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The Solvolysis of the Methyl 3-Tosyloxycyclohexanecarboxylates

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The acetolysis and formolysis of methyl *cis*-3-tosyloxycyclohexanecarboxylate (I) and methyl *trans*-3-tosyloxycyclohexanecarboxylate (II) have been shown to be normal. No rate acceleration is observed. The product formed is a mixture of olefins and the inverted acetate in each case.

Results

In connection with other studies concerning the rearrangement of disubstituted cyclohexane derivatives,[2,3] it became of importance to examine the solvolysis of the isomeric pair, methyl *cis*-3-tosyloxy cyclohexanecarboxylate (I) and methyl *trans*-3-tosyloxycyclohexanecarboxylate (II). Of importance was the question: would transannular participation manifest itself during these solvolyses, either structurally or kinetically? It is the purpose of the present report to answer this question.

The well known *cis*-3-hydroxycyclohexanecarboxylic acid was converted to its methyl ester and treated with *p*-toluenesulfonyl chloride to give I; and the *trans*-hydroxy acid similarly was converted to II. It also was found possible to separate by fractional crystallization the mixed isomers derived from methyl 3-hydroxycyclohexanecarboxylate.

The rate constants obtained for the solvolysis of I and II in acetic acid and formic acid are summarized in Table I, together with pertinent data for comparison from the work of Winstein and coworkers.[4,5]

TABLE I

RATES OF SOLVOLYSIS OF SUBSTITUTED CYCLOHEXYL TOSYLATES

Tosylate	$k_1 \times 10^5$ sec.$^{-1}$ Acetic acid, 75°	$k_1 \times 10^5$ sec.$^{-1}$ Formic acid, 40°	Rel. rate in acetic acid
Cyclohexyl	4.27[5]	28[a]	1.00
trans-4-*t*-Butylcyclohexyl (VII)	3.75[4]	23[a]	0.88
cis-4-*t*-Butylcyclohexyl (VIII)	10.2[4]	87[a]	2.39
cis-3-Carbomethoxycyclohexyl (I)	0.331 ± 0.008	0.62 ± 0.06	0.078
trans-3-Carbomethoxycyclohexyl(II)	1.59 ± 0.04	2.6 ± 0.2	0.37

[a] Interpolated from data at other temperatures, ref. 4.

Under the conditions of the solvolyses both elimination and substitution take place. From I there was isolated methyl *trans*-3-acetoxycyclohexanecarboxylate (III), 25%, and a mixture of methyl 3-cyclohexene-1-carboxylate (IV) and methyl 2-cyclohexene-1-carboxylate (V). III is the expected, normal, product of solvolytic substitution. The mixture of unsaturated esters, identified by infrared analysis, consisted largely of methyl 3-cyclohexene-1-carboxylate but contained 5–10% methyl 2-cyclohexene-1-carboxylate.

The products resulting from the acetolysis of II are similar. There was obtained methyl *trans*-3-acetoxycyclohexanecarboxylate (VI) in 20% yield and a mixture of IV and V, in similar ratio to that obtained above.

Discussion

The clean inversion accompanying the solvolysis of both I and II shows that the reactions are normal, and establishes the lack of transannular participation. Were such participation to occur, both I and II would be expected to give III.

The relative rate of solvolysis is also normal for each isomer in acetic acid. From the σ^*-value of Taft[6] for the carbomethoxyl group and from the recent correlation of Streitwieser[7] one may calculate the relative rate for I. In I both groups are equatorial, and hence the rate should be that of *trans*-4-*t*-butylcyclohexyl tosylate (VII), modified by the appropriate contribution for the polar influence of the carbomethoxy group. The calculated rate ratio of VII:I is 11:1. The observed ratio is 11:1. For II, the predominant conformation is probably that with the tosylate group in the axial position. This conclusion is reached by the following reasoning. The *A* value for the tosylate group is given by Winstein as 1.7.[4] The *A* value for the ester grouping may be estimated as being between that of ethyl and isopropyl, since there is branching adjacent to the ring. Using a value of 2.5, one concludes that the rate of reaction for II should show the same acceleration relative to I, that VIII shows relative to VII. The observed ratio, 4.5:1, is somewhat higher. However, there is an additional factor which requires consideration. The developing dipole associated with the solvolytic transition state is developing in a plane perpendicular to the dipole associated with the carbomethoxy group in II. In I, however, the developing charge separation will be developed largely in one plane at an angle of about 120°. This will make the polar retardation somewhat more effective for I than for II. Hence the rate ratio would be expected to be slightly larger for II to I, than the ratio of VIII to VII. The polar opposition to "ionization" is very similar to the polar assistance to ionization of *cis*- and *trans*-3-bromocyclohexanecarboxylic acids.[8] The acid dissociation constants of the acids show differences also due

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[2] D. S. Noyce and H. I. Weingarten, THIS JOURNAL, **79**, 3093 (1957).

[3] D. S. Noyce and H. I. Weingarten, *ibid.*, **79**, 3098 (1957).

[4] S. Winstein and N. J. Holness, *ibid.*, **77**, 5562 (1955).

[5] S. Winstein, E. Grunwald, R. E. Buckles and C. Hanson, *ibid.*, **70**, 816 (1948).

[6] R. W. Taft, Jr., *ibid.*, **75**, 4231 (1953).

[7] A. Streitwieser, Jr., *ibid.*, **78**, 4935 (1956).

[8] S. Siegel and J. G. Morse, *ibid.*, **75**, 3857 (1953).

to the direction of the bond dipole associated with the carbon–bromine bond.

The polar effect of the carbomethoxy group is more effective in retarding the rate. The rate ratio VII:I in formic acid is 40:1. This effect would be anticipated on the basis of the greater ionizing power of formic acid as solvent. The rate ratio in formic acid, 4.3, is likewise similar. The evidence clearly establishes that the solvolysis of I and II is normal.

The olefins fraction formed during the solvolysis also gives no evidence of transannular interaction. Exclusive formation of methyl 3-cyclohexene-1-carboxylate was observed in the elimination reaction accompanying the rearrangement of 3-methoxycyclohexanecarboxylic acid chloride. Were transannular interaction important, similar results would be expected. The difference in the relative rates of formation of the two olefins IV and V reflects the inductive influence of the ester grouping in stabilizing the hydrogen in the two position.

Experimental[9]

Methyl *cis*-3-Tosyloxycyclohexanecarboxylate (I).—An authentic 1-g. sample of *cis*-3-hydroxycyclohexanecarboxylic acid,[2,3] m.p. 131.6–132.0°, was converted to its methyl ester with diazomethane in ether. The ether solution was dried over magnesium sulfate, evaporated, and 1.3 g. of *p*-toluenesulfonyl chloride and 10 ml. of pyridine were added. The mixture was allowed to stand overnight. It was then poured into water, acidified and extracted with ether; the ether extract was washed with dilute sulfuric acid, sodium carbonate solution and dried. Crystallization from pentane of the residue obtained on evaporating the ether afforded 1.0 g. of methyl *cis*-3-tosyloxycyclohexanecarboxylate (I), m.p. 86.2–86.5°.

Anal. Calcd. for $C_{15}H_{20}O_5S$: C, 57.7; H, 6.5; S, 10.3. Found: C, 57.8; H, 6.7; S, 10.1.

Methyl *trans*-3-Tosyloxycyclohexanecarboxylate (II).—*trans*-3-Hydroxycyclohexanecarboxylic acid,[2,3] m.p. 118.8–119.6°, 0.1 g., was converted to authentic II as in the above experiment. The m.p. of the II thus obtained is 90.0–90.5°.

Anal. Calcd. for $C_{15}H_{20}O_5S$: C, 57.7; H, 6.5; S, 10.3. Found: C, 57.7; H, 6.5; S, 10.0.

Preparation and Isolation of the Methyl *cis*- and *trans*-3-Tosyloxycyclohexanecarboxylates (I and II).—A 34-g. (0.22 mole) sample of methyl 3-hydroxycyclohexanecarboxylate (mixed isomers) was dissolved in 100 ml. of pyridine and 45 g. (0.24 mole) of *p*-toluenesulfonyl chloride was added and allowed to stand overnight. The solution was then poured into water and extracted with 3:1 ether–pentane. The extracts were washed with water, dilute sulfuric acid and sodium carbonate solution, then dried over magnesium sulfate. The dry extracts, about 400 ml., were concentrated to three-fourths their volume and 700 ml. of *n*-pentane was added, making the ether–pentane ratio approximately 1:4. By a process of fractional crystallization and mechanical separation of the differently appearing crystals, 12 g. (18%) of I (polyhedral prisms), m.p. 85.5–86.3°, and 31 g. (47%) of crude I, m.p. 85–86°, were obtained. A dimorph of I was isolated first (m.p. 63°, long needles from *n*-pentane) but no longer appeared after the isolation of the higher melting form.

Also obtained was 13 g. (19%) of II (soft light plates), m.p. 89–90.5°.

Kinetic Procedure.—Acetic anhydride, 0.1%, was added to purified **acetic acid**, which analyzed for water content 0.01% by Karl Fischer titration. It was used in this form as solvent.

Formic acid was treated with boric anhydride and fractionated. It titrated 99.95% formic acid.

The volumetric equipment was calibrated, and the progress of the reactions was followed by potentiometric titration, with sodium acetate in acetic acid using a procedure similar to that of Winstein and Marshall.[10] For the acetolyses of I and II, the course of the reaction was followed to 80% completion.

The formolysis experiments were carried out on a much more limited basis and the rate constants are likely to be precise to only 10%.

Product Analysis of I Acetolysis.—I, 10 g. (0.032 mole), was dissolved in 100 ml. of acetic acid and 3.2 g. (0.032 mole) of potassium acetate was added. The flask, equipped with a spiral condenser capped by a calcium chloride tube, was placed on a steam-bath for 48 hours (about three half-lives). The solution was then poured into water, neutralized with solid sodium carbonate and extracted two times with pentane. The extracts were dried, evaporated and the products separated by fractional distillation. Fraction 1, weighing 1.9 g. (40%), proved on infrared analysis to be a mixture of methyl 2-cyclohexene-1-carboxylate and methyl 3-cyclohexene-1-carboxylate, b.p. 92–93° (40 mm.), $n^{25}\text{D}$ 1.4598. Fraction 2, 1.6 g. (25%), proved on infrared analysis to be methyl *trans*-3-acetoxycyclohexanecarboxylate, b.p. 110–112° (5 mm.), $n^{25}\text{D}$ 1.4521.

Product Analysis of II Acetolysis.—II, 10 g. (0.032 mole), was solvolyzed as in the above experiment for 12 hours on a steam-bath (about three half-lives) and also yielded two fractions on fractional distillation. Fraction one, b.p. 93–94° (40 mm.), weighed 1.3 g. (29%) and on infrared analysis proved to be a mixture of methyl 2-cyclohexene-1-carboxylate and methyl 3-cyclohexene-1-carboxylate, $n^{25}\text{D}$ 1.4589. Fraction two, weighing 1.3 g. (20%), was shown to be methyl *cis*-3-acetoxycyclohexanecarboxylate, b.p. 115–117° (5 mm.), by infrared spectrum.

Fraction two was hydrolyzed in the usual way and yielded 0.3 g. of *cis*-3-hydroxycyclohexanecarboxylic acid, m.p. 131–131.9° (no depression on admixture with an authentic sample).

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(9) Melting points are corrected; boiling points are uncorrected. Distillations were carried out with an 18″ modified Podbielniak column. Infrared spectra were recorded using a Baird infrared spectrometer in chloroform solutions at a concentration of 60 mg./ml. in a 0.1-mm. NaCl cell. Analyses are by the Microanalytical Laboratory of the University of California.

(10) S. Winstein and H. Marshall, THIS JOURNAL, **74**, 1120 (1952).