	66.0	34.0	66.0	34.0
31.86	19.40	34.08	0.143	0.075	97.3	65.6	34.4	65.6	34.4
Reaction B ^c									
23.22	14.24	20.88	0.150	0.079	102.2	65.5	34.5	65.5	34.5
23.12	14.72	22.00	0.142	0.078	98.2	64.5	35.5	64.5	35.5
22.92	15.01	22.40	0.138	0.078	96.4	63.9	36.1	63.9	36.1

^aAnalyses run on ODPN column at 90° and 75 ml./min. He flow rate.^bAnisole (0.1026 g.), total theoretical methyl ether product - 0.224 g. (from 0.50 g. brosylate).^cAnisole (0.0908 g.), total theoretical methyl ether product - 0.224 g. (from 0.50 g. brosylate).

TABLE XXII

ALKALINE METHANOLYSIS OF cis-PINOCARVYL BROSYLATE^a

Area, cm. ²		Reaction A ^b				Product, g.		Relative Amounts, %	
<u>trans</u> - Pinocarvyl Methyl Ether	Myrtenyl Methyl Ether	Anisole	<u>trans</u> - Pinocarvyl Methyl Ether	Myrtenyl Methyl Ether	Total % Yield	<u>trans</u> - Pinocarvyl Methyl Ether	Myrtenyl Methyl Ether	<u>trans</u> - Pinocarvyl Methyl Ether	Myrtenyl Methyl Ether
21.09	13.57	23.09	0.136	0.075	94.2	64.5	35.5		
22.14	13.18	22.26	0.148	0.076	100.0	66.1	33.9		
22.80	14.30	23.80	0.143	0.077	98.2	65.0	35.0		
		Reaction B ^c							
26.18	16.13	29.37	0.144	0.077	98.7	65.2	34.8		
26.78	16.11	30.61	0.142	0.073	96.0	66.0	34.0		
25.89	15.87	30.26	0.139	0.073	94.6	65.6	34.4		

^aAnalyses run on ODPN column at 90° and 75 ml./min. He flow rate.^bAnisole (0.1002 g.), total theoretical methyl ether product - 0.224 g. (from 0.5 g. brosylate).^cAnisole (0.1087 g.), total theoretical methyl ether product - 0.224 g. (from 0.5 g. brosylate).

TABLE XXIII

ALKALINE METHANOLYSIS OF 2-METHYLENECYCLOHEXYL BROSYLATE^a

Area, cm. ²		Reaction A ^b		Product, g.		Relative Amounts, %	
2-Methylene- cyclohexyl Methyl Ether	1-Cyclohexene- methyl Ether	Anisole	2-Methylene- cyclohexyl Methyl Ether	1-Cyclohexene- methyl Ether	Total Yield	2-Methylene- cyclohexyl Methyl Ether	1-Cyclohexene- methyl Ether
12.35	14.46	16.10	0.082	0.099	95.3	45.3	54.7
12.40	15.26	16.74	0.079	0.100	94.2	44.1	55.9
11.85	14.57	17.05	0.074	0.094	88.4	44.0	56.0
12.30	14.57	17.15	0.076	0.094	89.5	44.7	55.3
14.78	18.69	18.99	0.080	0.104	96.8	43.5	56.5
14.95	18.80	19.35	0.079	0.103	95.8	43.4	56.6
15.40	19.80	20.06	0.074	0.105	94.2	41.3	58.7
		Reaction B ^c					

^aAnalyses run on didecyl phthalate column at 105° and 100 ml./min. He flow rate.

^bAnisole (0.0958 g.), total theoretical methyl ether product - 0.190 g. (from 0.50 g. brosylate).

^cAnisole (0.0921 g.), total theoretical methyl ether product - 0.190 g. (from 0.50 g. brosylate).

TABLE XXIV

ALKALINE METHANOLYSIS OF cis-PINOCARVYL BROSYLATE WITH ADDED LITHIUM PERCHLORATE^a

Reaction A, 0.1M LiClO ₄ ^b									
Area, cm. ²		Product, g.				Relative Amounts, %			
<u>trans</u> - Pinocarvyl Methyl Ether	Myrtenyl Methyl Ether	Anisole	<u>trans</u> - Pinocarvyl Methyl Ether	Myrtenyl Methyl Ether	Total % Yield	<u>trans</u> - Pinocarvyl Methyl Ether	Myrtenyl Methyl Ether		
29.18	20.92	31.49	0.138	0.085	99.6	61.9	38.1		
30.43	21.50	33.15	0.137	0.083	98.2	62.3	37.7		
30.49	21.69	32.98	0.138	0.084	99.1	62.2	37.8		
Reaction B, 0.5M LiClO ₄ ^c									
19.91	22.70	17.64	0.098	0.096	86.6	50.5	49.5		
20.67	25.32	17.82	0.101	0.106	92.4	48.8	51.2		
21.10	25.17	18.54	0.099	0.101	89.3	49.5	50.5		

^aAnalyses run on ODPW column at 90° and 75 ml./min. He flow rate.^bAnisole (0.1002 g.), total theoretical methyl ether product - 0.224 g. (from 0.5 g. brosylate).^cAnisole (0.0582 g.), total theoretical methyl ether product - 0.224 g. (from 0.5 g. brosylate).

TABLE XXV

HYDROLYSIS OF cis-PINOCARVYL BROSYLATE^a

Area, cm. ²		Product, g.		Total % Yield	Relative Amounts, %	
<u>trans</u> - Pinocarveol	Myrtenol	<u>trans</u> - Pinocarveol	Myrtenol		<u>trans</u> - Pinocarveol	Myrtenol
16.61	15.87	0.047	0.047	92.2	50.0	50.0
17.61	16.56	0.049	0.048	95.1	50.5	49.5
17.40	16.61	0.048	0.047	93.1	50.5	49.5
Reaction A ^b						
24.88	24.74	0.048	0.050	96.1	49.0	51.0
26.64	25.58	0.049	0.049	96.1	50.0	50.0
27.23	26.80	0.047	0.048	93.1	49.5	50.5
Reaction B ^c						

^aAnalyses run on hyprose column at 145° and 100 ml./min. He flow rate.

^bBorneol (0.0459 g.), total theoretical alcohol product - 0.102 g. (from 0.25 g. brosylate).

^cBorneol (0.0470 g.), total theoretical alcohol product - 0.102 g. (from 0.25 g. brosylate).

TABLE XXVI

HYDROLYSIS OF 2-METHYLENECYCLOHEXYL BROSYLATE^a

		Reaction A ^b				Reaction B ^c		Relative Amounts, %	
2-Methylene- cyclohexanol	Area, cm. ² 1-Cyclo- hexene- methanol	Product, g.		Total % Yield	2-Methylene- cyclohexanol	1-Cyclo- hexene- methanol	Total % Yield	2-Methylene- cyclohexanol	1-Cyclo- hexene- methanol
		Borneol	2-Methylene- cyclohexanol						
12.39	17.12	12.48	0.069	0.098	41.3	58.7	98.8	41.3	58.7
12.98	17.64	14.42	0.062	0.087	41.6	58.4	88.2	41.6	58.4
13.43	17.22	14.80	0.063	0.083	43.2	56.8	86.4	43.2	56.8
15.15	19.91	15.98	0.069	0.093	42.6	57.4	95.9	42.6	57.4
14.85	19.58	17.22	0.063	0.085	42.6	57.4	87.6	42.6	57.4
15.68	20.54	17.63	0.065	0.087	42.8	57.2	89.9	42.8	57.2

^aAnalyses run on didecyl phthalate column at 145° and 100 ml./min. He flow rate.

^bBorneol (0.0901 g.), total theoretical alcohol product -- 0.169 g. (from 0.50 g. brosylate).

^cBorneol (0.0950 g.), total theoretical alcohol product -- 0.169 g. (from 0.50 g. brosylate).

TABLE XXVII

ALKALINE METHANOLYSIS OF cis-PINOCARVYL p-NITROBENZOATE^a

Reaction A ^b			
Area, cm. ²		<u>cis</u> - Pinocarveol, g.	Yield, %
<u>cis</u> - Pinocarveol	Borneol		
28.17	21.94	0.262	104.0
29.84	24.16	0.252	100.0
26.91	22.08	0.249	98.8
Reaction B ^b			
33.03	25.16	0.268	106.3
32.55	25.58	0.260	103.2
32.16	25.73	0.255	101.2

^aAnalyses run on hyprose column at 145° and 100 ml./min. He flow rate.

^bBorneol (0.2000 g.), total theoretical alcohol product - 0.252 g. (from 0.50 g. p-nitrobenzoate).

TABLE XXVIII

ALKALINE METHANOLYSIS OF trans-PINOCARVYL p-NITROBENZOATE^aReaction A^b

Area, cm. ²		<u>trans</u> - Pinocarveol, g.	Yield, %
<u>trans</u> - Pinocarveol	Borneol		
21.64	20.10	0.252	100.0
20.61	20.95	0.231	91.7
22.19	21.18	0.246	97.6
22.01	21.23	0.243	96.4

Reaction B^c

24.11	22.58	0.251	99.6
21.46	21.94	0.230	91.3
21.96	21.61	0.239	94.8

^aAnalyses run on hyprose column at 145° and 100 ml./min.
He flow rate.

^bBorneol (0.2075 g.), total theoretical alcohol product -
0.252 g. (from 0.50 g. p-nitrobenzoate).

^cBorneol (0.2080 g.), total theoretical alcohol product -
0.252 g. (from 0.50 g. p-nitrobenzoate).

TABLE XXIX

ALKALINE METHANOLYSIS OF 2-METHYLENECYCLOHEXYL p-NITROBENZOATE^aReaction A^b

2-Methylene- cyclohexanol	Area, cm. ² Borneol	2-Methylene- cyclohexanol, g.	Yield, %
11.63	7.29	0.235	109.3
16.10	11.89	0.199	92.6
17.03	12.48	0.201	93.5
17.67	11.46	0.227	105.6
11.63	7.70	0.222	103.7
12.83	8.96	0.211	98.1
12.91	8.98	0.212	98.6

Reaction B^c

17.29	13.58	0.220	102.3
17.26	14.01	0.213	99.1
17.40	13.70	0.220	102.3

^aAnalyses run on hyprose column at 145° and 100 ml./min.
He flow rate.

^bBorneol (0.1402 g.), total theoretical alcohol yield -
0.215 g. (from 0.50 g. p-nitrobenzoate).

^cBorneol (0.1649 g.), total theoretical alcohol yield -
0.215 g. (from 0.50 g. p-nitrobenzoate).

APPENDIX IV

TITRIMETRIC RATE DATA

This appendix contains the titrimetric rate data for the solvolysis of cis-pinocarvyl and 2-methylenecyclohexyl brosylate used to calculate rate constants (Tables XXX-XXXIV). Duplicate runs were made at each reaction condition.

In the tables for alkaline methanolysis, the brosylate concentration at time, t, is designated (a - x) and the sodium methoxide concentration at time, t, is designated (b - x).

TABLE XXX

METHANOLYSIS OF cis-PINOCARVYL BROSYLATE AT 5.1°Reaction A^a

Time, min.	0.03875M NaOH, ml. ^b	Ester Conc., moles/100 ml.	Reaction, %
2.25	0.64	10.85 x 10 ⁻⁴	18.6
8.50	1.56	7.28	45.4
13.00	1.97	5.70	57.2
18.67	2.36	4.18	68.6
24.00	2.60	3.25	75.5
30.25	2.86	2.25	83.1
37.50	2.99	1.74	86.9
54.33	3.16	1.08	91.9
91.00	3.35	0.35	97.4
6 Hours	1.72 ^c	13.33 (<u>c</u> ₀)	100

Reaction B^d

1.83	0.62	11.09 x 10 ⁻⁴	17.8
4.92	1.07	9.34	30.8
8.50	1.68	6.78	48.3
12.50	2.03	5.62	58.4
17.33	2.34	4.42	67.2
26.25	2.80	2.49	81.5
34.75	2.98	1.94	85.6
44.75	3.16	1.24	90.8
60.00	3.26	0.86	93.6
6 Hours	1.74 ^c	13.49 (<u>c</u> ₀)	100

^aBrosylate (0.5069 g.) in 100 ml. 10% acetone-methanol solution.

^bCorrected for 0.02 ml. reagent blank.

^c5-ml. aliquot.

^dBrosylate (0.5045 g.) in 100 ml. 10% acetone-methanol solution.

TABLE XXXI

METHANOLYSIS OF 2-METHYLENECYCLOHEXYL BROSYLATE AT 5.2°

Reaction A^a

Time, min.	0.03875M NaOH, ml. ^b	Ester Concn., moles/100 ml.	Reaction, %
11.00	1.99	5.70 x 10 ⁻⁴	57.5
14.92	2.28	4.57	65.9
18.00	2.48	3.80	71.7
21.75	2.67	3.06	77.2
25.00	2.79	2.60	80.6
29.00	2.94	2.02	84.9
32.75	3.03	1.67	87.5
37.00	3.09	1.44	89.3
42.00	3.13 ^c	1.28	90.5
6 Hours	1.73 ^c	13.41 (c _o)	100

Reaction B^d

2.00	0.87	9.88 x 10 ⁻⁴	25.4
5.25	1.34	8.06	39.2
8.00	1.65	6.86	48.2
11.50	1.98	5.58	57.9
18.00	2.44	3.79	71.4
25.75	2.82	2.32	82.5
36.83	3.07	1.35	89.8
53.00	3.22	0.77	93.6
71.00	3.28 ^c	0.54	95.9
6 Hours	1.71 ^c	13.25 (c _o)	100

^aBrosylate (0.4510 g.) in 100 ml. 10% acetone-methanol solution.

^bCorrected for 0.02 ml. reagent blank.

^c5-ml. Aliquot.

^dBrosylate (0.4504 g.) in 100 ml. acetone-methanol solution.

TABLE XXXII

ALKALINE METHANOLYSIS OF cis-PINOCARVYL BROSYLATE AT 5.1°Reaction A^a

Time, min.	0.03875M NaOH, ml. ^b	Ester Reacted, moles/100 ml.	(<u>a-x</u>)	(<u>b-x</u>)	$\frac{(\underline{a-x})}{(\underline{b-x})}$	Reacted, %
2.33	0.48	1.79×10^{-4}	11.31×10^{-4}	18.07×10^{-4}	0.626	13.7
4.75	0.83	3.15	9.95	16.71	0.596	24.0
7.75	1.22	4.66	8.44	15.20	0.555	35.6
12.00	1.67	6.40	6.70	13.46	0.498	48.9
15.67	2.00	7.68	5.42	12.18	0.445	58.6
20.75	2.30	8.84	4.26	11.02	0.387	67.5
28.00	2.60	10.01	3.09	9.35	0.314	76.4
39.75	2.83	11.09	2.01	8.77	0.229	84.7
60.00	3.14	12.10	1.00	7.76	0.129	92.4
6 Hours	4.27 ^c	13.10(<u>c₀</u>)				100

Reaction B^a

2.75	5.66 ^d	1.93×10^{-4}	11.25×10^{-4}	17.93×10^{-4}	0.627	14.6
8.75	1.29	4.93	8.25	14.93	0.553	37.4
11.33	1.58	6.05	7.13	13.81	0.516	45.9
17.75	2.10	8.07	5.11	11.79	0.433	61.2
20.50	2.26	8.69	4.49	11.17	0.402	65.9
24.75	2.48	9.54	3.64	10.32	0.353	72.4
30.50	2.70	10.39	2.79	9.47	0.295	78.8
38.25	2.90	11.17	2.01	8.69	0.231	84.7
57.75	3.19	12.29	0.89	7.57	0.118	93.2
6 Hours	4.28 ^c	13.18(<u>c₀</u>)				100

^aBrosylate (0.5000 g.) in 100 ml. 10% acetone-0.01986M methanolic sodium methoxide solution.

^bCorrected for 0.02 ml. reagent blank.

^c5-ml. aliquot.

^d20 ml. 0.01993M hydrochloric acid.

TABLE XXXIII

ALKALINE METHANOLYSIS OF 2-METHYLENECYCLOHEXYL BROSYLATE AT 5.2°

Reaction A^a

Time, min.	0.03875M NaOH, ml. ^b	Ester Reacted, moles/100 ml.	(<u>a-x</u>)	(<u>b-x</u>)	$\frac{(\underline{a-x})}{(\underline{b-x})}$	Reacted, %
1.83	1.69	7.68×10^{-4}	8.49×10^{-4}	13.38×10^{-4}	0.635	47.5
4.67	2.10	9.27	6.90	11.79	0.585	57.3
7.00	2.33	10.16	6.01	10.90	0.551	62.8
9.58	2.57	11.09	5.08	9.97	0.510	68.6
13.50	2.81	12.02	4.15	9.04	0.459	74.3
15.83	2.88	12.29	3.88	8.77	0.442	76.0
20.83	3.10	13.14	3.03	7.92	0.383	81.3
30.00	3.16	13.38	2.79	7.68	0.363	82.7
6 Hours	3.88	16.17(<u>c₀</u>)				100

Reaction B^c

2.67	1.39	6.52×10^{-4}	8.13×10^{-4}	14.54×10^{-4}	0.559	44.5
5.00	1.70	7.72	6.93	13.34	0.519	52.7
7.67	1.92	8.57	6.08	12.49	0.487	58.5
10.25	2.13	9.38	5.27	11.68	0.451	64.0
14.00	2.40	10.43	4.22	10.63	0.397	71.2
16.42	2.53	10.93	3.72	10.13	0.367	74.6
19.33	2.57	11.09	3.56	9.97	0.357	75.7
24.00	2.75	11.79	2.86	9.27	0.309	80.5
6 Hours	3.49	14.65(<u>c₀</u>)				100

^aBrosylate (0.5482 g.) in 100 ml. acetone-0.02106M methanolic sodium methoxide solution.

^bCorrected for 0.02 ml. reagent blank.

^cBrosylate (0.4961 g.) in 100 ml. acetone-0.02106M methanolic sodium methoxide solution.

TABLE XXXIV

 ALKALINE METHANOLYSIS OF cis-PINOCARVYL BROSYLATE
 WITH ADDED 0.5M LITHIUM PERCHLORATE AT 5.1°
Reaction A^a

Time, min.	0.03875M NaOH, ml. ^b	Ester Conc., moles/100 ml.	Reaction, %
2.17	1.03	7.83×10^{-4}	39.5
4.58	1.58	5.70	56.0
7.67	2.05	3.88	70.0
10.25	2.31	2.87	77.8
13.13	2.51	2.09	83.9
16.00	2.64	1.59	87.7
19.50	2.78	1.05	91.9
28.25	2.87	0.70	94.6
6 Hours	3.05	12.95(c ₀)	100

Reaction B^c

2.00	0.84	8.71×10^{-4}	33.5
4.00	1.44	6.39	51.2
6.67	1.93	4.49	65.7
8.67	2.14	3.68	71.9
11.58	2.42	2.55	80.5
15.33	2.59	1.93	85.3
17.75	2.68	1.58	87.9
20.75	2.80	1.12	91.5
6 Hours	3.09	13.10(c ₀)	100

^aBrosylate (0.5010 g.) in 100 ml. 10% acetone-0.02106M methanolic sodium methoxide solution (0.5M LiClO₄).

^bCorrected for 0.11 ml. reagent blank.

^cBrosylate (0.5025 g.) in 100 ml. 10% acetone-0.02106M methanolic sodium methoxide solution (0.5M LiClO₄).