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

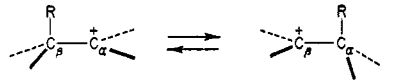
# Neighboring Carbon and Hydrogen. VIII. Solvolysis of Optically Active α-Phenylneopentyl Derivatives[1,2]

BY S. WINSTEIN AND BETSY K. MORSE

The question of the place of the so-called non-classical bridged structure in carbonium ion theory is discussed. For exploring where carbonium ion reactions need to be interpreted in terms of direct formation and subsequent direct reaction of a bridged cation, the α-phenylneopentyl system, with its high hindrance to solvent approach, and the near equivalence for conjugation purposes of the α-phenyl and the two β-methyl groups, represents one of the worthwhile test cases. Resolution of α-phenylneopentyl alcohol has been carried out and the solvolysis of the active *p*-toluenesulfonate and chloride has been studied. The steric results of slightly predominating inversion in the unrearranged product, and other facts, lend no support for a bridged structure for the cation in the present case. The facts are best accounted for with the classical description of the α-phenylneopentyl cation.

It has been clear for some time that isomerization within certain cations (I→II or II→I) involves very little activation energy since this kind of rearrangement competes, at times, so well with the collapse of the solvated cation to give normal solvolysis product. The latter process, itself, must not involve high activation energy. This means, at least, that the state involving *ca.* half-migration of the β-bonding electron pair and the accompanying R group (III a↔b↔c) has an energy not much in excess of the classical structure I. The question arises whether this state corresponds to a potential energy valley and, if so, whether the bridge structure III is, under certain circumstances, more stable than the classical structures I and II. The possibility of this kind of formulation for the carbonium ion was considered some years ago[3] and Nevell, de Salas and Wilson[3b] and Watson[3c] wrote the symbol V for a possible mesomeric carbonium ion (canonical structures IIIa and c). Allowing for canonical structure IIIb, as in somewhat analogous cases,[3a,4] one would write the symbol IV.

More recently, with the increased interest in cases where there is an over-supply of stable orbitals, bridged structures have been suggested for carbonium ions by Eyring,[5] Dewar[6] (symbol VI), Price[7] (symbol VII), Walsh,[8] Arcus[9] (symbol VIII) and others. Still not clear are: (a) whether I, II and IV all need explicit mention in any particular instance; (b) the energy of IV relative to I or II; and (c) the magnitude of any activation energy for processes such as I→IV or IV→II. Thus, Dewar[10] regards the π-complex (bridged) structure comparable in stability to the original structure (I), so that rearrangement by the route I→VI→II may require very little, if any, activation energy. But, in most cases, he regards it likely that a cation rearranges to a π-complex during the actual ionization process.



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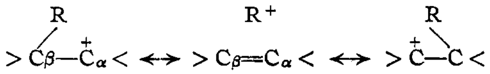
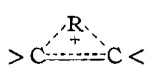


IIIa b c



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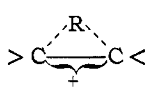

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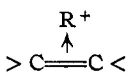

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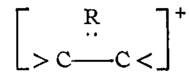

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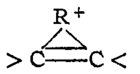
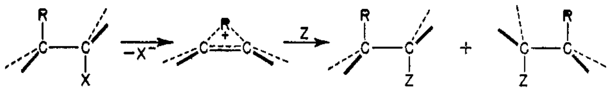


VIII

The question of the exact relative stabilities of I or II and IV and the other related questions are not easy to decide on theoretical grounds, especially when consideration is given the environment of the cation I or IV. In a polar solvent due regard needs to be given to the position of solvating species[11] and the substantial solvation energies involved. It seems likely, for example, that the bridged structure IV is associated with a smaller solvation energy than the classical structure I, and that a solvent could oppose the change from I to IV.

It is important to decide where carbonium ion reactions need to be interpreted in terms of direct formation and subsequent direct reaction of bridged cations IV. The stereochemical consequences for substitution and rearrangement connected with solvolysis of a halide or a similar derivative IX to X and XI are just those discussed in cases of participation by functional neighboring groups,[1a,12]



IX IV X XI

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[1] The results here presented were reported in summary at: (a) the American Chemical Society Eleventh National Organic Symposium, Madison, Wisconsin, June 21, 1949, page 65 of abstracts; (b) Montpellier, France, April 26, 1950 [*Bull. soc. chim.*, **18**, 55 (1951)].

[2] Taken in part from Ph.D. thesis of Betsy K. Morse, U. C. L. A., 1949.

[3] (a) Winstein and Lucas, This Journal, **60**, 836 (1938); (b) Nevell, de Salas and Wilson, *J. Chem. Soc.*, 1188 (1939); (c) Watson, "Annual Reports," 197 (1939); 120 (1941); "Modern Theories of Organic Chemistry," Oxford Univ. Press, Oxford, 1941, p. 208.

[4] Winstein and Lucas, This Journal, **61**, 1576 (1939).

[5] Eyring, *Ind. Eng. Chem.*, **35**, 511 (1943).

[6] Dewar, *J. Chem. Soc.*, 406, 777 (1946).

[7] Price, "Mechanisms of Reactions at Carbon-Carbon Double Bonds," Interscience Publishers, Inc., New York, N. Y., 1946, pp. 39-43.

[8] Walsh, *J. Chem. Soc.*, 89 (1947).

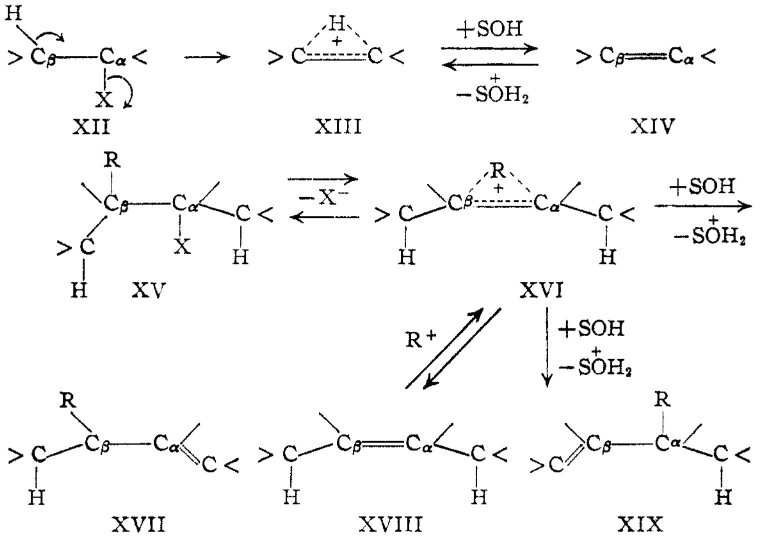
[9] Arcus, *Chemistry & Industry*, 442 (1947).

[10] Dewar, "The Electronic Theory of Organic Chemistry," Oxford Univ. Press, Oxford, 1949, page 212.

[11] Winstein, Grunwald and Jones, This Journal, **73**, 2700 (1951).

[12] *E.g.*, Winstein and Buckles, *ibid.*, **64**, 2780 (1942).

as Arcus[9] has already indicated.[13] Bridged structures could similarly be important in elimination (XII→XIII→XIV; XV→XVI→XVII or XIX), addition (XVIII→XVI→XV), or certain electrophilic substitutions (XVIII→XVI→XVII), using the usual stereo-electronic considerations.[1,12,14]



In approaching the question of the role of bridged structures in carbonium ion reactions, we have for one thing, sought stereochemical evidence in substitution and rearrangement for some suitable test systems discussed in this and other papers of this series. One of the worthwhile test systems has seemed to us to be the α-phenylneopentyl one, and in this article we report the resolution of α-phenylneopentyl alcohol XX and the results of the study of replacement reactions with the alcohol and some of its derivatives.

Our attention was first drawn to the α-phenylneopentyl system by the report of Skell and Hauser[15] that substitution reactions of α-phenylneopentyl bromide yielded largely unrearranged, together with some rearranged products.[16] If direct formation of a bridged structure in ionization of RX would be generally preferred were it not for solvent participation, the α-phenylneopentyl case, with its high hindrance to back-side solvent approach, should favor participation by neighboring methyl to give the species XXVI. Also, while this system is unsymmetrically substituted and thus seemingly permits scrutiny of both rearranged and unrearranged products, the substituents, a phenyl group on $C_\alpha$ and two methyl groups on $C_\beta$, have roughly equivalent ability to conjugate with cationic or olefinic centers. This factor would favor maintenance of the bridged structure XXVI.

The *dl*-α-phenylneopentyl alcohol (XX), m.p. 45°, was prepared in the conventional manner. It formed a liquid acetate, $n^{25}\text{D}$ 1.4859, and gave an acid phthalate in good yield, this being a useful way to separate the alcohol from tertiary rearrangement isomers, *e.g.*, 2-methyl-3-phenyl-2-butanol (XXI).

Resolution of XX was carried out in the usual manner through the acid phthalate using cinchonidine as the alkaloid. The resolution was carried to a high state of completion, the properties of the (+) and (−) isomers agreeing well in the case of the acid phthalates, m.p. 111–112° and 110–111°, and the resulting alcohols, m.p. 56.1–56.5° and 55.3–56.6°. The (+)-acetate from the (+)-alcohol was a solid, m.p. 46.5–48.5°.

The α-phenylneopentyl *p*-toluenesulfonate (XXIII, X = OTs) was *a priori* the best derivative for study in solvolysis because of the expected absence of rearrangement and configurational change attending its preparation from the alcohol. However, it was costly to work with because of instability and low yields in its preparation. The hindered character of the alcohol necessitated a long reaction period in the preparation of the *p*-toluenesulfonate, the yield being 16–17% from *dl* or (−)-alcohol. The *p*-toluenesulfonate gave all indications of structural homogeneity and solvolyzed in acetic acid (0.36 *M* in water) at 24.3° with a steady first order rate constant equal to (2.44 ± 0.10) × $10^{-5}$ sec.$^{-1}$ (Table II).

The bromide (XXIII, X = Br) was prepared from (−)-alcohol by the use of hydrogen bromide in petroleum ether, levorotatory product being obtained.

TABLE I

SOLVOLYSIS OF 0.06266 *M* α-PHENYLNEOPENTYL CHLORIDE IN 80% ETHANOL AT 50.00°

| Time, hr. | Vol. of 0.1145 *M* base | $\log \dfrac{V_\infty - V_0}{V_\infty - V}$ | $10^3 k$ hr.$^{-1}$ |
|---|---|---|---|
| 0 | 0.051 | ..... | .. |
| 18.4 | .171 | 0.00975 | 1.22 |
| 24.3 | .214 | .01330 | 1.26 |
| 48.9 | .362 | .02576 | 1.21 |
| 71.8 | .505 | .03814 | 1.22 |
| 147.2 | .935 | .07762 | 1.21 |
| 191.8 | 1.175 | .1013 | 1.22 |
| 258.9 | 1.502 | .1359 | 1.21 |
| 334.1 | 1.845 | .1753 | 1.21 |
| 427.8 | 2.250 | .2270 | 1.22 |
| 501.9 | 2.515 | .2645 | 1.21 |
| 573.7 | 2.776 | .3049 | 1.22 |
| 651.0 | 3.021 | .3466 | 1.23 |
| 744.2 | 3.278 | .3951 | 1.22 |
| 815.5 | 3.473 | .4359 | 1.23 |
| 912.7 | 3.681 | .4841 | 1.22 |
| | | Mean | 1.22 ± 0.01 |

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[13] Just as in the case of functional neighboring groups [ref. 1b and Winstein and Grunwald, THIS JOURNAL, **70**, 828 (1948)], it must be kept in mind that the stereochemical results corresponding to formation and opening of IV may, in some cases, be simulated by a dynamic pair of isomeric cations I and II. These one-sided structures could still involve quite serious delocalization of the $C_\beta$-R bonding pair. Also, even without this, but with restricted rotation about the $C_\alpha$–$C_\beta$ bond and a tendency in specific cases for the entering substituent to bond finally to $C_\alpha$ or $C_\beta$ on the side away from R, the same stereochemical results are possible.

[14] *E.g.*, Winstein, *et al.*, *ibid.*, **74**, 1113 (1952).

[15] P. Skell and C. R. Hauser, *ibid.*, **64**, 2633 (1942).

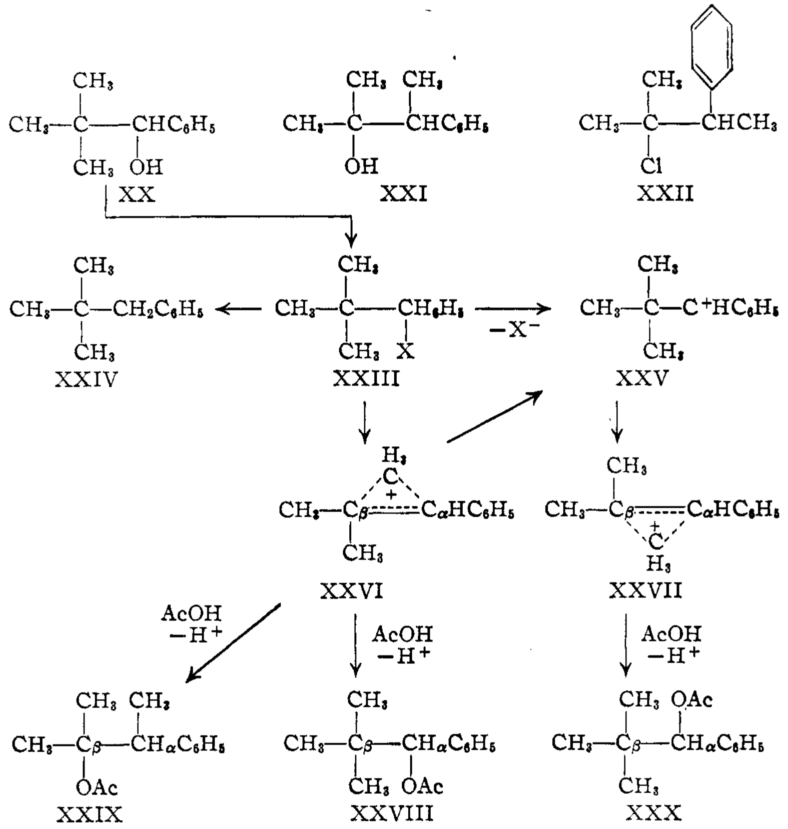
[16] We are indebted to Mr. Lionel Goldring for preliminary work on the resolution of α-phenylneopentyl alcohol in the summer of 1943. This work was then continued by B. K. Morse, but after being interrupted by circumstances connected with the war, it was not completed until 1948. While the work was in progress, Walsh[8] wrote the π-complex structure for Skell and Hauser's α-phenylneopentyl cation.

TABLE II

SUMMARY OF SOLVOLYSIS RATES

| Compound | Concn., $M$ | Temp., °C. | $k$, sec.$^{-1}$ | Solvent |
|---|---|---|---|---|
| $(CH_3)_3CCHClC_6H_5(SOCl_2)$ | 0.063 | 50.00 | $(3.36 \pm 0.03) \times 10^{-7a}$ | 80% EtOH |
| $(CH_3)_3CCHClC_6H_5(SOCl_2)$ | .03-0.05 | 74.83 | $(7.77 \pm 0.29) \times 10^{-6}$ | 80% EtOH |
| $(CH_3)_2CClCH(CH_3)C_6H_5$ (62.3%) | .016 | 50.00 | $(3.35 \pm 0.05) \times 10^{-5}$ | 80% EtOH |
| $(CH_3)_3CCHClC_6H_5$ ($PCl_3$ + Py) | .06 | 50.00 | $(3.27 \pm 0.13) \times 10^{-7}$ | 80% EtOH |
| $(CH_3)_3CCH(OTs)C_6H_5$ |  | 24.3 | $(2.44 \pm 0.10) \times 10^{-5}$ | AcOH, 0.36 $M$ $H_2O$ |
| $CH_3CHClC_6H_5$ |  | 50.0[17] | $1.64 \times 10^{-4b}$ | 80% EtOH |

[a] $\Delta H^{\pm} = 27.5$ kcal./mole; $\Delta S^{\pm} = -3.1$ e.u. [b] $\Delta H^{\pm} = 20.8$ kcal./mole; $\Delta S^{\pm} = -11.7$ e.u.



The derivative most convenient to work with was the α-phenylneopentyl chloride (XXIII, X = Cl). This could be prepared from the alcohol without structural rearrangement either with thionyl chloride or phosphorus trichloride. The α-phenylneopentyl chloride prepared from *dl*-alcohol with thionyl chloride could be shown to be homogeneous by scrutiny of the kinetics of its solvolysis. Data for a solvolysis run in 80% ethanol are given in Table I and it is seen that the rate constant, followed past 68% reaction, is very steady. The chloride XXII which would be formed from α-phenylneopentyl alcohol (XX) by Wagner–Meerwein rearrangement was prepared from the corresponding carbinol (XXI), and this proved more reactive in solvolysis than the α-phenylneopentyl chloride. In 0.016 $M$ solution, the first order solvolysis rate constant of XXII is $3.35 \times 10^{-5}$ sec.$^{-1}$ in 80% ethanol, some 100 times the value for α-phenylneopentyl chloride (Table II). Thus the presence of rearranged isomer XXII as a contaminant in α-phenylneopentyl chloride is easily detected. Scrutiny of the early part of the solvolysis of the chloride prepared from α-phenylneopentyl chloride (XX) and thionyl chloride showed the content of the more reactive isomer XXII must be below several parts per thousand.

The structure of α-phenylneopentyl chloride was verified by hydrogenolysis over palladized calcium carbonate to a hydrocarbon whose diacetylamino derivative[18] agreed in melting point with that of neopentylbenzene XXIV and not that of 2-methyl-3-phenylbutane.

The chloride from (+)-α-phenylneopentyl alcohol and thionyl chloride was dextrorotatory, the rotation being larger than that of the parent alcohol. By analogy with the results with other α-phenylalkanols and thionyl chloride, one would guess that retention of configuration very largely prevailed in the alcohol–thionyl chloride reaction due to the S$_{N}$i mechanism.[19] This configurational assignment was confirmed by making conditions more conducive to inversion and eventually obtaining predominant inversion.

The use of thionyl chloride and pyridine[20] which usually modifies the stereochemical result in the direction of inversion of configuration still gave chloride with configuration largely maintained. Going to phosphorus trichloride and pyridine[20] did give rise to a chloride with an inverted sign of rotation. This chloride was nearly as pure structurally as the other preparations, following good first order kinetics (Table II for rate constant) in its solvolysis in 80% ethanol from 10–76% reaction. The behavior in the early period indicated some 3 to 4% of the more reactive rearranged isomer. The hindered α-phenylneopentyl system does not favor the inversion mechanism, and the assumption is made that the stereochemical result with thionyl chloride alone is 100% retention. On this basis, the stereochemical results are 43% predominating retention with thionyl chloride and pyridine and 56% predominating inversion with phosphorus trichloride and pyridine.

On the basis of the observed rotations, configurations in the α-phenylneopentyl system are the

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[17] Ward, *J. Chem. Soc.*, **445**, 2285 (1927).

[18] Ipatieff and Schmerling, THIS JOURNAL, **59**, 1056 (1937); **60**, 1476 (1938).

[19] Cowdrey, Hughes, Ingold, Masterman and Scott, *J. Chem. Soc.*, 1252 (1937).

[20] Kenyon, Phillips and Taylor, *ibid.*, 382 (1931).

same when the sign of rotation is the same for the acid phthalate, alcohol, acetate, *p*-toluenesulfonate and chloride.

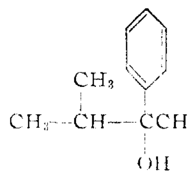
The solvolysis of *a*-phenylneopentyl bromide with aqueous silver nitrate had been investigated by Skell and Hauser,[15] who reported a maximum of 30% of rearrangement. Judging by melting point the alcohol from which the bromide was prepared was fairly impure. The bromide, $\alpha = -8.69°$ (1 dcm., homog.) from partially resolved (−)-alcohol, when treated with aqueous silver nitrate, gave a carbinol which contained only very little rearranged material since the melting point was only *ca.* 4° low. The optical rotation of the final alcohol was very low and, allowing for the fact that the alcohol used in preparing the bromide was 72% optically pure, the over-all steric result from alcohol to bromide to alcohol is of the order of 5% predominating inversion.

Acetolysis of the (−)-*p*-toluenesulfonate (XXIII, X = OTs) at room temperature in acetic acid containing lithium acetate, and the (−)-chloride (XXIII, X = Cl) with silver acetate in acetic acid at 75° gave acetates in 42 and 87% yields, respectively, with nearly identical refractive indices, slightly higher than that of pure *dl*-α-phenylneopentyl acetate. In the case of the acetate from the *p*-toluenesulfonate the rotation corresponded to 10% predominating inversion in the acetolysis.

The acetate product obtained in 87% yield from 79% optically pure (−)-chloride had a rotation which corresponded to 1.2% excess (+)-acetate. Partial saponification, preparation of the acid phthalate and resaponification gave nearly pure α-phenylneopentyl alcohol, whose rotation corresponded to 2.6% dextro. Further saponification gave an alcohol, m.p. 40–44°, nearly entirely α-phenylneopentyl alcohol, whose rotation corresponded to 1.3% dextro. Conversion of this carbinol to acid phthalate to remove any tertiary alcohol gave an acid phthalate, which on resaponification gave nearly pure α-phenylneopentyl alcohol, m.p. 44–45°, with a rotation which corresponded to 0.7% dextro.

Allowing for the fact that the original chloride was 79% resolved, the rotations at various stages in working up the α-phenylneopentyl product of treatment of the chloride with silver acetate in acetic acid point to *ca.* 1.5% predominating inversion.

The amount of rearranged product was small and the final isolated fraction which contained any tertiary alcohol constituted a *ca.* 2% yield, in contrast to the 46% yield, after all the manipulations, of α-phenylneopentyl alcohol. This puts a maximum figure of 4% of solvolysis proceeding with rearrangement. Even this is high, since the refractive index of the tertiary alcohol fraction was below that of XXI or the isomer XXXI, in just the direction of the change in refractive index when α-phenylneopentyl alcohol is dissolved in tertiary alcohol. The tertiary alcohol fraction showed no optical activity whatsoever.



XXXI

Thus there is no indication of a tendency for the results of solvolysis of α-phenylneopentyl derivatives to correspond to those expected from formation and opening of the bridged cation structure XXVI. The acetolysis product with the unrearranged structure XXVIII would, on this basis, have the retained configuration. Even if the bridged structure XXVI partly isomerized to another bridged structure XXVII (by way of XXV) before formation of acetolysis product XXX and XXVIII any survival of activity would be in the direction of retention. Instead, inversion predominates slightly. On the basis of the bridged structure XXVI the rearranged acetolysis product XXIX would be expected to be active, $C_\alpha$ being asymmetric. While we did not characterize the trace of rearranged material in the small fraction which would have contained it, any indication to be gained from the total absence of activity in the fraction is opposed to the bridged structure.

Therefore, in the present test system, the results of solvolysis in the range of solvents employed ($H_2O$ or AcOH) can be discussed on the basis of the classical description of the cation XXV. The small amount of predominant inversion (1.5–10%) from intervention of solvent slightly more often from the rear than from the front can be accounted for in the usual way.[11] This highly hindered α-phenyl case provides some further calibration when one notices that 10% inversion attending acetolysis of the *p*-toluenesulfonate is not too far below the *ca.* 16% inversion attending acetolysis of α-phenylethyl chloride.[21]

The rate of solvolysis of the α-phenylneopentyl chloride (and similarly that of the *p*-toluenesulfonate) (Table II) is of some interest since it is quite low. Reference to the solvolysis rate of α-phenylethyl chloride[17] in 80% ethanol at 50° listed in Table II gives the comparison

$$CH_3CHClC_6H_5,\ 490 > (CH_3)_3CCHClC_6H_5,\ 1$$

Triple β-methyl substitution in α-phenylethyl chloride is attended by a substantial decrease in solvolysis rate. This decrease is associated with an increase in $\Delta H^{\pm}$ of activation, from 20.8 to 27.5 kcal./mole, and a partly compensating increase in $\Delta S^{\pm}$ of activation, from −11.7 to −3.1 e.u. The slowness of α-phenylneopentyl is attributable to predominantly retarding steric effects. One of these is steric hindrance to solvation[11] and the change in $\Delta S^{\pm}$ is in line with reduced solvation of the transition state in the case of α-phenylneopentyl chloride solvolysis. The other steric effect is due to the steric strain associated with the planar arrangement of the $C_\beta$-$C_\alpha$H-$C_1C_2C_6$ skeleton in the cation XXXII, which is most favorable for resonance stabilization involving the phenyl group. The best compromise configuration will still correspond to a reduced stability. There are related cases where spectroscopic evidence exists for closely related steric effects,[22] and analogous effects on

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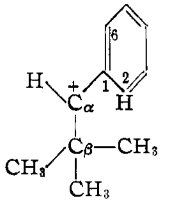
(21) Steigman and Hammett, This Journal, **59**, 2536 (1937).

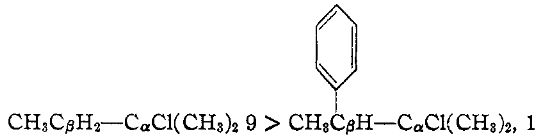
(22) *E.g.*, Tsatsas, *Bull. soc. chim.*, [5] **14**, 1011 (1947).



XXXII

solvolysis rates have recently been reported by Baddeley and Chadwick.[23]

It is of some interest to compare the solvolysis rate of the 2-methyl-3-phenyl-2-butyl chloride (XXII) with that of *t*-amyl chloride, for in XXII a β-phenyl group is present, $C_\alpha$ being tertiary in this case. Extrapolating the rate constant for *t*-amyl chloride[24] to 50° gives the comparison



$$CH_3C_\beta H_2—C_\alpha Cl(CH_3)_2\ 9 > CH_3C_\beta H(C_6H_5)—C_\alpha Cl(CH_3)_2,\ 1$$

As is to be expected,[14] the net retarding effect of the phenyl group is greater in the present case than for $C_\alpha$ secondary.

## Experimental

**2-Methyl-3-phenyl-2-butanol.**—Methyl α-phenylethyl ketone,[25] b.p. 69.5–72.5° (2.5–2.9 mm.), reported[26] b.p. 103–106° (22 mm.), semicarbazone m.p. 171–174° (reported[27] m.p. 170°), was prepared by methylation of phenylacetone.

The methyl α-phenylethyl ketone (36.9 g.) dissolved in an equal volume of ether, was added to a cooled 2.4 *M* solution of methylmagnesium bromide (24% excess). The reaction mixture was worked up in the usual way with saturated ammonium chloride solution and distillation from a few mg. of potassium carbonate gave rise to carbinol in 37% yield, b.p. 85.0–87.3° (4.8 mm.), $n^{25}D$ 1.5158, $d^{25}_4$ 0.9774; *MR*D 50.74, calcd. 50.92 (reported[28] b.p. 105–107° (12 mm.) $n^{20}D$ 1.51932, $d^{20}_4$ 0.9794).

**2-Phenyl-3-methyl-2-butanol.**—Isobutyrophenone, b.p. 83–84° (6 mm.), $n^{25}D$ 1.5170, was added to 30% excess 2.4 *M* methylmagnesium bromide solution. The complex was treated with saturated ammonium chloride solution, and the ethereal solution was dried over potassium carbonate. Distillation gave the desired carbinol, b.p. 77.0–77.5° (2.6–2.9 mm.), $n^{25}D$ 1.5137, $d^{25}_4$ 0.9694; *MR*D 50.98, calcd. 50.92.

*Anal.* Calcd. for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.65; H, 9.94.

**α-Phenylneopentyl Alcohol.**—This material was prepared from benzaldehyde and *t*-butylmagnesium chloride by the method of Conant and Blatt.[29] The product, b.p. 95–100° (10 mm.), obtained in an average yield of 45%, gave crystalline material, m.p. 42.3–42.8° after two recrystallizations from diethyl ether (77% recovery). Carbinol, b.p. 90–91.5° (5 mm.), m.p. 36–40° after one recrystallization from ether, was obtained in an over-all yield of 55% when the Grignard reaction was carried out with unfiltered *t*-butylmagnesium chloride solution and purified benzaldehyde.

The α-phenylneopentyl alcohol was contaminated with benzyl alcohol, the most pure product being obtained by saponification of the purified acid phthalate, m.p. 141–142°. This gave rise to carbinol, m.p. 44–45° (reported[28] m.p. 45°).

**α-Phenylneopentyl Acid Phthalate.**—The following procedure was used in the preparation of α-phenylneopentyl acid phthalate from 1 to 300-g. samples of the alcohol. α-Phenylneopentyl alcohol, Baker C.P. phthalic anhydride, and anhydrous pyridine were used in the molar ratios of 1:1.05:2, and the mixture was heated with an oil-bath for six hours at 95°. About 300 cc. of C.P. chloroform was added to the reaction mixture, and the solution was poured over ice and 10% excess concentrated C.P. hydrochloric acid. The chloroform solution was washed with water and dried over sodium sulfate, the chloroform was removed on the steam-cone, and the residual oil was mixed with twice its volume of petroleum ether (b.p. 20–40° or 30–60°) to give the crystalline product.

Pure α-phenylneopentyl alcohol, m.p. 44–45°, gave a 78% yield of acid phthalate, m.p. 123–124° (uncor.) from Skellysolve B, m.p. 142–143° from acetic acid (two crystalline modifications, mixed m.p. 143°). An α-phenylneopentyl acid phthalate sample, m.p. 140–141°, was recrystallized from ethyl acetate and Skellysolve C to yield a sample 123–124°. After recrystallization of this latter sample from acetic acid the m.p. was 143°.

On one occasion recrystallization from acetic acid and water produced an acid phthalate, m.p. 76–77°, with an equivalent weight 187.5 (calcd. for $C_{19}H_{20}O_4$: 312.4; calcd. for $C_{19}H_{20}O_4 \cdot C_2H_4O_2$: 186.2). Three recrystallizations did not change the melting point. After seven weeks over sodium hydroxide the sample had lost the acetic acid and the m.p. was now 142–143°.

*Anal.* Calcd. for $C_{19}H_{20}O_4$: C, 73.06; H, 6.45; neut. equiv., 312.4. Found: C, 72.86; H, 6.59; neut. equiv., 311.7.

**Resolution of α-Phenylneopentyl Alcohol.**—Merck and Co., Inc., cinchonidine alkaloid (47.1 g.) was dissolved in 3500 cc. of acetone after five hours under reflux. Fifty grams of α-phenylneopentyl acid phthalate (amount equivalent to the alkaloid) was added and the hot solution was filtered and stored at 4° for 3 or 4 days. The levo-cinchonidine α-phenylneopentyl phthalate (43%) m.p. 184–185° (dec.) (uncor.) (m.p. after one recrystallization from acetone, 188.3–188.6°) (dec.), $[\alpha]D$ −96 ± 1° (*c* 1.163, $CHCl_3$), which crystallized first, was removed by filtration and washed with acetone. Acetone was removed from the filtrate at room temperature under reduced pressure, to one-tenth of the volume. The cinchonidine α-phenylneopentyl phthalate which crystallized (about 7%) was removed by filtration and used in subsequent resolutions.

The levo-cinchonidine α-phenylneopentyl phthalate was converted to the acid phthalate by shaking it in chloroform solution (100 cc. C.P. chloroform) with twice the equivalent amount of 1 *N* hydrochloric acid. The chloroform solution was washed with an equivalent amount of 1 *N* hydrochloric acid, filtered and dried over anhydrous sodium sulfate. The chloroform was removed on a steam-bath and 35–40 cc. of Skellysolve B was added with constant stirring. Overnight at 4° the dextro-α-phenylneopentyl acid phthalate, m.p. 109–110° (cor.), $[\alpha]D$ +30.5 ± 0.5 (*c* 4.153, $CHCl_3$), m.p. after one recrystallization from aqueous acetic acid, 111–112°, crystallized in 84–92% yield.

Chloroform was added to the acetone solution containing the dextro-cinchonidine α-phenylneopentyl phthalate, and the acetone was distilled off. The chloroform solution was treated with 1 *N* hydrochloric acid as before, then filtered and dried. The solvent was removed, and the levo-acid phthalate crystallized with Skellysolve B in 42% yield. The levo-α-phenylneopentyl acid phthalate, m.p. 110–111°, $[\alpha]D$ −29.8° (*c* 4.800, $CHCl_3$), was recrystallized from ethyl acetate and Skellysolve B in 68% yield.

The (+) and (−) α-phenylneopentyl acid phthalates were dissolved in 20% sodium hydroxide (2.5 equivalents sodium hydroxide). The carbinols were obtained in 93% yield by steam distillation, extraction with ether and distillation. Dextro: m.p. 56.1–56.5° $[\alpha]^{25}D$ 30.6 ± 0.3 (*c* 3.593, acetone); levo: m.p. 55.3–56.6°, $[\alpha]D$ −30.3 ± 0.4 (*c* 3.640, acetone).

The over-all yields of dextro- and levo-α-phenylneopentyl alcohols from the *dl*-acid phthalate were 35 and 27%, respectively.

The levo-α-phenylneopentyl alcohol obtained from levo-acid phthalate which had not been recrystallized gave carbinol which was contaminated with benzyl alcohol as well as the dextro compound, m.p. 42.5–48.5°, $[\alpha]D$ −23.3 ± 0.4 (*c* 3.501, acetone).

**Separation of Carbinol Mixtures *via* the Acid Phthalates.**—Mixtures of α-phenylneopentyl alcohol and 2-methyl-3

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[23] Baddeley and Chadwick, *J. Chem. Soc.*, 368 (1951).

[24] (a) Brown and Fletcher, THIS JOURNAL, **71**, 1845 (1949); (b) Hughes, Ingold, Martin and Meigh, *Nature*, **166**, 679 (1950).

[25] Suter and Weston, THIS JOURNAL, **64**, 533 (1942).

[26] Norris and Olmsted, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1947, p. 144.

[27] Tsatsas, *Ann. chim.*, **1**, 342 (1946).

[28] Lepin, *Chem. Zentr.*, **83**, IV, 2080 (1912).

[29] Conant and Blatt, THIS JOURNAL, **50**, 551 (1928).

phenyl-2-butanol, were treated with phthalic anhydride, as in the described preparation of α-phenylneopentyl acid phthalate. The pyridine solution of α-phenylneopentyl acid phthalate, excess phthalic anhydride, and tertiary carbinol was poured over ice and allowed to stand for 15 to 30 minutes. The product was worked up in the usual fashion. The α-phenylneopentyl acid phthalate was separated from the tertiary carbinol in the last step, where the acid phthalate was crystallized from Skellysolve B or petroleum ether. The tertiary carbinol (as well as the unreacted secondary alcohol) was soluble in the large volume of solvent used and was obtained by evaporation of the solvent.

RESULTS OF THREE EXPERIMENTS

| α-Phenylneopentyl alc. in mixture, % | Yield acid phthalate, % | Yield tert. alcohol, % | M.p. acid phthalate, °C. |
|---|---|---|---|
| 100 | 78 | ... | 124–125 |
| 55 | 42 | 44 | 100–106 |
| 76 | 67 | 27 | 115–120 |

Pure α-phenylneopentyl alcohol gave acid phthalate in 78% yield, and the mixtures gave acid phthalate from the secondary alcohol component in approximately the same yield. The tertiary carbinol was nearly quantitatively accounted for.

**α-Phenylneopentyl Acetate.**—A mixture of 5.0 g. of α-phenylneopentyl alcohol, m.p. 42°, 6.23 g. of acetic anhydride and 2.76 g. of anhydrous sodium acetate was heated on an oil-bath for 5.5 hours at 90–110°. Ether was added to the mixture and the ethereal solution was poured over ice. The ether extract was washed with water and 5% sodium bicarbonate, dried over potassium carbonate, and distilled to give a 59% yield of α-phenylneopentyl acetate, b.p. 80–80.2° (2 mm.), $n^{25}_D$ 1.4859, besides a forerun (presumably partly benzyl acetate).

Ten grams of (+)-α-phenylneopentyl alcohol, m.p. 56°, $[\alpha]_D$ +30.6, was converted to the acetate by the same method. The product crystallized in 89% yield upon removal of the ether. Recrystallization from aqueous acetone gave material, m.p. 46.5–48.5°, $[\alpha]_D$ 53.6° (acetone, *c* 6.01).

*Anal.* Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79. Found: C, 75.62; H, 8.68.

The dextro-α-phenylneopentyl acetate, was hydrolyzed with 20% aqueous alcoholic sodium hydroxide to α-phenylneopentyl alcohol in 77% yield, m.p. 59°, $[\alpha]_D$ +29.9° (acetone, *c* 4.043).

**α-Phenylneopentyl *p*-Toluenesulfonate.**—This preparation was carried out by the general procedure used previously.[30] The *dl-p*-toluenesulfonate was prepared from 2- to 26-g. samples of α-phenylneopentyl alcohol, m.p. 42°. The pyridine solution was cooled initially in an ice–hydrochloric acid-bath, and the reaction period was one week at 4°. The *p*-toluenesulfonate, m.p. 75–76° from Skellysolve B, was obtained in an average yield of 16%; the equivalent weight in acetolysis was 323.2 (calcd. 318.4).

*Anal.* Calcd. for $C_{18}H_{22}SO_3$: C, 67.89; H, 6.96. Found: C, 67.93; H, 7.03.

The (−)-*p*-toluenesulfonate was prepared from 26 g. of (−)-alcohol, m.p. 55.3–56.6°, $[\alpha]^{25}_D$ −30.3°. The product, m.p. 72.5–72.8° from petroleum ether (b.p. 20–40°), α −3.13° (1 dcm., acetone, *c* 5.0), $[\alpha]_D$ −63°, was obtained in 17% yield.

*Anal.* Calcd. for $C_{18}H_{22}SO_3$: C, 67.89; H, 6.96. Found: C, 67.80; H, 7.04.

The dextro-α-phenylneopentyl *p*-toluenesulfonate prepared as above from the dextro-carbinol, m.p. 56.1–56.5°, decomposed about one-half hour after isolation from C.P. petroleum ether.

***levo*-α-Phenylneopentyl Bromide.**—*levo*-α-Phenylneopentyl alcohol, m.p. 48–49°, $[\alpha]^{25}_D$ −27.9 ± 0.3° ($CHCl_3$, *c* 4.777) was converted to the bromide by treatment with hydrogen bromide in petroleum ether over a five-hour period, 1 hour at 5–10° and 4 hours at room temperature. Working up the product in the usual way and distillation gave bromide in 60% yield, b.p. 88.5–89.5° (3–4 mm.), $\alpha_D$ −8.69° ± 0.01° (1 dcm., homog.), $[\alpha]^{25}_D$ −7.04, $n^{25}_D$ 1.5370, $d^{25}_4$ 1.2338, $MR_D$ 57.50 (calcd., 57.16), (reported[28] b.p. 109° (10 mm.), $d^{20}_4$ 1.2373, $n^{20}_D$ 1.53977).

*Anal.* Calcd. for $C_{11}H_{15}Br$: C, 58.16; H, 6.61. Found: C, 58.14; H, 6.68.

**α-Phenylneopentyl Chloride.**—The alcohol was added in small portions to excess purified thionyl chloride (2.5 moles per mole of alcohol) which was cooled in an ice–salt-bath and the solution was allowed to stand overnight at room temperature. Then excess thionyl chloride was removed under reduced pressure and the residue was dissolved in pure ether. The ethereal solution was washed with ice-water and cold 5% sodium bicarbonate solution; then it was dried over potassium carbonate and distilled. α-Phenylneopentyl chloride, b.p. 89.5–90.5° (6.7 mm.), $n^{25}_D$ 1.5142, $d^{25}_4$ 1.0104, $MR_D$ 54.42 (calcd. 54.26) was obtained in 88% yield from 5- to 25-g. quantities of *dl*-α-phenylneopentyl alcohol, m.p. 45°.

*Anal.* Calcd. for $C_{11}H_{15}Cl$: C, 72.31; H, 8.28. Found: C, 72.66; H, 8.49.

Samples of *dl*-α-phenylneopentyl chloride (0.3 g.) were subjected to hydrogenolysis in the presence of 1 g. of 2% palladized calcium carbonate in 0.4 *N* alcoholic potassium hydroxide according to the method of Busch and Stöve.[31] The filtered solution was concentrated by removal of alcohol and the reduction product was extracted with pure ether. The aqueous solution was concentrated, acidified and titrated by the Volhard method. Values of 19.35% and 19.52% chlorine were obtained (calcd. for $C_{11}H_{15}Cl$, 19.41%).

The reduction product obtained from the ether extract was nitrated using equal volumes of sulfuric and nitric acids by the procedure of Ipatieff and Schmerling.[18] A diacetylamino derivative m.p. 242–245° (uncor.) was obtained (reported[18] for the diacetylamino derivative of neopentylbenzene, m.p. 240–241°, for the diacetylamino derivative of 2-methyl-3-phenylbutane, m.p. 193°).

From fifteen grams of (+)-α-phenylneopentyl alcohol, m.p. 56°, $[\alpha]_D$ 31.6° (acetone, *c* 2.851) and thionyl chloride by the above procedure, there was obtained dextro chloride, b.p. 82–83° (4.5 mm.), $n^{25}_D$ 1.5142, $[\alpha]_D$ +40.68°, α +41.09° (1 dcm., homog.), in 87% yield.

Similarly, from 60 g. of levo-alcohol, m.p. 43–49°, $[\alpha]_D$ −22.3° (acetone, *c* 3.501), which was contaminated with benzyl alcohol, there was obtained levo-chloride, b.p. 88–89° (7.0 mm.), $n^{25}_D$ 1.5141, $[\alpha]_D$ −32.1°, α −32.39° (1 dcm., homog.), in 84% yield.

Ten grams of *dl*-α-phenylneopentyl alcohol, m.p. 44–45°, was dissolved in 9.65 g. anhydrous pyridine. To the solution, which was cooled in an ice–salt-bath, 14.5 g. of thionyl chloride was added slowly. The mixture was left at 0° for 15 minutes, then heated to 60° for half an hour and left overnight at room temperature. The mixture was poured over ice, and the product was taken up with Skellysolve B. The Skellysolve solution was washed with 1 *N* hydrochloric acid, 5% sodium bicarbonate solution, ice-water, then filtered and dried over potassium carbonate. Distillation gave α-phenylneopentyl chloride, b.p. 87.2–87.8° (6.3 mm.), $n^{25}_D$ 1.5141, in 43% yield. The same procedure with 10 g. of dextro-α-phenylneopentyl alcohol, m.p. 56°, $[\alpha]_D$ +31.6° (acetone, *c* 2.851), gave chloride, b.p. 82.2° (4.7 mm.), $n^{25}_D$ 1.5142, $[\alpha]_D$ +17.27° in 33% yield.

Ten grams of dextro-α-phenylneopentyl alcohol, m.p. 56°, $[\alpha]_D$ +31.6° (acetone, *c* 2.851), was dissolved in 5 g. of anhydrous pyridine. The pyridine solution was added to 16.8 g. of reagent grade phosphorus trichloride which was cooled in an ice–salt-bath. The mixture was warmed to 50° for half an hour, and then was allowed to remain overnight at room temperature. The mixture was poured over ice and the product was taken up in ether. The ether solution was washed with water and 10% sodium bicarbonate solution, then dried over potassium carbonate. Distillation gave rise to chloride, b.p. 80–81° (4.3 mm.), $n^{25}_D$ 1.5139, $[\alpha]_D$ −22.45°, in 22% yield.

**2-Methyl-3-phenyl-2-butyl Chloride.**—Seven grams of 2-methyl-3-phenyl-2-butanol, $n^{25}_D$ 1.5158, was treated with thionyl chloride by the procedure used with α-phenylneopentyl alcohol. The product was distilled to give material, b.p. 72–90° (7.4 mm.), $n^{25}_D$ 1.5159, $d^{25}_4$ 1.005, $MR_D$ 54.87 (calcd. for $C_{11}H_{15}Cl$, 54.26), Cl, 12.21 (calcd. for $C_{11}H_{15}Cl$, 19.41), in 67% yield. For the analysis, a weighed sample of the chloride was heated on the steam-bath for one-half hour with an aliquot of standard silver nitrate. After filtration, the excess silver nitrate was determined with standard so-

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(30) Winstein, Grunwald and Ingraham, THIS JOURNAL, **70**, 821 (1948).

(31) Busch and Stöve, *Ber.*, **49**, 1063 (1916).

dium thiocyanate solution. The product was only 62.3% alkyl chloride, and this was allowed for in the determination of the solvolysis rate (Table II). Olefinic material appeared to be the contaminant, the product decolorizing bromine solution in carbon tetrachloride.

**Solvolysis of (−)-α-Phenylneopentyl-*p*-toluenesulfonate.**—*levo*-α-Phenylneopentyl *p*-toluenesulfonate (7.74 g.), m.p. 72.5–72.8°, was added to 165 cc. 1 *M* lithium acetate in glacial acetic acid. The solution remained six days at room temperature. The solution was cooled in an ice-bath, and to it a 10% excess of 20% potassium carbonate was added gradually along with C.P. diethyl ether. When neutralization was complete the aqueous layer was extracted with ether. The combined ether solutions were washed with 10% potassium carbonate and dried over potassium carbonate. The product was distilled through a pear-shaped Claisen flask to give 2.11 g., 42%, of acetate, b.p. 105.8–106.2° (7 mm.), $n^{25}$D 1.4884, [α]$^{25}$D +5.31 (acetone, *c* 6.58) (α +0.35°, 1 dcm.).

**Treatment of (−)-α-Phenylneopentyl Bromide with Aqueous Silver Nitrate.**—Two grams of levo-bromide, b.p. 88.5–89.5° (3–4 mm.), [α]D −7.04 (homog.), was shaken with 1 *M* aqueous silver nitrate for 16 hours. The mixture was filtered, and the silver bromide was washed with ether. The filtrate was extracted with ether, and the ether solution was washed with water and then dried over potassium carbonate. The product was distilled through a modified Claisen flask to give material, m.p. 39.2–40.5°, α +0.06 ± 0.03° (1 dcm.), [α]D 1.5 ± 0.8 (*c* 4.069 $CHCl_3$).

**Treatment of (−)-α-Phenylneopentyl Chloride with Silver Acetate in Acetic Acid.**—Silver acetate, prepared from 61 g. of silver nitrate and 33 g. of sodium acetate in aqueous solution, was filtered, washed with glacial acetic acid and suspended in 360 ml. of 99.7% acetic acid to which sufficient acetic anhydride was added to make the resulting solution 1% in acetic anhydride. A 48.51-g. quantity of levo-α-phenylneopentyl chloride, [α]D −32.1°, $n^{25}$D 1.5141, was added to the silver acetate suspension and the mixture was heated on an oil-bath with stirring for 13.5 hours at 75°. Silver chloride, removed by filtration of the acetic acid solution, was recovered in 98% yield. The filtrate was concentrated by removal of the solvent at reduced pressure. The residue was dissolved in ether, and the ether solution was washed with 5% sodium bicarbonate, then dried over potassium carbonate. On distillation acetate, b.p. 95–100° (5.5–6.4 mm.), $n^{25}$D 1.4886, α +0.94 ± 0.02° (homo., 1 dcm.), [α]D +0.65° ± 0.14° (acetone, *c* 7.73) was obtained in 87.2% yield.

The acetate mixture (46.97 g.) was partially hydrolyzed by a half-hour reflux period with 20% aqueous sodium hydroxide (2.5 equivalents), and steam distillation. The distillate was extracted with pure ether and the ether solution was dried over potassium carbonate. After removal of the solvent, distillation gave, in 86% yield, an acetate–carbinol mixture, b.p. 98–102° (7 mm.), $n^{25}$D 1.4934. This acetate–carbinol mixture was subjected to treatment with phthalic anhydride and pyridine. The acid phthalate obtained in 30.7% yield on the basis of the total acetate mixture gave on saponification (75% yield) α-phenylneopentyl alcohol, m.p. 45° (without recrystallization), [α]D +0.8 ± 0.2° (acetone, *c* 3.766). The unsaponified portion was recovered from the Skellysolve B solution in 76% yield on the basis of the total acetate–carbinol mixture upon evaporation of the solvent. Upon distillation (80.8% recovery) the mixture had the following properties: b.p. 99–103° (5.6 mm.), $n^{25}$D 1.4881, and α +1.02 ± 0.02° (homo., 1 dcm.).

This acetate mixture (18.93 g.) was hydrolyzed by refluxing for 45 minutes in 20% sodium hydroxide (2.5 equiv.) diluted with an equal volume of ethanol. After the ethanol was removed by distillation, the carbinol was steam distilled and the carbinol was removed from the distillate by extraction with ether. The ether solution was dried, and the carbinol distilled to give, in 86.4% yield, material, b.p. 71–73° (1.6–2.6 mm.), m.p. 40–44° (directly), α +0.05 ± 0.01°, [α]D +0.48 ± 0.13° (*c* 10.37, acetone) (1.3% dextro by comparison with similar solution of (+)-alcohol).

The carbinol mixture was separated with pyridine and phthalic anhydride. An acid phthalate, m.p. 118–123° (uncor.) was obtained in 80.4% yield. The tertiary carbinol fraction, $n^{25}$D 1.5172, probably contaminated with some secondary alcohol and phthalic anhydride, was obtained in 11.7% yield (1.49 g.) from the C.P. petroleum ether solution. The tertiary carbinol fraction, $n^{25}$D 1.5048, α 0.00 ± 0.007° (1 dcm.) (acetone, *c* 13.16) was recovered in 50% yield upon distillation. Hydrolysis of the acid phthalate gave, in 88% yield, α-phenylneopentyl alcohol, m.p., after distillation but without recrystallization, 44–45°, α +0.04 (1 dcm.), [α]$^{21}$D +0.29 ± 0.09° (13.89 g./100 cc. acetone soln.) (0.7% dextro by comparison with similar solution of (+)-alcohol).

**Control on Active Acetate.**—Pure dextro-α-phenylneopentyl acetate, m.p. 46.5–48.5°, [α]D +53.6°, was heated for 14 hours at 75° with a mixture of silver acetate (0.6 mole per liter of solvent) and silver chloride (0.4 mole per liter of solvent) in glacial acetic acid, 5% in acetic anhydride. The recovered acetate had m.p. 46.5–49.5° and [α]D +55.4° (*c* 5.418, acetone).

**Rate Measurements.**—The 80% ethanol was prepared and solvolysis rates were determined as previously described[11,14] using the sealed ampoule technique.

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RECEIVED JUNE 11, 1951