

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CORNELL UNIVERSITY, ITHACA, N. Y.]

Highly Strained Bicyclic Systems. IX. The Acetolysis of 5,5-Dimethylbicyclo[2.1.1]hexyl 2 β -*p*-Toluenesulfonate¹

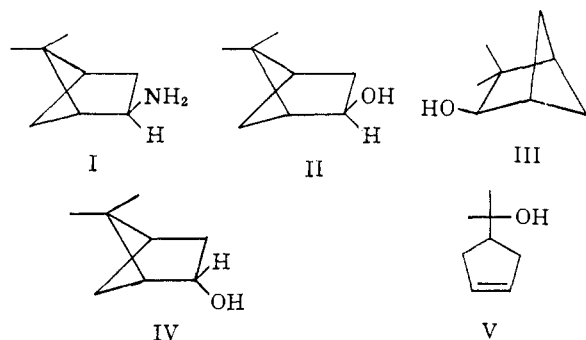
BY JERROLD MEINWALD² AND PAUL G. GASSMAN³

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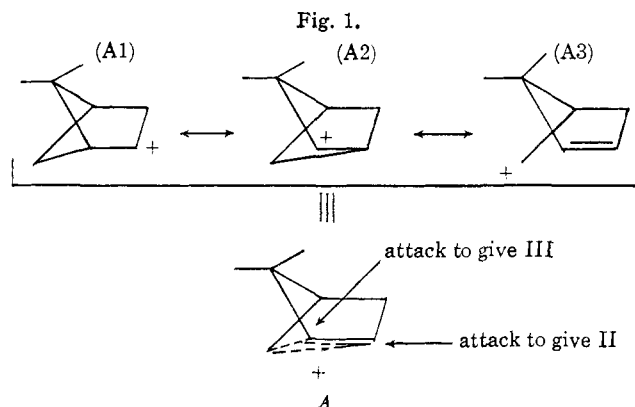
The preparation and acetolysis of 5,5-dimethylbicyclo[2.1.1]hexyl-2 β *p*-toluenesulfonate (VI) is described. Chromatography of VI on neutral alumina brings about rearrangement to an isomeric *p*-toluenesulfonate, VII. Acetolysis of VI at 75°, accompanied by internal return to give VII, proceeds at a rate comparable to that of cyclopentyl *p*-toluenesulfonate (X). When the small internal angle at C₂ of VI is taken into account, this result is interpreted as revealing a marked anchimeric assistance to ionization in VI. The steric preference for retention of configuration, giving the acetates of II and IV in a ratio of 11:1, combined with the apparent rate enhancement, supports the idea that VI ionizes to give the bridged ion A.

Introduction

One of our chief objectives in investigating the chemistry of the bicyclo[2.1.1]hexanes has been to gain some insight into the nature of the corresponding carbonium ions. Toward this end, the nitrous acid deamination of (-)-5,5-dimethylbicyclo[2.1.1]hexyl-2 β -amine (I) has recently been studied, and was found to give esters of the four isomeric alcohols II, III, IV and V in the relative amounts in 56%, 21%, 14% and 9%, respectively.¹ The possibility that II and III



were formed by opening of the bridged intermediate A (see Fig. 1) is an attractive one, which would provide a simple explanation for the predominant retention of configuration observed in this deamination.



Because of its obvious relation to this problem, we have studied the preparation and acetolysis of VI, the *p*-toluenesulfonate ester of II, with the results reported below. The acetolysis of VI was chosen for study in part because such a large amount of background data on related acetolyses has accumulated in the literature. Among the questions to which answers seemed desirable for this system, we may list: (1) What products result from the acetolysis of VI?

(1) For part VIII of this series, see J. Meinwald, P. G. Gassman and J. J. Hurst, *J. Am. Chem. Soc.*, **84**, 3722 (1962).

(2) Fellow of the Alfred P. Sloan Foundation.

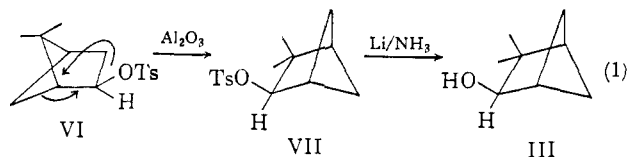
(3) Present address: Department of Chemistry, Ohio State University, Columbus, O.

More particularly, can the 5,5-dimethylbicyclo[2.1.1]hex-2-yl cation retain its integrity, or does it spring open to give monocyclic olefins? (2) What stereochemical results are characteristic of the reaction? (3) What kinetic behavior is observed? (4) What mechanistic picture of the reaction provides the simplest explanation of the product and rate observations? Here, the question of whether there are any stereochemical or kinetic reasons to postulate the formation of a bridged ion, such as A, analogous to those bridged ions B and C involved in the solvolyses of isobornyl and *exo*-norbornyl systems, is of special interest.⁴



Discussion

The preparation of the desired *p*-toluenesulfonate VI was carried out in the usual way by treating II with *p*-toluenesulfonyl chloride in dry pyridine. The product was a colorless, viscous oil which failed to crystallize, although its infrared spectrum was in accord with expectations. In an attempt to prepare a crystalline analytical sample, a petroleum ether solution of this ester was chromatographed on a column of neutral alumina. Petroleum ether eluted a beautifully crystalline toluenesulfonate, whose infrared spectrum, however, revealed it to be quite different from the ester originally placed on the column. In order to elucidate the nature of this readily obtained rearrangement product, it was reductively cleaved by treatment with lithium in liquid ammonia to a crystalline alcohol of composition C₈H₁₄O. This alcohol, which was inert to double bond reagents, and therefore bicyclic, was recognized as the Wagner-Meerwein rearrangement product III which might be expected to arise from II. It was identified by direct comparison with an authentic sample of III, independently synthesized from camphene¹ in connection with our earlier study of the deamination of I. These results are summarized in eq. 1.



In spite of this tendency of VI to rearrange, we were able to purify it successfully by molecular distillation at *ca.* 35°. Acetolysis at 75° in anhydrous acetic acid containing one molar equivalent of sodium acetate was

(4) For a convenient review of the literature in this area, see E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., New York, N. Y., 1959, p. 594, and also A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill Book Co., New York, N. Y., 1962.

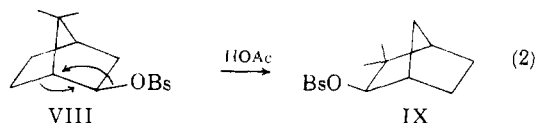
followed titrametrically using standard techniques.⁵ A rapidly downward drifting rate constant was observed.

One explanation of this drifting rate might be provided by the rearrangement of VI to a less reactive *p*-toluenesulfonate accompanying the solvolysis. Since the facile conversion of VI to VII (although under different experimental conditions) had already been encountered, the hypothesis that this same process was complicating the kinetic results was an obvious one. Analysis of the kinetic data on this basis gave a self consistent picture of the process, wherein VI rearranges to VII during the solvolysis. The last part of the solvolysis corresponds in rate to the solvolysis of VII itself ($k = 1.55 \times 10^{-5} \text{ sec.}^{-1}$ at 75.10°). This hypothesis was further substantiated by interruption of an acetolysis experiment at a point where over 98% of VI should have already rearranged or solvolyzed. The recovered tosylate proved to be pure VII, as anticipated, thus confirming the occurrence of internal return.

In order to determine the structures of the acetates derived from VI itself, these products were isolated from a reaction in which less than 2% of the solvolysis product should be derived from VII. Reductive cleavage of the mixed acetates, using lithium aluminum hydride, gave the four isomeric alcohols II (44%), V (35%),⁶ III (17%) and IV (4%). These products, which are the same as those obtained from the deamination of I, were identified, as described in our preceding paper, by the usual gas chromatographic and infrared techniques.

It is now appropriate to ask what these data mean. It seems most significant that retention of configuration (giving the acetate of II) is preferred to inversion (giving the acetate of IV) by a factor of 11:1, in spite of the fact that either direct displacement of *p*-toluenesulfonate anion by solvent or collapse of the simple carbonium ion A'' with solvent would be expected to favor the formation of inverted product. A parallel result in the deamination of I has been discussed on the basis of A as an intermediate; the assumption that VI also ionizes to give the bridged ion A would now appear to provide the simplest explanation for: (1) the preferred retention of configuration, (2) the formation of the rearranged tosylate VII by internal return and (3) the formation of the corresponding rearranged acetate (of III) by combination of A with solvent at the positive center adjacent to the *gem*-dimethyl group.

It is interesting to note, in this connection, that Winstein and Holness⁷ have reported some very similar behavior in the acetolysis of apoisobornyl brosylate (VIII). This reaction (see eq. 2) also shows a rapidly downward drifting first-order rate constant,



in this case due to internal return to give *exo*-camphenyl brosylate (IX), a substantially less reactive ester.

It must be noted, however, that the ring opening to give the acetate of the 3° , olefinic alcohol V and the displacement with inversion to give the acetate of IV do not appear to involve the bridged ion A as an immediate product precursor. These products might be considered to arise either by rearrangement of initially formed A to the more stable, bridged ion A', or

(5) S. Winstein, E. Grunwald and I. Ingraham, *J. Am. Chem. Soc.*, **70**, 821 (1948).

(6) An independent synthesis of V is described by J. Meinwald, P. G. Gassman and J. K. Crandall, *J. Org. Chem.*, **27**, 3366 (1962).

(7) S. Winstein and N. J. Holness, *J. Am. Chem. Soc.*, **77**, 3054 (1955).

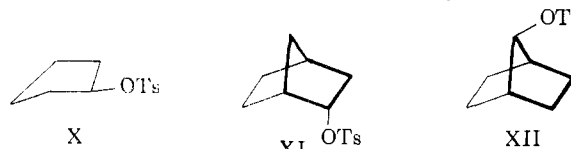
alternatively by direct ionization of VI to a classical ion A'', which in part gives the acetates of IV and V and in part stabilizes itself by bridging to give A.



This latter possibility is not completely satisfactory, however, since it is hard to see why A'' would rearrange to A rather than to A' (which should be preferred on the grounds that it can use a 3° carbon atom to help distribute the positive charge). The product analysis, therefore, gives evidence supporting the mechanism VI \rightarrow A \rightarrow A', with internal return from A giving VII, and with acetates being derived from both A and A'.

It should be possible to use the kinetic results to decide whether the initial ionization gives a resonance stabilized, bridged ion (A) directly, or whether the initial ion has a classical structure (A''). In the first instance, anchimeric assistance should lead to an enhanced reaction rate. Analysis of the kinetic data gives a first-order rate constant at 75° , $k_A = 5.61 \pm 0.14 \times 10^{-4} \text{ sec.}^{-1}$, for the liberation of *p*-toluenesulfonic acid from VI. The combined rate constant for disappearance of VI (solvolysis and rearrangement of VI to VII at 75°) is $k_A + k_R = 9.63 \pm 0.29 \times 10^{-4} \text{ sec.}^{-1}$. Thus, the rate constant for rearrangement to VII at 75° , $k_R = 3.98 \pm 0.39 \times 10^{-4} \text{ sec.}^{-1}$.

What these numbers are considered to mean depends very largely on the choice of an appropriate model compound. The seriousness of this choice is illustrated by the enormous differences in acetolysis rates (a spread of about 10^8) of cyclopentyl, *endo*-norbornyl and 7-norbornyl *p*-toluenesulfonates (X, XI and XII) each of which might at first sight be considered a fair standard of comparison.⁸ Cyclopentyl *p*-toluenesulfonate (X) comes to mind first, since any 2-substituted



bicyclo[2.1.1]hexyl compound can be regarded as a cyclopentyl derivative. The *endo*-norbornyl system (XI) might be more appropriate, however, since here the cyclopentyl ring is rigidly folded into an envelope conformation⁹ which should resemble more closely the geometry of VI than does the more flexible monocyclic system. Even the 7-norbornyl system (XII) might be relevant, since again it is a rigid version of the cyclopentyl moiety.

Schleyer has pointed out recently in an elegant study of the factors which may influence solvolysis rates in molecules of this type that a good argument can be made for the internal C-C-C angle at the carbon atom from which the anion leaves playing the dominant role in determining rate of ionization.⁸ Adopting this point of view, we need only estimate the relevant internal angles of the possible models and compare these to the corresponding internal angle for VI to estimate the expected "normal" reactivity of VI. Using Halford's relationship^{8,10} between carbonyl

(8) For good summaries of the relevant data see P. von R. Schleyer and R. D. Nicholas, *ibid.*, **83**, 182 (1961), and P. D. Bartlett and W. P. Giddings, *ibid.*, **82**, 1240 (1960).

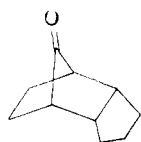
(9) F. V. Brutcher, T. Roberts, S. J. Barr and N. Pearson, *ibid.*, **81**, 4915 (1959).

(10) J. O. Halford, *J. Chem. Phys.*, **24**, 830 (1956); G. J. Karabatsos, *J. Org. Chem.*, **25**, 315 (1960).

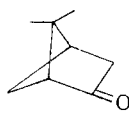
stretching frequencies and internal angles, the values shown in Table I are obtained. Assuming that these angles also represent those that the corresponding carbonium ions would have, we obtain the necessary estimates.

TABLE I

Ketone	Carbonyl stretching, cm.^{-1}	Calculated angle
Cyclopentanone	1750	102.5°
Norcamphor	1751	101.5°
<i>endo</i> -Trimethylenebicyclo[2.2.1]-heptan-7-one (XIII)	1770	92.5°
5,5-Dimethylbicyclo[2.1.1]-hexan-2-one (XIV)	1764	95.5°



XIII



XIV

From this analysis, it would appear that the geometry of VI is more closely related to that of XII (a difference of -3° between XIV and norcamphor) than XI (a difference of $+6^\circ$ between XIV and XIII). Assuming the validity of the correlation between angle and expected reaction rate, this would lead to the prediction that *in the absence of other effects*, VI should solvolyze at a rate somewhere intermediate between those of XI and XII. In fact, even though the exact functional relationship between angle and rate is unknown, one might expect a rate closer to that of the better model XII.

The experimental findings are presented in Table II. From these data, it is apparent that the reactivity of VI is very much greater than that anticipated simply on the basis of geometrical considerations.¹¹ This result, therefore, is in accord with the postulate that VI ionizes with participation of the one-carbon bridge adjacent to the departing tosylate group, giving the bridged ion A directly.

TABLE II

Sulfonate ester	Acetolysis rate constant, sec.^{-1} (T , °C.)
5,5-Dimethylbicyclo[2.1.1]hex-2-yl <i>p</i> -toluenesulfonate (VI)	5.61×10^{-4} (75.1)
Cyclopentyl <i>p</i> -toluenesulfonate (X) ^a	5.46×10^{-4} (74.6)
<i>endo</i> -Norbonyl <i>p</i> -toluenesulfonate (XI) ^b	0.6×10^{-4} (74.6)
7-Norbonyl <i>p</i> -toluenesulfonate (XII) ^c	4.6×10^{-11} (75)

^a S. Winstein, *et. al.*, *J. Am. Chem. Soc.*, **74**, 1127 (1952).
^b S. Winstein and D. Trifan, *ibid.*, **74**, 1147 (1952), extrapolated from brosylate. ^c S. Winstein, M. Shatavsky, C. Norton and R. B. Woodward, *ibid.*, **77**, 4183 (1955), extrapolated from 205°.

To summarize, the solvolysis of VI has yielded the same products as the deamination of I. In the non-rearranged product, there is an 11-to-1 preference for retention of configuration. The kinetic data indicate a rate enhancement compared with a hypothetical model. The stereochemical and kinetic data are, therefore, both in accord with the formation of a bridged ion in this reaction.

Acknowledgment.—The support of this work by a research grant from the National Science Foundation is acknowledged with pleasure.

(11) The exact amount of acceleration is hard to calculate, since the rate to be expected for a "normal" tosylate with a 95.5° internal angle and no anchimeric assistance remains unknown. Roughly, a rate factor in the range of 10^2 – 10^6 seems indicated. It should not go unmentioned, however, that there may be an appreciable steric contribution to this acceleration. This might be anticipated to arise from the proximity of the *syn*-5-methyl group to the 2 β -tosyl group, which might be responsible for considerable repulsive non-bonded interaction. In this context, it would be interesting to have data for the unmethylated bicyclo[2.1.1]hexyl-2-tosylate. Work along these lines is in progress.

Experimental

5,5-Dimethylbicyclo[2.1.1]hexan-2 β -ol Tosylate (VI).—To 1.00 g. of II in 3 ml. of dry pyridine was added 1.60 g. of *p*-toluenesulfonyl chloride at 0°. The reaction mixture was allowed to stand at 0° for 30 hours and was poured into ice-diluted hydrochloric acid. The quenched mixture was extracted with 30–60° petroleum ether. The organic solution was washed thoroughly with water and dilute sodium bicarbonate solution and finally dried over anhydrous magnesium sulfate. The drying agent was removed by filtration and the solvent was removed under reduced pressure. Removal of the last traces of solvent at 0.3 mm. gave 2.08 g. (94%) of VI. Molecular distillation at 35° and 10^{-4} mm. gave an analytical sample, n_D^{25} 1.5261.

Anal. Calcd. for $\text{C}_{15}\text{H}_{20}\text{SO}_2$: C, 64.25; H, 7.19; S, 11.44. Found: C, 64.44; H, 7.28; S, 11.23.

2,2-Dimethylbicyclo[2.1.1]hexane-3-ol Tosylate (VII).—Crude VI (1.458 g.) was chromatographed on a column of neutral alumina, 16×1 cm. Elution with 30–60° petroleum ether gave 552 mg. (38%) of the rearranged tosylate VII, m.p. 53–54°. This crystalline tosylate was saturated to bromine in carbon tetrachloride.

Anal. Calcd. for $\text{C}_{15}\text{H}_{20}\text{SO}_2$: C, 64.25; H, 7.19; S, 11.44. Found: C, 64.37; H, 7.20; S, 11.69.

2,2-Dimethylbicyclo[2.1.1]hexan-3-ol (III).—A solution of 200 mg. of VII in 25 ml. of anhydrous ether was added dropwise to a stirred solution of 0.55 g. of lithium in 50 ml. of liquid ammonia, the addition taking 15 minutes. After stirring for 4 hours, ammonium chloride was added and the ammonia was allowed to evaporate. The reaction mixture was diluted carefully with ether and water and stirred until no color remained. The ethereal solution was removed and dried over anhydrous magnesium sulfate. Removal of the drying agent and solvent gave 123 mg. of partially crystalline material. Repeated sublimation gave long, colorless needles, m.p. 106.5–107.0°. Vapor phase chromatography, infrared analysis and mixture melting point showed that this alcohol was identical with an authentic sample of III.¹

Kinetic Measurements.—The solvolysis reactions were run in anhydrous acetic acid solution,⁸ which was 0.0512 *N* in both sodium acetate and tosylate. The solvolysis temperature was $75.10 \pm 0.02^\circ$. One milliliter samples in individual sealed ampoules were removed at appropriate intervals and cooled in an ice-bath. After warming to room temperature, the 1-ml. aliquot was titrated with 0.0202 *N* perchloric acid in acetic acid using brom phenol blue as indicator.⁵ All rate measurements were followed for at least three half-lives.

Solvolysis of VII.—Acetolysis of VII under the conditions described above gave a rate constant of $1.55 \pm 0.01 \times 10^{-6}$ sec.^{-1} . Excellent first-order kinetics were observed in all runs.

Solvolysis of VI.—Acetolysis of VI under the conditions described above gave kinetic data which indicated a competitive solvolysis and rearrangement to a slower solvolyzing tosylate.

Due to the nature of the kinetics, most points were taken in the first half-life. The minimum number of points taken in any one run was eighteen. All runs were followed to at least 75% of completion. The kinetic data was interpreted according to the method of Young, Winstein and Goering.¹²

Product Analysis for Acetolysis of VI.—The solvolysis of 575 mg. of VI under the conditions described above was interrupted after 1 hour. This corresponded to greater than 98% reaction of VI. The solvolysis mixture was cooled to 0° and poured into a solution of 35 g. of sodium hydroxide in 200 ml. of water. The acetates and rearranged tosylate were extracted with 30–60° petroleum ether and dried over anhydrous magnesium sulfate. The drying agent was removed by filtration and the solvent was removed on a flash evaporator.

The residue was placed in a vacuum system and the acetates were distilled away from the rearranged tosylate at room temperature. This gave 235 mg. (41%) of VII. One recrystallization from 30–60° petroleum ether gave product with a melting point of 51.0–52.5°. The infrared spectrum of this product was identical to that of an authentic sample of VII.

The mixed acetates were diluted with 40 ml. of anhydrous ether and added dropwise to a stirred suspension of 1.00 g. of lithium aluminum hydride in 20 ml. of ether. After stirring for 2 hours at room temperature, the reaction mixture was hydrolyzed by dropwise addition of 4.00 g. of water. Removal of the inorganic salts by filtration, followed by evaporation of the solvent, gave 79 mg. (31%) of mixed alcohols. Vapor phase chromatography on 0.3% polyethylene glycol on glass heads at 100° indicated that the alcohol mixture consisted of 35% of V, 17% of III, 44% of II and 4% of IV. These alcohols were also separated on a 10-ft. preparative v.p.c. column (10% Carbowax 4000 on 80–100 mesh firebrick). Infrared spectra of the various alcohols were identical to the infrared spectra of authentic samples.

(12) W. G. Young, S. Winstein and H. L. Goering, *J. Am. Chem. Soc.*, **73**, 1958 (1951).