Tetrahedron Letters No. 14, pp. 473-476, 1961. Pergamon Press Ltd. Printed in Great Britain.

ABSENCE OF STERIC EFFECTS ON THE LEAVING GROUP IN S_N2 REACTIONS

Ernest L. Eliel and Rico P. Gerber

Department of Chemistry, University of Notre Dame

Notre Dame, Indiana

(Received 13 July 1961)

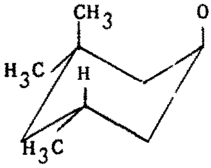
IT is well known,[1a] largely through the pioneering research of Polanyi and of Hughes and Ingold and their coworkers, that the rate of bimolecular nucleophilic displacement (S_N2) reactions is greatly retarded when there is steric hindrance to approach of the incoming nucleophile. In unimolecular nucleophilic displacement and elimination (S_N1-E_1) reactions there is no corresponding retardation; in fact recent work by H.C. Brown and by Bartlett and coworkers[1b,2] suggests that such reactions are subject to steric acceleration when the departure of the anion relieves strain in the starting molecule. It seemed to be of interest to investigate whether a corresponding steric acceleration could be produced in S_N2 reactions in cases where the departing group (but not the incoming group) were subject to steric compression.

A suitable system for the purpose of such study is the trans-3,3,5-trimethylcyclohexyl system. In the tosylate (I) the leaving p-toluenesulfonate group is crowded by the axial methyl group, but there is no interference with the approach of the incoming nucleophile. The extent of crowding

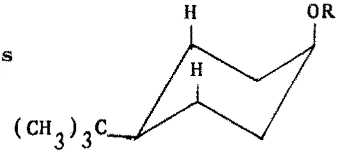
---

[1] cf. E.L. Eliel in M.S. Newman, Steric Effects in Organic Chemistry [a]pp. 73-79; [b]pp. 70-73. John Wiley, New York (1956).

[2] For a contrary view, see D.V. Banthorpe, E.D. Hughes and C.K. Ingold, J.Chem.Soc. 4054 (1960).



I R = Ts
II R = H



III R = Ts
IV R = H

of the tosylate group may be inferred from the axial CH_3-OH-H interaction in the corresponding alcohol (II) which was recently measured[3] to amount to approximately 3.7 kcal/mole. The axial CH_3-OTs-H interaction is probably about the same, for the axial OTs-H-H interaction in cis-4-t-butylcyclohexyl tosylate (III)[4] and the OH-H-H interaction in the corresponding alcohol (IV)[4] both amount to about 0.6-0.8 kcal/mole.

Alcohol II is readily available from isophorone[3,5] and, contrary to a previous report,[6] is readily converted to the tosylate I, m.p. 67.5° by treatment with p-toluenesulfonyl chloride in pyridine at 0° (Found: C, 64.67; H, 8.37. $C_{16}H_{24}O_3S$ requires: C, 64.85; H, 8.17). Treatment of I (0.05 mole) with sodium thiophenolate (from 0.10 g atom Na and 0.146 mole PhSH) in 87% ethanol for 2 days gave 1.25 g (22%) of a fraction boiling at 38°/38 mm and 2.80 g (25%) of a fraction boiling at 126-130°/1.6 mm. The infrared spectrum and analysis of the low boiling fraction, n_D^{20} 1.4400 after percolation through alumina, were compatible with the expected 3,3,5- or 3,5,5-trimethylcyclohexene structure. (Found: C, 86.59; H, 12.97. C_9H_{16} requires C, 87.02; H, 12.98). The high-boiling fraction, presumably cis-

---

[3] E.L. Eliel and H. Haubenstock, J.Org.Chem. In press.

[4] cf. E.L. Eliel, J.Chem.Educ. 37, 126 (1960). The values for the axial OH and OTs interactions have recently been confirmed in our laboratory by nuclear magnetic resonance spectroscopy, cf. E.L. Eliel, Chem. & Ind. 558 (1959).

[5] E.G. Peppiat and R.J. Wicker, J.Chem.Soc. 3122 (1955).

[6] I. Alkonyi, Chem.Ber. 92, 1130 (1959).

3,3,5-trimethylcyclohexyl phenyl sulfide, was oxidized to the sulfone, m.p. 135°, showing the characteristic sulfone bands at 1150 and 1300 cm^{-1} in the infrared. (Found: C, 67.70, 67.46; H, 8.30; 8.32. $C_{15}H_{22}O_2S$ requires: C, 67.65; H, 8.33).

It having been established that the reaction of I with thiophenolate in 87% ethanol does, in fact, give substitution and elimination rather than solvolysis products, the reaction was studied kinetically at 25.2°C under the conditions previously described.[7] Second-order kinetics were followed quite cleanly, the results being as follows:

Compound	NaSPh / ROTs	k (1/mole/sec. x 10^4)	k_s/k_e
I	1:1	6.97±0.10	0.348
	1:1	6.71±0.10	0.442
	1:2	6.65±0.14	0.477
	1:1	7.52±0.21	0.374
	1:2	6.88±0.26	0.380
I, average		6.95	0.404
III	1:1	7.84±0.10	0.833
	1:1	7.32±0.07	--
III, average		7.58	
III, lit.[8]		7.02	1.06

It is evident from the data that I reacts with thiophenolate at substantially the same overall rate as III, there being neither steric assistance nor steric hindrance of the reaction. In view of the fact that the steric compression energy in I would seem to exceed that in III by approximately 3 kcal/mole, this result is rather surprising. If the transition states for I and III had no compression energy due to the axial tosylate group left, the

---

[7] E.L. Eliel and R.G. Haber, J.Amer.Chem.Soc. **81**, 1249 (1959).

strain relief in III would be ca. 0.7 kcal/mole and that in I ca. 2.8 kcal/mole (one CH_3-H interaction of about 0.9 kcal/mole is left over in I) so that I should react ca. 30 times faster than III at 25°. That there is, in fact, no appreciable difference between I and III at all must mean that whatever compression energy there is in the ground state persists to nearly the same extent in the transition state.

We believe that the merged mechanism of substitution and elimination[8,9] may account for the apparent small change in geometry of the leaving group between the ground state and the transition state in the thiophenolate displacement reaction of cyclohexyl tosylates as well as for the lack of correlation between the overall rate (nearly identical for I and III) and the ratio of substitution to elimination (about twice as large for III as for I).

Studies of solvolysis[10] and bimolecular elimination reactions of compound I as well as studies of the stereoisomeric *cis*-3,3,5-trimethylcyclohexyl system should throw further light on the problems raised here. Such studies are in progress in our laboratory.

We acknowledge, with thanks, support of this work by the National Science Foundation.

---

[8] S. Winstein, D. Darwish and N.J. Holness, *J.Amer.Chem.Soc.* **78**, 2915 (1956).

[9] E.L. Eliel and R.S. Ro, *Tetrahedron* **2**, 353 (1958). See also ref. 7.

[10] *cf*. S. Nishida, *J.Amer.Chem.Soc.* **82**, 4290 (1960).