[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF NOTRE DAME]

Conformational Analysis. IV. Bimolecular Displacement Rates of Cyclohexyl *p*-Toluenesulfonates and the Conformational Equilibrium Constant of the *p*-Toluenesulfonate Group[1]

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RECEIVED FEBRUARY 16, 1957

Rates of displacement of *sec*-butyl tosylate, cyclohexyl tosylate and the *cis*- and *trans*-4-*t*-butylcyclohexyl, -4-methylcyclohexyl and -3-methylcyclohexyl tosylates with thiophenolate ion have been measured. The products of the reaction have been isolated in three instances. The displacement reaction is second order and is accompanied, in the case of the cyclohexyl, *cis*-4-*t*-butylcyclohexyl, *cis*-4-methylcyclohexyl and *trans*-3-methylcyclohexyl compound, by a surprisingly fast second-order elimination. The ratio of displacement rates of equatorial tosylate : axial tosylate : acyclic secondary tosylate is 1:19:80. The geometry of the transition state for the displacement reaction is discussed. The conformational equilibrium constant for tosylate is calculated to be 3.2 corresponding to a free energy difference of 0.7 kcal./mole between equatorial and axial tosylate. The consistency of the data is examined.

Introduction

Nucleophilic substitution reactions of the SN2 type involving cyclohexyl halides have been found to be quite slow as compared to similar reactions involving acyclic secondary halides.[3] The difference (by a factor of about 100) has been explained as being due to steric interference of the ring to backside attack[4] or as being a manifestation of "I-strain."[5] One weakness of the theoretical arguments is that, for lack of information, the axial or equatorial nature of the displaced halide substituent could not be taken into account.

Although many reactions of cyclohexyl compounds, such as esterification, ionic elimination, rearrangements, etc., have been studied as a function of the conformation of the substituent affected,[6] no complete study of conformational factors in bimolecular substitution is available. Difficulties might be expected in such a study due to the incursion of the unimolecular mechanism and of elimination reactions.[7] In the present work these difficulties were minimized by using thiophenolate, a highly nucleophilic reagent,[8] as substituting agent. The reactions of cyclohexyl and substituted cyclohexyl tosylates with sodium thiophenolate in 87% ethanol were found to be clean-cut second order in the reagents; moreover, the substitution reactions of the 4-*t*-butylcyclohexyl tosylates were found to give the *inverted* thioethers, so that both the kinetic and stereochemical criteria[9] indicated this reaction to be bimolecular (SN2). Unfortunately, in the case of those cyclohexyl tosylates (*cis*-4-*t*-butyl, *cis*-4-methyl, *trans*-3-methyl and unsubstituted) where the tosylate group is partly or entirely axial, substitution, even with the highly nucleophilic thiophenolate, was attended by second-order (presumably[9] bimolecular, E_2) elimination to the cyclohexene.[10] It was therefore necessary to follow the reaction by a double titration, an iodimetric one to follow the substitution reaction and an acidimetric one to follow the total (substitution and elimination) reaction, as suggested by the stoichiometric equations

$$C_6H_{11}OTs + C_6H_5SNa \longrightarrow C_6H_{11}SC_6H_5 + NaOTs$$

$$C_6H_{11}OTs + C_6H_5SNa \longrightarrow C_6H_{10} + NaOTs + C_6H_5SH$$

in which only the first reaction leads to a net consumption of thiophenol (followed iodimetrically), but both reactions consume base (with use of the appropriate indicator, sodium thiophenolate is basic and thiophenol is neutral).

Results

In Table I are listed the average values of all the rate constants determined in this work. (A complete list of all kinetic runs is contained in Table III in the Experimental.) By the method of computation employed (see Experimental) the iodometric titration gives k_S/k_E where k_S is the rate constant for substitution and k_E is the rate constant for elimination. The acidimetric titration gives $k_S + k_E = k_T$ (total bimolecular rate constant). From these the individual values of k_S and k_E are computed. The time unit used is the second, even though actual time measurements were made to the nearest minute in all reactions except that of *n*-butyl tosylate. Also listed in Table I are the conformational equilibrium constants derived from the rate constants by the equation[11] $K = (k_a - k)/(k - k_e)$ where k are the rate constants for the compounds indicated, k_a is the rate constant for the purely axial isomer *cis*-4-*t*-butylcyclohexyl tosylate (fixed conformation I) and k_e is the rate constant for the purely equatorial isomer *trans*-4-*t*-butylcyclohexyl tosylate (fixed

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(1) (a) Paper III, E. L. Eliel and R. S. Ro, THIS JOURNAL, **79**, 5992 (1957). (b) A preliminary account of the present work has appeared in *Chemistry & Industry*, 251 (1956).

(2) Texas Co. Fellow, 1954–1956. From the Ph.D. thesis of R. S. Ro.

(3) For a summary see E. L. Eliel in M. S. Newman's "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 121 *ff*.

(4) P. D. Bartlett and L. J. Rosen, THIS JOURNAL, **64**, 543 (1942); also discussed by S. J. Angyal and J. A. Mills, *Revs. Pure Appl. Chem.*, **2**, 185 (1952).

(5) H. C. Brown, R. S. Fletcher and R. B. Johannesen, THIS JOURNAL, **73**, 212 (1951); H. C. Brown and G. Ham, *ibid.*, **78**, 2735 (1956).

(6) *Cf.* D. H. R. Barton and R. C. Cookson, *Quart. Revs.*, **10**, 44 (1956).

(7) *E.g.*, H. R. Nace, THIS JOURNAL, **74**, 5937 (1952), observed considerable elimination in the methanolysis of epicholestanyl tosylate. R. J. Bridgewater and C. W. Shoppee, *J. Chem. Soc.*, 1709 (1953), found the substitution reaction of both 3-chlorocoprostanes with acetate to involve clean inversion suggesting a bimolecular mechanism, but complete kinetic data were not obtained.

(8) *Cf.* ref. 3, p. 156.

(9) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, Chapter VII.

(10) F. Winternitz and R. Dennilauler, *Bull. soc. chim. France*, 441 (1954), report that the reaction of cyclohexyl tosylate with sodium thiophenolate (solvent unspecified) gives phenyl cyclohexyl thioether in good yield.

(11) (a) S. Winstein and N. J. Holness, THIS JOURNAL, **77**, 5562 (1955); (b) see also E. L. Eliel and C. A. Lukach, *ibid.*, **79**, 5986 (1957).

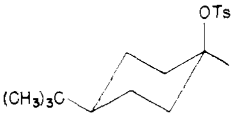
TABLE I

AVERAGE VALUES OF EXPERIMENTAL RATE CONSTANTS, CALCULATED SPECIFIC RATES OF SUBSTITUTION AND ELIMINATION AND CALCULATED CONFORMATIONAL EQUILIBRIUM CONSTANTS AND FREE ENERGY DIFFERENCES

Tosylate of	10^5k_T[a]	k_S/k_E	10^5k_S[a]	10^5k_E[a]	K	ΔK^0, kcal./mole
Cyclohexanol	18.35	1.22	10.09	8.26	3.24 3.12	$-0.68(k_S)$ $-\ .67(k_E)$
cis-4-*t*-Butylcyclohexanol (I)	70.19	1.06	36.12	34.07	0[b]	....
trans-4-*t*-Butylcyclohexanol (II)	1.95	Large	1.95	0	∞[b]	....
cis-4-Methylcyclohexanol	46.20	0.65	18.20	28.00	1.102 0.217	$-\ .06(k_S)$ $.90(k_E)$
trans-4-Methylcyclohexanol	2.58	Large	2.58	0	107	$-2.78(k_T)$
cis-3-Methylcyclohexanol	2.41	Large	2.41	0	149	$-2.95(k_T)$
trans-3-Methylcyclohexanol	59.30	1.20	32.35	26.95	0.124 0.284	$1.23(k_S)$ $0.74(k_E)$
Butanol-2	155.4	Large	155.4	0	.....	....
Butanol-1	839.7	Large	839.7	0	.....	....

[a] l. mole^{-1} sec.$^{-1}$ at 25.1°. [b] Assumed.

conformation II).[11a] ΔF^0 ($= -2.3\ RT \log K$) in the table is the free energy difference between the conformational isomers. Values of K and ΔF^0 computed from substitution rate constants are marked (k_S), those derived from elimination rates are marked (k_E); these two values are independently determined. In some cases it was found preferable to calculate the conformational equilibrium constants from the total rate constants[12]; such values are marked (k_T).



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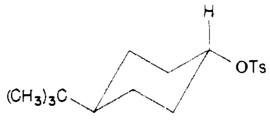
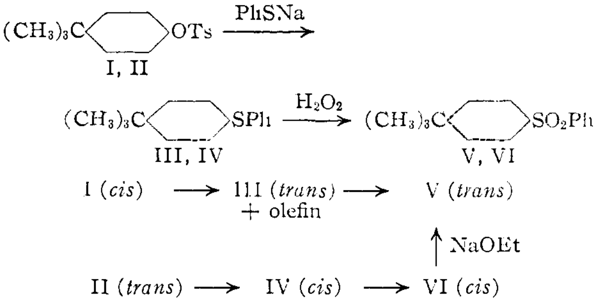


II

The rate data listed in Table I were supplemented by product studies in the case of cyclohexyl tosylate, the *cis*- and *trans*-4-*t*-butylcyclohexyl tosylates and the secondary acyclic tosylate, although, in the latter case, 2-octyl tosylate was examined instead of 2-butyl tosylate to facilitate isolation of the olefinic product if any. Cyclohexyl tosylate, under the condition of the kinetic experiments (reaction allowed to go to 95% completion), yielded cyclohexene, identified by its infrared spectrum and cyclohexyl phenyl thioether, identical in infrared spectrum with that of an authentic sample prepared by photochemical addition of thiophenol to cyclohexene.[13]



cis-4-*t*-Butylcyclohexyl tosylate (I) similarly gave *trans*-4-*t*-butylcyclohexyl phenyl thioether (III, 42%) and 4-*t*-butylcyclohexene (32%) in approximately the proportions demanded by the kinetic study. The *trans*-thioether III showed none of the diagnostic bands of its *cis* isomer IV (*vide infra*) in the infrared and was oxidized to a crystalline sulfone (V). *trans*-4-*t*-Butylcyclohexyl tosylate (II) with sodium thiophenolate (reaction time one month) gave only *cis*-4-*t*-butylcyclohexyl phenyl thioether (IV) and no olefin; the thioether IV was entirely distinct from the *trans* isomer III in infrared spectrum and, upon oxidation, gave a crystalline sulfone (VI) distinct from *trans*-4-*t*-butylcyclohexyl phenyl sulfone (V). The configuration of the sulfones was established by treatment of ether with ethanolic sodium ethoxide; this epimerized the *cis*-sulfone VI to the *trans*-isomer V but left the *trans* isomer V unchanged. Since on conformational grounds the *trans* isomer V (both substituents equatorial) should be more stable than the *cis* isomer VI (one substituent axial, one equatorial), the epimerization experiment confirms the configurations tentatively assigned on the basis of the S_N2 rule.[9] The reaction of 2-octyl tosylate gave some olefin (less than 6%) and a material which from its physical properties and analysis appeared to be 2-octyl phenyl thioether (87% yield).

Discussion

Before discussing the data in Table I, two curious aspects of the cyclohexyl tosylate–thiophenolate reaction should be pointed out. One is concerned with the unexpectedly large proportion of E_2 elimination occurring in the reaction of axial tosylates with thiophenolate. The rate of reaction of cyclohexyl tosylate with sodium hydroxide in 87% ethanol was found, in exploratory experiments, to be 0.810×10^{-5} l. mole^{-1} sec.$^{-1}$ or only about one-tenth of the rate of elimination with thiophenolate.[14] Further exploration of this phenomenon appears desirable.[15] The limited information available

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(12) This is legitimate since

$$K = \frac{k_a^S - k^S}{k^S - k_e^S} = \frac{k_a^E - k^E}{k^E - k_e^E} = \frac{k_a^S + k_a^E - (k^S + k^E)}{k^S + k^E - (k_e^S + k_e^E)} = \frac{k_e^T - k^T}{k_a^T - k_e^T}$$

(13) J. L. Cunneen, *J. Chem. Soc.*, 36 (1947).

(14) The ratio of *ca.* 10 for the specific rates of elimination with thiophenolate and alkoxide (or hydroxide), respectively, would seem to be a minimum, since it was not established that the reaction with alkoxide or hydroxide was entirely elimination.

(15) (a) While this work was in progress, P. B. D. de la Mare and C. A. Vernon, *J. Chem. Soc.*, 41 (1956), reported a similar observation in the reaction of thiophenolate with *t*-butyl chloride. (b) S. Winstein,

suggests that the efficacy of a base in bimolecular elimination may parallel its efficacy in bimolecular substitution (*i.e.*, nucleophilic character[8]) rather than its base strength; in other words, that there is a lack of parallel between rate and equilibrium in proton abstraction by bases, just as there is, in some instances, a lack of parallel between rate and equilibrium in the ionization of acids.[16] As expected[11b,17] the equatorial tosylates did not undergo appreciable bimolecular elimination.[18]

A second point of interest, established in exploratory experiments, is that the reaction of thiophenolate with cyclohexyl tosylate is greatly *accelerated* by increasing the proportion of water in the solvent, contrary to what might be predicted from known evidence in other SN2 reactions.[9,19]

According to the data in Table I, the ratio of bimolecular substitution rate constants for equatorial tosylate (II), axial tosylate (I) and acyclic (2-butyl) tosylate is 1:18.6:80. The ratio of 1:80 is similar to ratios of bimolecular substitution rate constants of cyclohexyl bromides and iodides to those of corresponding isopropyl halides,[3] as might be expected on the reasonable assumption that the halogen in cyclohexyl halide is largely equatorial. The ratio of 1:4.3 between axial cyclohexyl tosylate and acyclic tosylate is comparable in magnitude to that observed in SN1 reactions of cyclohexyl halides[3] and appears to be a manifestation of a relatively small amount of I-strain.[5,20] The more striking ratio is that of 1:18.6 between the equatorial and axial tosylate. Rather than to try to interpret this ratio in terms of I-strain[5] or steric hindrance to rearward attack,[4] we prefer to explain it in terms of differences in ground state energy and transition state energy levels between the two isomers.

It is evident from Fig. 1 that in a *symmetrical* substitution, such as that of an alkyl iodide by radioiodide, the transition state is the same for equatorially and axially substituted starting material, and the difference in specific rate should be entirely due to the difference in ground state energy levels. (This does not imply that the C–X and C–Y distances in the transition state—Fig. 1—need be the same. In fact, it is quite likely that the C–Y distances may be larger, since the originally axial group Y seems to be more crowded in the transition state.)

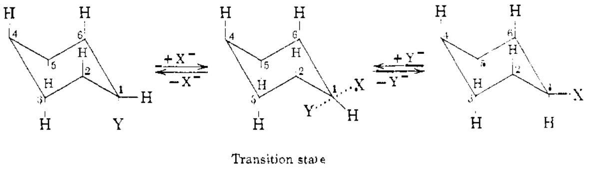

Fig. 1.

For an unsymmetrical substitution, such as that of a cyclohexyl tosylate by thiophenolate ion, there would also be some difference due to the unequal steric requirement of the incoming and outgoing groups (X and Y, respectively, for the axial isomer; Y and X, respectively, for the equatorial isomer).

The conformational equilibrium constant for cyclohexyl tosylate listed in Table I indicates that about 77% of the molecules exist with the tosylate group equatorial in equilibrium with 23% whose tosylate group is axial. The agreement of the constants K calculated from the substitution and elimination data (which are independent of each other) is very satisfactory. The difference of *ca.* 0.7 kcal./mole between the two ground states in Fig. 1 for a displacement of tosylate (equatorial or axial) by thiophenolate is not, however, sufficient to account for the entire difference in rate of substitution, which difference (by a factor of 19) corresponds to a difference in activation energy of $1.38 \times \log 19$ or 1.75 kcal./mole. It appears that about 1 kcal./mole of this difference is due to the unequal steric requirements of tosylate and thiophenoxide. This value does not appear unreasonably large.

The conformational free energy differences ΔF^0 (Table I) for *cis*- and *trans*-4-methylcyclohexyl tosylates should be related to that of cyclohexyl tosylate by the equations[11b] $\Delta F^0_{cis} = 1.8 - \Delta F^0_{\text{OTs}}$ and $\Delta F^0_{trans} = -1.8 - \Delta F^0_{\text{OTs}}$. Using $\Delta F^0_{\text{OTs}} = -0.7$ kcal./mole, the calculated values are $\Delta F^0_{cis} = 1.1$ kcal./mole and $\Delta F^0_{trans} = -2.5$ kcal./mole. The observed value for *trans*-4-methylcyclohexyl tosylate of −2.8 kcal./mole is in good agreement with the calculated, but in the case of the *cis* isomer, only the ΔF^0 value calculated from the elimination rate (0.90 kcal./mole) agrees with the calculated. The value calculated from substitution rate (−0.06 kcal./mole) appears to be affected by some unknown disturbing factor. The same factor does not seem to affect the *trans*-3-methylcyclohexyl tosylate; here the ΔF^0 values from substitution (1.23 kcal./mole) and elimination (0.74 kcal./mole) do not diverge too widely and bracket the calculated value of 1.1 kcal./mole.[21] *cis*-3-Methylcyclohexyl tosylate should exist in the diequatorial form to an even larger extent than the *trans*-4-isomer, since in the diaxial form of the *cis*-3-isomer a strong steric interaction between the axial methyl and

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D. Darwish and N. J. Holness, THIS JOURNAL, **78**, 2915 (1956), have reported that elimination occurs in the reaction of cyclohexyl tosylates with bromide ion. (c) See also C. W. Shoppee, H. C. Richards and G. H. R. Summers, *J. Chem. Soc.*, 4817 (1956).

[16] *E.g.*, R. G. Pearson and R. L. Dillon, THIS JOURNAL, **75**, 2439 (1953).

[17] D. H. R. Barton and W. J. Rosenfelder, *J. Chem. Soc.*, 1048 (1951); G. H. Alt and D. H. R. Barton, *ibid.*, 4284 (1954). However, bimolecular elimination of an equatorial substituent has been reported in ref. 15b.

[18] It should be stressed that the kinetic method employed here is not capable of detecting elimination when $k_S/k_E \gtrsim 10$, especially in slow runs where some consumption of thiophenol by oxidation is unavoidable.

[19] The same point was already suggested by the finding that the addition of benzene retards the reaction of *n*-butyl bromide with sodium 1-butylthiolate in benzene: O. R. Quayle and E. G. Royals, THIS JOURNAL, **64**, 226 (1942). See also P. B. D. de la Mare and C. A. Vernon, *J. Chem. Soc.*, 3679 (1954).

[20] Numerous factors may be responsible for the difference between axial cyclohexyl and 2-butyl tosylate. Because of the relatively easy rotation about carbon–carbon bonds of the 2-butyl compound, interactions between the incoming thiophenolate group, outgoing tosylate group and the hydrogen atom attached to C_1 with adjacent atoms in the transition state should be less for 2-butyl than for axial cyclohexyl. There is also a (probably smaller) difference in the two ground states, due to the extra 1–3 diaxial hydrogen–tosylate interaction in the cyclohexyl compound. We agree with H. C. Brown[5] that the magnitude of these factors is difficult to assess at the present time.

[21] The value of 0.98 kcal./mole computed from k_T would also give good agreement with the calculated. On the whole, k_T values are more reliable than k_S or k_E values, since they are not affected by the difficulties inherent in determining k_S/k_E.

axial tosylate group appears. The data (Table I) bear out this prediction.

The value of 0.7 kcal./mole for the difference in free energy between equatorial and axial tosylate is in poor agreement with a value of 1.7 kcal./mole deduced from solvolysis data by Winstein and Holness.[11a] The lower value appears quite reasonable, however, in view of the fact that the corresponding value for hydroxyl[1a,11] is 0.5–0.9 kcal./mole and the value for tosylate would not be expected to be very different, since the toluenesulfonyl moiety can be so rotated that it does not add to the interference of the axial oxygen atom with the axial hydrogen atoms at C_3 and C_5.[22]

Experimental

All melting points are uncorrected. Microanalyses by Micro-Tech Laboratories, Skokie, Ill., and Midwest Microlab, Inc., Indianapolis, Ind.

***p*-Toluenesulfonates.**—The preparation of the alkylcyclohexanols used in this study is described elsewhere.[1a,11b] The alcohol (0.03 mole) dissolved in 20 ml. of dry pyridine was added to 10 g. (0.05 mole) of *p*-toluenesulfonyl chloride in 20 ml. of pyridine at 0°. The solution was allowed to stand overnight at room temperature, poured into ice-cold 10% hydrochloric acid and extracted with ether. The ether extract was washed with dilute hydrochloric acid, water, aqueous sodium bicarbonate and again with water, dried over sodium sulfate and concentrated. Yields were of the order of 85%.

trans-4-*t*-Butylcyclohexyl tosylate melted at 89–90°, lit.[11b] 89.4–90.0°. *cis*-4-*t*-Butylcyclohexyl tosylate melted at 78–79°, lit.[11b] 79–80°. This material could be prepared in 30% yield from the *cis*-rich alcohol obtained[1a] by catalytic reduction of the ketone with platinum in acetic acid containing hydrogen chloride, the crude tosylate being recrystallized several times from ethyl acetate-petroleum ether (b.p. 30–60°). *trans*-4-Methylcyclohexyl tosylate melted at 70–71°, lit.[23] 70.8–71.8°. *cis*-4-Methylcyclohexyl tosylate melted at 71–72°, lit.[23] 72.0–72.8°.

cis-3-Methylcyclohexyl tosylate melted at 38–39° after recrystallization from 95% ethanol at −70°. *Anal.* Calcd. for $C_{14}H_{20}O_3S$: C, 62.65; H, 7.51. Found: C, 62.62; H, 7.60.

trans-3-Methylcyclohexyl tosylate similarly purified melted at 50–52°. *Anal.* Calcd. for $C_{14}H_{20}O_3S$: C, 62.65; H, 7.51. Found: C, 62.65; H, 7.21.

Cyclohexyl tosylate melted at 44–45°, lit.[24] 44–45°.

2-Butyl tosylate was purified by low-temperature crystallization. *Anal.* Calcd. for $C_{11}H_{16}O_3S$: C, 57.86; H, 7.06. Found: C, 57.83; H, 7.08.

n-Butyl tosylate boiled at 169° (4 mm.), $n^{20}\mathrm{D}$ 1.5046; lit.[25] b.p. 169° (4 mm.), $n^{20}\mathrm{D}$ 1.5085. *trans*-4-Phenylcyclohexyl tosylate[26] melted at 99–100°, lit.[27] 98.2–98.7°.

cis-4-Phenylcyclohexyl tosylate[26] melted at 119–120°. *Anal.* Calcd. for $C_{19}H_{24}O_3S$: C, 69.10; H, 6.71. Found: C, 68.94; H, 6.86.

Reaction of *p*-Toluenesulfonates with Sodium Thiophenolate. Cyclohexyl Tosylate.—A solution of 1.3 g. (0.056 g.-atom) of sodium and 6.8 g. (0.061 mole) of thiophenol in 100 ml. of 87% ethanol was mixed with a solution of 12.7 g. (0.053 mole) of cyclohexyl tosylate in 400 ml. of the same solvent and allowed to stand for five days when titration of an aliquot showed the reaction to be 95% complete. The solution was poured into ice-water and extracted repeatedly with ether. The combined ethereal extracts were washed successively with dilute aqueous sodium hydroxide, water and calcium chloride solution and dried over calcium chloride. Ether was removed through a column and the residue fractionated through a small Vigreux column at atmospheric pressure.

Cyclohexene began to come over at 65° and was identified by its infrared spectrum. Vacuum distillation of the residue produced cyclohexyl phenyl thioether, b.p. 90–104° (0.3 mm.), containing, according to its infrared spectrum, some diphenyl disulfide which was removed by percolation of a pentane solution of the crude product through an alumina column. The material recovered from the eluate had an infrared spectrum identical with that of an authentic sample of cyclohexyl phenyl thioether prepared by photochemical addition of thiophenol to cyclohexene,[13] b.p. 150–152° (12 mm.) (lit.[13] 135–137.5° (9 mm.)).

***cis*-4-*t*-Butylcyclohexyl Tosylate.**—The reaction of 31 g. (0.1 mole) of the tosylate I in 400 ml. of 87% ethanol with 100 ml. of 1.1 *N* sodium thiophenolate was allowed to proceed for two days and the product worked up as described above. There was obtained 4-*t*-butylcyclohexene (4.4 g., 32%) boiling at 55–57° (15 mm.), $n^{20}\mathrm{D}$ 1.4589 (after percolation through alumina to remove traces of sulfur compounds); lit.[11a] b.p. 65–66° (20 mm.), $n^{20}\mathrm{D}$ 1.4583; identical in infrared spectrum with an authentic sample[28]; and *trans*-4-*t*-butylcyclohexyl phenyl thioether (III, 10.5 g., 42%), b.p. 185–186° (14 mm.). The thioether contained some diphenyl disulfide, the bulk of which was removed by chromatography, yet the analysis showed some residual impurity.

Anal. Calcd. for $C_{16}H_{24}S$: C, 77.35; H, 9.74; S, 12.91. Found: C, 76.64; H, 9.43; S, 13.44.

The chromatographed thioether III was oxidized to the *trans*-sulfone V by means of 30% hydrogen peroxide-acetic anhydride-acetic acid.[29] The sulfone so obtained melted at 90–91° and was chromatographically homogeneous.

Anal. Calcd. for $C_{16}H_{24}O_2S$: C, 68.53; H, 8.63. Found: C, 68.37; H, 8.48.

***trans*-4-*t*-Butylcyclohexyl Tosylate.**—The reaction of II with sodium thiophenolate was carried out as described above for the *cis* isomer I, except that the reaction time was one month.[30] Distillation of the product gave no olefin but 14 g. (56%) of material boiling at 184–186° (13 mm.) which appeared to be mainly the desired thioether IV contaminated with some diphenyl disulfide which was removed by chromatography (recovery 10 g., 40%). The *cis*-thioether IV differed in infrared spectrum from the *trans* isomer III. Oxidation of IV as described above give *cis*-4-*t*-butylcyclohexyl phenyl sulfone (VI), chromatographically homogeneous, m.p. 115–116°, depressed to 57–81° by admixture of the isomer V.

Anal. Calcd. for $C_{16}H_{24}O_2S$: C, 68.53; H, 8.63. Found: C, 68.20; H, 8.53.

2-Octyl Tosylate.—The tosylate (42 g., 0.15 mole) was allowed to stand in a solution of 27 g. (0.2 mole) of sodium thiophenolate in 87% ethanol containing some excess thiophenol overnight. The product, worked up as described above, weighed 32 g. Distillation gave 1.4 g. of a forerun[31] boiling up to 105° (15 mm.) ($n^{20}\mathrm{D}$ 1.4272) and 28 g. (87%) of material boiling at 158.5–160° (15 mm.), $n^{20}\mathrm{D}$ 1.5220. considered as 2-octyl phenyl thioether (lit.[32] b.p. 178° (20 mm.)).

Anal. Calcd. for $C_{14}H_{22}S$: C, 75.60; H, 9.97. Found: C, 75.60; H, 9.93.

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(22) E_2 elimination data cited in ref. 11a would lead to a ΔF^0 value of −0.4 kcal./cal.—in much better agreement with the value (−0.7) found here. We suggest that the calculation of the conformational equilibrium constant *K* from solvolysis rates may be subject to error, since, because of the complexity of the reaction when considered in detail, the assumption that k_e and k_a for cyclohexyl tosylate are measured by the solvolysis rates of the corresponding *trans*- and *cis*-4-*t*-butyl compounds may be invalid.

(23) G. Stork and W. N. White, THIS JOURNAL, **78**, 4609 (1956).

(24) W. Hückel, O. Neunhoeffer, A. Gereke and E. Frank, *Ann.*, **477**, 143 (1929).

(25) V. C. Sekera and C. S. Marvel, THIS JOURNAL, **55**, 345 (1933).

(26) Attempts to obtain kinetic measurements for the 4-phenylcyclohexyl tosylates were frustrated by lack of solubility of the compounds in 87% ethanol.

(27) H. E. Ungnade, *J. Org. Chem.*, **13**, 361 (1948).

(28) Kindly provided by Prof. Saul Winstein.

(29) D. Swern, *Chem. Revs.*, **45**, 33, 35 (1949).

(30) The reaction vessel was sealed to avoid oxidation and placed in the dark. Attempts to carry out the reaction at reflux led to considerable olefin formation, presumably by an E_1 mechanism.

(31) This material, according to infrared spectrum, contained olefin. If it were all an octene, the yield would be 6%; however, this is unlikely in view of the boiling point and refractive index (*trans*-2-octene boils at 123° (750 mm.) and has $n^{20}\mathrm{D}$ 1.4128).

(32) J. Kenyon, H. Phillips and V. P. Pittman, *J. Chem. Soc.*, 1072 (1935).

Epimerization of *cis*-4-*t*-Butylcyclohexyl Phenyl Sulfone.—The sulfone VI (350 mg.) was boiled for 61 hr. with 20 ml. of 10% ethanolic sodium ethoxide. The solution was poured into water and extracted with ether which, after drying and concentration, left a residue melting at 84–87°. One recrystallization from 95% ethanol raised the melting point to 90–91°, undepressed by admixture with the *trans*-sulfone V but depressed to 80–90° by admixture of the starting *cis*-sulfone VI. Similar treatment of the *trans*-sulfone with sodium ethoxide only lowered the melting point to 86–89°, not depressed by admixture of pure *trans*-sulfone but depressed to 79–89° by admixture of *cis*-sulfone. In both cases the crude recovered sulfone was identical in infrared spectrum with the pure *trans* isomer V and different from the *cis*-isomer VI.

Kinetic Measurements.—Thiophenol was freshly distilled material. Ethanol was diluted with water to a density d^{20}_4 of 0.8258 ± 0.0015 corresponding to 87 ± 0.5% ethanol. Sodium thiophenolate solutions were prepared by dissolving clean sodium (*ca.* 0.69 g.) in 87% ethanol (*ca.* 150 ml.). filtering the solution, titrating it against standard acid and adding thiophenol in 5–10% excess over the calculated amount. Total base and thiophenol were titrated, respectively, by adding a measured volume of the thiophenolate solution to excess standard hydrochloric acid and back-titrating with base using methyl orange as an indicator and by adding a measured volume of the solution to excess glacial acetic acid and titrating with standard iodine solution.

The butyl tosylates were weighed, dissolved in 87% ethanol in a volumetric flask, placed in the thermostat at 25.1° (fluctuation less than 0.1°), and to an aliquot (pipetted into the reaction vessel) was added the required amount of thiophenolate solution at the same temperature by means of a pipet. Zero time was taken when half the thiophenolate solution had been delivered. The zero titer was calculated from the known concentrations. In the case of the slower-reacting cyclohexyl tosylates the weighed solid was placed in the reaction vessel, and solvent was added by means of a pipet, followed by similar addition of thiophenolate after temperature equilibrium had been reached. The zero titer was determined by immediate quenching of an aliquot and agreed well with the approximate titer calculated from the known amounts of reagents neglecting the volume of solid weighed out. For each kinetic run six or more well-spaced points were obtained and at each point two titrations (acidimetric and iodimetric) were carried out within one minute of each other. Most reactions were followed to 50–60% completion, except for the very slow runs which were followed to only 25% completion. In the fast reactions the infinity titer was occasionally checked and found to agree with the calculated. A typical run is shown in Table II.

Controls.—Solvolysis of all the tosylates used in this investigation in 87% ethanol in the absence of added base was checked and found to be responsible for less than 2% of the total reaction, except in the case of 2-butyl tosylate where it amounted to about 3%. In view of this, solvolysis was neglected in the calculation of the rate constants, a procedure which seems to be further justified by the absence of deviation from second-order kinetics.

Addition of thiophenol to olefin under the conditions of the kinetic experiment was checked by mixing cyclohexene, sodium thiophenolate and free thiophenol in 87% ethanol at the approximate concentrations of the kinetic runs. After 24 hr. no thiophenol had been consumed and no thioether was found to be present in the reaction mixture.

Since the specific rate for the reaction of *n*-butyl bromide with thiophenolate in 87% ethanol determined in preliminary experiments (17.5 × 10^{-3} l.mole^{-1}sec.$^{-1}$) was in apparent disagreement with the value found by Hine and Brader[33] (4.2 × 10^{-3} interpolated from measurements at temperatures other than 25°) in absolute methanol, the rate in absolute methanol was checked and found it to be 4.36 × 10^{-3} l.mole^{-1}sec.$^{-1}$ in good agreement with the literature value.[33] This experiment points up the considerable increase in rate observed on addition of water to the alcohol solvent.

TABLE II

REACTION OF 0.09795 *M* CYCLOHEXYL TOSYLATE WITH 0.1901 *M* SODIUM THIOPHENOLATE IN 87% ETHANOL AT 25.1°

Time, min.	Base,[a] ml.	[Na-SC_6H_5][b]	Iodine,[c] ml.	[Na-SC_6H_5[d] + C_6H_5SH]	10^3k_T[e]	k_S/k_E[f]
0	4.50	0.1901	21.40	0.2084	...	..
60	5.05	.1793	20.80	.2025	10.58	1.20
120	5.50	.1701	20.35	.1981	10.58	1.06
181	5.95	.1611	19.93	.1939	11.13	1.00
240	6.35	.1535	19.57	.1905	11.48	0.96
300	6.62	.1479	19.20	.1869	11.31	1.03
360	6.82	.1438	18.93	.1843	10.88	1.09
				Mean	10.99 ± 0.32	1.06 ± 0.06

[a] Ml. of 0.09980 *N* base required to back-titrate 15 ml. of 0.09336 *N* hydrochloric acid after quenching of 5-ml. aliquot of reaction mixture. [b] Sodium thiophenolate concentration in solution at time indicated calculated from previous column. These values represent $b - x$. [c] Ml. of 0.04867 *N* iodine (in aqueous KI) required to titrate solution of 5-ml. aliquot quenched in *ca.* 10 ml. of glacial acetic acid. [d] Total thiophenol concentration in solution at time indicated calculated from previous column. [e] Calculated from $k = \frac{2.303}{t(a - b)} \log \frac{b(a - x)}{a(b - x)}$ where $a = 0.9795$, $b = 0.1901$ and $x = 0.1901$ minus value in column 3 at time t. [f] This is measured by amount of substitution product at time t divided by amount of elimination product formed at time t or 0.2084 minus value in column 5 at time t divided by 0.1901 minus value in column 3 at time t (this is measure of total reaction product) diminished by the number in the numerator. *E.g.*, at 60 min. the value is [0.2084 − 0.2025]/[(0.1901 − 0.1793) − (0.2084 − 0.2025)].

TABLE III

REACTION OF TOSYLATES WITH SODIUM THIOPHENOLATE IN 87% ETHANOL AT 25°

Tosylate	[ROTs]	[C_6H_5SNa]	10^5k_T, l. mole^{-1} sec.$^{-1}$	k_S/k_E
Cyclohexyl	0.1502	0.2081	18.95 ± 0.27	[a]
	.09932	.09969	18.58 ± .50	[a]
	.09892	.1970	18.63 ± .49	[a]
	.1609	.09149	18.23 ± .50	1.45 ± 0.15
	.09795	.1901	18.32 ± .53	1.06 ± .06
	.1984	.08869	17.15 ± .10	1.18 ± .06
	.0980	.1891	18.63 ± .30	1.17 ± .10
cis-4-*t*-Butyl-cyclohexyl	.09994	.09696	70.57 ± 0.67	0.98 ± 0.10
	.06664	.06333	71.23 ± 0.87	1.15 ± .16
	.04440	.1227	71.05 ± 1.30	1.07 ± .07
	.04355	.1248	69.91 ± 2.50	1.06 ± .07
trans-4-*t*-Butyl-cyclohexyl	.04234	.07038	2.016 ± 0.116	Large
	.04353	.1239	1.883 ± .067	Large
	.06456	.1834	1.950 ± .083	Large
	.06676	.2245	1.950 ± .050	Large
cis-4-Methyl-cyclohexyl	.10006	.09766	43.32 ± 1.20	[a]
	.1005	.1786	43.88 ± 1.40	0.55 ± 0.03
	.09358	.2697	42.85 ± 1.23	.68 ± .03
	.07455	.1485	50.87 ± 0.70	.57 ± .03
	.09709	.09043	48.50 ± 1.35	[a]
	.07767	.1457	47.82 ± 0.50	0.79 ± 0.04
trans-4-Methyl-cyclohexyl	0.8639	.1808	2.550 ± 0.016	Large
	.08085	.09830	2.600 ± .050	Large
	.07457	.1849	2.567 ± .050	Large
	.07831	.1841	2.600 ± .033	Large
cis-3-Methyl cyclohexyl	.09908	.06191	2.388 ± .070	Large
	.06795	.12603	2.422 ± .071	Large
trans-3-Methyl-cyclohexyl	.08409	.1489	59.52 ± 0.10	1.24[b]
	.11181	.07130	58.48 ± .11	1.16[b]
	.08012	.15329	59.90 ± .02	1.20[b]
2-Butyl	.11	.05282	160.6 ± 3.2	Large
	.0550	.1056	150.3 ± 10.5	Large
1-Butyl	.03603	.1037	841.1 ± 5.8	Large
	.06903	.1122	847.2 ± 5.7	Large
	.03603	.02074	830.8 ± 19.4	Large

[a] Not determined—acidimetric titration only carried out. [b] Average of two values only.

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(33) J. Hine and W. H. Brader, THIS JOURNAL, **75**, 3964 (1953).

Because of upward drifts in k_S/k_E during some of the early runs which were apparently caused by oxidation, reaction vessels were purged with a slow stream of nitrogen during the removal of aliquots for titration. Even so, some drift in k_S/k_E persisted in the slow runs. In these cases, the value of the ratio obtained early in the titration was considered more significant and is reported in Table III.

Table III summarizes all the measurements carried out in this work. Table I contains average values calculated from Table III.

Acknowledgment.—This work was supported by a fellowship grant from The Texas Co. for which we are grateful.

NOTRE DAME, INDIANA

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

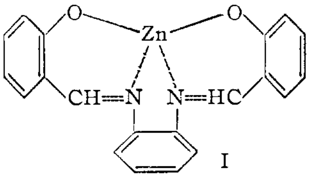
Heat Stability Studies on Chelates from Schiff Bases of Salicylaldehyde Derivatives[1]

BY C. S. MARVEL AND N. TARKÖY

RECEIVED JUNE 12, 1957

5,5'-Methylene-bis-salicylaldehyde has been prepared and converted to a polymeric Schiff base with a molecular weight of about 10,000 by heating with *o*-phenylenediamine. The metal chelates of this polymeric material are less heat stable than are the corresponding compounds prepared from salicylaldehyde itself. Some other effects of substitution on heat stability in this series have been noted.

The zinc chelate (I) of the condensation product of salicylaldehyde and *o*-phenylenediamine showed promising stability at 250°.[2] We have now prepared a related polymeric chelate. The monomeric dialdehyde II was obtained in 48% yield by treating salicylaldehyde with trioxane and sulfuric acid in acetic acid solution, a procedure that is analogous to that used by Smith[3] for the preparation of the corresponding diacid from salicylic acid.



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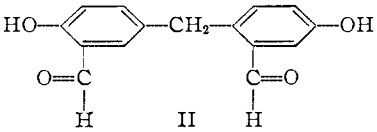


II

The yield of the dialdehyde is related to the amount of sulfuric acid catalyst used (see Table I) and this relationship can be rationalized on the assumption that the salicylaldehyde to formaldehyde ratio must be very high in order that the dialdehyde be formed rather than a polymeric product. It has been shown[4] that the rate of acid-catalyzed depolymerization of trioxane to formaldehyde bears a close correlation to the acid concentration of the reaction medium. Thus a low acid concentration helps keep the ratio of salicylaldehyde to formaldehyde favorable for the preparation of the dialdehyde.

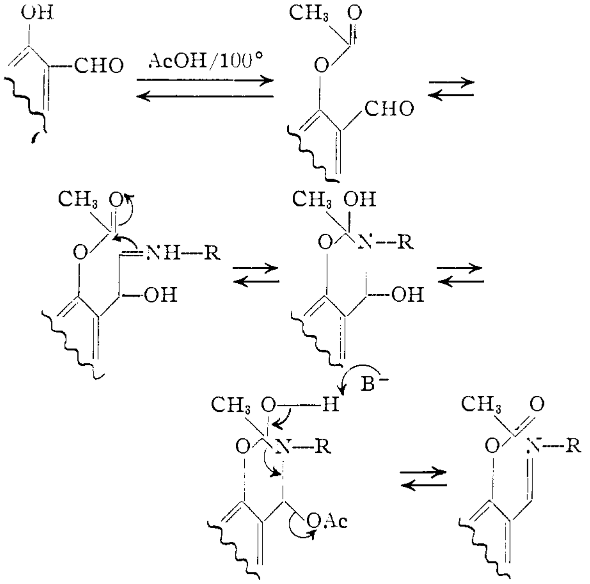
TABLE I

EFFECT OF ACID CONCENTRATION ON THE FORMATION OF DIALDEHYDE II

Temp. of reacn., °C.	Mole H_2SO_4 per l. CH_3CO_2H	Yield of dialdehyde, %
20	0.15	0
115	.3	18
105–110	.15	41.5
90–95	.07	42.8

The dialdehyde II was converted to a polymeric Schiff base by heating it with *o*-phenylenediamine in tetrahydrofuran solution. This gave a 65% yield of a yellow product (III) which had an inherent viscosity of 0.05 (concn. 1 g./100 ml.) in tetrahydrofuran. Attempts to determine the molecular weight of this polymer by the boiling point elevation method of Menzies and Wright[5] and by the Rast method[6] showed that the molecular weight was too great to be within the scope of either. The polymer shows weak absorption at 1652 cm.$^{-1}$ (in Nujol) in the infrared which indicates that there are aldehyde end groups.

The same polymer was obtained in 88% yield in less than a minute at water-bath temperature when acetic acid was used as the solvent. This marked catalysis by acetic acid may be due to some such sequence of reaction as



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(1) This work was performed under contract number AF-33(616)-3772 with the Materials Laboratory of Wright Air Development Center, Wright-Patterson Air Force Base, Ohio; Lt. L. E. Coleman, project engineer.

(2) C. S. Marvel, S. A. Aspey and E. A. Dudley, THIS JOURNAL, **78**, 4905 (1956).

(3) W. H. Smith, E. E. Sager and I. J. Siewers, *Anal. Chem.*, **21**, 133 (1949).

(4) R. P. Bell, K. N. Bascombe and J. C. M. Coutrey, *J. Chem. Soc.*, 1286 (1956).

(5) A. W. C. Menzies and S. L. Wright, Jr., THIS JOURNAL, **43**, 2315 (1921).

(6) K. Rast, *Ber.*, **55**, 1051, 3727 (1922).