Acetolysis of Some Cyclohexylnorbornyl Tosylates and the Case for Dipolar Effects in Cis–Exo Norbornanes

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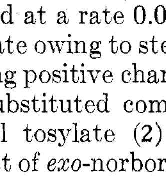
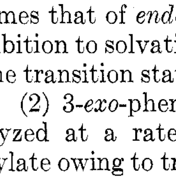
The acetolysis rates of the 3-cyclohexyl-, the 7-cyclohexyl-, and the 1-cyclohexyl-2-norbornyl tosylates have been determined. That 3-*exo*-cyclohexyl-2-*exo*-norbornyl tosylate reacted at about the same rate as the unsubstituted parent supports the explanation of an unfavorable dipolar interaction in the *exo*-3-phenyl analog causing its rate retardation. The 1-cyclohexyl-2-*exo* isomer reacted 146 times as fast as the unsubstituted parent, demonstrating again a significant positive charge accumulation at C-1 in the transition state for the 1-alkyl-2-*exo* tosylates. In the endo series the 3-*exo*-cyclohexyl isomer reacted 0.0910 times the rate of its unsubstituted parent, a retardation ascribed to steric inhibition to solvation of the developing positive charge in the transition state. The 3-*endo*-cyclohexyl- and 1-cyclohexyl-2-*endo* isomers reacted, respectively, 21 and 9.0 times as fast as their parent attributed to steric acceleration. A comparison of kinetic data for some 3-exo-substituted 2-*exo*-norbornyl tosylates with the data from some identically substituted 2-cyclohexyl brosylates revealed a greater rate depression in the norbornyl system. This supports the operation of a significant dipolar repulsive interaction in the acetolyses of the norbornyl compounds.

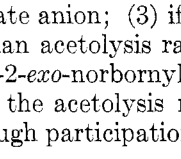
In prior papers we have reported upon the acetolysis rates for the four 3-phenyl-2-norbornyl tosylates, the four 3-*p*-anisyl-2-norbornyl tosylates, and the four 7-phenyl-2-norbornyl tosylates[1] as well as detailed analyses of the acetolysis products under kinetic and thermodynamic conditions.[2] These studies were conducted in order to assess the relationships between fixed geometries with definite dihedral angles and the rate-retarding inductive effects of aryl substituents, steric hindrance to ionization, and steric acceleration. In addition we anticipated that comparison of the rate data from 3-substituted norbornyl tosylates with the related 7-substituted compounds might provide information as to the amount of participation of the C_1–C_6 bond in the transition state for the exo compounds. Three of the reported relative rates were attributed to some "special effect" of phenyl not generally invoked to explain rate data: (1) 3-*exo*-phenyl-2-*endo*-norbornyl tosylate (**1**) acetolyzed at a rate 0.00392 times that of *endo*-norbornyl tosylate owing to steric inhibition to solvation of the developing positive charge in the transition state for the phenyl-substituted compound; (2) 3-*exo*-phenyl-2-*exo*-norbornyl tosylate (**2**) acetolyzed at a rate 0.00758 times that of *exo*-norbornyl tosylate owing to transition-state destabilization caused by a dipolar repulsive interaction between the phenyl π cloud and the developing tosylate anion; (3) if one compares ionization rates rather than acetolysis rates, the phenyl substituent in 1-phenyl-2-*exo*-norbornyl tosylate (**3**) has virtually no effect on the acetolysis rate of *exo*-norbornyl tosylate even though participation of the C_1–C_6 bond could lead to a transition state with positive charge generation at the tertiary benzylic position, which one would presume to be an energetically favorable process. This observed small effect of phenyl may also be due to the aforementioned dipolar repulsive interaction.



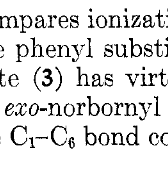
1



2



3



4

The rigid norbornane skeleton does not possess the conformational mobility of acyclic and simple monocyclic systems like cyclopentane and cyclohexane, and this rigid three-dimensional structure may provide an ideal system for the investigation of large steric effects.[3] As a consequence of this rigidity a preferred phenyl orientation in the ground state of a reacting species may remain so preferred in the transition state and lead to a rate retardation due to the preferential alignment. A different preferred phenyl orientation could lead to a rate acceleration, *viz.*, steric acceleration. For example, the overall effect of phenyl in the *cis–endo*-phenyl substituted isomer (**4**) is one of steric acceleration in which steric interactions are relieved in the transition state. In **4** the phenyl plane is presumably oriented in such a way that the dipolar repulsive interaction in the transition state is much less than that operating in **2**. Such preferential alignments of phenyls in **2**, **3**, and **4** have been demonstrated *via* compilation of nmr and ir spectral data.[4]

In an attempt to verify these factors contributing to the effects of the phenyl substituents on the acetolysis rates, we wished to determine acetolysis rates for substituted norbornyl tosylates lacking the phenyl substituent. Since the phenyl ring could be hydrogenated readily, we prepared the cyclohexyl derivatives from the available and characterized phenylnorbornanols. The cyclohexyl ring should have approximately the same bulk as phenyl and should transmit only a slight inductive electron-releasing effect to the reaction site. Herein we report the summations of our studies on the effects of cyclohexyl substituents on the acetolysis rates of *exo*- and *endo*-norbornyl tosylates.

All of the cyclohexyl derivatives were prepared by catalytic hydrogenation of the phenylnorbornanols with platinum oxide in acetic acid. One side reaction, that of partial esterification of the alcohol, frequently

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[1] D. C. Kleinfelter, E. S. Trent, J. E. Mallory, T. E. Dye, and J. H. Long, Jr., *J. Org. Chem.*, **38**, 4127 (1973).

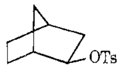
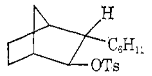
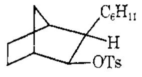
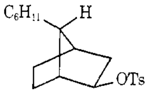
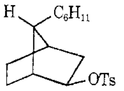
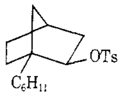
[2] D. C. Kleinfelter, M. B. Watsky, and W. E. Wilde, *J. Org. Chem.*, **38**, 4134 (1973).

[3] H. C. Brown and S. Ikegami, *J. Amer. Chem. Soc.*, **90**, 7122 (1968).

[4] (a) D. C. Kleinfelter, T. E. Dye, J. E. Mallory, and E. S. Trent, *J. Org. Chem.*, **32**, 1734 (1967); (b) D. C. Kleinfelter, *ibid.*, **32**, 3526 (1967); (c) D. C. Kleinfelter, *J. Amer. Chem. Soc.*, **89**, 1734 (1967).

TABLE I

KINETIC DATA FOR THE ACETOLYSES OF CYCLOHEXYL- (C_6H_{11}) SUBSTITUTED 2-*exo*-NORBORNYL TOSYLATES

Exo tosylate	Temp, °C	k_1, sec^{-1}	k_{rel} at 25°	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
 **5**-*x*	25.0[a]	2.40×10^{-5}	1.00	22.4	−4.6
 **6**-*x*	25.0[b]	3.64×10^{-5}	1.52	22.4	−3.6
	50.0	7.37×10^{-4}	(0.289)[c]		
 **7**-*x*	25.0	$2.50 \pm 0.16 \times 10^{-5}$	1.04	23.8	+0.14
	50.0	$6.02 \pm 0.16 \times 10^{-4}$	(0.00758)		
 **8**-*x*	25.0	$2.73 \pm 0.08 \times 10^{-5}$	1.14	23.3	−1.6
	50.0	$6.11 \pm 0.10 \times 10^{-4}$	(0.237)		
 **9**-*x*	50.0	4.37×10^{-5}	1.82	23.1	−0.91
	50.0	9.68×10^{-4}	(0.252)		
 **10**-*x*	25.0	3.51×10^{-3}	146		
			(3.98)		

[a] P. v. R. Schleyer, P. J. Stang, and D. J. Raber, *J. Amer. Chem. Soc.*, **92**, 4275 (1970). [b] Rate constants recorded without uncertainties (±) are extrapolated values reported due to some apparent internal return being involved. [c] Relative rates in parentheses are for the corresponding phenyl analogs.

occurred; therefore, the reaction product mixture was routinely treated with lithium aluminum hydride. Only 1-cyclohexyl-2-*endo*-norbornanol was not isolated as a pure compound. A small amount of epimeric exo alcohol was present. The sample of impure alcohol was converted to the tosylate mixture. After the mixture was allowed to sit for several days, all of the exo tosylate decomposed, leaving the endo tosylate unaffected. This partially decomposed mixture was used for the kinetic determinations without further purification.

Rate Data and Discussion.—Rate data for the acetolyses of the ten cyclohexylnorbornyl tosylates determined by us are listed in Tables I and II. The data for *exo*- and *endo*-norbornyl tosylates and relative rates for the analogous phenyl-substituted compounds are included for comparative purposes.

All of the 3- and 7-cyclohexyl-2-*exo*-norbornyl tosylates acetolyzed at rates *ca.* 1.0–1.8 times the rate of the unsubstituted parent (**5**-*x*). In the absence of any steric contribution to the reaction rates, one would predict a small inductive acceleration by virtue of the known electron-releasing effect of β and γ alkyl groups like cyclohexyl (δ^* for $C_6H_{11}CH_2$ −0.06; σ^* for $C_6H_{11}CH_2CH_2$ −0.03).[5] Two exo tosylates, **7**-*x* and **10**-*x*, deserve special consideration. The slow acetolysis rate for 2 of 0.00758 relative to **5**-*x* was attributed to the dipolar repulsive interaction. When the phenyl has been replaced by cyclohexyl as in **7**-*x*, the acetolysis rate is practically identical with that of **5**-*x*. When methyl and ethyl substituents are attached in the 1 position, rate increases relative to **5**-*x* of 51 and 78 are observed.[6] In these tosylates there must be significant positive charge buildup at C-1 in the transition state, contrary to the effect of the 1-phenyl substituent. The 1-cyclohexyl substituent in **10**-*x* causes a rate increase of 146 relative to **5**-*x*. The order of cyclohexyl (σ^* −0.15) > ethyl (σ^* −0.100) > methyl (σ^* 0.000) is the order of inductive effects of the groups rather than the Baker–Nathan order.[7] Streitweiser[8] has found that the rates of solvolysis of tertiary chlorides in 80% ethanol follow the inductive order, *i.e.*, the σ^* values for the R substituent groups. Relief of steric interactions between the 1-alkyl groups and the exo tosylate substituent may also accelerate the acetolysis rates relative to **5**-*x*. The order of steric substituent constants (E_s)[9] of cyclohexyl (−0.79) > ethyl (−0.07) > methyl (0.00) is also in line with the relative rates observed. Regardless of the effects contributing to cause the acceleration by the cyclohexyl over that of the methyl and ethyl groups, by analogy with the modest effect of a 3-cyclohexyl group on the acetolysis of an exo tosylate there must be significant positive charge generation at C-1 in the transition state for all of the 1-alkyl substituted 2-exo tosylates.

Of the four 3- and 7-cyclohexyl-2-*endo*-norbornyl tosylates, the 7-anti substituted compound (**8**-*n*) and

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(5) R. W. Taft, Jr., in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., Wiley, New York, N. Y., 1956, p 619; σ^* for $C_6H_{11}CH_2CH_2$ is obtained by dividing σ^* for $C_6H_{11}CH_2$ by 2.8 (see p 592).

(6) D. C. Kleinfelter and P. v. R. Schleyer, 138th National Meeting of the American Chemical Society, New York, N. Y., Sept 1960, Abstracts, p 432; D. C. Kleinfelter, *Diss. Abstr.*, **22**, 428 (1961); J. A. Berson in "Molecular Rearrangements," Part I, P. de Mayo, Ed., Interscience, New York, N. Y., 1963, p 182.

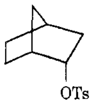
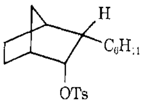
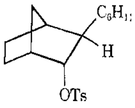
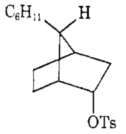
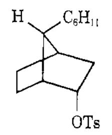
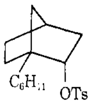
(7) J. W. Baker and W. S. Nathan, *J. Chem. Soc.*, 1840, 1844 (1935).

(8) A. Streitweiser, Jr., *J. Amer. Chem. Soc.*, **78**, 4935 (1956).

(9) Reference 5, p 598.

TABLE II

KINETIC DATA FOR THE ACETOLYSES OF CYCLOHEXYL- (C_6H_{11}) SUBSTITUTED 2-*endo*-NORBORNYL TOSYLATES

Endo tosylate	Temp, °C	k_1, sec^{-1}	k_{rel} at 25°	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
 5-*n*	25.0[a]	8.14×10^{-8}	1.00	26.5	−2.0
 6-*n*	25.0[b]	1.70×10^{-6}	20.9	26.6	+4.1
	50.0	5.81×10^{-5}	(2.35)[c]		
	75.0	1.21×10^{-3}			
 7-*n*	25.0[b]	7.40×10^{-9}	0.0910	28.3	−0.72
	75.0	$8.27 \pm 0.10 \times 10^{-6}$	(0.00392)		
	100.0	$1.38 \pm 0.01 \times 10^{-4}$			
 8-*n*	25.0[b]	1.12×10^{-7}	1.38	26.2	−2.6
	75.0	$7.45 \pm 0.08 \times 10^{-5}$	(0.286)		
	100.0	$9.92 \pm 0.16 \times 10^{-4}$			
 9-*n*	25.0[b]	6.17×10^{-8}	0.758	27.1	−0.72
	75.0	$4.93 \pm 0.03 \times 10^{-5}$	(0.367)		
	100.0	$7.17 \pm 0.11 \times 10^{-4}$			
 10-*n*	25.0[b]	7.32×10^{-7}	8.99	24.8	−3.5
	75.0	$3.43 \pm 0.07 \times 10^{-4}$	(0.695)		
	100.0	$4.00 \pm 0.10 \times 10^{-3}$			

[a] See footnote *a*, Table I. [b] Extrapolated from higher temperatures; also see footnote *b*, Table I. [c] See footnote *c*, Table I.

the 7-syn substituted compound (**9**-*n*) acetolyzed at rates close to that of the unsubstituted parent (**5**-*n*). The acetolysis rate for 3-*exo*-cyclohexyl-2-*endo*-norbornyl tosylate (**7**-*n*) is 0.0910 times that of **5**-*n*. However, this rate is still *ca.* 23 times faster than that of the phenyl analog (**1**). Of course, some of the phenyl rate retardation is due to the inductive effect of the substituent group. The E_s substituent constants for phenyl and cyclohexyl are −0.90 and −0.79, respectively;[9] *i.e.*, the bulk of a phenyl is presumed to be greater than that of a cyclohexyl. The relative steric effects of these substituents should depend on their rotational alignments with respect to the interacting reaction center. In the cyclohexane system the conformational free-energy differences, $-\Delta G_x°$ values in kcal/mol, for methyl, ethyl, and isopropyl are within the same range.[10] Presumably the methyls of an axial ethyl or isopropyl group may be rotated into positions where they cause no extra interference with the syn-axial ring hydrogens. On this basis the bulk of a cyclohexyl group should not be significantly different from that of an isopropyl group. The ortho hydrogens of phenyl can also be oriented away from axial hydrogens by rotation about the phenyl to cyclohexane bond axis. The $-\Delta G°$ values for phenyl and isopropyl by the same experimental method of equilibration in anhydrous ether are *ca.* 2.6[11] and 1.84–2.20,[12] respectively. The values for cyclohexyl and isopropyl by the nmr method in CCl_4 are 2.5[13] and 2.22 ± 0.08.[14] On the basis of these data a phenyl is slightly larger than a cyclohexyl substituent and a greater steric effect by the former might be expected. The relative steric effects of a 3-*exo*-phenyl *vs.* a 3-*exo*-cyclohexyl substituent on $LiAlH_4$ reduction of a 2-norbornanone may be obtained from the relative amounts of exo and endo alcohols formed. Reduction of 3-*exo*-phenyl-2-norbornanone gave an approximate 2.0:1.0 ratio of endo to exo alcohol, while reduction of the 3-exo-cyclohexyl analog gave only endo alcohol. Through this analogy one might expect a greater inhibition to solvation by the phenyl group.[15] Regardless of the magnitude of the difference between phenyl and cyclohexyl, the rate retardation demonstrated by **7**-*n* may be attributed to steric inhibition to solvation of the developing positive charge in the transition state.

While 3-*exo*-phenyl-2-*exo*-norbornyl tosylate (**2**) undergoes acetolysis quite slowly, presumably owing to

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(10) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Wiley, New York, N. Y., 1965, p 44.

(11) E. L. Eliel and M. N. Rerick, *J. Amer. Chem. Soc.*, **82**, 1367 (1960).

(12) E. L. Eliel and T. J. Brett, *J. Amer. Chem. Soc.*, **87**, 5039 (1965).

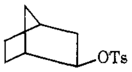
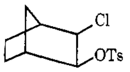
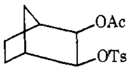
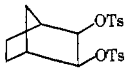
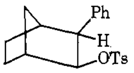
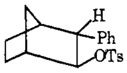
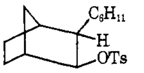
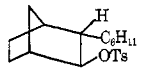
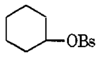
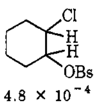
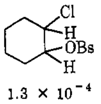
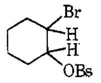
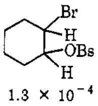
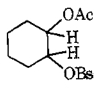
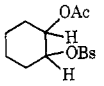
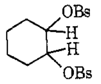
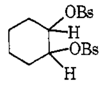
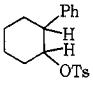
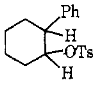
(13) J. Reisse, J. C. Celotti, D. Zimmermann, and G. Chiurloglu, *Tetrahedron Lett.*, 741 (1962).

(14) A. H. Lewin and S. Winstein, *J. Amer. Chem. Soc.*, **84**, 2464 (1962).

(15) The problems associated with attempts to equate ketone addition reactions with nucleophilic solvent approach to carbonium ions have been cited previously. See ref 1 and H. C. Brown and J. Muzzio, *J. Amer. Chem. Soc.*, **88**, 2811 (1966). These problems should be minimized when the comparisons are made between two substituents on the same carbon atom.

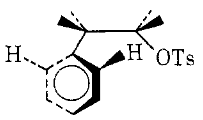
TABLE III

KINETIC DATA FOR THE ACETOLYSES OF SOME 3-SUBSTITUTED 2-*exo*-NORBORNYL TOSYLATES AND SOME 2-SUBSTITUTED CYCLOHEXYL BROSYLATES AND TOSYLATES

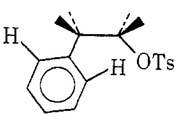
Compd	 **5-*x***	 **12**	 **13**	 **14**		
k_{rel} at 75°	1.00[a]	3.25×10^{-5} [b]	5.10×10^{-5} [a]	2.89×10^{-6} [a]		
Compd	 **2**	 **15**	 **7-*x***	 **6-*x***		
k_{rel} at 75°	1.73×10^{-2}	3.81×10^{-1}	1.58	1.62		
Compd						
k_{rel} at 74.9°	1.00[c]	4.8×10^{-4}	1.3×10^{-4}	1.05×10^{-1}	1.3×10^{-4}	
Registry no.		41914-94-7	41914-95-8	41914-96-9	41914-97-0	
Compd						
k_{rel} at 74.9°	2.40×10^{-1}	3.8×10^{-4}	6.9×10^{-5}	7.7×10^{-5}	1.21×10^{-1} [d]	1.93[d]
Registry no.	41914-98-1	41914-99-2	41915-00-8	27892-06-4	(75°)	(75°)

[a] J. R. Lambert and A. G. Holcomb, *J. Amer. Chem. Soc.*, **93**, 2994 (1971); the k_1 for **5-*x*** reported in this reference is 5.88×10^{-3} sec^{-1} while that calculated from **5-*x*** using the data in Table I is 6.31×10^{-3} sec^{-1}. Since we are using the k_{rel} for two of the compounds from Lambert and Holcomb, we are employing their value for **5-*x***. [b] H. L. Goering and M. J. Degani, *J. Amer. Chem. Soc.*, **91**, 4506 (1969); the listed k_{rel} was calculated from this reference and from data found in P. G. Gassman and J. M. Hornback, *J. Amer. Chem. Soc.*, **94**, 7010 (1972). Goering and Degani report a k_{rel} to 7-*syn*-chloro-2-*exo*-norbornyl tosylate at 78.2°, and Gassman and Hornback list data for this syn isomer from which a k at 75° was calculated. Then a k for **12** was calculated by assuming that the k_{rel} to the syn isomer would not be changed by the difference of only 3.2°. [c] S. Winstein, E. Grunwald, and L. L. Ingraham, *J. Amer. Chem. Soc.*, **70**, 821 (1948); E. Grunwald, *ibid.*, **73**, 5458 (1951). [d] H. C. Brown, K. J. Morgan, and F. J. Chloupek, *J. Amer. Chem. Soc.*, **87**, 2137 (1965); the data are relative to cyclohexyl tosylate at 75°. No correction was attempted for the different leaving group or the temperature difference of 0.1°.

the unfavorable dipolar interaction, a similar effect of equivalent magnitude cannot be operating in the endo isomer (**4**) since a rate acceleration (2.35 times) relative to **5-*n*** is observed. If the C–OTs bond is located directly below the plane of the benzene ring (see **11-*x*** below), then the destabilization of the transition state is presumed to be at a maximum. Such an arrangement would be approached by the exo isomer (**2**). If the C–OTs bond is located in the same plane as that defined by the benzene ring (see **11-*n*** below), then the dipolar contribution to the destabilization of the transition state should be at a minimum with only the inductive effect through the σ bonds affecting the rate. In this latter case steric acceleration should be at a maximum. Since there is some ground-state interaction between the endo phenyl π cloud and the cis-endo substituent, as shown from nmr and ir studies,[4] then the rate of the endo tosylate **4** reflects all three possible rate-influencing factors operating simultaneously, *i.e.*, the inductive effect through the σ framework (rate retardation), the dipolar effect through space, or field effect (rate retardation), and the steric effect (rate acceleration). If one were to accept the premise that a phenyl is larger than a cyclohexyl group, then the observed rates for **4** and **6-*n*** should be close to one another if no dipolar field effect were operating in **4**. That this effect is influencing the rate to some extent is revealed by the acetolysis rate for the cyclohexyl compound (**6-*n***), which is *ca.* 21 times faster than that of **5-*n***.



11-*x*



11-*n*

Finally, one of the most surprising rates was that exhibited by 1-cyclohexyl-2-*endo*-norbornyl tosylate (**10-*n***), which acetolyzed *ca.* 9.0 times faster than **5-*n***. Both the 1-methyl- and 1-ethyl-2-*endo* tosylates acetolyzed at the same rate (1.13 times **5-*n***).[6] Since the dihedral angle between the 1- and 2-endo substituents is considered to be *ca.* 79°,[16] steric interactions between said substituents would presumably be slight. However, the only tenable explanation for the observed rate of **10-*n*** is that of some relief of ground-state interactions between the cyclohexyl and OTs substituents in the transition state, *viz.*, steric acceleration. In the 1-ethyl compound the CH_3 may be rotated away from any potentially unfavorable interaction at the 2 position. However, when one of the CH_2 protons is replaced by CH_3 as in isopropyl, or in the structurally analogous cyclohexyl case (here a CH_2 proton is replaced by CH_2R), then some steric interaction may be present. The norbornane ring should be equatorially attached to the cyclohexane ring. By positioning the tertiary axial proton toward C-2 of the norbornane ring, the cyclohexane's 2-methylene group may then interact with the C-2 endo-OTS substituent. The equatorial attachment of isopropyl or cyclohexyl to a cyclohexane ring with the tertiary axial hydrogen directed toward a 2-positioned substituent would not cause a similar unfavorable interaction.[17]

The Case for Dipolar (Field) Effects in Cis–Exo Norbornanes.—Table III lists some relative rates for

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(16) F. A. L. Anet, *Can. J. Chem.*, **39**, 789 (1961).

(17) This difference can be seen best with the aid of molecular models. In a previous paper (ref 4b) it was shown that there is some interaction between a 1-phenyl substituent and the 2-tosylate aromatic protons. The tosyloxy protons appear at δ 7.83 and 7.31 in 7-*anti*-phenyl-2-*exo*-norbornyl tosylate (no interaction possible), while the same protons appear at δ 7.45 and 7.04 in 1-phenyl-2-*endo*-norbornyl tosylate.

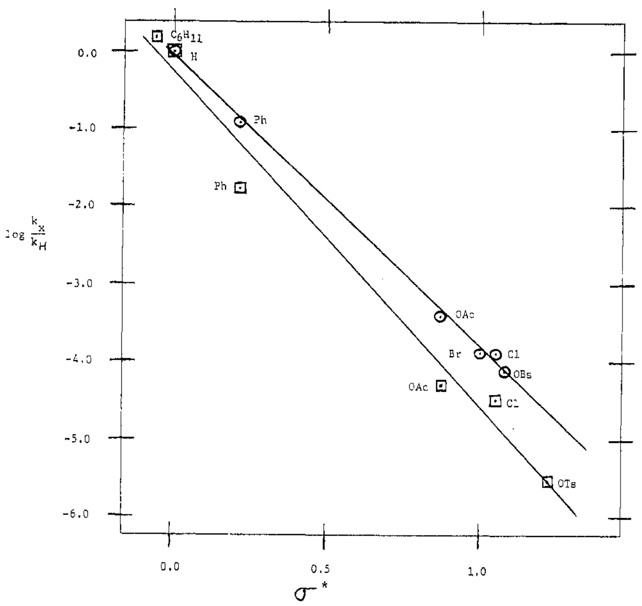

Figure 1.—Plot of log k_X/k_H *vs.* σ^* for the acetolysis of 2-substituted cyclohexyl brosylates (○) and 3-exo-substituted 2-*exo*-norbornyl tosylates (□). $\rho = -3.77$, $r = -0.99$ for cyclohexyl compounds; $\rho = -4.34$, $r = -0.985$ for the norbornyl compounds. σ^* for OAc of 0.87 was calculated from the σ_I of 0.39 using the formula $\sigma_I = (0.45)\sigma^*_{XCH_2}$; see ref 5, p 594. Although σ^* values for OBs and OTs are not listed in the literature, they have been included in the plots. Using these data, σ^* values of -1.08 and -1.22 for OBs and OTs, respectively, may be obtained.

some *exo*-norbornyl tosylates and some cyclohexyl brosylates and tosylates. We offer a rationalization of these data which will support our hypothesis that an adverse dipolar or field effect is operating to a large extent in the acetolyses of **2** and **3**. Four of the 3-exo-substituted tosylates listed can exhibit rate retardation *via* inductive effects through the σ system as well as through space (field effect). The relative rates shown, Ph > OAc > Cl > OTs, are what one would expect based on σ^* substituent constants (XCH_2). The only cis and trans compounds studied bearing one of these substituents (Ph) are **2** and 3-*endo*-phenyl-2-*exo*-norbornyl tosylate (**15**). The rate of **2** is 22 times slower than that of **15** at 75°. The problem with the other 3-exo-substituted tosylates revolves around estimates of what one would expect the cis substituents to exert on the acetolysis rates; *i.e.*, how much slower should their rates be relative to their trans (3-endo-substituted) isomers.

Since the rigid norbornane system does not enjoy the flexibility of acyclic or alicyclic systems, the unfavorable dipolar effect is presumably at a maximum in the cis–exo-substituted norbornanes. In the cyclohexane system where the dihedral angles between adjacent substituents are 60° or more, such a dipolar effect should operate to a smaller extent. The cis cyclohexane compounds represent the best model compounds for measuring the overall inductive effects, since neighboring-group participation is inoperative in these stereoisomers. The rates of the two dibrosylates are practically the same, since no neighboring-group participation operates in the trans isomer as well. Once again the relative rates shown, Ph > OAc > Cl = Br > OBs, are what one would expect based on σ^* substituent constants. The relative effects of the substituents in the two systems may be revealed by the $\rho\sigma^*$ plots shown in Figure 1. This figure illustrates that the rate depressions caused by exo Ph, OAc, Cl, and OTs substituents in the norbornane system are greater than those observed by the same substituents (OBs rather than OTs) in the cyclohexane system. The magnitude of these relative rate depressions in the two systems ranges from 2.7 (OBs or OTs) to 7.5 (OAc). The cis cyclohexane system may be complicated somewhat by the possibility of the leaving brosylate (or tosylate) occupying either the equatorial or axial position. The interaction of an axial tosylate group with the syn-axial hydrogens is relieved when one goes to the carbonium ion intermediate or to the corresponding transition state which resembles the intermediate.[18] Hence, the greater the percentage of molecules reacting with the OTs or OBs groups axial, the faster will be the rate. This complication is maximized in the *cis*-2-phenylcyclohexyl tosylate, where the free energy difference between Ph and OTs is such that most of the reacting molecules would have the OTs in the axial position. In addition, some of the rate acceleration in this tosylate has been ascribed to steric acceleration combined with H participation.[19] For these reasons we have used the relative rate for the *trans*-2-phenylcyclohexyl tosylate in our $\rho\sigma^*$ plot.[20] Neighboring phenyl group participation is inoperative in the acetolysis of this compound.

Georing and Degani[21] have mentioned that the rate difference between 3-*exo*-chloro-2-*exo*-norbornyl tosylate (**12**) and 3-*endo*-chloro-2-*exo*-norbornyl tosylate (**16**) should be less than the *ca.* 4 difference in the cyclohexyl system. Since the two dibrosylates acetolyze with approximately the same rates, the difference in the 2-chlorocyclohexyl brosylates may be attributed to some small amount of neighboring chloro participation in the trans compound. As mentioned previously, tosylate **2** acetolyzes at a rate which is 22 times slower than that of **15**. Based on our previous rationale, the difference in rates between **12** and **16** may actually turn out to be significantly greater than 4.

In the 1-substituted 2-*exo*-norbornyl system a phenyl substituent accelerates the acetolysis rate by a factor of only 3.91 while an alkyl group causes a rate increase of 51–146, indicative of significant positive charge generation in the transition state for the 1-alkyl substituted compounds. The lack of significant rate enhancement in **3** may also be explained by the unfavorable dipolar effect previously discussed with reference to the cis–exo isomer (**2**). A dipolar effect may be used to explain why a 1-methoxy substituent in **17** exerts a much smaller rate-accelerating effect than a 1-methyl substituent[22] whereas in other systems methoxy prevails over methyl in their abilities to delocalize positive charge. A dipole–dipole repulsive interaction has been suggested as a possible explanation for the small (2.9) exo:endo ratio in the acetolysis rates of the 1-cyanoapoisobornyl (**18**) and 1-cyanoapobornyl (**19**) brosylates,[23] in which the rate of the exo brosylate is

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[18] G. S. Hammond, *J. Amer. Chem. Soc.*, **77**, 334 (1955); see, *e.g.*, ref 10, p 84.

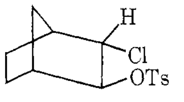
[19] H. C. Brown, K. J. Morgan, and F. J. Chloupek, *J. Amer. Chem. Soc.*, **87**, 2137 (1965).

[20] When the *trans*-2-phenylcyclohexyl tosylate is not included, a ρ of -3.81 is obtained, $r = -0.999$.

[21] H. L. Goering and M. J. Degani, *J. Amer. Chem. Soc.*, **91**, 4506 (1969).

[22] Footnote *a*, Table I.

[23] R. Muneyuki and T. Yano, *J. Amer. Chem. Soc.*, **92**, 746 (1970).



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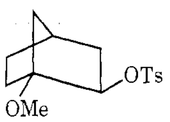

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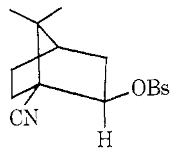

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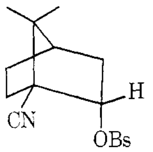

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retarded by a factor of 1.71×10^{-7} (relative to apoisobornyl) while for the endo brosylate this difference (relative to apobornyl) is reduced to 2.43×10^{-4}. Presumably the dipolar effect is quite small in the endo brosylate (ϕ between CN and OBs is *ca.* 79°) wherein the inductive effect through the σ system exerts the greater influence. We intend to determine the acetolysis rates of the 3-endo-substituted 2-exo isomers of **12**, **13**, and **14** to test the hypotheses set down in this publication.

Experimental Section

Melting points were determined in soft capillary tubes using a Hoover capillary melting point apparatus (Arthur H. Thomas Co., Philadelphia, Pa.) and are uncorrected. A Varian A-60 nmr spectrometer, calibrated with tetramethylsilane (δ 0) and chloroform (δ 436.5 Hz), was used for the nmr determinations. Chemical shifts are presumed correct to ±0.01 ppm. Microanalyses were carried out by F. B. Strauss Microanalytical Laboratory, Oxford, England. All ether and ligroin solutions of products were dried over anhydrous sodium sulfate prior to removal of solvent. Ligroin was distilled over potassium permanganate and had bp 40–55°.

Preparation of the Cyclohexylnorbornanols.—All of the cyclohexylnorbornanols were prepared from the known phenylnorbornanols by catalytic hydrogenation. A typical procedure follows. The phenylnorbornanol (*ca.* 5 g) was dissolved in a minimum amount of acetic acid. Platinum oxide (*ca.* 200 mg) was added, and the mixture was subjected to *ca.* 40 psi of hydrogen in a Paar bomb apparatus for 24 hr or until no more hydrogen was taken up. After filtration the acetic acid solution was poured into water. If the product solidified it was filtered and washed with dilute sodium hydroxide and then with water. If the product did not solidify, the oil was extracted with ligroin, the ligroin solution was washed with dilute sodium hydroxide and dried, and the solvent was removed at reduced pressure. The resultant solid or oil was dissolved in ether, stirred with $LiAlH_4$ (*ca.* 1.0 g) to reduce any acetate that formed, and worked up in the standard manner. The cyclohexylnorbornanol was crystallized and/or recrystallized from ligroin. The melting points and chemical shifts of the H-2 protons are listed in Table IV. The *p*-toluenesulfonates were prepared in the usual manner.[24] Their melting points are listed in Table V.

Reduction of 3-*exo*-Cyclohexyl-2-norbornanone.—An ether solution of 3-*exo*-cyclohexyl-2-norbornanone (0.83 g, 0.0043 mol), prepared by the oxidation of 3-*exo*-cyclohexyl-2-*endo*-norbornanol with 8 *N* chromic acid in acetone held at 0°, was reduced with 0.5 g of $LiAlH_4$ in the standard manner.[25] Nmr analysis showed only the H-2 absorption at δ 3.87, characteristic of the endo isomer. No appreciable absorption at δ 3.73 for the exo isomer was observed.

TABLE IV

PHYSICAL DATA FOR CYCLOHEXYLNORBORNANOLS

	Norbornanol[a]			
Registry no.	Cyclohexyl	OH	Mp, °C	Nmr[b] (H-2), ppm
38935-69-2	3-*n*	2-*x*	70.5–71.5	3.13
38935-68-1	3-*n*	2-*n*	57.0–57.5	4.21
38935-70-5	3-*x*	2-*x*	Oil	3.73
38935-71-6	3-*x*	2-*n*	65–67	3.87
38935-72-7	7-*a*	2-*x*	78–79	3.71
38935-73-8	7-*a*	2-*n*	83–86	4.04
38935-74-9	7-*s*	2-*x*	116–117	3.80
38935-75-0	7-*s*	2-*n*	101.0–101.5	4.34
41915-10-0	1	2-*x*	71–73	3.63
41915-11-1	1	2-*n*	Semisolid	3.87

[a] Satisfactory combustion analytical data for C, H (±0.4%) were reported for these compounds: Ed. [b] CCl_4 solution.

TABLE V

PHYSICAL DATA FOR CYCLOHEXYLNORBORNYL TOSYLATES

Tosylate[a]	Mp, °C
6-*x*	78–80
6-*n*	103–106
7-*x*	61–62.5
7-*n*	111–112
8-*x*	55–57
8-*n*	80–81
9-*x*	58.5–59
9-*n*	102–103
10-*x*	105–107
10-*n*	110–111

[a] Satisfactory combustion analytical data for C, H (±0.3%) were reported for these compounds: Ed.

Kinetic Procedures.—Anhydrous acetic acid was prepared by distillation from acetic anhydride. Substrate concentrations for tritrimetric kinetics were generally 0.040 ± 0.010 *M*. The method of Winstein[26] was employed for the titrimetic tosylate acetolyses. Bromthymol Blue and Crystal Violet were used as indicators. All tosylates displayed good first-order kinetics. Eight titrimetric points were usually taken per kinetic run and most acetolyses were followed to 70% reaction or greater.

Acknowledgment.—We wish to thank Mr. R. A. Ralston for the least-squares analysis for Figure 1. J. M. M. wishes to acknowledge support by a Union Carbide Fellowship (1967–1968) and a Petroleum Research Fellowship (1968–1969).

Registry No.—**2**, 10472-63-6; **5**-*x*, 959-42-2; **5**-*n*, 840-90-4; **6**-*x*, 41915-15-5; **6**-*n*, 41915-16-6; **7**-*x*, 41939-31-5; **7**-*n*, 41915-17-7; **8**-*x*, 41915-18-8; **8**-*n*, 41915-19-9; **9**-*x*, 41915-20-2; **9**-*n*, 41915-21-3; **10**-*x*, 41915-23-5; **10**-*n*, 41915-22-4; **15**, 10561-82-7; 3-*endo*-phenyl-2-*exo*-norbornanol, 944-56-9; 3-*endo*-phenyl-2-*endo*-norbornanol, 10381-59-6; 3-*exo*-phenyl-2-*exo*-norbornanol, 10472-45-4; 3-*exo*-phenyl-2-*endo*-norbornanol, 10561-84-9; 7-*anti*-phenyl-2-*exo*-norbornanol, 14181-16-9; 7-*anti*-phenyl-2-*endo*-norbornanol, 41770-32-5; 7-*syn*-phenyl-2-*exo*-norbornanol, 14181-14-7; 7-*syn*-phenyl-2-*endo*-norbornanol, 41770-08-5; 1-phenyl-2-*exo*-norbornanol, 14182-93-5; 1-phenyl-2-*endo*-norbornanol, 14182-96-8.

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(24) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Wiley, New York, N. Y., 1967, p 1180.

(25) W. G. Brown, *Org. React.*, **6**, 469 (1951).

(26) S. Winstein, C. Hansen, and E. Grunwald, *J. Amer. Chem. Soc.*, **70**, 812 (1948).