Molecular Rearrangements. XVII. The Deaminations of D- and L-*erythro*-1-Amino-1,2-diphenylpropanol-2 and of D-2-Amino-1,1-diphenylpropane[1]

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The radiochemical and stereochemical consequences of the deamination, accompanied by phenyl migration, of D- and L-*erythro*-1-amino-1,2-diphenyl-(1-*phenyl*-C[14])-propanol-2 (IV) have been studied. It is established that the major products, α- or β-benzhydryl-*phenyl*-C[14] methyl ketone (V) were formed with an average of 73.5% inversion and 26.5% retention of configuration at the migration termini. There was no α-phenylpropiophenone formed, thus establishing that no methyl migration occurred during these rearrangements. These results exclude the intervention of initially formed bridged ion intermediates in the deamination of IV. Similar studies were conducted upon two modifications of stereospecifically phenyl-labeled D-2-amino-1,1-diphenylpropane (VII), which underwent deamination to yield L-(+)-*threo*-1,2-diphenylpropanol-1 (55%, *threo*-VIII) and D-(+)-*erythro*-1,2-diphenylpropanol-1 (11%, *erythro*-VIII), 6-7% of olefins and 25-27% of materials which were not identified. These results indicate open carbonium ion formation during the deamination of VII, and are best interpreted in terms of ground-state control of the intermediate open ions. The absolute configuration of D-(−)-phenylglycine has been confirmed through the series of reactions just discussed by the conversion of (+)-aminodesoxybenzoin to (−)-2-amino-1,1,2-triphenylethanol which had been shown previously (ref. 17) to possess the L-configuration. The radiochemical results serve to establish the configurations of D-(+)- and L-(−)-2-amino-1,1-diphenylpropane (VII).

In 1957, we reported[3] the successful synthesis of optically active 2-amino-1,1-diphenylpropanol-1 (I) stereospecifically labeled in only one of the two phenyl groups. Upon subsequent deamination, it was demonstrated that whereas the labeled phenyl migrated with inversion, the unlabeled phenyl migrated with retention of configuration at the migration terminus (Fig. 1). We therefore postulated[3] as the simplest explanation that the open carbonium ion intermediates A and B underwent phenyl migration faster than they underwent rotation about the C—C[⊕] bond. The observation that stereoselective topside migration of phenyl is possible during the rearrangement of I indicates that bridged ions[4] and neighboring[5] group participation are not so important to the mechanism of deamination as several groups of investigators recently have implied.[6,7] Although the evidence[4,5] for bridged ion intermediates in certain solvolytic reactions seems overwhelming, there is not yet,

in our opinion, adequate experimental justification for such intermediates in the deamination reaction. Following are the reasons:

(1) The well-known[5] enhancement of rate owing to neighboring-group participation has never, to our knowledge, been established during a deamination reaction. In fact, the few kinetic studies which have been made for aromatic diazotization[8] or for aliphatic deaminations[8] indicate that the slow or "rate-controlling" step in both reactions is either nitrosation itself or the formation of the nitrosating agent, a situation in which neighboring-group assistance, in the aliphatic case, would not appear to be of much importance. The disappearance of large differences in migratory aptitudes between *p*-anisyl, *p*-tolyl and phenyl[9] upon deamination of primary amines is quite consistent with a mechanism in which all steps after nitrosation are fast, and of very low activation energy requirements.

(2) Whereas bridging[4] and neighboring-group participation[5] are usually synonymous with stereospecificity, the reverse, although sometimes[7] tacitly assumed, is not true. That is, stereospecificity is *not* synonymous with bridging[4] nor with neighboring-group participation,[10] as has been emphasized by Winstein and co-workers[11] and demonstrated experimentally[10] in this Laboratory.

(3) Finally, replacement of an amino group by hydroxyl with predominant inversion of configuration has been ascribed to direct displacement through an "SN2-like process."[6e] Although such a process is possible, an alternate explanation could be that open, non-bridged ions do not suffer attack equally from both sides by the entering group. This has been demonstrated for the open 1,2,2-triphenylethylcarbonium ion.[10] The observations that α-phenylethylamine can yield α-phenylethanol

(1) This paper is based upon work performed at Oak Ridge National Laboratory, which is operated by Union Carbide Corporation for the Atomic Energy Commission. Portions of this research were presented at the Eighth Conference on Reaction Mechanisms, Princeton, N. J., September 8, 1960, and at the Conference on Use of Radioisotopes in the Physical Sciences and Industry, Copenhagen, Denmark, September 15, 1960.

(2) Department of Chemistry, Duke University. Professor Wilder was a Research Participant of the Oak Ridge Institute of Nuclear Studies, Feb.-June, 1958.

(3) B. M. Benjamin, H. J. Schaeffer and C. J. Collins, *J. Am. Chem. Soc.*, **79**, 6160 (1957). In the foregoing paper we used the configurational assignments of H. I. Bernstein and F. C. Whitmore, *ibid.*, **61**, 1324 (1939). (+)-1,1-Diphenyl-2-aminopropanol-1, however, is related to D-(−)-alanine [A. McKenzie, R. Roger and G. O. Wills, *J. Chem. Soc.*, 779 (1926)] which, in turn, has been related to D-(+)-glyceraldehyde [M. L. Wolfrom, K. V. Lemieux and S. M. Olin, *J. Am. Chem. Soc.*, **71**, 2870 (1949)]. The configurational assignments of Fig. 1 are therefore correct.

(4) D. J. Cram, *ibid.*, **71**, 3863, 3883 (1949).

(5) S. Winstein and co-workers, *ibid.*, **74**, 113, 1127, 1140, 2165, 2171 (1952); **75**, 147, 155 (1953), and many subsequent and preceding papers.

(6) (a) J. D. Roberts and C. M. Regan, *J. Am. Chem. Soc.*, **75**, 2069 (1953); (b) J. D. Roberts and M. Halmann, *ibid.*, **75**, 5759 (1953); (c) J. D. Roberts, C. C. Lee and W. H. Saunders, *ibid.*, **76**, 4501 (1954); (d) R. H. Mazur, W. N. White, D. A. Semenow, C. C. Lee, M. S. Silver and J. D. Roberts, *ibid.*, **81**, 4390 (1959); (e) E. Renk and J. D. Roberts, *ibid.*, **83**, 878 (1961); (f) A. W. Fort and R. E. Leary, *ibid.*, **82**, 494 (1960).

(7) (a) A. Streitwieser, Jr., *J. Org. Chem.*, **22**, 861 (1957); (b) A. Streitwieser, Jr., and W. D. Schaeffer, *J. Am. Chem. Soc.*, **79**, 2888 (1957).

(8) (a) H. Schmid and G. Muhr, *Ber.*, **70**, 421 (1937); H. Schmid and A. Woppmann, *Monatsh.*, **83**, 346 (1952); H. Schmid and R. Pfeiffer, *ibid.*, **84**, 829, 842 (1953); H. Schmid, *ibid.*, **85**, 424 (1954). (b) E. D. Hughes, C. K. Ingold and J. H. Ridd, *J. Chem. Soc.*, 88 (1958).

(9) D. Y. Curtin and M. C. Crew, *J. Am. Chem. Soc.*, **76**, 3719 (1954); B. M. Benjamin and C. J. Collins, *ibid.*, **78**, 4952 (1956).

(10) C. J. Collins, W. A. Bonner and C. T. Lester, *ibid.*, **81**, 466 (1959); **78**, 5587 (1956).

(11) S. Winstein and E. Grunwald, *ibid.*, **70**, 835 (1948); S. Winstein and B. K. Morse, *ibid.*, **74**, 1134 (1952); S. Winstein and L. L. Ingraham, *ibid.*, **77**, 1739 (1955).
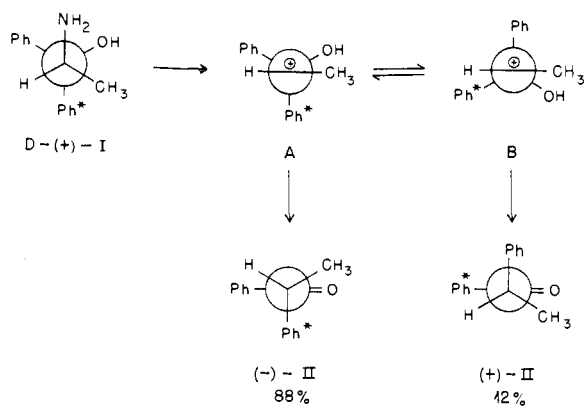
Fig. 1.

Fig. 2.

or α-phenylethyl acetate with inversion or retention, depending upon the solvent employed,[12] and that D-(−)-aminodesoxybenzoin[13] yields D-(−)-benzoin can also be explained on the same basis.

It appeared to us that the results obtained[3] in the deamination of stereospecifically labeled (+)-I (Fig. 1) foreshadowed a completely new field of research in which the novel technique previously[3] employed could be applied to a series of deamination reactions involving 1,2-shifts for the purpose of determining what factors influence the relative proportions of topside and backside attack exhibited by the migrating group. Since topside attack by the migrating group with retention of configuration (corresponding in Fig. 1 to the pathway (+)-I → B → (+)-II) is presumed to be associated with open carbonium ion formation, whereas backside attack with inversion could be a consequence either of bridged or of open carbonium ion intermediates, a comparison of the relative amounts of topside versus backside attack in several different systems should allow us to estimate the relative importance of bridging and neighboring-group participation. We make the basic assumption that if in a given deamination topside attack with retention of configuration through open carbonium ion intermediates can account for a significant proportion of reaction, then neighboring-group participation accompanied by bridging cannot be important in that same deamination. This follows, for it has been well established[5] that participation or "anchimeric assistance"[14] imparts such a driving force to the reaction that the same reaction without such "anchimeric assistance" (that is, through open carbonium ion intermediates) cannot compete ratewise, sometimes by several orders of magnitude. We accordingly synthesized, resolved and related the absolute configurations of erythro-1-amino-1,2-diphenyl-2-propanol-phenyl-C[14] (IV), 2-amino-1,1-diphenylpropane (VII, stereospecifically labeled in one or the other of the two phenyl groups), erythro-1-amino-1-phenyl-2-p-tolylpropanol-2 (erythro-IX, chain-labeled in the 1-position), threo-1-amino-1-phenyl-2-p-tolylpropanol-2 (threo-IX), and the erythro and threo isomers of 1-amino-1-phenyl-2-o-tolylpropanol-2 (XIX).[15]
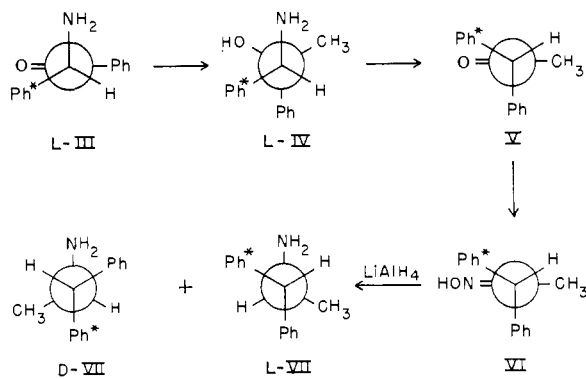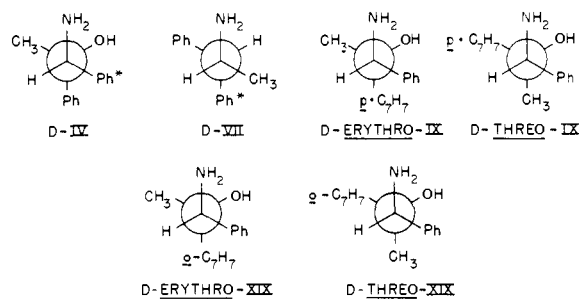
(12) E. Ott, Ann., 488, 186 (1931).

(13) A. McKenzie and D. J. Pirie, Ber., 69, 876 (1936).

(14) S. Winstein, C. R. Lindgren, H. Marshall and L. L. Ingraham, J. Am. Chem. Soc., 75, 148 (1953), footnote 3.

In the present paper we discuss the radiochemical and stereochemical consequences of the deamination of compounds IV and VII. In subsequent papers[16] the reactions of the threo and erythro isomers of IX and XIX will be reported.

Methods and Results

The proposed syntheses of appropriately labeled L-IV and of D- and L-VII are shown in Fig. 2. We anticipated that racemic aminodesoxybenzoin (III) would be used as the starting material, since it appeared that erythro-IV should be more easily resolved and also more optically stable than III. The absolute configurations of the enantiomers of III had not been determined previously, so we related L-(+)-III and L-(+)-IV to L-(−)-2-amino-1,1,2-triphenylethanol (XVIII) as shown in Fig. 3, L-(−)-XVIII having previously been related[17] to L-(+)-phenylglycine. The configuration of L-(+)-phenylglycine has been reported by Ingold, et al.,[18] and is twice confirmed by our own work. The first confirmation follows through the

(15) The D- or L-designations employed in this paper always refer, in those compounds containing two asymmetric carbon atoms, to the carbon atom containing the amino group, or the lone functional group. Thus (−)-erythro-1-amino-1-phenyl-2-p-tolylpropanol-2 is assigned the D-configuration because the no. 1 carbon possesses the same arrangement of hydrogen, amino and phenyl groups as does D-(−)-phenylglycine (vide infra); the terms "erythro" or "threo" then define the configuration of the no. 2 carbon. The "erythro" isomer is that diastereomer in which the largest number of identical or similar groups can be brought into eclipsed positions. We have arbitrarily chosen the functional groups amino and hydroxyl as similar to each other, and the aryl groups phenyl and p-tolyl or o-tolyl as similar to one another in naming the diastereomers discussed in this paper (see also footnote 20).

(16) (a) B. M. Benjamin and C. J. Collins, J. Am. Chem. Soc., 83, 3662 (1961); (b) C. J. Collins, M. Staum and B. M. Benjamin, to be submitted.

(17) A. McKenzie and A. C. Richardson, J. Chem. Soc., 123, 79 (1923); A. McKenzie and G. O. Wills, ibid., 127, 283 (1925).

(18) B. C. Hibbin, E. D. Hughes and C. K. Ingold, Chemistry & Industry, 933 (1954).

Fig. 3.

Fig. 4.
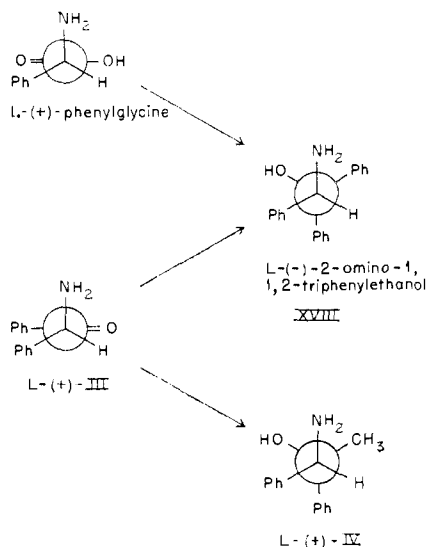
work of McKenzie and Pirie[19] from our experiments relating (+)-III and L-(+)-phenylglycine, and the second confirmation stems from the relation of stereospecifically labeled (+)-2-amino-1,1-diphenylpropane (VII), through deamination, to D-(+)-*threo*- and L-(+)-*erythro*-1,2-diphenylpropanol-1 (VIII), whose configurations have been established by Abd Elhafez and Cram.[20]

Because there existed no *a priori* method of ensuring the total stereoselectivity of the reaction sequence given in Fig. 2, we carried out the experiments illustrated in Fig. 4, in order to determine whether or not it would be possible to oximinate the model compound benzhydryl-$^2H_1$ phenyl ketone-C^{14} (XI) and then reduce the oxime XII to the amine hydrochloride XIII without loss of deuterium. It was reasoned that if the deuterium label of structure XI could survive the reaction sequence XI → XII → XIII, then in all probability the reaction sequence V → VI → VII could also be carried out without racemization of the labeled phenyl. The numbers under the structures of Fig. 4 refer to the carbon-14 contents of the compounds expressed as relative molar radioactivities. This series of reactions was carried out twice. In the first run the oximination XI → XII was performed in low yield under mild conditions. Infrared analyses of ketones XI and XVI indicated ketone XI to be devoid of hydrogen in the benzhydryl position, whereas ketone XVI contained approximately 26% hydrogen in the benzhydryl position. This is a very good check with the carbon-14 data shown in Fig. 4, and indicates that no deuterium was lost during the sequence X → XI → XII → XIII → XIV. In the second experiment, forcing conditions were used during oximination in order to increase the yield of XII. Results of infrared

(19) A. McKenzie and D. J. C. Pirie, *Ber.*, 67, 876 (1936); see also G. Drefahl and H. Crahmer, *ibid.*, 91, 745 (1958).

(20) F. A. Abd Elhafez and D. J. Cram, *J. Am. Chem. Soc.*, 74, 5849 (1952). These authors assign the D- or L-designations to the various isomers of VIII on the basis of a different convention than that used in the present paper. We have employed, for internal consistency, the genetic relation of the no. 1 carbon to D or L mandelic acid [K. Mislow, *J. Am. Chem. Soc.*, 73, 3954 (1951)].
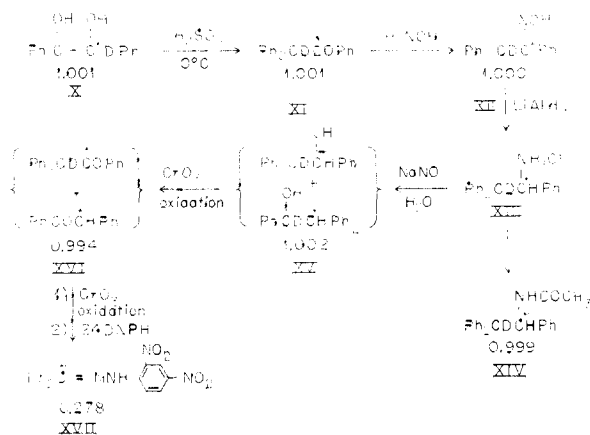
analyses indicated considerable loss of deuterium from XVI (about 55%) in excess of the 28% to be expected on basis of the carbon-14 data. Nuclear magnetic resonance spectra[21] of all of the samples of Fig. 4 except XIII indicated approximately 40% loss of deuterium during the forced oximination, but no loss of deuterium during the transformations XII → XIII → XIV. From the n.m.r. data it could be calculated that approximately 25% rearrangement had taken place during the deamination XIII → XV, again in very good agreement with the radiochemical data of Fig. 4. We therefore concluded that under sufficiently mild conditions the oximination V → VI should take place without interchange of Ph and Ph*, and that the lithium aluminum hydride reduction VI → VII could be performed also with maintenance of the optical integrity of the benzhydryl position.

erythro-(+)-IV, *erythro*-(−)-IV and their corresponding hydrochlorides were synthesized through the action of methylmagnesium iodide upon carbon-14-labeled, racemic aminodesoxybenzoin (III), followed by resolution through the (+)-tartrate and (+)-10-camphorsulfonate salts. Through deamination, under conditions previously reported,[3] followed by oximination and reduction (Fig. 2), the two separate enantiomers were converted to the isotope position isomers of (±)-2-amino-1,1-diphenylpropane (VII) illustrated in Figs. 5 and 6. The distribution of radioactivity between the two labeled phenyl groups of compounds V and VII (Figs. 5 and 6) is established in the following paragraph. From the two racemic mixtures of VII produced, it was possible to isolate α-(+)-VII and β-(+)-VII by resolution through their salts with (+)-camphoric and (+)-camphorsulfonic acids. It was established, by subjecting the reaction products to vapor phase chromatography, that no α-phenylpropiophenone was present in the ketone fraction and thus that no methyl migration had occurred during rearrangement of *erythro*-IV.

The two optically active, isotope position isomers α-(+)-VII and β-(+)-VII were converted to their hydrochlorides, dissolved in water at 25° and subjected to deamination by the gradual addition of solid potassium nitrite. Reisolation, from aliquots of the product, of optically pure α- and

Fig. 5.

Fig. 6.

a The *erythro* isomer of VIII is formed in very small yield (see Fig. 1). Therefore, it was not possible to purify these degradation products to the same extent as the degradation products from the *threo*-isomer. The values given here, therefore, are within experimental error identical with the more accurate values given for the degradation products from D-(+)-*threo*-VIII.
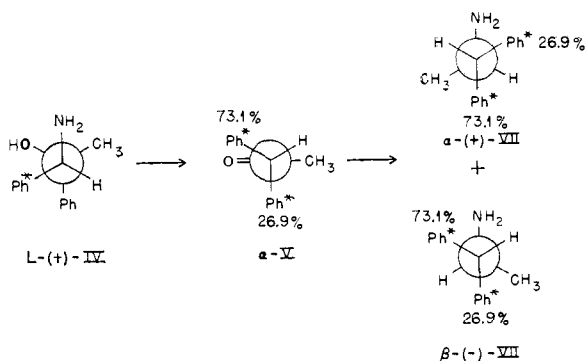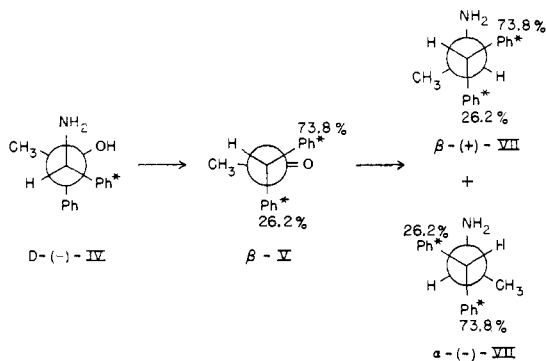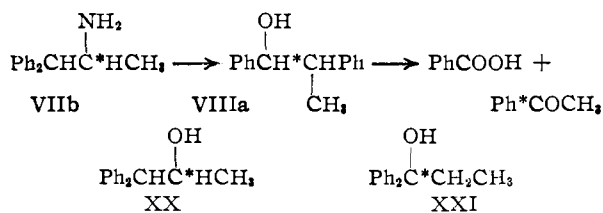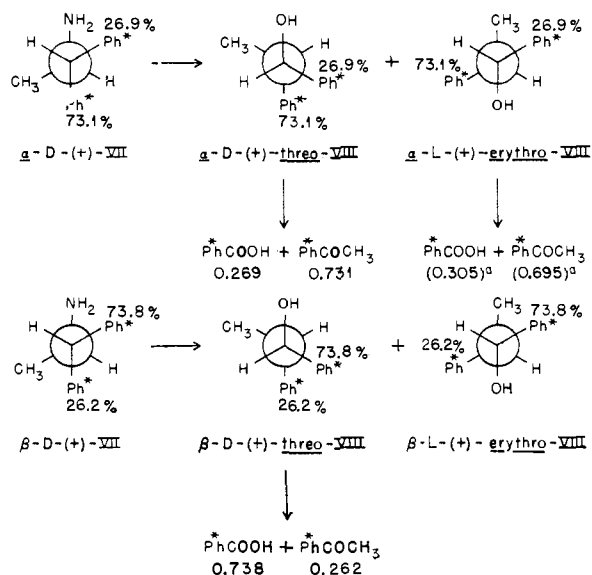
Fig. 7,

β-D-(+)-*threo*-VIII and α-L-(+)-*erythro*-VIII was followed by oxidation of each to samples of benzoic acid and acetophenone. Radioactivity assay of these degradation fractions (the acetophenone-C^{14} was converted to the oxime) allowed us to calculate the distribution of radioactivity in the products of deamination. These results are summarized in Fig. 7. Several additional experiments were performed: (a) An aliquot of the reaction product was subjected to vapor phase chromatography to determine whether any olefinic products had been formed. A fraction amounting to 6–7% of the total product and consisting of three olefinic components was found. Since two of the peaks correspond to two products from the deamination of 1-amino-1,2-diphenylpropane,[22] we presume that *cis*- and *trans*-α-methylstilbene were produced. The third component may be 1,1-diphenylpropene-1. (b) To another aliquot was added a weighed amount of racemic *threo*-VIII. Reisolation and purification of the racemate and the pure enantiomer, followed by radioactivity assay, permitted the calculation that optically pure (+)-*threo*-VIII was formed on deamination of (+)-*threo*-VII unaccompanied by (−)-*threo*-VII. (c) Racemic 2-amino-1,1-diphenylpropane-2-C^{14} (VIIb) was syn-

(22) B. M. Benjamin and C. J. Collins, unpublished work.

thesized, subjected to the same conditions of deamination, and the isotope dilution technique was employed to determine the yields of *threo*-VIIIa (54.8%) and *erythro*-VIIIa (10.6%). Carbinol VIIIa was oxidized to benzoic acid and acetophenone, and these fragments were assayed for radioactivity, by which it was demonstrated that no scrambling of the chain label took place, and that all of the carbon-14 in VIIIa was in the 2-position of the propane nucleus. (d) Isotopic dilution experiments upon the deamination product of VIIb demonstrated the absence of 1,1-diphenylpropanol-2 (XX) and of 1,1-diphenylpropanol-1 (XXI) as well as of starting amine. (e) Finally, VIIIa was subjected to the conditions of the deamination reaction for a prolonged period, then oxidized to acetophenone and benzoic acid. Radioactivity assay of these fragments demonstrated that no scrambling of the carbon-14 label took place under the reaction conditions.

Discussion

From the data just presented, we can draw the following conclusions: (1) The compounds α-(+)-VII and β-(+)-VII are not discretely labeled but contain carbon-14 distributed between the two phenyl groups in the ratio 0.735:0.265, as shown in the formulas of Fig. 7 (this is the average value for the two degradation experiments upon α- and β-D-(+)-*threo*-VIII). This is equivalent to saying that the observed scrambling of carbon-14 must have taken place during the deamination of D- and L-*erythro*-1-amino-1,2-diphenylpropanol-2 (IV, Figs. 5 and 6) and not during the rearrangement (Fig. 7) of 2-amino-1,1-diphenylpropane (VII). This conclusion is based on the argument which follows: Shown in Fig. 8 is a scheme for the deamination-rearrangement of α-D-(+)-VII. In order to sim-
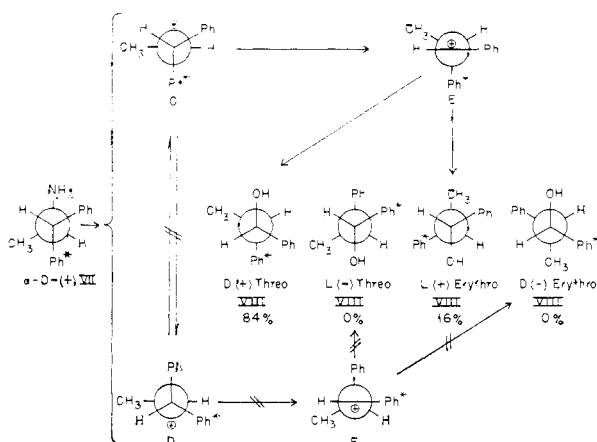
Fig. 8.

plify the discussion that phenyl with the excess carbon-14 is shown as labeled.

If we neglect for the moment the question of whether the intermediates C, D, E and F are bridged or open carbonium ion intermediates, it can be seen that each of the four possible products—representing two enantiomers each of *threo-* and *erythro-*VIII—is formed through a separate and experimentally distinguishable pathway. The key to our ability to thus distinguish these pathways is the fact that D- and L-*threo*-VIII should possess opposite distributions of radioactivity, as should D- and L-*erythro*-VIII, whereas D-(+)-*threo*-VIII and L-(+)-*erythro*-VIII should possess identical radioactivity distributions, as should the L-(−)-*threo* and D-(−)-*erythro* diastereomers. Therefore, from our data we can immediately say that ions D and F make no contribution to the reaction, and that the only pathways through which D-(+)-VII underwent deamination was through ions C and E, because: (a) isotope dilution experiments demonstrated the absence of L-(−)-*threo*-VIII, and (b) the radioactivity distributions of the reisolated D-(+)-*threo*-VIII and L-(+)-*erythro*-VIII are identical within experimental error.[23]

(2) Since D-(+)-*threo*-VIII (Fig. 8) and L-(+)-*erythro*-VIII were both formed from the same intermediate (carbonium ion E), the former through attack of hydroxyl from above the plane of the carbonium center (as oriented in Fig. 8) and the latter from below the plane, then at least to the extent that L-(+)-*erythro*-VIII is produced, E must exist as an open, unbridged ion. Since it has already been demonstrated[10] that the open, unbridged 1,2,2-triphenylethylcarbonium ion is not attacked equally by hydroxyl ion from both sides due probably to steric shielding by *ortho*-hydrogen, we prefer the interpretation that ions C and E are also open, unbridged ions. Additional evidence for the open-ion character of the intermediates in

such deamination reactions is to be found in the two succeeding papers[15,16] and in the ensuing paragraph.

(3) The formation of carbonium ion C to the exclusion of ion D is most probably a consequence of control of intermediate formation by the "ground-state" conformations of VII. This conclusion follows from a comparison of the conformations possible for 2-amino-1,1-diphenylpropanol-2 (I-1, I-2 and I-3) with those possible for 2-amino-1,1-diphenylpropane (VII-1, VII-2 and VII-3).
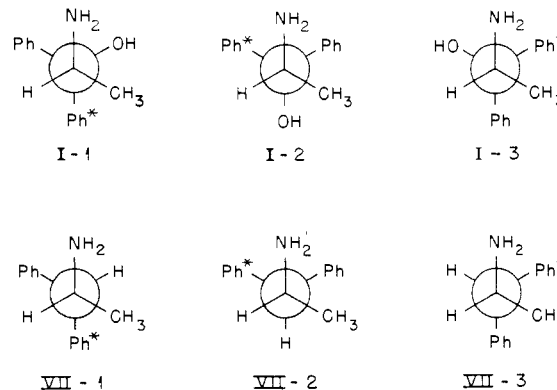
Although it seems clear that hydrogen is by far the smallest group in compounds I and VII, the relative effective bulks of the amino-, hydroxy- and methyl-groups are not so easy to assess.[24] On a steric basis alone, therefore, a qualitative decision concerning the relative abundances of conformations I-1, I-2 and I-3 would be difficult to make. Not so, however, for the conformations of VII, since it seems highly unlikely that VII-2 and VII-3—each with two hydrogens adjacent—could ever compete in relative stability with conformation VII-1. We propose, therefore, that the previous[3] results (Fig. 1) upon the deamination of (+)-I are best explained by assuming conformations I-1 and I-2 are present in approximately the relative proportions of 88:12, thus upon deamination producing in this same proportion ions A and B, which go directly to their respective products (−)-II and (+)-II. The present data (Figs. 7 and 8) are similarly best explained by assuming that VII-1 is the only important "ground-state" conformation and that it, upon loss of nitrogen, goes directly to the open carbonium ion C, which then rearranges to E with resulting formation of D-*threo*-VIII and L-*erythro*-VIII. We consider it unlikely that bridged ions are directly formed in these deaminations, for not only is the invocation unnecessary, but one would expect the driving force for participation[5] of phenyl through "anchimeric" assistance[14] to be greater in the rearrangement of I than in the rearrangement of VII, owing to the enhancement of such assistance through the presence of the electron-rich hydroxyl group of I.[25] If we

(23) The present data allow, it is true, the migration of the un-labeled phenyl of D-VII (Fig. 8) through a *cis*-transition state to the backside of the migration terminus. This possibility would also account for the observed scrambling of the carbon-14 label. Such an alternative mechanism has been ruled out, we believe, by the data of the ensuing paper (ref. 16a), in which (−)-*erythro*-1-amino-1-phenyl-2-*p*-tolylpropanol-2 (IX) has been found to undergo deamination under the same reaction conditions with 74% inversion and 26% retention of configuration. These results are identical, within experimental error, with the results reported here for the deamination of IV.

(24) The relative effective bulks of methyl and phenyl are also in some doubt owing to the recent discovery that the effective shielding ratio of phenyl to methyl can vary from 10 to 0.45 as the addend to biacetyl is changed from phenyllithium to phenylmagnesium iodide, phenylmagnesium bromide and phenylmagnesium chloride: J. H. Stocker, P. Sidisunthorn, B. M. Benjamin and C. J. Collins, *J. Am. Chem. Soc.*, **82**, 3913 (1960).

make the unfounded assumption, therefore, that the rearrangements of I and VII through backside migration of phenyl proceed through participation which produces bridged ion intermediates, then we would be unable to explain why (+)-I produces on deamination 12% of (+)-II (corresponding to 24% open carbonium intervention) when (+)-VII which should suffer more topside migration of phenyl (corresponding to ion D, Fig. 8), actually undergoes none.[26]

(4) The rearrangements of phenyl-labeled D- and L-IV, Figs. 5 and 6, can best be interpreted through the mechanism outlined in Fig. 9. The isomer D-(−)-IV, labeled in the 1-phenyl group, is used as an illustration. It is interesting that even when we postulate "ground-state control" of the products, as in Fig. 9, our data demand that the intermediate ions undergo a certain degree of rotation, for in the absence of methyl migration (which would presumably take place through ions H or L) it is necessary at least that ion K or ion L suffer 60° rotation to ion M, in order to account for the 26.5% topside attack by phenyl. It should also be pointed out that whereas our experiments[3] (see Fig. 1) upon the deamination of (+)-I ruled out the possibility of phenyl migration through a *cis* transition state, since both ion A and ion B proceed to produce through *trans* transition states, such is not the case for the rearrangement of IV. Thus (see Fig. 9) although 73.5% of the reaction occurs through ion G which, when phenyl migrates, places Ph* and CH₃ *trans* one to the other, 26.5% of the reaction proceeds to produce through ion M, which places Ph* and CH₃ in *cis* eclipsed positions in the transition state. This very fact is almost conclusive evidence against the formation of bridged ions through participation, since such a mechanism would require, according to the rules set down[6,7] for other deamination reactions, that at least 53% (or twice the amount of topside migration) of the reaction must of necessity proceed through open carbonium ions, thus indicating the absence of the acceleration to be expected in well-documented[5] cases of neighboring-group participation.

(5) The stereochemistry of the processes intervening between L-(+)-IV in its conversion through V, VI and VII to α-D-(+)-*threo*-VIII and α-L-(+)-*erythro*-VIII now becomes clear on the basis of our knowledge of the fate of the carbon-14 labels. Since the configurations of reactants (L-IV) and products (D-*threo*-VIII and L-*erythro*-VIII) are known, we have been able to assign the configurations of all intermediate compounds, making the one assumption that in the rearrangements of IV and VII, phenyl migration has taken place predominantly through backside 1,2-shifts involving *trans* transition states.

(25) S. Winstein, C. R. Lindegren, H. Marshall and L. L. Ingraham, *J. Am. Chem. Soc.*, **75**, 153 (1953).

(26) Our hesitancy to invoke bridged ions in the present work should not be interpreted to mean that we believe such non-classical ions can never intervene during these and other deamination reactions. It is, of course, possible that bridged ions could serve as intermediates between two interconverting classical ions. In the absence of any compelling evidence for the existence of non-classical ions as intermediates in the reactions discussed here and in light of the positive evidence for open, unbridged, non-classical ions, we believe it necessary to present the simplest possible mechanism which is consistent with all of the facts.
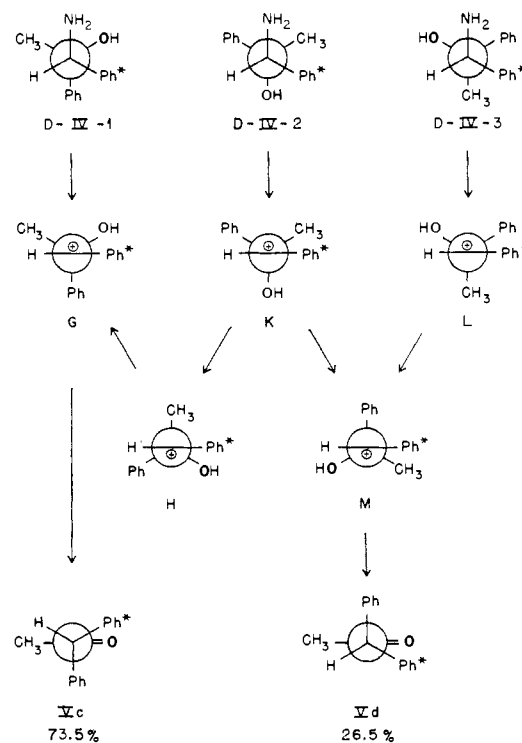

Fig. 9.

(6) Finally, the complete lack of methyl migration during rearrangement of IV is somewhat surprising in view of the considerable fraction of methyl migration observed by Cram and McCarty[27] during the deamination of *threo-* and *erythro-*2-amino-3-phenylbutane. The explanation may lie in the higher stabilization of charge by phenyl in the ions G, H, K, L (Fig. 9) than would be expected by methyl in the 3-phenyl-2-butyl carbonium ion. Such stabilization would increase, whereas the more localized charge of the 3-phenyl-2-butyl carbonium ion would decrease the activation energy for both phenyl and methyl migration, thus minimizing the differences between them.

Experimental

erythro-1-Amino-1,2-diphenyl-2-propanol-1-*phenyl*-C¹⁴ (IV).—2-Phenyl-C¹⁴-acetophenone (phenyl-labeled desoxybenzoin), prepared by the Friedel–Crafts reaction between benzene and phenyl-C¹⁴-acetyl chloride, was converted to the isonitroso derivative.[28] The product was reduced with stannous chloride to the stannic chloride complex salt of phenyl-labeled aminodesoxybenzoin.[29] The dry powdered salt, 87.5 g., was added in small portions to the Grignard reagent prepared from 2 moles of methyl iodide and 2 moles of magnesium. The reaction mixture was allowed to stand at room temperature overnight. Hydrolysis of the complex was accomplished with ammonium chloride solution. The ether layer was separated and the aqueous layer was extracted several times with ether. The combined ether extracts were treated with Norite and filtered. Crude racemic aminoalcohol remained when the ether was evaporated. After crystallization from ethanol there remained 19.8 g. of pure IV, m.p. 110°.[30]

Resolution of IV.—The aminoalcohol IV was mixed with 13.5 g. of *d*-tartaric acid in 150 ml. of 75% alcohol. The mixture was heated until all solid material was dissolved.

(27) D. J. Cram and J. E. McCarty, *J. Am. Chem. Soc.*, **79**, 2866 (1957).

(28) V. Meyer and L. Oelkers, *Ber.*, **21**, 1303 (1888).

(29) R. Pschorr and F. Bruggemann, *ibid.*, **35**, 2740 (1902).

(30) A. McKenzie and A. K. Mills, *ibid.*, **62**, 1788 (1937).

Fractional crystallization of the resulting tartaric acid salt produced a pure material, $[\alpha]^{25}$D $-3°$ (water).

Anal. Calcd. for $C_{19}H_{23}NO_7$: C, 60.46; H, 6.14. Found: C, 60.36; H, 6.08.

The foregoing tartrate was treated with dilute sodium hydroxide to liberate the free resolved aminoalcohol, which was dissolved in ethanol and converted directly to the hydrochloride salt by the addition of excess concentrated hydrochloric acid; $[\alpha]^{25}$D $-52.3°$ (alcohol).[30]

The mother liquors from crystallization of the tartrate salt were treated with dilute sodium hydroxide. The free aminoalcohol was collected and mixed with an equimolar amount of *d*-10-camphorsulfonic acid in alcohol–water mixture. The salt which separated was crystallized four times; $[\alpha]^{25}$D $56°$ (alcohol).[30] The free amine was recovered from this and salt converted to the hydrochloride, $[\alpha]^{25}$D $52.5°$ (alcohol).[30]

erythro-1-Amino-1,2-diphenyl-2-propanol-2-C^{14} (IVb).— Carboxyl-labeled phenylacetyl chloride-C^{14} was converted to IVd in a manner strictly analogous to that employed in the synthesis of the phenyl-labeled isomer. The aminoalcohol was converted to the hydrochloride salt, crystallized twice, and dried in vacuum for further use.

Proof of Radiochemical Structure of IV.—A sample of phenyl-labeled aminoalcohol (0.21 g., 4.493 mc./mole), recovered from filtrates left over after resolution, was dissolved in 10 ml. of acetic acid and 0.123 g. of chromic oxide was added. The solution was heated to 75° on the steam-bath for 1 hour, then diluted with 125 ml. of water. Organic materials were recovered by ether extraction. The combined ether extracts were washed thoroughly with sodium bicarbonate solution and the ether was evaporated. The small amount of oily material containing acetophenone, benzaldehyde and benzoic acid was taken up in 10 ml. of ethanol and was treated with 0.018 mole of 2,4-dinitrophenylhydrazine reagent. The mixture was allowed to stand at room temperature for a half-hour. The precipitated 2,4-dinitrophenylhydrazone of acetophenone was collected on a filter and crystallized three times. To the 91 mg. of derivative remaining was added 8 mg. of non-radioactive 2,4-dinitrophenylhydrazone of benzaldehyde as hold-back carrier and the compound was crystallized twice more; m.p. 250°, 0.0729 ± 0.0006 mc./mole. This is 1.6% of the original radioactivity of the aminoalcohol.

1,1-Diphenyl-C^{14}-acetone (α-V).—A solution of 24.9 g. of the resolved hydrochloride salt, $[\alpha]^{25}$D $-52.3°$, of phenyl-C^{14}-labeled aminoalcohol in 500 ml. of 25% acetic acid was treated with 7 g. of sodium nitrite in 20 ml. of water. After a half-hour, 3 g. more of sodium nitrite was added and the solution was stirred for an additional hour. The oily product was extracted with ether. The ether solution was washed thoroughly with water and sodium bicarbonate solution and the ether was evaporated. There remained 19.5 g. of oily material which was not further purified. In a previous run with non-radioactive starting material the ketone was recovered as a solid material by crystallization from hexane; m.p. 60°.[31]

2-Amino-1,1-diphenyl-C^{14}-propane (VII).—The phenyl-C^{14}-labeled diphenylacetone α-V, 19.5 g., was dissolved in a mixture of 50 ml. of ethanol and 50 ml. of pyridine and 20 g. of hydroxylamine hydrochloride was added. The mixture was heated to reflux for 3 hours and then poured into 500 ml. of cold water. The precipitate of solid oxime was collected on a filter, and was crystallized once from alcohol; yield 13.2 g., m.p. 163°.[31] The oxime was added to a slurry of 10 g. of lithium aluminum hydride in 500 ml. of diisopropyl ether. After the mixture was heated at reflux temperature for 20 hours, the solvent was removed by evacuation with a water aspirator. Ethyl ether was added and the complex was hydrolyzed with just enough water to cause the precipitated alumina to become grainy. The alumina was removed from the ether solution by filtration and the filter cake was washed thoroughly with ether. The volume of solution was reduced to about 500 ml. and to this was added 3 *M* hydrochloric acid. A mass of crystals of 2-amino-1,1-diphenylpropane hydrochloride separated and this was collected on a filter and dried; 11.5 g., m.p. 180°.[32] Treatment of the amine hydrochloride with dilute sodium

hydroxide gave the free amine; 9.5 g., m.p. 60°.[32] An additional 2 g. of amine was recovered from the acidic filtrates; yield 97%.

2-Amino-1,1-diphenylpropane-2-C^{14} (VIIb).—The amine VIIb labeled with carbon-14 in the 2-position of the chain was synthesized from chain-labeled aminoalcohol-C^{14} IVb using exactly the same procedures described above for synthesis of the ring-labeled amine VII. A yield of 10.4 g. (66%) of pure VIIb, m.p. 182°, was obtained from 16 g. of 1,1-diphenylpropanone-2-C^{14}-oxime. A small amount of oxime was recovered.

Radiochemical Structure Proof of VIIb.—The oxime, 0.5 g., recovered above after reduction to amine VIIb, was dissolved in 10 ml. of acetic acid and 1.5 g. of chromic oxide was added, followed by a few drops of sulfuric acid. The solution was heated to boiling for 5 minutes and then poured into water. Benzophenone was recovered from the mixture and converted to the 2,4-dinitrophenylhydrazone. There was no radioactivity in the derivative, proving that the oxime and thus also the amine VIIb were labeled only in the 2-position.

Resolution of VII.—Racemic amine, 12 g., in 25 ml. of alcohol was mixed with 13.5 g. of *d*-10-camphorsulfonic acid in 200 ml. water. The solid which separated was collected on a filter and crystallized three times from water containing a little alcohol; m.p. 270°, $[\alpha]^{25}$D 10.8° (alcohol).

Anal. Calcd. for $C_{25}H_{33}NO_4S$: C, 67.67; H, 7.50. Found: C. 67.95; H, 7.41.

The salt was treated with dilute sodium hydroxide to obtain the free amine which was crystallized from hexane; m.p. 81°, $[\alpha]^{25}$D 10.7° (alcohol).

Anal. Calcd. for $C_{15}H_{17}N$: C, 85.44; H, 8.14. Found: C, 85.18; H, 8.12.

The (+)-amine, 3.7 g., was dissolved in 5 ml. of alcohol and 25 ml. of 3 *M* hydrochloric acid was added. The precipitated amine hydrochloride was crystallized from dilute hydrochloric acid; 3.5 g., sublimes above 250°, $[\alpha]^{25}$D $-24.6°$ (alcohol), 3.617 ± 0.003 mc./mole. In another run, 2 g. of (−)-amine hydrochloride was obtained, $[\alpha]^{24}$D $-25.4°$, 4.493 ± 0.001 mc./mole.

Free amine, 10.2 g., recovered from the filtrates of the *d*-10-camphorsulfonic acid salt, was dissolved in 30 ml. of alcohol containing 10.2 g. of *d*-camphoric acid. Crystallization was induced by adding 35 ml. of water to the warm solution and allowing it to stand undisturbed for several hours. The salt was crystallized four times from alcohol–water mixture; 8.3 g., m.p. 95° dec., $[\alpha]^{24}$D 20.3° (alcohol). The compound contained water of crystallization.

Anal. Calcd. for $C_{25}H_{33}NO_4 \cdot H_2O$: C, 69.90; H, 8.21. Found: C, 69.96; H, 8.27.

The free (−)-amine obtained from the *d*-camphoric acid salt was crystallized from hexane; m.p. 82°, $[\alpha]^{24}$D $-10.8°$ (alcohol).

Anal. Calcd. for $C_{15}H_{17}N$: C, 85.26; H, 8.11. Found: C, 85.61; H, 8.16.

The (+)-amine hydrochloride was prepared from the above (−)-amine. This was mixed with a small amount of (+)-amine hydrochloride from previous runs and the material was crystallized from dilute hydrochloric acid; sublimes above 250°, $[\alpha]^{21}$D 25.7°, 3.416 ± 0.012 mc./mole.

Anal. Calcd. for $C_{15}H_{18}NCl$: C, 72.71; H, 7.32. Found: C, 72.64; H, 7.32.

Deamination of 2-Amino-1,1-diphenylpropane (VII).— The following is a description of a typical deamination of VII. A sample, 3.3825 g., of the resolved hydrochloride salt, $[\alpha]^{25}$D $-24.6°$, α-(−)-VII hydrochloride, originating from aminoalcohol (L-(+)-IV) hydrochloride, $[\alpha]$ $-52.3°$, was dissolved in 100 ml. of water. To this was added 26 ml. of 1 *M* hydrochloric acid and 5.5 g. of potassium nitrite in 10 ml. of water. The temperature was maintained at 25° while stirring for 1.5 hours. The oily product which was extracted with ether weighed 3.186 g., $[\alpha]^{25}$D 30° (chloroform). The material was dissolved in hexane and passed through a 6″ × 3/4″ column containing Fisher alumina (80–200 mesh). A small amount of a hydrocarbon, 0.197 g., 7.5%, was obtained by elution of the column with 500 ml. of hexane. Elution of the column was continued with 250 ml. of 5% methanol in ether. When the solvent was evaporated and the residue was dried in vacuum overnight there remained 2.4 g. of material, $[\alpha]^{25}$D 37° (ethanol).

(31) A. McKenzie and R. Roger, *J. Chem. Soc.*, **125**, 844 (1924).

(32) J. Levy, P. Gallais and D. Abragam, *Bull. soc. chim.*, [4] **43–44**, 872 (1928). These authors report that the sole product upon deamination of VII is the olefin, 1,1-diphenylpropene-2.

A small amount of yellow radioactive material remained on the column.

Distribution of Carbon-14 in the Deamination Products of α-(−)-VII Hydrochloride.—The carbinol fraction of the deamination products recovered from the alumina column mentioned in the foregoing section was taken up in a small amount of hexane and placed in the refrigerator to crystallize. The solid crystals were collected on a filter, washed with cold hexane and crystallized again. Thus there was obtained 0.8 g. of pure L-(+)-1,2-diphenyl-1-propanol (α-L-(+)-*threo*-VIII), m.p. 61-61.5° (capillary), [α]^{25}D 47.5°. Filtrates were saved for subsequent recovery of the *erythro*-carbinol. The *threo*-carbinol was oxidized to α-methyldesoxybenzoin by dissolving it in 8 ml. of pyridine and adding the solution to a mixture of 0.8 g. of chromic oxide in 8 ml. of pyridine at 15°. The mixture was stirred at room temperature for 1 hour and then was poured into 200 ml. of water. Oily material was extracted with ether. The ether solution was washed with dilute hydrochloric acid and then with water. When the ether was evaporated 0.72 g. of residue remained. The ketone was separated from unreacted carbinol by chromatography on Fisher alumina. Thus 0.67 g. (93%) of α-methyldesoxybenzoin (racemized on the alumina) was recovered, m.p. 49° (capillary). The ketone was treated with 0.2 g. of sodium hydroxide and 0.6 g. of amyl nitrite in 7 ml. of alcohol at 0° for 2 days. In the manner described previously,[8] there was recovered from the reaction mixture pure benzoic acid, 0.9736 ± 0.0030 mc./mole, and pure acetophenone oxime, 2.643 ± 0.001 mc./mole.

The residue, 1.5 g., left in the filtrates after recovery of L-(+)-*threo*-1,2-diphenylpropanol, was treated with 1.35 g. of *p*-nitrobenzoyl chloride in 11 ml. of pyridine. The mixture was heated on the steam-bath for 2 hours and then poured into water. Crystallization of the recovered ester resulted in separation of two fractions. The high melting fraction was the *p*-nitrobenzoate of L-(+)-*threo*-1,2-diphenyl-1-propanol, m.p. 170°. The low melting fraction, melting point indefinite above 125°, was hydrolyzed by heating it in the presence of 25 ml. of 10% sodium hydroxide for 12 hours. A small amount of carbinol (α-L-(+)-*erythro*-VIII) which was recovered from the hydrolysis medium was crystallized three times from hexane; yield 0.2 g., m.p. 73°, [α]^{25}D 69.2° (chloroform). This material was pure L-(+)-*erythro*-1,2-diphenyl-1-propanol. It was cleaved in the same way as the *threo* isomer. Only 30 mg. of benzoic acid could be recovered, 1.082 ± 0.005 mc./mole. The acetophenone oxime, 50 mg., could not be completely purified; m.p. 55-58° (capillary), 2.459 mc./mole. The above information is outlined in Fig. 6. A similar experiment involving the deamination of the hydrochloride salt or β-(+)-VII, [α]^{25}D −25.4°, which was derived from aminoalcohol (D-(−)-IV) hydrochloride, [α]^{25}D +52.5°, is also outlined in Fig. 6.

Distribution of Carbon-14 in the Deamination Products of VIIb (Chain Labeled).—The deamination of 10.78 g. of racemic VIIb hydrochloride, 4.866 ± 0.014 mc./mole, conducted exactly as described elsewhere in the Experimental part, gave 10.42 g. of crude product, which was diluted to 200 ml. with alcohol in a volumetric flask. Two 10-ml. aliquots were removed and set aside for determination of the yields of *threo*- and *erythro*-1,2-diphenyl-1-propanol as described in the next section. The solvent was evaporated from the remaining 180 ml. and the residue was treated with 8.24 g. of *p*-nitrobenzoyl chloride in 25 ml. of pyridine. The ester was recovered and crystallized three times; m.p. 144°, 5.5 g. This was hydrolyzed to recover pure *threo*-1,2-diphenyl-1-propanol. This carbinol was oxidized and cleaved, by the method already described, to benzoic acid, 0.0186 mc./mole, and acetophenone oxime, 4.741 ± 0.012 mc./mole. Thus, since the benzoic acid was not radioactive and the acetophenone oxime contained almost all of the original radioactivity of the carbinol, the deamination rearrangement of IVb occurs without scrambling of the chain label.

Determination of Yields of Products in the Deamination of VIIb (Chain Labeled).—To one 10-ml. aliquot reserved from the experiment described in the foregoing section there was added 1.0215 g. of pure non-radioactive *threo*-1,2-diphenylpropanol. The carbinol was reisolated as the *p*-nitrobenzoate ester and crystallized four times; m.p. 144°, 0.9669 ± 0.0036 mc./mole. To the second 10-ml. aliquot was added 1.5702 g. of pure non-radioactive *erythro*-

1,2-diphenyl-1-propanol. The *erythro*-carbinol was recovered by crystallization from hexane six times; m.p. 50-51° (capillary), 0.1476 ± 0.0001 mc./mole. Thus the yield of *threo*-carbinol was 54.85% and the yield of *erythro*-carbinol was 10.64%.

In another experiment 1.3102 g. of the hydrochloride of VIIb amine was deaminated. The product was dissolved in 200 ml. of ethanol in a volumetric flask and then divided into four 50-ml. aliquots. One aliquot was used to determine the yield of *threo*-carbinol by adding to it 0.8230 g. of non-radioactive carbinol and reisolating it as the *p*-nitrobenzoate ester; m.p. 144°, 0.7988 ± 0.0011 mc./mole. The yield of *threo*-1,2-diphenyl-2-propanol in this run was therefore 57.59%. To the second aliquot was added 1.5003 g. of 1,1-diphenyl-2-propanol which, when reisolated and crystallized four times, m.p. 62°, was not radioactive. To the third aliquot was added 1.000 g. of 1,1-diphenyl-1-propanol, which reisolated, m.p. 94°, and found to be non-radioactive. To the fourth aliquot was added 0.8458 g. of racemic non-radioactive VII. The amine was reisolated as the hydrochloride salt and was not radioactive. Thus the deamination product contained no unreacted amine and neither 1,1-diphenyl-1-propanol nor 1,1-diphenyl-2-propanol.

In an attempt to determine the yield of racemic *threo*-carbinol formed upon deamination of optically active amine, a sample of the hydrochloride of (β-(−)-VII), [α] 25.6°, 3.554 ± 0.016 mc./mole, was treated with sodium nitrite. To the reaction product was added 1.2127 g. of pure non-radioactive racemic *threo*-1,2-diphenylpropanol. The mixture of carbinols then was treated with 2.1 g. of *p*-nitrobenzoyl chloride in pyridine. The benzoate ester was recovered and fractionally crystallized. The first material recovered after seven crystallizations was D-(−)-*threo*-1,2-diphenyl-2-propyl-*p*-nitrobenzoate, m.p. 170°, [α]^{24}D −91.9° (chloroform), 1.894 ± 0.007 mc./mole. This corresponds to a yield of 65.1% of the D-(−)-*threo*-carbinol. From the filtrates was recovered an ester fraction which, after repeated fractional crystallization, yielded almost completely racemic *threo*-1,2-diphenyl-2-propyl-*p*-nitrobenzoate, m.p. 144°, [α] −3.42° (chloroform), 1.038 ± 0.002 mc./mole. From these data it can be calculated that there was no racemic and consequently no (+)-*threo*-carbinol in the reaction product.

Attempted Isomerization of *threo*-1,2-Diphenyl-1-propanol.—A sample of radioactive *threo*-carbinol-C^{14} was prepared by deamination rearrangement of phenyl-labeled aminoalcohol IV. The carbinol was purified by crystallization and subsequent decomposition of its *p*-nitrobenzoate ester. The pure *threo*-carbinol, 0.8798 g., 3.671 ± 0.024 mc./mole, was subjected to conditions identical with the deamination experiments described above. The organic fraction was isolated and to it was added 1.5249 g. of pure non-radioactive *erythro*-1,2-diphenyl-1-propanol. The *erythro*-carbinol was recovered by four crystallizations from hexane, m.p. 50-51° (capillary), and when assayed for carbon-14 it was found to be completely dead. Therefore the *threo*-carbinol does not isomerize under deamination conditions.

(−)-2-Amino-1,1,2-triphenylethanol (XVIII).—Aminodesoxybenzoin (III) was resolved by the method of McKenzie and Walker.[33] A one-gram sample of the solid aminoketone hydrochloride, [α]^{25}D 221.5° (alcohol), was added to the Grignard reagent from 1.5 g. of magnesium and 9 g. of bromobenzene. The reaction mixture was heated for 2 hours at the end of which water was added. The ether layer was separated by decantation and the ether was allowed to evaporate in a current of air. The residue was crystallized from ethanol; m.p. 130°, [α]^{25}D −238° (alcohol, concn. = 1). McKenzie and Wills[34] prepared the same (−)-aminoalcohol from (+)-phenylglycine.

Model Experiments on Compound X → XVII (Fig. 4) to Determine Extent of Deuterium Loss during Oximination (XI → XII) and Lithium Aluminum Hydride Reduction (XII → XIII).—1,1,2-Triphenylethylene-2-^{2}H$_1$-2-C^{14} glycol (X), 8.528 ± 0.014 mc./mole, was prepared and converted to benzhydryl-^{2}H$_1$ phenyl ketone-C^{14} (XI), 8.523 ± 0.06 mc./mole, as described previously.[35] To 10 g. of XI was added 11 g. of hydroxylamine hydrochloride and 78 ml. of

(33) A. McKenzie and N. Walker, *J. Chem. Soc.*, 646 (1928).

(34) A. McKenzie and G. O. Wills, *ibid.*, 127, 283 (1925).

(35) C. J. Collins, W. T. Rainey, W. B. Smith and I. A. Kaye, *J. Am. Chem. Soc.*, 81, 460 (1959).

pyridine. The mixture was boiled 2 hours, then 78 ml. of ethanol was added and the boiling was continued another 90 minutes. The mixture was quenched with water and the reisolated solid was shown to be only partially converted to oxime, so it was boiled for 16 hours with 80 ml. of pyridine, 80 ml. of ethanol and 11 g. of hydroxylamine hydrochloride, at which time 11 g. more of hydroxylamine hydrochloride was added and the heating was continued an additional 3 hours. The mixture was poured into water and the collected, crude solid had a melting point of 175°. Upon three crystallizations from chloroform–hexane, the melting point of the material became constant at 181°. The oxime XII had a radioactivity content of 8.519 ± 0.004 mc./mole. Five grams of XII was treated in ether with an excess of lithium aluminum hydride, and the mixture was stirred at room temperature for 4 days. The reduction mixture was treated with water until a grainy precipitate was obtained, and the ether was decanted, dried, and treated with anhydrous HCl to yield 2.5 g. of the amine hydrochloride XIII. A portion of XIII was made basic and converted to the amide XIV, m.p. 208°, 8.504 ± 0.02 mc./mole. To 1.19 g. of XIII in 120 ml. of water and 10 ml. of N HCl was added 2.25 g. of sodium nitrite. From the reaction mixture was isolated 801 mg. of crude product which upon treatment with Norite in hexane and subsequent crystallization produced 582 mg. of pure white carbinol XV, m.p. 87°, 8.532 ± 0.013 mc./mole. To 297 mg. of XV in 5 ml. of acetic acid was added 350 mg. of CrO_3 in 2 ml. of water. The mixture was left 1 hour at room temperature, warmed on a steam-bath 2–3 minutes, then poured into water. The solid ketone XVI, 275 mg., was collected on a filter and washed with water. It had a melting point of 138°. After one crystallization from ethanol, the material was assayed for radioactivity, 8.486 ± 0.06 mc./mole. After oxidation to benzophenone, the 2,4-dinitrophenylhydrazone XVII was shown to have a molar radioactivity of 2.365 ± 0.03 mc./mole.

The infrared spectrum of ketone XI showed a strong absorption at 8.1 μ and a medium absorption at 11.1 μ, characteristic for deuterium substitution alpha to a carbonyl group, and no adsorption at 8.4 μ, characteristic for the corresponding ketone devoid of deuterium. From the infrared spectrum of ketone XVI it could be calculated that the benzhydryl position contained 45% deuterium and 55% hydrogen.[36] Nuclear magnetic resonance spectroscopy[37] showed that ketone XI possessed only deuterium in the benzhydryl position, whereas the oxime XII and the amide XIV contained 57% and 63%, respectively, of the original deuterium in this same position. Carbinol XV contained 45% of the original deuterium in the benzhydryl position, 15% deuterium at the no. 1 carbon position, and 40% of the molecules contained no deuterium. Ketone XVI contained 49% of the original deuterium in the benzhydryl position. Thus the n.m.r., infrared and carbon-14 data are all in very close agreement. The n.m.r. data indicate that during the oximation about 40% loss of deuterium occurred, but that the lithium aluminum hydride reduction caused no deuterium loss. The oximation was therefore repeated under milder conditions, in which 1 g. of ketone XI, 1 g. of hydroxylamine hydrochloride, 2.7 ml. of pyridine and 7 ml. of ethanol were heated under reflux for 4.5 hours, during which time (after 3.5 hours) another gram of hydroxylamine hydrochloride was added. The isolated oxime XII (0.64 g., m.p. 182°) was treated as before, except that lithium aluminum hydride reduction was carried out for 2 hours in refluxing isopropyl ether. The infrared spectrum of ketone XVI from this second experiment showed that 74% of the original deuterium had remained in the molecule, very close to the percentage expected (72.2%) from the carbon-14 data of the first experiment.

(36) Performed by Mr. A. Tsiomis.

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Molecular Rearrangements. XVIII. The Deamination of *erythro*- and *threo*-1-Amino-1-phenyl-2-*p*-tolyl-2-propanol[1]

BY BEN M. BENJAMIN AND CLAIR J. COLLINS

The deaminations of optically active *erythro*- and *threo*-1-amino-1-phenyl-2-*p*-tolyl-2-propanol (III) have been studied. Whereas the *erythro* isomer yields *p*-methylbenzhydryl methyl ketone (IV) in which inversion predominates over retention in the ratio of 74:26, the *threo* isomer produces IV in which the ratio of inversion to retention is 43:57. These data clearly establish the open carbonium character of the intermediates. The absence of α-phenyl-4′-methylpropiophenone (V) in either deamination product rules out methyl migration during both reactions.

Introduction

In the preceding paper[2] were reported the radiochemical and stereochemical consequences of the deaminations of D- and L-*erythro*-1-amino-1,2-diphenyl-2-propanol (I), labeled in the 1-phenyl group with carbon-14. The results of this investigation, together with the mechanistic interpretation, are given in Fig. 1. Since these data revealed[2] that the deaminations involved an average of 73.5% phenyl migration with inversion of configuration and 26.5% phenyl migration with retention of configuration, we did not invoke bridged ions[3]

or neighboring group participation[4] in our rationalization of the mechanism of the reaction. Our conclusion rested on the assumption that topside attack of migrating phenyl through ions B or D to the extent of 26.5% (Fig. 1) must of necessity require complete cleavage of the carbon–nitrogen bond, which in turn demands that an open carbonium ion must be formed. Although it has been implied[5] that rearrangement accompanied by stereospecificity is synonymous with bridged or "nonclassical" ionic intermediates, such cannot be the case in the deamination of *erythro*-I, for one of the properties of neighboring group participation leading to bridged ions is its well-demonstrated[4] ability to enhance the rate considerably over the rate of the same reaction, were it to proceed solely through open carbonium ions. Since, in the deamination of I, the portion of the reaction which, stoichiometrically at least, could conceivably go through ini-

(1) This paper is based upon work performed at Oak Ridge National Laboratory, which is operated for the Atomic Energy Commission by Union Carbide Corporation. Portions of this research were presented at the Eighth Conference on Reaction Mechanisms, Princeton, N. J., September 8, 1960, and at the Conference on Use of Isotopes in Research and Industry, Copenhagen, Denmark, Sept. 15, 1960.

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(3) D. J. Cram, *ibid.*, **71**, 3863 (1949).

(4) A. Streitwieser, Jr., *J. Org. Chem.*, **22**, 861 (1957).

(5) See however, A. Streitwieser, Jr., and C. E. Coverdale, *ibid.*, **81**, 4277 (1959).