trans,trans,trans-2-Carboxy-4-hydroxy-5-bromocyclohexanecarboxylic acid lactone-(2,4) (VIIIa) was obtained in 80% yield from VIIa, mp 129–130° (ethyl acetate), ν_{max} 1790 and 1720 cm^{-1}. Esterification of VIIIa with diazomethane gave VIIIb, mp 89–90° (benzene), ν_{max} 1790–1740 cm^{-1}. *Anal.* Calcd for $C_8H_{11}BrO_4$: C, 41.1; H, 4.2. Found: C, 41.3; H, 4.2.

Methyl *trans,trans,trans*-2-carboxy-4-hydroxy-5-chlorocyclohexanecarboxylate lactone-(2,4) (XIb) was prepared in 40% yield from Xa and subsequent esterification with diazomethane, mp 92° (ethanol), ν_{max} 1800 and 1740 cm^{-1}. *Anal.* Calcd for $C_9H_{11}ClO_4$: C, 49.4; H, 5.0; Cl, 16.2. Found: C, 50.0; H, 5.1; Cl, 16.1.

Methyl *cis*-2-carboxy-*cis*-4-hydroxy-*trans*-5-chlorocyclohexanecarboxylate lactone-(2,4) (XIIb) was obtained from XIIIa and subsequent esterification with diazomethane, bp 150–155° (0.5 mm), ν_{max} 1800 and 1740 cm^{-1}. *Anal.* Calcd for $C_9H_{11}ClO_4$: C, 49.4; H, 5.0; Cl, 16.2. Found: C, 49.4; H, 5.0; Cl, 16.0.

Registry No.—Vb, 26595-97-1; VIIa, 26595-79-9; VIIb, 26595-80-2; VIIIa, 26595-81-3; VIIIb, 19914-90-0; Xa, 26595-83-5; Xb, 26595-84-6; XIb, 26595-85-7; XIIb, 26595-86-8; XIIIa, 26595-87-9; XIIIb, 26595-88-0; XIII anhydride, 26595-89-1; XIVa, 26595-90-4; XIVb, 26595-91-5; XVa, 26595-92-6; XVb, 19914-94-4; XVI, 26595-94-8; XVIIb, 19914-95-5; *trans*-2-carboxy-*cis*-4-chloro-*trans*-5-bromocyclohexanecarboxylic acid dimethyl ester (from Table I), 26595-96-0.

Solvolysis Studies of Cycloalkylcarbinyl Tosylates. Effect of Adjacent Ring Size on the Rates and Products. Ionization Constant Determinations of Cycloalkanecarboxylic Acids

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First-order titrimetric rate constants, activation parameters, and products were determined for the acetolysis of cycloalkylcarbinyl tosylates of ring size five through twelve. First-order formolysis rate constants were also determined for the series, and trifluoroacetolysis first-order rate constants were determined for cyclohexyl-, cyclononyl-, and cycloundecylcarbinyl tosylates. Ionization constants were measured for the cycloalkanecarboxylic acids of ring size five through twelve. A small rate spread was observed for the series, with the maximum rate being observed for cyclononylcarbinyl tosylate. The observed rate profiles closely parallel the cycloalkane ring strain profile calculated from combustion data. The products (seven- through twelve-membered rings) were mainly 1-methylcycloalkenes, which were shown by deuterium substitution in one case to arise *via* a 1,2-hydride shift. The rate spread was considered to be due to nucleophilic hydrogen participation at the transition state (k_Δ). A smaller contribution of a solvent assisted (k_s) pathway also contributed to the total solvolytic rate. Hydrogen participation is proposed as being directly related to relief of ring strain (six- through twelve-membered rings). Inductive contributions of the adjacent ring are also of importance. Cyclopentylcarbinyl tosylate appears to solvolyze *via* a nonclassical ion (carbon participation) to yield ring expanded products.

In the mechanistic analysis of solvolytic reactions of primary substrates it has been proposed that there are competing pathways for displacement of the leaving group. These routes have been designated as k_Δ (anchimerically assisted ionization) and k_s (anchimerically unassisted ionization) and depend on the solvent and substrate structure.[2,3] The suggestion has been made that the k_s route is the nucleophilic solvent assisted process[4] and we shall adopt this terminology in this manuscript and return to the original definition of Winstein.[3]

These pathways are simultaneous processes and no crossover occurs between them. In solvents of high ionizing power and low nucleophilicity such as trifluoroacetic acid, the k_Δ/k_s ratios for primary substrates are much higher than in formic acid.[2,5] The solvolyses of primary tosylates have also been performed in fluorosulfuric acid[6,7] and sulfuric acid.[8]

The formation of carbonium ions or ion pairs (k_c route) from primary substrates seems highly unlikely as these cations are perhaps far too unstable to exist in solution.[9-12] A strong nucleophilic solvent bond is indicated in the solvolysis of these substrates proceeding through the k_s route. On the basis of rate, solvent, and isotope effects in the solvolysis of ethyl trifluoromethanesulfonate, it was concluded that substantial bonding to a nucleophilic solvent molecule at the transition state was required even with such a good leaving group as the trifluoromethanesulfonate anion.[13]

On the basis of these pathways (k_s and k_Δ) for primary substrate solvolyses, it has been concluded by Schleyer and coworkers[14] that the presence of any rearranged product in the solvolysis of simple primary systems can be taken as *prima facie* evidence for neighboring group participation.

This picture of competing k_Δ and k_s routes, with no interconversion between them, has been successfully utilized in the interpretation of the solvolysis

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rates of 2-arylethyl tosylates.[15-18] In these cases one must include a term for the fraction of phenonium ions which go on to product and do not undergo internal return.

The solvolytic study of a series of cycloalkylcarbinyl tosylates seemed of considerable interest to determine the effect of adjacent ring size on the rates and products. The effect of having a primary reaction center adjacent to a ring could lead to three competitive solvolytic pathways: (a) k_s route, (b) k_Δ route with carbon participation, and (c) k_Δ route with hydrogen participation. It appeared that hydrogen participation (k_Δ) might be the most energetically favorable process in the six- through twelve-membered ring systems since a tertiary cation would be formed while carbon participation would lead to a ring-expanded secondary cation. The magnitude of the k_s route is difficult to estimate. However, if a strong solvent bond occurs at the transition state (k_s route) leading to unrearranged product, then the k_Δ route in order to be competitive may not have a rate considerably greater than the k_s route.[4]

Previous Studies.—The acetolyses of the small ring systems, cyclopropylcarbinyl tosylate[19-21] and cyclobutylcarbinyl tosylate,[22] have been reported and discussed. The acetolysis of cyclopentylcarbinyl *p*-nitrobenzenesulfonate at 80° yields 62% cyclohexene and 18% cyclohexyl acetate.[23] The acetolysis of cyclohexylcarbinyl tosylate at 115° yields less than 2% ring-expanded products[24,25] and cycloheptylcarbinyl brosylate is reported to yield only unrearranged acetate.[26] Acetolysis rates have been reported and discussed for cyclopentylcarbinyl brosylate,[27] cyclohexylcarbinyl brosylate,[27,28] and cycloheptylcarbinyl brosylate.[26,29]

Nitrous acid deaminations of cycloalkylcarbinyl amines have been studied. Cyclopropylcarbinylamine leads to an alcohol mixture containing 47% cyclobutanol[30] and cyclobutylcarbinylamine yields mainly cyclopentanol.[31] In the deaminations of the medium to large size cycloalkylcarbinylamines, significant amounts of ring-expanded products have been obtained.[32-35] The deaminations of isobutylamine and various deuterated analogs have been extensively studied and the mechanisms discussed.[36-38] The pyrolyses of cyclohexylcarbinyl tosylate,[24] cyclohexylcarbinyl mesylate,[39] cyclohexylcarbinyl borate,[40] and cyclobutylcarbinyl borate[40] have been reported. Cyclopentyl- and cyclohexylcarbinyl acetates have also been pyrolyzed and yield the corresponding methylenecycloalkanes.[41-43]

Synthetic Methods.—The cycloalkylcarbinyl tosylates (five- through twelve-membered rings) were prepared from the corresponding alcohols.[44] Cycloheptylcarbinol was prepared by lithium aluminum hydride reduction of cycloheptanecarboxylic acid.[45] Cyclononylcarbinol and cyclodecylcarbinol were prepared from the corresponding 2-carbethoxycycloalkanones by the following sequence: (a) preparation of the ethylene thioketal by reaction with boron trifluoride etherate and 1,2-ethanedithiol; (b) desulfurization of the thioketal with Raney nickel to yield the carbethoxycycloalkane; and (c) lithium aluminum hydride reduction to the carbinol. Cyclodecylcarbinol was also obtained by lithium aluminum hydride reduction of 1-carbomethoxycyclodecene in refluxing 1,2-dimethoxyethane.

Cyclooctylcarbinyl tosylate, deuterated at the ring position holding the tosylate carbon, was prepared from β-*d*-carbethoxycyclooctane by lithium aluminum hydride reduction and subsequent tosylation. Deuteration of the ester was accomplished with ethereal triphenymethyl sodium followed by addition of ethanol-d_1.[46]

Cyclooctane-, cyclononane-, and cyclododecanecarboxylic acids were prepared by hydrolysis of the corresponding esters. Cyclodecane- and cycloundecanecarboxylic acids were prepared by catalytic hydrogenation of the corresponding 1-carboxycycloalkenes. These latter compounds were obtained by a modified Favorskii reaction on cycloundecanone and cyclododecanone, respectively, according to the procedure described by Garbisch.[47]

Kinetic Procedures.—The acetolysis and formolysis titrimetric procedures were similar to those of Winstein and coworkers[48] and Roberts and coworkers.[49] The sealed ampoule technique was utilized for the acetolyses and formolyses run above 50°. The solvolyses were run in buffered media except where noted. The trifluoroacetolysis procedure was essentially that of Peterson and coworkers.[50] The samples were quenched in methanol and the decrease in the ultraviolet absorption maximum at 273 mμ was followed.

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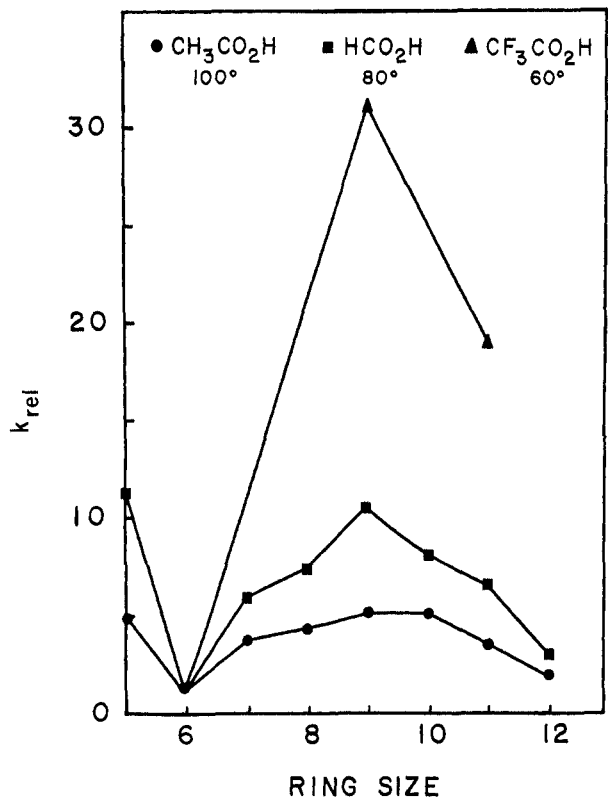

Figure 1.—Variation of the solvolysis rates (k_t) of the cycloalkylcarbinyl tosylates with the ring size.

Solvolysis Products.—The products produced under acetolysis conditions were determined. The cycloalkylcarbinyl tosylates were solvolyzed at about 120°. The analyses were performed by nmr or vpc or a combination of these two procedures. The procedure is described in the Experimental Section.

Ionization Constant Determinations.—As a possible probe into the inductive effect of the adjacent ring, the ionization constants of the five- through twelve-membered cycloalkanecarboxylic acids were determined in 50% aqueous ethanol. The procedure followed was essentially that of Hahn and coworkers with minor modifications.[51]

Results and Discussion

The calculated first-order titrimetric rates constants (k_t) for the acetolyses of the cycloalkylcarbinyl tosylates are tabulated in Table I.

The relative rate data (cyclohexylcarbinyl tosylate as the reference compound) are plotted in Figure 1. One notes a maximum in the acetolysis rates at the nine-membered ring carbinyl system.

Although the ring size effect in the tosylates studied is small, it is consistent for both acetolysis temperatures. The agreement of the rate data with previously published rates is generally good as shown in Table II.

The activation parameters are tabulated in Table III.

It is interesting to compare the general curve shape of Figure 1 with the plot of the ring strain *vs.* ring size data shown in Figure 2. The curve profiles are remarkably similar.

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TABLE I

CYCLOALKYLCARBINYL TOSYLATES. ACETOLYSIS RATE DATA[a]

Ring size	Temp, °C[b]	$k_t \times 10^5$ sec^{-1} [c]
5	100.0	2.54 ± 0.10
	130.0	38.10 ± 0.9
6	100.0	0.534 ± 0.021
	130.0	9.53 ± 0.26
7	100.0	1.92 ± 0.10
	130.0	33.7 ± 0.7
8	100.0	2.37 ± 0.10
	(100.0)	(2.33 ± 0.17)[d]
	130.0	44.7 ± 1.9
9	100.0	2.75 ± 0.13
	130.0	48.3 ± 2.8
10	100.0	2.68 ± 0.21
	(100.0)	(2.44 ± 0.21)[d]
	130.0	39.4 ± 3.2
11	100.0	1.89 ± 0.09
	130.0	31.8 ± 1.4
12	100.0	1.01 ± 0.08
	130.0	19.9 ± 0.7
β-*d*-8	100.0	1.80 ± 0.12

[a] A preliminary report of these data was presented at the First Northeast Regional Meeting of the American Chemical Society, Boston, Mass., Oct 15, 1968, Abstract No. 205. [b] Temperature deviation ±0.10°. [c] Average of two or more kinetic runs; the error is the average standard deviation. [d] Without sodium acetate.

TABLE II

ACETOLYSIS OF CYCLOALKYLCARBINYL TOSYLATES. RATE COMPARISONS WITH PUBLISHED DATA

Ring size	Temp, °C	$k_t \times 10^6$ sec^{-1} This study[a]	Lit. value	Ref
5	80	3.23	2.99[a,b]	27
5	80	3.23	3.25[a,c]	23
6	80	0.592	0.500[a,b]	27
6	100	5.34	5.06	28
6	100	5.34	3.88	25
7	65	0.360	0.383[a,b]	26

[a] With sodium acetate present. [b] Data published for *p*-bromobenzenesulfonate (OBs) ($k_{OBs} = 3k_{OTs}$). [c] Data published for *p*-nitrobenzenesulfonate (ONs) ($k_{ONs} = 11.1\ k_{OTs}$).

TABLE III

ACETOLYSIS OF CYCLOALKYLCARBINYL TOSYLATES. ACTIVATION PARAMETERS

Ring size	E_a, kcal	ΔS^*, eu
4[a]	25.1	−8.7
5	27.0 ± 0.8	−9.2 ± 2.7
6	28.7 ± 0.9	−7.7 ± 2.7
7	28.5 ± 1.0	−5.8 ± 3.5
8	29.3 ± 0.9	−3.2 ± 3.0
9	28.5 ± 1.1	−5.0 ± 3.9
10	26.6 ± 1.6	−10.1 ± 5.5
11	28.1 ± 0.9	−6.8 ± 3.2
12	29.8 ± 1.6	−3.5 ± 5.6
i-Bu[b]	28.9 ± 0.5	−7.8 ± 1.9

[a] Data from ref 22. [b] S. Winstein and H Marshall, *J. Amer. Chem. Soc.*, **74**, 1120 (1952).

The major acetolysis product (C-7 through C-12) as shown in Table IV is the 1-methylcycloalkene. This product could arise by a 1,2-hydride shift followed by proton loss from the tertiary cation or by elimination to form the methylenecycloalkane followed by rearrangement to the endocyclic olefin. Small amounts of 1-methylcycloalkyl acetates and methylenecyclo-

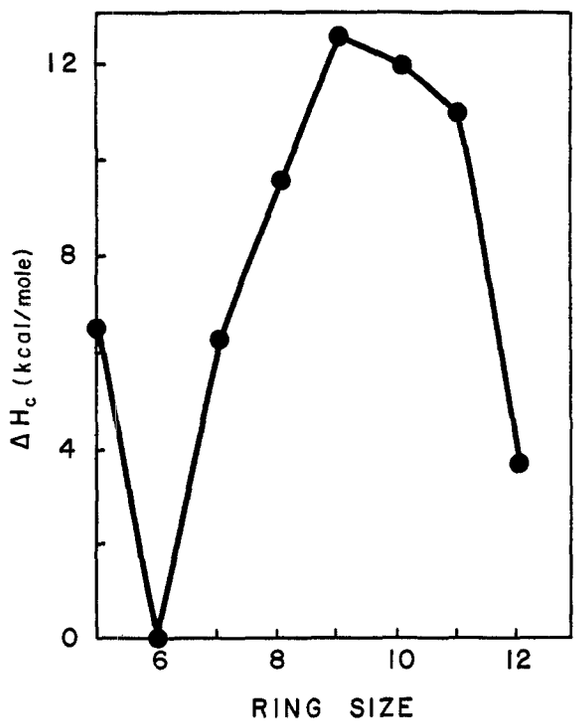


Figure 2.—Correlation of the ring size with the ring strain energy from combustion data.

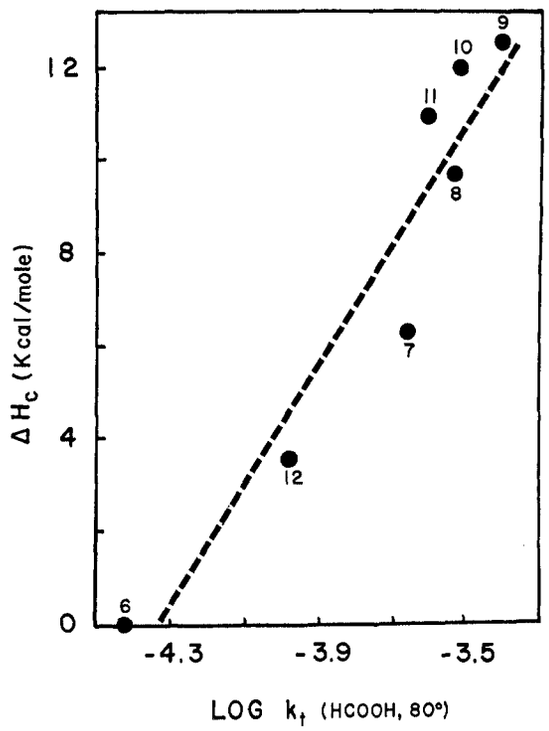
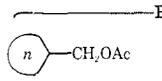
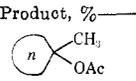
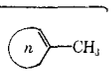


Figure 3.—Correlation of the formolysis rates (log k_t) of the cycloalkylcarbinyl tosylates at 80° with the ring strain energy from combustion data.

TABLE IV

CYCLOALKYLCARBINYL TOSYLATES. ACETOLYSIS DATA

Ring size, n	Product, % 		
4[a]	<1		
5[b]	60.5	1.1	1.6
6	49	5	46
7[c]	12.9	1.2	82.4
8	15.9	1.7	82.4
9	12		88
10	5		95
11	11		89
12	21.9	2.9	75.2
i-Bu[d]	~17		

[a] Also 78% cyclopentyl acetate; data from ref 22. [b] Also 9.2% cyclohexene and 27.6% cyclohexyl acetate. [c] Also 3.5% methylenecycloheptane. [d] Data from ref 2.

alkanes were also found along with unrearranged acetate. No ring expanded products were found except in the cases of cyclopentylcarbinyl tosylate and cyclobutylcarbinyl tosylate. These latter two cases will be discussed separately.

Since the acetolysis data for the cycloalkylcarbinyl tosylates showed a small rate variation among the compounds studied, it was of interest to utilize buffered formic acid as the solvent (less nucleophilic and higher ionizing power). The formolysis rate data (k_t) are tabulated in Table V and show the same rate pattern as the acetolysis (Figure 1) with a rate range of 11. The rate enhancement compared to acetic acid is about 100 (Table VI). The formolysis rates correlate to some extent (excluding cyclopentylcarbinyl tosylate) with ring strain as shown in Figure 3.

Trifluoroacetic acid is a much better ionizing solvent and a poorer nucleophile than acetic or formic acid.[2,5] A rate decrease would be expected for a substrate dependent on nucleophilic solvent participation. On the other hand its greater ionizing power would accentuate any rate enhancement due to hydrogen participation.

The trifluoroacetolysis of the six-, nine-, and eleven-membered ring carbinyl tosylates (Table VII and Figure 1) shows a further rate separation, a factor of 31 be-

TABLE V

CYCLOALKYLCARBINYL TOSYLATES. FORMOLYSIS RATE DATA

Ring size	Temp, °C[a]	$k_t \times 10^4$ sec^{-1}[b]
5	80.0	4.29 ± 0.30
6	80.0	0.388 ± 0.015
	100.0	2.83 ± 0.18
7	80.0	2.23 ± 0.10
8	80.0	2.86 ± 0.15
9	80.0	4.08 ± 0.23
10	80.0	3.11 ± 0.11
11	80.0	2.53 ± 0.08
12	80.0	1.11 ± 0.14[c]

[a] Temperature deviation ±0.10°. [b] Average of two kinetic runs; the error is the average standard deviation. [c] One run only.

TABLE VI

SOLVOLYSIS OF CYCLOALKYCARBINYL TOSYLATES. RATE COMPARISONS

Ring size	$k_{HCO_2H}/k_{CH_3CO_2H}$	$k_{CF_3CO_2H}/k_{CH_3CO_2H}$
5	133	
6	65	419
7	102	
8	114	
9	131	2460
10	88	
11	115	2030
12	109	

TABLE VII

CYCLOALKYLCARBINYL TOSYLATE. TRIFLUOROACETOLYSIS RATE DATA

Ring size	Temp, °C[a]	$k_t \times 10^5$ sec^{-1}[b]
6	60.0	2.13 ± 0.12
	80.0	14.2 ± 1.3
9	60.0	66.7 ± 6.2
11	60.0	40.2 ± 2.2

[a] Temperature deviation ±0.10°. [b] Average of two kinetic runs; the error is the average standard deviation.

tween the six- and nine-membered ring compounds. The rate increase for trifluoroacetolysis over acetolysis (Table VI) is greater than 2000 for the nine- and eleven-membered rings indicating a possible increase in hydrogen participation for these rings. Cyclohexylcarbinyl tosylate, on the other hand, exhibits a rate increase of only 419 in trifluoroacetic acid compared to the rate in acetic acid.

The activation data for cyclohexylcarbinyl tosylate in the three solvent systems are tabulated in Table VIII. Pritzkow and Schoppler[52] have solvolyzed a

TABLE VIII

SOLVOLYSIS OF CYCLOHEXYLCARBINYL TOSYLATE. ACTIVATION PARAMETERS[a]

Solvent[b]	$k_1 \times 10^{-9}$ sec^{-1} [a]	E_a, kcal	ΔS^*, eu[a]
CH_3CO_2H	0.309	28.7 ± 0.9	−7.7 ± 2.7
HCO_2H	41.4	26.0 ± 1.6	−7.0 ± 5.6
CF_3CO_2H	406	22.3 ± 2.2	−15.0 ± 7.6

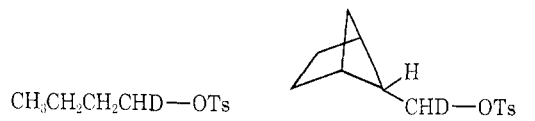
[a] Calculated at 25°. [b] Buffered with the sodium salt of the acid.

number of simple (RCH_2CH_2OTs where R = *n*-alkyl) primary alkyl tosylates in buffered acetic acid and reported second-order kinetics. Cyclohexylcarbinyl tosylate was also reported to show a second-order acetolysis rate in the presence of potassium acetate although no experimental data were given.[28]

As a check on the first-order reaction rates, cyclooctyl- and cyclodecylcarbinyl tosylates were solvolyzed in unbuffered acetic acid. First-order rate constants were obtained (Table I) with only 2 and 9% decreases, respectively, compared to the buffered studies, which are within the range of a normal salt effect.

The solvolysis rates (k_t) of isobutyl tosylate in ethanol, acetic acid, and formic acid have been analyzed in terms of competing k_Δ and k_s routes.[2] The magnitude of k_s was approximated by assigning the yield of unrearranged solvolysis product to this route with the remainder being assigned to k_Δ (hydrogen or methyl participation). In acetic acid (75°), 79% of the reaction proceeds through the k_Δ route. At 100°, 17% of isobutyl acetate is produced in the acetolysis reaction. In the trifluoroacetolysis of isobutyl tosylate no evidence for a second-order reaction was found as k_s was not affected by added sodium trifluoroacetate (second-order rate constants were observed for CH_3OTs, EtOTs, and *n*-PrOTs under these conditions). The k_Δ route predominates in the trifluoroacetolysis of isobutyl tosylate. Wiberg and Hess[22] have previously analyzed the solvolyses of isobutyl tosylate *via* SN1 and SN2 mechanistic routes. The validity of their product dissection must be questioned since no account is taken in this analysis of the route by which rearranged olefin arises.[2]

Streitwieser[53] has solvolyzed chiral 1-*d*-*n*-butyl tosylate (**1**) in formic acid and obtained inverted 1-*d*-*n*-butyl formate. Wiberg and Hess[22] have prepared and solvolyzed optically active *endo*-bicyclo[2.1.1]-hexane-5-meth-d_1-yl tosylate (**2**) in unbuffered acetic acid at 108°. The primary alcohol that was isolated after separation and reduction with lithium aluminum



1 **2**

hydride had undergone complete inversion, thus indicating the k_s origin of the unrearranged acetate.

Product studies were not done on chiral cycloalkylcarbinyl tosylates. However, the above reported cases of inversion in the solvolysis of primary tosylates argue strongly for a k_s route to unrearranged acetate products.

Therefore, the product data were used to separate the titrimetric rate constants (k_t) into k_Δ and k_s paths[2] using the following relationships.

$$k_t = k_\Delta + k_s \qquad \frac{k_\Delta}{k_s} = \frac{P_1 \text{ (rearranged)}}{P_s \text{ (unrearranged)}}$$

The data are given in Tables IX and X. The rates

TABLE IX

RATES OF k_Δ AND k_s PATHS FOR THE ACETOLYSIS OF CYCLOALKYLCARBINYL TOSYLATES AT 100°

Ring size	$k \times 10^5$ sec^{-1}	
	k_s	k_Δ
4[a]	0.43	42
5	1.55	0.99
6	0.26	0.27
7	0.25	1.67
8	0.37	1.98
9	0.33	2.42
10	0.13	2.57
11	0.21	1.67
12	0.22	0.78
i-Bu[b]	0.06	0.32

[a] Data from ref 22, k_Δ route with carbon participation. [b] Data from ref 2.

TABLE X

SOLVOLYSIS OF CYCLOALKYLCARBINYL TOSYLATES. RELATIVE RATES

n	k_t CH_3CO_2H, 100°	k_t CH_3CO_2H, 130°	k_Δ[a] CH_3CO_2H, 100°	HCO_2H,[b] 80°	CF_3CO_2H,[b] 60°
5	4.8	4.0	3.7	11.1	
6	1.0	1.0	1.0	1.0	1.0
7	3.6	3.5	6.2	5.8	
8	4.4	4.7	7.3	7.4	
9	5.2	5.1	9.0	10.5	31.3
10	5.1	4.1	9.5	8.0	
11	3.5	3.3	6.2	6.5	18.9
12	1.9	2.1	2.9	2.9	

[a] Corrected for k_s product. [b] Use of k_t; no products were determined, but k_Δ probably constitutes the major pathway.

(52) W. Pritzkow and H. Schoppler, *Chem. Ber.*, **95**, 834 (1962).

(53) A. Streitwieser, Jr., *J. Amer. Chem. Soc.*, **77**, 1117 (1955).

for the k_s and k_Δ paths shown in Table IX are slightly greater than for isobutyl tosylate, with the exception of cyclopentylcarbinyl tosylate, a special case. A rate spread of about 10 is shown for the k_Δ path.

A note of caution should be introduced here. Schleyer and coworkers[14] have obtained chiral adamantylcarbinyl acetate which showed complete *retention* of configuration from the acetolysis of chiral adamantylcarbinyl tosylate (d_1). The adamantylcarbinyl system cannot be directly compared to the cycloalkylcarbinyl systems. Still, the possibility must be kept in mind that solvent attack on an intermediate hydrogen-bridged ion could also yield the cycloalkylcarbinyl acetates which would have the retained configuration; however, the tertiary product would be strongly favored.

Let us compare the relative rates in the three solvents as shown in Table X. The relative acetolysis rates at the two temperatures are about the same, and correction of the acetolysis rates for the k_s product leads to a relative rate sequence which is virtually identical with that for the formolyses (in formic acid the k_Δ route predominates). The trifluoroacetolyses show a further expanded rate range and in the same direction.

Bartlett and coworkers[23] and Kotani and coworkers[24] have subjected, respectively, cyclopentyl- and cyclohexylcarbinyl acetates to acetolysis conditions and found no rearrangement products. Thus the k_s product is not a source of further products. Methylenecyclopentane has been shown to rearrange to 1-methylcyclopentene and 1-methylcyclopentyl acetate under acetolysis conditions.[23] As a further probe into the elimination mechanism, methylenecyclooctane and methylenecyclodecane were subjected to acetolysis conditions and were found to rearrange to the corresponding 1-methylcycloalkenes. The tertiary acetates, 1-methylcyclohexyl acetate and 1-methylcyclododecyl acetate, formed the corresponding 1-methylcycloalkenes under acetolysis conditions.

To distinguish between a mechanism involving a 1,2-hydride shift or an elimination mechanism, β-*d*-cyclooctylcarbinyl tosylate was solvolyzed. The acetolysis product ratios were comparable to those found for the undeuterated compound. The 1-methylcycloalkene contained a deuterium in the methyl group corresponding to 100% 1,2-hydride shift (nmr analysis). The unrearranged acetate still contained the β-deuterium, further substantiating the k_s nature of its origin.

In the acetolysis of β-*d*-cyclooctylcarbinyl tosylate at 100°, an isotope effect of 1.32 (k_H/k_D) was observed. Winstein and Takahashi[54] have reported a k_H/k_D ratio of 2.26 at 25° (1.85 calculated at 100°) for the acetolysis of 3-*d*-3-methyl-2-butyl tosylate. Since the product arises mainly from hydrogen (deuterium) migration, this value may indicate the degree of hydrogen participation at the transition state.

A free-energy plot of k_t (acetolysis rates) of the cycloalkylcarbinyl tosylates *vs.* the observed cycloalkyl tosylate acetolysis rates is shown in Figure 4. The agreement is good considering the different nature of the transition states involved (solvent participation effects) and prompts some conclusion. The dependence of cycloalkyl tosylates rates on relief of ring strain

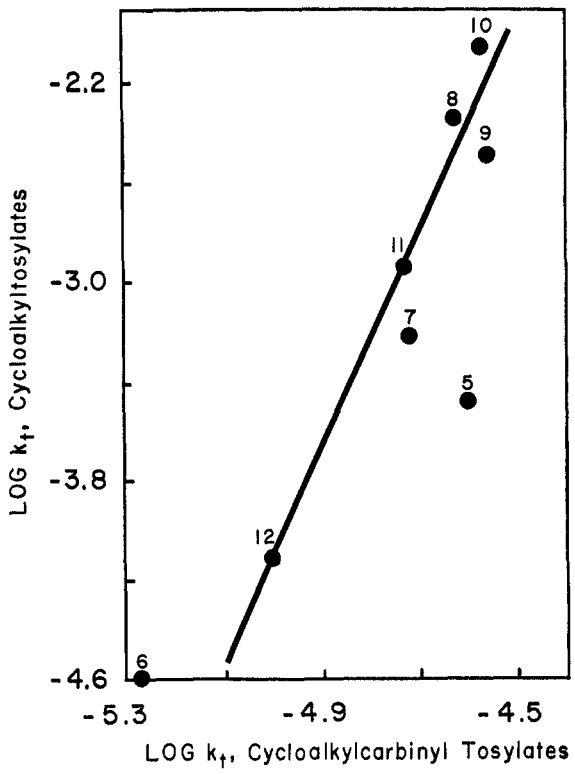


Figure 4.—Correlation of the acetolysis rates (log k_t) of the cycloalkyl tosylates at 50° with the acetolysis rates (log k_t) of the cycloalkylcarbinyl tosylates at 100°.

has been proposed.[55] Linear relationships have been found in the alicyclic series of rings five through ten, *e.g.*, the borohydride reductions of cycloalkanones and the acetolyses of the cycloalkyl tosylates. The correlation of Figure 4 (five ring excluded) might be construed as evidence for hydrogen participation as the major path with resultant partial release of ring strain in the solvolysis of the cycloalkylcarbinyl tosylates. A correlation between rates and expected hydrocarbon strain release has been proposed as evidence for anchimeric assistance in the rearrangement of a series of esters derived from bicyclo[*m.n.*0]alkane-1-methanols.[56]

The mechanistic route for the six- through twelve-membered cycloalkylcarbinyl tosylates appears to be an ionization anchimerically assisted by hydrogen participation (k_Δ) to lead to a tertiary cation along with a competitive pathway with nucleophilic solvent attack at the primary center (k_s) to lead to unrearranged acetate (Scheme I).

The parallelism of the solvolytic rate profile with the ring size *vs.* ring strain plot suggests that hydrogen bridging is to some extent related to partial release of internal ring strain; *i.e.*, rings of greatest internal strain can release nonbonded repulsions by hydrogen participation at the transition state thus making the ring carbon more sp^2 in character. In solvents of increasingly poorer nucleophilicity, the migrating hydrogen would supply a greater proportion of the nucleophilic driving force ($k_\Delta \gg k_s$).

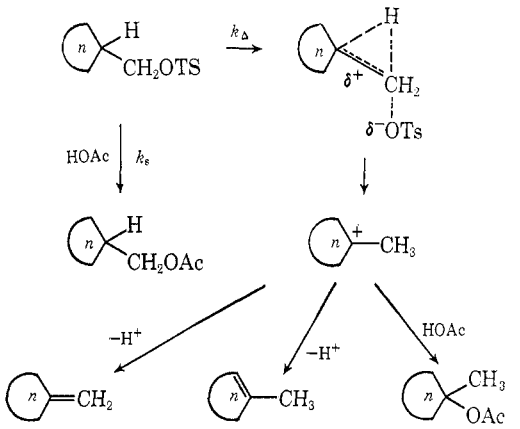
In the case of cyclohexylcarbinyl derivatives, there is little tendency for a hybridization change of ring carbon from sp^3 to sp^2 since the ring conformation

(54) S. Winstein and J. Takahashi, *Tetrahedron*, **2**, 316 (1958).

(55) H. C. Brown and K. Ichikawa, *ibid.*, **1**, 221 (1957).

(56) W. G. Dauben, J. L. Chitwood, and K. V. Scherer, Jr., *J. Amer. Chem. Soc.*, **90**, 1014 (1968).

SCHEME I
ACETOLYSIS OF CYCLOALKYLCARBINYL TOSYLATES. REACTION PATHWAYS

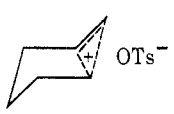


is already strain-free. This is reflected in the slower rate of acetolysis of cyclohexylcarbinyl tosylate and the equality of the k_s and k_Δ contributions to k_t (Table IX).

Cyclopentylcarbinyl and cyclobutylcarbinyl tosylates are special cases. The formolysis and acetolysis rates of these compounds are as high as for cyclononyl- and cyclodecylcarbinyl tosylates. The acetolysis products (Table IV) included 37% ring expanded products, and Bartlett[23] has found 80% ring expansion in the acetolysis of cyclopentylcarbinyl *p*-nitrobenzenesulfonate. Separation of the tosylate rate into k_Δ and k_s paths gives a k_s (Table IX) which is inconsistent with the other values of the k_s reaction for the series. Bartlett obtained only 5% unrearranged acetate, but the difference may be explained on the basis of difference in leaving groups and a much different temperature.

Olah and coworkers[57] have studied the formation of 1-methylcyclopentyl cation from various cyclohexyl and methylcyclopentyl precursors, in the appropriate antimony pentafluoride systems. Although they have found this cation to be the only species present at −60°, equilibrium mixtures at 25° contain 77% cyclohexane derivatives. They favor a protonated cyclopropane intermediate in the reaction mechanism.

Bartlett[23] proposed the nonclassical "stage" **3** as a transition state or intermediate in the acetolysis of cyclopentylcarbinyl *p*-nitrobenzenesulfonate. Judging from the agreement in rates observed, it seems logical



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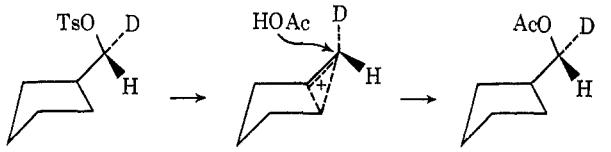
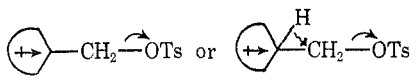
that the tosylate would solvolyze through a similar "stage." One of Bartlett's basic objections to direct initial formation of the classical ion was the difference in cyclohexene–cyclohexyl acetate ratios between the solvolyses of the cyclopentylcarbinyl ester (3.4:1) and the cyclohexyl ester (7.7:1). If the classical ion were formed directly by carbon migration, these ratios should be the same. The "folded" nonclassical ion would be geometrically less favorable for proton elimination than the flatter classical ion.

The existence of this ion also might help to explain the higher apparent k_s rate previously noted. Solvent attack on **3** could yield cyclopentylcarbinyl acetate, as well as ring expanded products. Cyclopentylcarbinyl acetate with retained configuration would be expected.



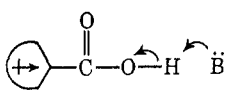
If one compares the ring expanded product fraction with that from the 1,2-hydride shift, a carbon to hydrogen participation ratio of 13.6:1 is obtained for the tosylate and a ratio of 5.3:1 is obtained for the *p*-nitrobenzenesulfonate. It would then appear that as the leaving group becomes better, carbon participation becomes less important. In the extremely energetic deamination of cyclopentylcarbinyl amine,[33] a carbon–hydrogen migration ratio of 4:1 was found which is consistent with this theory. This may be due to an entropy effect which requires more substrate and solvent reorganization for a carbon shift than for hydrogen.

Ionization Constants of Cycloalkanecarboxylic Acids.—Inductive effects of the ring may also play a role in the solvolysis of the cycloalkylcarbinyl tosylates.



Electron donation by the ring would stabilize the species proceeding through the k_s route or the intermediate formed *via* the k_Δ route. In addition, the hydrogen migration (k_Δ) would lead to release of internal nonbonded interactions.

As a probe into the inductive contribution to the solvolysis reaction of the cycloalkylcarbinyl tosylates, it would be desirable to have a model reaction which is dependent only on the inductive effect of the ring. The ionization of cycloalkanecarboxylic acids can perhaps provide such a model.



In the acids, an increase in electron density at the carbonyl carbon would decrease the ease of ionization thus decreasing the acidity. As the ring size is increased, one might expect a progressive decrease in acidity due to the inductive contribution of the methylene groups. This decrease should level off, as the effect of an additional methylene group is attenuated at a greater distance from the carboxyl group. An inverse correlation should be expected between the ionization constants of the cycloalkanecarboxylic acids and the solvolysis rates of the cycloalkylcarbinyl tosylates (if inductive effects only are operative and solvent effects are mutually similar).

The ionization constants of the cycloalkanecarboxylic acids of ring size five through twelve were measured. The data, presented in Table XI and Fig-

(57) G. A. Olah, J. M. Bollinger, C. A. Cupas, and J. Lukas, *J. Amer. Chem. Soc.*, **89**, 2692 (1967).

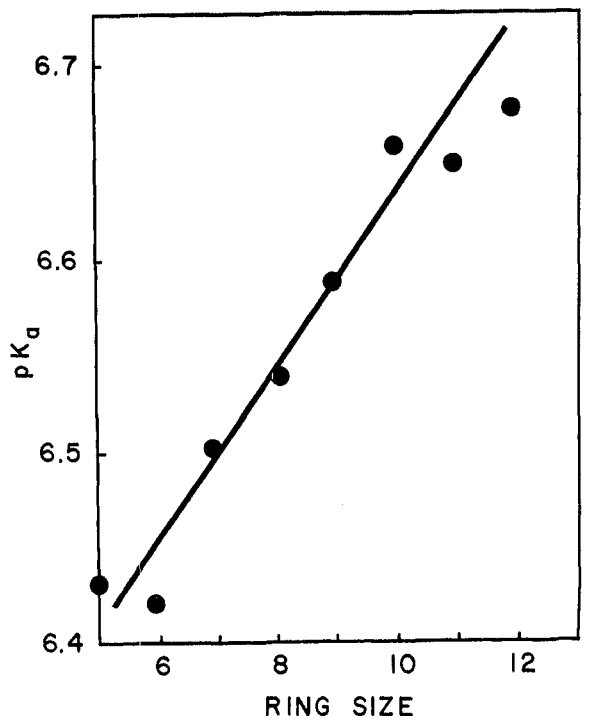


Figure 5.—Plot of the pK_a of the cycloalkanecarboxylic acids *vs.* the ring size.

TABLE XI
IONIZATION CONSTANTS OF CYCLOALKYLCARBOXYLIC ACIDS

Ring size	pK_a	$K_a \times 10^7$
5	6.43 ± 0.01	3.73
6	6.42 ± 0.01	3.79
7	6.50 ± 0.02	3.13
8	6.54 ± 0.01	2.87
9	6.59 ± 0.01	2.55
10	6.66 ± 0.01	2.17
11	6.65 ± 0.01	2.21
12	6.68 ± 0.02	2.08
i-Bu	6.24 ± 0.01	5.68

ure 5, show a steady increase in pK_a up to about the ten-membered ring, leveling off at that point, presumably due to the attenuation of the inductive effect.

Correlation of the pK_a values with the formolysis rates of the cycloalkylcarbinyl tosylates is reasonable for the six- through nine-membered rings, as shown in Figure 6. This lends some support to the idea that the hydrogen participation in these cases may be partially inductive in nature. However, solvation effects are also of importance in the measurement of ionization constants, and the relative magnitude of these effects is impossible to assess. The ionization constants for the cycloalkanecarboxylic acids were measured in 50% aqueous ethanol, while the solvolyses of the cycloalkylcarbinyl tosylates were done in acetic, formic, and trifluoroacetic acids.

Conformational effects also are important, although the carbinyl tosylate group would be expected to be in an equatorial position, well away from the bulk of the ring. The larger, less rigid rings might serve to inhibit solvation of the carbinyl tosylate group, thus offsetting the greater inductive effect. If this occurred, however, the rate decrease should also be reflected in the k_s rates, which is not the case (see Table IX).

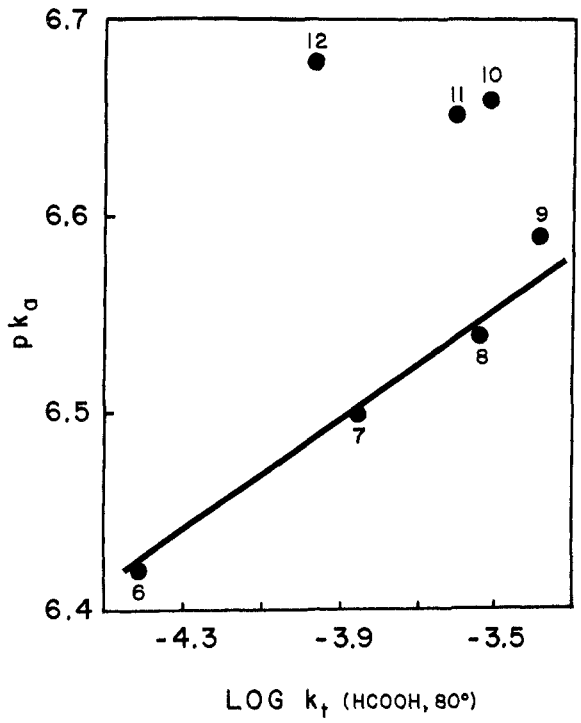


Figure 6.—Correlation of the formolysis rates (log k_t) of the cycloalkylcarbinyl tosylates at 80° with the pK_a values of the cycloalkanecarboxylic acids.

Conclusions

The solvolyses of the cycloalkylcarbinyl tosylates with ring sizes of six through twelve proceed with a rate spread due to nucleophilic hydrogen bridging at the transition state. The intermediate 1-methylcycloalkyl cation produced by the 1,2-hydride shift then yields the 1-methylcycloalkene by loss of a proton or reacts with solvent to form the tertiary ester.

The hydrogen bridging is directly related to the relief of ring strain offered by formation of the sp^2 center in the ring and partially to an inductive effect due to electron release by the ring, which could also stabilize the developing positive center. A direct SN2 displacement by solvent (k_s), which yields the unrearranged ester, is competitive with the hydrogen bridging (k_A). The reaction pathways are summarized in Scheme I.

Cyclopentylcarbinyl tosylate appears to solvolyze by way of a nonclassical ion yielding ring-expanded products. The considerably higher "apparent" k_s rate may be evidence to indicate that the nonclassical ion is indeed an intermediate.

Experimental Section

Nuclear magnetic resonance spectra (nmr) were taken on a Varian A-60 spectrometer. The peak positions are reported in ppm from internal tetramethylsilane as the reference and carbon tetrachloride as solvent. Ultraviolet measurements were taken with a Cary 14 spectrophotometer. Vapor phase chromatographic analyses were performed on an Aerograph A-90-P instrument. The microanalyses were performed by the MHW Laboratories, Garden City, Mich. All melting and boiling points are uncorrected.

A. Synthetic Section. General Procedures. Thioketalization. Method A.[58]—The β-keto ester (5 g) was dissolved in 15 ml of 1,2-ethanedithiol, and 1 ml of boron trifluoride etherate

(58) J. F. Tinker, *J. Org. Chem.*, **16**, 1417 (1951).

was added. The reaction mixture was protected by a drying tube, left at room temperature overnight, and then heated at 60° for 2 hr. After cooling, 25 ml of ether was added, and the reaction mixture washed first with several portions of 10% aqueous sodium hydroxide, then with saturated aqueous sodium chloride, and dried over anhydrous magnesium sulfate. The ether was removed on an aspirator, and the residue was distilled at reduced pressure to yield the thioketal ester.

Desulfurization. Method B.[59]—Active Raney nickel (5 teaspoons of 50% slurry in water, Wm. Grace no. 28, ~40 g of Ni) was placed in a 250-ml erlenmeyer flask equipped with a ground glass joint and fitted with a condenser. The slurry was washed with five 50-ml portions of ethanol to remove the water, and 4 g of thioketal dissolved in 50 ml of ethanol was added. The mixture was heated at gentle reflux (bath temperature 80–90°) for 3 days.

The reaction mixture was cooled and filtered, and the nickel residue was washed with methylene chloride. The filtrate was dried over anhydrous magnesium sulfate, the solvent removed on an aspirator, and the residue distilled at reduced pressure to yield the cycloalkyl carboxylic ester.

Lithium Aluminum Hydride Reduction. Method C.[45]—A suspension of 2.5 g of lithium aluminum hydride in 75 ml of dry ether was stirred at room temperature in a flask equipped with a drying tube, condenser, and addition funnel. A solution of ester to be reduced (0.1 mol) in 20 ml of dry ether was added dropwise with stirring. After addition was complete, the reaction mixture was allowed to reflux for 2 hr and cooled. The excess lithium aluminum hydride was destroyed by careful addition of water, and the resulting salts were dissolved with 10% hydrochloric acid. The layers were separated and the aqueous phase was extracted twice with ether. The combined organic phases were washed with saturated sodium chloride and dried over anhydrous magnesium sulfate, and the ether was removed on the aspirator. The residue was distilled at reduced pressure.

Tosylation. Method D.[45]—The alcohol to be tosylated was dissolved in dry pyridine (3 ml/1 g of alcohol) and cooled to 0° in an ice bath. The *p*-toluenesulfonyl chloride (10% molar excess) was dissolved in 3 ml of dry pyridine and also cooled to 0°. The two solutions were mixed, and the tightly stoppered flask was placed in the refrigerator overnight. The reaction mixture was poured into ice water, and the mixture extracted with petroleum ether. The extract was washed with 10% hydrochloric acid, 10% sodium bicarbonate, and water. The organic phase was dried over anhydrous magnesium sulfate and placed in the freezer to crystallize.

Hydrolysis. Method E.[60]—The ester to be hydrolyzed (2 g) was added to 20 ml of 25% sodium hydroxide and refluxed overnight. The reaction mixture was cooled, acidified to congo red with 10% hydrochloric acid, and extracted with ether. The ether extract was washed with saturated sodium chloride and dried over anhydrous magnesium sulfate, and the ether was removed on the aspirator. The residue was distilled at reduced pressure.

Acetylation of the Cycloalkylcarbinols and Cycloalkanols. Method F.[61]—The alcohol to be esterfied (2 g) was dissolved in 20 ml of dry pyridine, and 8 ml of acetic anhydride was added. The mixture, protected with a drying tube, was refluxed for 1 hr and cooled.

The reaction mixture was poured into 75 ml of ice water and then extracted with methylene chloride. The extract was washed with 10% hydrochloric acid, then with water, and dried over anhydrous potassium carbonate, and the solvent was removed on an aspirator. The residue was distilled at reduced pressure.

Preparation of Reference *tert*-Acetates from the Corresponding Ketones. Method G.—Magnesium turnings (0.06 g-atom) were placed in a 100-ml flask fitted with a condenser and an addition funnel and protected with a drying tube. A solution of methyl iodide (4.26 g, 0.03 mol) in 20 ml of dry ether was slowly added with stirring, maintaining a slow reflux rate. The mixture was allowed to reflux an additional 15 min, and a solution of 0.025 mol of the parent ketone in 10 ml of ether was added slowly, with cooling. After addition was complete, the mixture was stirred for 10 min, and then 20 ml of acetic anhydride was added with stirring. The reaction mixture was poured into ice water and extracted with ether. The extract was washed with saturated aqueous sodium bicarbonate and aqueous sodium chloride and dried over anhydrous magnesium sulfate; the ether was removed on an aspirator. The residue was distilled at reduced pressure.

Thioketals.—The thioketals were prepared from the β-keto esters *via* the general procedure A and the physical properties and analytical data are detailed in Table XII.

TABLE XII

THIOKETAL FORMATION USING METHOD A

Thioketal ring size	Registry no.	% yield	Bp (mm), mp, °C
8[a]	26600-30-6	84	124 (0.15)
9[a]	26600-31-7	83	39–41
10[a]	26600-32-8	73	146 (0.1)
12[a]	26600-33-9	89	95–96

[a] Satisfactory combustion analytical data (±0.35) have been obtained on these compounds. Ed.

Carbethoxycycloalkanes.—The general procedure B was utilized to desulfurize the thioketals. The experimental results are tabulated in Table XIII.

TABLE XIII

ESTERS FORMED BY DESULFURIZATION USING METHOD B

Carbethoxycycloalkane ring size	Registry no.	% yield	Bp (mm), °C
8[a]	26600-34-0	87	83 (0.2)
9[a]	26600-35-1	81	75 (0.1)
10[a]	26600-36-2	87	83 (0.2)

[a] Table XII, footnote *a*. Ed.

Cycloalkylcarbinols.—The general procedure C was utilized to convert the esters to the corresponding cycloalkylcarbinols. The results are summarized in Table XIV.

TABLE XIV

CYCLOALKYLCARBINOLS PREPARED BY PROCEDURE C

Cycloalkylcarbinol ring size	Registry no.	% yield	Bp (mm), °C
7[a]		92	45–48 (0.08)[b]
9[c]	26600-37-3	87	79–80 (0.5)
10[c]	3668-38-0	89	86–88 (0.3)

[a] Starting from cycloheptanecarboxylic acid. [b] Reference 45, bp 79–82° (4 mm). [c] Table XII, footnote *a*. Ed.

Cyclodecylcarbinol from Cyclododecanone.—The synthesis of 1-carbomethoxycycloundecene was accomplished from cyclododecanone following the procedure of Garbisch and Wohllebe.[47] This ester was converted to cycloundecanone, and cycloundecanone was converted to 1-carbomethoxycyclodecene. Reduction of the latter compound with lithium aluminum hydride in refluxing 1,2-dimethoxyethane led to cyclodecylcarbinol. This method constitutes an efficient synthesis of this carbinol.

Preparation of the Tosylates.—The general procedure described in method D was followed and the results are listed in Table XV. The nmr data are listed in Table XVI.

β-*d*-Cyclooctylcarbinyl Tosylate. A. β-*d*-Carbethoxycyclooctane.[46]—A solution of triphenylmethylsodium (*ca.* 0.0452 mol) was prepared according to the method of Renfrow and Hauser[62] and transferred under nitrogen pressure to a 1-l. flask equipped with a magnetic stirrer. Carbethoxycyclooctane (2.54 g, 0.0138 mol) was added, and the reaction mixture was stirred at room temperature under nitrogen. After 1 hr, 20 ml (0.334 mol) of ethanol-d_1 was added, and the mixture was stirred for 2 hr. Dilute acetic acid (10%, 200 ml) was added, the mixture was transferred to a separatory funnel, and the aqueous layer was discarded. The ether solution was washed with water and

(59) R. Mozingo, D. E. Wolf, S. A. Harris, and K. Folkers, *J. Amer. Chem. Soc.*, **65**, 1013 (1943).

(60) O. Kamm and J. B. Segur, "Organic Synthesis," Coll. Vol. I, Wiley New York, N. Y., 1941, p 391.

(61) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," Wiley, New York, N. Y., 1964, p 247.

(62) W. B. Renfrow and C. R. Hauser, "Organic Synthesis," Coll. Vol. II, Wiley, New York, N. Y., 1943, p 607.

TABLE XV

CYCLOALKYLCARBINYL TOSYLATES

Cycloalkylcarbinyl tosylate ring size	Registry no.	% yield	Mp, °C
5[a]	21856-53-1	98	8–11
6	3725-11-9	79	30–31[b]
7[a]	16472-98-3	94	41–42
8[a]	16472-97-2	77	23–24
9[a]	26600-43-1	84	32.5–34
10[a]	26630-78-4	86	22–24
11[a]	26600-44-2	91	18.5–20
12[a]	26600-45-3	64	64–65

[a] Table XII, footnote *a*. Ed. [b] C. F. Wilcox, Jr., and S. S. Chibber, *J. Org. Chem.*, **27**, 2332 (1962), mp 32–33°.

TABLE XVI

NMR SPECTRA OF THE CYCLOALKYLCARBINYL TOSYLATES

Cycloalkylcarbinyl tosylate ring size	A_2B_2, q, 4 H aromatic H	d, 2 H, RCH_2OTs	s, 3 H, $-CH_3$	Ring envelope
5	7.49	3.82	2.45	0.9–1.9, 9 H
6	7.51	3.75	2.45	1.0–1.8, 11 H
7	7.50	3.71	2.41	1.0–2.0, 13 H
8	7.51	3.72	2.43	1.49, 15 H (1.71, shoulder)
9	7.50	3.72	2.42	1.45, 17 H
10	7.50	3.72	2.48	1.45, 19 H
11	7.50	3.78	2.42	1.38, 21 H
12	7.51	3.80	2.44	1.29, 23 H

saturated sodium chloride and dried over anhydrous magnesium sulfate; the ether was removed on the aspirator. The residue was distilled at reduced pressure yielding β-*d*-carbethoxycyclooctane in 77% yield (2.08 g), bp 53–56° (0.2 mm), bp 51–53° (0.2 mm), for the undeuterated compound. The nmr spectrum showed absorption at δ 4.05 (q, 2 H, $CH_3\mathbf{CH_2}O$–), 1.58 (envelope, 14 H, ring), and 1.22 (t, 3 H, $\mathbf{CH_3}CH_2O$–). The absorption for the β proton at δ 2.4 in the β-H ester was absent.

B. β-*d*-Cyclooctylcarbinol.—Method C was used to convert 2.00 g (0.17 mol) of the parent ester to β-*d*-cyclodecylcarbinol in 98% yield (1.47 g). The product distilled at 54–56° (0.1 mm). The nmr spectrum showed absorption at δ 5.21 (s, 1 H, –**OH**), 3.28 (s, 2 H, $R\mathbf{CH_2}OH$), and 1.59 (envelope, 14 H, ring).

C. β-*d*-Cyclooctylcarbinyl Tosylate.—Method D was used to convert 1.47 g (0.0102 mol) of the parent alcohol to β-*d*-cyclooctylcarbinyl tosylate in 96% yield (2.82 g). The product was recrystallized from pentane and was an oil at room temperature. The nmr spectrum showed absorption at δ 7.51 (A_2B_2 quartet, 4 H, aromatic protons), 3.73 (s, 2 H, $R\mathbf{CH_2}OTs$), and 1.48 (envelope, 14 H, ring).

Reference Acetates.—The reference primary and secondary acetates were prepared *via* general procedure F. Some of the substances were not obtained analytically pure but structures were unambiguously assigned by nmr spectroscopy. These data are tabulated in Tables XVII and XVIII.

The general procedure G was used to prepare the tertiary acetates listed in Table XIX, which also summarizes the nmr data.

Carboxylic Acids.—Cyclooctane-[63] and cyclononanecarboxylic acids were prepared *via* the hydrolysis following procedure E of the corresponding carbethoxycycloalkanes. The hydrolysis of 1-carbomethoxycyclodecene yielded 1-cyclodecenecarboxylic acid. The 1-cyclodecenecarboxylic acid was catalytically hydrogenated to cyclodecanecarboxylic acid.[63] Cycloundecanecarboxylic acid was prepared *via* catalytic hydrogenation of 1-cycloundecenecarboxylic acid which had been prepared from hydrolysis *via* procedure E of 1-carbomethoxycycloundecene (prepared from cycloundecanone using the procedure of Garbisch and Wohllebe[47]). Cyclododecanecarboxylic acid was prepared *via* hydrolysis of carbethoxycyclododecane. The nmr data for the cycloalkanecarboxylic acids are tabulated in Table XX along with pertinent literature references.

B. Kinetics (Kinetic Procedures).—The procedures described below are well known and closely follow the references cited. The standard acetolysis technique was used below 100° and the sealed ampoule technique for higher temperature acetolyses and for the formolyses.

Acetolysis (Standard Technique).[48,49]—The tosylate to be solvolyzed (0.2–0.7 mmol) was weighed into a 25-ml volumetric flask and dissolved in 10 ml of a 0.1 *N* solution of sodium acetate in acetic acid. The flask was immersed in a constant temperature bath and allowed to come to temperature equilibrium. Aliquots (1-ml portions) were pipetted into 6 ml of 50:50 pentane–acetic acid quench solution contained in a 25-ml erlenmeyer. One drop of 1% crystal violet indicator in acetic acid was added, and the sample was titrated with 0.025 *N* perchloric acid in acetic acid. The first sample was taken as zero time; for each sample, the time, bath temperature, and titrant volume were recorded. The infinity sample was taken after at least 12 half-lives had elapsed. The bath temperature in general varied to the extent of ±0.05°.

Acetolysis (Sealed Ampoule Technique).—The tosylate to be solvolyzed (0.5–0.9 mmol) was weighed into a small flask and dissolved in 10.0 ml of a 0.1 *N* solution of sodium acetate in acetic acid. Nine 1-ml aliquots were removed and sealed in small glass ampoules. The ampoules were placed in a constant temperature bath and allowed to come to temperature equilibrium. The first sample was taken as zero time. Each ampoule was rinsed with ether to remove traces of bath oil, carefully wiped, broken, and placed in a 125-ml erlenmeyer. A quench of 50:50 pentane–acetic acid (6 ml) and two drops of 1% crystal violet in acetic acid were added. The sample was titrated with standard 0.025 *N* perchloric acid in acetic acid. The time, titrant volume, and bath temperature were recorded for each sample; the temperature varied over a ±0.1° range. The infinity sample was allowed to remain in the bath for at least 12 half-lives.

Acetolysis (Unbuffered Technique).—The procedure was the same as for the standard and sealed ampoule techniques, except that the tosylate was dissolved in 10.00 ml of stock acetic acid, and 1 ml of 0.1 *N* sodium acetate in acetic acid was added with the quench solution to neutralize the *p*-toluenesulfonic acid formed during the reaction. The excess sodium acetate was titrated as for the other techniques.

Formolysis.—The formolysis procedure was exactly the same as for the sealed ampoule acetolysis technique, except that sodium formate in formic acid was used in place of sodium acetate in acetic acid.

Trifluoroacetolysis.[50]—The tosylate to be solvolyzed was weighed into a 25-ml flask and dissolved in 10.00 ml of a 0.125 *N* solution of sodium trifluoroacetate in trifluoroacetic acid. Eight aliquots of about 1.2 ml were removed and sealed in small glass ampoules. The ampoules were placed in a constant temperature bath and allowed to come to temperature equilibrium; the first sample was taken as zero time. Each ampoule was removed from the bath, quickly cooled to room temperature, opened, and a 1-ml aliquot was removed. The aliquot was quenched by pipetting directly into about 45 ml of methanol in a 50-ml volumetric flask. The flask was then made up to the mark with methanol, and the ultraviolet absorbance was measured at the 273.0 mμ maximum. The spectrophotometer was zeroed at 280.0 mμ with the actual sample. The time, uv absorbance, and bath temperature were recorded for each sample; the temperature varied over ±0.1°. The infinity sample was allowed to remain in the bath for at least 7 half-lives.

Calculations (Titrimetric Procedures).—The first-order titrimetric rate constants and the activation parameters were calculated according to the standard procedures.[64] The calculations were performed on an IBM computer using an appropriate program. The data treatment was the same for the spectrophotometric monitoring of the trifluoroacetolysis except that absorption data were used in the first-order rate expression.

Error Treatment.—The error in the activation energy was calculated according to the procedure outlined by Wiberg.[65]

(63) J. G. Traynham and J. S. Dehn, *J. Amer. Chem. Soc.*, **89**, 2139 (1967).

(64) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," Wiley, New York, N. Y., 1964.

(65) K. B. Wiberg, "Physical Organic Chemistry," Wiley, New York, N. Y., 1964, p 378.

TABLE XVII

CYCLOALKYLCARBINYL ACETATES FROM PROCEDURE F

Cycloalkylcarbinyl acetate ring size	Registry no.	% yield	Bp (mm), °C	d, 2 H, RCH_2OAc	s, 3 H, $-OCOCH_3$	Ring envelope
5		51	29–31 (1)[a]	3.80	1.95	1.1–1.8, 9 H
6	937-55-3	66	39–40 (0.7)[b]	3.90	1.95	1.0–1.9, 11 H
7	26600-50-0	54	55–56 (0.7)	3.79	1.95	1.6–1.8 13 H
8	26600-51-1	88	110 (11)	3.78	1.98	1.5–1.6, 15 H
9	26630-81-9	83	(Crude)	3.81	1.98	1.51, 17 H
10[c]	26600-52-2	42	(Crude)	3.82	1.95	1.51, 19 H
11	26600-53-3	63	100–101 (0.7)	3.82	1.98	1.46, 21 H
12	26660-54-4	52	116 (0.7)	3.85	1.98	1.38, 23 H

[a] R. C. Schreyer, *J. Amer. Chem. Soc.*, **74**, 3242 (1954), bp 45–50° (5 mm). [b] A. Favorsky and I. Borgmann, *Chem. Ber.*, **40**, 4863 (1907), bp 199–201° (740 mm). [c] Also contaminated with 51% 1-methylcyclodecene and 7% methylenecyclodecane.

TABLE XVIII

NMR SPECTRA OF SECONDARY ACETATES PREPARED *via* PROCEDURE F

Cycloalkyl acetate ring size	Registry no.	% yield	Bp (mm), °C	Broad s, 1 H, R_2CHOAc	s, 3 H, $-OCOCH_3$	Ring envelope
6[a]	622-45-7	67	38 (1)	4.64	1.95	1.2–1.85, 10 H
7[b]	18631-70-4	68	44–45 (1.2)	4.82	1.93	1.57, 12 H
8[c]	772-60-1	86	92 (11)	4.86	1.92	1·60, 16 H
12[d]	6221-92-7	73	97–98 (0.7)	4.91	1.92	1.35, 18 H

[a] L. Brunel, *Ann. Chim.*, 6, 207 (1905), bp 175°. [b] M. Kobelt, P. Barman, V. Prelog, and L. Ruzicka, *Helv. Chim. Acta*, **32**, 256 (1949), bp 95–96° (11 mm). [c] Reference *b*, bp 95–96° (11 mm). [d] Reference *b*, bp 141–142° (11 mm).

TABLE XIX

NMR DATA AND YIELDS OF TERTIARY ACETATES PREPARED *via* PROCEDURE G

1-Methyl-1-cycloalkyl acetate ring size	Registry no.	% yield	Bp (mm), °C	s, 3 H, CH_3OCO-	OAc | $CH_3-C=$ and ring envelope
5[a]	26600-59-9	21	36–38 (6.5)	1.91	1.65–1.5, 11 H
6[b]	16737-30-7	32	32–33 (0.3)	1.91	1.4–1.6, 13 H
7[c]	26600-61-3	15	45–46 (0.3)	2.01	1.4–1.9, 15 H
8	26600-62-4	3	Crude	1.89	1.2–1.7, 17 H
12	26600-63-5	86	41–45	1.89	1.1–1.6, 25 H

[a] A. C. Cope, D. Ambros, E. Ciganek, C. F. Howell, and Z. Jacura, *J. Amer. Chem. Soc.*, **82**, 1750 (1960), bp 66–67° (30 mm). [b] Reference *a*, bp 75–76° (17 mm). [c] Reference *a*, bp 74–74.5° (17 mm).

TABLE XX

LITERATURE AND NMR COMPARISONS OF THE CYCLOALKANECARBOXYLIC ACIDS

Cycloalkanecarboxylic acid ring size	Registry no.	Bp (mm), °C	s, 1 H, $-COOH$	Broad m, 1, $>CHCOOH$	Ring envelope
8[a]	4103-15-5	96–97 (0.3)	12.08	2.50	1.5–2.0, 14 H
9[b]	3667-74-1	94 (0.15)	12.19	2.52	1.3–2.0, 16 H
10[c]	3203-36-9	115 (0.13)	12.09	2.70	1.4–1.9, 18 H
11[d]	831-67-4	107 (0.1)	12.04	2.50	1.3–1.9, 20 H
12[e]	884-36-6	93–95	11.69	2.35	1.1–1.8, 22 H

[a] Reference 63, bp 108° (0.12 mm). [b] Reference 63, bp 118° (0.15 mm). [c] Reference 63, bp 122–123 (0.11 mm). [d] Societe des Usines Chimiques Rhone-Poulenc, French Patent Addn 78253; *Chem. Abstr.*, **57**, 16437*f* (1962), bp 118° (0.06 mm). [e] P. LaFont and Y. Bonnet, French Patent 1,286,709; *Chem. Abstr.*, **57**, 16437*b* (1962), mp 98°.

The error in the entropy of activation was calculated according to the equation also proposed in this reference.

C. Product Studies (General Procedure).—An amount of tosylate sufficient to produce a solution of concentration equivalent to the kinetic runs was dissolved in 50 ml of glacial acetic acid containing 0.41 g of sodium acetate. The solution was refluxed (120°) for at least 12 half-lives, cooled, diluted with 200 ml of water, and extracted with pentane. The combined extracts were washed with saturated aqueous sodium bicarbonate and saturated aqueous sodium chloride and dried over anhydrous magnesium sulfate. The vpc analyses were performed on the crude extract. The nmr analyses were performed on the residue after the pentane had been carefully fractionated off. The vpc ratios were determined by relative peak areas on a 9-ft Apiezon L column. Peaks were generally identified by the enrichment technique for the olefins and acetates. Ring-expanded secondary acetates were eliminated as possible products by the use of the enrichment technique with authentic samples. The product analysis in certain cases was performed by a combination of the nmr and vpc analyses. The product analyses are detailed in Table IV.

Stability Studies.—Under solvolysis conditions, 1-methylcyclohexyl acetate formed mainly 1-methylcyclohexene, 1-methylcyclododecyl acetate yielded 1-methylcyclododecene, cyclodecylcarbinyl acetate showed no change, methylenecyclooctane was converted to 1-methylcyclooctene, and methylenecyclodecane was converted to 1-methylcyclodecene.

D. Ionization Constant Determinations[51] (Apparatus).—The titration apparatus consisted of a jacketed titration vessel of 90-ml capacity, two burets, two electrodes, a nitrogen inlet, and a magnetic stirrer. Water from a constant temperature bath maintained at 25 ± 0.06° was circulated through the jacket.

The burets were of the automatic-zero type with integral reservoirs; they were filled by nitrogen pressure and protected by drying tubes filled with Ascarite. One buret (25 ml) delivered carbon dioxide-free ethanol, and one buret (5 ml) delivered aqueous carbonate-free sodium hydroxide. The electrodes were Fisher No. 13-639-12 (glass) and No. 13-639-52 (calomel); a Beckman Model G pH meter was used for the titrations. The nitrogen was passed through two gas washing bottles filled with 50% aqueous ethanol, and the titration vessel was covered with a sheet of parafilm.

Procedure.—A sample of the acid (about 0.33 mmol) was placed in the titration vessel and dissolved in 25 ml of ethanol, with stirring. Carbon dioxide-free water (25 ml) was pipetted in, and the solution allowed to come to thermal equilibrium (10–15 min). The initial pH reading was taken and a 0.5-ml aliquot of 0.02 *N* sodium hydroxide was added, followed by a 0.5-ml aliquot of ethanol. The mixture was stirred for 30 sec and allowed to stand for 15 sec, and the pH reading was taken. About 30 readings per run were taken in this manner, up to pH 11. Nitrogen flow was maintained throughout the run.

Solutions.—Carbon dioxide-free distilled water was prepared by boiling distilled water for 5 min, stoppering the flask, and allowing it to cool. Carbon dioxide-free ethanol was prepared by bubbling dry nitrogen through absolute ethanol for 20–30 min.

Carbonate-free sodium hydroxide was prepared by dissolving reagent grade sodium hydroxide (4 g) in 4 ml of carbon dioxide-free water and allowing to stand. A 1.1-ml portion of the supernatant 50% solution was diluted to 1 l., which was approximately 0.02 *N*. The solution was standardized against potassium hydrogen phthalate with phenolphthalein indicator.

The pH 4.00 buffer (25°) was prepared by dissolving 10.2114 g (0.05 mol) of potassium hydrogen phthalate in 1 l. of carbon dioxide-free water. The pH 9.18 buffer (25°) was prepared by dissolving 19.0687 g (0.05 mol) of sodium borate decahydrate (borax) in 1 l. of carbon dioxide-free water.

Calculations.[66]—The pK_a values were calculated at each point and corrected for H^+ activity below pH 7 and for OH^- activity above pH 7. The following equations were used.

pH 0-7 $pK_a = pH + [(HA) - (H^+)] - \log [(A^-) + (H^+)]$

pH 7 $pK_a = pH + \log (HA) - \log (A^-)$

pH 7-14 $pK_a = pH + \log [(HA) + (OH^-)] - \log [(A^-) - (OH^-)]$

The activity corrections were assumed to be the same for 50% ethanol as for water; the constant pK_a values obtained support this assumption. It was also assumed that the pH reading was equal to the logarithm of the reciprocal of the hydrogen ion concentration; no correction was made for the liquid-junction potential.

The pK_a values were converted to K_a values, averaged, and reconverted to an average pK_a. The pK_a value with the largest deviation from the average was discarded, and a new average pK_a determined. The process was repeated until the largest deviation was less than 0.03 pH unit. The calculations were performed on an IBM 1130 computer. The values are presented in Table XI.

Registry No.—β-*d*-Carbethoxycyclooctane, 26600-46-4; β-*d*-cyclooctylcarbinol, 26600-47-5; β-*d*-cyclooctylcarbinyl tosylate, 26600-48-6; cycloalkylcarbinyl acetate (5 ring size), 26600-49-7.

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(66) A. Albert and E. P. Serjeant, "Ionization Constants of Acids and Bases," Wiley, New York, N. Y., 1962.

The Chemistry of Acylsalicylamides. I. The Base-Catalyzed Decomposition of *O*-Benzyloxycarbonylglycyl-*N*-ethylsalicylamide

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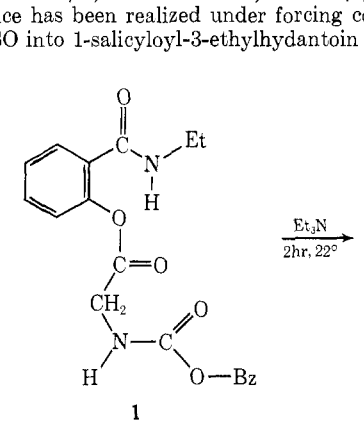
The structure of the major product obtained when *O*-benzyloxycarbonylglycyl-*N*-ethylsalicylamide (**1**) is treated with triethylamine is shown to be 3-(*N*-ethylacetamido)-1,3-benzoxazine-2,4-dione (**3**). The extensive ring–chain tautomerism potentially open to this substance has been realized under forcing conditions by conversion of **3** upon treatment with dimsyl sodium in DMSO into 1-salicyloyl-3-ethylhydantoin (**8**).

In the course of an investigation of the properties of benzyloxyamino acid esters of *N*-ethylsalicylamide,[1] we noted a ready decomposition of these substances under basic conditions and a formation of benzyl alcohol, along with one of a series of new, highly crystalline, neutral substances. Ring–chain tautomerism of an unusually rich kind was a possible complication for these species, and in this paper we wish to present evidence which establishes the structure of the simplest of these species and which determines the facility with which it equilibrates with its tautomers.

When *O*-benzyloxycarbonylglycyl-*N*-ethylsalicylamide[2] (**1**) is treated in acetonitrile solution with triethylamine, a red, tarry mixture of products is formed from which a highly crystalline substance, X, $C_{12}H_{12}N_2O_4$, is readily isolable. Careful saponification of this



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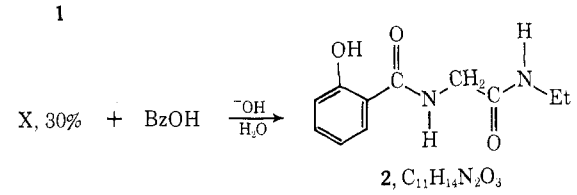

2, $C_{11}H_{14}N_2O_3$

substance results in a nearly quantitative conversion to salicyloylglycine ethylamide (**2**), an observation which establishes an amide insertion reaction of the

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(1) D. S. Kemp and R. B. Woodward, *Tetrahedron*, **21**, 3019 (1965); D. S. Kemp, *ibid.*, **23**, 2001 (1967); D. S. Kemp, Ph.D. Thesis, Harvard University, 1964.

(2) D. S. Kemp, S. W. Wang, G. Busby III, and G. Hugel, *J. Amer. Chem. Soc.*, **92**, 1050 (1970).