4. Norbornanes

Part 19

The Inductive Model for Norbornyl Cation Formation

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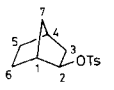
Two CH_3 groups at C(6) of 2-*exo*- (**10a**) and 2-*endo*-norbornyl *p*-toluenesulfonate **11a** lower their solvolysis rates in 80% EtOH by factors of 28 and 16, respectively. A spirocyclopropyl group including C(6), as in **21a** and **22a**, reduces the rate of *exo*- and *endo*-ionization by factors of 250 and 8, respectively. The geminally dimethyl-substituted tosylates **10a** and **11a** yield the 2-*exo*-alcohol **10b**, whereas the spirocyclopropyl-substituted tosylates **21a** and **22a** furnish rearranged 3-brendanol **23**. These findings are readily rationalized by the inductive model, according to which norbornyl cation formation is controlled by the inductive effect of dorsal substituents.

Substituents at C(4), C(5), C(6), and C(7) of 2-*exo*- and 2-*endo*-norbornyl *p*-toluenesulfonate (tosylate) **1** and **2**, respectively, control solvolysis rates by their inductive (*I*) effect only [1]. This follows from the observed linear correlation of the logarithms of the rate constant $\log k$ with the inductive constants of the substituents σ_I^q [2] at these positions according to the equation $\log k/k_0 = \rho_I \sigma_I^q$, which, in addition to other data [3], precludes steric effects as a significant rate and product-controlling factor[1]).



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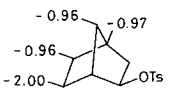

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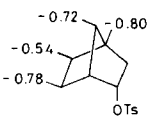

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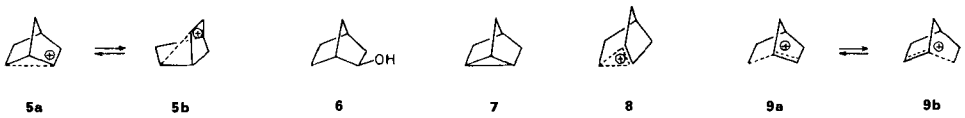
However, reaction rates are far more sensitive to substituents at C(6) than to those at other positions, as illustrated by the size of the reaction constants ρ_I [1d]. The ρ_I values for the 2-*exo*- and 2-*endo*-norbornyl tosylates determined to date in 80% EtOH are summarized in **3** and **4**. These values [4] are uniformly higher for *exo*- than for *endo*-ionization. The difference $\Delta\rho_I$ is especially large for C(6) ($\Delta\rho_I = 1.22$) and is considered to be responsible for the large *exo*/*endo*-rate ratio of more than 300 observed for the parent tosylates **1** and **2** [1].

Furthermore, the higher rate of **1** was ascribed to the favorable alignment of C(6) for dorsal participation in *exo*-ionization to form the unsymmetrically bridged ion **5a**. The latter equilibrates rapidly with its enantiomer **5b** by a degenerate rearrangement, which is observably slowed down by $-I$ substituents at C(6) [4]. These substituents reduce bridg-

[1]) For a review, see [4].

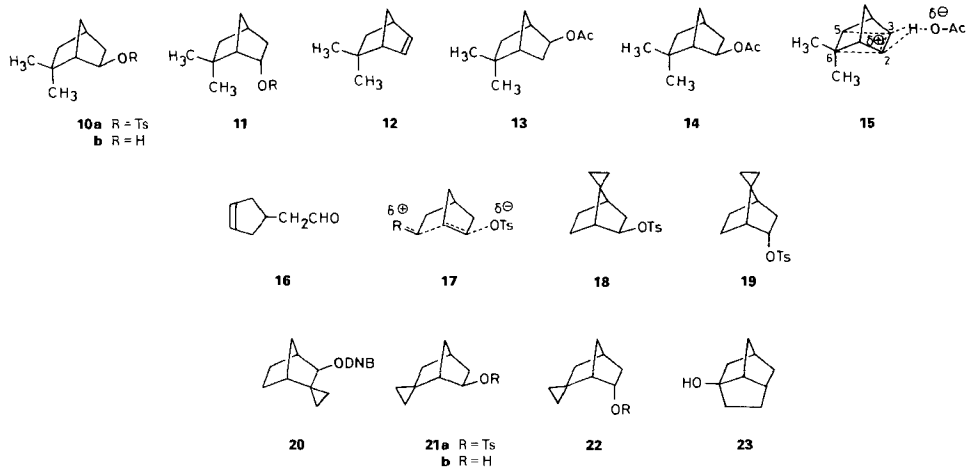


5a **5b** **6** **7** **8** **9a** **9b**

ing and, hence, lead to 2-*exo*- and 2-*endo*-substitution. The dotted line in **5a** and **5b** signifies a weak bonding interaction which results from an inductive shift of electron density from C(6) toward the electrophilic center at C(2). As evidenced by the relatively low ρ_I of -0.72 for C(7) in **4**, dorsal assistance to *endo*-ionization is hindered, presumably because bridging of C(7) to C(2) would afford a cation that is more strained than **5**. Hydrolysis, therefore, yields 2-*exo*-norbornanol **6** with inversion of configuration [1a] [4].

Other closely related rationales for norbornyl cation formation have been proposed previously[2]). Thus, according to *Winstein* [6] the two electrons constituting the C(1)–C(6) σ-bond participate selectively in *exo*-ionization, thereby forming the symmetrically bridged nonclassical cation **8**. In this structure, the positive charge is assumed to be shared equally by C(1) and C(2) and, to a lesser degree, by C(6) [7]. More recently *Jensen* and *Smart* [8] suggested that C,C-hyperconjugative delocalization of the strained C(1)–C(6) σ bond in the ionization of **1** leads to the asymmetrical cation **9a**. For stereoelectronic reasons, this kind of stabilization is not feasible in *endo*-ionization. As pointed out by *Brown* [5], the cation **9a** retains the geometry of **1** and would, therefore, still have to equilibrate rapidly with its enantiomer **9b** to explain the formation of racemic 2-*exo*-norbornanol **6** from optically active **1** [6][3]).

The latter two models are not easily reconciled with certain reports in the literature. Thus, *Schleyer et al.* [7] observed that the introduction of two CH_3 groups at C(6), as in **10a**, lowers the acetolysis rate relative to that of the parent tosylate **1** by a factor of 25 at 25°, whereas an increased rate would be expected on the basis of the nonclassical and C,C-hyperconjugative model, for both imply a transfer of positive charge from C(2) to C(6) in the transition state. The ionization rate of the 2-*endo*-tosylate **11a**, in which the



10a R = Ts **b** R = H **11** **12** **13** **14** **15** **16** **17** **18** **19** **20** **21a** R = Ts **b** R = H **22** **23**

[2]) See the comprehensive review [5].

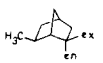
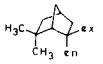
[3]) Confirmed in an unpublished work with *Bruno Schaub*.

geminal methyl groups should have little or no effect on the rate, is reduced by a similar factor of twenty. *Schleyer et al.* attributed these rate decreases to steric deceleration, implying that the transition states for **10a** and **11a** are more crowded than the ground states[4]).

More recently, we have shown that a 6-*exo*- or a 6-*endo*-CH_3 group reduces the solvolysis rate of 2-*exo*- and 2-*endo* norbornyl tosylates according to their small electron attracting $-I$ effect at an sp^3 C-atom ($\sigma_I^q = 0.11$) [2], as illustrated by k^{rel} in *Table 1*. This finding supports the assumption that the larger rate decrease caused by the geminal methyl groups in **10a** and **11a** is due mainly to their combined $-I$ effects. This view is also borne out by *McGreer*'s study [9] of the addition of AcOH to 6,6-dimethylnorbornene **12**, which showed that twice as much acetate **13** than the expected isomer **14** is obtained. It appears then that C(6)–C(2) bridging is somewhat weaker than C(5)–C(3) bridging in the transition state **15** for proton transfer. It is also noteworthy that 2-*exo*-norbornyl tosylates **1** bearing *n*-electron donors at C(6), such as $(CH_3)_2N$, HO, CH_3O, and CH_3S, react 1261 to 40 times faster than calculated on the basis of their σ_I^q values. Furthermore, quantitative fragmentation takes place in these cases yielding the unsaturated aldehyde **16** by subsequent hydrolysis [1a]. It is also of interest that the transition state for fragmentation **17** resembles those implied by the nonclassical and C,C-hyperconjugative models.

In a study designed to reveal charge dispersal from C(2) to C(1), as demanded by the nonclassical model, *Wilcox* and *Jesaitis* [10] compared the acetolysis rates of **1** and **2** with those of the corresponding 7-spirocyclopropyl derivatives **18** and **19**, respectively. Participation of the C(1)–C(6) σ-bond should increase the ionization rate of the *exo*-tosylate **18** substantially, while the rate of the *endo*-tosylate **19** should not be affected. In fact, the rates of both epimers differed only little from those of the respective parent tosylates **1** and **2**. Therefore, very little σ participation is indicated in the transition state for **18**. In contrast, the 3,5-dinitrobenzoate (DNB) of 3-spirocyclopropyl-2-*exo*-norbornanol **20** reacted *ca.* 10^3 times faster than the parent ester, clearly illustrating the large stabilizing

Table 1. *Rate Constants for Solvolysis of* 2-exo- *and* 2-endo-*Norbornyl* p-*Toluenesulfonates in 80% EtOH at 70.0°*, k_{rel}, *and* exo/endo-*Rate Ratios* (*ex* and *en* denote an *exo*- or an *endo*-OTs group, respectively)

	k_{exo}	k_{exo}^{rel}	k_{endo}	k_{endo}^{rel}	k_{exo}/k_{endo}
	$2.62 \cdot 10^{-2}$ [a])	1	$8.42 \cdot 10^{-5}$	1	311
	$1.09 \cdot 10^{-2}$ [b])	1/2.4	$6.02 \cdot 10^{-5}$	1/1.4	181
	$5.58 \cdot 10^{-3}$ [c])	1/5	$1.18 \cdot 10^{-5}$	1/7	473
	$9.39 \cdot 10^{-4}$ [d])	1/28	$5.31 \cdot 10^{-6}$	1/16	178
	$1.05 \cdot 10^{-4}$ [d])	1/250	$1.09 \cdot 10^{-5}$	1/8	10

[a]) [14]. [b]) [1a]. [c]) [3]. [d]) This work.

[4]) Actually, a case for steric acceleration could be made since the stretching of the C(1)–C(6) and C(2)–C(6) bonds in **8** should relieve strain.

effect of the cyclopropyl group on an adjacent cationic center. It is noteworthy that the high *exo*/*endo*-rate ratio of *ca.* 10^3 for **18** and **19** observed by *Wilcox* and *Jesaitis* [10] is also in accord with the inductive model which predicts normal bridging of C(6) in *exo*-ionization of **18**, but even less bridging of C(7) than in **2** in *endo*-ionization of **19** due to the considerable $-I$ effect of the cyclopropyl ring[5]).

The significance of the work described above warranted its extention to a study of the 6-spirocyclopropyl-2-*exo*- and 2-*endo*-norbornyl tosylates **21a** and **22a**[6]).

According to the nonclassical model, the cyclopropyl group should again enhance the rate of the *exo*-tosylate **21a**, if appreciable positive charge were generated at the adjacent C(1) in the transition state. In contrast, the inductive model predicts a marked decrease in rate compared to the parent tosylate **1**, because the $-I$ effect of the cyclopropyl group should lower the tendency of C(6) to bridge the incipient cationic center at C(2). In this communication, the rate constants in 80% EtOH for the tosylates **21a** and **22a** are reported together with those of the 6,6-dimethyl-2-*exo*- and 2-*endo*-tosylates **10a** and **11a**, respectively.

The preparation of the compounds **10**, **11**, **21**, and **22** and the identification of their hydrolysis products in 70% dioxane are described in [12]. Also described in [12] is the resolution of the racemic alcohol **10b** into optically active **10b** (m.p. 30–31.5°; $[\alpha]_D^{25} - 5.14$ ($c = 1.33$, THF)) which furnished the optically active tosylate **10a** (m.p. 52.5–53.5°; $[\alpha]_D^{25} - 4.63°$ ($c = 1.36$, THF)). Solvolysis of the latter should lead to racemic product, if ionization is followed by a degenerate rearrangement, as observed in the hydrolysis of the optically active parent tosylate **1**[3]).

Results. – The rate constants were measured conductometrically [13] at three temperatures *(Table 2)*. Hydrolysis of the *exo*-tosylate **10a** yielded 92% of the corresponding

Table 2. *First-Order Rate Constants for* 10^{-3} M *Solutions in 80% EtOH, and Activation Parameters*

Compound	T [°]	k [s^{-1}]	$\Delta H^{\neq}$ [kcal/mol]	$\Delta S^{\neq}$ [cal/mol·degree]
10a	59.83	$3.30 \cdot 10^{-4}$	22.6	− 6.9
	69.95	$9.31 \cdot 10^{-4}$		
	70.00[a])	$9.39 \cdot 10^{-4}$		
	80.17	$2.50 \cdot 10^{-3}$		
11a	70.00[a])	$5.31 \cdot 10^{-6}$	27.3	− 3.4
	99.90	$1.43 \cdot 10^{-4}$		
	109.90	$3.85 \cdot 10^{-4}$		
	120.10	$1.00 \cdot 10^{-3}$		
21a	70.00[a])	$1.05 \cdot 10^{-4}$	23.6	− 8.1
	79.67	$2.80 \cdot 10^{-4}$		
	89.70	$7.31 \cdot 10^{-4}$		
	99.55	$1.77 \cdot 10^{-3}$		
22a	70.00[a])	$1.09 \cdot 10^{-5}$	24.5	− 10.1
	99.54	$2.04 \cdot 10^{-4}$		
	109.35	$4.89 \cdot 10^{-4}$		
	119.42	$1.14 \cdot 10^{-3}$		

[a]) Extrapolated.

[5]) *E.g.* The p*K*a of cyclopropylamine and 2-propylamine are 9.1 and 10.63, respectively [11].

[6]) We thank Prof. *P. von R. Schleyer*, Erlangen, for drawing attention to this problem.

Table 3. *Yield of Products and Reaction Conditions in 70% Dioxane*

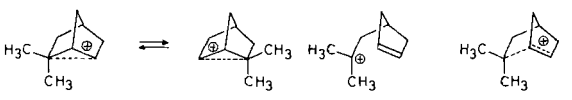
Reactand	T [°C]	Time [min]	Products (Yields)
10a	70	120	**10b** (92%); **12** (8%)
11a	110	440	**10b** (100%)
21a	90	160	**23** (100%)
22a	110	235	**23** (100%)

exo-alcohol **10b** with complete retention, beside 8% 5,5-dimethylnorbornene **12** (*Table 3*). The *endo*-tosylate **11a** yielded the *exo*-alcohol **10b** only, *i.e.* with complete inversion. Solvolysis of optically active **10a** in 70% dioxane or in 80% EtOH and dry EtOH led to completely inactive, *i.e.* racemized product. Hydrolysis of both *exo*- and *endo*-tosylates **21a** and **22a** led to a quantitative yield of the unknown tricyclo[4.2.1.$0^{3,7}$]nonan-3-ol (3-brendanol) **23**, m.p. 88–89.6°, which was identical with a sample prepared by an independent route [12].

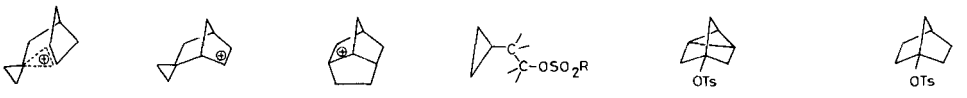
Discussion. – According to the C,C-hyperconjugative model [8], CH_3 groups at C(6) of **1** should facilitate the participation of the C(1)–C(6) σ-bond and thereby increase the rate of *exo*-ionization selectively. As shown in *Table 1*, the opposite effect is observed, for the 6,6-dimethyl derivative **10a** reacted 28 times slower (at 70°) than the parent tosylate, thus confirming *Schleyer*'s earlier measurements in AcOH [7]. It is noteworthy that the 2-*endo*-tosylate **11a** reacted 16 times more slowly than the parent tosylate **2**, which leaves little room for specific σ participation in *exo*-ionization. Also, rate reduction should be larger for *endo*- than for *exo*-ionization, if steric hindrance of the former were a crucial factor [5].

The formation of 92% *exo*-alcohol **10b** from **10a** with retention, beside 8% elimination to **12**, and of 100% *exo*-alcohol **10b** from **11a** with inversion indicates a transient bridged intermediate **24a**, which reacts with H_2O on the *exo*-side only. Furthermore, the alcohol **10b** recovered from hydrolysis of optically active **10a** was completely racemized, indicating that the cation **24a** equilibrates faster with its enantiomer **24b** than it is captured by H_2O. It is significant that neither **10a** nor **11a** underwent fragmentation to the monocyclic tertiary carbenium ion **25**, a species that differs from the C,C-hyperconjugated cation **26** only in the degree to which the C(1)–C(6) bond is broken. On the other hand, the above results are well accomodated by the inductive model.

This applies also to the solvolysis of the 6-spirocyclopropyl derivatives **21a** and **22a** which react 250 and 8 times, respectively, slower than the corresponding parent compounds **1** and **2**, thereby causing a remarkable drop of the *exo*/*endo* ratio from 311 to 10



24a **24b** **25** **26**



27 **28** **29** **30** **31** **32**

(Table 1). This result is in agreement with the earlier finding, *i.e.* that the inductivity of C(6) for *exo*-ionization is much larger than that of C(7) for *endo*-ionization [1a] [1b] [4]. Again, the results are less easily rationalized with the nonclassical model, which assumes that a substantial positive charge develops at C(1) in the transition state leading to the symmetrically bridged cation **27**. In contrast, the inductive model predicts that the $-I$ effect of the cyclopropyl group reduces bridging and hence the rate of ionization to the cation **28**. The latter subsequently undergoes a 1,3-shift to form the brendyl cation **29**, the precursor of **23**. Cyclopropane-to-cyclopentane ring enlargements in the solvolysis of β-cyclopropylethyl sulfonates **30** have been observed before and studied by *Sauers* and *Uebersax* [16], *Dewar* and *Harris* [17], and *Rhodes* and coworkers [18]. There is also precedence for the strong rate-retarding $-I$ effect of the cyclopropane ring in S_N1 reactions. A striking example was reported by *Chernier et al.* [19], who found that 4-nortricyclyl tosylate **31** reacted 10^5 times slower than 1-norbornyl tosylate **32**. The authors suggest that at least part of this large rate reduction is due to the $-I$ effect of the cyclopropane ring, in which all three C-atoms are located dorsal to the leaving group.

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