verted to the phthalic acid ester of VA; weight 9.2 g., m. p. 127–128° (flakes from ethyl acetate and petroleum ether). The filtrates were combined, concentrated and converted to the acid ester which was allowed to crystallize from ethyl acetate and petroleum ether until about half of the material had appeared. This substance was collected (weight 5 g.) and submitted to the resolution procedure described above to give 1.5 additional grams of acid phthalate of VA.

The combined filtrates were concentrated and converted to the free acid ester which was submitted to a four-cycle fractional crystallization procedure with ethyl acetate and petroleum ether as solvent. In each case the material that first crystallized was rich in racemate. A total of 4.5 g. of the phthalic acid ester of VB was obtained, m. p. 127–128° (flakes).

Resolution of the 3-Nitrophthalic Acid Ester of VI.—A mixture of 100 g. of the 3-nitrophthalic acid ester of VI, 65 g. of cinchonine and 500 ml. of acetone was heated to the boiling point and slowly cooled. The needles that separated were collected and twice recrystallized from a mixture of chloroform and acetone. The salt (55 g.) was converted to the 3-nitrophthalic acid ester of VIA; weight 30 g., m. p. 138–139° (needles from ethyl ether and petroleum ether).

The filtrates were combined, concentrated and converted to the acid ester which was mixed with 50 g. of cinchonidine and 300 ml. of acetone. The needles that separated were recrystallized twice from acetone to give 25 g. of salt which was converted to 13 g. of white needles (from ether and petroleum ether) of the 3-nitrophthalic acid ester of VIB, m. p. 139–140°.

The filtrates were combined, concentrated and converted to the acid ester which was subjected to the resolution procedure described above to produce 9 additional grams of the 3-nitrophthalic acid ester of VIA (m. p. 139–140°) and 13 additional grams of the 3-nitrophthalic acid ester of VIB, m. p. 139–140°.

Hydrolysis of the Phthalic Acid Esters of III, V and VA to III, V and VA, Respectively, and the 3-Nitrophthalic Acid Esters of IV, VI, IVA, IVB, VIA, and VIB to IV, VI, IVA, IVB, VIA and VIB, Respectively.—The procedure used for the above introconversions is illustrated by the hydrolysis of the 3-nitrophthalic acid ester of VIA to VIA alcohol. A mixture of 36 g. of the ester, 10 g. of potassium hydroxide, 10 g. of sodium hydroxide and 100 ml. of water was heated at reflux for twelve hours. The mixture was then cooled, extracted twice with petroleum ether, the extracts combined and washed with water, dried and evaporated to an oil. This oil was distilled to give 15.6 g. of VIA, b. p. 121° (17 mm.).

Acknowledgment.—The author wishes to express his thanks to Welton Burney, who performed the analysis of the compounds reported in this paper.

Summary

1. The compounds 2-phenyl-3-pentanol and 3-phenyl-2-pentanol have been prepared and completely resolved into the eight optically pure stereoisomers.

2. Tentative stereochemical structures have been assigned to each isomer.

LOS ANGELES, CALIFORNIA RECEIVED MARCH 14, 1949

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

Studies in Stereochemistry. III. The Wagner–Meerwein Rearrangement in the 2-Phenyl-3-pentanol and 3-Phenyl-2-pentanol Systems[1]

BY DONALD J. CRAM

Paper II[2] of this series reported the primary resolutions of 2-phenyl-3-pentanol into racemates III[3] and IV followed by the secondary resolution of each of these racemates into IIIA, IIIB and IVA and IVB, respectively. The structural isomer, 3-phenyl-2-pentanol, was also resolved to give racemates V and VI, and subsequently VA, VB and VIA and VIB, respectively. Tentative assignments of configuration for each of these isomers were suggested. This paper reports the results of an investigation of the acetolyses of the *p*-toluenesulfonates of III, IV, V, VI, IIIA, IVA, VA and VIA.

Results

Table I records the physical properties, analyses and yields of the *p*-toluenesulfonates of III, IV, V, VI, IIIA, IVA, IVB, VA, VIA and VIB. In each case the acetolysis of these substances was conducted at 70° and for thirty hours in anhydrous glacial acetic acid containing enough potassium acetate to neutralize the *p*-toluenesulfonic acid as it formed. The mixtures of acetate products were hydrolyzed to the corresponding mix-

TABLE I

PHYSICAL AND ANALYTICAL DATA PERTAINING TO THE *p*-TOLUENESULFONATES OF THE ISOMERS OF 2-PHENYL-3-PENTANOL AND 3-PHENYL-2-PENTANOL

Isomer	M. p., °C.	Yield, %	Formula	Analyses, % Calcd. C	H	Found C	H
III	90–91[a]	67	$C_{18}H_{22}SO_3$	67.89	6.97	67.82	7.17
IV	67–68	68	$C_{18}H_{22}SO_3$	67.89	6.97	67.73	7.18
V	40–41	63	$C_{18}H_{22}SO_3$	67.89	6.97	67.98	7.18
VI	Oil[b]	45	$C_{18}H_{22}SO_3$	67.89	6.97	68.02	7.22
IIIA	100–101	71	$C_{18}H_{22}SO_3$	67.89	6.97	67.92	7.18
IVA	86–87	66	$C_{18}H_{22}SO_3$	67.89	6.97	68.12	7.06
IVB	86–87	75	$C_{18}H_{22}SO_3$	67.89	6.97	67.82	7.17
VA	71–72	85	$C_{18}H_{22}SO_3$	67.89	6.97	67.75	6.78
VIA	41–42	69	$C_{18}H_{22}SO_3$	67.89	6.97	67.86	7.18
VIB	41–42	68	$C_{18}H_{22}SO_3$	67.89	6.97	67.76	7.25

[a] All of the compounds except VI crystallized as needles from low-boiling petroleum ether. [b] This compound was never obtained in a crystalline state. Purification was accomplished through repeated precipitation of the substance from low-boiling petroleum ether at Dry Ice temperature followed by high vacuum drying of the oil at room temperature.

---

(1) This paper was presented in part before the Organic Division of the American Chemical Society, San Francisco Meeting, March, 1949.

(2) Cram, THIS JOURNAL, **71**, 3871 (1949).

(3) The numbering system has been maintained from paper to paper in this investigation.

TABLE II

DATA ON ACETOLYSIS OF *p*-TOLUENESULFONATES OF THE RACEMATES OF 2-PHENYL-3-PENTANOL AND 3-PHENYL-2-PENTANOL

p-Toluenesulfonate	Yield,[a] of olefin, %	Solid deriv. product	M. p., °C. solid deriv.	Yield[a] solid deriv., %	Composition of known mixt.	M. p., °C. known mixt.	M. m. p. known mixt. and solid derivative, °C.
III	31	P. A. E.[b]	129–131[c]	30	32% P. A. E.[b] III 68% P. A. E.[b] V	129–131	129–131
V	29	P. A. E.[b]	128–130	33	33% P. A. E.[b] III 67% P. A. E.[b] V	128–130	128–130
IV	14	N. P. A. E.[d]	147–149[e]	34	31% N. P. A. E.[d] IV 69% N. P. A. E.[d] VI	147–149	147–149
VI	11	N. P. A. E.[d]	148–150	36	29% N. P. A. E.[d] IV 71% N. P. A. E.[d] VI	148–150	148–150

[a] This yield is based on the *p*-toluenesulfonate of the respective alcohol. [b] P. A. E. stands for phthalic acid ester. [c] A mixed melting point determination of this substance with the phthalic acid ester obtained from the acetolysis of the *p*-toluenesulfonate of V produced no depression. [d] N. P. A. E. stands for 3-nitrophthalic acid ester. [e] A mixed melting point determination of this substance with the 3-nitrophthalic acid ester obtained from the acetolysis of the *p*-toluenesulfonate of VI produced no depression.

tures of alcohols which were converted to mixtures of solid derivatives.

Table II records the yields and compositions of the products of the acetolysis experiments performed on the racemic *p*-toluenesulfonates of III, V, IV and VI. The products were identified in the first two experiments (III and V) by conversion to the phthalic acid ester mixtures, which melted at 129–131° and 128–130°, respectively (mixed melting point, 128–130°). Figure 1 records the plot of composition against melting point of known mixtures of phthalic acid esters of III and V, and mixed melting point determinations of the unknown and known mixtures served to identify the unknown mixture from both a qualitative and quantitative point of view.

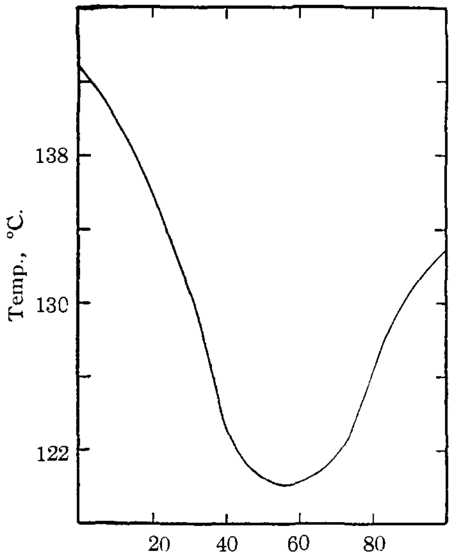


Fig. 1.—Melting point-composition diagram of the acid phthalates of III and V.

The products of the acetolysis experiments performed on the racemic *p*-toluenesulfonates of IV and VI were converted to mixtures of 3-nitrophthalic acid esters which melted at 147–149° and 148–150°, respectively (mixed melting point, 148–150°). Figure 2 records the plot of composition against melting point of known mixtures of the 3-nitrophthalic acid esters of IV and VI, and mixed melting point determinations of the unknown mixtures served to identify both quantitatively and qualitatively the compositions of the unknowns.

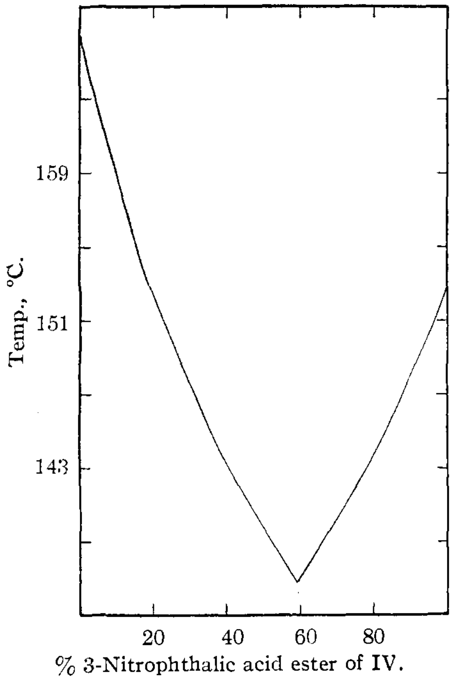
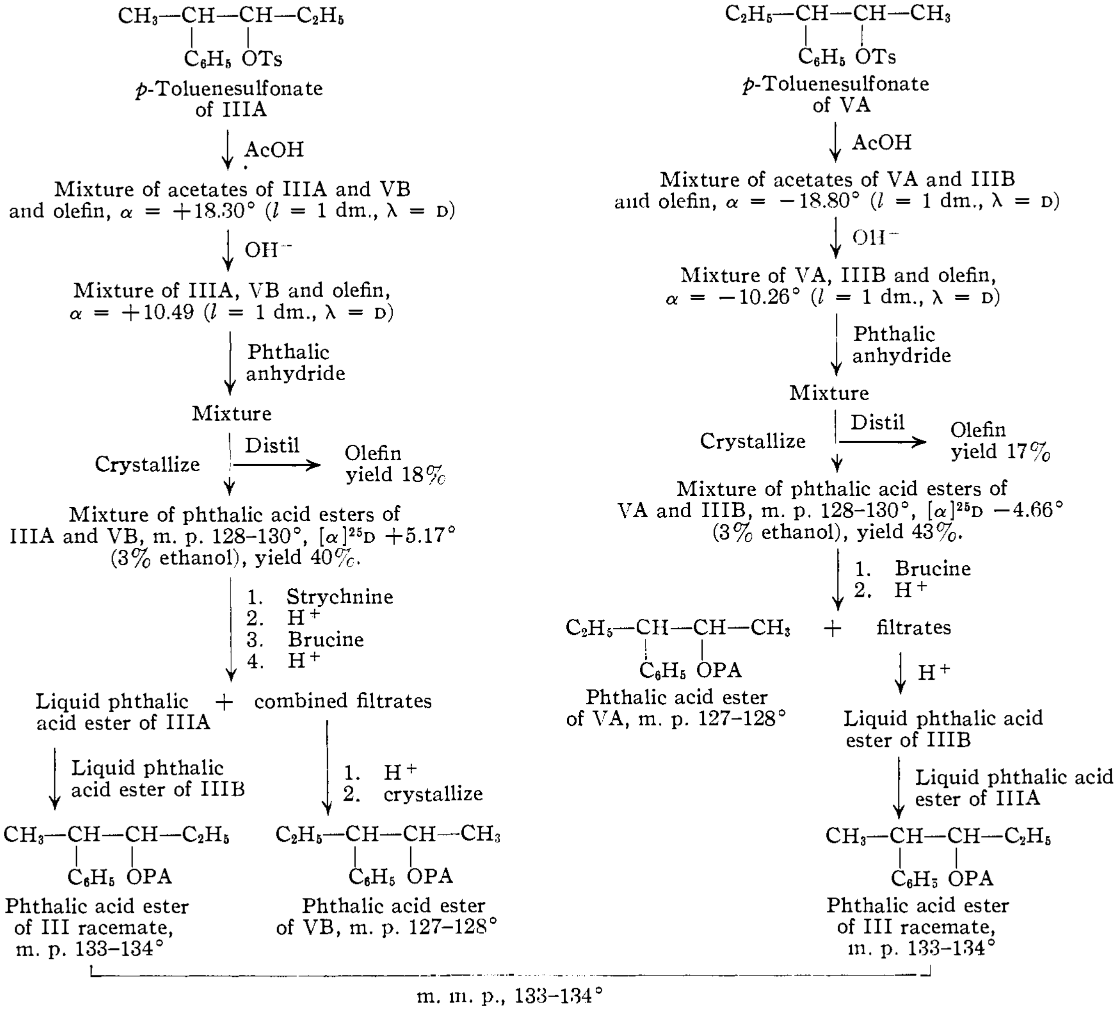


Fig. 2.—Melting point-composition diagram of the 3-nitrophthalic acid esters of IV and VI.

The methods employed for the determination of the products of the acetolysis experiments performed on the *p*-toluenesulfonates of IIIA and VA are outlined below. Special isolation procedures had to be used to demonstrate the qualitative composition of the products of each reaction, because the phthalic acid esters of IIIA and IIIB are liquids and hence a melting point–composition plot of mixtures of this derivative of IIIA and VB on the one hand and VA and IIIB on the other was impossible.



The procedure used for the determination of the compositions of the products of the acetolysis experiments performed on the *p*-toluenesulfonates of IVA and VIA is outlined in the following scheme. Figure 3 plots the variation of melting point with composition of mixtures of the 3-nitrophthalic acid esters of IVA and VIA. The qualitative and quantitative determinations of the compositions of the unknown mixtures were made through the use of mixed melting point determinations between the known and unknown mixtures.

For purposes of relating the configurations of VIA to VA, the *p*-toluenesulfonate of VIA was subjected to the action of potassium acetate[4] dissolved in absolute ethyl alcohol. The product (mixture of acetate and ether) was hydrolyzed and converted to the phthalic acid ester which proved to be the ester of VA.

Discussion

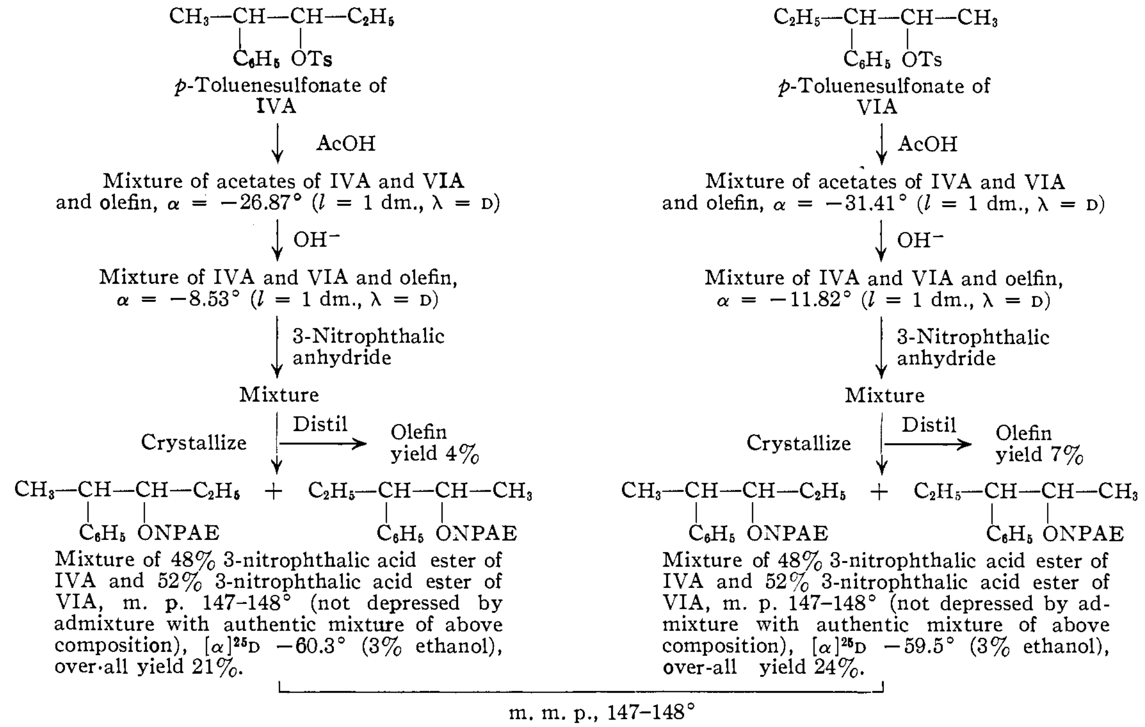
The above results clearly indicate that a partial rearrangement of the carbon skeleton has taken place during the acetolysis of the *p*-toluenesulfonates of the isomers of 2-phenyl-3-pentanol and 3-phenyl-2-pentanol (p. 3879).

This rearrangement appears to be stereospecific, at least as far as the main products of the reaction are concerned. The material that did not rearrange underwent a displacement reaction with complete retention of configuration. Thus in each case a mixture of rearranged and unrearranged acetate was obtained. These results are in complete agreement with what would be predicted from the interpretation given to the behavior of the analogous 3-phenyl-2-butanol system reported in paper I of this series.[5] The fact that rearrangement was found in both racemate series of the 2-phenyl-3-pentanol and 3-phenyl-2-pentanol systems provides strong evidence that rearrangement also took place in *both* racemate series of the 3-phenyl-2-butanol system. The *p*-toluenesulfonate of IIA must then have given acetate of IIA by two routes, one involving rearrangement, and the other not, even though there is no way of distin-

---

[4] This reaction results in simple inversion of the carbon atom bearing the oxygen and is analogous to the reaction reported in paper I (THIS JOURNAL, **71**, 3863 (1949)) of this series in which the *p*-toluenesulfonate of IA was converted to the acetate of IIA.

[5] Cram, THIS JOURNAL, **71**, 3863 (1949).



$CH_3—CH(C_6H_5)—CH(OTs)—C_2H_5$

p-Toluenesulfonate of IVA

↓ AcOH

Mixture of acetates of IVA and VIA and olefin, $\alpha = -26.87°$ (l = 1 dm., λ = D)

↓ OH^-

Mixture of IVA and VIA and olefin, $\alpha = -8.53°$ (l = 1 dm., λ = D)

↓ 3-Nitrophthalic anhydride

Mixture

Crystallize ↓ Distil → Olefin yield 4%

$CH_3—CH(C_6H_5)—CH(ONPAE)—C_2H_5$ + $C_2H_5—CH(C_6H_5)—CH(ONPAE)—CH_3$

Mixture of 48% 3-nitrophthalic acid ester of IVA and 52% 3-nitrophthalic acid ester of VIA, m. p. 147–148° (not depressed by admixture with authentic mixture of above composition), $[\alpha]^{25}D$ −60.3° (3% ethanol), over-all yield 21%.

$C_2H_5—CH(C_6H_5)—CH(OTs)—CH_3$

p-Toluenesulfonate of VIA

↓ AcOH

Mixture of acetates of IVA and VIA and olefin, $\alpha = -31.41°$ (l = 1 dm., λ = D)

↓ OH^-

Mixture of IVA and VIA and oelfin, $\alpha = -11.82°$ (l = 1 dm., λ = D)

↓ 3-Nitrophthalic anhydride

Mixture

Crystallize ↓ Distil → Olefin yield 7%

$CH_3—CH(C_6H_5)—CH(ONPAE)—C_2H_5$ + $C_2H_5—CH(C_6H_5)—CH(ONPAE)—CH_3$

Mixture of 48% 3-nitrophthalic acid ester of IVA and 52% 3-nitrophthalic acid ester of VIA, m. p. 147–148° (not depressed by admixture with authentic mixture of above composition), $[\alpha]^{25}D$ −59.5° (3% ethanol), over-all yield 24%.

m. m. p., 147–148°

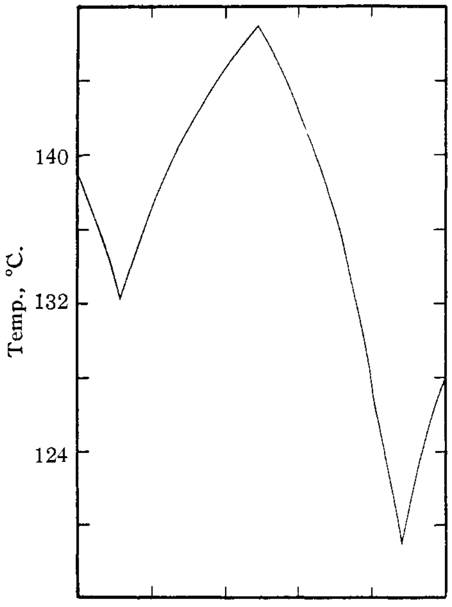
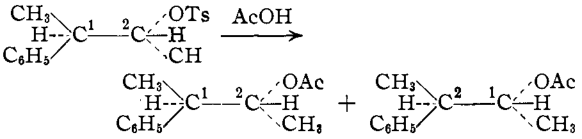


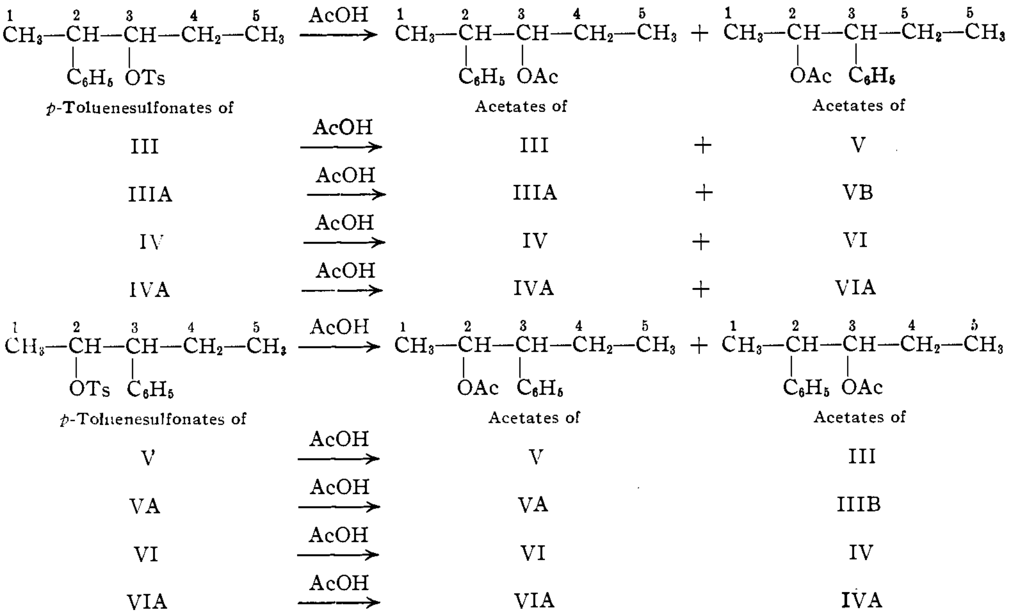
Fig. 3.—Melting point–composition diagram of the 3-nitrophthalic acid esters of IVA and VIA.

guishing between the products coming from the two paths.



From an experimental point of view, the 3-phenyl-2-pentanol and 2-phenyl-3-pentanol systems are much more difficult to study because the products of the reactions are mixtures of two structural isomers whose properties are very similar. As a result, the products were identified as mixtures of solid derivatives, and in only two cases were the two components separated. This method of analysis served well for a qualitative determination of the isomeric products, but is indicative in only a crude way of the relative amounts of each isomer produced in the reaction. Thus from the acetolysis of the *p*-toluenesulfonates of racemates III, IV, V and VI was ultimately obtained in each case approximately a seven to three ratio of 3-phenyl-2-pentanol derivative to 2-phenyl-3-pentanol derivative. When IVA and VIA esters were employed, however, the ratio was about one to one. This discrepancy is probably due to the interesting fact that the 3-nitrophthalic acid esters of IVA and VIA form a molecular compound in a one to one ratio (see Fig. 3), and that this molecular compound is more insoluble in the crystallization solvent than the VIA component (the melting point of the molecular compound is higher than either pure component). Hence the molecular compound crystallized preferentially.

The good agreement between the relative amounts of each isomer produced (see Table II) from the reactions of the III, V, IV, and VI esters, however, was probably not fortuitous, and can safely be interpreted as meaning that the 3-phenyl-2-pentanol isomer was produced in somewhat larger quantities than was the 2-phenyl-3-pentanol isomer, regardless of which series the starting mate-



$$\overset{1}{\mathrm{CH_3}}{-}\underset{\mathrm{C_6H_5}}{\overset{2}{\mathrm{CH}}}{-}\underset{\mathrm{OTs}}{\overset{3}{\mathrm{CH}}}{-}\overset{4}{\mathrm{CH_2}}{-}\overset{5}{\mathrm{CH_3}} \xrightarrow{\mathrm{AcOH}} \overset{1}{\mathrm{CH_3}}{-}\underset{\mathrm{C_6H_5}}{\overset{2}{\mathrm{CH}}}{-}\underset{\mathrm{OAc}}{\overset{3}{\mathrm{CH}}}{-}\overset{4}{\mathrm{CH_2}}{-}\overset{5}{\mathrm{CH_3}} + \overset{1}{\mathrm{CH_3}}{-}\underset{\mathrm{OAc}}{\overset{2}{\mathrm{CH}}}{-}\underset{\mathrm{C_6H_5}}{\overset{3}{\mathrm{CH}}}{-}\overset{5}{\mathrm{CH_2}}{-}\overset{5}{\mathrm{CH_3}}$$

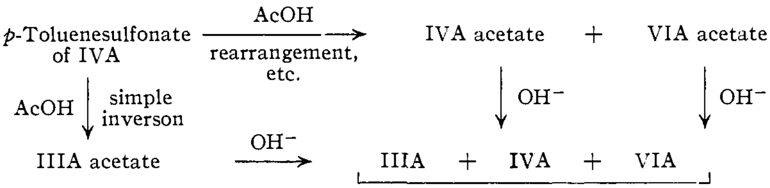
p-Toluenesulfonates of		Acetates of		Acetates of
III	$\xrightarrow{\mathrm{AcOH}}$	III	+	V
IIIA	$\xrightarrow{\mathrm{AcOH}}$	IIIA	+	VB
IV	$\xrightarrow{\mathrm{AcOH}}$	IV	+	VI
IVA	$\xrightarrow{\mathrm{AcOH}}$	IVA	+	VIA

$$\overset{1}{\mathrm{CH_3}}{-}\underset{\mathrm{OTs}}{\overset{2}{\mathrm{CH}}}{-}\underset{\mathrm{C_6H_5}}{\overset{3}{\mathrm{CH}}}{-}\overset{4}{\mathrm{CH_2}}{-}\overset{5}{\mathrm{CH_3}} \xrightarrow{\mathrm{AcOH}} \overset{1}{\mathrm{CH_3}}{-}\underset{\mathrm{OAc}}{\overset{2}{\mathrm{CH}}}{-}\underset{\mathrm{C_6H_5}}{\overset{3}{\mathrm{CH}}}{-}\overset{4}{\mathrm{CH_2}}{-}\overset{5}{\mathrm{CH_3}} + \overset{1}{\mathrm{CH_3}}{-}\underset{\mathrm{C_6H_5}}{\overset{2}{\mathrm{CH}}}{-}\underset{\mathrm{OAc}}{\overset{3}{\mathrm{CH}}}{-}\overset{4}{\mathrm{CH_2}}{-}\overset{5}{\mathrm{CH_3}}$$

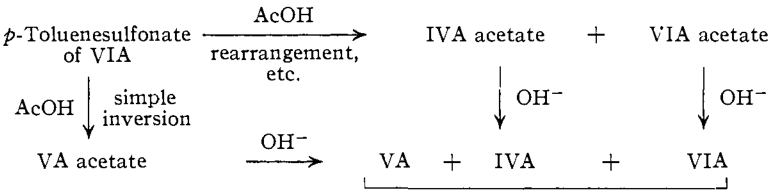
p-Toluenesulfonates of		Acetates of		Acetates of
V	$\xrightarrow{\mathrm{AcOH}}$	V		III
VA	$\xrightarrow{\mathrm{AcOH}}$	VA		IIIB
VI	$\xrightarrow{\mathrm{AcOH}}$	VI		IV
VIA	$\xrightarrow{\mathrm{AcOH}}$	VIA		IVA

rial belonged to. The striking fact about the data is that the *p*-toluenesulfonates of the structural isomers, III and V, produced the same products in the same ratios, and that the *p*-toluenesulfonates of the structural isomers IV and VI gave analogous results. When the optically active *p*-toluenesulfonates of IIIA and VA were used, the rotations of the whole samples of the acetate products were taken and the values proved to be of almost equal magnitude but of opposite sign (+18.30 and −18.80°, respectively). This relationship of the rotations was maintained through the conversions of the acetates to the alcohols, and the subsequent conversions to the phthalic acid esters. These data are excellent evidence that in these two runs the products were qualitatively and quantitatively the same but of opposite configurations.

The data obtained for the acetolysis of the *p*-toluenesulfonates of the optically active isomers, IVA and VIA, are not as conclusive. The yields of the solid derivatives are only about half of the yields obtained in the runs involving the esters of IIIA and VA as starting materials. Undoubtedly more material was lost during the purification of the solid derivatives in the former cases due to the formation of a molecular compound between the two components. However, the poor agreement between the rotations of the impure acetate products of the IVA and VIA runs suggests that small amounts of side reactions interfered. A plausible explanation for the direction which the rotations took is to assume that a small amount of direct displacement took place with simple inversion at the carbon atom bearing the oxygen during the acetolysis of the *p*-toluenesulfonates of IVA and VIA. Thus the ester of IVA would give small amounts of acetate of IIIA and subsequently the alcohol, IIIA, and the ester of VIA would give small amounts of acetate of VA and subsequently the alcohol, VA.



mixture, $\alpha = -8.53$, $l = 1$ dm. (λ = D)
(IIIA, $[\alpha]^{25}\mathrm{D}$ +12.40°; IVA, $[\alpha]^{25}\mathrm{D}$ −7.32°; VIA, $[\alpha]^{25}\mathrm{D}$ −20.37°)[6]



mixture, $\alpha = -11.82°$, $l = 1$ dm. (λ = D)
(VA), $[\alpha]^{25}\mathrm{D}$ −16.89°; IVA, $[\alpha]^{25}\mathrm{D}$ −7.32°; VIA, $[\alpha]^{25}\mathrm{D}$ −20.37°)[6]

The positive rotation of IIIA would tend to cancel some of the negative rotation of the mixture of IVA and VIA, whereas the negative rotation of VA would not affect very much the negative rotation of the mixture of IVA and VIA.

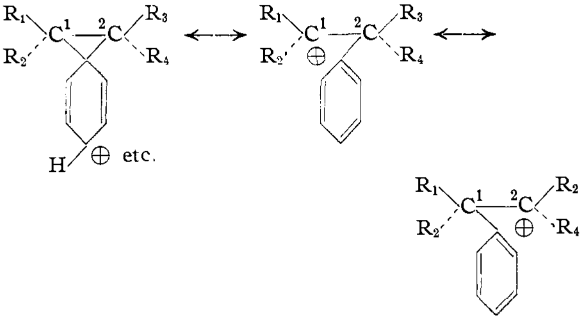
The relative yields of olefin obtained from the acetolysis reactions are consistent with the con-

---

(6) These rotations of the pure alcohols were reported in paper II of this series (THIS JOURNAL, **71**, 3871 (1949)).

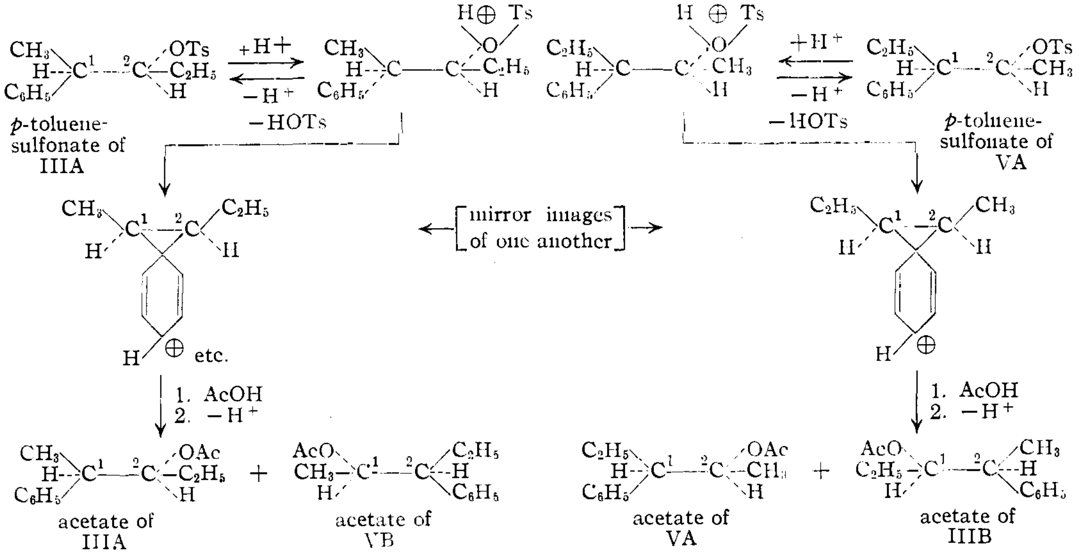
figurational assignments of III, IV, V, and VI (racemic alcohols) made in part II[2] of this series. The yield of olefin obtained from the acetolysis of the *p*-toluenesulfonate of IA (see paper I[5] of this series) was 26% as compared to a yield of 9.5% obtained from the *p*-toluenesulfonate of IIA. Since the *p*-toluenesulfonates of III and V gave yields of olefin amounting to 31 and 29%, respectively, and the *p*-toluenesulfonates of IV and VI, yields of 14 and 11%, respectively, it seems probable that the configurations of III and V are analogous to I on the one hand, and the configurations of IV and VI are analogous to II on the other. Further evidence for this analogy is found in paper IV of this series, along with definite proof that IVA possesses a configuration analogous to that of IIA.

Enough information is now at hand to rationalize the experimental results and the deductions based on these results in terms of a mechanistic interpretation of the acetolysis reaction of the *p*-toluenesulfonates of IIIA, IVA, VA and VIA. In the generalized cyclic ionic species shown, if R_1 and R_3 are methyl groups and R_2 and R_4 are hydrogens, the cycle possesses a plane of symmetry.



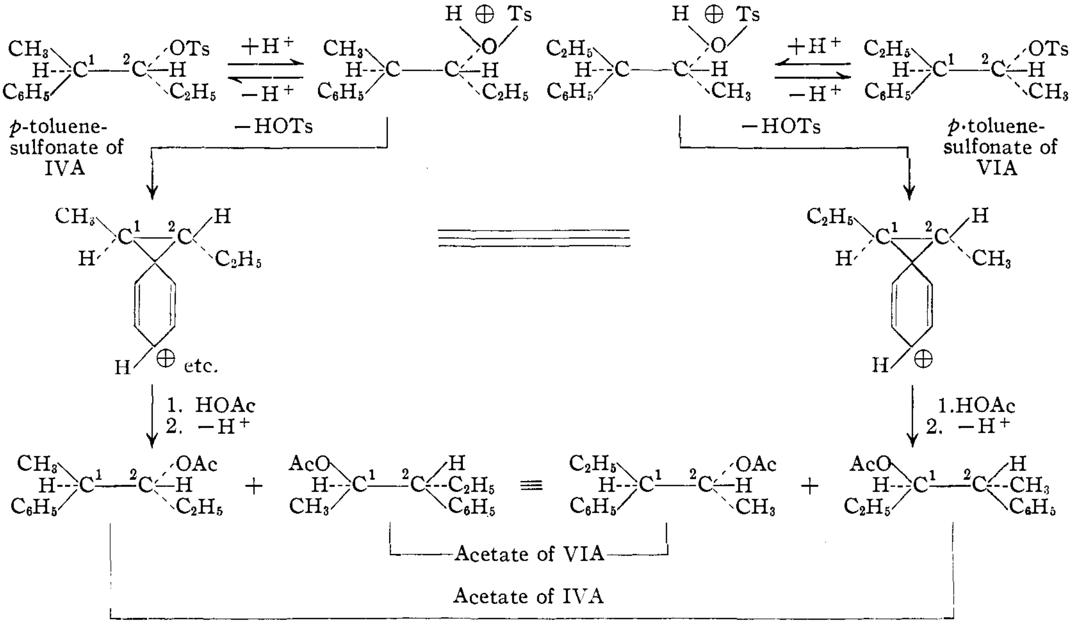
This intermediate was postulated as being formed during the acetolysis of the *p*-toluenesulfonates of either IA or IB.[5] Opening of the cycle at carbon atoms 1 or 2 (with equal probability) leads to racemic I acetate.[7] If R_1 and R_4 are methyl groups and R_2 and R_3 are hydrogens, the cycle is asymmetric, and can be formed only from the *p*-toluenesulfonate of IIA. When such a cycle is opened, the same product (acetate of IIA) is obtained whether the cycle is opened at carbon atoms 1 or 2. Such an intermediate was postulated in the acetolysis of the *p*-toluenesulfonate of IIA. If R_1 is a methyl group, R_3 an ethyl group, and R_2 and R_4 are hydrogens, the cycle is asymmetric, and would be formed from the *p*-toluenesulfonates of either IIIA or VB, these two structural isomers possessing a pseudo-enantiomorphic configurational relationship to one another. Furthermore, when the cycle is opened at carbon atom 2, acetate of IIIA would be obtained, and when the cycle is opened at carbon atom 1, acetate of VB is produced. If both reactions occur, a mixture would be obtained. The composition of the mixture would be independent of whether the starting material was one or the other isomer (IIIA or VB configuration) if no competing side reactions interfered. If R_1 is a methyl group, R_4 an ethyl group and R_2 and R_3 are hydrogens, the cycle is asymmetric, and would be formed from the *p*-toluenesulfonates of either IVA or VIA, these two structural isomers possessing an analogous configurational relationship to one another. When this cycle is opened at carbon atom 2, the acetate of IVA is obtained, and when opened at carbon atom 1, the acetate of VIA is produced. When both reactions occur, a mixture would result, the composition of which would be independent of which of the two starting materials the cycle came from.

The following scheme summarizes the argument.



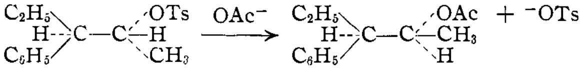
---

[7] The reasonable assumption has been made that inversion occurs at the carbon atom bearing the oxygen when the cycle closes, and that a second inversion occurs at the point where the cycle is opened.



The interesting fact that a small excess of 3-phenyl-2-pentanol derivative over 2-phenyl-3-pentanol derivative was obtained in each case (see Table II) independent of which racemate series was involved is explainable on the hypothesis that the cyclic intermediate ions are always asymmetric. The cycle is opened by a collision with an acetic acid molecule more often at the carbon atom bearing a methyl group than at the carbon atom bearing an ethyl group because of the slightly greater steric hindrance an ethyl group offers over that of a methyl group in the nucleophylic bimolecular displacement reaction.

The assignments of relative configurations of VA and VIA were substantiated by the inversion of the carbon bearing the oxygen bond of the *p*-toluenesulfonate of VIA by acetate ion in absolute ethanol. Although ether of undetermined configuration was the main product of the reaction, a small amount of solid derivative of VA was isolated.



p-Toluenesulfonate of VIA

Acetate of VA

Although any one experimental observation in the series of investigations reported in the first three papers of this series does not substantiate the general hypothesis of a carbocyclic ionic intermediate, the long sequence of facts become coherent only in terms of such a hypothesis. The formulation of the fundamental ideas early in the work was of great help not only in designing systems to broaden the experimental evidence but also in predicting products of reactions and thereby aiding in the experimental work. However, there has been no evidence obtained that the mechanism presented above applies to Wagner–Meerwein rearrangements in systems that are not closely similar to the one at hand. Since, in a sense, the reactions studied above amount to an aromatic substitution of an alkyl group for an alkyl group in a benzene ring, the results of this study should be relevant to the general question of the mechanism of aromatic substitution.

Experimental

Syntheses of the *p*-Toluenesulfonates of III, IV, V, VI, IIIA, IVA, IVB, VA, VIA and VIB.—The procedure used for the above syntheses is illustrated by the conversion of III to the *p*-toluenesulfonate of III. A mixture of 3.85 g. of III, 4.46 g. of pure *p*-toluenesulfonyl chloride and 10 ml. of pure dry pyridine was allowed to stand at room temperature for twenty-four hours. The mixture was then shaken with a cooled mixture of benzene and excess 2 *N* sulfuric acid, and the organic layer was washed successively with 2 *N* sulfuric acid, water, dilute alkaline solution and water. The organic layer was then dried, the solvent was evaporated under reduced pressure and at room temperature, and the resulting oil was crystallized and recrystallized from a low boiling petroleum ether and benzene mixture to give 5.0 g. of ester, m. p. 90–91° (white needles).

Acetolysis of the *p*-Toluenesulfonates of III, V, IV, VI, IVA, VIA, IIIA and VA.—The same procedure was used for the acetolyses of the *p*-toluenesulfonates of all of the above isomers. The acetates produced were hydrolyzed to the respective alcohols and solid derivatives were prepared by completely analogous methods. The following procedure is representative.

The *p*-toluenesulfonate of III (3.45 g.), 79 ml. of glacial acetic acid, 0.79 ml. of acetic anhydride and 1.5 g. of freshly fused potassium acetate was heated at 70° for thirty hours, cooled, and shaken with a mixture of petroleum ether and a large volume of water. The organic layer was separated, washed first with water, then with dilute alkaline solution and again with water. The solvent was evaporated and distilled to give 1.91 g. of mixture of acetate and olefin. This mixture was hydrolyzed by heating at reflux temperature for twenty-four hours in a mixture of 10 ml. of water and 1.91 g. of potassium hydroxide. The mixture was then cooled, extracted with petroleum ether, the extract was washed with water, dried, evaporated and distilled. The 1.50 g. of the mixture of alcohols and olefin obtained was heated at 100° for one hour with 1.50 g. of phthalic anhydride and 2 ml. of pyridine. This mixture was cooled, shaken with a mixture of ethyl ether and excess of 2 N sulfuric acid, the ether layer was washed with water, dried and evaporated to an oil. This oil was crystallized from ethyl acetate and petroleum ether and recrystallized from these same solvents to produce 1.00 g. of acid phthalate, m. p. 129–131°, m. m. p. with a mixture of 32% acid phthalate of III and 68% acid phthalate of V (m. p. 129–132°), 129–132°, m. m. p. with an equal weight of the acid phthalate of III, 121–127°, m. m. p. with an equal weight of the acid phthalate of V, 137–142°.

The combined filtrates were evaporated to an oil and this oil was subjected to distillation under 18 mm. of pressure to give 0.50 g. of olefin.

When the *p*-toluenesulfonate of V (6.8 g.) was subjected to the above procedures, 3.8 g. of a mixture of acetate and olefin was obtained which was converted to 3.0 g. of a mixture of olefin and alcohol. Conversion of the mixture to the acid phthalate gave 2.22 g. of a recrystallized mixture of acid esters, m. p. 128–130°, m. m. p. with a mixture of 33% acid phthalate of III and 67% acid phthalate of V (m. p. 128–130°), 128–130°, m. m. p. with an equal weight of the acid phthalate of III, 121–126°, m. m. p. with an equal weight of acid phthalate of V, 136–141°. Olefin (0.90 g.) was recovered from the filtrates.

Acetolysis of the *p*-toluenesulfonate of IV (3.71 g.) produced 2.0 g. of a mixture of acetate and olefin which on hydrolysis gave 1.55 g. of a mixture of alcohol and olefin. Treatment of this mixture with 3-nitrophthalic acid ester produced 1.40 g. of a recrystallized mixture of acid esters, m. p. 147–149°, m. m. p. with a mixture of 31% 3-nitrophthalic acid ester of IV and 69% 3-nitrophthalic acid ester of VI (m. p. 147–149°) 147–149°, m. m. p. with an equal weight of the 3-nitrophthalic acid ester of IV, 139–145°, m. m. p. with an equal weight of the 3-nitrophthalic acid ester of VI, 152–161°. A total of 0.24 g. of olefin was recovered from the filtrates.

Acetolysis of the *p*-toluenesulfonate of VI (3.90 g.) produced 2.45 g. of a mixture of acetates and olefin which upon hydrolysis gave 1.75 g. of a mixture of alcohols and olefin. Conversion of the mixture of the 3-nitrophthalic acid ester produced 1.55 g. of recrystallized material, m. p. 148–150°, m. m. p. with a mixture of 29% 3-nitrophthalic acid ester of IV and 71% of the same derivative of VI (m. p. 148–150°), 148–150°, m. m. p. with an equal weight of the 3-nitrophthalic acid ester of IV, 139–146°, m. m. p. with an equal weight of the same derivative of VI, 154–163°. A total of 0.20 g. of olefin was obtained from the filtrates.

When the *p*-toluenesulfonate of IVA (2.4 g.) was subjected to acetolysis, 1.32 g. of a mixture of acetate and olefin was obtained, $\alpha = -26.87°$ (l = 1 dm.) and hydrolysis of the mixture produced 0.88 g. of a mixture of olefin and alcohol, $\alpha = -8.53°$ (l = 1 dm.). Conversion of this material to the 3-nitrophthalic acid ester produced 0.58 g. of recrystallized product, m. p. 147–148°, $[\alpha]^{25}\text{D}$ $-60.3°$ (3% in ethanol), m. m. p. with a mixture of 48% of the 3-nitrophthalic acid ester of IVA and 52% of the 3-nitrophthalic acid ester of VIA (m. p. 147–148°), 147–148°, m. m. p. with an equal weight of IVA, 134–141°, m. m. p. with an equal weight of VIA, 138–142°. From the filtrates was isolated 0.05 g. of olefin.

Acetolysis of the *p*-toluenesulfonate of VIA (5.0 g.) produced 2.90 g. of a mixture of alcohol and olefin, $\alpha = -31.41°$ (l = 1 dm.), which when hydrolyzed gave 2.20 g. of a mixture of alcohol and olefin, $\alpha = -11.82°$ (l = 1 dm.). This material was converted to the 3-nitrophthalic acid ester derivative to give 1.33 g. of recrystallized material, m. p. 147–148°, $[\alpha]^{25}\text{D}$ $-59.5°$ (3% in ethanol), m. m. p. with a mixture of 48% 3-nitrophthalic acid ester of IVA and 52% 3-nitrophthalic acid ester of VIA (m. p. 147–148°), 147–148°, m. m. p. with an equal weight of 3-nitrophthalic acid ester, of IVA, 131–136°, m. m. p. with an equal weight of the same derivative of VIA, 137–142°. A total of 0.15 g. of olefin was obtained from the filtrate.

Acetolysis of the *p*-toluenesulfonate of IIIA (2.4 g.) produced 1.26 g. of a mixture of acetate and olefin, $\alpha = +18.30°$ (l = 1 dm.) which when hydrolyzed gave 0.94 g. of a mixture of alcohol and olefin, $\alpha = +10.49°$ (l = 1 dm.). Conversion of this material to the acid phthalate gave 0.96 g. of recrystallized derivative, m. p. 128–130°, $[\alpha]^{25}\text{D}$ $+5.17°$ (3% in ethanol). Olefin (0.19 g.) was obtained in the usual way from the filtrates.

A mixture of 0.80 g. of the above mixture, 0.70 g. of strychnine and 10 ml. of acetone was allowed to stand and the material that separated was recrystallized from acetone and shaken with a mixture of ethyl ether and excess dilute sulfuric acid. The organic layer was washed with water, dried, the solvent was evaporated and the resulting oil mixed with 0.50 g. of brucine and 5 ml. of acetone. The material that separated was recrystallized from acetone and shaken with a mixture of ether and excess dilute sulfuric acid, the organic layer was washed with water, dried and evaporated to an oil, weight, 155 mg. This material was mixed with 155 mg. of the acid phthalate of IIIB (this material is an oil and was prepared by hydrolysis of the pure 3,5-dinitrobenzoate of IIIB[2] with subsequent esterification of the alcohol obtained). When dissolved in an equal volume of ethyl acetate and a small amount of petroleum ether added, the oil crystallized to give 250 mg. of the acid phthalate of III, m. p. 133–134°, mixed melting point with an authentic sample, 133–134°.

The filtrates from the crystallizations of the strychnine and brucine salts were evaporated to dryness, shaken with an excess of dilute sulfuric acid and ether, the ether layer was washed with water, dried and evaporated to an oil. Crystallization of this material from ethyl acetate and petroleum ether and recrystallization of the product from the same solvents gave 0.54 g. of the acid phthalate of VB, m. p. 127–128°, m. m. p. with an authentic sample, 127–128°. A sample of this material was mixed with an equal weight of the acid phthalate of VA and the mixture recrystallized from ethyl acetate and petroleum ether, m. p. 143–144°, m. m. p. with an authentic sample of the acid phthalate of V, 143–144°.

Acetolysis of the *p*-toluenesulfonate of VA (5.0 g.) produced 2.80 g. of a mixture of acetate and olefin, $\alpha = -18.80°$ (l = 1 dm.), which on hydrolysis gave 2.17 g. of a mixture of olefin and alcohol, $\alpha = -10.26°$ (l = 1 dm.). Conversion of this material to the acid phthalate gave 2.11 g. of recrystallized material, m. p. 128–130°, $[\alpha]^{25}\text{D}$ $-4.66°$ (3% in ethanol). Olefin (0.40 g.) was obtained from the filtrate in the usual way.

A solution of 1.5 g. of the above material and 1.8 g. of brucine dissolved in 10 ml. of acetone was allowed to stand and the salt that separated was recrystallized and converted back to the phthalic acid ester; weight 0.70, m. p. 128–129°, m. m. p. with an authentic sample of the acid phthalate of VA, 128–129°. A small amount of this material was mixed with an equal weight of the same derivative of VB and recrystallized from ethyl acetate and petroleum ether, m. p. 143–144°, m. m. p. with an authentic sample of the acid phthalate of V, 143–144°.

The filtrates from the crystallization of the salt were concentrated and shaken with a mixture of excess dilute sulfuric acid solution and ether, the organic layer was washed with water, dried, and evaporated to an oil, weight 0.52 g. A small amount of this oil (50 mg.) was mixed with an equal amount of the oil obtained by treatment of IIIA with phthalic anhydride (the non-crystalline phthalic acid ester of IIIA), and the mixture was crystallized and recrystallized from ethyl acetate and petroleum ether; weight 55 mg., m. p. 133–134°, m. m. p. with an authentic sample of the phthalic acid ester of III, 133–134°.

Inversion of the *p*-Toluenesulfonate of VIB to Produce the Acetate of VB.—A solution of 10 ml. of absolute ethanol, 1.0 g. of *p*-toluenesulfonate of VIB and 3.0 g. of freshly fused potassium acetate was held at reflux for fifteen hours. The mixture was then cooled and shaken with a mixture of water and petroleum ether (low boiling).

The organic layer was washed three times with water, dried, evaporated to an oil and distilled to give 0.40 g. of oil. This material was treated with 0.20 g. of phthalic anhydride and 2 ml. of pyridine at 100° for one hour, cooled and shaken with a mixture of benzene and dilute sulfuric acid (excess). The organic layer was washed with water, dried, evaporated and the oil submitted to distillation; weight of ether 0.27 g.

The material that did not distil was crystallized and recrystallized three times from a mixture of ethyl acetate and petroleum ether to give 32 mg. of acid phthalate of VB; m. p. 126–128°, m. m. p. with an authentic sample, 127–129°.

A sample of this material was mixed with an equal weight of the acid phthalate of VA and the mixture crystallized from ethyl acetate and petroleum ether; m. p. 143–144°, m. m. p. with an authentic sample, 143–144°.

Acknowledgment.—The author wishes to thank Welton Burney for the analyses reported in this paper.

Summary

1. The *p*-toluenesulfonates of the isomers of 3-phenyl-2-pentanol and 2-phenyl-3-pentanol (III, IV, V, VI, IIIA, IVA, VA and VIA) were prepared and submitted to acetolysis, and the mixtures of acetates obtained were hydrolyzed to the respective mixtures of alcohols, of which solid derivatives were prepared. From the *p*-toluenesulfonate of either III or V was obtained a mixture of III and V derivatives, from the *p*-toluenesulfonate of either IV or VI was obtained a mixture of derivatives of IV and VI, from the *p*-toluenesulfonate of either IVA or VIA was obtained a mixture of derivatives of IVA and VIA, from the *p*-toluenesulfonate of IIIA was obtained a mixture of derivatives of IIIA and VB, and from the *p*-toluenesulfonate of VA was obtained a mixture of derivatives of IIIB and VA. These results have been interpreted as constituting evidence that a Wagner–Meerwein rearrangement takes place in each system and in a highly stereospecific manner, and that the stereochemistry of these reactions can be explained only on the basis of carbocyclic, asymmetric ionic intermediates.

2. Additional evidence has been obtained for the relative configurations of the above isomers.

LOS ANGELES, CALIFORNIA RECEIVED MARCH 14, 1949

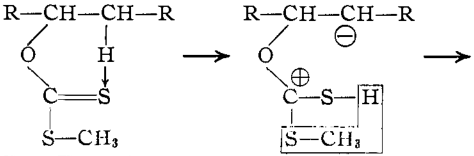
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

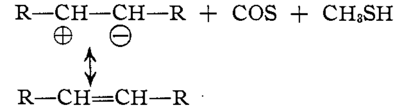
Studies in Stereochemistry. IV. The Chugaev Reaction in the Determination of Configuration of Certain Alcohols

BY DONALD J. CRAM

The results of rearrangement studies of the *p*-toluenesulfonates of the isomers of 3-phenyl-2-butanol led in paper I[1] of this series to an assignment of relative configurations to the four stereoisomers. The determination of the relative configurations by an independent method is desirable, and the use of the Chugaev reaction offers not only an attractive and unique method of accomplishing this end, but also offers a means of extending our knowledge of the steric course and mechanism of the Chugaev reaction itself. Since these two problems are completely interdependent, the purpose of this investigation is to show consistency between what is already known about the configurations of the starting material, and what is already known about the stereochemistry of the Chugaev reaction.

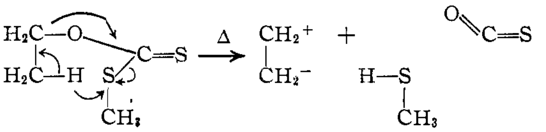
Stevens and Richmond[2] have suggested that the lack of rearranged olefins as products of this reaction can be explained by assuming that intramolecular hydrogen bonding prior to the proton elimination takes place, and that the reaction can be pictured as follows.





These authors did not state whether the proton was pulled from the carbon before or during the breaking of the carbon oxygen bond, but the diagram implies the former.

Hückel, *et al.*,[3] found that decomposition of the xanthate of *l*-menthol produced about 30% Δ^2-menthene and 70% Δ^3-menthene, and the xanthate of *d*-neomenthol decomposed to give 80% Δ^2-menthene and 20% Δ^3-menthene. Since the hydrogen, loss of which leads to Δ^3-menthene, lies *cis* to the carbon–oxygen bond in the xanthate of *l*-menthol, and *trans* in the xanthate of *d*-neomenthol, the 70% Δ^3-menthene produced by the xanthate of *l*-menthol represents in effect a *cis* elimination reaction, and the 20% Δ^3-menthene obtained from the xanthate of *d*-neomenthol a *trans* elimination reaction. The stereochemistry of the reactions that produced Δ^2-menthene are not clear. These authors interpret the reaction as taking place by a completely concerted proc-



---

[1] Cram, THIS JOURNAL, **71**, 3863 (1949).

[2] Stevens and Richmond, *ibid.*, **63**, 3132 (1941).

[3] Hückel, Tapp and Legutke, *Ann.*, **543**, 191 (1940).