Rates of Solvolysis of Di-p-toluenesulfoxycyclohexanes

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In the previous paper[1] it was reported that *trans*-1,3-di-*p*-toluenesulfoxycyclohexane, in which one of two toluenesulfoxyl groups was axial and the other equatorial in stable form, was solvolyzed more rapidly than the cis form, in which two toluenesulfoxyl groups were equatorial in stable form, in agreement with the general rule as described below. However, it was unexpectedly observed that solvolysis of *trans*-4-hydroxy- or -acetoxy-cyclohexyl *p*-tosylate in which two substituents were equatorial proceeded at a rate twice as fast as that of the corresponding cis isomer in which one of two substituents was axial and the other equatorial[2]. In connection with the unexpected result mentioned above it was desirable to study further the configuration and the reactivity of the 4-substituted cyclohexyl *p*-tosylates.

In the present work, also in relation to the problem mentioned above, the solvolysis of 1, 2- and 1, 4-di-*p*-toluenesulfoxycyclohexanes (described as ditosylates in this paper) has been made.

Experimental

Samples. — *cis*- and *trans*-Cyclohexane-1,2- and -1,4-diols used as starting materials were those which were previously prepared[2,3]. Each of them was treated in pyridine at 0 to 5°C with two equivalent quantities of *p*-toluenesulfonyl chloride according to the conventional method, and the resulting ditosylate was recrystallized from a mixture of benzene and ligroin. The ditosylates obtained in this way had respectively the following melting points.

Position of tosyl groups	M. p. (reported m. p.), °C
cis-1,2	129∼130 (128.5∼129.5[4])
trans-1,2	109∼110 (109[4])
cis-1,4	98∼98.5 (98∼99[5])
trans-1,4	159 (159°[5])

Procedure for Rate Measurements.—Solvolysis rates were measured at 99.8°C in ethanol (98.5% by weight), in methanol (99.5% by weight) and in acetic acid containing a slight excess of acetic anhydride, by the usual ampoule technique[1,2]. Concentrations (all given at room temperature) of ditosylates were in the range from 0.005 to 0.01 mol./l., since they are less soluble in these solvents, especially in alcohol. Solvolysis of 1, 4-ditosylates was performed in 0.01 mol./l. in acetic acid and also in 0.005 mol./l. in methanol since the solubility of the compounds in ethanol was very small, and that of 1, 2-ditosylates was performed in ethanol. The reactions were followed by titrating at intervals for the sulfonic acid liberated or the alkali consumed during the solvolysis. Titrations in acetic acid were carried out with a 0.05 N solution of anhydrous sodium acetate or *p*-toluenesulfonic acid in acetic acid using bromophenol blue as indicator. In methanol and ethanol, a 0.05 N aqueous solution of sodium hydroxide or hydrogen chloride was used as a standard solution for titration with phenolphthalein as indicator. Rate constants were calculated from the formula:

$$k_1=(1/t)\ln\{a/(a-x)\}$$

in which a was the initial concentration of ditosylate and x was the concentration of sulfonic acid liberated at time t.

Results and Discussion

The solvolysis of the di-tosylates will proceed substantially in two steps as described below, and therefore a real solvolysis rate constant for each of them is not shown by the averaged value of the rate constants calculated from the formula. In fact, a calculated rate constant increased gradually during the alcoholysis and the acetolysis, and decreased gradually during the alcoholysis in the presence of a small amount of sodium alcoholate, in agreement with the behavior of 3-methylcyclohexyl *p*-tosylate and 1, 3-di-*p*-toluenesulfoxycyclohexanes previously reported[1]. But, in all cases, since the differences between the rate constants and the averaged rate constant in the solvolysis were within 5%, the solvolysis could be approximately expressed as the first order reaction. Table I lists the data for a run with *cis*-1,4-ditosylate in acetic acid. It is seen that, though the first order rate constant increases gradually during the solvolysis, it is approximately constant.

The mean rate constants of the acetolysis of the 1, 4-ditosylates were not substantially changed by the addition of a small quantity

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[1] N. Mori, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **80**, 1458 (1959).

[2] N. Mori, This Bulletin, **33**, 1332 (1960).

[3] N. Mori, ibid., **33**, 1144 (1960).

[4] R. Criegee and H. Stanger, *Ber.*, **69**, 2753 (1936).

[5] L. N. Owen and P. A. Robins, *J. Chem. Soc.*, **1949**, 320.

TABLE I. ACETOLYSIS OF *cis*-1,4-DI-*p*-TOLUENESULFOXYCYCLOHEXANE AT 99.8°C

Time, min.	Ditosylate, mol.×10^2	$k_1\times10^2$/min.
0.0	1.03	
40.0	0.92	0.269
100.0	0.786	0.267
160.0	0.666	0.269
280.0	0.448	0.294
400.0	0.304	0.303
		Mean 0.280

of anhydrous sodium acetate, and therefore the acetolysis is predominantly of the unimolecular type. On the other hand, since the mean rate constants of the alcoholysis were decreased by the addition of sodium alcoholate, and under this condition the rate constant decreased during the solvolysis as described above, a part of the alkaline alcoholysis consists of the bimolecular displacement and elimination reactions based on a back-side attack on carbon and hydrogen coincident with the departure of the toluenesulfoxyl group. The rate constants and the relative rates for the isomeric di-tosylates are summarized in Tables II and III.

TABLE II. RATE CONSTANTS OF SOLVOLYSIS OF DI-*p*-TOLUENESULFOXYCYCLOHEXANES

Position of tosyl groups	Tosylate, mol./l.	Solvent	Alkali, mol./l.	$k_1\times10^2$/min.
cis-1,4	0.005	M	0.020 a	2.8
〃	0.005	M	0.013 a	1.7
〃	0.005	M		1.1
〃	0.010	A	0.023 b	0.292
〃	0.010	A		0.280
trans-1,4	0.005	M	0.018 a	1.7
〃	0.005	M	0.013 a	1.5
〃	0.005	M		1.2
〃	0.010	A	0.023 b	0.603
〃	0.010	A		0.614
cis-1,2	0.005	E	0.015 c	0.39
trans-1,2	0.005	E	0.015 c	0.069
cis-1,3 1)	0.010	E	0.025 c	1.5
〃	0.010	A	0.026 b	0.195
trans-1,3 1)	0.010	E	0.025 c	3.5
〃	0.011	A	0.027 b	0.209
trans-4-acetoxy cyclohexyl tosylate 2)	0.026	A		1.61

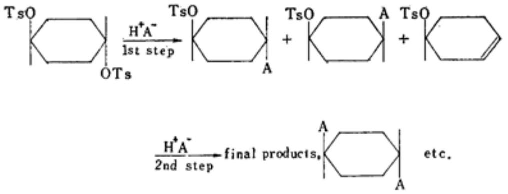
A, acetic acid; M, methanol; E, ethanol; a, sodium methoxide; b, sodium acetate; c, sodium ethoxide.

TABLE III. RELATIVE RATES OF SOLVOLYSIS OF 1,4-DI-*p*-TOLUENESULFOXYCYCLOHEXANES

	MeOH[a]	MeOH[b]	MeOH[c]	AcOH[d]	AcOH[c]
k_{cis}	10.0	6.0	4.0	1.04	1.0
k_{trans}	2.8	2.4	2.0	0.98	1.0
$k_{\text{cis}}/k_{\text{trans}}$	1.6	1.1	0.9	0.48	0.45

a, contained sodium methoxide in 0.02 mol./l.
b, contained sodium methoxide in 0.013 mol./l.
c, not contained alkali.
d, contained sodium acetate in 0.023 mol/l.

Mechanism of Solvolysis.—The solvolysis of the ditosylates proceeds substantially in two steps where in the first step three monotosylates are produced and in the second step they are converted into final products. For example, in the case of *trans*-1,4-ditosylate, the process is illustrated by the following formula:



where H^+A^- is the solvent and Ts is the tosyl group.

In the present work, it has been observed that a calculated rate constant increased gradually during the neutral alcoholysis and the acetolysis. The increase in the rate constants is probably due to the fact that the reaction rate in the second step is higher than that in the first step, as explained for the similar behavior of 1,3-di-*p*-toluenesulfoxycyclohexanes1). This suggestion is supported for example by the experimental facts that the acetolysis rate of *trans*-4-acetoxycyclohexyl *p*-tosylate is 1.7 times that of the *trans*-1,4-ditosylate and 3.4 times that of the *cis*-1,4-ditosylate, and that 2-acetoxycyclohexyl *p*-tosylates6) and 2-hydroxycyclohexyl *p*-brosylates3) are rapidly solvolyzed, but 1,2-ditosylates are not acetolyzed.

Relative Rate $k_{\text{cis}}/k_{\text{trans}}$.—The relation between conformation and reactivity in a rigid cyclohexane system is very important. An axial group is sterically more strained and therefore, in general, more ionizable or easier to depart than an equatorial group. In the labile cyclohexane system, the trans form of cyclohexyl *p*-tosylate with a group such as the acetoxyl group6) at the β-position is solvolyzed more rapidly than the cis isomer, but *trans*-2-substituted cyclohexyl *p*-tosylates and *p*-brosylates with a group such as *p*-bromobenzenesulfoxyl6), nitroxyl7), and hydroxyl3) group are solvolyzed at a slightly faster or slower rate than the corresponding cis forms. *trans*-3-Alkyl8),

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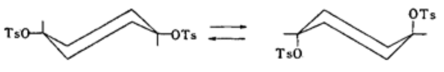
6) S. Winstein, E. Grunwald and L. L. Ingraham, *J. Am. Chem. Soc.*, **70**, 821 (1948).

7) S. J. Cristol and B. Franzus, ibid., **79**, 2488 (1957).

8) S. Winstein and H. J. Holmess, ibid., **77**, 5562 (1955).

hydroxy[1], acetoxy[1] or methoxycarbonyl[9] cyclohexyl *p*-tosylate is solvolyzed more rapidly than the corresponding cis from. Further, *cis*-4-alkylcyclohexyl *p*-tosylate is solvolyzed more rapidly than the trans form[8]. The *trans*-1, 4-ditosylate has the two possible chair conformations as follows:



trans (e, e) trans (a, a)

The trans (e, e) is more stable than the trans (a, a). On the other hand, the cis form has only one chair conformation as follows:

cis (e, a) cis (a, e)

where Ts is the toluenesulfonyl group.

Similarly, also in the case of the 1, 2-ditosylates, the cis form has two chair conformations and the trans form only one. From those facts it is expected that the solvolysis rates of the *cis*-1, 2- and 1, 4-ditosylates are higher than that of the corresponding trans forms.

In the present work, the 1, 2-ditosylates were not solvolyzed in acetic acid after being heated for 20 hr. at 100°C, as reported by Criegee[4]. They were, however, sowewhat ethanolyzed and especially solvolyzed more rapidly in the presence of sodium alcoholate and the relative rate $k_{\mathrm{cis}}/k_{\mathrm{trans}}$ was 5.6 (see Table II). Winstein[6] reported that the relative rate of acetolysis (75°C) of 1, 2-dibromobenzenesulfoxycyclohexanes was 1.1, although the rate constants of those brosylates were very low. Those facts are in agreement with the expectation described above.

In the solvolysis of the 1, 4-ditosylates, the trans form was solvolyzed in acetic acid unexpectedly at a rate 2.2 times faster than the cis form. Also, a similar result was obtained in the acetolysis of 1, 4-dibromobenezenesulfoxycyclohexanes[10] and the ratio of k_{cis} to k_{trans} was 0.78. Those facts are substantially similar to the results previously obtained in the solvolysis of 4-hydroxy- and 4-acetoxycyclohexyl tosylates[2], and are not explained by the rule as described above. Up to the present, the author can not give reasons for the fact that the trans form was acetolyzed more rapidly than the cis form. However, the methanolysis of the ditosylates, especially in the presence of alkali, proceeded more rapidly than their acetolysis and the cis form was methanolyzed more rapidly than the trans form. Thus, the ratio of k_{cis} to k_{trans} was 0.9 in methanol without alkali, 1.1 in methanol with NaOMe in 0.013 mol./l. and 1.6 in methanol with NaOMe in 0.02 mol./l.

Solvent and Alkali Effects.—In general, in unimolecular reaction solvation with solvent is very important, and the solvolysis rate in acetic acid is higher than that in ethanol. Further, such an enhancement in the rate in going from ethanol to acetic acid is nicely shown in the case of unsubstituted and substituted cyclohexyl tosylates. For example, the ratio of k_{EtOH} to k_{AcOH} for the cis form (with a-tosyl group) of 4-*tert*-butylcyclohexyl tosylate is 0.87 and that for the trans form (with e-tosyl group) 0.72[8]. On the other hand, primary alkyl tosylates, which are sensitive to a nucleophilic attack, are more reactive in ethanol than in acetic acid, such as those shown by the solvent-rate sequences[11] (EtOH : AcOH) for MeOTs, EtOTs and *iso*-BuOTs respectively to be 80 : 1, 39 : 1 and 6.2 : 1 at 75°C.

Furthermore, a carbon atom having an a-tosyl group is more easily attacked by a nucleophilic agent than that having an e-tosyl group, and the bimolecular reaction[12] of *cis*-*tert*-butylcyclohexyl tosylate with phenolate ion proceeds more rapidly than that of the trans form.

In the present work, however, the ditosylates were solvolyzed more rapidly in alcohol, especially in the presence of alkali, than in acetic acid and the solvolysis rate of the cis forms with the a-tosyl group was enhanced more than that of the trans forms without such a group, in going from acetic acid to alcohol containing alkali. Therefore, the alcoholysis and the alkaline alcoholysis of the di-tosylates probably involve bimolecular nucleophilic attack on carbon or hydrogen in the rate-determining step, similar to the primary alkyl tosylates, but in contrast to the general cyclohexyl tosylates.

Summary

Rates of solvolysis of *cis*- and *trans*-1, 2- and -1, 4-di-*p*-toluenesulfoxycyclohexanes were measured at 99.8°C in methanol or in acetic acid. In all cases, the solvolysis was approximately of first order.

Mean rate constants of the solvolysis increased in going from acetic acid to alcohol, and were enhanced by the addition of a small

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[9] D. S. Noyce and H. J. Weingarten, ibid., **79**, 3103 (1957).

[10] N. Mori, unpublished work. The k_1 of the cis form was 1.13 and that of the trans form 1.44 at 99.8°C.

[11] S. Winstein and H. Marshall, *J. Am. Chem. Soc.*, **74**, 1120 (1952).

[12] E. L. Eliel and R. S. Ro, ibid., **79**, 5995 (1958).

amount of alkali, in agreement with the behavior in solvolysis of primary alkyl tosylates.

The 1, 2-isomers were not solvolyzed in acetic acid in 20 hr., and in ethanol containing EtONa in 0.02 mol./l., the ratio of k_{cis} to k_{trans} was 5.6.

In the case of the 1, 4-isomers, the ratio was ca. 0.5 in acetic acid, 0.9 in methanol without alkali, 1.1 in methanol with MeONa in 0.013 mol./l. and 1.6 in methanol with MeONa in 0.02 mol./l.

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