Kinetics of Reactions of Piperidine with Nitrophenyl Esters of *p*-Toluenesulfonic and Mesitylenesulfonic Acids. The Miserable Effect of *ortho*-Methyl Groups[1]

J. F. BUNNETT[2] AND J. Y. BASSETT, JR.[3]

Venable Chemical Laboratory, University of North Carolina, Chapel Hill, North Carolina

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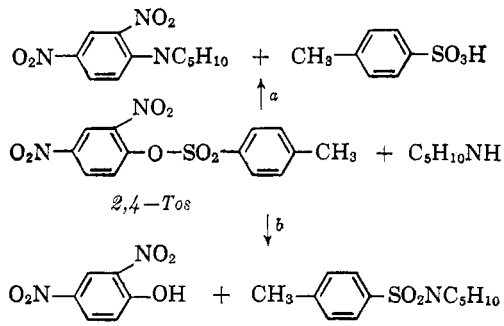
These esters are cleaved by piperidine with scission of both S—O and C—O bonds. Rates of S—O scission are decreased only four- to eightfold by introduction of two methyl groups *ortho* to sulfur. All of this modest change can be attributed to the electronic influence of the methyl groups. *The two ortho methyls provide no detectable steric hindrance of nucleophilic substitution at sulfonate sulfur.* Both C—O and S—O scission are some 2.5-fold faster with *ortho*-nitrophenyl esters than with their *para* isomers.

We have shown[4] that 2,4-dinitrophenyl *p*-toluenesulfonate (*2,4-Tos*) is cleaved by piperidine in two senses. The C—O bond may be severed (route *a*) or S—O scission may occur (route *b*). Route *a*



is somewhat preferred; in 60% dioxane–40% water, 67% of cleavage occurs with C—O scission. it was similarly observed that two methyl groups *ortho* to sulfur did not greatly diminish the fraction of S—O scission. These results indicated that *ortho*-methyl groups only slightly retarded nucleophilic attack on sulfonate sulfur. This was a striking result in view of the enormous hindrance which two *ortho* methyl groups provide to nucleophilic attack on the carbonyl carbon in benzoic esters.[5]

We now report a direct kinetic study of these reactions. Table I summarizes our results concerning piperidine cleavage of *2,4-Tos* and *2,4-Mes* in methanol solution; the data for the former compound stem from an earlier study.[6]

The fact that addition of piperidine hydrochloride (the last two runs) had no significant effect on either the over-all rate or the ratio of C—O to S—O scission shows that salt effects are minor and that

TABLE I

REACTIONS OF PIPERIDINE WITH 2,4-DINITROPHENYL *p*-TOLUENE- AND MESITYLENESULFONATES IN METHANOL AT 0°[a]

Substrate	$[C_5H_{10}NH]_0$, *M*	10^3k_ψ,[b] sec.$^{-1}$	10^3k_{tot},[c] l. mole^{-1} sec.$^{-1}$	%, C—O scission	10^3k_C,[c] l. mole^{-1} sec.$^{-1}$	10^3k_S,[c] l. mole^{-1} sec.$^{-1}$
2,4-Tos[d]	0.0406	3.33	8.10	55	4.46	3.64
2,4-Mes	.0195	1.04	5.34	81.4	4.34	1.00
	.0203	1.09	5.37	81.4	4.37	1.00
	.0406	2.36	5.81	81.0	4.70	1.11
	.0400[e]	2.32	5.80	83.5	4.84	0.96
	.0800[e]	4.98	6.22	83.5	5.20	1.02

[a] Photometric analysis; substrate 0.001 *M* throughout. [b] k_ψ is total pseudo-first-order rate coefficient for all reactions consuming substrate. [c] k_{tot}, k_C, and k_S are, respectively, second-order rate coefficients for the sum of C—O and S—O scission, and for C—O and S—O scission separately. [d] Data from ref. 6. [e] Piperidine hydrochloride, in half the concentration of $C_5H_{10}NH$, was also present.

We also observed that introduction of two methyl groups *ortho* to sulfur had only a modest effect on the ratio of C—O to S—O scission. In 60% dioxane, piperidine cleaved 2,4-dinitrophenyl mesitylenesulfonate (*2,4-Mes*) with *ca.* 85% rupture of the C—O bond. In the piperidine cleavage of *o*- and *p*-nitrophenyl toluene- and mesitylene-sulfonates (*2-Tos*, *4-Tos*, *2-Mes*, and *4-Mes*, respectively), methoxide ion plays no role, either as a competing nucleophile[6] or as a basic catalyst. The fact that the second-order coefficients are substantially independent of piperidine concentration shows that the reaction is first order in piperidine. The slight rise in k_{tot} or k_C with increase in piperidine concentration is evidently another example of a general medium or polar molecule effect which has been

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(2) Brown University, Providence, Rhode Island.

(3) R. J. Reynolds Fellow, 1956–1957. This paper is based on the Ph.D. thesis of J. Y. Bassett, Jr., October, 1957.

(4) J. F. Bunnett and J. Y. Bassett, Jr., *J. Am. Chem. Soc.*, **81**, 2104 (1959).

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encountered in similar reactions and which does not appear to constitute base catalysis.[7]

Comparison of the k_C values for the two esters shows, as one might have anticipated, that introduction of methyl groups *ortho* to sulfur has virtually no effect on the rate of substitution at carbon. The k_S values indicate that the two methyl groups retard displacement at sulfur about fourfold.

The inference[4] that *ortho* methyl groups only slightly decelerate substitution at sulfonate sulfur is thus supported. However, since the interesting k_S values represent differences between numbers about five times larger, similar values of greater precision were desired.

Reaction of piperidine with phenyl *p*-toluenesulfonate was inconveniently slow, and so kinetics of piperidine cleavage of the *ortho* and *para* mononitrophenyl esters of the two sulfonic acids were studied. Ratios of C—O to S—O scission were determined by product isolation experiments,[4] and rates were followed by bromometric titration. Results are set forth in Table II.

TABLE II

REACTIONS OF PIPERIDINE WITH *o*- AND *p*-NITROPHENYL *p*-TOLUENE- AND MESITYLENESULFONATES IN 60% DIOXANE–40% WATER (V./V.) AT 46.0°

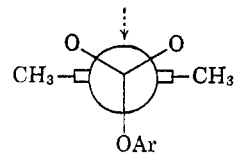
Substrate	$10^5 k_\psi$[c] sec.$^{-1}$	% S—O scission[d]	$10^5 k_S$,[e] M^{-1} sec.$^{-1}$	$10^5 k_C$,[e] M^{-1} sec.$^{-1}$
4-*Tos*[a]	19.0, 20.4	90	16.6	1.84
2-*Tos*[a]	41.6	88	36.2	4.9
4-*Mes*[b]	1.47, 1.46	58	2.10	1.52
2-*Mes*[a]	9.28, 9.42	62	5.71	3.50

[a] $[C_5H_{10}NH]_0$ = 1.013 *M*. [b] $[C_5H_{10}NH]_0$ = 0.405 *M*. [c] See footnote *b*, Table I. [d] From data in ref. 4. [e] See footnote *c*, Table I.

Again substitution at sulfur is but little affected by two *ortho* methyl groups. In the 2-nitro series, the deceleration is 6.3-fold and in the 4-nitro series, 7.9-fold. If the electronic effects of *ortho* methyls are represented by *para*-methyl sigma values, and if displacement at sulfur has a Hammett rho value[8] of about +2.5, the whole of the deceleration can be attributed to electronic effects of the methyl groups. For a similar reaction, saponification of phenyl esters of *m*- and *p*-substituted benzenesulfonic acids,[9] which is known to occur *via* displacement at sulfur,[10] rho is +2.3. Bearing in mind that other small factors, such as London interactions between piperidine and the *ortho*-methyl groups,[11] may have some influence on substitution rate, one cannot altogether exclude the possibility that the methyl groups exert some steric hindrance.

We can say, however, that *steric hindrance of nucleophilic attack on sultonate sulfur by ortho methyl groups is so small that it cannot be detected in the system studied.*

Molecular models indicate that I is the favored conformation for an aryl ester of mesitylenesulfonic acid. I shows a perspective view of the molecule along the axis of the S—C bond from the sulfur end.



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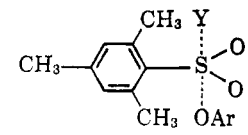

II

The horizontal bar represents the benzene ring, and the *ortho* methyl groups are shown. In this conformation the back side of the sulfur atom with respect to the cleavable S—O bond is wide open to attack by a nucleophile (along the line of the dashed arrow).

One does not know whether bimolecular nucleophilic substitution at sulfonate sulfur occurs concertedly, as at saturated carbon, or with discrete bond-making and (later) bond-breaking steps, as is the rule at unsaturated carbon.[12] If the former, the transition state geometry is perhaps that of a trigonal bipyramid, as in reactions of the familiar Walden inversion type. The C—S and the twin S—O bonds are imagined to lie in a plane, with the Y—S and S—OAr bonds linear and perpendicular thereto. If this plane is also that of the benzene ring, as in II, the distance from methyl carbon to nearest oxygen is 2.81 Å.[13] In conformation I of the ester before reaction, the corresponding distance is 2.85 Å.

Since both these values are less than the sum (3.4 Å.) of the van der Waals radii[14] of the methyl group and oxygen atom, a small increase in compressive strain might be expected to attend formation of the transition state.[15] The computed

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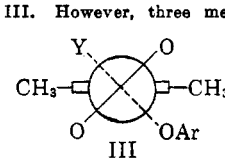
(11) J. F. Bunnett, *J. Am. Chem. Soc.*, **79**, 5969 (1957); J. D. Reinheimer and J. F. Bunnett, *ibid.*, **81**, 315 (1959).

(12) J. F. Bunnett, "Theoretical Organic Chemistry: Proceedings of the Kekulé Symposium," Butterworths, London, 1959, p. 144.

(13) Distance computations are based on the following bond length values: C_{methyl}—C_{Ar}, 1.52 Å.; C_{Ar}—C_{Ar}, 1.395 Å.; C_{Ar}—S, 1.84 Å; S—O, 1.42 Å. Trigonal (120°) angles were assumed at aromatic carbons and at sulfur in the transition state, and tetrahedral (109° 28′) at sulfur in the ester itself. These values are chosen from data in "Interatomic Distances," Spec. Pub. No. 11, The Chemical Society, London, 1958.

(14) J. A. A. Ketelaar, "Chemical Constitution," 2nd ed., Elsevier Publishing Co., Amsterdam, 1958, p. 201.

(15) The methyl carbon to oxygen distance is greater in transition state conformation III. However, three methyl-oxygen and one



III

methyl-Y interactions are now of first importance, compared to two primary methyl-oxygen interactions in II.

decrease in methyl-oxygen separation is small, however, and may be illusory. It is based on the assumption that the S—O bonds in the transition state are the same length as in the initial state and form an angle of 120°. If they become longer in the transition state and/or the O—S—O angle is slightly diminished, the computed decrease in methyl-oxygen separation disappears.

Thus may our inability to detect steric hindrance of nucleophilic attack on sulfur be rationalized.

The foregoing discussion in terms of a synchronous displacement mechanism constitutes no endorsement of that mechanism. Geometry approaching that of II is probable also for the transition state of either the first or second step of a two-step mechanism *via* an intermediate complex. Steric effects on the two mechanisms should be similar.

ortho-Methyl groups also slightly retard displacement at nitrophenyl carbon. k_C for the toluenesulfonates is higher by 1.4- and 1.2-fold in the *o*- and *p*-nitrophenyl series, respectively. The electronic effect of the methyl groups is presumed to be responsible.

ortho:para **Ratios.**—Data of Table II show that k_C and k_S are larger, in both the toluene- and mesitylenesulfonate series, for *ortho* nitro esters than for their *para* isomers. The margin of superiority of the *ortho* esters varies somewhat, but in all cases lies between 2.2 and 2.7.

ortho-Halonitrobenzenes are known to react with amines faster than their *para* isomers.[16] It has been proposed[16] that a favorable electrostatic or hydrogen-bonding interaction in the *ortho* transition states is responsible. Adjacent positively charged nitrogen (of the amine reagent) and negatively charged oxygen (of the *ortho* nitro group) are thought to interact so as to mutually satisfy needs which would otherwise have to be met by solvation. Solvation of the transition state is thereby reduced, and a more favorable entropy of activation is the consequence. This effect has been termed "built-in solvation."

One would expect the same effect to operate when a sulfonoxy group rather than a halogen atom was being displaced. That *ortho* k_C exceed *para* k_C is therefore intelligible.

It is unexpected, however, that *ortho* k_S are greater than *para* k_S by about the same margin. That built-in solvation through direct interaction of nitro oxygens with amine nitrogens is responsible seems unlikely because (a) these atoms are now in a 1,7-relationship, (b) the nitro oxygens are possibly less negative than in the transition state for substitution at carbon (depending on what mechanism prevails for substitution at sulfur), and (c) the London forces interpretation of reagent-dependence of the sense of cleavage of 2,4-dinitrophenyl *p*-toluenesulfonate implies that the reagent attacking sulfur does not closely approach the 2-nitro group. It is conceivable that the two poles may interact at longer range *via* hydrogen bonding with relay through an intervening water molecule. Utilization of one solvent molecule in this way may be entropically advantageous compared to the alternative of several molecules of solvation. Definitive evidence on this question would be welcome.

(16) J. F. Bunnett and R. J. Morath, *J. Am. Chem. Soc.*, **77**, 5051 (1955).

Experimental

Preparation of the esters and purification of solvents have been described.[4]

The kinetic experiments of Table I were performed as described by Bunnett, Garbisch, and Pruitt.[6]

Kinetic Experiments of Table II.—The substrate concentration was about 0.032 *M* except in runs with *4-Mes*, where it was about 0.014 *M*. A weighed quantity of substrate was placed in a 100-cc. volumetric flask (250 cc. in *4-Mes* runs), dissolved in *ca.* 80 cc. (or *ca.* 230 cc.) of 60% dioxane–40% water (v./v.), and placed in the thermostat at 45.98 ± 0.02°. A flask containing *ca.* 15 cc. of pure piperidine and another containing extra solvent were also allowed to come to thermostat temperature. Ten cubic centimeters of piperidine was pipetted into the volumetric flask which was then filled to the mark with solvent, shaken thoroughly, and replaced in the bath. Samples were taken with a 5-cc. pipet (10 cc. for *4-Mes*) and quenched in 50 cc. of 10% aqueous hydrochloric acid contained in a 125-cc. glass-stoppered flask. A standard brominating solution (potassium bromate plus excess potassium bromide in water) was added from a buret until a yellow color persisted. The flask was stoppered and shaken vigorously for 1 min., excess potassium iodide (in water) was added, and the iodine liberated was titrated with sodium thiosulfate and starch indicator. From the number of equivalents of bromine consumed, it was necessary to subtract the number consumed by a standard blank (piperidine and solvent, quenched in the usual way); the "blank" titre was on the order of 1% of the infinity titre.

TABLE III

REACTION OF 2-NITROPHENYL *p*-TOLUENESULFONATE (2-*Tos*) WITH PIPERIDINE AT 46.0°; A TYPICAL RUN[a]

Time (min.)	Milli-equiva-lents Br_2 used[b]	Meq. Br_2 used (corr.)	Conc. cleavage products, *M*	[2-*Tos*], *M*	3 + log [2-*Tos*][c]
1.3	0.028	0.032	[0.0016	0.0307	1.487
3.0	.057	.064	.0032	.0291	1.464
6.0	.100	.113	.0057	.0266	1.425
10.0	.145	.165	.0082	.0241	1.382
15.0	.186	.212	.0106	.0217	1.336
21.0	.213	.242	.0121	.0202	1.306
27.0	.256	.291	.0146	.0177	1.248
34.0	.328	.373	.0186	.0137	1.137
41.0	.358	.407	.0204	.0119	1.076
48.0	.375	.426	.0213	.0110	1.042
56.1	.436	.496	.0248	.0075	0.875
64.0	.469	.533	.0266	.0057	.756
∞	.563				
∞	.571	.645	.0322		
∞	.566				

[a] Initial concentrations: [2-*Tos*]$_0$ = 0.0323; [$C_5H_{10}NH$]$_0$ = 1.013 *M*. [b] After subtraction of the blank titre of 0.006 meq. [c] The slope was 1.09×10^{-2}, and k_ψ 2.50×10^{-2} min.$^{-1}$ or 4.16×10^{-4} sec.$^{-1}$.

From titration of standard samples of *o*- and *p*-nitrophenol and *o*- and *p*-nitrophenylpiperidine it was discovered that only *p*-nitrophenol consumes the expected four equivalents per mole under the conditions of bromination used. The other three products consumed fewer equivalents, as follows: *o*-nitrophenol, 3.6; *p*-nitrophenylpiperidine, 3.1; *o*-nitrophenylpiperidine, 2.9. It was therefore necessary to apply a correction factor to each titer, taking into account also the ratios in which the two types of product are formed from each substrate. The correction factors used were: *4-Tos*, 4.0/3.9; *2-Tos*, 4.0/3.52; *4-Mes*, 4.0/3.62; *2-Mes*, 4.0/3.33.

Use of these correction factors did not much affect the values of rate coefficients. "Corrected" coefficients were mostly about 10% higher than those computed without use of the correction. The greatest increase (about 25%) was with *2-Mes*. The values in Table II are all "corrected."

A pseudo-first-order rate coefficient was reckoned (graphically) for each run, and converted to a second-order coefficient by dividing by the piperidine concentration. The latter was multiplied by the experimentally determined fractions of C—O and S—O scission to give, respectively, k_C and k_S.

It was determined that the substrates are not brominated under the conditions of the analysis.

Data for a typical run are given in Table III.

Deamination of 1,2,2-Tri(*p*-anisyl)ethylamine-1-C^{14}

WILLIAM A. BONNER AND THOMAS A. PUTKEY[1]

Department of Chemistry, Stanford University, Stanford, California

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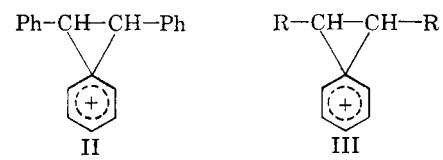
1,2,2-Tri(*p*-anisyl)ethylamine-1-C^{14} (VI, 2.592 mc./mole) was subjected to deamination with nitrous acid, producing 1,2,2-tri(*p*-anisyl)ethanol-1,2-C^{14} (X). Oxidation of the latter to the corresponding ketone, followed by cleavage with alkali afforded di(*p*-anisyl)methane (0.432 mc./mole) and *p*-anisic acid (2.083 mc./mole). These results, indicating a *p*-anisyl migration of only 17% during the deamination, contrast sharply to the 26–28% phenyl migration noted during similar deamination of 1,2,2-triphenylethylamine-1-C^{14}. A rationalization of this observation is offered, involving the suggestion that the cationic charge distribution at the migration terminus is important in determining relative migratory tendencies in 1,2-shifts.

In recent years we have studied solvolytic[2] and deamination[3] reactions in the 1,2,2-triphenylethyl system by both radiochemical[2,3] and stereochemical[4] techniques, with the purpose of gaining information as to the type of cationic intermediate (open, classical *vs.* nonclassical, bridged) through which such reactions proceed. All our data, both radiochemical and stereochemical, could be qualitatively and quantitatively interpreted in terms of equilibrating, classical 1,2,2-triphenylethyl carbonium ion intermediates such as I, with bridged phenonium structures such as II being specifically excluded. These conclusions contrasted sharply to those reached by Cram and co-workers[5] in their studies of solvolytic reactions in the 3-phenyl-2-butyl and similar systems and to related deamination reactions,[6,7] wherein convincing evidence was presented for the intervention (partial or complete) of nonclassical phenonium ion intermediates such as III. One possible reason

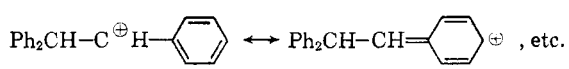
$$Ph_2C_\beta H-C_\alpha^{\oplus}HPh \rightleftarrows PhC_\beta^{\oplus}H-C_\alpha HPh_2$$

I

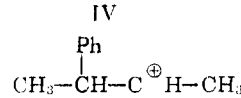


II III

for such mechanistic differences arises from the fact that the open 1,2,2-triphenylethyl carbonium ion may be resonance stabilized as a hybrid (IV) of lower energy than the corresponding bridged ion II. The 3-phenyl-2-butyl carbonium ion (V), on

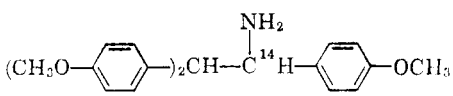


IV



V

the other hand, has no such effective means of stabilization and presumably is therefore a higher energy species than the corresponding bridged ion III (R = CH_3). In the hope of gaining further insight into questions such as these we have now



VI

(1) The authors are indebted to the National Science Foundation (NSF-G9479) for its generous support of this investigation.

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(3) W. A. Bonner and C. J. Collins, *ibid.*, **78**, 5587 (1956).

(4) C. J. Collins, W. A. Bonner, and C. T. Lester, *ibid.*, **81**, 466 (1959); C. J. Collins, J. B. Christie, and V. F. Raaen, *ibid.*, **83**, 4267 (1961).

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