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EXO/ENDO SOLVOLYSIS RATE RATIOS IN CONSTRAINED 2-NORBORNYL SYSTEMS

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Summary: Tetracyclo[6.2.1.0^{2,6}.0^{5,10}]undec-3-yl derivatives (6 - 8) show typically high tertiary exo/endo solvolysis rate ratios, but the ratios for secondary reactants are suppressed. The rate and product data support the theory of anchimeric assistance in the parent exo-2-norbornyl solvolysis.

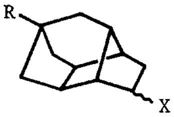
Exo/endo rate and product ratios have been central to efforts to characterize the intermediates in solvolysis of 2-norbornyl derivatives.[1] Winstein[2] originally attributed the high rate ratio for the parent secondary brosylates 1 (Scheme I) - see also 2[3]- to anchimerically assisted ionization of the exo isomer with formation of a symmetrically bridged cation, 9.[4] Brown subsequently discovered the exo/endo ratio also to be large for tertiary norbornyl reactants, 3,[5] where anchimeric assistance must be much less important. He proposed steric inhibition of endo ionization as a common explanation for both secondary and tertiary systems.[1,6]

Low exo/endo rate ratios have been observed for a variety of secondary sulfonates in which the 2-norbornyl skeleton is incorporated into a larger polycyclic framework constrained against bridged ion formation.[7-10] Among these the exo-5,6-trimethylene-2-norbornyl system,[8] 4 and 5, provides a particularly serious stumbling block for Brown's steric interpretation.[9] The extra ring away from the reaction site would not be expected to introduce any steric complication under ordinary reaction, and indeed the tertiary esters 5 have virtually the same reactivities as their norbornyl counterparts 3 and exhibit a characteristically high exo/endo rate ratio. In contrast, the secondary exo/endo ratio for 4 drops dramatically. This singular behavior is easily explained as the result of inhibited anchimeric assistance. In exo-4, sigma bridging during ionization would require the 5,6-trimethylene substituent "to move toward the more crowded endo environment, increasing the strain. The system resists this change, resulting in a decreased rate for the exo isomer and a decreased exo/endo rate ratio."[10]

Scheme I. Exo/endo solvolysis rate ratios at 25.0 °C

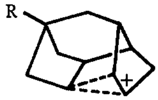
1 **2**

4



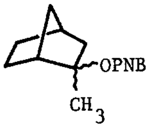
6 **7**

9



10

	1	2	4	6	7
R =				H	CH_3
X =	OBs	OTs		OBs	OTs
HOAc	348[a]	292[b]	19.5[e]		5.3
60% EtOH	1160[c]	1010[d]	5.3 (EtOH)[e]	16.8	



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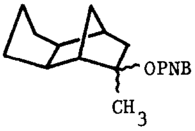

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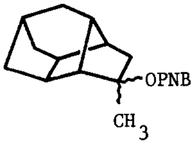

8

	3	5	8
80% acetone	885[f]	420[g]	164 (60% acetone)

[a] Ref 2. [b] Ref 3. [c] Calculated from data in Harris, J. M.; Mount, D. L.; Raber D. J. *J. Am. Chem. Soc.* **1978**, *100*, 3139 with the assumption that k(OBs)/k(OTs) = 5.0; see Roberts, D. D. *J. Org. Chem.* **1972**, *37*, 1510. [d] Lenoir, D. *Chem. Ber.* **1975**, *108*, 2055. [e] Ref 8a. [f] Ref 5b. [g] Ref 8b,c.

Table I. Solvolysis Rate Constants

Reactant	Solvent	Temp, °C	$k_1 \times 10^5$, s^{-1}	ΔH^{*a} ΔS^{*b}
exo-**6**	80% Me_2CO	57.0	123	
		49.6	54.2	23.1
		35.0	9.33	-2.1
		25.0	2.56[c]	
	60% EtOH	25.0	98.6	22.6
		0.0	2.76	3.4
exo-**7**	HOAc	70.0	87.7	
		62.8	36.3	25.2
		55.0	14.8	0.4
		42.9	3.36	
		25.0	0.282[c]	
endo-**6**	80% Me_2CO	75.0	97.2	22.7
		49.6	6.83	-7.5
		25.0	0.342[c]	
	60% EtOH	49.6	86.8	20.3
		25.0	5.87	-9.7
endo-**7**	HOAc	82.0	68.0	25.7
		70.0	18.0	-0.9
		60.0	5.74	
		25.0	0.0531[c]	
exo-**8**	60% Me_2CO	100.0	133	23.3
		75.0	13.0	-9.7
		25.0	0.0393[c]	
endo-**8**	60% Me_2CO	151.0	104	25.2
		129.4	20.5	-13.4
		115.2	6.02	
		25.0	0.000239[c]	

[a] Kcal/mol. [b] Cal/deg-mol. [c] Interpolated or extrapolated from data at other temperatures.

We have now examined the solvolytic behavior of the even more rigid 2-norbornyl analogs **6** - **8**.[11,12] The tetracyclic ring system of these substrates, as indicated by molecular models and empirical force-field calculations,[13] should cause minimal deformation at the norbornyl reaction site in both reactant ground states and the corresponding classical secondary and tertiary carbenium ions. Formation of a bridged ion, **10**, from *exo*-**6** or *exo*-**7**, on the other hand, should be strongly resisted due to strain increase.

The measured rate constants are listed in Table I. As seen in Scheme I, the tertiary *exo/endo* ratio in **8** remains high. The similarity of data for **3**, **5** and **8** as well as for a broad set of aryl analogs of **3** and **5**[8b-d] indicates a common steric origin for epimeric tertiary 2-norbornyl rate differentials.

This is not the case in the secondary series. Low exo/endo rate ratios are observed for **6** and **7**, as well as for **4** and other related models,[7] in contrast to **1** and **2**. Again the principal effect is found to be diminished reactivity for the constrained exo reactants. The disparity in comparative secondary and tertiary epimeric rate differences between **1** - **3**, on one hand, and **4** - **8**, on the other, reveals the absence of any comprehensive steric factor. The results are well explained instead by geometric inhibition in the larger polycyclic systems of the bridging proposed by Winstein to assist ionization of *exo*-**1** and *exo*-**2**. The alternative hyperconjugative explanation advocated by some[14] is unsatisfactory. Stabilization by delocalization with minimal nuclear movement should have been undiminished by the ring-system extensions in *exo*-**4**, *exo*-**6**, and *exo*-**7**.

Comparison of the products of buffered acetolysis of systems **7** and **2**[15] supports the conclusion drawn from the kinetics. Rigid *exo*-**7** produced 2.0±0.2% of the corresponding endo acetate along with 89.3% of the exo acetate and 8.7% of the symmetrical olefin, an enhancement of endo product formation relative to that from parent *exo*-**2**[15b,d] by a factor of *ca* 90. The substitution product from *endo*-**7** also contained 0.5% of endo acetate, whereas ester with retained configuration has not been detected from a simple *endo*-2-norbornyl sulfonate.[15] The solvolysis of constrained reactants **7** thus reflects the behavior expected from localized ion-pair mechanisms, with small but differing amounts of nucleophilic solvent involvement.[16] The bridged 2-norbornyl ion **9** accomodates the much higher preference for exo product formation observed from *exo*-**2**.

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REFERENCES AND NOTES

(1) Leading review: Brown, H. C.; with comments by Schleyer, P. v. R. "The Nonclassical Ion Problem"; Plenum: New York, 1977.

(2) Winstein, S.; Morse, B. K.; Grunwald, E.; Jones, H. W.; Course, J.; Trifan, D.; Marshall, H. J. Am. Chem. Soc. 1952, 74, 1127. Winstein, S.; Trifan, D. Ibid. 1952, 74, 1147, 1154.

(3) Schleyer, P. v. R.; Donaldson, M. M.; Watts, W. E. J. Am Chem. Soc. 1965, 87, 375.

(4) For recent evidence in favor of a bridged structure for the stable 2-norbornyl cation see Schleyer, P. v. R.; Chandrasekhar, J. J. Org. Chem. 1981, 46, 225 and references therein.

(5) (a) Brown, H. C.; Chloupek, F. J. Am. Chem. Soc. 1964, 86, 1248. (b) Ikegami, S.; Vander Jagt, D. L.; Brown, H. C. Ibid. 1968, 90, 7124.

(6) Brown, H. C. In "The Transition State"; Special Publication No. 16, The Chemical Society: London, 1962; pp 140-158. Brown, H. C.; Chloupek, F. J.; Rei, M.-H. J. Am. Chem. Soc. 1964, 86, 1248. For recent evidence to the contrary see Grob, C. A.; Günther, B.; Hanreich, R. Tetrahedron Lett. 1981, 22, 1211.

(7) (a) Winstein, S.; de Vries, L. J. Am. Chem. Soc. 1960, 82, 5363. (b) Corey, E. J.; Glass, R. S. Ibid. 1967, 89, 2600. (c) Baker, R.; Mason, T. J. J. Chem. Soc. (B) 1971, 1144. (d) Howe, R. K.; Carter, P.; Winstein, S. J. Org. Chem. 1972, 37, 1473. (e) Freeman, P. K.; Stevenson, B. K. J. Am. Chem. Soc. 1973, 95, 2890. (f) Rothberg, I.; Fraser, J.; Garnick, R.; King, J. C.; Kirsch, S.; Skidanow, H. J. Org. Chem. 1974, 39, 870. (g) Battiste, M. A.; Timberlake, J. F.; Paquette, L. A.; Degenhardt, C. R.; Martin, J. T.; Hedaya, E.; Su, T. M.; Theodorpulos, S. J. Chem. Soc., Chem. Commun. 1977 , 941. See also (h) Nickon, A.; Weglein, R. C.; Mathew, C. T. Can. J. Chem. 1981, 59, 302.

(8) (a) Takeuchi, K.; Oshika, T.; Koga, Y. Bull. Chem. Soc. Jpn. 1965, 38, 1318. (b) Brown, H. C.; Vander Jagt, D. L.; Schleyer, P. v. R.; Fort, R. C., Jr.; Watts, W. E. J. Am. Chem. Soc. 1969, 91, 6848. (c) Brown, H. C.; Gundu Rao, C.; Vander Jagt, D. L. Ibid. 1979, 101, 1780. See also (d) Takeuchi, K.; Kurosaki, T.; Okamato, K. Tetrahedron 1980, 36, 1557.

(9) Reference 1, pp 209-215.

(10) Brown, H. C.; Gundo Rao, C. J. Org. Chem. 1979, 44, 3536.

(11) Presented in part at the Second Chemical Congress of the North American Continent, Las Vegas, Nevada, August 24-29, 1980, Abstract ORGN-361.

(12) Synthetic entry to compounds 6 and 8 was gained through the corresponding ketone: Godleski, S. A.; Schleyer, P. v. R.; Osawa, E.; Inamoto, Y.; Fujikura, Y. J. Org. Chem. 1976, 41, 2596. The preparation of compounds 7 will be described in a forthcoming full paper.

(13) To be reported in the full paper.

(14) Kosower, E. M. "An Introduction to Physical Organic Chemistry"; Wiley: New York, 1968; pp 130-143. Jensen, R. R.; Smart, B. E. J. Am. Chem. Soc. 1969, 91, 5688. Traylor, T. G.; Hanstein, W.; Berwin, H. J.; Clinton, N. A.; Brown, R. S. Ibid. 1971 , 93, 5715. Fischer, W.; Grob, C. A.; von Sprecher, G.; Waldner, A. Tetrahedron Lett. 1979, 1901, 1905. Grob, C. A.; Waldner, A. Ibid. 1980, 21, 4429, 4433.

(15) (a) Winstein, S.; Clippinger, E.; Howe, R.; Vogelfanger, E. J. Am. Chem. Soc. 1965, 87, 376, and preceding work. (b) Goering, H. L.; Schewene, C. B. Ibid. 1965, 87, 3516. (c) Lee, C. C.; Lam, L. K. M. Ibid. 1966, 88, 2831. (d) Brown, H. C.; Kawakami, J. H.; Liu, K.-T. Ibid. 1970, 92, 5536.

(16) Bentley, T. W.; Schleyer, P. v R. J. Am. Chem. Soc. 1976, 98, 7658.

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