(29) The skeleton of **67** appears as a partial structure of a natural product: M. Kaneda, R. Takahashi, Y. Iitaka, and S. Shibata, *Tetrahedron Lett.*, 4609 (1972). A simple derivative of **67** has recently been synthesized.[24l]
(30) For structures like **67**, the Allinger 1971 force field probably overestimates Pitzer strain: E. Osawa, J. B. Collins, and P. v. R. Schleyer, *Tetrahedron*, in press.
(31) ^{13}C NMR spectra of the isolated intermediate for which the structure of **67** was assigned are also consistent with its configurational isomer, **69** (Table I).[12] However, **69** is calculated to be 34 kcal/mol more strained than **67** and hence can be safely rejected.
(32) (a) Z. Majerski, A. P. Wolf, and P. v. R. Schleyer, *J. Labelled Compds.*, **6**, 179 (1970); (b) Z. Majerski, P. v. R. Schleyer, and A. P. Wolf, *J. Am. Chem. Soc.*, **92**, 5731 (1970); (c) Z. Majerski, S. H. Liggero, P. v. R. Schleyer, and A. P. Wolf, *J. Chem. Soc., Chem. Commun.*, 1596 (1970).
(33) A. Nickon and R. C. Weglein, *J. Am. Chem. Soc.*, **97**, 1271 (1975).
(34) The allowed ±60° range of deviation of dihedral angle from the ideal values of zero or 180° is based on the fact that the 1,2-methyl shift involving a dihedral angle of 60° on the adamantane framework does not occur even under forcing conditions.[32] The use of a narrower range, say ±45° from ideal values, would simplify Table II. We become, however, more selective in the next stage (see text).
(35) These assumptions imply that both sp^2 and sp^3 alignment factors[33] are considered, since both stepwise and concerted mechanisms are likely to occur for the 1,2-skeletal shift. While concerted mechanisms often prevail in solvolytic reactions,[36] 1,2 shifts initiated by hydride abstraction with strong acids have been traditionally considered to involve free carbonium ions.[3,6,7] However, we have recently presented some kinetic, albeit indirect, evidence indicating the operation of concerted mechanism in hydride abstraction with trifluoromethanesulfonic acid.[10,37] Since we have no firm grounds to reject either of these two mechanisms, and our present goal is to consider all possible Wagner–Meerwein shifts among 69 isomers of $C_{11}H_{18}$, we tentatively follow the dual policy.
(36) S. H. Liggero, R. Sustmann, and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **91**, 4571 (1969).
(37) The apparent rate of disappearance of **29** upon contact with acid catalyst is 2×10^4 times faster than that of **27**.[10] The large rate difference appears to be in accord with the proposed pathways. The isomerization of **29** to **34** is indicated to be slightly exothermic, whereas the paths **27** → **33**, **61** are endothermic.
(38) Review: G. D. Sargent in "Carbonium Ions", Vol. III, G. A. Olah and P. v. R. Schleyer, Ed., Wiley-Interscience, New York, N.Y., 1971, p 1099.
(39) Y. Inamoto et al., unpublished results.
(40) N. Takaishi, Y. Inamoto, K. Tsuchihashi, K. Aigami, and Y. Fujikura, *J. Org. Chem.*, **41**, 771 (1976).
(41) N. Takaishi, Y. Inamoto, K. Aigami, K. Tsuchihashi, and H. Ikeda, *Synth. Commun.*, **4**, 225 (1974).
(42) (a) T. Katsushima, Y. Yamaguchi, and M. Kawanisi, *J. Chem. Soc., Chem. Commun.*, 692 (1975). (b) The calculated enthalpy of **60**, equal to that of **48** and 2 kcal/mol higher than that of **49**, is consistent with this assignment. If the 2 kcal/mol uphill barrier **49** → **48** cannot be overcome under the reaction conditions employed, the barrier **49** → **60** should not be overcome either. However, this barrier is barely outside of our accuracy range of energy calculations and the argument may not be valid.
(43) Subsequent to completion of this work, two homoprotoadamantanes, **54** and **65**, have been studied as the starting materials of acid-catalyzed rearrangements. No methylprotoadamantane intermediate could be found: N. Takaishi, Y. Inamoto, K. Aigami, Y. Fujikura, E. Osawa, M. Kawanisi, and T. Katsushima, *J. Org. Chem.*, in press.
(44) Our previous paper[12] suggested two routes for the generation of **61** from **40**. Clearly, there are many more alternatives, as shown in Figure 1. The shortest route is **40** → **51** → **61**.
(45) The fifth possibility of isomerization of **29** is the one that leads to **1**. While this step appears feasible energetically (Table I), the bond alignment factor is unfavorable.
(46) (a) H. L. Goering and M. F. Sloan, *J. Am. Chem. Soc.*, **83**, 1397, 1992 (1961); (b) R. W. Thies and L. E. Schick, *ibid.*, **98**, 456 (1974); (c) J. A. Berson and R. Reynolds-Warnhoff, *ibid.*, **84**, 682 (1962).
(47) (a) The sixth path from **20** is rejected; it is the one leading to **22**, which is about 10 kcal/mol more strained than **20**. (b) Y. Inamoto et al., submitted for publication.
(48) Y. Inamoto et al., to be published. The previous report[12] wherein methylisotwistane structures were assigned to the methyl-containing intermediates was wrong.
(49) Taking a single, reverse step from each of **73** and **74** to suggest **10** and/or **19** as their progenitors, as has been done in the previous paper,[12] may be oversimplification. Other undetected methyltricyclodecane intermediates may be involved.
(50) P. v. R. Schleyer, J. E. Williams, and K. R. Blanchard, *J. Am. Chem. Soc.*, **92**, 2377 (1970). Used in conjunction with Engler force field[18] calculations.
(51) D. Lenoir, R. E. Hall, and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **96**, 2138 (1974).
(52) Note that we assumed that the reverse reactions **77** → **10** and **77** → **19** do not take place.

Structural Effects in Solvolytic Reactions. 22. Effect of Ring Size on the Stabilization of Developing Carbocations as Revealed by the Tool of Increasing Electron Demand

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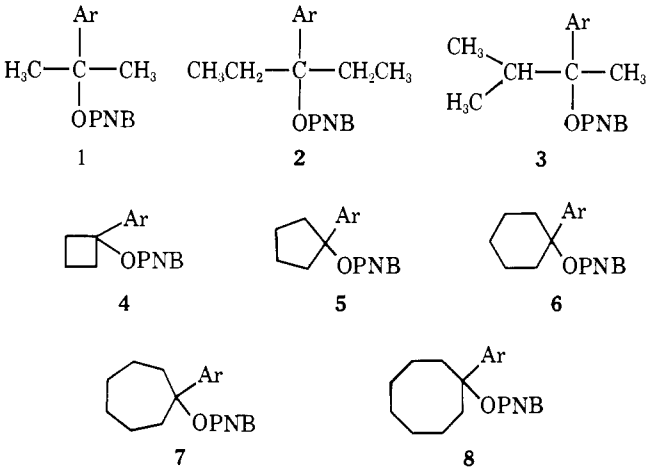
Abstract: Representative aryldialkylcarbinyl (RR'ArCOPNB) and 1-aryl-1-cycloalkyl ($(\overbrace{CH_2)_{n-1}}C$ArOPNB) *p*-nitrobenzoates were synthesized and their rates of solvolysis in 80% aqueous acetone determined in order to examine the electron deficiency in the developing carbocationic center as measured by the tool of increasing electron demand. A rough parallelism exists between the observed rates and the ρ^+ values: *tert*-cumyl (R, R' = Me), −4.72; 2,3-dimethyl-2-butyl (R = *i*-Pr; R' = Me), −4.76; 3-pentyl (R, R' = Et), −4.52; 1-cyclopropyl ($n = 3$), −5.15; 1-cyclobutyl ($n = 4$), −4.91; 1-cyclopentyl ($n = 5$), −3.82; 1-cyclohexyl ($n = 6$), −4.60; 1-cycloheptyl ($n = 7$), −3.87; and 1-cyclooctyl ($n = 8$), −3.83. The similarity in the ρ^+ values for the *tert*-cumyl, 2,3-dimethyl-2-butyl, and 3-pentyl derivatives indicates that the stabilizing effect of the alkyl groups (methyl, ethyl, and isopropyl) on the developing cationic center must be nearly the same. The high negative values observed for the cyclopropyl and cyclobutyl derivatives are attributed to the effect of I-strain in destabilizing the cationic center, resulting in an increased demand on the aryl system for electronic contributions to stabilize the electron deficiency. The marked difference in the relatively high (−) value in ρ^+ for cyclohexyl as compared to the other ring systems (five, seven, and eight) is attributed to the resistance of the conformationally stable cyclohexyl system to the introduction of an sp^2 cationic center in contrast to the ready accommodation of such a center in the more crowded five-, seven-, and eight-ring systems (I-strain). The 1-methyl-1-cycloalkyl *p*-nitrobenzoates were also synthesized and solvolyzed. In these systems the tool of increasing electron demand yields results entirely consistent with earlier studies based primarily upon direct comparison of rates.

For many years solvolysis rates have been utilized to arrive at an understanding of the factors influencing the stability of carbonium ions.[2,3] A remarkably consistent body of knowledge has been built up in this way.[4,5]

One possible difficulty has been the necessity of comparing the rate with a suitable model system.[6,7] Occasionally this can lead to ambiguities.[8] The tool of increasing electron demand appears to minimize such ambiguities.[8]

This tool was introduced for the study of participation and it appears to yield unambiguous conclusions in a variety of systems where such participation may be involved.[5] Thus it has established major π participation in 7-norbornenyl[9] and 5-methyl-2-norbornenyl[10] systems and important π conjugation in the cyclohex-2-enyl systems.[11] The results indicated the 2-norbornenyl system to be a borderline case with incursion of π participation observed only with the more electron-demanding groups.[12] The tool also confirmed $\pi\sigma$ conjugation in the 3-nortricyclyl[8] and 1-aryl-1-cyclopropyl-1-ethyl systems.[13] More recently we applied this tool to establish unambiguously the presence of carbon ($\pi\sigma$) participation in Coates' cation,[14] supporting the conclusion arrived at earlier based on solvolytic measurements[15] and the study of the cation under stable ion conditions.[16] However, the tool has failed to detect σ participation in 2-bicyclo[2.1.1]hexyl[17] and 2-norbornyl,[18] two fascinating systems where σ participation is often postulated.[5]

The effect of ring size on rates of solvolysis had been studied earlier.[19,20] Interesting differences in rates were observed, attributed to I-strain effects.[19] We decided to examine the utility of the tool of increasing electron demand in such systems. Accordingly, we undertook to synthesize and solvolyze a number of 1-aryl-1-cycloalkyl derivatives together with some related aliphatic derivatives for comparison (**1–8**). (Several



of these (**1**,[21] **3**,[13] **5**,[22] and **6**[11]) have been utilized as models in earlier studies, but are included here to provide complete data for the discussion and comparison.)

It should be pointed out that Tanida previously studied the solvolytic behavior of several 1-aryl-1-cycloalkyl chlorides over a limited range of reactivity.[23] We included these systems in our present study in order to have data for our standard solvolytic conditions (*p*-nitrobenzoates in 80% acetone) so as to make a direct comparison of the reactivities and ρ^+ values of the various systems without introducing correction factors and approximations.

Results

Synthesis. The Grignard reagents prepared from *p*-bromoanisole, bromobenzene, *p*-bromobenzotrifluoride, and 3,5-bis(trifluoromethyl)bromobenzene and magnesium in ether were added to the appropriate ketones to furnish the tertiary alcohols. The alcohols were converted into the *p*-nitrobenzoates by treating their lithium salts with *p*-nitrobenzoyl chloride in THF.[12]

Solvolysis. The rates of solvolysis of the *p*-nitrobenzoates were measured in 80% aqueous acetone utilizing the standard procedure.[8] The solvolyses at higher temperatures were carried out in sealed ampules and the rates were extrapolated to 25 °C. In some cases the synthesis of the *p*-nitrobenzoates of the tertiary anisyl alcohols proved exceedingly difficult owing to their reactivity and instability. In such cases the benzoates were synthesized and the rates for the *p*-nitrobenzoates were calculated by multiplying the rate of benzoate by the factor 20.8.[24] The pertinent rate data and activation parameters are summarized in Table I.

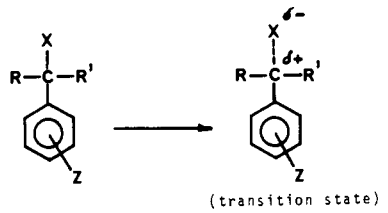
Discussion

Two major factors influencing the rates of solvolysis are the change in steric strain accompanying the transformation from the ground state to the transition state and the effectiveness with which the electron deficiency in the developing cationic center in the transition state is delocalized into the molecular structure.

Thus the enhanced rate of solvolysis of tri-*tert*-butylcarbinyl *p*-nitrobenzoate is attributed to relief of strain accompanying partial ionization in the transition state.[25] The reduced rate of solvolysis of *endo*-2-norbornyl tosylate is attributed to steric hindrance to ionization resulting from the rigid U-shaped structure of the system.[26]

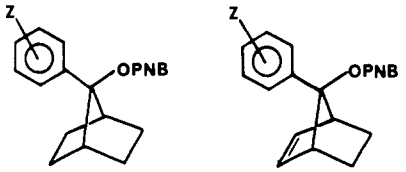
On the other hand, the enhanced rate of solvolysis of 1-phenyl-1-cyclohex-2-enyl *p*-nitrobenzoate (152 000) over 1-phenyl-1-cyclohexyl *p*-nitrobenzoate (1.00) is attributed to delocalization of charge into the allylic system.[11]

The Gassman-Fentiman approach[9] provides an alternative means of evaluating the electron deficiency of the developing cationic center in a system undergoing ionization. The greater the electron deficiency at the developing cationic center, the



greater should be the demand on the aromatic ring for electronic stabilization. By examining the effect produced by representative substituents (normally *p*-CH_3O, *p*-H, *p*-CF_3, 3,5-$(CF_3)_2$) it is possible to express this electron demand in terms of ρ^+.

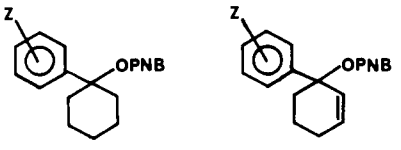
For example, the 7-aryl-7-norbornyl *p*-nitrobenzoates reveal a large (−) ρ^+, $\rho^+ = -5.27$ for **9**.[9] The major increase in ρ^+ to −2.30 for **10** establishes that the rate of solvolysis of this



ρ+ -5.27 -2.30

system is far less dependent on the electronic contributions from the substituents Z, a result of stabilization of the cationic center by π participation of the double bond.

Similarly, 1-aryl-1-cyclohexyl *p*-nitrobenzoate (**6**) exhibits



ρ+ -4.60 -2.52

a ρ^+ of −4.60, revealing high electron demand, but somewhat lower than that in **9**. The introduction of a double bond in the allylic position, as in **11**, increases ρ^+ to −2.52.[11]

Thus, π conjugation in **11** greatly stabilizes the electron-deficient center and it makes far smaller demands on the substituent Z for further stabilization.

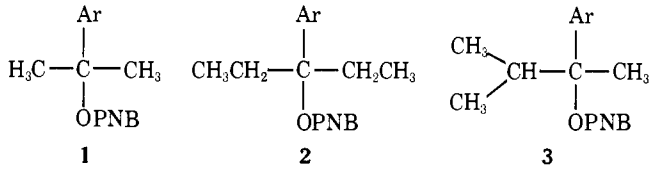
Table I. Rate Data for the Solvolysis of *p*-Nitrobenzoates in 80% Aqueous Acetone

System	OPNB	$k_1 \times 10^6$, s^{-1} T_1, °C	T_2, °C	25 °C	$\Delta H^{\neq}$, kcal mol^{-1}	$\Delta S^{\neq}$, eu
1	*p*-CH_3O			372		
	p-CH_3	577 (75)	37.5 (50)	1.54[a]	23.8	−5.1
	p-H	391 (100)	33.6 (75)	0.072[a]	24.8	−8.2
	p-CF_3	238 (150)	25.7 (125)	8.36×10^{-5} [a]	29.2	−6.7
	3,5-$(CF_3)_2$	219 (175)	22.2 (150)	7.50×10^{-7} [a]	33.9	−0.3
2	*p*-CH_3O			60.3		
	p-H	76.7 (100)	6.66 (75)	0.0149[a]	24.6	−11.7
	p-CF_3	108 (150)	9.83 (125)	1.22×10^{-5} [a]	31.5	−2.9
	3,5-$(CF_3)_2$	151 (175)	15.1 (150)	4.17×10^{-7} [a]	34.3	−0.1
3	*p*-CH_3O			65.3		
	p-H	100 (100)	7.11 (75)	9.51×10^{-3} [a]	26.7	−5.7
	p-CF_3	117 (150)	10.7 (125)	1.36×10^{-5}	31.4	−2.8
	3,5-$(CF_3)_2$	122 (175)	10.9 (150)	1.43×10^{-7} [a]	35.8	2.8
4	*p*-CH_3O	306 (50)		14.4	22.8	−4.2
	p-H	321 (125)	28.8 (100)	1.84×10^{-3} [a]	27.8	−5.0
	p-CF_3	26.2 (150)	2.24 (125)	1.93×10^{-6} [a]	32.3	−3.7
	3,5-$(CF_3)_2$	23.7 (175)	2.0 (150)	1.68×10^{-8}	36.7	1.5
5	*p*-CH_3O			3980[b]		
	p-H	926 (75)	61.6 (50)	2.6[a]	23.7	−4.8
	p-CF_3	98.1 (100)	7.54 (75)	0.012[a]	25.9	−7.9
	3,5-$(CF_3)_2$	76.2 (125)	7.02 (100)	4.9×10^{-4} [a]	27.6	−8.6
6	*p*-CH_3O			67.3		
	p-H			0.0146[a]		
	p-CF_3	19.6 (125)	1.35 (100)	3.05×10^{-5} [a]	30.9	−2.8
	3,5-$(CF_3)_2$	124 (175)	11.9 (150)	2.66×10^{-7} [a]	34.7	0.4
7	*p*-CH_3O			563[b]		
	p-H	332 (75)	20.0 (50)	0.752[a]	24.5	−4.3
	p-CF_3	404 (125)	33.4 (100)	1.54×10^{-3} [a]	28.9	−2.1
	3,5-$(CF_3)_2$	383 (150)	36.1 (125)	5.43×10^{-5} [a]	31.0	−1.4
8	*p*-CH_3O			6610[b]		
	p-H	161 (50)		7.52	22.9	−5.3
	p-CF_3	363 (100)	25.6 (75)	0.0335[a]	26.8	−2.9
	3,5-$(CF_3)_2$	290 (125)	22 (100)	7.17×10^{-4} [a]	29.8	−0.4

[a] Extrapolated from data at higher temperatures. [b] Calculated by multiplying the rate of benzoate by the factor 20.8.[24]

$\pi\sigma$ participation in Coates' cation[14] and $\pi\sigma$ conjugation in nortricyclyl[8] and 1-aryl-1-cyclopropyl-1-ethyl[13] have similar effects in making ρ^+ more positive. Thus it does not appear to matter whether the cationic center is stabilized by conjugation or by participation; ρ^+ becomes more positive. The question we set out to answer is whether simple alkyl groups can have a significant effect upon ρ^+ through variations in hyperconjugative contributions, or whether I-strain in cycloalkyl systems can have such effects.

Alkyl Systems. The data summarized in Table I indicates that simple alkyl groups, such as methyl, ethyl and isopropyl, do not have a significant effect on ρ^+ as indicated by the values: −4.72 for **1**, −4.52 for **2**, and −4.76 for **3**.



1 **2** **3**

ρ^+ −4.72 −4.52 −4.76

The large negative, essentially constant ρ^+ values indicate that hyperconjugative stabilization of the cationic center by the alkyl groups do not provide significant differences in such stabilization, resulting in significant differences in the electronic demand on the aryl group. Possibly the slightly more positive value of ρ^+ in **2** is indicative of a slightly greater stabilization of the cationic center by the two ethyl groups as compared to the two methyl groups in **1** or the methyl and isopropyl groups in **3**. However, it appears safer at this stage in the development of the tool to consider only larger effects.

Cycloalkyl Systems. It was pointed out earlier that alicyclic compounds exhibit considerable changes in reactivity with changes in the number of carbon atoms in the ring. This is true both for S_N2 and S_N1 reactions, as well as for the reactions of cyclic ketones.[27] For example, the bimolecular displacement reactions of cyclopropyl, cyclobutyl, and cyclohexyl halides are very slow compared to the corresponding reactions of simple acyclic secondary halides and the corresponding derivatives of cyclopentane and cycloheptane.[28,29]

Similarly the solvolytic reactivities of secondary alicyclic tosylates increase in the order cyclooctyl > cycloheptyl, cyclopentyl, cyclobutyl ≫ cyclohexyl ≫ cyclopropyl.[20,30,31] From a study of the solvolysis of simpler tertiary cycloalkyl chlorides, not complicated by molecular rearrangements, the reactivities follow the order cyclooctyl > cycloheptyl ≈ cyclopentyl ≫ cyclohexyl > cyclobutyl.[19]

The effect of ring size on chemical reactivity was accounted for in terms of I-strain—the increase in internal strain in a cyclic structure resulting from alterations in bond angles and constellations accompanying a change in the coordination number of a ring atom in the course of the reaction.[19]

In this way the inertness of cyclopropane and cyclobutane derivatives to solvolysis (in systems where rearrangements are not involved) is attributed to the additional strain involved in incorporating an sp^2 carbonium carbon atom with a preferred angle of 120° into a small ring.

The inertness of cyclohexyl derivatives in solvolytic reactions is attributed to the additional strain accompanying the introduction of an sp^2 carbonium atom into the nicely staggered,

Table II. Rates of Solvolysis of Tertiary 1-Methyl-1-cycloalkyl *p*-Nitrobenzoates in 80% Aqueous Acetone

$(CH_2)_{n-1}$C(OPNB)CH_3	$k_1 \times 10^6$, s^{-1}			$\Delta H^{\ddagger}$,	$\Delta S^{\ddagger}$,
n	T_1, °C	T_1, °C	25 °C	kcal mol^{-1}	eu
4	4.3 (150)	0.377 (125)	3.73×10^{-7}[a]	32.0	−8.0
5	236 (125)	23.0 (100)	2.11×10^{-3}[a]	26.9	−7.9
6	247 (150)	24.9 (125)	5.48×10^{-5}[a]	30.1	−4.4
7	528 (125)	50.6 (100)	4.21×10^{-3}[a]	27.1	−6.0
8	287 (100)	23.1 (75)	0.042[a]	25.4	−7.0

[a] Calculated from data at higher temperatures.

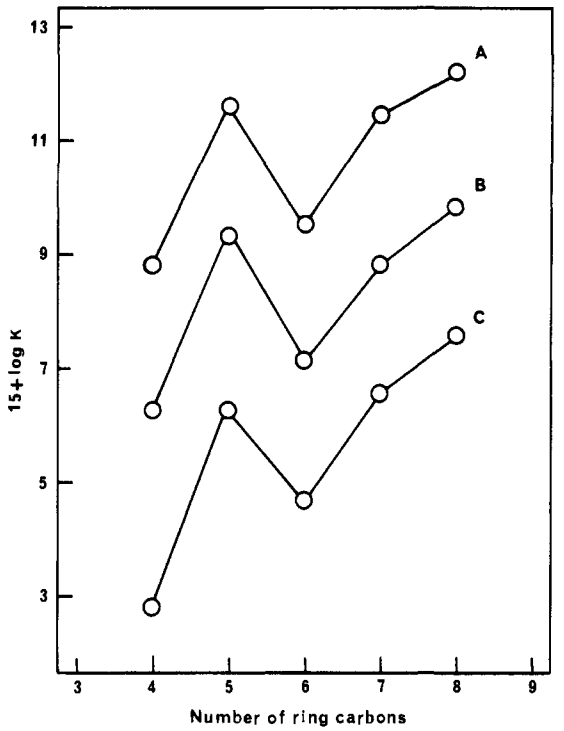
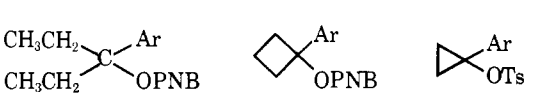


Figure 1. Effect of ring size on the rate of solvolysis of (A) 1-methyl-1-cycloalkyl chlorides in 80% ethanol, (B) 1-phenyl-1-cycloalkyl *p*-nitrobenzoates in 80% acetone, and (C) 1-methyl-1-cycloalkyl *p*-nitrobenzoates in 80% acetone.

essentially strain-free cyclohexyl system. On the other hand, the greater reactivity of cyclopentyl, cycloheptyl, and cyclooctyl systems is attributed to the relief of nonbonded interaction accompanying the transformation of a tetrahedral ring atom into one with only three neighbors.

Although we did not include the 1-aryl-1-cyclopropyl *p*-nitrobenzoates in this study, it is evident from recent data on the solvolysis of 1-aryl-1-cyclopropyl tosylates[32] and 1-methyl-1-cyclopropyl triflates[33] that the reactivities of these derivatives are indeed very slow. Indeed, estimation of the value of ρ^+ at 25 °C from Depuy's data for the solvolysis of 1-aryl-1-cyclopropyl tosylates in acetic acid gives ρ^+ −5.15, more negative than that realized for the acyclic derivatives (**1–3**). The value for the cyclobutyl derivatives also reveals a large negative value.



ρ^+ −4.52 −4.91 −5.15

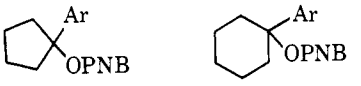
Thus, the difficulty of incorporating an sp^2 atom into the ring results in the developing cationic center being highly electron demanding resulting in relatively large electron supply from the aryl group and relatively large (−) ρ^+ value.

Table III. Relative Rates of 1-Phenyl-1-cycloalkyl and 1-Methyl-1-cycloalkyl *p*-Nitrobenzoates and 1-Methyl-1-cycloalkyl Chlorides

$(CH_2)_{n-1}$C(R)X	Rel rate, 25 °C		
n	R = Ph; X = OPNB[a,b]	R = Me; X = OPNB[a,b]	R = Me; X = Cl[c,d]
4	0.126	0.0068	0.21
5	178.0	38.0[e]	124.0
6	1.00	1.00[e]	1.00
7	51.5	76.8[e]	108.0
8	515.0	766.0	286.0

[a] This study. [b] In 80% aqueous acetone. [c] Reference 19. [d] In 80% aqueous ethanol. [e] For properties and pertinent references, see E. N. Peters and H. C. Brown, *J. Am. Chem. Soc.*, 97, 2892 (1975).

The ρ^+ values for the cyclopentyl and cyclohexyl derivatives parallel the solvolysis rates. Thus the relatively reactive cyclopentyl derivatives exhibit a ρ^+ value of −3.82, whereas the



5 6

ρ^+ −3.82 −4.60

less reactive cyclohexyl derivatives exhibit one of −4.60. Similarly, the relatively reactive cycloheptyl and cyclooctyl derivatives exhibit ρ^+ values that are close to that for the cyclopentyl system.

7 8

ρ^+ −3.87 −3.83

The question arises as to whether this parallelism between the value of ρ^+ for the 1-aryl-1-cycloalkyl systems and their reactivities is fortuitous, arising from varying hindrance to rotation of the aryl group at the developing cationic center. Accordingly, we synthesized the 1-methyl-1-cycloalkyl *p*-nitrobenzoates and examined their reactivities. The results (Table II) reveal the same pattern of reactivity.

In certain systems one must be careful in comparing tertiary chlorides with tertiary *p*-nitrobenzoates. The latter can be subjected to considerably greater F-strain, facilitating the ionization.[34] However, comparison of the 1-phenyl-1-cycloalkyl *p*-nitrobenzoates, 1-methyl-1-cycloalkyl *p*-nitrobenzoates, and 1-methyl-1-cycloalkyl chlorides reveal a common pattern of reactivity (Table III, Figure 1).

I-Strain as a Factor in ρ^+. In all previous cases examined, significant decreases in the absolute value of ρ^+ were associated with increasing electron supply to the developing carbocationic center (**9** and **10**, **6** and **11**). Can this be the source of the difference between the observed value of ρ^+ in the cycloalkyl derivatives?

For example, can we account for the relatively large difference between 1-aryl-1-cyclopentyl (ρ^+ −3.82) and 1-aryl-1-cyclohexyl (ρ^+ −4.60) in terms of a greater electron supply from the more strained cyclopentyl system? However, the even more strained 7-aryl-7-norbornyl, 1-aryl-1-cyclopropyl, and 1-aryl-1-cyclobutyl systems all reveal considerably high absolute values of ρ^+.

The parallelism of the observed ρ^+ values with the relative reactivities of these ring systems, previously accounted for in terms of I-strain effects, is remarkable. It suggests that both the relative reactivities and the relative values of ρ^+ may have their origin in I-strain.

It is evident that the strain accompanying the introduction of an sp^2 center in the 7-norbornyl, cyclopropyl, or cyclobutyl systems must result in a large demand by that center for additional electron density. In these systems the low rate of ionization and the large negative values of ρ^+, i.e., −5.27, −5.15, and −4.91, are reasonable.

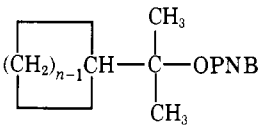
Similarly, the introduction of an sp^2 center in the nicely staggered strain-free cyclohexyl system results in bond oppositions and considerable strain. Here also the slow rate of ionization and the large (−) value of ρ^+, −4.60, are reasonable.

In these systems the higher energies of activation for the reactions cause the transition state to come further along the reaction coordinate. The species is more ionized, closer to the cationic intermediate. The higher electron deficiency makes a greater demand on the aryl group and its substituents for electronic stabilization.

But how can bond opposition forces in the cyclopentyl, cycloheptyl, and cyclooctyl systems result in more positive values of ρ^+? The strain in the ground state is partially dissipated in the transition state. The energy of activation is reduced by such strain relief. According to the Hammond postulate,[35] the transition state for such systems will not be so far along on the reaction coordinate. The development of the electron deficiency in the transition state will be less, and the center will make a smaller demand on the aryl system for stabilization.[36]

It should be pointed out that a similar explanation was previously suggested by Schleyer for the results of Tanida on the solvolysis of several 1-aryl-1-cycloalkyl chlorides.[23]

On this basis, it appears reasonable to account for the observed variation in both reactivity and ρ^+ in terms of I-strain effects. Variation in hyperconjugative contributions, resulting from the strain in the five-, seven-, and eight-membered rings is possible, but no evidence for such effects is now available. We are exploring systems of the type



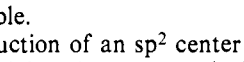
to explore the possibility that such strain can result in enhanced electronic contributions to an electron-deficient center.

Conclusion

The tool of increasing electron demand provides an objective measure of the electron deficiency at the developing carbonium ion center, in the transition state for the solvolysis. This electronic unsaturation is estimated from the sensitivity of the reaction to substituents, in the aromatic ring, as measured by ρ^+. Electronic contributions, either conjugation or participation, which stabilize the cationic center result in diagnostic changes in ρ^+. In ring systems, either destabilization of the cationic center by angle strain effects or enhancement of the ionization by relief of bond opposition forces, both manifestations of I-strain effects, can be detected by corresponding changes in the values of ρ^+.

Table IV. Properties of *p*-Nitrobenzoates[a]

System	OPNB	Mp, °C	Yield, %	Anal.
2	*p*-CH_3O	100–101	71	C, H, N
	p-H	80–81	69	C, H, N
	p-CF_3	94.5–95	57	C, H, N, F
	3,5-$(CF_3)_2$	99–100	68	C, H, N, F
4	*p*-CH_3O	96–98	22	C, H, N
	p-H	101–102	85	C, H, N
	p-CF_3	96–97	87	C, H, N, F
	3,5-$(CF_3)_2$	83–84	70	C, H, N, F
	CH_3	85–86	85	C, H, N
7	*p*-H	121–121.5	69	C, H, N
	p-CF_3	132	62	C, H, N, F
	3,5-$(CF_3)_2$	119	64	C, H, N, F
8	*p*-H	105 dec	58	C, H, N
	p-CF_3	99–100	60	C, H, N, F
	3,5-$(CF_3)_2$	102–103	63	C, H, N, F
	CH_3	89–90	78	C, H, N

[a] For  with n = 5, 6, and 7, see footnote *e*. Table III.

Experimental Section

Preparation of *p*-Nitrobenzoates. The tertiary alcohols were prepared by the addition of the appropriate Grignard reagents to the ketone. Alcohols from cycloheptanone and cyclooctanone were used for the *p*-nitrobenzoate preparation without further purification since they were found to undergo dehydration on distillation. The *p*-nitrobenzoates were prepared by treating their lithium salts with *p*-nitrobenzoyl chloride.[8] The properties of the *p*-nitrobenzoates are listed in Table IV.

Kinetic Procedure. The procedure employed in determining the rate constants is essentially the same as described earlier.[8] The rate constants are reproducible to ±1% and the ρ^+ values ±0.1.

Products. With the exception of the cyclopropyl derivatives, which undergo solvolysis with varying amount of ring opening,[32] the other ring derivatives here discussed (n = 4, 5, 6, 7, and 8) undergo solvolysis to give unrearranged alcohols and olefins. It is of interest that the solvolysis of the 1-aryl-1-cyclobutyl *p*-nitrobenzoates proceeded to give only the unrearranged alcohols, without significant amounts of the olefins detected.

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Aminolysis of Thionesters

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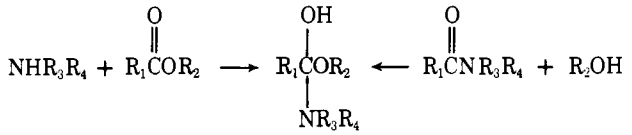
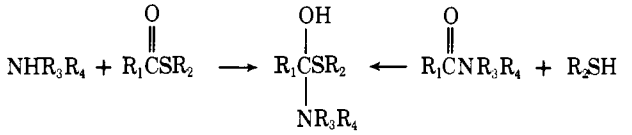
Abstract: Rates of reaction of *p*-nitrophenyl thionbenzoate (I) and *p*-nitrophenyl benzoate (II) with a series of primary amines and one secondary amine were measured. The pK_a's of the conjugate acids of the amines studied range from 5.6 to 11. In contrast to the reaction of hydroxide ion, which is about equally reactive toward I and II, amines react up to 200 times faster with I than with II. Structure-reactivity correlations show a change in rate determining step in the aminolysis of I, consistent with rate limiting breakdown of a zwitterionic tetrahedral intermediate with moderately basic amines and rate limiting attack of highly basic amines. The break occurs with a less acidic leaving group than does the corresponding break in oxygen ester aminolysis and suggests that the tetrahedral intermediate formed from thionesters is more reactive than that formed from oxygen esters. This reactivity stems from the enhanced ability of sulfur to expel leaving groups.

The mechanism of aminolysis of esters has recently received extensive attention.[1-4] This reaction is of special interest because one or more of the tetrasubstituted intermediates involved (III, its zwitterionic form, conjugate acid, and conjugate



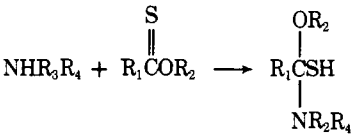
III

base) are also formed in the acylation of chymotrypsin and other serine proteases by amides.[3] A similar intermediate, IV,



IV

is formed by the analogous acylation reaction of papain[5] and other cysteine proteases,[6] and is also generated in the aminolysis of thiolesters.[7] A closely related intermediate, V, is formally derived from the aminolysis of thionesters. We report here the first data on thionester aminolysis, which demonstrate the actual existence of V.

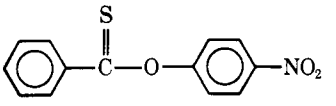


V

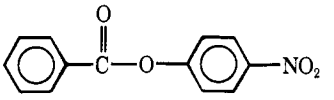
Aminolysis reactions of thionesters show extensive mechanistic similarity to the corresponding reactions of oxygen esters, but with differences which lend insight into the role of the carbonyl heteroatom in acyl transfer and thionacyl transfer reactions.

Results

p-Nitrophenyl thionbenzoate (I), a thionester with a highly



I



II

acidic leaving group, undergoes reaction with amines and with hydroxide ion with liberation of *p*-nitrophenol or *p*-nitrophenoxide ion. Because I is sparingly soluble in water, reaction products and rates were determined in a mixed solvent containing 20% acetonitrile and 80% water by volume. Aminolysis and hydrolysis reactions of the corresponding oxygen ester, *p*-nitrophenyl benzoate (II), were studied, for the purposes of comparison, in the same mixed solvent.

The pseudo-first-order rate constants for the hydrolysis of I were identical when measured spectrophotometrically at either 288 (destruction of the -C(=S)O- chromophore[8]) or 400 nm (production of *p*-nitrophenoxide). From the rate constants shown in Figure 1 it can be seen that the reaction obeys the simple rate law

$$k_{obsd} = k_1 [OH^-] + k_0 \quad (1)$$

For comparison, rate constants for the hydrolysis of II under identical conditions are also included in Figure 1. For neither ester was buffer catalysis observed. The rates of uncatalyzed, or water, reactions (k_0) were too slow to be measured accurately at the pH values studied.