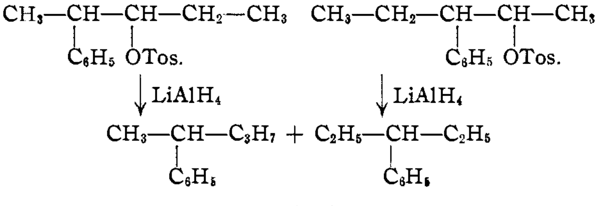
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Studies in Stereochemistry. VIII. Molecular Rearrangements During Lithium Aluminum Hydride Reductions in the 3-Phenyl-2-pentanol and 2-Phenyl-3-pentanol Systems(1)

BY DONALD J. CRAM

The molecular rearrangements that occur during the reduction with lithium aluminum hydride of the *p*-toluenesulfonates of the isomers of the 2-phenyl-3-pentanol and 3-phenyl-2-pentanol systems have been studied. All of the isomers undergo both a simple reduction reaction and a reduction with rearrangement to give mixtures of 2- and 3-phenylpentane, as well as elimination reactions to give both rearranged and unrearranged olefin. Methods of analyses of mixtures of 2- and 3-phenylpentane based on infrared and polarimetric measurements have been developed. Optically pure 2-phenylpentane has been synthesized. The mechanism and stereochemistry of the rearrangement reaction is discussed, and a correlation between the degree of rearrangement and the steric requirements for rearrangement has been made.

Paper VII(2) in this series presented evidence for a Wagner-Meerwein rearrangement taking place during the reduction of the *p*-toluenesulfonates of the various isomers of 3-phenyl-2-butanol with lithium aluminum hydride, as well as evidence that at least most of the olefin that accompanies the reduction arises through a *trans* elimination reaction. Since the products of both direct reduction and reduction with rearrangement are of the same structure, and in one racemate series of the same configuration, more information concerning the mechanism of the reaction could be gathered if the products of rearrangement were different from the products of simple replacement. The 3-phenyl-2-pentanol and 2-phenyl-3-pentanol systems offer such an advantage both as to the reduction products and the olefinic products of the reaction. In addition to this advantage, a novel method of product analysis presents itself based on the fact that of the two reduction products, 2-phenylpentane and 3-phenylpentane, the former has one center of asymmetry whereas the latter, although arising from a molecule containing two centers of asymmetry, is itself optically symmetric.



$$\mathrm{CH_3{-}\underset{C_6H_5}{CH}{-}\underset{OTos.}{CH}{-}CH_2{-}CH_3} \qquad \mathrm{CH_3{-}CH_2{-}\underset{C_6H_5}{CH}{-}\underset{OTos.}{CH}{-}CH_3}$$

$$\downarrow \mathrm{LiAlH_4} \qquad\qquad \downarrow \mathrm{LiAlH_4}$$

$$\mathrm{CH_3{-}\underset{C_6H_5}{CH}{-}C_3H_7 + C_2H_5{-}\underset{C_6H_5}{CH}{-}C_2H_5}$$

Methods

The four stereomers of both 3-phenyl-2-pentanol and 2-phenyl-3-pentanol were prepared in optically pure state and the *p*-toluenesulfonates of the B series(3) were prepared. In each case the *p*-toluenesulfonates of the enantiomorphs are less soluble in the crystallization solvents than the same derivatives of the racemates, and thus even higher optical purity is to be expected in the derivatives than in the starting alcohols.

Highly pure samples of both racemic (VII) and resolved 2-phenylpentane (VIIB) as well as 3-phenylpentane were needed for the analytical procedures. Racemic 2-phenylpentane was prepared by the treatment of acetophenone with propylmagnesium bromide followed by dehydration of the tertiary alcohol. Continuous removal of the water was necessary to drive this elimination reaction to completion. Catalytic reduction of the olefinic mixture produced crude racemic 2-phenylpentane. A carboxyl group was placed in the para-position of the benzene ring for use as a handle for carrying out resolution, as well as to provide solid compounds amenable to purification. The formulations trace these interconversions. That optical purity was obtained in the resolution(4) of 4-(2′-pentyl)-benzoic acid (VIII) is shown by the approach of the rotation of the acid to a maximum value with continued recrystallization of the quinine salt. This acid was also prepared by a second method to completely remove an ambiguity introduced into the literature by G. Hennion and S. McLease(5) regarding the physical properties of this compound. This second approach (see Experimental) was analogous to that used by Marvel(6) for the preparation of *p*-*s*-butylbenzoic acid. The conversion of resolved 2-phenylpentane back into 4-(2′-pentyl)-benzoic acid without any loss of the original optical activity indicates that none of the reactions in the cycle of operations involved any racemization at the asymmetric carbon atom. Pure 3-phenylpentane (IX) was prepared by a completely analogous series of reactions. The *p*-(2′,4′-dinitrobenzenesulfenyl) derivatives of these isomers were also prepared.(7) Table I reports the physical properties and analyses of the compounds involved in these syntheses.

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(1) Parts of this paper were presented before the Organic Division of the American Chemical Society, Chicago Meeting, September, 1950.

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

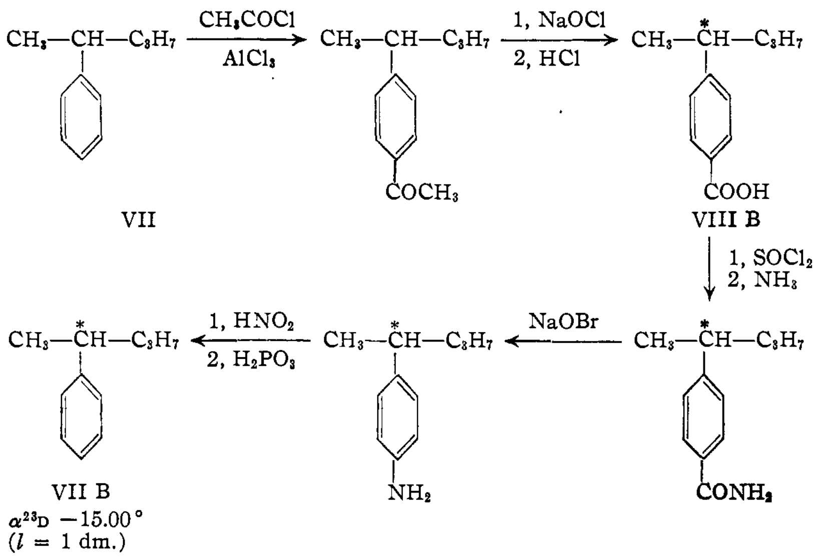
(3) The preparations and resolutions of most of these compounds were reported in Paper II of this series, *ibid.*, **71**, 3781 (1949). The numbering system for the various stereomers is carried into the present investigation. Evidence for optical purity of the starting materials is found in the Experimental part. The relative configurations of these starting materials have all been determined [D. J. Cram, *ibid.*, **71**, 3883 (1949)].

(4) This resolution is patterned after that employed by C. S. Marvel, R. L. Frank and E. Prill [*ibid.*, **65**, 1647 (1943)] to resolve *p*-*s*-butylbenzoic acid. Attempts were made to put the carboxyl group in the *ortho* position to bring the handle closer to the asymmetric carbon atom, but the synthetic difficulties proved prohibitive. An approach analogous to that used by P. Harrison, J. Kenyon and J. Shephard [*J. Chem. Soc.*, 659 (1926)] for the resolution of *p*-*s*-butylaniline was tried, but appeared unpromising.

(5) These authors, THIS JOURNAL, **64**, 2421 (1942), reported the synthesis of "*p*-*s*-amylacetophenone" and "*p*-*s*-amylbenzoic acid," the latter compound having a m.p. of 103–104° and the melting point of the semicarbazone of the ketone was given as 173–174°. These compounds were prepared from "*s*-amylbenzene." These physical constants are in disagreement with those of 4-(2′-pentyl)-benzoic acid and in agreement with those of 4-(3′-pentyl)-benzoic acid found in the present investigation.

(6) J. Copenhaver, M. Roy and C. S. Marvel, *ibid.*, **57**, 1311 (1935).

(7) C. M. Buess and N. Kharasch, Abstracts of Papers Presented Before Meeting of the American Chemical Society, September, 1949, pp. 3017.



resolved through 24 recrystallizations of the quinine salt, $\alpha^{23}\text{D}$ −23.3° (c = 3%, ethanol)

Figure 1 records the infrared absorption spectra of 2- and 3-phenylpentane. The differences in optical densities at $\lambda = 10.15\ \mu$, $\lambda = 11.33\ \mu$, and $\lambda = 12.02\ \mu$ were used for analyses of unknown mixtures of the two hydrocarbons. Figure 2 records the calibration curves at these wave lengths prepared from known mixtures, and in each case Beer's law applies. Figure 3 records the plot of the observed rotations of mixtures of optically pure (−)-2-phenylpentane mixed with various amounts of 3-phenylpentane. Again the plot is almost linear.

The reactions were carried out by dissolving the

TABLE I

PHYSICAL AND ANALYTICAL DATA PERTAINING TO COMPOUNDS INVOLVED IN THE SYNTHESES OF 2- AND 3-PHENYLPENTANE

Compounds 4-(2′-Pentyl)-	M.p., °C.	B.p., °C.	Mm.	Yield, %	$n^{25}\text{D}$	$[\alpha]^{23}\text{D}$	Formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
Acetophenone	.....	148–149	14	95	1.5137	....	$C_{13}H_{18}O$	82.04	81.89	9.53	9.58
Benzoic acid (*rac.*)	71–72	.....	..	74	....	.....	$C_{12}H_{16}O_2$	74.96	75.03	8.34	8.47
Benzoic acid (−)	54–55	.....	..	14	....	−23.3[a]	$C_{12}H_{16}O_2$	74.96	74.68	8.34	8.39
Benzamide (*rac.*)	114–115	.....	..	92	....	.....	$C_{12}H_{17}NO$	75.36	75.37	8.95	8.70
Benzamide (−)	108–109	.....	..	90	....	−21.9[a]	$C_{12}H_{17}NO$	75.36	75.46	8.95	8.93
Aniline (*rac.*)	.....	133	15	82	1.5283	.....	$C_{11}H_{17}N$	80.84	80.67	10.49	10.66
Aniline (−)	.....	131–132	19	84	1.5282	−22.3[b]	$C_{11}H_{17}N$	80.84	80.79	10.49	10.73
Benzene (−)	.....	193	..	67	1.5458	−15.0[c]	$C_{11}H_{16}$	89.12	89.05	10.88	11.09
Bromobenzene	.....	152	..	15	1.5332	.....	$C_{11}H_{15}Br$	58.13	58.76	6.65	6.64
Acetophenone semicarbazone (*rac.*)	175–177	.....	..	82	....	.....	$C_{14}H_{21}N_3O$	67.98	67.71	8.56	8.83
Acetophenone semicarbazone (−)	174–176	.....	..	87	....	.....	$C_{14}H_{21}N_3O$	67.98	67.94	8.56	8.72
Acetanilide (*rac.*)	105–106	.....	..	95	....	.....	$C_{13}H_{19}NO$	76.05	76.06	9.33	9.35
Acetanilide (−)	104–106	.....	..	94	....	−22.2[a]	$C_{13}H_{19}NO$	76.05	76.01	9.33	9.05
Phenyl 2′,4′-dinitrophenyl sulfide (*rac.*)	62.3	.....	..	47	....	.....	$C_{17}H_{18}N_2SO_4$	58.95	58.81	5.25	5.14
Compounds 4-(3′-Pentyl)-											
Acetophenone	.....	148–150	16	93	1.5151	.....	$C_{13}H_{18}O$	82.04	82.22	9.53	9.64
Benzoic acid	104–105	.....	..	89	....	.....	$C_{12}H_{16}O_2$	74.96	74.92	8.34	8.71
Benzamide	127–128	.....	..	94	....	.....	$C_{12}H_{17}NO$	75.36	75.23	8.95	8.71
Aniline	.....	130	15	83	1.5287	.....	$C_{11}H_{17}N$	80.84	80.78	10.49	10.53
Benzene	.....	189.5	752	73	1.4861	.....					
Acetophenone semicarbazone	165–166	.....	..	79	....	.....	$C_{14}H_{21}N_3O$	67.98	67.84	8.56	8.57
Phenyl 2′,4′-dinitrophenyl sulfide	86–87	.....	..	63	....	.....	$C_{17}H_{18}N_2SO_4$	58.95	58.81	5.25	5.14
Other compounds											
1-(2′-Chlorophenyl)-1-butanol		118–120	10	70	1.5037	.....	$C_{10}H_{13}ClO$	65.04	64.98	7.11	7.07
1-(2′-Chlorophenyl)-1-ethanol		114–116	14	34	1.5418	.....	C_8H_9OCl	61.37	61.45	5.79	5.87

[a] Absolute ethanol, $c \cong 3.3\%$. [b] $[\alpha]^{25}\text{D}$ on pure liquid, d^{25}_4 0.9278. [c] $\alpha^{23}\text{D}$, l = 1 dm.

TABLE II

DATA PERTAINING TO THE TREATMENT OF THE *p*-TOLUENESULFONATES OF THE ISOMERS OF 2-PHENYL-3-PENTANOL AND 3-PHENYL-2-PENTANOL WITH LITHIUM ALUMINUM HYDRIDE

Run no.	Tos. of	Solv.[a]	T, °C.	Wt. tos., g.	Wt.[b] ol. +phen.-pent., g.	%[c] Ol. in mix.	% Phen.[d] pents. in mixt.	α^{23}D[e] Mix. of 2- and 3-Phenpent. Olefin remov.		% 2-Phenylpentane in mixture of alkylbenzenes Mix. with olefin remov. By α[g]	By infrared at $\lambda(\mu)$ 10.15	11.33	12.02	Mix. from reductions By α[g]	By infrared at $\lambda(\mu)$ 10.15	11.33	12.02
								Olefin remov.	Olefin reduc.[f]								
1	IIIB	Ether	25	7.0	2.82	34	60	−14.44[e]	−10.46°	96	96	95	96	70	98	96	97
2	IVB	Ether	25	7.0	2.97	29	62	−13.38	+10.95	89	88	88	88	73	91	90	90
3	VB	Ether	25	7.0	2.94	31	50	+0.74	+0.52	5	6	7	5	3	6	7	6
4	VIB	Ether	25	7.0	2.73	12	71	−2.61	−2.58	18	18	18	16	18	19	18	19
5	VB	Dioxane	25	5.0	1.66	..	48[h]	+0.09[h]	......	0.6	6	3	2	..	..	..	..
6	VB	Triethylamine	25	7.0	2.53	52	43	+0.66	......	4.4	6	5	4	..	..	..	..
7	VIB	Tetrahydrofuran	64	7.0	2.20	..	68	−1.24	......	8	10	9	8	..	..	..	..

[a] In each case the solvents were distilled from lithium aluminum hydride before use. The runs made in ether were all aliquots of a homogeneous solution of $LiAlH_4$ in ether, 5.8 g. per 100 ml. of solution. The other runs were heterogeneous and were in the presence of large excesses of $LiAlH_4$. [b] This is the weight of distilled material (in each case the small pot residue was neutral). [c] The amount of olefin was estimated by the hydrogen uptake in an ethanol solution with a Ra Ni catalyst. Since the amount of Ra Ni was hard to measure and since some hydrogen was absorbed on the surface, these values are only estimates. [d] These values are based on the weights of olefin-free hydrocarbon actually obtained. In each case n^{25}D 1.4860 ± 0.0002 unless otherwise specified (n^{25}D $\cong$ 1.4860 for both pure 2- and 3-phenylpentane). [e] l = 1 dm., no solvent. [f] In runs 1 and 2 for these olefin-free mixtures, n^{25}D 1.4857; in run 3, n^{25}D 1.4838; and in run 4, n^{25}D 1.4849. [g] These values are calculated on the basis that optically pure 2-phenylpentane has an α^{23}D ±15.00° (l = 1 dm.). [h] This mixture of 2- and 3-phenylpentanes was contaminated as shown by n^{25}D 1.4869.

sulfonate esters in a clear solution of lithium aluminum hydride in the solvent used for the reaction, and allowing the mixture to stand eight hours. The excess lithium aluminum hydride was decomposed with cold concentrated alkali, and the olefin-alkylbenzene mixture was isolated. The amount of olefin produced was estimated by hydrogenating a portion of the reaction product.

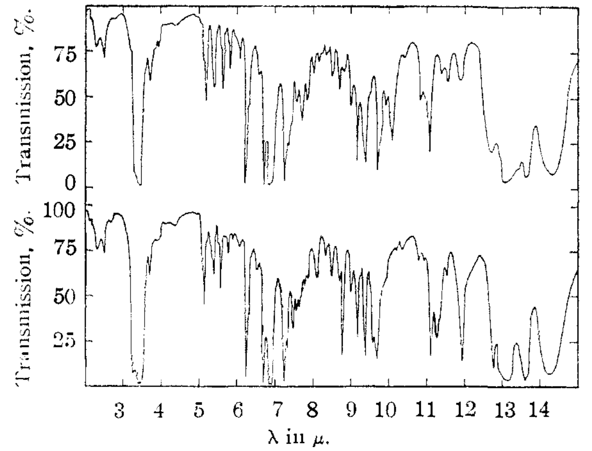


Fig. 1.—Infrared spectra, Baird spectrograph with NaCl prism, homogeneous films, 0.1 mm. thick: upper curve, 2-phenylpentane; lower curve, 3-phenylpentane.

Attempts to remove olefin from the reaction mixtures by extraction of the pure hydrocarbon with concentrated sulfuric acid were unsuccessful, due to the rapid racemization of the optically active 2-phenylpentane in the presence of concentrated sulfuric acid.[8] Thus when pure (−)-2-phenylpentane (α^{23}D = −15.0°, l = 1 dm.) was shaken with five successive portions of concentrated sulfuric acid, 2% of the activity of the hydrocarbon was lost. However, when olefin was added to a mixture of 40% (−)-2-phenylpentane and 60% 3-phenylpentane (α^{23}D −5.63°, l = 1 dm.), and the resulting solution was shaken with five successive portions of concentrated sulfuric acid, the recovered olefin-free

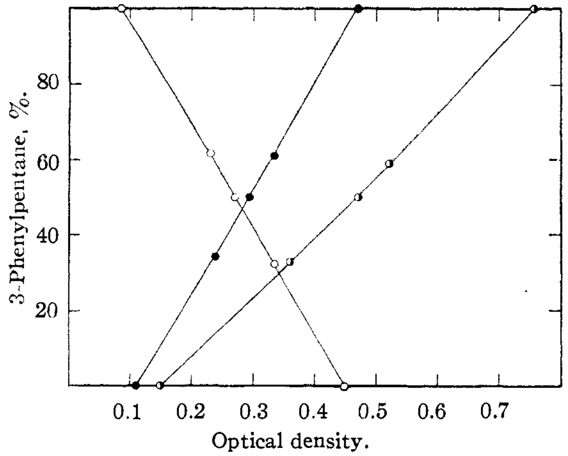


Fig. 2.—Plots of optical density against % composition of known mixtures of 2- and 3-phenylpentane: ●, λ = 11.33 μ; ◑, λ = 12.02 μ; ○, λ = 10.15 μ. Beckman IR2 Spectrophotometer, NaCl prism, slit width = 0.92 mm., homogeneous films, 0.03 mm. thickness.

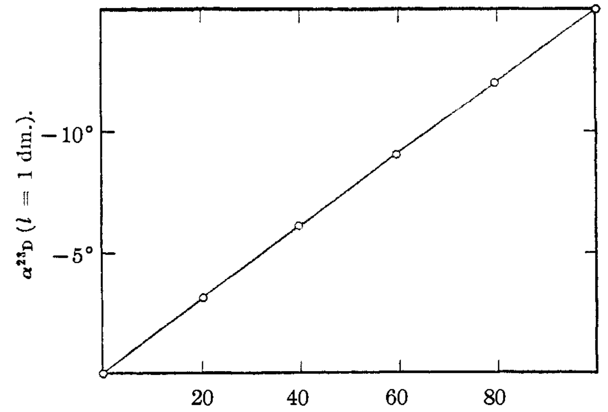


Fig. 3.—Plot of observed rotation against % of (−)-2-phenylpentane in mixtures of (−)-2- and 3-phenylpentane.

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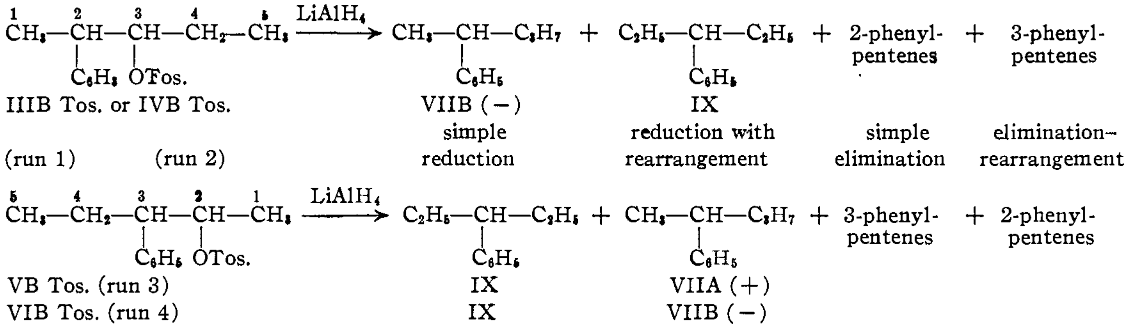
(8) These results are in agreement with the racemization of optically active hydrocarbon with concentrated sulfuric acid reported by A. Burwell and P. Gordon [THIS JOURNAL, **70**, 3129 (1948)]. In this investigation it was also noted that olefin catalyzes the racemization.



$$\overset{1}{CH_3}-\underset{C_6H_5}{\overset{2}{CH}}-\underset{OTos.}{\overset{3}{CH}}-\overset{4}{CH_2}-\overset{5}{CH_3} \xrightarrow{LiAlH_4} \underset{C_6H_5}{CH_3-CH}-C_3H_7 + \underset{C_6H_5}{C_2H_5-CH}-C_2H_5 + \text{2-phenyl-pentenes} + \text{3-phenyl-pentenes}$$

IIIB Tos. or IVB Tos. (run 1) (run 2)

VIIB (−) simple reduction

IX reduction with rearrangement

simple elimination

elimination–rearrangement

$$\overset{5}{CH_3}-\overset{4}{CH_2}-\underset{C_6H_5}{\overset{3}{CH}}-\underset{OTos.}{\overset{2}{CH}}-\overset{1}{CH_3} \xrightarrow{LiAlH_4} \underset{C_6H_5}{C_2H_5-CH}-C_2H_5 + \underset{C_6H_5}{CH_3-CH}-C_3H_7 + \text{3-phenyl-pentenes} + \text{2-phenyl-pentenes}$$

VB Tos. (run 3) IX VIIA (+)

VIB Tos. (run 4) IX VIIB (−)

mixture of alkylbenzenes had lost 23% of its optical activity.

A successful method of removing olefin from the hydrocarbon mixture was developed making use of the fact that 2,4-dinitrobenzenesulfenyl chloride adds quantitatively to the carbon–carbon double bond.[9] When a mixture of 2- and 3-phenylpentane (α^{23}D −4.77°, l = 1 dm., n^{25}D 1.4860) was added to about an equal weight of a mixture of 2- and 3-phenylpentenes[10] and the resulting solution was heated with a large excess of 2,4-dinitrobenzenesulfenyl chloride, all of the olefin reacted to form the adduct, the alkylbenzenes being untouched. Recovery of the original 2- and 3-phenylpentane mixture was accomplished through extraction of these hydrocarbons into pentane, the resulting solution being submitted to chromatographic adsorption. The recovered hydrocarbon was unchanged in its physical properties (α^{23}D −4.77°, l = 1 dm., n^{25}D 1.4860).

The above method was applied to the reaction products obtained by the treatment of the sulfonate esters with lithium aluminum hydride. The resulting olefin-free mixtures were then submitted to infrared and polarimetric analyses.

Table II records the yields and the results of the product analysis. The agreement between the infrared analyses at the three wave lengths is within a per cent. whenever the sample is free of contaminants, and the agreement of values can be used as an index of purity, as well as a criterion of the validity of the methods. The excellent agreement between the analyses from the infrared data and the analyses derived from the rotation argues for the reliability of both methods.

Since reduction of the olefins in the original olefin–alkylbenzene reaction products gave only 2- and 3-phenylpentane, the products of the hydrogenation experiments were also submitted to polarimetric and infrared analyses. From the results of these analyses, the results of the hydrogenation experiments and the results obtained by analyses of the samples of alkylbenzene from which olefin had been removed, the amount of rearranged and unrearranged olefin produced in the reaction can be roughly estimated. From the polarimetric data, the amount of optically active olefin produced both with and without rearrangement can be calculated.[11]

Results

The results of experiments 1–4 (Table II) provide evidence that four sets of products are produced when the *p*-toluenesulfonates of the 3-phenyl-2-pentanols and 2-phenyl-3-pentanols are treated with ether solutions of lithium aluminum hydride.

These products are the result of simple reduction, reduction with rearrangement, simple elimination and elimination with rearrangement. The agreement between the polarimetric and infrared analyses of VIIB and IX (free of olefin) in runs 1 and 2 indicates that the simple reduction reaction occurs without any alteration of the stereochemistry at carbon atom 2 of the starting material.[12] On the other hand, this same agreement in runs 3 and 4 provides evidence that the rearrangement–reduction reaction is stereospecific and that carbon atom 2 of the starting material has been inverted during the rearrangement. The fact that 2-phenylpentane of opposite configuration is produced in runs 1 and 3 in spite of the starting materials both belonging to the *threo* series[2] is a consequence of the stereochemical relationships involved[3] (see Discussion section).

The extent to which the reduction–rearrangement reaction takes place as compared to the simple reduction reaction varies somewhat with both the configuration and structure of the starting material. Thus configuration IIIB produces a ratio of 24 to 1 (simple reduction to rearrangement–reduction reactions); IVB, 7.3 to 1; VB, 16 to 1; and VIB 4.5 to 1. Since the differences between the sulfonate esters of IIIB and IVB lie only in configuration, the differences in the above ratios must be due to steric effects, the same being true of the differences in the sulfonates of VB and VIB.

In any given run (of runs 1–4) the infrared analysis of the mixture of VII and IX produced by freeing the reaction product from olefin is roughly the same as the analysis of the mixture of VII and IX produced by reducing the olefin in the reaction mixture. Thus when a relatively large amount of rearrangement occurred to produce 2- or 3-phenylpentane, the amount of rearranged olefin produced was also relatively large and *vice versa*. However, since an exact calculation of the amount of rearranged olefin formed in each experiment would involve small differences between relatively large numbers, only the qualitative observation can be made.

In runs 1 and 2, a comparison of the polarimetric and infrared analyses of the two alkylbenzene mix-

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[9] N. Kharasch and C. M. Buess, THIS JOURNAL, **71**, 2724 (1949).

[10] The preparation and properties of these olefins will be reported in a later paper in this series.

[11] It has been demonstrated (unpublished results) that a small amount (~3%) of racemization occurs when optically pure 3-phenyl-1-butene is reduced with Raney Ni to 2-phenylbutane. Undoubtedly a small amount of an analogous reaction occurred when optically active olefin was reduced in the present experiments.

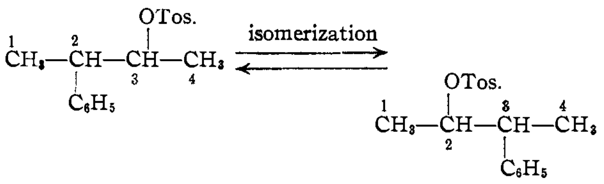
[12] No evidence is available to indicate whether the reaction goes with retention or inversion of configuration at carbon atom 3.

tures (one produced by olefin removal, the other by olefin reduction) indicates that small amounts of an optically active olefin must have been produced which could be reduced to optically active 2-phenylpentane. This olefin probably arose by the loss of *p*-toluenesulfonic acid from the starting material in such a way as to give the unconjugated and optically active 4-phenyl-2-pentene. Similar comparisons in run 4 indicate that small amounts of this same olefin were produced in the rearrangement–elimination reaction.

Marked differences in the extent to which rearrangement took place resulted from a variation in the character of the solvent. Although in runs 3 and 5 the starting material was the same, the ratio of simple reduction to reduction–rearrangement reaction is 16 to 1 whereas in run 5 the ratio is at least 49 to 1. Each of the solutions in which the reactions were conducted were saturated with respect to the same sample of lithium aluminum hydride (Metal Hydrides, Inc.).[13] It can be concluded that the higher the concentration of lithium aluminum hydride in the reducing solution, the greater is the amount of rearranged alkylbenzene produced.

Discussion

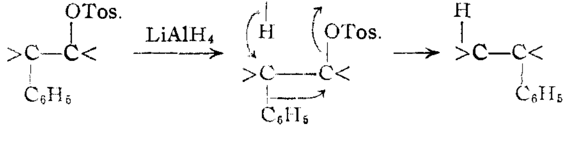
The production of both rearranged olefin as well as rearranged alkylbenzene in the above experiments suggests that both of these substances arise from a common precursor, which itself is a rearrangement product of the starting material. This hypothesis is strengthened by two further facts: the larger the amount of rearranged alkylbenzene formed, the larger the amount of rearranged olefin observed; the higher the concentration of lithium aluminum hydride in the solvent the greater the amount of rearranged product observed. Evidence for an isomerization reaction during the solvolyses of the *p*-toluenesulfonates of the isomers of 3-phenyl-2-butanol has already been reported,[14] the rate of this rearrangement being very sensitive to the ionizing power of the solvent. Therefore it is reasonable to suppose that an analogous isomerization reaction occurs in the present investigation.[15] The disturbing feature about such an isomerization reaction is that it must go with great rapidity, and must be comparable to the rate at which the isomerization reaction occurs in formic acid at the same temperature.[14] However, since the ability of the isomerization reaction to compete with simple reduction and elimination reactions seems to correlate far better with the concentration of lithium aluminum hydride in the solvent than with the ionizing power of the pure solvent (dioxane is a more ionizing solvent than ethyl ether), it seems probable that the hydride exerts a catalytic effect on the isomerization reaction.[16]



Since the isomerization reaction has been shown to go through a bridged ion-pair (phenonium sulfonate) as an intermediate in acetic and formic acids as solvent,[14] the same intermediate probably also exists in the present case. The question as to whether the reduction–rearrangement reaction occurs by an exchange reaction involving the phenonium sulfonate ion-pair or by a simple reduction of isomerized sulfonate ester becomes pertinent. Although some reduction product could have arisen by the former path, the fact that rearranged olefin was also formed suggests that at least the greater part of rearranged alkylbenzene must have come from rearranged sulfonate ester.[17]

The following formulations summarize the conclusions with regard to the mechanisms of these reactions, and also set forth the stereochemical relationships that exist between the various isomeric starting materials and their reaction products.

A comparison of the structures of the *cis* and *trans* ion-pairs reveals that in the former a methyl and ethyl group are forced into a configuration in which both groups are on the same side of the three-membered ring whereas in the latter the two groups are distributed on the opposite sides of the ring. Molecular models of these two configurations reveal that due to the bulk of the methyl and ethyl groups, the *cis* configuration is strained whereas the *trans* configuration is free of the same kind of strain. These steric considerations provide a likely explanation of why starting materials of the *erythro* configuration (compounds II, IV and VI) give a higher percentage of rearranged to unrearranged alkylbenzene than starting materials of the *threo* configuration (compounds I, III, V). The fact that the *p*-toluenesulfonate of IA gives more rearrangement (about 10%) than the same ester of III or V[2] is a consequence of the smaller bulk of a methyl as compared to an ethyl group. Thus two methyl groups are more compatible on the same side of a three-membered ring than a methyl and an ethyl group.



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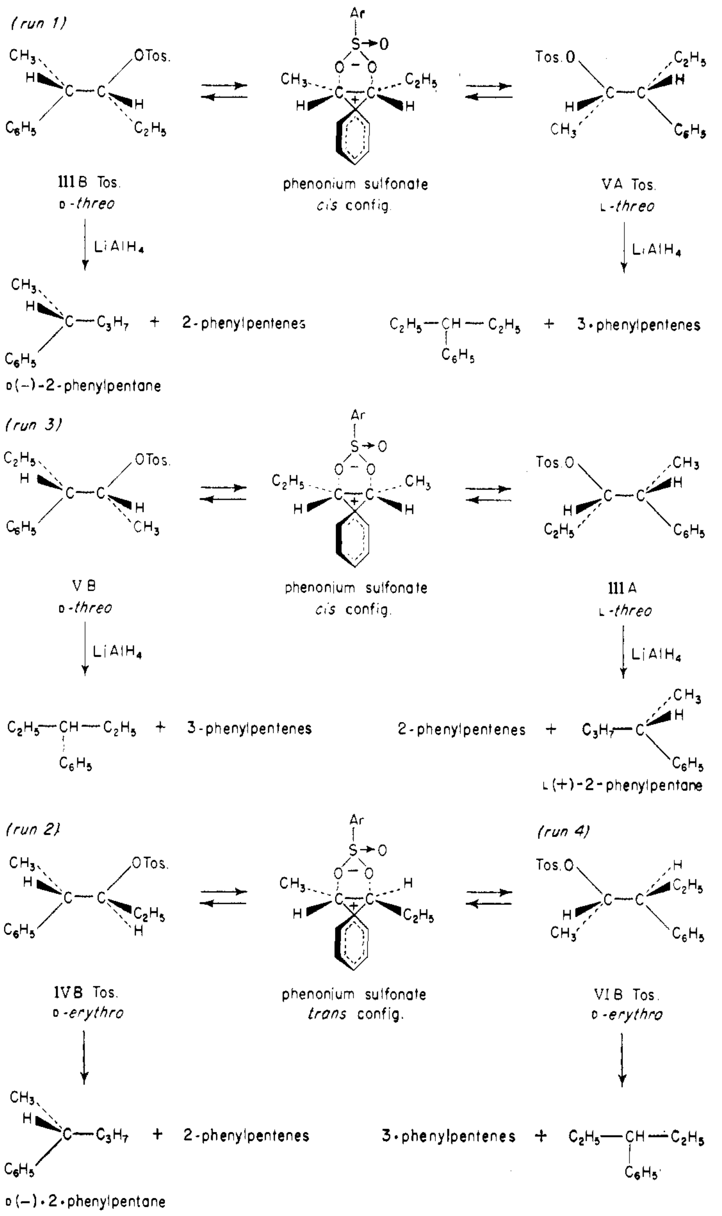
[13] The solubility of this sample of lithium aluminum hydride in ether (5.8 g. per 100 ml. of solution) is considerably less than the solubility that has been previously reported [A. Finholt, A. Bond and H. Schlesinger, THIS JOURNAL, **69**, 1201 (1947)]. These authors found the following solubilities: 25–30 g. of hydride per 100 g. of ethyl ether; 13 g. per 100 g. of tetrahydrofuran: 0.1 g. per 100 g. of dioxane.

[14] D. J. Cram, *ibid.*, **74**, 2129 (1952).

[15] Many other explanations of the data have been considered. One of the more attractive alternative mechanisms is one in which a completely concerted (one transition state) reduction-rearrangement reaction occurs. The chief points against such a mechanism at the present time are that no analogy for such a process exists, and that two separate mechanisms for the production of rearranged alkylbenzene and rearranged olefin would have to be envisioned, resulting in a less economical explanation.

[16] Such a catalysis is reminiscent of the catalytic effect that the addition of small amounts of *p*-toluenesulfonic acid had on the isomerization reaction in acetonitrile (ref. 2). H. C. Brown (private communication) has suggested that AlH_3 (a weak acid) is the actual catalyst here, and not the relatively basic $LiAlH_4$.

[17] Evidence that phenonium sulfonate ion-pairs do not go directly to olefin (in glacial acetic acid) was obtained in Paper VI of this series [THIS JOURNAL, **74**, 2137 (1952)].



Experimental

The Alcohols IIIB, IVB, VB and VIB and Their *p*-Toluenesulfonates.—These alcohols and their enantiomers were prepared in fairly large quantities (30 g. or more) by procedures already outlined.[3] Two of the alcohols (IIIB and VB) as well as their *p*-toluenesulfonates have not been previously reported. Since optical purity is critical in the present investigation, the rotations for the eight alcohols are reported here: IIIA, $[\alpha]^{23}\text{D}$ +12.47°; IIIB, $[\alpha]^{23}\text{D}$ −11.79°; IVA, $[\alpha]^{23}\text{D}$ −7.47°; IVB, $[\alpha]^{23}\text{D}$ +7.56°; VA, $[\alpha]^{23}\text{D}$ −17.40°; VB, $[\alpha]^{23}\text{D}$ +16.76°; VIA, $[\alpha]^{23}\text{D}$ −20.19°; VIB, $[\alpha]^{23}\text{D}$ +21.06°. The alcohols IIIB and VB were obtained in an optically pure state by fractional crystallization of their acid phthalates, followed by hydrolysis to give colorless oils.

Anal. Calcd. for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found for IIIB: C, 80.23; H, 9.67. Found for VB: C, 79.95; H, 10.00. The *p*-toluenesulfonates were prepared by a procedure already outlined,[3] yield for IIIB derivative, 73%, m.p. 100.5–101.5°; yield for VB derivative, 82%, m.p. 71–72°. *Anal.* Calcd. for $C_{18}H_{22}SO_3$: C, 67.89; H, 6.98. Found for IIIB derivative: C, 67.82; H, 7.01. Found for VB derivative: C, 68.01; H, 7.15.

Preparation of Crude Phenylpentanes.—The procedure is illustrated with the preparation of 3-phenylpentane. To a Grignard reagent prepared from 108 g. of magnesium and 409 g. of ethyl bromide in ether was added 400 g. of propiophenone over a period of one hour. The mixture was decomposed on ice and ammonium chloride, purified through extraction, and the product was distilled, weight 365 g., b.p. 108–110° (14 mm.). This material was mixed with 2 g. of *p*-toluenesulfonic acid and heated at reflux temperature under 14 mm. of pressure, the water being collected by trapping it in the reflux return. After one mole of water had been eliminated the product was washed with base, dried and distilled, b.p. 82–83° (14 mm.), $n^{25}\text{D}$ 1.5208, weight 295 g. A mixture of 130 g. of olefin and 20 g. of freshly prepared Raney Ni was stirred in an atmosphere of hydrogen until no more hydrogen was absorbed, and the product was distilled, b.p. 189°, $n^{25}\text{D}$ 1.4868.

The position isomer, 2-phenylpentane was prepared by an analogous procedure with comparable yields.

Acylation of the Phenylpentanes.—The procedure is illustrated with the preparation of 4-(2′-pentyl)-acetophenone. To a mixture of 217 g. of crude 2-phenylpentane, 192 g. of acetyl chloride and 600 ml. of carbon disulfide was added, over a period of one hour, 220 g. of aluminum chloride. The mixture was stirred for half an hour, and poured onto ice and concentrated hydrochloric acid. The product was extracted into pentane, the resulting solution was washed with water, dilute base and dilute acid, the solvent was evaporated, and the residual oil was distilled under reduced pressure to give 265 g. of product, b.p. 148–149° (14 mm.).

The semicarbazones were prepared in the usual way.

When the acetyl chloride was added to a mixture of hydrocarbon, solvent and aluminum chloride the yield of product was cut to 32%, the rest of the starting material having gone to acetophenone and dialkylbenzenes.

Oxidation of the Alkylacetophenones to Alkylbenzoic Acids.—The procedure is illustrated by the preparation of 4-(2′-pentyl)-benzoic acid.

Calcium hypochlorite[18] (700 g.) was warmed with 2800 ml. of water and shaken with a solution of 140 g. of potassium hydroxide and 490 g. of potassium carbonate in 1400 ml. of water. The resulting sludge was filtered, and to the filtrate was added with vigorous stirring and at such a rate to maintain the temperature between 50° and 70°, 265 g. of 4-(2′-pentyl)-acetophenone (the solution of potassium hypochlorite was preheated to 60°). The mixture was stirred until clear and for an additional half an hour, cooled and mixed with a solution of 30 g. of potassium bisulfite in 200 ml. of water. When the solution was acidified with hydrochloric acid, the product precipitated, and recrystallization of the product from methanol and water gave 191 g. of white prisms, m.p. 71–72°.

This acid was also prepared by a method completely analogous to that used by Marvel, *et al.*,[4,6] for the preparation of *p*-*s*-butylbenzoic acid, but in the present work the yields were inferior. The product melted at 71–72°, undepressed by admixture with the material prepared by the other method.

Resolution of 4-(2′-Pentyl)-benzoic Acid.—To a boiling solution of 223 g. of quinine dissolved in 2 l. of 95% ethanol was added 223 g. of the acid. The salt that separated was recrystallized twenty-four times from 95% ethyl alcohol, in each case using enough solvent to just dissolve the salt at reflux temperature. Decomposition of the salt produced 21.5 g. of acid, m.p. 54–55°, $[\alpha]^{23}\text{D}$ −23.3° (3.3% solution in absolute ethanol). That optical purity was obtained is shown by the rotations of small samples of acid prepared from the salt at various stages of recrystallization: after sixteen recrystallizations, $[\alpha]^{23}\text{D}$ −19.5°; after eighteen, $[\alpha]^{23}\text{D}$ −22.5°; after twenty, $[\alpha]^{23}\text{D}$ −23.4°. Another

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(18) This procedure is patterned after that reported by M. Newman and H. Holmes ("Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 428) for the preparation of β-naphthoic acid.

12.4 g. of material, m.p. 54–55°, $[\alpha]^{23}\text{D}$ −23.2° was recovered by fractional crystallization of second crops.

Fractional crystallization of the acid obtained from various filtrates gave 135 g. of racemic acid, m.p. 70–72°, and 31 g. of (+) acid, $[\alpha]^{23}\text{D}$ +12.3°, m.p. 50–58°.

Conversions of the Alkylbenzoic Acids to Alkylbenzamides.—A mixture of 30 g. of (−)-4-(2′-pentyl)-benzoic acid, 30.g. of purified thionyl chloride and 2 ml. of pyridine was warmed to 50° for three hours, cooled and poured with stirring onto a mixture of ice and concentrated ammonium hydroxide. The product that separated was recrystallized from ethanol and water to give needles, weight 27.5 g., m.p. 108–109°, $[\alpha]^{23}\text{D}$ −21.9° (3.3% in abs. ethanol).

Rearrangement of the Alkylbenzamides to Alkylanilines.[19]—To a solution prepared from 6.63 g. of sodium and 209 ml. of methanol was added with cooling 27.5 g. of 4-(2′-pentyl)-benzamide followed by 23 g. of bromine. The mixture was cautiously warmed[20] to reflux temperature and held there for ten minutes, after which the solvent was evaporated under reduced pressure to a mixture of salt and oil. The oil was extracted with pentane, and after evaporation of the solvent the resulting oil was held at reflux for ten hours in a solution of 50 g. of potassium hydroxide dissolved in 35 ml. of water and 110 ml. of methanol. The amine was recovered through extraction with pentane and distillation of the concentrate to give 20.2 g. of product, b.p. 131–132° (19 mm.), $[\alpha]^{25}\text{D}$ −22.3° (liquid), d^{25}_{4} 0.9278, $n^{25}\text{D}$ 1.5282.

The N-acetyl derivatives of these amines were made in the usual way.

The partially resolved (+)-4-(2′-pentyl)-benzoic acid was converted to partially resolved (+)-4-(2′-pentyl)-aniline by the procedure outlined above, $\alpha^{23}\text{D}$ +12.04° (l = 1 dm.), b.p. 138–139° (18 mm.), $n^{25}\text{D}$ 1.5283. An attempt was made to completely resolve this amine through the *d*-tartaric acid salt, but six recrystallizations of the salt from 20% ethanol–80% water solution brought the rotation only to $\alpha^{23}\text{D}$ +13.71° (l = 1 dm.), and the attempt was abandoned.

Conversion of Alkylanilines to Alkylbenzenes.[21]—To a mixture of 69 ml. of concentrated hydrochloric acid, 40 ml. of water, 18.85 g. of 4-(2′-pentyl)-aniline and 30 ml. of glacial acetic acid held at −5° was added slowly with stirring 8.4 g. of sodium nitrite dissolved in 20 ml. of water. The temperature was not allowed to go above 0°. Precooled hypophosphorous acid (180 ml. of a 50% solution) was then added at a rate commensurate with holding the temperature below 0°. The mixture was then stirred for half an hour and allowed to stand at 0° for 24 hours. Extraction of the product with pentane followed by fractional distillation of the product resulted in 11.22 g. of pure hydrocarbon as the main product, b.p. 193°, $n^{25}\text{D}$ 1.4858 (first and last drop), $\alpha^{23}\text{D}$ −15.00° (l = 1 dm.).

Reaction of the Alkylbenzenes with 2,4-Dinitrobenzenesulfenyl Chloride.[7]—To a solution of 0.20 g. of 2,4-dinitrobenzenesulfenyl chloride in 10 ml. of ethylene dichloride at 0° was added 0.20 g. of aluminum chloride and 0.3 g. of 3-phenylpentane. After standing for ten minutes the mixture was shaken with benzene and ice, and the benzene layer was washed with water, dried and passed through a short column of alumina. The column filtrate was evaporated, the product was crystallized and recrystallized from ethyl alcohol, wt. 110 mg., m.p. 86–87° (yellow flakes).

Attempts to Prepare 2-(2′-Pentyl)-benzoic Acid.—In an attempt to prepare 2-(2′-pentyl)-benzoic acid, 157 g. of *o*-chloroacetophenone[22] was treated with *n*-propylmagnesium bromide (33.6 g. of Mg plus 172 g. of propyl bromide) in the usual way. As the reaction proceeded a large quantity of propylene was liberated and a stable crystalline complex separated from the ether mixture which was collected and ether washed, weight 180 g. Decomposition of the complex with acid, extraction and distillation of the product gave 54 g. of 1-(2′-chlorophenyl)-ethanol, b.p. 114–116° at 14 mm.

Isolation of the product which did not separate from the original Grignard reaction produced 75 g. of a mixture, b.p. 114–140° (14 mm.), which was abandoned.

In another attempt to prepare 2-(2′-pentyl)-benzoic acid, *o*-chlorobenzamide was treated with methylmagnesium bromide to produce *o*-chloroacetophenone, but apparently only dehydration to *o*-chlorobenzonitrile occurred because the product when treated with propylmagnesium bromide gave 1-(2′-chlorophenyl)-butanone as shown by its conversion to 1-(2′-chlorophenyl)-butanol by reduction with hydrogen using a platinum catalyst. Since the steps were not developed nor intermediates characterized, the experimental details will not be published.

The Removal of Olefins from Mixtures of Olefins and 2- and 3-Phenylpentane.—An attempt to develop a procedure for removal of olefin from the alkylbenzenes by extraction of the mixture with 96% sulfuric acid was made. A total of 8 g. of (−)-2-phenylpentane ($\alpha^{23}\text{D}$ −15.0°, l = 1 dm., $n^{25}\text{D}$ 1.4858) was shaken with five successive 10-ml. portions of concentrated sulfuric acid (in each case the period of shaking was one minute and the time allowed for separation of layers was three minutes). The rotation of the recovered hydrocarbon (7.2 g., $n^{25}\text{D}$ 1.4859) had dropped to $\alpha^{23}\text{D}$ −14.73° (l = 1 dm.). All of the sulfuric acid layers were colorless.

Similar extraction of pure 3-phenylpentane (b.p. 189°, $n^{25}\text{D}$ 1.4861) produced with each extraction a somewhat yellow sulfuric acid layer, in each case the color being of about the same intensity.

To a mixture of 3.0 g. of 40% (−)-2-phenylpentane and 60% 3-phenylpentane, ($n^{25}\text{D}$ 1.4860, $\alpha^{23}\text{D}$ −5.63°, l = 1 dm.) was added 0.38 g. of 3-phenyl-2-pentene and 0.31 g. of 2-phenyl-2-pentene, and this mixture was shaken with five successive 4-ml. portions of concentrated sulfuric acid (the layers were shaken for one minute and allowed to separate for three minutes in each case). The first sulfuric layer was deep orange, the others light yellow. The recovered hydrocarbon (2.2 g., $n^{25}\text{D}$ 1.4860, $\alpha^{23}\text{D}$ 4.34°, l = 1 dm.) had lost 23% of its optical activity, indicating that olefin catalyzes isomerization and loss of activity.[8]

The above procedures for removal of olefin were abandoned in favor of the following method. To a mixture of 2 g. of pure 3-phenylpentane and 1 g. of (−)-2-phenylpentane (physical constants of the mixture were $\alpha^{23}\text{D}$ −4.77°, l = 1 dm., $n^{25}\text{D}$ 1.4860) was added 1.0 g. of 3-phenyl-2-pentene and 1.0 g. of 2-phenyl-2-pentene. The resulting solution ($n^{25}\text{D}$ 1.4928) was heated for half an hour on the steam-bath with 15 ml. of glacial acetic acid and 10 g. of 2,4-dinitrobenzenesulfenyl chloride. The mixture was then cooled, poured into 100 ml. of pure pentane, and the pentane layer was shaken with six successive portions of water (the yellow precipitate was discarded), dried and passed through a column of 40 g. of alumina, the column being washed with an additional 30 ml. of pentane. Evaporation of the solvent followed by distillation of the product gave the original olefin-free mixture of 2- and 3-phenylpentane, $n^{25}\text{D}$ 1.4860, $\alpha^{23}\text{D}$ −4.77° (l = 1 dm.), weight 2.7 g.

Procedure for the Treatment of the *p*-Toluenesulfonates with Lithium Aluminum Hydride.—This procedure is illustrated by the treatment of the *p*-toluenesulfonate of VIB with lithium aluminum hydride.

To 100 ml. of a clear solution of ether (containing 5.80 g. of hydride) which had been filtered from a large excess of lithium aluminum hydride was added 7.0 g. of the *p*-toluenesulfonate of VIB. The mixture was allowed to stand at room temperature for ten hours, and the large excess of lithium aluminum hydride was decomposed by mixing with ice. The resulting sludge was shaken with pure pentane and dilute hydrochloric acid, and the organic layer was washed with water, a sodium bicarbonate solution and then dried; the solvent was evaporated through a short column, and the product was distilled, wt. 2.73 g., $n^{25}\text{D}$ 1.4921, $\alpha^{23}\text{D}$ −2.57° (l = 1 dm.). The small pot residue was neutral.

This mixture (2.00 g.) was freed from olefin by the procedure outlined above to give 1.41 g. of product, $n^{25}\text{D}$ 1.4861, $\alpha^{23}\text{D}$ −2.61°, (l = 1 dm.) which was directly submitted to infrared analysis.

The amount of olefin in the original mixture was estimated by submitting 0.566 g. of the original product of the reaction to quantitative hydrogenation by addition of the hydrocarbon to an equilibrated mixture of hydrogen, 1.0 ml. of Raney Ni and 10 ml. of ethanol (appropriate standardizing runs using pure olefins indicated the method accurate to ±5%). The olefin content was estimated from the hydro-

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(19) This procedure is a modification of that reported by E. Wallis and J. Lane ("Organic Reactions," Vol. III, John Wiley and Sons, Inc., 1946, p. 283) for the preparation of pentadecylamine.

(20) The reaction is exothermic and care must be taken that the mixture does not leave the flask.

(21) This reaction was effected by a modification of the procedure reported by N. Kornblum ("Organic Reactions," Vol. II, John Wiley and Sons, Inc., N. Y., 1944, p. 262, for the reduction of *p*-aminotoluene.

(22) L. Thorpe and E. Brunskill, THIS JOURNAL, **37**, 1260 (1915).

gen uptake, and the hydrocarbon was recovered through shaking the reduced mixture with water and pure pentane. The pentane layer was washed with water, dried and passed through 20 g. of activated alumina. The column filtrate was evaporated through a column and the residue was flash-distilled. This product (0.364 g., $n^{25}\text{D}$ 1.4861) was submitted directly to infrared analysis.

LOS ANGELES, CALIFORNIA RECEIVED AUGUST 16, 1951

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

Studies in Stereochemistry. IX. Phenonium Sulfonate Ion-pairs in the Substitution and Elimination Reactions in the 2-Phenyl-3-pentanol and 3-Phenyl-2-pentanol Systems

BY DONALD J. CRAM

The products of the solvolyses in glacial acetic acid of the *p*-toluenesulfonates of the stereoisomers of 3-phenyl-2-pentanol and 2-phenyl-3-pentanol have been analyzed. With regard to the acetate products of the reaction, the sulfonate ester of D-*erythro*-3-phenyl-2-pentanol and D-*erythro*-2-phenyl-3-pentanol give essentially the same mixture of 58% D-*erythro*-2-acetoxy-3-phenylpentane and 42% D-*erythro*-3-acetoxy-2-phenylpentane. Analogously, the sulfonate ester of D-*threo*-3-phenyl-2-pentanol gives about the same mixture of 58% D-*threo*-2-acetoxy-3-phenylpentane and 42% L-*threo*-3-acetoxy-2-phenylpentane as does the sulfonate ester of L-*threo*-2-phenyl-3-pentanol. Simple solvolysis reactions without involvement of the phenyl group account for only minor amounts of acetate product. These facts are interpreted in terms of phenonium sulfonate ion-pairs as intermediates in these reactions.

The production of widely differing balances of olefinic products in the solvolyses of the four sulfonate esters provides evidence that the olefin and acetate products arise through at least two different primary processes. The presence of rearranged olefin (both conjugated and unconjugated) among the products in each experiment is interpreted as evidence for an isomerization reaction, the *p*-toluenesulfonate of D-*erythro*-3-phenyl-2-pentanol giving the *p*-toluenesulfonate of D-*erythro*-2-phenyl-3-pentanol and *vice versa*, and the *p*-toluenesulfonate of D-*threo*-3-phenyl-2-pentanol giving the *p*-toluenesulfonate of L-*threo*-2-phenyl-3-pentanol and *vice versa*. Different ratios of conjugated to unconjugated 2-phenylpentene were obtained from the *p*-toluenesulfonates of D-*erythro*-2-phenyl-3-pentanol and D-*threo*-2-phenyl-3-pentanol. These differences are interpreted in terms of the steric requirements for the formation of a phenyl *vs.* a hydrogen-bridge from materials of the *erythro* as compared to the *threo* configuration.

Paper III of this series[1] reported the results of the solvolyses in glacial acetic acid of the *p*-toluenesulfonates of the stereoisomers of IIIA, IVA, VA and VIA.[2] Only a qualitative study of the nature of the acetate products was reported, and no examination of the products of the elimination reaction was made. The present investigation deals with a quantitative study of the acetate and olefinic products of the solvolysis reactions.

Methods and Results

The solvolysis reactions and methods of isolation of the alcoholic and olefinic fractions from the reaction mixtures were carried out by procedures analogous to those reported in Papers V[3a] and VI[3b] in which the solvolyses of the *p*-toluenesulfonates of the isomers of 3-phenyl-2-butanol were studied. Table I reports the analyses and rotations of the acetates, propionates and benzoates of the optically pure isomers of 3-phenyl-2-pentanol and 2-phenyl-3-pentanol. The yields of the olefinic and alcoholic products from the solvolysis reactions are reported in Table II, along with the rotations of the alcoholic products obtained in the various runs. The acetates, propionates and benzoates of the alcoholic mixtures from the solvolysis experiments were also prepared and their rotations are reported in Table II.

Figure 1 reports the infrared spectra of IIIB, IVB, VB and VIB, and Table III reports the optical densities of the substances at the eight wave lengths which were most amenable to the analysis of mixtures of these four compounds (or of their enantiomers). The differences in the optical densities

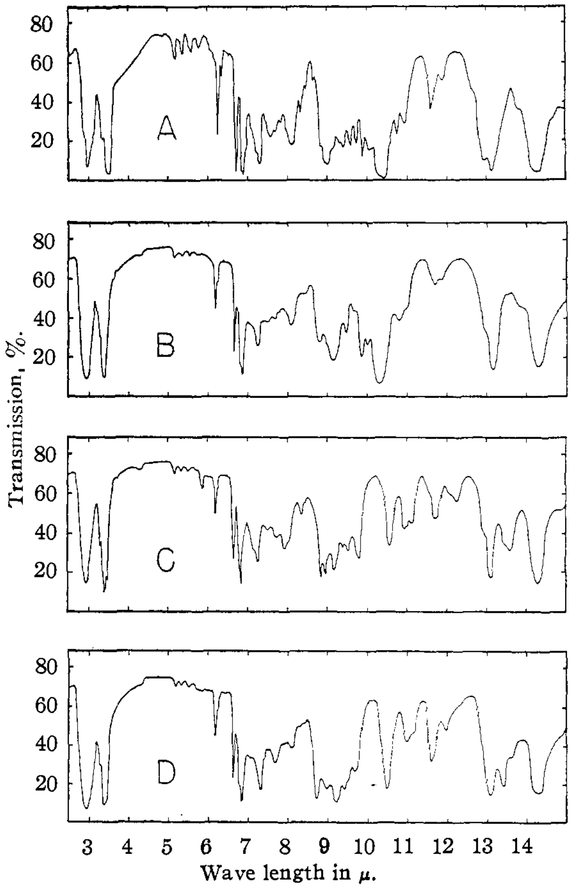

Fig. 1.—Infrared spectra, homogeneous samples, NaCl prism: A, D-*threo*-2-phenyl-3-pentanol (IIIB), cell thickness = 0.03 mm.; B, D-*erythro*-2-phenyl-3-pentanol (IVB), cell thickness = 0.01 mm.; C, D-*threo*-3-phenyl-2-pentanol (VB), cell thickness = 0.01 mm.; D-*erythro*-3-phenyl-2-pentanol (VIB), cell thickness = 0.01 mm.

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[1] D. J. Cram, THIS JOURNAL, **71**, 3871 (1949).

[2] The numbering system for these isomeric pentanols has been maintained from paper to paper. The relationships of all of the configurations of the substances to D-glyceraldehyde are reported in Paper VII [*ibid.*, **74**, 2149 (1952)] of this series.

[3] (a) D. J. Cram, *ibid.*, **74**, 2129 (1952); (b) *ibid.*, **74**, 2137 (1952).