[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Studies in Stereochemistry. XXVII. Conformational Control of the Migrating Group in the Deamination of 3-Phenyl-2-butylamine[1]

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The optically pure stereoisomers of 3-phenyl-2-butylamine have been deaminated in acetic acid and the products examined. With the *threo* isomer, methyl migration from C_β dominated over phenyl migration by a factor of 1.5 to 1, whereas with the *erythro* isomer, phenyl migration from C_β exceeded methyl migration by a factor of about 8 to 1. Methyl migration could not be detected when the stereoisomeric 3-phenyl-2-butyl tosylates were acetolyzed. These results coupled with those of others support the following hypothesis. Neither solvent nor neighboring group participation play much role in the breaking of the $C-N_2^+$ bond, and the fate of the *high energy open carbonium ion* thus created is determined by the relative proximity of the various neighboring groups and of solvent molecules. The relative positions of these species are therefore determined by the conformational populations of the starting diazotized amine. The products of methyl migration were partially optically active at the migration origin, this benzyl carbon atom having been partially inverted during the methyl migration. This result provides some evidence for the intervention of a *bridged methyl carbonium ion* intermediate in the rearrangement.

The propensity of the deamination reaction of aliphatic amines for initiating molecular rearrangements has been established by a large number of investigations. A number of recent mechanistic studies and observations have a direct bearing on the present research. Bernstein and Whitmore[2] demonstrated that the highly stereospecific rearrangement of (−)-1,1-diphenyl-2-amino-1-propanol to (+)-1,2-diphenyl-1-propanone observed much earlier by McKenzie, *et al.*,[3] occurred with inversion at the migration terminus. Roberts and co-workers[4c] found both methyl and hydrogen migration in the deamination of *n*-propylamine, but in this and other systems could find no evidence for the intervention of either hydrogen-[4a] or methyl-bridged carbonium ions.[4c,d] In the deamination of various *p*-substituted β-phenylethylamines, these authors[4b] observed a much smaller difference between the migratory aptitudes of *p*-nitrophenyl, phenyl and *p*-methoxyphenyl than had been observed in studies involving leaving groups other than N_2^+. Burr and Ciereszko[5] found in parallel studies of β-aryl-β-phenylethyl systems that with OH as a leaving group much greater differences in migratory aptitudes of phenyl and substituted phenyl were observed than when the leaving group was N_2^+. Curtin and co-workers[6] in an elegant study of the semipinacolic deamination reaction of various diastereomeric 2-phenyl-2-aryl-1-phenyl (or methyl)-1-ethylamines demonstrated that that aromatic nucleous migrated which gave a transition state where the bulky (non-migrating) groups attached to the two asymmetric carbon atoms were distributed *trans* to one another.

The present study describes the deaminative acetolysis of the optically pure diastereomers of 3-phenyl-2-butylamine (I). This system possesses certain peculiar advantages for mechanistic studies. (1) The acetolysis of 3-phenyl-2-butyl tosylate has been thoroughly studied,[7] and the effects of differences between tosylate and N_2 as leaving group can be assessed. (2) The intervention of "ethylenephenonium ions" as intermediates in the migration of phenyl from C_β to C_α can be detected making use of the symmetry properties of this system. (3) The three groups on C_β, phenyl, methyl and hydrogen, all compete with one another in undergoing Wagner–Meerwein rearrangements, and in this system a correlation between the amounts of each group which migrate and the known configurations of the starting material is possible. (4) The system allows the stereochemistry of methyl migration to be examined at the migration origin (C_β).

Three of the four optically pure stereomers of the 3-phenyl-2-butylamine system were prepared and their configurations determined in a previous study.[8] All four of the optically pure benzamide derivatives were reported.[8] In the current investigation the fourth isomeric amine possessing the D(−)-*erythro* configuration was prepared by the simple inversion in dioxane of the tosylate of optically pure D(−)-*threo*-3-phenyl-2-butanol. The rotation of this amine (α^{25}D −9.20°, *l* 1 dm., neat) compares favorably with that of its enantiomer prepared by direct resolution (α^{25}D +9.01°, *l* 1 dm., neat).

The methods of analysis and separation of the products of the deamination of the active isomers of 3-phenyl-2-butylamine are recorded in the Experimental, along with a number of control experiments on the solvolyses, the separations and the analyses.

Discussion

Table I records the yields of the various alcohol components obtained from the deaminative acetolysis of the stereomers of 3-phenyl-2-butylamine, as well as those obtained in previous studies[7] of the acetolyses under similar conditions of the tosylates

(1) This work was sponsored by the Office of Ordnance Research, U. S. Army.

(2) H. I. Bernstein and F. C. Whitmore, THIS JOURNAL, **61**, 1324 (1939).

(3) A. McKenzie, R. Roger and G. O. Wills, *J. Chem. Soc.*, 779 (1926).

(4) (a) J. D. Roberts and J. A. Yancey, THIS JOURNAL, **74**, 5943 (1952); (b) J. D. Roberts and C. M. Regan, *ibid.*, **75**, 2069 (1953); (c) J. D. Roberts and M. Halmann, *ibid.*, **75**, 5759 (1953); (d) J. D. Roberts and J. A. Yancey, *ibid.*, **77**, 5558 (1955).

(5) (a) J. G. Burr, Jr., and L. S. Ciereszko, *ibid.*, **74**, 5426 (1952); (b) **74**, 5431 (1952).

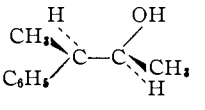
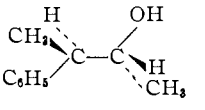
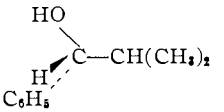
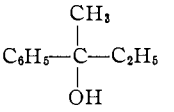
(6) (a) P. I. Pollak and D. Y. Curtin, *ibid.*, **72**, 961 (1950); (b) D. Y. Curtin and P. I. Pollak, *ibid.*, **73**, 992 (1951); (c) D. Y. Curtin, E. E. Harris and P. I. Pollak, *ibid.*, **73**, 3453 (1951); (d) D. Y. Curtin and E. K. Meislich, *ibid.*, **74**, 5518 (1952); (e) **74**, 5905 (1952); (f) D. Y. Curtin and M. C. Crew, *ibid.*, **76**, 3719 (1954); (g) **77**, 354 (1955).

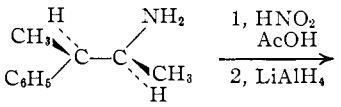
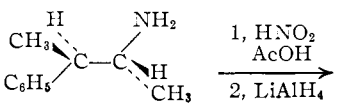
(7) (a) D. J. Cram, *ibid.*, **71**, 3863 (1949); (b) **74**, 2129 (1952); (c) **74**, 2137 (1952).

(8) D. J. Cram and J. E. McCarty, *ibid.*, **76**, 5740 (1954).

TABLE I

ALCOHOLIC PRODUCTS OF THE DEAMINATIVE AND TOSYLATE ACETOLYSIS OF THE 3-PHENYL-2-BUTYL SYSTEMS[a,b]

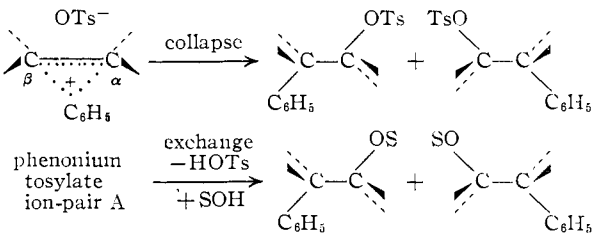
	Yield[b] *threo*, % Active	Racemic	Yield[b] *erythro*, % Active	Racemic	Yield,[b] % Active	Racemic	Yield,[b] %	Yield alcohol fraction,[c] %
 1, HNO_2, AcOH; 2, $LiAlH_4$	6	19	14	5	5	27	24[d]	50
[L(+)-*threo*-I] L(+)-*threo*-3-phenyl-2-butyl tosylate; 1, AcOH; 2, $LiAlH_4$	0.5	85	1	2.5	0	0	11	70
 1, HNO_2, AcOH; 2, $LiAlH_4$	6	0	68	0	0.2	6	20[d]	50
[L(+)-*erythro*-I] L(+)-*erythro*-3-Phenyl-2-butyl tosylate; 1, AcOH; 2, $LiAlH_4$	5	0	89	0	0	0	6	74

[a] The deaminative and tosylate acetolysis (ref. 7c) were both run at room temperature. However, a complete analysis of the secondary alcohol components of tosylate acetolysis was made only on product obtained from runs at 75° (ref. 11b). Enough data were obtained at both temperatures to indicate the patterns of results to be almost identical. The ratios of the various secondary alcohols to one another were taken from the runs at 75°. [b] Total alcohol fraction = 100%. [c] Starting amine or tosylate = 100%. [d] These are maximum values. Actual values are probably lower (see Experimental).

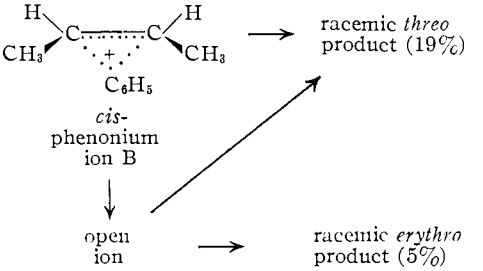
of the stereomers of 3-phenyl-2-butanol (III). In the deamination reaction each diastereomer gave appreciable but different amounts of products resulting from simple solvolysis (no rearrangement), from phenyl migration, from hydrogen and from *methyl migration*. In the tosylate solvolysis, the products of phenyl migration (3-phenyl-2-butanol) clearly dominated in both diastereomeric series, with small amounts of hydrogen migration, very small amounts of simple solvolysis product, and *no detectable product* from *methyl migration*.

Phenonium Ions as Intermediates in the Deamination Reaction.—In the tosylate solvolyses, both the high stereospecificity[7] and the enhancement of the rate of ionization[9] point to predominant phenyl participation in ionization. A complete analysis of the data for the *threo*-3-phenyl-2-butyl tosylate acetolysis[7c] provided the ratio 66/1 for phenyl over solvent participation in ionization and the ratio of 8/1 for hydrogen over solvent participation. Although a detailed calculation could not be carried out for the *erythro* isomer, it is clear that similar factors apply.[7b] In this and in similarly constituted systems,[10] phenonium tosylate ion-pairs (A) have been demonstrated to result from phenyl participation in ionization. These intermediates can collapse in either direction to give tosylate or can undergo anion exchange to give solvolyzed product. In acetic acid for the *threo*-3-phenyl-2-butyl system, collapse occurs four times as frequently as exchange.[7b]

A very different pattern of products arises in the deaminative acetolysis. That phenyl migrates from C_α to C_β is clear from the fact that in the *threo* series 24% of the alcoholic product is racemic 3-phenyl-2-butanol (III), 19% *threo* and 5% *erythro*. That simple substitution occurs to almost the same extent is indicated by the 20% of active 3-phenyl-2-butanol (6% *threo* and 14% *erythro*) obtained. With the *erythro* isomer, the high yield of product (68%) of configuration identical to that of starting material (substitution with retention) indicates that here as well phenyl migration occurred, although the symmetry properties of the system prevent its direct detection. The 6% of *threo* product indicates a somewhat lower degree of simple solvolysis in this as compared to the *threo* series.

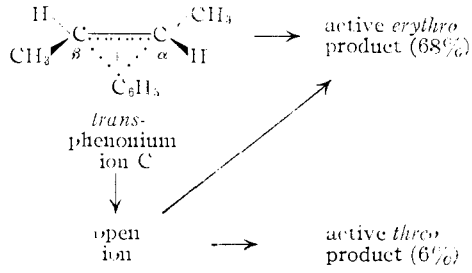


These results indicate a moderate degree of stereospecificity for the process involving phenyl migration but of a much lower order than was observed in tosylate solvolysis. Of the 25% of *threo* product from *threo* starting material, 19% was racemic, pointing to the intervention of the internally compensated phenonium ion (B) as an



(9) S. Winstein and K. C. Schreiber, THIS JOURNAL, **74**, 2165 (1952).
(10) (a) D. J. Cram, *ibid.*, **71**, 3883 (1949); (b) **74**, 2159 (1952).

intermediate. This intermediate appears to have been disposed of both by direct ring opening to give *threo* product and by giving racemic open ion which in turn could go to either racemic *threo* or *erythro* material. This phenonium ion is then different in some respect from that produced from tosylate solvolysis, which only underwent direct ring opening to give racemic *threo* product. This point will be discussed later. In the *erythro* series, the phenonium ion produced is asymmetric, and direct ring



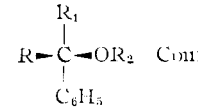
opening at either Cα or Cβ would give active material of the same configuration as the starting material. If this bridged ion gave open ion, this intermediate would be optically active and would give a mixture of active *threo* and *erythro* product. The results suggest that *direct ring opening* predominated in both series, but some rearranged, racemic, open ion is needed to explain the production of 5% racemic *erythro* product obtained from active *threo* starting material.

The Question of Bridged Methylcarbonium Ions as Intermediates in the Wagner–Meerwein Rearrangement.—Although bridged methylcarbonium ions frequently have been discussed[11] and deliberately sought for, not a shred of evidence for their intervention as reaction intermediates has been forthcoming. Some evidence has been obtained from rate comparisons in the solvolysis of neopentyl and more ramified tertiary systems for neighboring methyl participation in ionization,[12] but this means only that the *transition state for ionization is a hybrid* which *possesses some methyl bridged character*. It has not been demonstrated whether this transition state leads to a discrete bridged ion or directly to rearranged open ion.

In the present investigation some evidence for a bridged methylcarbonium ion is presented. From *threo*-amine was obtained alcohol, 32% of which was the product of methyl migration (1-phenyl-2-methyl-1-propanol or II) and from *erythro*-amine 6% was similarly rearranged. Of this rearranged material, 16% was optically active in the *threo* and 3% in the *erythro* runs. The stereochemistry of this rearrangement can be determined only if the relative configurations of reactant and product are known. The configurations of the starting materials have been established relative to D-glyceraldehyde,[8] but the configuration of 1-phenyl-2-methyl-1-propanol (II) has never been determined by chemical interconversions. However, the configuration of this compound can be assigned with a high probability of correctness relative to that of D-glyceraldehyde through the use of Freudenberg's displacement rule.[13,14] Levene, Mikeska and Marker[15] gathered the rotational data set forth in Table II, which when coupled with the known[16] configuration of 1-phenyl-1-ethanol allows the configurations of the other alcohols of Table II to be assigned the structures there set forth. The stereochemistry of the methyl migration thus becomes known and is formulated in Chart I.[17]

TABLE II

CONFIGURATIONS AND MOLECULAR ROTATIONS OF ALKYL SUBSTITUTED BENZYL ALCOHOLS AND DERIVATIVES



Configurational assignment

	Molecular rotations, R_2		
R_1	H[a]	Ac[a]	APTH[b,c]
CH_3	−52.5°	−194°	+32.0°
C_2H_5	−39.4°	−186°	−10.6°
$(CH_2)_2CH_3$	−34.9°	−178°	−21.0°
$CH(CH_3)_2$	−31.4°	−199°[d]	−62.6°
$(CH_2)_3CH_3$	−28.2°	−163°	−36.1°

[a] $M^{25}D$ (l 1 dm., neat). [b] Acid phthalate. [c] $M^{25}D$ (l 1 dm., c 0.01 M, ethanol). [d] From the present investigation.

Any mechanism used to explain this methyl migration must satisfy three main facts. (1) Both racemic and active product were obtained from both diastereomers. (2) The ratios of racemic to active product differ widely for the two diastereomers (*threo*, 5/1; *erythro*, 30/1). (3) In the production of optically active II, the migration origin was inverted. A completely concerted mechanism[18] by which all of the product was produced is thus eliminated, although the very remote possibility remains that the active portion of product arose by a completely concerted process, and the racemic material by a multistage course involving carbonium ions devoid of asymmetry. A mechanism in which *all of the product* arose from such a carbonium ion is also eliminated.

The data support the mechanistic scheme set forth in Chart I.[19] Here the *threo*-amine goes to a methyl bridged asymmetric carbonium ion with inversion of the migration terminus, the phenyl and methyl groups being *trans* to one another. Similarly the *erythro*-amine goes to a methyl bridge, also asymmetric, in which the methyl and

(11) (a) D. J. Cram and J. D. Knight, THIS JOURNAL, **74**, 5831 (1952); (b) S. Winstein and B. K. Morse, *ibid.*, **74**, 1133 (1952); (c) J. D. Roberts, M. Halmann and J. A. Yancey, ref. 8c and 8d; (d) H. C. Brown and R. B. Kornblum, THIS JOURNAL, **76**, 1510 (1954).

(12) (a) P. D. Bartlett, *Bull. soc. chim. France*, [5] **18**, C100 (1919); (b) P. D. Bartlett and M. Stiles, THIS JOURNAL, **77**, 2806 (1955); (c) P. D. Bartlett and M. S. Swain, *ibid.*, **77**, 2801 (1955); (d) S. Winstein and H. Marshall, *ibid.*, **74**, 1120 (1952).

(13) K. Freudenberg, W. Kuhn and I. Bumann, *Ber.*, **63B**, 2380 (1930).

(14) The authors are indebted to Professor H. S. Mosher for bringing this to our attention and wish to express their appreciation.

(15) (a) P. A. Levene and L. A. Mikeska, *J. Biol. Chem.*, **70**, 355 (1926); (b) P. A. Levene and R. E. Marker, *ibid.*, **97**, 381 (1932).

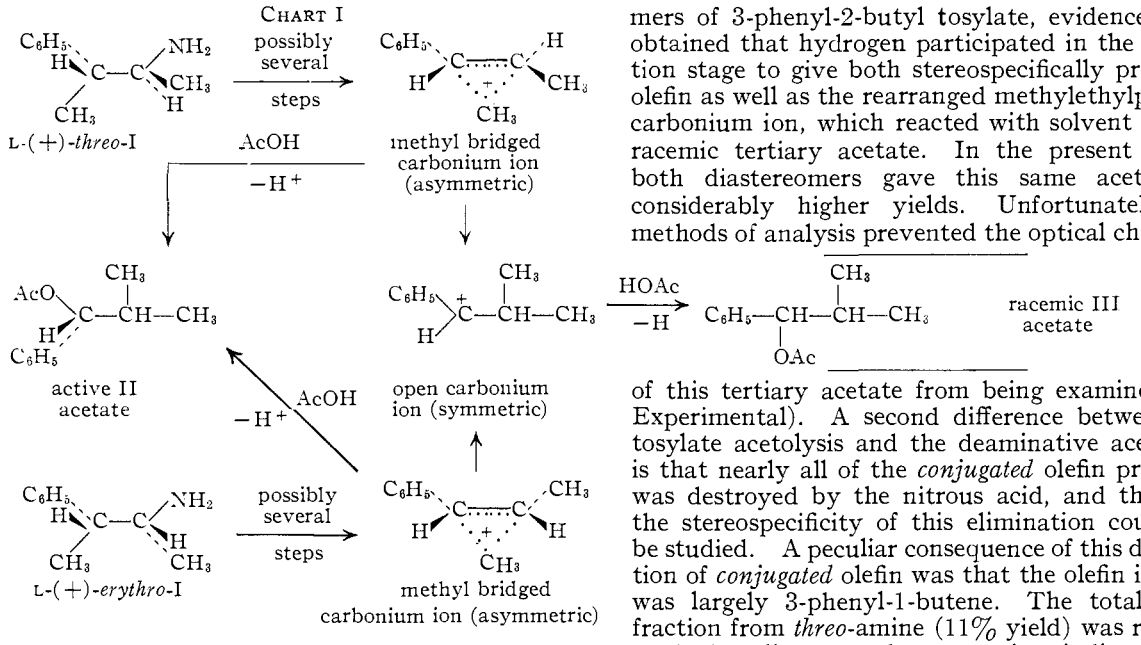
(16) K. Mislow, THIS JOURNAL, **73**, 3954 (1951).

(17) In the configurational formulations of this paper, that enantiomer which is convenient for portrayal is depicted. The fact that in some cases the other enantiomer was actually used in no way affects the principles involved.

(18) A completely concerted Wagner–Meerwein rearrangement (all bonds made and broken in the same transition state) has never been demonstrated and is very improbable.

(19) The stages intervening between starting material and the bridged ion are discussed in a later section.

CHART I



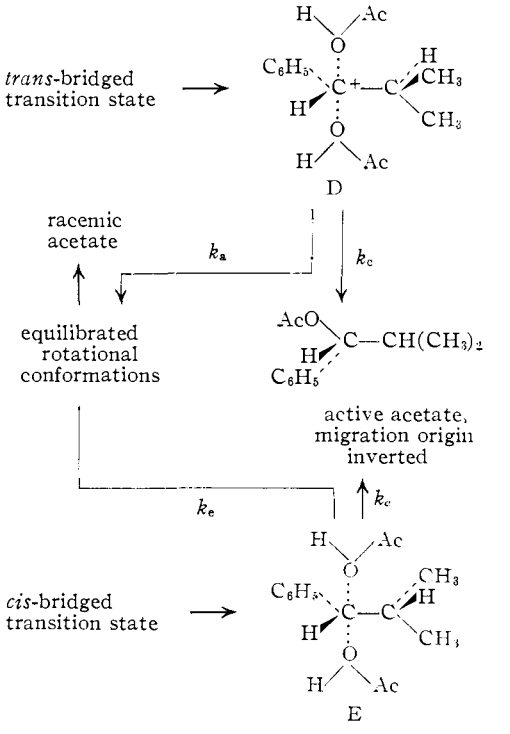
phenyl groups are *cis* to one another. Each of these bridged ions partition between two processes, one involving ring opening at the benzyl carbon to give directly (one transition state) optically active rearranged acetate with the migration origin inverted, the other involving ring opening to give the symmetrical phenyl isopropylcarbonium ion which goes to racemic rearranged acetate. Since the two bridges are diastereomerically related, they would partition differently between these two processes. The *trans* bridge from *threo* material might be expected to be the more stable of the two, and therefore to be the species more favorably disposed to undergo ring opening by solvent to give active product, as is indeed observed.

A second mechanistic scheme should also be considered (Chart II), in which the methyl bridges are transition states, not discrete intermediates. Thus *threo* material passing through a *trans* bridged transition state might give a rearranged disolvated open ion (D) which differs from that from *erythro* material (E) in rotational conformation. Should k_c be the same order of magnitude as k_e, optically active acetate with the migration origin inverted could arise. That D or E collapse *directly* from both sides with equal probability to give racemic material is unlikely, since the steric situation distinctly favors entrance from the top. The ratio of k_c/k_e should differ for D and E, and the greater stability of D should favor a higher value for this ratio, leading to a higher degree of optical activity for rearranged acetate, as was observed.

Of these two explanations, that involving the methyl bridge as a discrete intermediate is preferred on both the basis of simplicity and analogy. Since the leaving group in this deamination reaction is a nitrogen molecule, mechanisms involving rearranged ion-pairs or open carbonium ions solvated by nitrogen on one side and solvent on the other are highly unlikely.

The Hydrogen Migration in the Deamination Reaction.—In the acetolysis of the active diastereomers of 3-phenyl-2-butyl tosylate, evidence[7c] was obtained that hydrogen participated in the ionization stage to give both stereospecifically produced olefin as well as the rearranged methylethylphenylcarbonium ion, which reacted with solvent to give racemic tertiary acetate. In the present study, both diastereomers gave this same acetate in considerably higher yields. Unfortunately the methods of analysis prevented the optical character of this tertiary acetate from being examined (see Experimental). A second difference between the tosylate acetolysis and the deaminative acetolysis is that nearly all of the *conjugated* olefin produced was destroyed by the nitrous acid, and therefore the stereospecificity of this elimination could not be studied. A peculiar consequence of this destruction of *conjugated* olefin was that the olefin isolated was largely 3-phenyl-1-butene. The total olefin fraction from *threo*-amine (11% yield) was reduced to 2-phenylbutane whose rotation indicated the olefin to be free of conjugated material and to have arisen by a completely stereospecific process. This fact prohibits the intervention of phenonium ions in the production of this unconjugated olefin, a point also demonstrated for the tosylate solvolyses. The olefin from *erythro*-amine (4%) reduced to 2-phenylbutene whose activity was only about 80% of what was to be expected from the completely unconjugated olefin which had arisen by a completely stereospecific path. Apparently a small amount of conjugated olefin survived the nitrous acid in this particular run.

CHART II



The Differences in Mechanism Between N_2 and OTs^- as Leaving Groups in Solvolyses.—The above results clearly demonstrate rather gross differences in the mechanisms for the deaminative and tosylate solvolyses. In the deaminative reaction the first stage is very probably the formation of a diazonium ion, which dissociates to a nitrogen molecule and a carbonium ion of some kind. The diazonium ion for aliphatic systems is unstable, and the production of an exceedingly stable nitrogen molecule in the dissociation process should give rise to an exceptionally high energy carbonium ion.[20] The driving force for this reaction should come from the formation of nitrogen[20] and not from neighboring group or solvent participation. Thus neighboring group or solvent probably become involved to an appreciable extent only at a later stage, that is, only after the production of a little-solvated, high energy, very short lived, *open* carbonium ion. The stereochemical consequences of this latter possibility will be examined as applied to the system at hand.

Chart III formulates the three conformations for each of the diastereomeric diazonium ions. Utilizing the principles developed earlier,[21] it seems probable that IV > V > VI and VII > VIII > IX in relative thermodynamic stability, and that in the diazonium ions the populations are distributed accordingly. The process of dissociation probably does not involve rotating any of these substituents through an eclipsed geometry, and the three open ions produced from each of the diastereomers fall into the same stability order as do the conformations of the starting diazonium ion. Since the geometry for the transition states for dissociation lies somewhere between that of the diazonium ion and the open ion,[22] the activation energies for dissociation of the three conformers should be very similar. Therefore, the relative populations of the three open ions from each diastereomer would be similar to those of the starting diazonium ions. If these open, flat carbonium ions are of such high energy that their half-lives are much less than the half-lives of their rotation through 60° about the C_β–C_α bond, then their fate is determined by the relative proximity of their nearest neighbors (solvent or β-substituents). Thus the relative nucleophilicity of these neighbors plays a minor role and the relative conformational populations of the starting diazonium ion become controlling in the ultimate balance of products. In such a scheme, the neighboring β-substituents must still approach the face of the carbonium ion opposite from that which the nitrogen left but for a reason different from that in which the β-substituents actually participate in carbonium ion formation. If F, one of the three conformations of a diazonium ion, dissociates to give open carbonium ion G, then "a" on C_β is flanked by "d" and "e" on C_α. Thus "a" is the only substituent on C_β which is eclipsed

F G

with the relatively unsolvated and empty p-orbital of the short lived "hot" carbonium ion. Other groups (b and c) could become involved only if rotation about C_β–C_α occurred to the extent of either 60 or 120°.

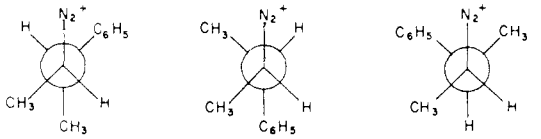
This hypothesis suggests that in the deamination of *threo*-3-phenyl-2-butylamine, methyl migration should exceed phenyl which should exceed hydrogen migration. The data (Table I) show that methyl accounted for 32%, phenyl for 24% and hydrogen migration for a maximum of 24% of the acetate produced.[23] For the *erythro* series, the hypothesis would predict that phenyl would predominate over hydrogen, which would exceed methyl migration. Of the acetate produced by this diastereomer (Table I), up to 68% could have involved phenyl[24] migration, a maximum of 20% hydrogen and only 6% methyl migration.

Two features make it unlikely that eclipsing effects in the formation of bridged transition states control the migrating group in these diastereomeric series. (1) These eclipsing effects played little or no role in either selecting the migrating group or effecting the rates of ionization for the acetolysis of the diastereomers of 3-phenyl-2-butyl tosylate. If eclipsing effects were important in this system, they certainly would be more likely to assert themselves in tosylate solvolysis where driving forces due to neighboring group participation are present. (2) The groups that are being eclipsed are rather small (*e.g.*, two methyl groups during phenyl migration in the *threo* series). In other reactions in other systems, the "*cis* effect" becomes important only when a medium and large or two large groups become involved.[25]

Tosylate and halide solvolyses differ in a second important respect from deaminative solvolyses.

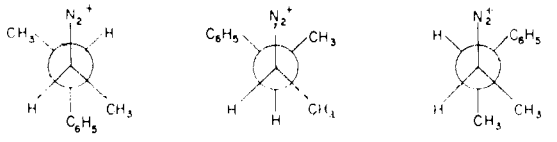
CHART III

Conformations of the L(+)-*threo*-diazonium ion



IV V VI

Conformations of the L(+)-*erythro*-diazonium ion



VII VIII IX

(20) This point has been made previously by Burr and Ciereszko (ref. 9b) and by D. Y. Curtin and M. C. Crew (ref. 10f).

(21) (a) F. A. Abd Elhafez and D. J. Cram, THIS JOURNAL, **74**, 5846 (1952); (b) **74**, 5851 (1952).

(22) Hammond's postulate [*ibid.*, **77**, 334 (1955)] would suggest that for this very exothermic reaction, the transition state would resemble the starting material in geometry.

(23) These values could be slightly in error as measures of the extent of each substituent migration since rearranged open carbonium ions could also give small amounts of conjugated olefin which was then destroyed by nitrous acid.

(24) A small part of this 68% undoubtedly arose by simple solvolysis with retention of configuration.

(25) D. Y. Curtin, *Record Chem. Progress* (*Kresge-Hooker Sci. Lib.*), **15**, 111 (1954).

Although ion-pair intermediates have been demonstrated[7b,26] in a number of halide and tosylate solvolyses, no such species can intervene in the deamination reaction with N_2 as the leaving group. Such a molecule would not even be expected to solvate the carbonium ion it was leaving, as is probable with the conjugate acid of an ester, ether or alcohol dissociates. Unlike the phenonium tosylate produced in tosylate solvolysis of the 3-phenyl-2-butyl system,[7b] a phenonium ion produced from a high energy, open ion would be relatively naked and reactive. Unlike the phenonium tosylate ion-pair, this bridged ion might not only capture solvent, but also give rearranged open ion which in turn could capture solvent. Such a process might explain the production of the 5% of racemic *erythro*-acetate produced from active *threo*-amine.

This amount of acetate produced by *simple solvolysis* is greater in the deaminative than in the tosylate solvolysis. In the former, *threo* material gave 6% acetate with retention and 14% with inversion as compared to 0.6% retention and 4% inversion in the latter. From *erythro*-amine, 6% acetate resulted from simple acetolysis with inversion, whereas with tosylate, 4% acetate. The amount of acetate resulting from simple acetolysis with retention could not be measured. The relatively higher amount of simple solvolysis in the deamination reaction probably reflects the ability of solvent to compete better with neighboring groups for a less hindered open carbonium ion than for either the back side of a saturated carbon atom or either side of an ion-pair. Again it would appear that in passing from tosylate solvolysis to the deamination reaction selectivity based on steric effects becomes more important at the expense of electronic effects.

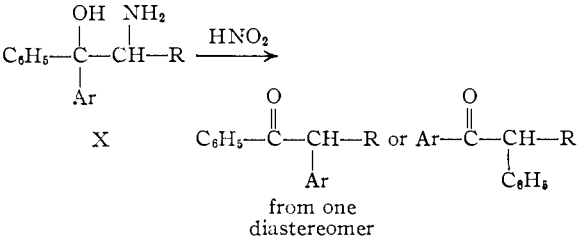
Other Solvolytic Deamination Reactions.—The general interpretation of the course of the deamination reaction in the present study is consistent with the results obtained in a wide variety of systems. Bartlett and Knox[27] observed that although the deamination of 1-apocamphylamine to give 1-apocamphanol or 1-chloroapocamphane occurred readily, attempts at substitution at this bridge-head carbon utilizing other leaving groups (H_2O^+ or Cl) failed even under brutal conditions. Thus participation by solvent or neighboring groups does not seem to be a necessary condition for dissociation in this deaminative substitution.

The demonstration by Bernstein and Whitmore[2] that the migration terminus is inverted in the deaminative rearrangement of 1,1-diphenyl-2-amino-1-propanol does not necessarily mean that phenyl participated in the dissociation of the diazonium ion. The most stable rotational conformation of the diazonium ion places one phenyl oriented 180° from the N_2 leaving group and a short lived, high energy, open carbonium ion produced by dissociation is sterically oriented to best attack this phenyl group, thus giving the observed stereochemical result.

The numerous observations[4b,5,6f] that the difference in migratory aptitude of various *p*-substituted phenyls became diminishingly small in the deamination reaction as compared to other carbonium ion-forming reactions are consistent with the concept of dissociation of the diazonium ion without neighboring group participation in the deamination reaction.

The high energy carbonium ion produced in the deamination reaction does not show any more tendency to rearrange than does the carbonium ion formed by simple ionization of an alkyl bromide or tosylate, at least in the α-phenylneopentyl system. Here the fate of the α-phenylneopentyl carbonium ion produced from a variety of leaving groups is similar.[11b,28]

Curtin, *et al.*, outlined two possible reasons why in the deamination of a series of diastereomeric amino alcohols X the migrating aryl group should be different for each diastereomer.[6a] In the first explanation, the relative stability of the various conformations of the starting molecule was considered as the controlling feature. However, it was pointed out[6g] that if the rate of conformational



equilibration is fast compared to rearrangement, the activation energy for one group migrating compared to a second in a given diastereomer is independent of the relative populations of the conformations of the initial molecule. The second and preferred[6g] explanation deals with the difference in energy of the transition states for rearrangement of two competing migrating groups in the same molecule, that transition state being the more stable in which the non-migrating groups are distributed *trans* to one another.[6a,6g] Implicit in both of these explanations is the assumption that the transition state for migration and for dissociation are one and the same; in other words, that the neighboring group participates in the dissociation. If on the other hand one assumes that a discrete intermediate, an open carbonium ion, intervenes between the dissociation and rearrangement processes, the analysis of this semipinacolic deamination reaction becomes similar to that applied to the deaminative Wagner–Meerwein rearrangement in this paper. Thus the first of Curtin's original hypotheses[6a] that the migrating group is controlled by the relative populations of conformations of the starting material might still apply to these pinacolic deamination reactions.

In the deamination of substituted cyclohexylamines, conformation control of the migrating

(26) (a) S. Winstein and D. Trifan, THIS JOURNAL, **74**, 1147, 1154 (1952); (b) D. J. Cram and F. A. Abd Elhafez, *ibid.*, **75**, 3189 (1953); (c) H. L. Goering, J. P. Blanchard and E. Silversmith, *ibid.*, **76**, 5409 (1954); (d) C. G. Swain, L. E. Kaiser and T. E. C. Knee, *ibid.*, **77**, 4681 (1955); (e) S. Winstein, E. Clippinger, A. H. Fainberg, R. Heck and G. C. Robinson, *ibid.*, **78**, 328 (1956).

(27) P. D. Bartlett and L. H. Knox, *ibid.*, **61**, 3184 (1939).

(28) (a) P. S. Skell and C. R. Hauser, *ibid.*, **64**, 2633 (1942); (b) A. Brodhag and C. R. Hauser, *ibid.*, **77**, 3024 (1955); (c) I. Dostrovsky and D. Samuel, *J. Chem. Soc.*, 658 (1954).

group seems to be enforced.[29] In simple solvolysis, however, both equatorially and axially oriented cyclohexylamines give mainly equatorially oriented alcohols.[30] This fact is consistent with a high energy, relatively unsolvated carbonium ion intermediate whose stereochemical fate is controlled not by solvent participation in ionization, but by the relative proximity of solvent molecules to the equatorial or axial faces of the carbonium ion once the nitrogen molecule has left. Apparently the same carbonium ion is created from *cis* to *trans* diastereomers and solvent molecules can get closer to the equatorial than the axial face of the ion, thus giving equatorially oriented alcoholic product.

Experimental

Preparation of Optically Pure D(−)-*erythro*-3-Phenyl-2-butylamine.—The procedure employed is identical to that used previously[8] to make the benzamide of this amine,[8] except that a large enough amount of material was used to allow isolation of the amine itself. From 4.92 g. of D(−)-*threo*-3-phenyl-2-butyl tosylate[7a,b] (m.p. 64.8–65.1°, prepared from optically pure alcohol) was obtained 0.432 g. of D(−)-*erythro*-3-phenyl-2-butylamine as a colorless oil, $n^{25}D$ 1.5157, $\alpha^{26}D$ −9.21° (*l* 1 dm., neat).

Anal. Calcd. for $C_{10}H_{15}N$: C, 80.46; H, 10.15. Found: C, 80.39; H, 10.37.

The enantiomer of this amine prepared by direct resolution gave $\alpha^{25}D$ +9.01° (*l* 1 dm., neat).[8]

Resolution of 2-Methyl-1-phenyl-1-propanol (II).—The racemic acid phthalate of this substance was resolved[15] in 24% yield (racemate = 100%) to give active acid phthalate, m.p. 93.6–94.1°, $[\alpha]^{23}D$ +45.1 (*c* 3.5, $CHCl_3$), lit.[15] $[\alpha]^{20}D$ +21.08° (*c* 9.2, solvent not reported). Further recrystallizations of the brucine salt (methanol–water) or of the acid phthalate (ether–pentane) did not change these values. Hydrolysis of this ester gave alcohol II in 94% yield, $n^{25}D$ 1.5113, $\alpha^{23}D$ +20.6° (*l* 1 dm., neat), $[\alpha]^{23}D$ +48.3° (*c* 6.7, ether), lit.[15] $[\alpha]^{20}D$ +47.7° (*c* 6.8, ether).

Preparation of L(−)-*threo*-2-Acetoxy-3-phenylbutane, D-(+)-*erythro*-2-Acetoxy-3-phenylbutane, (+)-1-Acetoxy-2-methyl-1-phenylpropane and 2-Acetoxy-2-phenylbutane.—L(−)-*threo*-2-Acetoxy-3-phenylbutane and D(+)-*erythro*-2-acetoxy-3-phenylbutane were prepared from L(+)-*threo*-3-phenyl-2-butanol ($n^{25}D$ 1.5160, $\alpha^{26}D$ +27.25°, *l* 1 dm., neat) and D(−)-*erythro*-3-phenyl-2-butanol ($n^{25}D$ 1.5168, $\alpha^{25}D$ −0.62°, *l* 1 dm., neat) by methods already reported[7b] in 93 and 96% yields, respectively, $n^{25}D$ 1.4877, $\alpha^{25}D$ −7.80° (*l* 1 dm., neat) and $n^{25}D$ 1.4877, $\alpha^{26}D$ +32.38° (*l* 1 dm., neat). The literature[7b] reports $n^{25}D$ 1.4877, $\alpha^{23}D$ −8.08° (*l* 1 dm., neat) and $n^{25}D$ 1.4877, $\alpha^{25}D$ +32.55 (*l* 1 dm., neat) for these compounds. (+)-1-Acetoxy-2-methyl-1-phenylpropane was prepared in an entirely analogous fashion from optically pure (+)-2-methyl-1-phenyl-1-propanol, $n^{25}D$ 1.5113, $\alpha^{25}D$ +21.57 (*l* 1 dm., neat), in a 96% yield, $n^{25}D$ 1.4853, $\alpha^{26}D$ +104.68° (*l* 1 dm., neat).

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 74.96; H, 8.38. Found: C, 75.06; H, 8.20.

Racemic 2-acetoxy-2-phenylbutane was prepared as before[7c] in 35% yield, $n^{25}D$ 1.4946 (lit.[7c] 1.4944).

Deamination Reactions of 3-Phenyl-2-butylamine.—Four reactions were carried out, one with optically pure L(+)-*erythro*-isomer, one with the optically pure D(−)-*threo*-isomer, one with partially optically pure D(−)-*erythro*-isomer and one with partially optically pure L(+)-*threo*-isomer. The reactions were all carried out in the same way, but in the two runs involving optically pure materials, different methods of isolation and analysis were employed from in the two runs involving partially optically pure amines. The procedure for the reaction itself is illustrated utilizing L(+)-*erythro*-3-phenyl-2-butylamine (run 1). To 4.63 g. of amine[8] ($\alpha^{23}D$ +8.91°, *l* 1 dm., neat; $n^{25}D$ 1.5159) dissolved in 300 ml. of dry glacial acetic acid was added over a period of 30 minutes, 31.4 g. of potassium nitrite. During this addition the temperature was held at 25–27° through external cooling. The resulting solution was stirred vigorously for one hour and shaken with 1.5 l. of water and 200 ml. of pure pentane. The aqueous layer was again washed with pentane, the pentane extracts were thoroughly washed with water, with dilute base, dried, and the solvent was evaporated through a short column. The residual oils were treated differently depending on which run was involved (see next section).

Isolation of Products from the Deamination Reaction; Method I.—This procedure is illustrated with the work up of the oil obtained from the deamination reaction in run 1 (see above). The residual oil was dissolved in 100 g. of anhydrous glacial acetic acid and maintained at 75° for 26 hours. This procedure has been demonstrated previously[7c] to completely convert 2-acetoxy-2-phenylbutane to olefin. Removal of this acetate in runs 1 and 2 simplified the analysis of the remaining components. The mixture was cooled, diluted with 1 l. of water and extracted twice with pure pentane. The pentane solution was washed with dilute sodium carbonate solution, water, dried, and the solvent was evaporated through a short column. The residual oil was a mixture of olefin, ketone and three acetates. The ketone was removed as follows: This oil was dissolved in 150 ml. of methanol containing 15 ml. of water, 15 g. of trimethylacethydrazine ammonium chloride (Girard reagent "T"), 4.1 g. of sodium acetate and 3.0 g. of glacial acetic acid. The resulting solution was heated at reflux for 90 minutes, cooled, diluted with 1 l. of water and extracted with pure pentane. The pentane extract was washed with dilute sodium bicarbonate solution, water, dried, and the solvent was evaporated through a short column. The residual oil was dissolved in dry ether and added to a slurry of 1.3 g. of lithium aluminum hydride in dry ether. In this fashion the acetates were converted to the parent alcohols. The excess hydride was decomposed with dilute hydrochloric acid, and the aqueous phase was extracted with pure pentane. The combined ether and pentane solutions were washed with dilute sodium bicarbonate solution, dried, and the solvent was evaporated through a short column. The residual oil was subjected to chromatography on 150 g. of activity I alumina[31] under pure pentane. The olefin fraction was washed from the column with pure pentane and was twice distilled at 18 mm. to give 0.43 g. (10% yield) of this product. The alcohol fraction was washed from the column with ethanol, the resulting solution being evaporated. The residual oil was distilled at 1 mm. through a short-path still to give 1.86 g. or 40% yield of a mixture of diastereomeric 3-phenyl-2-butanols and 2-methyl-1-phenyl-1-propanol, $\alpha^{23}D$ +3.18° (*l* 1 dm., neat), $n^{25}D$ 1.5167. This material was subjected to quantitative infrared analysis to determine the amount of each of the above three alcohols in the mixture (see later section). A sample (0.74 g.) of this alcohol fraction was converted by the pyridine–acetic anhydride method to acetate in 95% yield, $\alpha^{24}D$ −27.55° (*l* 1 dm., neat), $n^{25}D$ 1.4874. To 0.90 g. of the alcohol fraction was added 25 ml. of glacial acetic acid containing 2.5 g. of acetic anhydride and 0.25 g. of *p*-toluenesulfonic acid monohydrate, and the resulting solution was maintained at 75° for 18 hours. This treatment was demonstrated in control experiments (see later section) to completely racemize and partially convert to olefin the 2-methyl-1-phenyl-1-propanol component and to leave the diastereomeric 3-phenyl-2-butanols intact. The solution was cooled, diluted with 400 ml. of water, extracted with pure pentane, and the pentane extracts were washed with dilute base, dried and evaporated through a short column. The residual oil was dissolved in dry ether and added to a slurry of 0.3 g. of lithium aluminum hydride. This procedure converted any acetates formed back to alcohols. The olefin–alcohol mixture was isolated in the usual way and chromatographed on 50 g. of activity I alumina[31] as before. The fraction eluted with methanol was distilled at 15 mm. to give 0.72 g. of colorless oil, $\alpha^{23}D$ +3.21° (*l* 1 dm., neat). A sample (0.43 g.) of this alcohol was converted by the acetic anhydride–pyridine method to the acetate in 95% yield, $\alpha^{26}D$ −26.96° (*l* 1 dm., neat), $n^{25}D$ 1.4879. The rotational data on the alcohol and acetate before and after racemization of the 2-methyl-1-phenyl-1-propanol coupled

(29) (a) D. Nightingale and M. Maienthal, THIS JOURNAL, **72**, 4823 (1950); (b) D. Y. Curtin and S. Schmukler, *ibid.*, **77**, 1105 (1955).

(30) (a) J. A. Mills, *J. Chem. Soc.*, 260 (1953); (b) A. K. Bose, *Experientia*, **9**, 256 (1953); (c) W. G. Dauben, R. C. Tweit and C. Mannerskantz, THIS JOURNAL, **76**, 4420 (1954).

(31) H. Brockman and H. Schodder, *Ber.*, **74**, 78 (1941).

with the rotations of synthetic mixtures allowed the optical character of the three components to be determined (see later section).

In run 2, 4.70 g. of optically pure D(−)-*threo*-3-phenyl-2-butylamine[8] was employed, $\alpha^{23}D$ −42.33° (*l* 1 dm., neat), $n^{25}D$ 1.5143. From this was obtained 0.53 g. or 13% yield of olefin and 1.80 g. or 38% yield of the three isomeric alcohols, $\alpha^{23}D$ −5.78° (*l* 1 dm., neat), $n^{25}D$ 1.5143. This alcohol fraction was submitted directly to infrared analysis. A sample of this alcohol was converted to its acetate in 96% yield, $\alpha^{23}D$ +0.05° (*l* 1 dm., neat), $n^{25}D$ 1.4869. A portion of this alcohol (0.86 g.) was submitted to the action of *p*-toluenesulfonic acid in acetic acid as above to give a mixture of the two active diastereomers and racemic 2-methyl-1-phenyl-1-propanol, wt. 0.61 g., $\alpha^{23}D$ −4.21° (*l* 1 dm., neat). A sample of this alcohol was converted to its acetate by the acetic anhydride–pyridine method in 94% yield, $\alpha^{26}D$ +8.41° (*l* 1 dm. neat), $n^{25}D$ 1.4872.

Isolation of Products from the Deamination Reaction; Method II.—This procedure differs from method I in the following respects: (1) The original mixture obtained from the solvolysis (ketone, olefin and four acetates) was not heated to 75° to remove 2-phenyl-2-acetoxybutane but was treated directly with Girard reagent to remove ketone. (2) The olefin was examined by its reduction to 2-phenylbutane and measurement of this substance's optical purity. In this procedure olefin came only from deamination reaction itself. (3) The infrared analysis was performed on the final mixture of three alcohols, the two diastereomers of 3-phenyl-2-butanol and racemized 2-methyl-1-phenyl-1-propanol. The procedure is illustrated with run 4.

From the acetolysis of 9.83 g. of L(+)-*threo*-3-phenyl-2-butylamine[8] ($\alpha^{24}D$ +6.42°, *l* 1 dm., neat; $n^{25}D$ 1.5142) was obtained an oil which was 15.2% optically pure. This material was treated with Girard reagent "T" as in method I, and the product was reduced with lithium aluminum hydride as in method I. The product was chromatographed as in method I, the olefin fraction after distillation amounting to 1.03 g. (12% yield) and the alcohol fraction to 4.90 g. (50% yield).

This olefin fraction was reduced to 2-phenylbutane as follows. To a suspension of platinum black (from 50 mg. of PtO_2) in 25 ml. of methanol was added 0.51 g. of the olefinic fraction, and the mixture was shaken under 752 mm. of hydrogen. After hydrogen uptake had stopped (76 ml.), the mixture was filtered, and the filtrate was shaken with 350 ml. of water and pure pentane. The pentane extract was washed with water, dried and the solvent was evaporated through a short column. The residual oil was distilled through a short-path still to give 0.45 g. of crude 2-phenylbutane. Careful fractional distillation of this material (0.30 g.) gave 0.23 g. of L(+)-2-phenylbutane, $\alpha^{23}D$ +3.82° (*l* 1 dm., neat), $n^{25}D$ 1.4878. Optically pure 2-phenylbutane has a rotation $\alpha^{23}D$ +24.2° (*l* 1 dm., neat), $n^{25}D$ 1.4878.[32] This material is therefore 15.8% optically pure as compared to the 15.2% optical purity of the starting amine. Thus only optically pure 3-phenyl-1-butene survived the deaminative solvolysis.

The alcohol fraction (2.00 g.) was submitted to the action of an acetic acid, acetic anhydride and *p*-toluenesulfonic acid mixture to racemize 2-methyl-1-phenyl-1-propanol and destroy 2-phenyl-2-butanol, the procedure being the same as in method I. The product was reduced with lithium aluminum hydride as before and chromatographed on alumina. The olefin obtained (mixture of 2-phenylbutenes from dehydration of 2-phenyl-2-butanol) was distilled to give 0.38 g. (11% yield) of material, $n^{25}D$ 1.5190. Distillation of the alcohol fraction gave 1.09 g. (27% yield) of material, $\alpha^{23}D$ +0.63° (*l* 1 dm., neat), $n^{25}D$ 1.5147. This material was submitted to infrared analysis. A sample (0.76 g.) of this alcohol was converted by the acetic anhydride–pyridine method to acetate in 96% yield, $\alpha^{24}D$ −1.18° (*l* 1 dm., neat), $n^{25}D$ 1.4873.

In run 3, 10.0 g. of D(−)-*erythro*-amine[8] was employed, $\alpha^{25}D$ −4.01° (*l* 1 dm., neat), $n^{25}D$ 1.5160, 45% optically pure. From this material was obtained 0.463 g. of olefin (5% yield) and 5.05 g. of alcohol (50% yield). The total olefin fraction was reduced as before to give 0.396 g. of distilled 2-phenylbutane. Careful fractionation of 0.300 g. of this material gave 0.232 g. of 2-phenylbutane, $n^{25}D$ 1.4878, $\alpha^{24}D$ −8.70° (*l* 1 dm., neat), 36% optically pure.

(32) D. J. Cram, THIS JOURNAL, **74**, 2149 (1952).

A portion of the alcohol fraction (2.00 g.) was treated with *p*-toluenesulfonic acid as in the other runs to give, after lithium aluminum hydride reduction and chromatography, an olefin and alcohol fraction. The olefin fraction (distilled), wt. 0.215 g. (6% yield), came from the decomposition of 2-phenyl-2-butanol. The alcohol fraction (distilled) amounted to 1.22 g. (30% yield), $n^{25}D$ 1.5166, $\alpha^{24}D$ −1.42° (*l* 1 dm., neat) and was submitted to infrared analysis. This alcohol was converted to its acetate by the acetic anhydride–pyridine method in 94% yield, $\alpha^{24}D$ +12.53° (*l* 1 dm., neat).

Demonstration of the Presence of 2-Methyl-1-phenyl-1-propanol Among the Products of Deaminative Acetolysis of D(−)-*threo*-3-Phenyl-2-butylamine.—Because the product of methyl migration was unexpected in this deamination, qualitative proof of its presence was sought. A deamination reaction was run utilizing the conditions and isolation procedure of run 2 except that 35% optically pure (−)-*threo*-amine was employed. A portion (0.78 g.) of the alcoholic product (this material had not been treated with *p*-toluenesulfonic acid at 75°) was converted to its acid phthalate. The resulting oil was subjected to partition chromatography on 164 g. of a mixture of one part of silicic acid to two parts of Celite made up in 1% ethanol in chloroform. Elution of the material with 1% ethanol in chloroform resulted in a partial fractionation of the acid phthalates. Four fractions, each containing about 0.35 g. of solute, were collected. These materials were crystallized and recrystallized from chloroform–pentane to a constant melting point. The material from the first fraction (9 mg., m.p. 131.8–132.2°) gave a m.m.p. of 133–133.8° with authentic acid phthalate of racemic 2-methyl-1-phenyl-1-propanol[15] (m.p. 133.7–134°). The other fractions, although obtained in somewhat larger amounts, gave melting points and mixed melting points which indicated them to be mixtures of acid phthalates.

Preparation of the Acetates of Various Alcohols; Pyridine–Acetic Anhydride Method.—This preparation will be illustrated with the conversion of (+)-2-methyl-1-phenyl-1-propanol to (+)-1-acetoxy-2-methyl-1-phenylpropane. To 7.0 g. of (+)-2-methyl-1-phenyl-1-propanol[15] ($\alpha^{26}D$ +21.57°, *l* 1 dm., neat; $n^{25}D$ 1.5113) was added 30.0 g. of acetic anhydride and 75 g. of anhydrous pyridine. The resulting solution was heated on a steam-bath for 3 hours. At the end of this time, 250 ml. of water and 100 g. of ice were added, and the resulting mixture was extracted twice with pure pentane. The pentane extracts were combined, washed with water, dilute hydrochloric acid, dilute sodium bicarbonate and dried. The pentane was evaporated through a short column. The residual oil was subjected to chromatography on a 4 × 35 cm. column (140 g.) of alumina made up in pure pentane. The column was washed with pure pentane (the pentane washes were discarded) and was eluted with a solution of 10% ether in pentane. The ether–pentane was evaporated through a short column and the residual oil was distilled through a short-path still at 15 mm. to give 8.5 g. of (+)-1-acetoxy-2-methyl-1-phenylpropane,[15] $\alpha^{26}D$ 104.68° (*l* 1 dm., neat), $n^{25}D$ 1.4853.

Control Experiments.—The following experiment demonstrates: (1) that the solvolysis products once formed are stable, (2) that the ketone could be quantitatively removed, (3) that 2-acetoxy-2-phenylbutane is completely converted to olefin at 75° in glacial acetic acid and (4) the three secondary acetates are not fractionated during the isolation procedure. A mixture of 0.89 g. of L(−)-*threo*-3-acetoxy-2-phenylbutane ($\alpha^{24}D$ −7.80°, *l* 1 dm., neat; $n^{25}D$ 1.4877), 0.90 g. of (+)-acetoxy-2-methyl-1-phenylpropane ($\alpha^{26}D$ +104.68°, *l* 1 dm., neat; $n^{25}D$ 1.4853) gave $\alpha^{25}D$ +41.72° (*l* 1 dm., neat) and $n^{25}D$ 1.4870. To this mixture was added 0.60 g. of 2-acetoxy-2-phenylbutane ($n^{25}D$ 1.4946), 0.20 g. of acetophenone ($n^{25}D$ 1.5343) and 0.09 g. of 3-phenyl-2-butanone ($n^{25}D$ 1.5104). This mixture was subjected to the exact conditions of the deamination reaction, and the isolation procedure of method I (the final acid treatment of the alcohols was omitted). The product was 0.38 g. of olefin ($n^{25}D$ 1.5214) and 1.00 g. of alcohol, a sample (0.60 g.) of which was converted to its acetate, wt. 0.65 g., $n^{25}D$ 1.4871, $\alpha^{24}D$ +41.84° (*l* 1 dm., neat). The initial mixture of acetates had $\alpha^{25}D$ +41.72° (*l* 1 dm., neat) and $n^{25}D$ 1.4870.

That treatment of the 2-acetoxy-3-phenylbutanes and 2-acetoxy-2-phenylbutane with lithium aluminum hydride yields the corresponding alcohols in an essentially quantitative manner has been demonstrated previously.[7b] The

following experiment shows that 1-acetoxy-2-methyl-1-phenylpropane may be converted to 2-methyl-1-phenyl-1-propanol in a similar fashion and in a similarly high yield. A sample of 1.03 g. of (+)-1-acetoxy-2-methyl-1-phenylpropane, $\alpha^{26}D$ +104.7° (*l* 1 dm., neat), was prepared from the corresponding alcohol, $\alpha^{26}D$ +21.57° (*l* 1 dm., neat) $n^{25}D$ 1.5113. Reduction of this material with lithium hydride by the ordinary procedure gave 0.83 g. of (+)-2-methyl-1-phenyl-1-propanol, $n^{25}D$ 1.5112, $\alpha^{26}D$ +21.59° (*l* 1 dm., neat).

To demonstrate that (+)-acetoxy-2-methyl-1-phenylpropane was stable to the treatment at 75° in glacial acetic acid (no *p*-toluenesulfonic acid) used to decompose 2-acetoxy-2-phenylbutane, the following experiment was run. To 20 ml. of glacial acetic acid was added 0.8 ml. of acetic anhydride and 1.00 g. of (+)-1-acetoxy-2-methyl-1-phenylpropane, $\alpha^{26}D$ +104.7° (*l* 1 dm., neat), $n^{25}D$ 1.4853, and the resulting solution was heated at 75° for 26 hours. Isolation of the material in the usual way gave 0.96 g. of starting material, $\alpha^{26}D$ +104.3° (*l* 1 dm., neat), $n^{25}D$ 1.4853.

The following experiment demonstrates the facts: (1) conjugated olefin is destroyed under the conditions of the deaminative solvolysis, (2) unconjugated olefin survives without racemization and (3) active unconjugated olefin can be catalytically reduced to 2-phenylbutane essentially without racemization. To 0.28 g. of D(−)-3-phenyl-1-butene, $\alpha^{23}D$ −5.62° (*l* 1 dm., neat), $n^{25}D$ 1.5054,[33a] was added 0.13 g. of *cis*-2-phenyl-2-butene ($n^{25}D$ 1.5402)[33b] and 0.08 g. of *trans*-2-phenyl-2-butene ($n^{25}D$ 1.5193). This mixture was dissolved in 100 g. of glacial acetic acid, and 10.3 g. of solid potassium nitrite was added in eight portions with vigorous stirring over a period of 30 minutes. The resulting mixture was stirred for 45 minutes, and the product was subjected to the isolation procedure outlined in method II for the isolation and reduction of olefin except that the treatment with Girard reagent was omitted. For the catalytic reduction of olefin, 25 ml. of methanol and 25 mg. of platinum oxide were used, 37 ml. of hydrogen being absorbed (750 mm. and 22°). The D(−)-2-phenylbutane obtained amounted to 0.15 g., $n^{25}D$ 1.4878, $\alpha^{24}D$ −23.62° (*l* 1 dm., neat). The literature reports for optically pure L(+)-2-phenylbutane, $\alpha^{23}D$ +24.2° (*l* 1 dm., neat), $n^{25}D$ 1.4878.[32]

The following experiment demonstrates that: (1) (+)-2-methyl-1-phenyl-1-propanol racemized at 75° in glacial acetic acid in the presence of *p*-toluenesulfonic acid; (2) 2-acetoxy-2-phenylbutane is converted to olefin by this treatment. To 25 g. of glacial acetic acid containing 2.5 g. of acetic anhydride and 0.25 g. of *p*-toluenesulfonic acid monohydrate was added 1.00 g. of 2-phenyl-2-butanol ($n^{25}D$ 1.5167) and 0.90 g. of (+)-2-methyl-1-phenyl-1-propanol ($\alpha^{24}D$ +21.34°, *l* 1 dm., neat; $n^{25}D$ 1.5113), and the resulting solution was heated at 75° for 18 hours. The product was isolated, subjected to a lithium aluminum hydride treatment and chromatographed as in methods I and II. The olefin fraction amounted to 0.89 g., $n^{25}D$ 1.5192. The recovered (+)-2-methyl-1-phenyl-1-propanol (0.61 g.) gave $n^{25}D$ 1.5113, $\alpha^{24}D$ +0.13° (*l* 1 dm., neat) which corresponds to 99.4% racemization. The relatively poor recovery of this alcohol (68%) and the good recovery of olefin (101% based only on 2-acetoxy-2-phenylbutane) indicates that some of the secondary alcohol dehydrated to olefin.

The optical and structural stability of the diastereomeric 3-phenyl-2-butanols to the action of glacial acetic acid and *p*-toluenesulfonic acid at 75° was demonstrated as follows: A mixture of 0.90 g. of L(+)-*threo*-3-phenyl-2-butanol ($\alpha^{25}D$ +31.61°, *l* 1 dm.; $n^{25}D$ 1.5166), 25 g. of glacial acetic acid, 2.5 g. of acetic anhydride and 0.25 g. of *p*-toluenesulfonic acid monohydrate was maintained at 75° for 18 hours. The product was subjected to the lithium aluminum hydride and chromatographic procedures of methods I and II. No olefin could be isolated. Only L(+)-*threo*-3-phenyl-2-butanol was isolated (0.72 g., 80% recovery), $\alpha^{24}D$ +31.51° (*l* 1 dm., neat; $n^{25}D$ 1.5164). Since this *threo* isomer is the one that racemizes on ionization,[7a,b] the stability of this isomer demonstrates the stability of the *erythro* isomer as well.

The following experiments were run to measure the over-all accuracy of the isolation and analytical procedure used in the latter part of method I. Two synthetic mixtures of the three secondary alcohols were made up, mixture 1 simulating the composition of alcohols obtained in run 1 and mixture 2 simulating that of run 2. The composition of mixture 1 was as follows: 0.010 g. of (+)-2-methyl-1-phenyl-1-propanol ($\alpha^{23}D$ +21.21°, *l* 1 dm., neat; $n^{25}D$ 1.5113), 0.082 g. of racemic 2-methyl-1-phenyl-1-propanol ($n^{25}D$ 1.5113), 0.103 g. of L(+)-*threo*-3-phenyl-2-butanol ($\alpha^{25}D$ +31.61°, *l* 1 dm., neat; $n^{25}D$ 1.5167) and 0.917 g. of L(+)-*erythro*-3-phenyl-2-butanol ($\alpha^{26}D$ +0.76°, *l* 1 dm., neat; $n^{25}D$ 1.5163). This mixture had $\alpha^{24}D$ +4.52° (*l* 1 dm., neat), $n^{25}D$ 1.5167. A portion was converted to acetate by the usual method in 93% yield, $\alpha^{24}D$ −25.9° (*l* 1 dm., neat). The composition of alcohol was therefore: the benzyl alcohol, 8% (11% optically pure); *threo*-alcohol, 9% (100% optically pure); *erythro*-alcohol, 82% (100% optically pure). The composition of mixture 2 was as follows: 0.068 g. of (+)-2-methyl-1-phenyl-1-propanol ($\alpha^{23}D$ +21.21°, *l* 1 dm., neat; $n^{25}D$ 1.5113), 0.356 g. of racemic 2-methyl-1-phenyl-1-propanol ($n^{25}D$ 1.5113), 0.108 g. of L(+)-*threo*-3-phenyl-2-butanol ($\alpha^{24}D$ +31.67°, *l* 1 dm., neat; $n^{25}D$ 1.5167), 0.215 g. of racemic *threo*-3-phenyl-2-butanol ($n^{25}D$ 1.5167), 0.199 g. of L(+)-*erythro*-3-phenyl-2-butanol ($\alpha^{26}D$ +0.76; *l* 1 dm., neat; $n^{25}D$ 1.5163), and 0.063 g. of racemic *erythro*-3-phenyl-2-butanol ($n^{25}D$ 1.5163). This mixture had $\alpha^{24}D$ +5.82° (*l* 1 dm., neat), $n^{25}D$ 1.5142. A portion of this alcohol was converted to its acetate in 92% yield, $\alpha^{24}D$ −0.50° (*l* 1 dm., neat). The composition of mixture 2 was therefore: the benzyl alcohol, 42% (16% optically pure); *threo*-alcohol, 32% (33% optically pure); *erythro*-alcohol, 26% (76% optically pure).

Mixtures 1 and 2 (0.50 g. each) were submitted to the action of acetic acid and *p*-toluenesulfonic acid at 75° for 18 hours, the product being put through the lithium aluminum hydride and chromatographic procedures employed in runs 1 and 2. The alcohol obtained from mixture 1 (0.36 g.) gave $\alpha^{24}D$ +4.59 (*l* 1 dm., neat), and its acetate (92% yield) gave $\alpha^{26}D$ −28.49° (*l* 1 dm., neat). The alcohol from mixture 2 (0.30 g.) gave $\alpha^{24}D$ +4.75° (*l* 1 dm., neat), and its acetate gave $\alpha^{26}D$ −8.72° (*l* 1 dm., neat). Infrared analysis (see later section) of the final alcohol obtained by acid treatment of mixture 1 was as follows: the benzyl alcohol, 6%; *threo*-alcohol, 9%; *erythro*-alcohol, 84%. Analysis of final alcohol from mixture 2 was: the benzyl alcohol, 37%; *threo*-alcohol, 35%; *erythro*-alcohol, 28%.

This experiment demonstrates that no selective loss of *threo*- or *erythro*-alcohol occurs during this acid treatment, but that a small selective loss of 2-methyl-1-phenyl-1-propanol occurs. Racemization and partial loss of this alcohol in mixture 1 made practically no difference in the rotations of alcohols or acetates as was the case in run 1. Racemization and partial loss of the benzyl alcohol in mixture 2 changed the rotation from +5.82 to +4.75° as compared to a change in rotation of run 2 from −5.78 to −4.20°. The changes in rotation of the acetates are far more significant: mixture 2, from −0.50 to −8.72°; run 2, from +0.05 to +8.41°.

To demonstrate that (+)-2-methyl-1-phenyl-1-propanol is stable under the conditions used for the saponification of its acid phthalate, the following experiment was run. To 250 ml. of 0.32 *N* sodium hydroxide was added 0.529 g. of (+)-2-methyl-1-phenyl-1-propanol ($\alpha^{22}D$ +20.41°, *l* 1 dm., neat). The resulting mixture was brought to reflux and allowed to steam distil. The alcohol was isolated in the usual way to give 0.465 g. of material, $\alpha^{23}D$ +20.60° (*l* 1 dm., neat).

Infrared Analysis of Alcohol Mixtures.—These analyses were made on a Perkin–Elmer infrared spectrophotometer, model 21, NaCl prism and cells, utilizing liquid films 0.030 mm. thick. The optical densities of 2-methyl-1-phenyl-1-propanol (II) and *threo*- and *erythro*-3-phenyl-2-butanol (III) were determined at those wave lengths most advantageous for analysis. The optical densities of the unknowns were then determined. The amounts of these components were calculated by solving simultaneous equations assuming that Beer's law applied. Synthetic mixtures of the three components were then made which approximated the unknowns (to within 3% for each component based on the final values for each unknown), and these were then analyzed similarly. The unknown mixtures were now corrected to the known for deviations in Beer's law. Table III records samples of raw intensity data. Table IV records the percentage compositions of alcohol obtained in the

(33) Literature (ref. 11c) reports for these olefins: (a) $\alpha^{22}D$ −6.39°, 1 dm., neat; $n^{25}D$ 1.5055; (b) $n^{25}D$ 1.5402; (c) $n^{25}D$ 1.5193.

four solvolytic runs corrected to the known synthetic mixtures. The facts that these percentages add up to almost 100% and that calculations based on different wave lengths give similar values indicate the absence of other components in the mixtures. The infrared analyses of the alcohols obtained in the control experiments were done the same way.

TABLE III

OPTICAL DENSITIES AT THE WAVE LENGTHS USED FOR INFRARED ANALYSES OF ALCOHOL MIXTURES

Composition, %			Optical density at λ in μ (slit width in mm.)				
threo	*erythro*-		8.00	8.33	8.85	10.06	12.41
III[a]	III[b]	II[c]	(0.142)	(0.148)	(0.163)	(0.222)	(0.322)
100	0	0	0.498	0.210	0.920	0.080	0.080
0	100	0	.324	.163	.626	.080	.081
0	0	100	.398	.418	.208	.275	.205
Unknown from run 1			.346	.180	.638	.091	.088
8	87	5	.348	.181	.639	.091	.095
Unknown from run 2			.426	.272	.590	.152	.129
36	33	31	.430	.262	.621	.142	.125

[a] *threo*-3-Phenyl-2-butanol, $n^{25}D$ 1.5167. [b] *erythro*-3-Phenyl-2-butanol, $n^{25}D$ 1.5163. [c] 2-Methyl-1-phenyl-1-propanol, $n^{25}D$ 1.5113.

The differences in results in Table IV between runs 1 and 3 and between 2 and 4 result from the fact that in runs 1 and 2 the analyses were made *before* the 2-methyl-1-phenyl-1-propanol was racemized and partially destroyed by treatment at 75° with an acetic acid–*p*-toluenesulfonic acid mixture. In runs 3 and 4 the analyses were made *after* this treatment. When runs 3 and 4 are corrected for loss of this component (as measured in the foregoing control experiments), the analyses for runs 1 and 3 and for 2 and 4 correspond to one another with a 1% maximum deviation.

The yields of 2-phenyl-2-butanol reported in Table I are based on the differences in total alcohol obtained in runs 1 and 3 and in 2 and 4. In runs 1 and 2 the acetate of 2-phenyl-2-butanol was destroyed before the alcohol was isolated. In runs 3 and 4 this acetate was preserved and carried into the alcohol initially isolated. Since almost twice as much amine was used as starting material in runs 3 and 4 as in 1 and 2, the mechanical losses in runs 1 and 2 were proportionately higher. Therefore the yields of 2-phenyl-2-butanol in Table I represent maximum values.

Calculations of the Optical Activities of Components in Alcohol Mixtures.—The infrared analyses give the percentages of the three secondary alcohol components both before and after the racemization of the 2-methyl-1-phenyl-1-propanol component. The optical activities of the *threo*- and *erythro*-alcohols were calculated as follows. After the benzyl alcohol was racemized, only the *threo*- and *erythro*-alcohols contributed to the rotation of the mixture. As noted earlier,[7b] the rotation of active *threo*-alcohol is about 30° and that of active *erythro*-alcohol is only about 1°, whereas the rotation of active *threo*-acetate is only 8° and that of *erythro*-acetate is about 32°. The optical purities of these two components were calculated first by solving two simultaneous equations in two unknowns, assuming the rotational contributions of the active alcohols and the active acetates were additive and that the racemized 2-methyl-1-phenyl-1-propanol component or its acetate had no effect on these rotations. Synthetic mixtures of these estimated compositions were then made, and the rotations of their alcohols and acetates used to calculate composition. The unknowns were then corrected to the knowns for the small deviations in additivity of the components. This gave the optical compositions of the *threo*- and *erythro*-alcohols both before and after the racemization of the 2-methyl-1-phenyl-1-propanol. The optical composition of this benzyl alcohol was then calculated making use of rotations of the alcohols and their acetates before the racemization reaction, the infrared data and the rotations of optically pure 2-methyl-1-propanol and its acetate. Fortunately the rotation of the acetate of 2-methyl-1-phenyl-1-propanol (105°) is an order of magnitude higher than those of the other acetates. Again additivity of the rotations of each component was assumed, synthetic mixtures of similar compositions were made and analyzed, and the unknowns were corrected to the knowns for small deviations in additivity of the components. Although these last calculations depend on a large number of separate experimentally determined values and are therefore not very accurate, there is no doubt about the following points. (1) The product of methyl migration from *threo*-amine is somewhere between 12 and 20% optically pure and of an identifiable configuration. (2) The product of methyl migration from *erythro*-amine is somewhere between 0 and 8% optically pure and of an identifiable configuration.

TABLE IV

RESULTS OF INFRARED ANALYSES OF ALCOHOLS FROM DEAMINATIVE ACETOLYSES

Run no.[a]	Configuration st. mat.	% *threo*- III[b] 1st.[c]	2nd.[d]	% *erythro*- III[b] 1st.[c]	2nd.[d]	% II[b] 1st.[c]	2nd.[d]	Total,[b] % 1st.[c]	2nd.[d]
1	L(+)-*erythro*	8	9	87	87	5	5	100	101
2	D(−)-*threo*	36	35	33	33	30	32	99	100
3	D(−)-*erythro*	8	9	84	84	9	8	101	101
4	L(+)-*threo*	33	34	25	25	42	42	100	101

[a] Run numbers throughout paper correspond. [b] Unknowns corrected to knowns of almost identical composition (3% maximum difference for any component). [c] Based on optical densities at λ 8.00, 10.06 and 12.41 μ. [d] Based on optical densities at λ 8.00, 8.33 and 8.85 μ.

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