BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 46, 1795—1797 (1973)

Solvolysis of *cis*- and *trans*-4-*t*-Butylcyclohexyl Tosylates in *N*-Methylacetamide. Rates and Products Distribution

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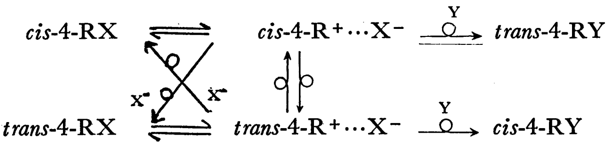
(Received November 16, 1972)

Solvolysis of *cis*- and *trans*-4-*t*-butylcyclohexyl tosylates (RX) in wet *N*-methylacetamide (H_2O content: 0.06—0.94 wt%) was carried out to give olefins (77—93%), 4- and 3-*t*-butylcyclohexyl acetates (ROAc) (6—22%), and 4- and 3-*t*-butylcyclohexanols (ROH) (2—4%). In *N*-methylacetamide with water (0.06%, wt) *trans*-4-RX gave *cis*-4-ROAc containing 18% *trans*-4-ROAc whereas *cis*-4-RX yielded *trans*-4-ROAc containing only 3% of *cis*-4-ROAc. In the course of solvolysis (75% completion) *trans*-4-RX was isomerized to *cis*-4-RX (5.9%), whereas *cis*-4-RX gave only 0.3% *trans*-4-RX. These results are characteristic of solvolysis in this amide solvent when compared with those in other hydroxylic solvents. Stereochemical results obtained from the present studies on the solvolysis in *N*-methylacetamide can not be explained by the hypothetical hydrogen-bridged carbonium ion intermediate proposed for the solvolysis of *cis*-4-RX. The nature of *N*-methylacetamide as a solvolytic solvent is discussed especially with regard to the effect of its polymeric structure on the steric course of solvolysis.

In previous studies on the solvolysis of *cis*- and *trans*-4-*t*-butylcyclohexyl tosylates (RX) in various hydroxylic solvents such as phenol, acetic acid, or 60% aqueous acetone, we demonstrated that the solvolytic *cis*-*trans* isomerization and 1,2-rearrangement of these tosylates, which respectively afford their geometrical isomers and their 3-derivatives (*cis*-and *trans*-3-RX), occur concurrently.[1] It was concluded that an appreciable part of the retained products is actually produced by double inversion, as is shwon in the following scheme, and the hypothesis of the hydrogen-bridged carbonium ion intermediate[2] is not necessary for an explanation of the formation of the retained products.



(X=OTs, Y=Nucleophile)

Scheme 1.

An investigation of these phenomena was extended to a non-hydroxylic solvent, solvolysis of this system in *N*-methylacetamide being carried out. This amide is known to possess a large dielectric constant[3] and

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[1] a) K. Okamoto, S. Saitô, and H. Shingu, This Bulletin, **42**, 3298 (1969); b) *ibid.*, **43**, 3008 (1970).

[2] a) S. Winstein and N. J. Holness, *J. Amer. Chem. Soc.*, **77**, 5562 (1955); b) V. J. Shiner, Jr., and J. G. Jewett, *ibid.*, **87**, 1382 (1965); c) N. C. G. Campbell, D. M. Muir, R. R. Hill, J. H. Parish, R. M. Southan, and M. C. Whiting, *J. Chem. Soc.*, *B*. **1968**, 355.

[3] G. R. Leader and J. F. Gormly, *J. Amer. Chem. Soc.*, **73**, 5731 (1951); the dielectric constant of *N*-methylacetamide was determined to be 169.7 at 35 °C.

TABLE 1. SOLVOLYSIS PRODUCTS FROM *cis*- AND *trans*-4-*t*-BUTYLCYCLOHEXYL TOSYLATES AT 75 °C

Solvent:	*N*-Methylacetamide[a]					PhOH−PhH[b] 1:1 by wt		AcOH[c]	
(H_2O concn., wt%)	(0.06)[d]	(0.06)[d]	(0.89)	(0.12)	(0.94)				
ROTs:	*cis*	*trans*	*cis*	*trans*	*trans*	*cis*	*trans*	*cis*	*trans*
Base:	Pyridine					Et_3N		NaOAc	
Cyclohexenes:									
Yield %	88.5	93.2	91.5	82.9	77.2	87.0	72.5	87.0	79.2
Composition %									
4-*t*-Butyl	100.0	100.0	100.0	100.0	100.0	97.4	95.3	96.6	93.0
3-*t*-Butyl	0.0	0.0	0.0	0.0	0.0	2.6	4.1	3.2	6.3
1-*t*-Butyl	0.0	0.0	0.0	0.0	0.0	0.0	0.6	0.2	0.7
Cyclohexyl Acetates or Cyclohexyl Phenyl Ethers:									
Yield %	5.7	7.0	8.4	17.1	22.4	8.7	9.4	12.8	21.9
Composition %									
trans-4-*t*-Butyl	96.1	18.0	96.1	9.2	1.2	55.0	12.9	57.0	1.8
cis-4-*t*-Butyl	3.1	77.6	1.3	88.3	97.6	20.4	69.2	5.5	89.0
trans-3-*t*-Butyl	0.8	0.0	2.6	0.0	0.0	13.7	12.8	35.2	2.3
cis-3-*t*-Butyl	0.0	4.4	0.0	2.5	1.2	10.9	5.1	2.3	6.9
Cyclohexanols or Cyclohexylphenols:									
Yield %	2.4	2.0	3.1	3.9	4.4	1.6	4.4		
Composition %									
trans-4-*t*-Butyl	96.9	28.7	97.5	12.3	2.0				
cis-4-*t*-Butyl	3.1	65.3	1.0	84.8	96.4				
trans-3-*t*-Butyl	0.0	0.0	1.5	0.0	0.0				
cis-3-*t*-Butyl	0.0	6.0	0.0	2.9	1.6				

a) ROTs concn.: 0.0922—0.0925 M; Pyridine concn.: 0.0973 M.

b) Ref. 6; ROTs concn.: 0.0913—0.0987 M; Et_3N concn.: 0.106—0.123 M.

c) Ref. 2c; data at 100 °C; NaOAc concn.: 0.05 M.

d) k_1's for *cis*- and *trans*-4-RX are 8.92×10^{-5} and 2.23×10^{-5} (sec^{-1}), respectively.

TABLE 2. COMPOSITION OF RECOVERED TOSYLATES IN THE PARTIAL SOLVOLYSIS OF *cis*- AND *trans*-4-*t*-BUTYLCYCLOHEXYL TOSYLATES AT 75 °C

ROTs	Solvent	Completion %	Composition %			
			trans-4-RX	*cis*-4-RX	*trans*-3-RX	*cis*-3-RX
cis	*N*-Methylacetamide[a]	75.0[b]	0.3	97.6	0.0	2.1
cis	PhOH-PhH (1:1 by wt)[c]	75.5	1.1	88.3	0.0	10.6
cis	AcOH[d]	74.3	2.2	82.9	0.0	14.9
trans	*N*-Methylacetamide[a]	75.0[b]	94.1	5.9	0.0	0.0
trans	PhOH-PhH (1:1 by wt)[c]	73.6	96.7	0.7	2.6	0.0

a) H_2O content: 0.05 wt%. b) Calculated from reaction time. c) Ref. 1a. d) Ref. 1b.

would be a typical solvolytic solvent. It is anticipated that the negative end of the dipole could probably solvate the carbonium ion more strongly than that of the hydroxylic solvents.

In this paper we report on the results of examination of solvolytic *cis-trans* isomerization and 1,2-rearrangement of tosylates, as well as of the rates and products studies on the solvolysis of *cis*- and *trans*-4-RX in *N*-methylacetamide. The factors determining the steric course of solvolysis are discussed in connection with the nature of the amide as a solvolytic solvent.

Results and Discussion

The solvolysis of both *cis*-4-RX and *trans*-4-RX was carried out in *N*-methylacetamide containing a small amount of water (0.06—0.94 wt%) and pyridine (equimolar amount to the tosylate). The yields and compositions were determined by means of vpc. The compositions of recovered tosylates from partially-solvolyzed reaction mixtures were determined by the method previously reported.[1b] The data are summarized in Tables 1 and 2 together with data pertinent to other solvent systems.

Both tosylates displayed good first-order behavior and the reaction proceeded at a similar rate to that of ethanolysis.[2a] This is in line with the expectation based on the *Y* value of *N*-methylacetamide.[4,5] As observed in S_N1 solvolysis in other solvents,[2,6] *cis*-4-RX is solvolyzed more rapidly than *trans*-4-RX in

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[4] a) E. Grunwald and S. Winstein, *ibid.*, **70**, 846 (1948); b) A. H. Fainberg and S. Winstein, *ibid.*, **78**, 2770 (1956).

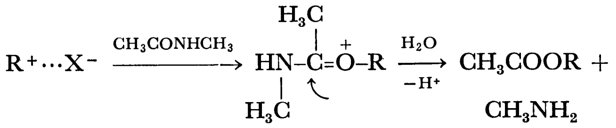
[5] K. Okamoto, M. Dohi, and S. Saitô, unpublished results; the *Y* value for *N*-methylacetamide has been determined to be −2.234.

[6] K. Okamoto, S. Saitô, and H. Shingu, This Bulletin, **42**, 3288 (1969).

the amide by a factor of 4.0 at 75 °C (2.5—3.1 for other solvents) (Table 1). The kinetic results imply that *N*-methylacetamide is a typical solvolytic solvent.

The major product of solvolysis in the amide for both tosylates has been proved to be an olefin, exclusively 4-*t*-butylcyclohexene. This is in sharp contrast to the case of other solvent systems in which small amounts of isomeric 3- and 1-*t*-butylcyclohexenes are accompanied with 4-*t*-butylcyclohexene.

The substitution products for both tosylates are composed of a major portion of 4- and 3-*t*-butylcyclohexyl acetates (ROAc) and a minor portion of 4- and 3-*t*-butylcycohexanols (ROH). The formation of ROAc could be elucidated by a mechanism similar to the nucleophilic intervention by acetone to furnish an oxonium ion in the solvolysis of 2-octyl brosylate in 80% methanolic acetone.[7] Thus, nucleophilic attack by the amide on $R^{+}\cdots X^{-}$ would be likely to produce an oxonium ion whose subsequent reaction with water furnishes ROAc as follows.



$$R^{+}\cdots X^{-} \xrightarrow{CH_3CONHCH_3} \underset{H_3C}{HN}-\overset{H_3C}{C}{=}\overset{+}{O}-R \xrightarrow[-H^{+}]{H_2O} CH_3COOR + CH_3NH_2$$

The yields of ROAc for solvolysis in the amide containing various amounts of water is a function of water concentration. This means that the second step in the above scheme is $B_{AC}2$ between the carbonyl-carbon in the pre-formed oxonium ion and water.

The composition percentage of the retained ROAc (18%) produced from the *trans*-4-RX (H_2O content: 0.06 wt%) significantly exceeds that of ROAc (3.1%) produced in the *cis*-4-RX solvolysis (H_2O content: 0.06 wt%), the formation of the rearranged ROAc being substantially less favored particularly in the case of *cis*-4-RX solvolysis. The results differ from those for the other solvent systems[2,6] (Table 1). It should be noted that the abnormal stereochemical results are incompatible with the expectation from the hypothetical hydrogen-bridged carbonium ion intermediate,[2] since such a carbonium ion should produce much of the retained or rearranged products *in the cis-4-RX solvolysis.*

The nature characteristic of this amide solvent became more evident when the composition of the recovered tosylates was examined (Table 2).

The extent of 1,2-rearrangement of the tosylate is greatly diminished, being comparable with the significant decrease in the rearranged products. Solvation of the cation by the amide in $R^{+}\cdots X^{-}$ may suppress the migration of *β*-hydrogen.

With regard to the superiority of *trans-cis* isomerization (5.9%) over *cis-trans* isomerization (0.3%), the following explanations are given. The amide might be operative as a nucleophile in the form of an extended polymer,[8] which would diminish the extent of attack by amide on *trans*-4-$R^{+}\cdots X^{-}$ from the back, since the approach of such a bulky nucleophile should enlarge the steric repulsion toward 1,3,5-triaxial hydrogens.[9] This would make it possible for the released tosylate anion (X^{-}) to compete affectively with polymerized amide to produce *cis*-4-RX from *trans*-4-RX by the S_N2-like attack on *trans*-4-$R^{+}\cdots X^{-}$ from the back (Scheme 1).

The decrease in the extent of retention for ROAc in the higher water contents, observed in the case of *trans*-4-RX solvolysis, might be explained as follows. The increase in water content lowers the degree of association of amide, increasing the extent of attack by the amide from the back on *trans*-4-$R^{+}\cdots X^{-}$, and decreasing the retained ROAc (Table 1).

The fact that the compositions of ROAc and ROH vary with the change in water content of the amide suggests the existence of an intermolecular complex between water and the amide, which competes with polymerized amide as a nucleophile to produce ROH.

Experimental

Materials. *N*-Methylacetamide was prepared according to Alelio and Ried,[10] and the water content was determined by means of Karl Fischer titration. *trans*-4-*t*-Butylcyclohexanol was prepared by the method of E. L. Eliel *et al.*,[11] other reagents being provided by the methods previously reported.[6]

Rate Measurements. Titrimetric rates were followed by placing the flask containing reaction mixture into an oil bath (75 °C±0.03) and removing 1 ml of an aliquot at various time intervals. The aliquots were transferred to a separatory funnel using 20 ml of ether and the ether solution was extracted three times with 10 ml of water. The aqueous solution was titrated with a standard aqueous sodium hydroxide using phenolphthalein as an indicator. It was not possible to obtain an experimental infinity titer, and therefore, tosylate concentrations at time *t* were calculated on the basis of the theoretical infinity titer. The rate constants were calculated graphically and are shown in Table 1, footnote (d).

Product Analysis and Unchanged Tosylate Analysis. The procedures were carried out as reported.[1b] except for the use of tlc for the separation of mixtures of products instead of column chromatography. The results are shown in Tables 1 and 2.

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[7] H. Weiner and R. A. Sneen, *J. Amer. Chem. Soc.*, **85**, 2181 (1963); **87**, 287 (1965).

[8] It is considered that the much higher dielectric constant of *N*-methylacetamide is due to the formation of extended polymer by hydrogen bonding (Ref. 3).

[9] The axial approach of the incoming amide should be hindered to a greater extent than the equatorial approach. For instance, S_N2 rate ratio ($k_{cis}/k_{trans}=31$ for the reaction of 4-*t*-butylcyclohexyl system with sodium thiophenoxide in 87% ethanol) is much greater than the value *ca.* 3 as expected from the ground-state energy differences alone (E. L. Eliel and R. S. Ro, *J. Amer. Chem. Soc.*, **79**, 5995 (1957)). Thus, the equatorial derivative undergoes S_N2 displacement more slowly, owing to its larger steric hindrance to the approach of the nucleophile in addition to its lower ground-state energy than the axial isomer. See also E. L. Eliel, N. L. Allinger, S. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience, New York, N. Y. (1965), pp. 86—88.

[10] G. F. D. Alelio and E. E. Ried, *J. Amer. Chem. Soc.*, **59**, 109 (1937).

[11] E. L. Eliel, R. J. L. Martin, and D. Nasipuri, "Organic Syntheses," Vol. 47, p. 16 (1967).