Studies in Stereochemistry. XXXIX. Phenonium *vs.* Open Ions in Solvolyses of 3-Phenyl-2-butyl Tosylate and Its *p*-Nitro Derivative[1,2]

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Abstract: The solvolytic behavior of the optically active stereomers of 3-phenyl-2-butyl tosylate (I-OTs) and those of the *p*-nitro derivative (II-OTs) are compared and found to be dramatically different. The nitro group is far removed from the reaction site, and depresses the tendency of phenyl to act as a neighboring group without interfering at all sterically, and only in a minor way electronically with the ability of solvent to participate in ionization. The acid phthalates of the optically active diastereomers of I-OH were nitrated to produce the diastereomers of II-OH, whose tosylates were subjected to acetolysis, formolysis, and trifluoroacetolysis. Acetolysis at 100° of optically pure L-*threo*-II-OTs gave a 13% yield of secondary acetate (7% *threo* and 93% *erythro*) and 68% olefin. Hydrolysis of the acetate and oxidation of the derived alcohol gave ketone 4 ± 2% racemized. Formolysis at 50° of L-*threo*-II-OTs gave an 11% yield of secondary formate (30% *threo* and 70% *erythro*) and a 72% yield of olefin. Ketone derived from the formate was 25 ± 2% racemized. Trifluoroacetolysis of racemic *threo*-II-OTs at 72° gave a 9% yield of trifluoroacetate (95% *threo* and 5% *erythro*) and a 57% yield of olefin. In acetolysis at 100°, 94% optically pure L-*erythro*-II-OTs gave a 9% yield of secondary acetate (10% *erythro*, 90% *threo*) and 57% olefin. The derived ketone was not detectably racemized. In formolysis at 50°, the same tosylate gave a 9% yield of secondary formate (37% *erythro*, 63% *threo*) and 59% olefin. The derived ketone was not detectably racemized. Trifluoroacetolysis of racemic *erythro*-II-OTs gave a 10% yield of secondary ester (28% *threo*, 72% *erythro*) and 69% olefin. In all product runs sufficient salt of the solvent was present to neutralize the *p*-toluenesulfonic acid generated. The effect of the nitro group on the stereochemical course of these reactions is best visualized through comparison of values for I-OTs and II-OTs of k_r/k_i, the rate constant for the ionization processes leading to *tosylate* or *carboxylate* esters of *retained* configuration over the rate constant of ionization processes leading to similar products of inverted configuration. In acetolysis, k_r/k_i = 105, 0.078, 101, and 0.11 for *threo*-*p*-H, *threo*-*p*-NO_2, *erythro*-*p*-H, and *erythro*-*p*-NO_2, respectively. In formolysis, k_r/k_i values for the same four compounds are 10^4, 0.43, . . ., and 0.59, respectively. In trifluoroacetolysis, minimum values of k_r/k_i were 19 for *threo*-*p*-NO_2 and 2.6 for *erythro*-*p*-NO_2. The rates of appearance of *p*-toluenesulfonic acid (rate constant, k_t) and of racemization (rate constant, k_α) of the *threo* isomers were measured in the three solvents, and the rates of racemization (ionization) for the *p*-H and *p*-NO_2 compounds were compared through the following ratios: $(k_\alpha^H/k_\alpha^{NO_2})^{50°}_{AcOH}$ = 190; $(k_\alpha^H/k_\alpha^{NO_2})^{25°}_{HCO_2H}$ = 560; $(k_\alpha^H/k_\alpha^{NO_2})^{0.7°}_{CF_3CO_2H}$ = 36,000. These results demonstrate unequivocally that *aryl and solvent are in competition with one another in nucleophilically assisting ionization at the back face of the incipient carbonium ion.* The kinetic results demonstrate that phenyl assists ionization more than *p*-nitrophenyl by factors of 190, 560, and 36,000 in passing from acetic to formic to trifluoroacetic acids. This order is expected on the basis that C_6H_5 > *p*-$NO_2C_6H_4$ and CH_3CO_2H > HCO_2H > F_3CCO_2H in nucleophilicity. The stereochemical results clearly demonstrate that phenonium ions are the principal intermediates in the trifluoroacetic acid with both *p*-H and *p*-NO_2 compounds, and in formic and acetic acids with the *p*-H system. In acetic acid, open ions dominate with the *p*-NO_2 compound, and in formic acid with the same compound, open and bridged ions are of almost equal importance. The new results fully support the phenonium ion thesis put forward in 1949 to account for the stereochemical results of acetolysis of the 3-phenyl-2-butyl tosylates.

The phenonium ion was first proposed[3a,b] as a discrete intermediate to explain the stereochemical course of acetolysis of the stereomers in the 3-phenyl-2-butyl tosylate system (I-OTs). This bridged ion was later named,[3c] and solvolytic studies were extended to formic acid[3c] and supplemented by kinetic comparisons between this and model systems.[3c,4a] Substitution of the *p*-hydrogen in I-OTs with methoxyl was found to potentiate the ability of aryl to participate in ionization, and thereby even more stringently control the stereochemical outcome of the solvolytic reactions.[4b,c] In a study of the deamination of the optically pure diastereomers of 3-phenyl-2-butylamine in acetic acid,[3g] the product distribution was found to be entirely different than in the tosylate acetolysis, and correlated not with neighboring group or solvent participation in breaking the C–N bond, but with the expected conformational populations of the ground state. Thus, "hot" open carbonium ions were the first intermediates, whose fates depended on their nearest neighbors (solvent or β substituents).

Study of the products and stereochemistry of sol-

(1) This research was sponsored by the U. S. Army Research Office, Durham, N. C. The authors express their thanks.

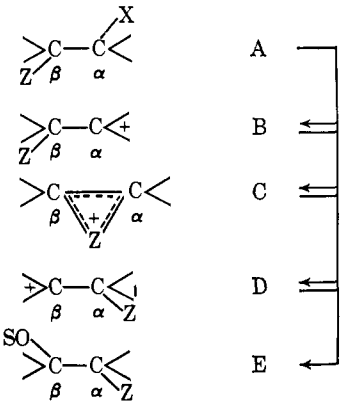
(2) Some of the results of this paper were published as a communication: D. J. Cram and J. A. Thompson, *J. Am. Chem. Soc.*, **89**, 6766 (1967).

(3) (a) D. J. Cram, *ibid.*, **71**, 3863 (1949); (b) D. J. Cram, *ibid.*, **71**, 3875 (1949); (c) D. J. Cram, *ibid.*, **74**, 2129 (1952); (d) D. J. Cram and F. A. Abd Elhafez, *ibid.*, **75**, 3189 (1953); (e) D. J. Cram, H. L. Nyquist, and F. A. Abd Elhafez, *ibid.*, **79**, 2876 (1957); (f) D. J. Cram, *ibid.*, **86**, 3769 (1964); (g) D. J. Cram and J. E. McCarty, *ibid.*, **79**, 2866 (1957).

(4) (a) S. Winstein, B. K. Morse, E. Grunwald, K. C. Schrieber, and J. Corse, *ibid.*, **74**, 1113 (1952); (b) S. Winstein and R. Baker, *ibid.*, **86**, 2071 (1964); (c) S. Winstein and G. C. Robinson, *ibid.*, **80**, 169 (1958); (d) S. Winstein and K. Schrieber, *ibid.*, **74**, 2165 (1952); (e) S. Winstein, M. Brown, K. C. Schrieber, and A. H. Schlesinger, *ibid.*, 74, 1140 (1952).

volytic reactions of a large number of β-arylethyl esters in which the substituents at C_α and C_β were varied led to the conclusion[5] that open and bridged phenonium ions compete with one another, and a generalized mechanism (see Chart I) was developed. With respect

Chart I



to this scheme, the following summarizing statements were made.[5] "These examples indicate that open ions B and D intervene in reaction sequences when they can be either ordinary tertiary or secondary benzyl carbonium ions. When B and D are ordinary secondary carbonium ions, their intervention in the Wagner–Meerwein sequence appears to depend on the particular system and on its environment.... The occurrence of a C stage (a bridged ion intermediate) has been demonstrated only for systems in which the migrating group is aryl or a methylene that is part of a bicyclic system.

The use of the kinetic technique has proven useful in gaining evidence for the absence of the B stage in rearrangements not amenable to stereochemical scrutiny, as well as for obtaining quantitative data regarding the tendency for migration to occur as a function of substituents at C_α and C_β."

The possibility that two unsymmetrical phenonium ions might be substituted for a single symmetrical phenonium ion in the 3-phenyl-2-butyl tosylate system and its homologs was discussed in detail,[3d,e] but the final conclusion reached was:[3e] "No evidence now exists which either suggests or demands the substitution of a dynamic equilibrium between unsymmetrical bridged carbonium ions for a single symmetrical bridged carbonium ion in systems where C_α and C_β carry the same substituents. Bridged ions such as C can provide a simpler and therefore better explanation of the facts until new evidence intrudes."

The interpretation of the stereochemical and kinetic results of tosylate solvolysis in the 3-phenyl-2-butyl system in terms of a phenonium ion has been challenged repeatedly by Brown,[6] who has chosen to interpret both the stereochemical and kinetic data in terms of equilibrating open ions with special conformational and steric properties. This alternative was discussed on many occasions by Winstein and the senior author in the early 1950's, and both of us concluded that the acetolysis and formolysis data on the 3-phenyl-2-butyl tosylate system were uniquely explained on the basis of a phenonium ion.[7]

Solvolyses rates of I-OTs isomers and 2-butyl tosylate are close to one another.[4a] Without taking into consideration the inductive effect of the phenyl, the fact that I-OTs ionizes faster than it solvolyzes, or the difference between steric inhibition of solvation of the transition states of the two systems, Brown, *et al.*,[6b] questioned that phenyl-assisted ionization in acetolysis of I-OTs on the basis of the above near equality of rates. These authors explained the high retention of configuration observed for I-OTs solvolysis on the basis of elaborate and unprecedented assumptions concerning nonbenzylic secondary carbonium ion behavior.[6b] In a later article, Brown, *et al.*,[6c] refer to Collins, *et al.*,[8] who are alleged to show consistency between the product ratios and "reasonable values for phenyl migration, rotational isomerization, and capture of the ions by solvent for open ions generated in acetolysis of the diastereomeric 3-phenyl-2-butyl tosylates." These authors' *mathematical model*[8] suffers from the facts that only half of the total number of ionic conformations were treated, ionization was assumed to occur exclusively from only one of three possible conformations for the starting material, and the product ratios generated were directly dependent on rate constant ratios that were assumed, not measured. Rather than describing reality, the model that emerges from these calculations reflects more the disregard of important conformations for both the starting tosylates and the presumed intermediate secondary ions.

(5) D. J. Cram in 'Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley & Sons, Inc., New York, N. Y., 1956, pp 259–261, and references quoted therein.

(6) (a) H. C. Brown, "The Transition State," Special Publication No. 16, The Chemical Society, London, 1962, p 140; (b) H. C. Brown, K. J. Morgan, and F. J. Chloupek, *J. Am. Chem. Soc.*, **87**, 2137 (1965); (c) H. C. Brown and C. J. Kim, *ibid.*, **90**, 2082 (1968).

(7) This historical statement is included to correct that of Brown in ref 6c, who correctly attributes the equilibrating open ion concept to Winstein [S. Winstein, *Bull. Soc. Chim. France*, **18**, C 55 (1951), and S. Winstein and E. Grunwald, *J. Am. Chem. Soc.*, **70**, 828 (1948)], but who incorrectly states that "Cram has taken a position which appears to be in opposition to that expressed by Winstein." In actual fact, the possibility of substituting two equilibrating open ions for a bridged ion to explain stereochemical results was never suggested as applying to the 3-phenyl-2-butyl tosylate acetolysis, but was mentioned as a possibility in entirely different contexts.

A second Brown claim requires correction. He states, "Cram's present position also appears to be in conflict with his earlier position taken to account for his observations in the deaminative acetolysis of 3-phenyl-2-butylamines.[3g] In that study he proposed that a "hot" unbridged 3-phenyl-2-butyl cation could undergo both rapid migration of the neighboring group and rapid substitution, faster than the rate of rotation about the central carbon–carbon bond, resulting in retention. On the other hand, it is his belief that the "cold" 3-phenyl-2-butyl cation, produced in the solvolysis of the tosylate, must be bridged to achieve substitution with retention." The facts are as follows. Deamination of the *threo* amine gave secondary acetate with a *threo/erythro* ratio of 1.3, in contrast to the tosylate acetolysis that gave a ratio of 24. If the stereospecific "internal return" component is also included, a *threo/erythro* ratio of 105 was observed for tosylate + acetate produced on ionization of the system in acetic acid. Thus, the deamination of *threo*-3-phenyl-2-butylamine produced very little net retention, whereas the tosylate ionization produced a great deal. This striking difference in stereochemistry, as well as in migratory aptitude for β substituents between the deaminative and tosylate acetolysis, was interpreted[3b,g] as the difference between behavior of an open ion formed without assistance of solvent or a neighboring group (deamination), and a bridged ion formed with assistance of a neighboring phenyl. Our position has not changed in this interpretation, and the notions and the data are mutually consistent. Apparently, Brown failed to notice the difference between the *threo/erythro* ratios of products for the deamination (1.3) and tosylate reactions (24 or 105) in the *threo* series.

(8) C. J. Collins, B. M. Benjamin, and M. H. Lietzke, *Ann.*, **687**, 150 (1965).

Table I. Solvolysis Products of Tosylates of 3-(*p*-Nitrophenyl)-2-butanol (II-OTs)[a]

Run no.	Isomer of II-OTs	Solvent	Temp, °C	Time, hr	% yield of olefin	% yield of sec. ester[b]	—Ester composition— % *threo*[b]	% *erythro*[b]
1	L-*threo*	CH_3CO_2H	100	38	68	13[c]	7	93
2	L-*erythro*	CH_3CO_2H	100	38	57	9	90	10
3	L-*threo*	HCO_2H	50[d]	38[d]	72	11	30	70
4	L-*erythro*	HCO_2H	50[d]	38[d]	59	9	63	37
5	(±)-*threo*	CF_3CO_2H	72	12	57	9	95	5
6	(±)-*erythro*	CF_3CO_2H	72	12	69	10	28	72

[a] Concentrations of tosylate ester were 0.15 *M*, and of base were slightly greater. [b] These results were reproduced several times. [c] In a similar run made at 75° for purposes of calculating partial rate factors at that temperature, the yield after correcting to complete reaction was 17%. [d] At the end of this time at this temperature the mixture was heated at 75° for 3 hr.

Table II. First-Order Solvolyses Rate Constants

Run no.	Tosylate	Solvent	Temp,[a] °C	Method	$k \times 10^6$, sec^{-1}[b]
7	*threo*-II	AcOH	74.98	Tit.	1.52 ± 0.09
8	*erythro*-II	AcOH	74.98	Tit.	1.68 ± 0.03
9	*threo*-II	AcOH	100.66	Tit.	28.6 ± 0.5
10	*erythro*-II	AcOH	100.66	Tit.	30.1 ± 0.7
11	L-*threo*-II	AcOH	75.25	Pol.	1.68 ± 0.02
12	L-*threo*-II	AcOH	100.50	Pol.	30.8 ± 0.5
13	L-*threo*-II	HCO_2H	49.85	Pol.	13.9 ± 0.2
14	L-*threo*-II	HCO_2H	65.40	Pol.	89.2 ± 1.0
15	D-*threo*-I	CF_3CO_2H	0.70	Pol.	1060 ± 10
16	L-*threo*-II	CF_3CO_2H	42.00	Pol.	9.28 ± 0.06
17	L-*threo*-II	CF_3CO_2H	56.90	Pol.	51.8 ± 0.3
18	2-(*p*-Nitrophenyl)ethyl	AcOH	100.52	Tit.	1.95 ± 0.02

[a] ±0.05°. [b] Average of two runs; standard deviations are recorded.

The present study was initiated to generate an *experimental model* for open ion formation and behavior in a system as close as possible to I-OTs, but one in which phenyl participation did not control the rate, and phenonium ion intermediates did not control the stereochemical relationships between starting materials and products. The 3-(*p*-nitrophenyl)-2-butyl tosylate stereomers (II-OTs) were selected for study. The presence of the nitro group was expected to reduce the nucleophilic character of the aryl to the point where it no longer assisted in the ionization step. However, the remote *p*-nitro group should in no way affect the balance of diastereomeric products that arise from nonaryl-assisted ionization of the *threo* and *erythro* starting materials. Thus, II-OTs serves as a splendid kinetic and stereochemical model for open-chain behavior in the 3-phenyl-2-butyl system. If the rates of ionization of I-OTs and II-OTs turned out to be close together and both systems gave products with high retention, the Brown–Collins open-chain model is worth consideration. If I-OTs should ionize appreciably faster than II-OTs, and if the high retention results of I-OTs should not be observed for II-OTs, then the original phenonium ion interpretation is required.

A second objective of the present study was to investigate more thoroughly the competition between aryl and solvent to act as nucleophile in the ionization of the 3-aryl-2-butyl tosylate system. The direct observation of phenonium ions in sulfur dioxide–antimony pentafluoride by Olah, *et al.*,[9] correlates with the earlier observation that formic acid as a highly ionizing but poor nucleophilic solvent promoted aryl over solvent involvement in ionization more than did acetic acid.[3c,4e] Trifluoroacetic acid as a solvolytic medium has been found to be even less of a nucleophilic competitor of aryl than formic acid,[10a] and seemed to bridge the gap between formic acid on the one hand and sulfur dioxide–antimony pentafluoride on the other with respect to nucleophilicity and ionizing power. In the present study it seemed possible that even the *p*-nitrophenyl group had some chance of exceeding trifluoroacetic acid in nucleophilic competition for the ion formed from the 3-aryl-2-butyl tosylate system.

Results

Starting Materials and Products. The optically pure phthalic acid ester of L-*threo*-I was prepared as before,[3a] nitrated, and hydrolyzed to give L-*threo*-II. Similar treatment of 94% optically pure 3-nitrophthalic acid ester of L-*erythro*-I[3a] gave 94% optically pure L-*erythro*-II. The tosylates of these materials were prepared, and submitted to acetolysis, formolysis, and trifluoroacetolysis for product analysis. In each case the reaction was carried out in the presence of enough salt of the acid solvent to neutralize the *p*-toluenesulfonic acid generated in the reactions. The products were isolated by extraction procedures, and were separated into olefin and ester fractions by chromatography. The relative amounts of *threo* and *erythro* solvolysis products were determined by nmr analysis

(9) G. A. Olah, M. B. Comisarow, E. Namanworth, and B. Ramsey, *J. Am. Chem. Soc.*, **89**, 5259 (1967).

(10) (a) J. E. Nordlander and W. G. Deadman, *ibid.*, **90**, 1590 (1968); (b) see also P. E. Peterson, R. E. Kelley, Jr., R. Belloli, and K. A. Sipp, *ibid.* **87**, 5169 (1965).

Table III. Activation Parameters for Solvolyses of *threo*-Tosylates

Data taken from	Temp, °C	Tosylate of	Solvent	$\Delta H^{\neq}$, kcal/mol Based on k_α	$\Delta H^{\neq}$, kcal/mol Based on k_t	$\Delta S^{\neq}$, eu Based on k_α	$\Delta S^{\neq}$, eu Based on k_t
Ref 4a	50	I	CH_3CO_2H	25.9	26.3	−1.1	−2.9
Runs 7, 9	50	II	CH_3CO_2H	29.1	29.0	−1.8	−2.1
Ref 4c,e	50	III	CH_3CO_2H	26.1[a]	26.3	3.4[a]	5.6
Runs 13, 14	25	II	HCO_2H	25.3	...	−2.5	...
b	25	I	CF_3CO_2H	...	16.1	...	−14.1
Runs 16, 17	25	II	CF_3CO_2H	23.3	...	−8.1	...

[a] k_α for III-OTs (*threo*-3-anisyl-2-butyl tosylate) at 50° was calculated from k_t at 50°, assuming the same k_α/k_t as that measured at 25°. [b] Private communication from S. Winstein and A. Diaz, solutions contained sodium trifluoroacetate.

using the difference in chemical shift of the methyl group in the diastereomeric acetates. The formates and trifluoroacetates were converted to their corresponding acetates for determination of their diastereomeric balance. Control experiments demonstrated these conversions to be nonselective. Table I reports the results.

The composition of the olefinic mixture was not determined. Control experiments demonstrated that the ester products once formed neither decomposed nor epimerized under the reaction conditions. Previous experiments demonstrated that olefins formed in acetolysis and formolysis of the diastereomers of I-OTs were stable under conditions of their formation.[3c] The reasonable assumption is made that substitution of a nitro group in the *para* position of these phenylbutenes should not alter this condition. However, a control experiment demonstrated that trifluoroacetic acid added to the terminal olefin, 3-phenyl-1-butene, in 10 hr at 72° to give 93% secondary ester and 7% olefin. The ester formed was 42% *threo* and 58% *erythro*. Should such addition also occur to the terminal *p*-nitro olefin, a similar nonstereospecific result is expected. An addition reaction of trifluoroacetic acid to the internal olefins would undoubtedly give tertiary ester, which would revert to olefin at the temperature employed. Such behavior was observed with the 2-phenyl-2-butenes in formic acid.[3c]

Attempts to separate the *threo* from the *erythro* esters by glpc and column chromatography failed. In order to determine the amount of racemization that took place during acetolysis and formolysis, the alcohols produced by hydrolysis of ester products were oxidized to the corresponding 3-(*p*-nitrophenyl)-2-butanone under neutral conditions.[11] As expected, the L-*erythro*-II-OTs gave nonracemized acetate or formate. The L-*threo*-II-OTs gave acetate 4 ± 2% racemized, and formate 25 ± 2% racemized. A control experiment established that no racemization or diastereomer selection occurred during hydrolysis, oxidation, or purification of the product.

Kinetics. Table II summarizes the kinetic results. Titrimetric acetolysis rates of optically active *threo*- and *erythro*-II-OTs were followed by titrating the liberated *p*-toluenesulfonic acid with standard sodium acetate in glacial acetic acid.[4] Polarimetric formolysis and trifluoroacetolysis rates were observed by measuring the changes in optical rotations of the kinetic solutions by the ampoule aliquot technique. All kinetic solutions were unbuffered, and the reactions exhibited good first-order behavior through two half-lives. Each run was made in duplicate, and the rate constant reported was the average of the two values. From seven to nine points were determined per run, and the infinity point was determined after about ten half-lives at 100°.

Table III lists the activation parameters calculated from the rate constants of Table II, or taken from the literature.

To determine the inductive effect on rate of acetolysis of a remote nitro group in a β-aryl system in which phenyl does not assist appreciably in ionization,[12] 2-(*p*-nitrophenyl)ethyl tosylate was prepared and its rate of acetolysis measured. Table II records the results of this and the other kinetic runs.

Discussion

The stereochemical and kinetic results previously obtained for solvolysis of the I-OTs system and its *p*-methoxy derivative will be contrasted with those obtained for II-OTs in the present investigation. Both the product and kinetic results indicate that solvent and β-aryl compete with one another in nucleophilically assisting the ionization of these tosylates. The product results indicate that when aryl participates in ionization of the tosylates, a phenonium ion intervenes as an intermediate in the reaction.

Products of Solvolysis. In acetic acid, L-*threo*-I-OTs gave 53% acetate (and 35% olefin) composed of 95% racemic *threo*, 0.6% L-*threo*, 1.2% L-*erythro*, and 2.8% racemic *erythro* material. In the same solvent, D-*erythro*-I-OTs gave 68% acetate (and 23% olefin) composed of 96% D-*erythro* and 4% D-*threo* material.[13] In formic acid, L-*threo*-I-OTs gave a 70% yield of formate which was >99% racemic *threo*, <0.1% L-*threo* and <0.01% L-*erythro* material. In the same solvent, D-*erythro*-I-OTs gave a 71% yield of formate which was >99% D-*erythro* and <0.5% D-*threo* material.[3c] These stereochemical results are uniquely

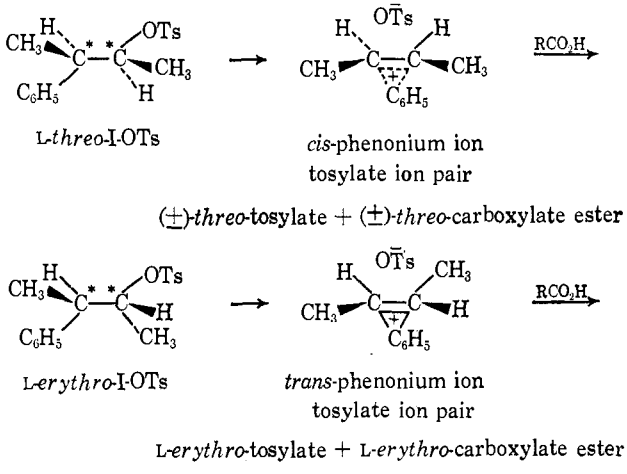
(11) K. E. Pfitzner and J. G. Moffatt, *J. Am. Chem. Soc.*, 87, 5670 (1965).

(12) (a) C. C. Lee, G. P. Slater, and J. W. Spinks, *Can. J. Chem.*, 35, 1417 (1957); (b) E. F. Jenny and S. Winstein, *Helv. Chim. Acta*, 41, 807 (1958); (c) W. H. Saunders, S. Asperger, and P. H. Edison, *J. Am. Chem. Soc.*, 80, 2421 (1958); (d) S. Winstein, C. R. Lindegran, H. Marshall, and L. L. Ingraham, *ibid.*, 80, 2421 (1958).

(13) The composition of acetate from D-*erythro*-I-OTs is reported as an average of that obtained from rotation and from infrared methods.[3c] Small computational errors were made in the original paper,[3c] and are corrected here. These corrections in no way change the argument.

explained by the phenonium ion mechanism depicted in Chart II. The fact that acetate product of retained

Chart II



configuration had undergone a 50% rearrangement was demonstrated by reresolution of the racemic *threo* product from acetolysis of ^{14}C-1 labeled L-*threo*-I-OTs.[14]

Phenonium tosylate ion-pair return is an important factor in acetic acid and less important in formic acid which is a better dissociating medium.[4d] Since *cis*-phenonium ion formed from (−)-L-*threo*-I-OTs is symmetrical, only racemic products can arise from this intermediate. Therefore, the ratio of the rate constant for racemization (k_α) to that for appearance of *p*-toluenesulfonic acid (k_t) is a direct measure of ion-pair return. For (−)-L-*threo*-I-OTs in acetic acid, k_α/k_t = 4.41 at 75°, and in formic acid, k_α/k_t = 1.18 at 25°.[4d] Essentially the same results were obtained from product data that indicated that in acetolysis, 80% of the racemic *threo* acetate came from racemized starting material and 20% directly from active starting material. In formolysis 75% of the racemic *threo* formate came directly from active starting material and 25% from racemized starting material.[3c] A value of k_α/k_t equal to 4.2 at 75° was determined for acetolysis of *erythro*-I-OTs through ^{14}C scrambling experiments.[14]

Substitution of a *p*-methoxyl group in I-OTs for the *p*-hydrogen to give 3-(*p*-anisyl)-2-butyl tosylate (III-OTs) greatly enhances the nucleophilicity of the aryl.[4b] Thus, acetolysis of *threo*-III-OTs produced 99.7% acetate and 0.3% terminal olefin. The acetate was >99.9% racemic *threo* material with no measurable *erythro* contaminant (<0.1%). The ratio, k_α/k_t, for (+)-*threo*-III-OTs was 4.6 at 25°.[4c]

The behavior of I-OTs, II-OTs, and III-OTs can best be compared through use of partial rate factors, which provide a measure of the stereochemical course of the substitution and tosylate rearrangement reactions. If k_r is the rate constant for production of carboxylic ester plus tosylate ester of retained configuration and k_i that for esters of inverted configuration, then k_r/k_i ratios can be calculated from product data coupled with k_α/k_t values.[3d,e] Thus, $k_r/k_i = k_\alpha/k_t$ (yield of carboxylate ester of retained configuration/yield of carboxylic ester of inverted configuration). Table IV lists values for k_r/k_i for acetolysis and formolysis for most of the optically active diastereomers of I-OTs, II-OTs, and III-OTs. Comparison of the titrimetric and polarimetric rate constants for *threo*-II-OTs in acetic acid at 75° and at 100° (Table II) indicates them to be almost the same, as is expected from the nature of the products (Table I). The same is undoubtedly true for the other acetolysis and formolysis runs of II-OTs (runs 7–14 of Table III). Thus, the values of k_r/k_i for II-OTs reflect the simple diastereomeric product data of Table I.

Table IV. Ratios of Retention–Inversion Partial Rate Factors That Reflect the Stereochemical Course of Solvolyses

Tosylate	*para* subst	$(k_r/k_i)^{75°}_{AcOH}$	$(k_r/k_i)^{50°}_{HCO_2H}$	$(k_r/k_i)^{0°}_{CF_3CO_2H}$
L-*threo*-III	CH_3O	>4600	...	...
L-*threo*-I	H	105	10,000	...
D-*erythro*-I	H	101	...	...
L-*threo*-II	NO_2	0.078	0.43	>19
L-*erythro*-II	NO_2	0.11	0.59	>2.6

The values of k_r/k_i in acetic acid vary in a systematic manner from over 4600 for the *p*-methoxy substituted system to 105 for the parent (*p*-hydrogen) system to 0.08–0.11 for the *p*-nitro system. The total spread in stereochemical result is about 50,000. Clearly, neighboring aryl and solvent are in competition with one another in providing nucleophilic assistance in ionization. With a *p*-methoxy substituent, aryl dominates by over 10^3; with a *p*-hydrogen, aryl dominates by 10^2; and with a *p*-nitro substituent, acetic acid dominates over aryl by about 10^1. Thus, the stereochemical course of substitution in this secondary system can be changed from high retention to high inversion in acetic acid by simply changing the nature of a remote substituent. The values for the *p*-nitro substituent serve as a model for the stereochemical outcome of solvolysis for this secondary system in the absence of neighboring aryl assistance in ionization. The fact that rearrangement occurred at most to the extent of a few per cent in the *threo*-*p*-nitro system but to the extent of almost exactly 50% in the other two *threo* systems correlates with the high inversion observed in the *p*-nitro and the high retention found for the *p*-hydrogen and *p*-methoxy systems.

The high inversion observed in the *p*-nitro system in acetic acid also correlates with the stereochemical result found in simple secondary systems such as 2-octyl tosylate, which gives high inversion in the same solvent.[15]

Unfortunately, data are missing for the *p*-methoxy system in formic acid. The difference in k_r/k_i values for the *p*-H and *p*-nitro systems in formic acid is about 20,000 with the scale moved toward the retention side. Thus, in the *p*-hydrogen system, aryl firmly directs the stereochemical course of the reaction toward re-

(14) W. B. Smith and M. Showalter, *J. Am. Chem. Soc.*, **86**, 4136 (1964).

(15) (a) A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp 59 and 73; (b) A. Streitwieser, Jr., and T. D. Walsh, *Tetrahedron Letters*, 27 (1963).

Table V. Rate Constant Ratios for Ionization of Tosylates Based on k_α Comparisons

Based on data from	Solvent	Temp, °C	Rate constant ratios[a] $(k^H/k^{NO_2})_{threo}$	Rate constant ratios[a] $(k^{CH_3O}/k^{NO_2})_{threo}$
Ref 4c,d, 13 Runs 8, 10–12	CH_3CO_2H	50	190	15,000
Ref 4d Runs 13, 14	HCO_2H	25	560	...
Runs 15–17	CF_3CO_2H	0.70	36,000	...

[a] Superscripts in rate constant ratios refer to *para* substituent in the phenyl group.

tention. Even in the *p*-nitro system, a small amount of aryl involvement in ionization is detectable, since $k_r/k_i \sim 0.5$. These values correlate with the facts that in formic acid the *threo*-*p*-hydrogen system gave 50% rearrangement (complete racemization), and the *p*-nitro system (*threo* plus *erythro*) was about 12% rearranged (24% racemized). The movement of the scale toward aryl involvement in passing from acetic to formic acid correlates with the decrease in nucleophilicity of the solvent.

The scanty product data in trifluoroacetic acid bear out the trends observed in passing from acetic to formic acid. Thus, *threo*-II-OTs (*p*-nitro system) in trifluoroacetic acid gives a k_r/k_i value of >2.6.[16] In this solvent even the *p*-nitrophenyl group competes successfully with solvent in directing the reaction into a stereochemical course of retention. These findings are in full accord with what would be expected on the basis of the results of Nordlander, *et al.*,[10a] in other systems.

The absolute yields of ester produced also correlate roughly with the stereochemical results. Thus, the higher the value of k_r/k_i in a given solvent, the higher the yield of ester product. For example, the *threo* isomers in acetic acid gave acetate yields of >99%, 53%, and 13% for the *p*-methoxy, *p*-hydrogen, and *p*-nitro systems, respectively.[17] At the same time, k_r/k_i values decreased from >4600 to 105 to 0.08. Thus, aryl participation in ionization favors ester product (formed with retention), whereas nonaryl involvement in ionization favors olefin products. Thus, solvent plays a multiple role in its competition with the aryl for directing the course of reaction toward various products. It can act as either a nucleophile to give inverted product, or as a base to give olefin. The olefin produced without rearrangement from *erythro*- and *threo*-I in acetic acid was observed to arise largely by a *trans* elimination.[18] Possibly, the proton became hydrogen bonded to acetic acid in the same transition state that involved the breaking of the carbon–oxygen bond. Just as in the mechanism for producing inverted acetate in simple secondary systems, differing amounts of involvement of solvent can be envisioned in the production of olefin. Thus, aryl as a nucleophile is in competition with solvent acting as either a nucleophile leading to inverted acetate, or a base leading to olefin (*trans* elimination). The source of olefin products is complicated by β-hydrogen migration.[18]

Kinetics. The steric environment in a given diastereomeric series of the two asymmetric centers should be independent of the nature of the *para* substituent in the 3-aryl-2-butyl tosylates. Thus, in comparisons of the rates of ionization of I-, II-, and III-OTs, the degrees of steric inhibition of solvation at both the front and back faces of the incipient open ions should be independent of the *para* substituent. The rates of ionization to form open ions should be sensitive only slightly to the character of the *para* substituent, since the energy of the transition states leading to open ion should be subject to only the small differences between the three substituents' inductive effect operating from the remote *para* position.

The stereochemical evidence of the last section demonstrated that both diastereomers of II-OTs (*p*-nitro system) ionized in acetic and formic acids with very little assistance from the aryl group. Therefore, this system provides a superb kinetic model for ionization without aryl involvement in the other two systems. Even though the *p*-nitrophenyl group did become involved in ionization in trifluoroacetic acid, the products of that involvement were only a fraction of the total (including olefin). Thus, comparisons of the rates of ionization in the three systems provides a simple means of estimating the rate increase due to neighboring aryl participation in the *p*-hydrogen and *p*-methoxy systems. The rate constant for change in rotation, k_α, provides the best measure of ionization rate. Similarly, $(k_x/k_{NO_2})_\alpha$ values provide the best measure of the rate factor increase due to substituting hydrogen or methoxy for a nitro group in the *para* position of the phenyl ring. Table V lists the values calculated for these ratios in the various solvents. In some cases the rate constants had to be extrapolated to the same temperature through use of the activation parameters listed in Table III and those already published.

The rate enhancement factor in acetic acid for phenyl over *p*-nitrophenyl in the *threo* series is 190. The factor in the same solvent for *p*-anisyl over *p*-nitrophenyl is 15,000. In formic acid the factor for phenyl over *p*-nitrophenyl (*threo*) is 560, and in trifluoroacetic acid is 36,000. Although a small part of these rate factors may be attributable to the difference in the remote inductive effect of the *p*-nitro group on the one hand and *p*-hydrogen or *p*-methoxyl on the other,

(16) The values are minimal for two reasons: (a) since k_t was not measured, they were calculated by setting $k_\alpha/k_t = 1$, while the actual ratio is probably greater (S. Winstein and A. Diaz report in a private communication that L-*threo*-I-OTs exhibits $k_\alpha/k_t = 1.8$ in buffered solution at 25°); (b) terminal olefin adds trifluoroacetic acid to give the diastereomeric secondary esters in almost equal amounts, and to the extent that such addition occurs, the k_r/k_i values would be correspondingly reduced.

(17) Even more striking are comparisons of the absolute yields of racemic *threo* acetates from L-*threo*-tosylates of I, II, and III. Thus, in passing from the *p*-nitro to the *p*-hydrogen system this yield increased by a factor of 100. Replacement of the *p*-nitro group with a *p*-methoxyl increased this yield by a factor of 200.

(18) D. J. Cram, *J. Am. Chem. Soc.*, 74, 2134 (1952).

most of the factor is undoubtedly due to phenyl or *p*-anisyl participation in ionization. The product data indicated that even the *p*-nitrophenyl group exerted considerable stereochemical control over the reaction in trifluoroacetic acid, which indicates some aryl participation. Thus, the value, $(k_H/k_{NO_2})_{CF_3CO_2H}$ = 36,000, is minimal as an indication of phenyl participation in ionization.

The question remains as to the size of the remote inductive effect of the *p*-nitro on the rate factors in II-OTs. A general impression of the order of magnitude of this inductive effect is available by comparing the rates of acetolysis of 2-phenylethyl tosylate[12d] and 2-(*p*-nitrophenyl)ethyl tosylate. Since phenyl rearranges in acetolysis of the former compound only 11%, the *p*-nitrophenyl should rearrange little, if at all, in the latter system. The partial rate factor due to nucleophilic solvent involvement for 2-phenylethyl tosylate (k_s) is $0.89k_t$, whereas $k_s = k_t$ for the *p*-nitro compound. At 100°, $k_s^H/k_s^{NO_2} = 1.5$. Although a somewhat larger inductive effect is expected for secondary open ion formation, the difference should not be large.

A better but imperfect measure of the magnitude of this inductive effect in a secondary system involves a comparison of the values of k_s for the secondary open ion components in the acetolysis of I-OTs and II-OTs. Because of the large amount of olefin produced from II-OTs (and the smaller amount from I-OTs), and because an indeterminate amount probably came from open ion, an exact measure of k_s cannot be calculated. However, if open ions from I-OTs and II-OTs each partitioned the same way between inverted acetate and other products, then $k_s^H/k_s^{NO_2}$ = [k_t^H (yield inverted acetate)]/[($k_t^{NO_2}$ (yield inverted acetate)]. This ratio provides the best measure of the inductive effect available, and in acetolysis at 75°, $(k_s^H/k_s^{NO_2})_{threo} \sim 4.4$. As expected, the inductive effect of the nitro group in the secondary system is more than in the primary. Correction for this inductive effect leaves a factor of 43 increase in rate in acetic acid due to phenyl participation in ionization for *threo*-I-OTs. If the inductive effect rate factor was 4.4 in formic and trifluoroacetic acid as well, the rate increase due to phenyl participation would be 128 and ~8000, respectively.

Brown and Kim[6c] state, "Indeed, a detailed examination of the rates of solvolysis of symmetrically substituted β-phenylalkyl derivatives reveals little or no rate enhancements." These authors seem devoted to the rate factors of 4.0 and 3.5 assigned to phenyl participation which grow out of comparisons of rates of acetolysis (not ionization) of *threo*- and *erythro*-I-OTs and 2-butyl tosylate. Our factors of 43 in acetic, 128 in formic, and 8000 in trifluoroacetic acid demonstrate that comparisons between I-OTs and 2-butyl tosylate are as superficial and misleading as are comparisons between the rates of solvolysis of β,β,β-triphenylethyl tosylate and I-OTs.[6c] Factors of 43, 128, and 8000 are large enough to put neighboring phenyl in almost complete control of both the stereochemical course of the substitution reaction, and the importance of aryl migration. Had these rate factors been of the order of 10^6 instead of in the range 10^1–10^3, the acetolysis products would have been little changed. For example, in acetolysis of L-*threo*-I-OTs, the acetate produced was 95% *threo* out of a theoretical maximum of 100%, and phenyl migrated to the extent of over 49% out of a theoretical maximum of 50%. A rate factor in the millions would have provided an increase in *threo* acetate of only 5% and of phenyl-migrated acetate of less than 1%.

Differences in the relative importance of phenonium ions in the I, II, and III systems do not produce any correlation between neighboring group participation in ionization and the partitioning of activation energies between entropy and enthalpy terms. Although such correlations have been observed in the *p*-phenylethyl tosylate system,[19] they have not appeared in other than this primary system.[4a,e] Electrophilic solvent involvement with the tosylate group during ionization of secondary systems probably makes the largest contribution to lowering the entropy of activation, and "drowns out" changes in the less important nucleophilic contributions as the *para* substituent is changed.

Correlations of Rates with σρ. Neighboring phenyl involvement in carbonium ion formation represents an intramolecular example of electrophilic aromatic alkylation. The interesting question arises as to whether the partial rate factors for ionization with aryl participation (k_Δ) in the I-OTs, II-OTs, and III-OTs systems can be correlated by σ or σ^+ values. In acetolysis of (+)-*threo*-III-OTs (*p*-methoxy system), the virtual absence of products other than racemic *threo* acetate indicates that $k_\Delta^{75°} = k_\alpha = 1.82 \times 10^{-2}$ sec^{-1}. In acetolysis of L-*threo*-I-OTs (*p*-hydrogen) a small correction must be made for starting material that goes to product through open ion. In this system, $k_\Delta^{75°} = k_\alpha - k_t$ (yield of all products other than racemic *threo*) = 2.09×10^{-4} sec^{-1}. For L-*threo*-II-OTs (*p*-nitro), $k_\Delta^{75°} = k_\alpha$ (yield of racemic carboxylate ester) = $(1.1 \pm 0.6) \times 10^{-8}$ sec^{-1}. A plot of log k_Δ *vs.* σ gives a line with a slight curvature in one direction, while a plot of k_Δ against σ^+ provides a line with considerably more curvature in the opposite direction (Figure 1). The inability of σ and σ^+ to better correlate k_Δ values can be due to a number of factors. (1) Methoxy and nitro groups are at the far ends of the scale of substituent constants and frequently do not fall on plots whose slopes are largely determined by other substituents. (2) Neighboring aryl should respond to a different blend of various effects of substituents than are observed in the reactions used to define σ and σ^+ values.[20] For example, in the reactions used to define σ or σ^+ no three-membered rings are formed with the attendant types of orbital rehybridization and the response of substituents to such rehybridization. (3) The position of the transition state along the reaction coordinate is expected to change substantially by changing the substituent (see discussion in final section).

An average ρ value of −6.3 was extracted from the σ points by averaging the slopes of the three two-point lines, and an average ρ value of −4.2 was obtained similarly from the σ^+ points. The average slope from the former points understandably is much greater than

(19) S. Winstein and R. Heck, *J. Am. Chem. Soc.*, 78, 4801 (1956).
(20) (a) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Company, Inc., New York, N. Y., 1940, p 186; (b) L. M. Stock and H. C. Brown, *Advan. Phys. Org. Chem.*, 1, 35 (1963).

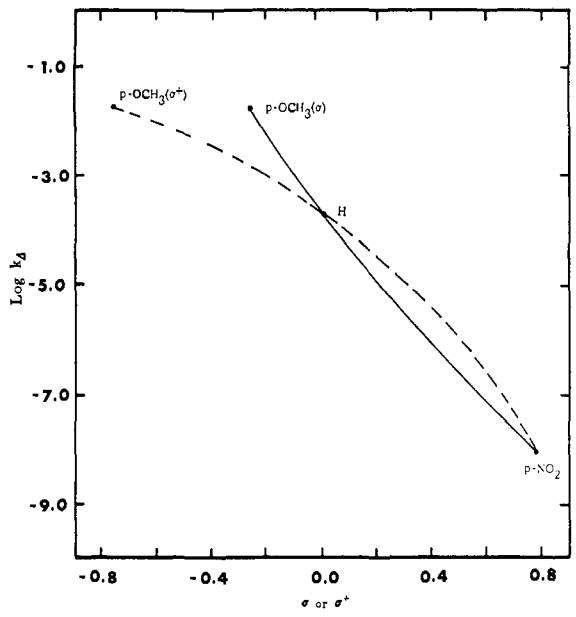


Figure 1. Correlation of the partial rate factors for ionization with aryl participation (k_Δ) with σ and σ^+ constants for acetolysis of 3-aryl-2-butyl tosylates at 75°.

that of the reaction used to define σ (benzoic acid ionization), while the average slope from the latter points is less than that of the reaction used to define σ^+ (−4.5 for cumyl chloride solvolysis). Some success has been realized with $\sigma^+\rho$ plots where phenyl participation is involved,[21] and failure of this correlation has also been reported.[22]

Phenonium *vs.* Open Ion Models. By selection of kinetic data that does not measure ionization rates, and by overlooking the differences in steric inhibition of solvation of ions generated from 2-butyl tosylate and 3-phenyl-2-butyl tosylate, Brown, *et al.*,[6] conclude that "the minor factors of 4.0 . . . for the acetolysis of *threo*- and *erythro*-3-phenyl-2-butyl tosylates do not appear to be compatible with the postulated formation of relatively stable phenonium ion intermediates."[6c] These authors[6b] explained the stereochemical results of the I-OTs system with five assumptions. (1) Ionization occurs to give open ion pairs only when phenyl and tosyl are *trans* for steric reasons, the tosyl group swelling as it ionizes. (2) The ion pair is unsolvated from the back because of the blocking effect of the phenyl in its resting state. (3) The phenyl migrates back and forth faster than rotation occurs about the central C–C bond, and faster than solvent attacks the ion pair. Solvent is blocked from the back by migrating phenyl (windshield-wiper effect). (4) Rotation about the central C–C bond in the ion pair is slowed because of the steric necessity of phenyl and tosylate anion remaining *trans* to one another. (5) Capture of the ion pair occurs from the front because of the blocking ability of the phenyl at the back and because of solvation of the anion.

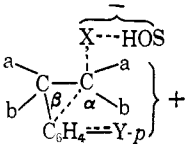
Our *p*-hydrogen and *p*-nitro starting states are stereochemically identical. Assumptions 1, 2, 4, and 5 apply equally well to our *p*-hydrogen and *p*-nitro systems. The *p*-nitro group slows down the rate of aryl migration, and hence assumption 3 for the *p*-nitro system would not apply. Now the question arises as to whether a phenyl that migrates is different sterically than a *p*-nitrophenyl that does not. The two should be the same since little of an open ion pair's lifetime is spent in the transition state for migration. To attribute the steric effects of a transition state to a ground state because of rapid migration is folly, and violates transition-state theory. Clearly, the aryl groups in the two starting materials present the same steric inhibition to solvation from the back in transition states leading to open ion pairs, whether they be solvated carbonium ion tosylate or less likely, oxonium tosylate ion pairs. Thus, the Brown model (allegedly justified[6c] by Collins' mathematics[8]) predicts similar k_r/k_i ratios for the *p*-hydrogen and *p*-nitro systems. Furthermore, since the Brown model excludes aryl participation in ionization, the only difference in ionization rates the model predicts must be due to the small inductive effect.

The Brown model is completely incompatible with the results on both stereochemical and kinetic grounds. Instead of k_r/k_i values being similar for *p*-hydrogen and *p*-nitro systems, they differ by factors of 800–1800 in acetic acid and by a factor of 23,000 for the *threo* isomer in formic acid. Instead of the rates of ionization for the *p*-hydrogen and *p*-nitro systems differing by factors of 1.5–4.4 (remote inductive effect), they differ by factors that range from 190 in acetic acid to 560 in formic acid to 36,000 in trifluoroacetic acid. In contrast, these results are consistent in detail with the original interpretation[3] in which solvent and aryl compete with one another for nucleophilic assistance in ionization at the back of secondary carbon. In nucleophilicity, $CH_3CO_2H > HCO_2H > CF_3CO_2H$, and p-$CH_3OC_6H_4 > C_6H_5 > p$-$NO_2C_6H_4$. By combining the most nucleophilic solvent (AcOH) with the least nucleophilic aryl group (p-$NO_2C_6H_4$), nucleophilic solvent assistance produces a relatively slow rate and a stereochemical course of the reaction to give ester with high inversion. However, in the least nucleophilic solvent (CF_3CO_2H), the high net retention observed with p-$NO_2C_6H_4$ indicates that aryl participation dominated the reaction. The extent to which phenyl as a nucleophile dominates over solvent depends on the solvent. In acetic acid the domination was nearly complete and in formic acid overwhelming. With *p*-methoxyphenyl, the domination of aryl over acetic acid as a nucleophile also was overwhelming. Here is a continuity of behavior based on reaction mechanism which logically extrapolates to the direct spectroscopic observation of phenonium ions by Olah, *et al.*,[9] who used a solvent (SO_2–SbF_5) which exhibits essentially no nucleophilicity, high ionizing power, and a neighboring phenyl with phenonium ion stabilizing methyl or methoxyl substituents. An open secondary carbonium ion formed *without nucleophilic assistance from either acetic acid or neighboring phenyl is envisioned by Brown for the 3-phenyl-2-butyl system.*[6b] Such a naked carbonium ion has no place in this picture, explains nothing, and is in conflict with a body of experimental data. Nonnucleophilically solvated nonbenzyl secondary carbonium ions may be generated in deamination reactions with nitrogen as leaving group,[3g] or

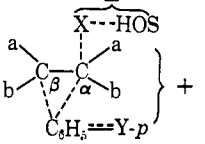
(21) R. Heck and S. Winstein, *J. Am. Chem. Soc.*, 79, 3432 (1957).
(22) F. R. Jensen and R. J. Ouellette, *ibid.*, 85, 367 (1963).

possibly in extremely nonnucleophilic solvents in the absence of neighboring groups, but clearly not in the acetolysis of 3-phenyl-2-butyl tosylate. The stereochemical results and conclusions of the original 1949 phenonium ion paper[3a] have in no basic way been modified by any new data or any new ideas.

Relationship between Bridged Ions and Transition States Leading to Bridged Ions. The question of the structural relationship between symmetrical ethylene phenonium ions and the phenonium ion producing transition state invites speculation. We envision a whole family of *transition state structures* which reflect different degrees of bond making and breaking, all leading to the same type of bridged ion, and all involving *some* σ *bonding* between aryl and C_α. At one extreme this bonding may be very weak as in the summarizing structure IV in which aryl has migrated only a short way toward a centered position. At the other extreme, the bonding may be very strong as in summarizing structure V in which aryl is closer to a centered position.



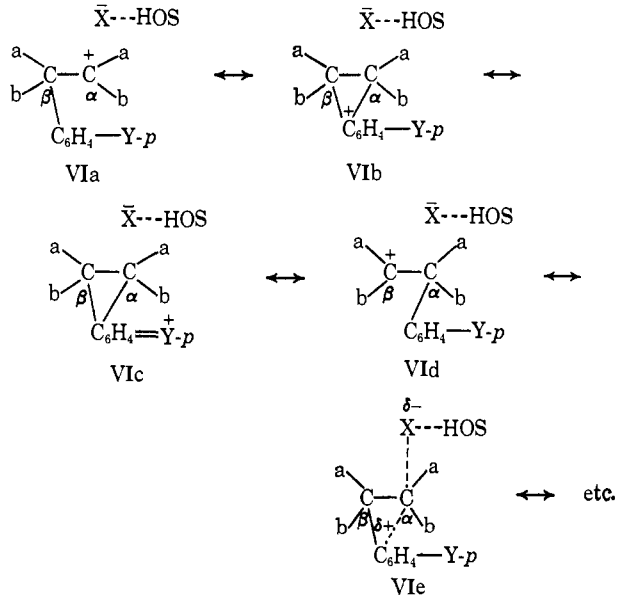
IV



V

The exact bond orders in any particular transition state can be thought of as reflecting a blend of canonical resonance structures of which VIa–VIe of Chart III are illustrative. The exact blend in β-arylethyl systems depends on structural features such as α and β substituents, the position and character of aryl substituents, and the character of the leaving group. At least as important are environmental features such as the electrophilicity and dielectric properties of the medium. The rate changes that accompany changes in a and b, in X and Y, and in HOS are undoubtedly accompanied by serious structural changes, particularly with respect to the aryl–C_α bond distance. For example, the transition state leading to bridge for II-OTs in trifluoroacetic acid might be rich in VIa with a small contribution from VIb, but little contribution from the other structures. The aryl–C_α bond in this transition state would be long, but so also would be the C–X bond, and C_α would carry much of the positive charge. In contrast, the transition state for III-OTs in acetic acid might be rich in VIc and VIe, with a relatively short aryl–C_α bond. Structures such as VId would be expected to be greatest for I-OTs in trifluoroacetic acid, but relatively unimportant compared to VIa and VIb. In all transition states, VId is envisioned as making only a minor contribution.

Chart III



The important part of this mechanistic picture is the large number of structural variables for the transition state for aryl bridging. With so many structural changes available, the notion that the structure of the transition state *must resemble in detail* the structure of the first intermediate is empty, and has neither theoretical nor empirical support. This hypothesis is limited to endothermic reactions[23] and was never meant to apply to highly complex transformations, or to act as an arbiter of mechanistic detail. We see no reason why a large variety of transition-state structures cannot converge on a bridged ion of the same or very similar properties. The vast changes in rate of the systems at hand with changes in solvent and the *para* substituent point to big changes in endothermicity, and yet only at the extreme ends of the scale does the stereochemical course of the reactions change, and then only because the rate of the reaction that involves neighboring phenyl participation is much exceeded by the rate of nucleophilic solvent participation in ionization.

The vast increases in rate of reaction of I-OTs in passing from acetic to formic to trifluoroacetic acids reflect increases in the electrophilic participation of solvent which, in turn, results in increases in the participation of aryl in the transition states leading to the bridged ion. In terms of resonance structure blends, structure VIb would become increasingly important and VIe less important as this rate increased. Although still minor, VId should also increase in importance. At the same time, the aryl–C_α bond distance should become shorter as VIb became more important.

Experimental Section

All melting points and boiling points are uncorrected. Infrared spectra were recorded for all compounds on a Beckman IR-5 spectrophotometer. Solutions were 5–10% in spectrograde chloroform as solvent. Nuclear magnetic resonance (nmr) spectra were recorded for all compounds on a Varian Associates A-60 spectrometer in deuteriochloroform with 2% tetramethylsilane as internal standard. Optical rotations were taken in a jacketed 1-dm cell on a Perkin-Elmer Model 141 polarimeter. The observed rotations were generally $\pm 0.005°$.

Most solvents used were reagent grade. Diethyl ether was Mallinckrodt Analytical Reagent. Pyridine was Karl Fischer reagent grade (Matheson Coleman and Bell), stored over potassium hydroxide pellets. Technical pentane was distilled before use. Dry acetic acid for acetolysis reactions and dry formic acid for formolysis reactions were prepared as described previously.[24] Trifluoroacetic acid (Matheson Coleman and Bell) was dried by refluxing it with 2% by weight trifluoroacetic anhydride (Eastman)

(23) G. S. Hammond, *J. Am. Chem. Soc.*, 77, 334 (1955).
(24) D. J. Cram and F. L. Harris, Jr., *ibid.*, **89**, 4642 (1967).

for 4 hr and distilling; a center cut was taken, bp 72°. This material was made 1% by weight in trifluoroacetic anhydride.

L-*threo*- and L-*erythro*-3-(*p*-Nitrophenyl)-2-butanols (L-*threo*-II and L-*erythro*-II). The phthalic acid ester of L-*threo*-I was prepared by a former procedure[3a] to give material, $[\alpha]^{25}D$ 27.6° (*c* 3, 95% ethanol), mp 99.5–100.5° (lit.[3a] $[\alpha]^{25}D$ 25.2° (*c* 3, 95% ethanol), mp 101–102°). To 33 ml of 90% nitric acid was added 15.0 g of the above ester by slowly sifting the finely ground solid into the rapidly stirring acid over a period of 30 min. The temperature was maintained at −15 to −20° during and for 15 min after addition. The reaction mixture was then poured into a mixture of ice and water, and this mixture was extracted with dichloromethane. The organic extract was washed twice with water and dried. Evaporation of the solvent left a solid which was recrystallized from ethyl acetate–petroleum ether (bp 30–60°) (3:1) to yield 9.2 g of phthalic acid ester of L-*threo*-II (54%), mp 139–140°. The infrared spectrum had two strong absorptions due to the nitro group (1350 and 1530 cm^{-1}).[25] This compound was not investigated further, but was then mixed with 33 ml of 2 *N* aqueous potassium hydroxide and 200 ml of reagent grade tetrahydrofuran and refluxed 20 hr. After evaporating most of the tetrahydrofuran, water was added and the mixture extracted with ethyl ether. The ethereal solution was washed successively with water, 2 *N* sulfuric acid, and water and dried. The solvent was evaporated leaving an oil which crystallized, and was recrystallized from ethyl ether–pentane (3:2) to give 3.3 g of L-*threo*-II (64% as long white needles), $[\alpha]^{25}D$ +39.2° (*c* 3, 95% ethanol), mp 59–60°. The nmr spectrum showed the following absorptions: aromatic protons (multiplet, 4.04 protons) centered at τ 2.22; methine proton (symmetrical quintet, 1.01 protons) centered at 6.07; methine proton (symmetrical quintet, 1.01 protons) centered at 7.13; hydroxyl proton (singlet, 1.09 protons) at 7.48; methyl protons (doublet, J = 7 cps, 3.00 protons) centered at 8.63; and methyl protons (doublet, J = 7 cps, 2.92 protons) centered at 8.91. *Anal.* Calcd for $C_{10}H_{13}NO_3$: C, 61.53; H, 6.71. Found: C, 61.83; H, 6.55.

The 3-nitrophthalic acid ester of L-*erythro*-I was prepared as described previously[3a] to give material, $[\alpha]^{25}D$ −32.6° (*c* 3, 95% ethanol), mp 142–144° (lit.[3a] $[\alpha]^{25}D$ −34.6° (*c* 3, 95% ethanol), mp 144–145°). To 35 ml of 90% nitric acid was added 14.3 g of the above ester, and the reaction was carried out as described for the L-*threo* ester. The reaction mixture was then poured into a mixture of ice and water and the solid which formed was isolated by filtration (because of its insolubility in organic solvents), washed several times with water, and dried under vacuum in a desiccator. This material was recrystallized twice from ethyl acetate–petroleum ether (3:1) to give 8.0 g of 3-nitrophthalic acid ester of L-*erythro*-II (49%), mp 162–163°. Infrared absorption bands due to the nitro group were the same for this as for the above L-*threo* ester. This compound was not investigated further but was saponified to the alcohol in a manner identical with that described for the above compound to give 2.7 g of a light yellow oil. This material could not be crystallized, but was chromatographed over 150 g of silica gel. Treatment of the column with 500 ml of ether–pentane (1:9) and 500 ml of ether–pentane (35:65) failed to remove any material. Subsequent elution with 500 ml of ether–pentane (1:1) produced 2.5 g of L-*erythro*-II (62% as a light yellow oil), $[\alpha]^{25}D$ +15.6° (*c* 3, 95% ethanol). The nmr spectrum of the substance was identical with that of L-*threo*-II. *Anal.* Calcd for $C_{10}H_{13}NO_3$: C, 61.53; H, 6.71. Found: C, 61.30; H, 6.78.

Tosylates of L-*threo*- and L-*erythro*-3-(*p*-Nitrophenyl)-2-butanols (L-*threo*- and L-*erythro*-II-OTs). To a solution of 6.7 g of L-*threo*-II in 10 ml of pyridine was added 8.5 g of *p*-toluenesulfonyl chloride. The resulting solution was stirred at room temperature for 10 hr, during which time solid material precipitated. To the mixture was added excess 2 *N* sulfuric acid, and the mixture was extracted with ethyl ether. The ethereal solution was washed with water and dried. The solvent was evaporated leaving an oily residue which was crystallized and recrystallized from benzene–petroleum ether (1:1) to give 9.0 g of L-*threo*-II-OTs (76% as fine white needles), $[\alpha]^{25}D$ 29.4° (*c* 3, $CHCl_3$), mp 79–80°. The infrared spectrum of the compound contained a broad peak at 1530 cm^{-1} due to both the NO_2 and SO_2 groups and an absorption at 1180 cm^{-1} due to SO_2.[25] *Anal.* Calcd for $C_{17}H_{19}NO_5S$: C, 58.45; H, 5.48. Found: C, 58.42; H, 5.48.

To a solution of 2.3 g of L-*erythro*-II in 3 ml of pyridine was added 2.9 g of *p*-toluenesulfonyl chloride. The reaction and isolation were carried out as described above to yield 4.0 g of L-*erythro*-II-OTs (95% as a thick yellow oil) which could not be crystallized, $[\alpha]^{25}D$ +8.0° (*c* 1, $CHCl_3$). The infrared spectrum was identical with that of the L-*threo* isomer. *Anal.* Calcd for $C_{17}H_{19}NO_5S$: C, 58.45; H, 5.48. Found: C, 58.59; H, 5.70.

Acetates of *threo*- and *erythro*-3-(*p*-Nitrophenyl)-2-butanols (*threo*- and *erythro*-II-Acetates). To 0.30 g of *threo*-II was added 0.37 g of pyridine and 0.47 g of acetic anhydride. The mixture was stirred and heated at 70° for 4 hr, cooled, excess 2 *N* sulfuric acid added, and extracted with ethyl ether. The ethereal solution was washed with water and dried. The solvent was removed and the oily residue heated to 85° under high vacuum (to remove traces of acetic anhydride) to give 0.28 g of *threo*-II-acetate (76% as a light yellow oil) which could not be crystallized. The infrared spectrum showed a strong carbonyl absorption at 1735 cm^{-1} and had the following nmr spectrum: aromatic protons (multiplet, 4.00 protons) centered at τ 2.19; methine proton (symmetrical quintet, 1.10 protons) centered at 4.85; methine proton (symmetrical quintet, 1.07 protons) centered at 6.92; acetoxy methyl protons (singlet, 3.03 protons) at 8.08; two methyl groups (multiplet, 6.30 protons) centered at 8.73. *Anal.* Calcd for $C_{12}H_{15}NO_4$: C, 60.75; H, 6.37. Found: C, 60.84; H, 6.19.

To 0.16 g of *erythro*-II was added 0.19 g of pyridine and 0.25 g of acetic anhydride. The reaction and product isolation were carried out as above to give an oil which was crystallized from petroleum ether to give 0.12 g of *erythro*-II-acetate (61% as light yellow needles), mp 63–65°. The infrared spectrum was very similar to that for the *threo* isomer. The aromatic and methine protons gave the identical nmr spectrum as the *threo* isomer, and the remaining part of the spectrum is as follows: acetoxy methyl protons (singlet, 3.08 protons) at τ 7.90 and two methyl groups (symmetrical quartet, 6.43 protons) centered at 8.74. *Anal.* Calcd for $C_{12}H_{15}NO_4$: C, 60.75; H, 6.37. Found: C, 60.88; H, 6.33.

Acetolysis of L-*threo*- and L-*erythro*-3-(*p*-Nitrophenyl)-2-butyl Tosylates (L-*threo*-II-OTs and L-*erythro*-II-OTs). A solution was prepared by dissolving 2.45 g of L-*threo*-II-OTs and 0.69 g of freshly fused potassium acetate in 50 ml of a mixture of 99% dry glacial acetic acid and 1% acetic anhydride. This solution was held at 100° for 38 hr and cooled and 100 ml of ether–pentane (1:3) was added. The resulting mixture was extracted three times with 200-ml portions of water and dried. The solvent was evaporated and the resulting oily residue (1.3 g) was chromatographed over 260 g of silica gel. Elution successively with: 0.6 l. of pentane produced nothing; 1.6 l. of ether–pentane (2:98) produced 0.837 g of a light yellow mixture of liquid olefins (68%); 2.5 l. of ether–pentane (5:95) first produced 0.064 g of a yellow oil not identified (but an nmr spectrum suggested it to be rearranged 2-(*p*-nitrophenyl)-2-butyl acetate (3.8%)) and then 0.215 g of a yellow oil found to be a mixture of *threo*- and *erythro*-II-acetates (13%). The infrared spectrum of the olefin mixture gave a weak absorption in the C=C region (1660 cm^{-1}) and the characteristic peaks for the nitro group,[25] but no other functional groups were visible. Olefinic protons were observed in the nmr, and this liquid had a neat rotation $\alpha^{25}D$ +2.2° (*l* 1). The acetate fraction was found to be a mixture of 7% *threo*- and 93% *erythro*-II-acetates by nmr analysis.

A solution was prepared by dissolving 1.50 g of L-*erythro*-II-OTs and 0.41 g of freshly fused potassium acetate in 30 ml of a mixture of 99% dry glacial acetic acid–1% acetic anhydride. The reaction was carried out as described above to give a yellow liquid residue (0.60 g) which was chromatographed over 120 g of silica gel in a manner analogous to that described above. The initial eluted material was an olefinic mixture (0.42 g, 57%); the next eluted material amounted to only about 10 mg (possibly rearranged acetate, 1%); the last material eluted was the secondary acetate mixture (0.090 g, 9%) found by nmr analysis to be 10% *threo*- and 90% *erythro*-II-acetates.

A solution was prepared by dissolving 1.82 g of L-*threo*-II-OTs and 0.51 g of freshly fused potassium acetate in 37 ml of a mixture of 99% dry glacial acetic acid–1% acetic anhydride. This solution was held at 75° for 407 hr (about three half-lives), and the products were isolated (*vide supra*). The mixture of olefins amounted to 0.678 g (73%), and the secondary acetate, which was shown by nmr analysis to be 7% *threo* and 93% *erythro*, amounted to 0.190 g (15%).

***threo*-3-(*p*-Nitrophenyl)-2-butyl Formate (*threo*-II-Formate).** To a solution of 1.0 g of *threo*-II in 0.4 ml of 90% formic acid was added three drops of 6 *N* sulfuric acid, and the resulting mixture was heated at 70° for 10 hr. The reaction mixture was then cooled

(25) K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, Inc., San Francisco, Calif., 1962, pp 50, 55.

and ethyl ether added, and the resulting solution was extracted with two portions of water and dried. The solvent was evaporated, leaving 0.70 g of *threo*-II-formate (61% as a light yellow oil). The infrared spectrum of this compound contained a carbonyl absorption at 1730 cm^{-1} and the nmr spectrum contained the following: aromatic protons (multiplet, 4.0 protons) centered at τ 2.17, formoxy proton (singlet, 0.99 proton) at 2.02, methine proton (symmetrical quintet, 0.80 proton) centered at 4.72, methine proton (symmetrical quintet, 1.05 protons) centered at 6.89, methyl protons (multiplet, 6.37 protons) centered at 8.70. *Anal.* Calcd for $C_{11}H_{13}NO_4$: C, 59.18; H, 5.87. Found: C, 59.27; H, 5.76.

Formolysis of L-*threo*- and L-*erythro*-3-(*p*-Nitrophenyl)-2-butyl Tosylates (L-*threo*-II-OTs and L-*erythro*-II-OTs). A solution was prepared by dissolving 3.80 g of L-*threo*-II-OTs and 0.73 g of sodium formate in 76 ml of dry formic acid. The resulting solution was placed in a round-bottomed flask, fitted with a drying tube, and heated at 50° for 38 hr and then at 75° for an additional 3 hr. After cooling, the mixture was shaken with 150 ml of ether–pentane (1:3) and 300 ml of water. The aqueous layer was discarded, and the organic phase was extracted with 200-ml portions of water and dried. The solvent was evaporated, leaving 1.85 g of an oily residue which was chromatographed over 370 g of silica gel. Elution successively with: 0.7 l. of pentane produced nothing; 2.0 l. of ether–pentane (2:98) produced 1.378 g of a light yellow liquid which was shown by infrared and nmr spectra to be a mixture of olefins (72%) having a neat rotation $\alpha^{25}D$ +1.0° (1 dm); 3.0 l. of ether–pentane (5:95) initially produced about 0.070 g of a yellow oil (unidentified) and then 0.256 g of a yellow oil determined to be a mixture of *threo*- and *erythro*-II-formates (11%). This latter material possessed infrared and nmr properties which were almost identical with those of the authentic II-formate described above. This mixture of formates was converted to the corresponding mixture of acetates in 55% yield (*vide infra*). Analysis by nmr showed this mixture to be 30% *threo* and 70% *erythro*.

A solution was prepared by dissolving 2.70 g of L-*erythro*-II-OTs and 0.52 g of sodium formate in 54 ml of dry formic acid. The reaction was carried out as described above to yield a yellow liquid residue (1.10 g) which was chromatographed over 200 g of silica gel in a manner analogous to that just described. The first material eluted was the olefin mixture (0.811 g, 59%) which had a neat rotation $\alpha^{25}D$ +0.65° (1 dm). An unidentified yellow oil (7 mg) was eluted next, and lastly the formate mixture (0.165 g, 9%) was eluted. This mixture was converted to the corresponding mixture of acetates in 62% yield (*vide infra*) and found by nmr analysis to be 37% *erythro* and 63% *threo*.

Trifluoroacetate of a Mixture of 3-(*p*-Nitrophenyl)-2-butanol Diastereomers (II-Trifluoroacetate). A mixture of 0.60 g of 3-(*p*-nitrophenyl)-2-butanol, 120 g of trifluoroacetic anhydride, and 0.60 g of pyridine was stirred for 6 hr at room temperature. An excess of 2 *N* sulfuric acid was then added and the product extracted with ethyl ether. The ethereal solution was washed with water and dried. The solvent was removed leaving an oil. This material was chromatographed over 30 g of silica gel. Elution of the column with ether–pentane (5:95) produced 0.42 g of the ester (47%) as a yellow oil. The infrared spectrum showed a carbonyl absorption at 1770 cm^{-1}. The following nmr spectrum was obtained: aromatic protons (multiplet, 4.00 protons) centered at τ 2.20, methine proton (symmetrical quintet, 0.88 proton) centered at 4.73, methine proton (symmetrical quintet, 0.71 proton) centered at 6.80, two methyl groups (multiplet, 6.50 protons) centered at 8.65. *Anal.* Calcd for $C_{12}H_{12}F_3NO_4$: C, 49.49; H, 4.15. Found: C, 49.70; H, 4.03.

Trifluoroacetolysis of *threo*- and *erythro*-3-(*p*-Nitrophenyl)-2-butyl Tosylates (*threo*- and *erythro*-II-OTs). The solvolysis medium was prepared by dissolving 0.58 g of anhydrous sodium carbonate in 70 ml of dry trifluoroacetic acid (1% in trifluoroacetic anhydride) and adding 1.3 g of trifluoroacetic anhydride. To this solution was added 3.47 g of *threo*-II-OTs, and the resulting solution was refluxed (72°) for 12 hr. After cooling the solution, 100 ml of ether–pentane (1:3) was added and the resulting mixture extracted three times with 200-ml portions of water and dried. The solvent was removed, and the resulting oily residue (1.32 g) was chromatographed over 250 g of silica gel. Elution with 1.5 l. of ether–pentane (1:99) produced 0.996 g of a light yellow liquid, shown to be olefinic by its infrared and nmr spectra (57%). Elution with 2 l. of ether–pentane (5:95) produced 0.268 g yellow oil, shown by comparison of its tlc, infrared, and nmr properties with an authentic sample to be the trifluoroacetate of II (9.3%). Conversion of this ester to the acetate (*vide infra*) in 40% yield and subsequent nmr analysis showed it to be a mixture of 95% *threo* and 5% *erythro* isomers.

The solvolysis medium was prepared by dissolving 0.50 g of anhydrous sodium carbonate in 60 ml of dry trifluoroacetic acid (1% in trifluoroacetic anhydride) and adding 1.10 g of trifluoroacetic anhydride. To this solution was added 2.99 g of *erythro*-II-OTs. The reaction was carried out as described above for the *threo* isomer to give 1.31 g of an oily residue which was chromatographed on 250 g of silica gel. Elution with 1.6 l. of ether–pentane (1:99) removed 1.055 g of a yellow liquid shown to be olefinic (69%), and further elution with 2 l. of ether–pentane (5:95) produced 0.263 g of a yellow oil which was shown to be the trifluoroacetate of II (10%). Conversion of this ester to the corresponding acetate (*vide infra*) in 36% yield and subsequent nmr analysis showed it to be a mixture of 72% *erythro* and 28% *threo* isomers.

Representative Conversion of Ester Products of Solvolyses to the Corresponding Mixture of Diastereomeric 3-(*p*-Nitrophenyl)-2-butanols. Diastereomeric mixtures of II-acetates from acetolysis, of II-formates from formolysis, and of II-trifluoroacetates from trifluoroacetolysis were all converted to the corresponding mixture of alcohols by the same method. A representative reaction is the following. To 9.5 ml of methanol were added 0.187 g of a mixture of *threo*- and *erythro*-II-acetates and three drops of concentrated hydrochloric acid; the resulting solution was refluxed for 15 hr, cooled, and excess methanol and methyl acetate evaporated. The residue (0.102 g) was dissolved in ethyl ether, extracted with water, and dried; the solvent was evaporated leaving a residue that was shown to be pure II by comparing its tlc and spectral properties with authentic alcohol (0.092 g, 60%). Control experiments (*vide infra*) demonstrated that the ester diastereomeric balance was maintained in the resulting alcohol.

L- and D-3-(*p*-Nitrophenyl)-2-butanone. The oxidation of II to ketone was carried out under neutral conditions as described by Pfitzner and Moffatt.[11] A mixture of 0.10 g of L-*threo*-II, 1.25 ml of dimethyl sulfoxide, 0.04 ml of pyridine, and 0.02 ml of trifluoroacetic acid was prepared and 0.31 g of dicyclohexylcarbodiimide added. The mixture was stoppered and allowed to stir at room temperature for 10 hr, after which the dicyclohexylurea which had formed was filtered and 20 ml of ethyl ether added. This solution was extracted successively with two, 30-ml portions of pH 7.1 phosphate buffer and two, 30-ml portions of water. The mixture was filtered again and dried, and the solvent was evaporated. The resulting oil was subjected to filtration chromatography over 3 g of silica gel. Elution with 70 ml of pentane removed unidentified, fast moving material. This was followed by elution with about 70 ml of ether–pentane (5:95) to remove solid material. This material was then sublimed at 50° (0.4 mm) to yield 38 mg of L-3-(*p*-nitrophenyl)-2-butanone (38% as white crystals), $[\alpha]^{25}D$ −192° (*c* 1, chloroform), mp 51.5–52.5°. The infrared spectrum showed a strong carbonyl absorption at 1710 cm^{-1}, and the nmr spectrum was the following: aromatic protons (multiplet, 4.00 protons) centered at τ 2.13, methine proton (quartet, J = 7 cps, 1.00 proton) centered at 6.00, methyl protons (singlet, 3.30 protons) at 7.84, methyl protons (doublet, J = 7 cps, 3.30 protons) centered at 8.52. *Anal.* Calcd for $C_{10}H_{11}NO_3$: C, 62.17; H, 5.74. Found: C, 62.47; H, 5.86.

The identical oxidation was performed on 94 mg of L-*erythro*-II (94% optically pure) to yield 32 mg of L-3-(*p*-nitrophenyl)-2-butanone, $[\alpha]^{25}D$ −181° (*c* 1, chloroform), mp 50.5–52.0°.

Control Experiment to Demonstrate the Stability of a Mixture of Diastereomeric 3-(*p*-Nitrophenyl)-2-butyl Acetates to Acetolysis Conditions and to Demonstrate Nonselectivity in Oxidation of the Resulting Alcohol Mixture. A mixture of 0.147 g of L-*threo*-II-acetate and 0.066 g of racemic *erythro*-II-acetate (69:31) was prepared and shown by nmr analysis to be 71% *threo* and 29% *erythro*. This mixture (0.200 g) was dissolved in a solution of 1.25 g of anhydrous *p*-toluenesulfonic acid (0.0073 mol) and 0.83 g of freshly fused potassium acetate (0.0083 mol) in 60 ml of dry glacial acetic acid. The resulting solution was held at 100° for 50 hr, cooled, and acetate isolated (*vide supra*). This acetate mixture (0.167 g) was reanalyzed by nmr, showing 68% *threo* and 32% *erythro*. Conversion of this mixture to the corresponding alcohol mixture (0.113 g) by transesterification and subsequent oxidation produced ketone with $[\alpha]^{25}D$ −137° (*c* 1, chloroform). Therefore, 71% optically pure L-ketone was produced as expected.

Control Experiment to Demonstrate Nonselectivity in the Hydrolysis of a Diastereomeric Mixture of 3-(*p*-Nitrophenyl)-2-butyl Acetates and in Acylation of the Corresponding Mixture of Alcohols. A diastereomeric mixture of II-acetates was prepared and shown by

Table VI. First-Order Polarimetric Rate Studies

Solvent	Temp, °C	Obsd rotation: Initial	Obsd rotation: Final	k, sec^{-1}
HOAc	75.25 ± 0.03	0.685	0.040	(1.68 ± 0.02) × 10^{-6}
HOAc	75.25 ± 0.03	0.685	0.040	
HOAc	100.50 ± 0.05	0.966	0.071	(3.08 ± 0.05) × 10^{-5}
HOAc	100.50 ± 0.05	0.968	0.068	
HCO_2H	49.85 ± 0.03	0.616	0.042	(1.39 ± 0.02) × 10^{-5}
HCO_2H	49.85 ± 0.03	0.611	0.043	
HCO_2H	65.40 ± 0.03	0.590	0.044	(8.92 ± 0.10) × 10^{-5}
HCO_2H	65.40 ± 0.03	0.587	0.044	

nmr analysis to be 60% *threo* and 40% *erythro*. This mixture (193 mg) was both converted to the corresponding alcohols and reconverted to the acetates by the methods described above (120 mg). Analysis by nmr showed that the mixture was 60% *threo* and 40% *erythro*, and thus the hydrolysis and acylation reactions were nonselective.

Control Experiment to Demonstrate the Stability of a Mixture of Diastereomeric 3-(*p*-Nitrophenyl)-2-butyl Formates to Formolysis Conditions. A mixture of *threo*- and *erythro*-II-formates was prepared and separated into two parts. One portion (0.20 g) was dissolved in a solution of 0.97 g of anhydrous *p*-toluenesulfonic acid (0.0056 mol) and 0.45 g of sodium formate (0.0066 mol) in 50 ml of dry formic acid. The resulting solution was held at 75° for 4 hr and cooled and the formate reisolated (*vide supra*) to give 0.17 g. This formate mixture and the formate mixture which was not subjected to formolysis conditions were each converted to the corresponding diastereomeric mixtures of II-acetates. Analysis of these acetate mixtures by nmr showed one to be 76% *threo* and 24% *erythro* and the other to be 77% *threo* and 23% *erythro*, demonstrating that formolysis conditions do not affect the diastereomeric balance of the product esters, once formed.

Control Experiment to Demonstrate the Stability of a Diastereomeric Mixture of 3-(*p*-Nitrophenyl)-2-butyl Trifluoroacetates to Trifluoroacetolysis and to Demonstrate Nonselectivity in the Ester Hydrolysis. A mixture of *threo*- and *erythro*-II was prepared and part of this mixture converted directly to the corresponding mixture of acetates. Analysis by nmr showed it to be 17% *threo* and 83% *erythro*. The remaining alcohol mixture was converted to the corresponding mixture of trifluoroacetates (0.15 g) which was dissolved in 10 ml of dry trifluoroacetic acid containing sodium trifluoroacetate and the mixture was refluxed for 25 hr. The ester was reisolated in the usual way (0.12 g) and converted to the corresponding mixture of acetates. Analysis by nmr demonstrated it to be 17% *threo* and 83% *erythro*.

Effect of Trifluoroacetolysis Medium on 3-Phenyl-1-butene. A solution was prepared by adding 0.24 g of dry sodium carbonate and 0.69 g of *p*-toluenesulfonic acid to a mixture of 0.53 g of trifluoroacetic anhydride in 25 ml of trifluoroacetic acid. To this solution was added 0.22 g of 3-phenyl-1-butene.[26] The solution was refluxed for 10 hr, cooled, water was added, and the mixture extracted with pentane. The extract was washed with water and dried. The solvent was evaporated and the resulting liquid analyzed by vapor phase chromatography (vpc) on a Perkin-Elmer Model 151 vapor fractometer. The column used was 23% pimelonitrile on 60–80 Firebrick, 3 ft in length. At 89° (10 psi of helium), the olefin had a retention time of 7.3 min and that of the trifluoroacetate was 25.3 min. It was found (by the cut and weigh method) that 7% of the liquid was olefin and 93% was ester. These compounds were separated by silica gel chromatography by eluting with pentane, and the ester obtained was converted to alcohol. This alcohol was then analyzed by vpc on the same instrument using a 3-ft column of 10% hyprose on Chromosorb W. At 75° (10 psi of helium), the *erythro* alcohol had a retention time of 19.3 min and the *threo* alcohol retention time was 13 min (ester retention time is 0.7 min). Analysis (cut and weigh) showed the mixture to be 42% *threo* and 58% *erythro*-I.

Tosylate of 2-(*p*-Nitrophenyl)ethanol. From 20.0 g of 2-phenylethyl acetate was prepared 2.4 g of 2-(*p*-nitrophenyl)ethanol,[27] mp 61–62° (lit.[27] mp 62°). This alcohol (2.0 g) was added to 3.4 g of *p*-toluenesulfonyl chloride and 4.0 ml of pyridine. The reaction and work-up were carried out as described above for other tosylates to give a solid. This material was recrystallized from benzene–petroleum ether (1:1) to give 2.8 g of 2-(*p*-nitrophenyl)ethyl tosylate (73% as white crystals), mp 131.5–132.5°. *Anal.* Calcd for $C_{15}H_{15}NO_5S$: C, 56.06; H, 4.71. Found: C, 55.98; H, 4.65.

Titrimetric Acetolysis Rate Studies of the Tosylates of *threo*- and *erytho*-3-(*p*-Nitrophenyl)-2-butanols (*threo*-II-OTs and *erythro*-II-OTs) and the Tosylate of 2-(*p*-Nitrophenyl)ethanol. The kinetic procedure used and treatment of the data are identical with that described previously.[24] Each run was made in duplicate, and the rate constant chosen was usually the average of the two values. From seven to nine points were recorded during the first two half-lives, and the infinity point was determined after about ten half-lives at 100° for each run. Isomer *threo*-II-OTs gave: at 74.98 ± 0.03°, k = (1.58 ± 0.15) × 10^{-6} sec^{-1} and k = (1.46 ± 0.04) × 10^{-6} sec^{-1}; at 100.66 ± 0.05°, k = (2.78 ± 0.02) × 10^{-5} sec^{-1} and k = (2.95 ± 0.09) × 10^{-5} sec^{-1}. Isomer *erythro*-II-OTs gave: at 74.98 ± 0.03°, k = (1.72 ± 0.05) × 10^{-6} sec^{-1} and k = (1.64 ± 0.03) × 10^{-6} sec^{-1}; at 100.66 ± 0.05°, k = (2.76 ± 0.10) × 10^{-5} sec^{-1} and k = (3.26 ± 0.04) × 10^{-5} sec^{-1}. The tosylate of 2-(*p*-nitrophenyl)ethanol gave: at 100.52 ± 0.05°, k = (1.90 ± 0.02) × 10^{-6} sec^{-1} and k = (2.00 ± 0.02) × 10^{-6} sec^{-1}.

Polarimetric Acetolysis and Formolysis Rate Studies of L-*threo*-3-(*p*-Nitrophenyl)-2-butyl Tosylate. Solutions of L-*threo*-II-OTs in acetic acid (0.0594 *M*) and in formic acid (0.0496 *M*) were prepared in volumetric flasks and 1.2-ml aliquots were withdrawn and sealed into clean ampoules. These ampoules were then thermostated at the designated temperatures, an ampoule was cooled to 0° for each point, and stored at 5° until all points in a run could be determined. Each ampoule was then opened, and the rotation was determined at 25° and λ 436 mμ. For each run, eight or nine points were determined in the first two half-lives and each run was done in duplicate. The acetolysis infinity points were determined after more than ten half-lives at 100°, while the formolysis half-lives were determined after more than ten half-lives at 75°. Small corrections were made in each point for the estimated component of the rotation due to optically active products. The ampoules corresponding to the same point in the duplicate runs were quenched simultaneously, and the average of their rotations was used to compute the rate constant (the data then being treated as before[24]) (see Table VI).

Polarimetric Trifluoroacetolysis Rate Studies of D-*threo*-3-Phenyl-2-butyl Tosylate and L-*threo*-3-(*p*-Nitrophenyl)-2-butyl Tosylate (D-*threo*-I-OTs and L-*threo*-II-OTs). Solutions of D-*threo*-I-OTs (0.049 *M*) and L-*threo*-II-OTs (0.029 *M*) in trifluoroacetic acid were prepared in volumetric flasks (because of the extreme reactivity of D-*threo*-I-OTs, its solution was prepared rapidly with chilled solvent and used immediately). A jacketed 1-dm polarimeter cell (1-ml capacity) was then filled with each solution successively, and with thermostated water circulating, the rotations were measured at intervals at λ 436 mμ (D-*threo*-I-OTs) or λ 546 mμ (L-*threo*-II-OTs). For the first 2 half-lives, 10 or 11 points were taken and the infinity points were determined after more than 10 half-lives. The infinity rotations were close to zero and no corrections were necessary. Duplicate runs were made and the rate constant chosen was the average of the two. Isomer D-*threo*-I-OTs gave: at 0.70 ± 0.05°, k = (1.06 ± 0.01) × 10^{-3} sec^{-1} and k = (1.05 ± 0.02) × 10^{-3} sec^{-1}. Isomer L-*threo*-II-OTs gave: at 42.00 ± 0.05°, k = (9.26 ± 0.06) × 10^{-6} sec^{-1} and k = (9.30 ± 0.06) × 10^{-6} sec^{-1}; at 56.90 ± 0.05°, k = (5.24 ± 0.03) × 10^{-5} sec^{-1} and k = (5.13 ± 0.02) × 10^{-5} sec^{-1}.

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