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

# Studies in Stereochemistry. XII. Molecular Rearrangements in the 3,4-Dimethyl-4-phenyl-3-hexanol System

BY DONALD J. CRAM AND JACK D. KNIGHT

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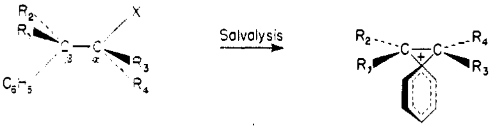
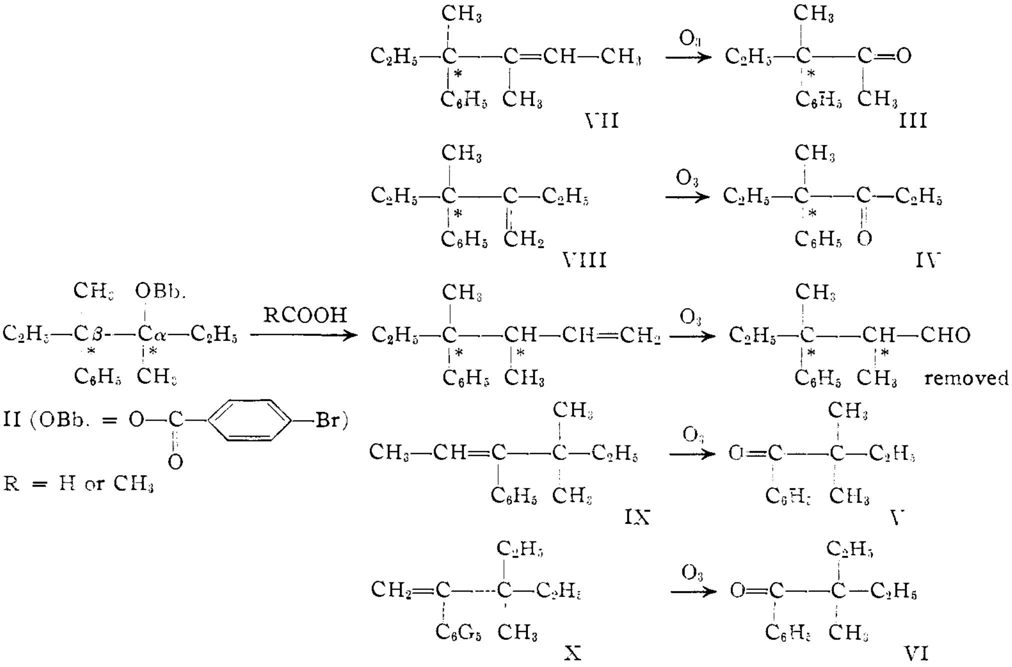
Two optically pure diastereomerically related isomers of 3,4-dimethyl-4-phenyl-3-hexyl-*p*-bromobenzoates were solvolyzed in dry acetic and formic acids. The results suggest the following conclusions. (1) In the quaternary–tertiary system represented by 3,4-dimethyl-4-phenyl-3-hexanol, intramolecular rearrangements take place involving mainly the phenyl and methyl groups as migrating species, with the ethyl group becoming involved to only a minor extent. (2) The phenyl group migrates at least twelve times as frequently as the methyl group in acetic acid. (3) The phenyl group migrates by two mechanisms, one stereospecific, the other non-stereospecific in character. (4) A simple elimination reaction accompanies the molecular rearrangements, and this reaction is also partially stereospecific and partially non-stereospecific in nature when conducted in acetic acid. (5) In formic acid, multi-stage reactions occur in which the products of the initial reaction undergo further reaction to produce conjugated olefin (products of methyl and ethyl migrations). The methyl group migrates roughly thirty-five times as frequently as the ethyl group. The mechanisms of these reactions are discussed.

The occurrence of phenonium ions (A) as discrete intermediates in the Wagner–Meerwein rearrangement has been demonstrated in the following systems (I): $R_1 = R_3 = CH_3$, $R_2 = R_4 = H$ and $R_1 = R_4 = CH_3$, $R_2 = R_3 = H$[1a,1b]; $R_1 = CH_3$, $R_3 = C_2H_5$, $R_2 = R_4 = H$ and $R_1 = CH_3$, $R_4 = C_2H_5$,



I (X = OTos. or OBros.)

$R_2 = R_3 = H$[1c,1d]; $R_1 = C_2H_5$, $R_3 = CH_3$, $R_2 = R_4 = H$ and $R_1 = C_2H_5$, $R_4 = CH_3$ and $R_2 = R_3 = H$.[1c,1d] The widely recognized electronic and steric differences in reactivity at secondary, tertiary and quaternary carbon atoms suggested that a study of the reactions of the 3,4-dimethyl-4-phenyl-3-hexanol system (II, $R_1 = R_3 = CH_3$, $R_2 = R_4 = C_2H_5$, *threo* isomer; $R_1 = R_4 = CH_3$, $R_2 = R_3 = C_2H_5$, *erythro* isomer) would reveal substantial differences in the course of the substitution, rearrangement and elimination reactions in this β-quaternary-α-tertiary system (II) as compared to the β-tertiary-α-secondary systems (I) studied previously. Paper XI of this series reports the synthesis and tentative assignment of relative configuration to the four stereoisomers of II,[2] whereas this paper reports the results of the solvolyses of the *threo*- and *erythro*-*p*-bromobenzoates of II in formic and acetic acids.



## Results

Preliminary experiments indicated that at 25° in pure glacial acetic acid the *p*-bromobenzoate of *threo*-II[2] was soluble, but that no detectable reaction occurred in 60 hours. Therefore the solvolyses experiments (runs 1 and 2) were conducted at 75° in this solvent, conditions under which only olefinic products were produced. Although in formic acid at 25° the esters of I appeared to react readily (runs 3 and 4), the rate of consumption of starting mate-

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[1] (a) D. J. Cram, THIS JOURNAL, **71**, 3863 (1949); (b) **74**, 2129 (1952); (c) **71**, 3875 (1949); (d) **74**, 2159 (1952).

[2] D. J. Cram and J. D. Knight, *ibid.*, **74**, 5835 (1952).

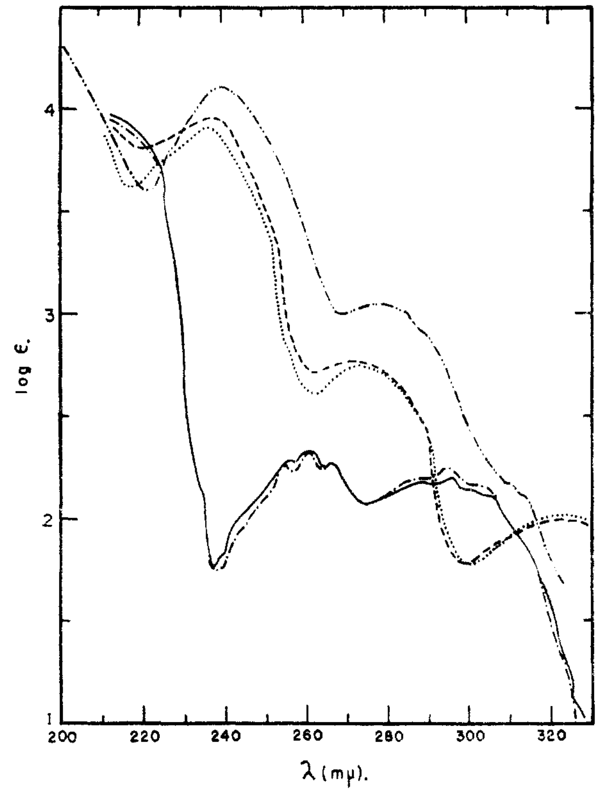


Fig. 1.—Ultraviolet absorption spectra of ketones in cyclohexane, Cary Spectrophotometer, Model 11PMS: —··—, acetophenone; ----, 1-phenyl-2-methyl-2-ethyl-1-butanone; ..... 1-phenyl-2,2-dimethyl-1-butanone; —, 4-methyl-4-phenyl-3-hexanone; -·-, 3-methyl-3-phenyl-2-pentanone.

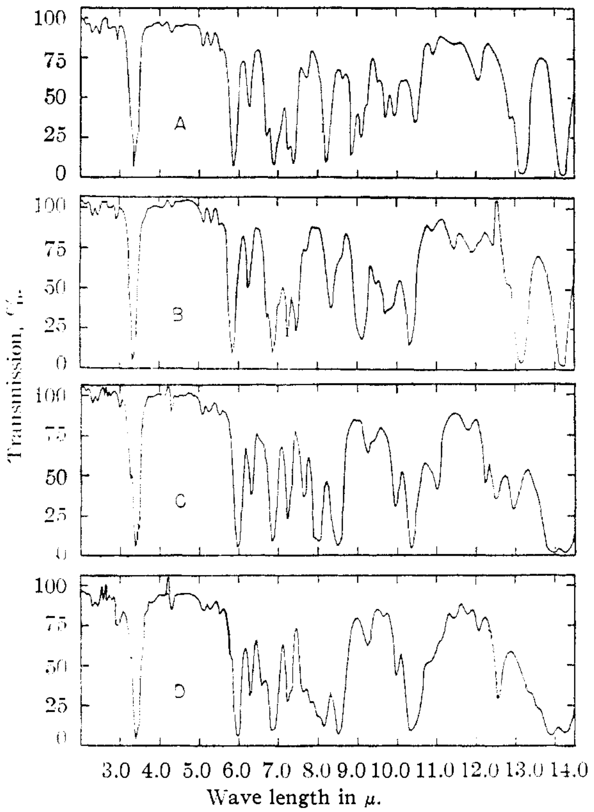
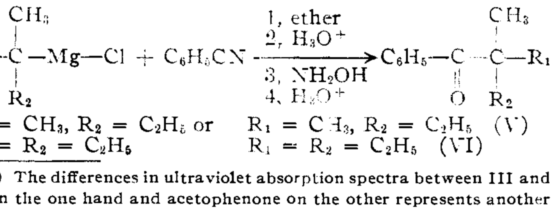


Fig. 2.—Infrared absorption spectra of ketones: liquid films 0.03 mm. thickness, NaCl prism, Beckman spectrophotometer (model I.R.2T): A, 3-methyl-3-phenyl-2-pentanone; B, 4-methyl-4-phenyl-3-hexanone; C, 1-phenyl-2,2-dimethyl-1-butanone; D, 1-phenyl-2-methyl-2-ethyl-1-butanone.

rial was severely limited by the low solubility of the esters in formic acid. Again only olefinic products were obtained. The nature of these products was ascertained by submitting the olefinic mixtures to ozonolysis. The aldehydic components of the resulting mixtures were removed through the use of silver oxide, and the ketonic products were submitted to polarimetric and spectral analyses. The diagram sketches the structural relationships between the starting esters and the final ketonic products. Ketone V could arise only as a product of a methyl migration, and ketone VI as a product of an ethyl migration from the $\beta$- to the $\alpha$-carbon atom.

The optically pure (+)- and (−)-isomers of III and IV were reported previously,[2] and ketones V and VI were prepared by the action of the appropriate Grignard reagent on benzonitrile as shown below. In each case the ketones were purified through their crystalline oxime derivatives. Figure 1 records the ultraviolet absorption spectra of ketones III, IV, V, VI and acetophenone,[3] and Fig. 2, the infrared absorption spectra of III, IV, V and VI. Table I reports the optical densities of these ketones at those wave lengths in the infrared most advantageous for analysis of unknown mixtures of the com-



$$R_1-\overset{\displaystyle CH_3}{\underset{\displaystyle R_2}{C}}-Mg-Cl + C_6H_5CN \xrightarrow[\text{3, }NH_2OH \;\; \text{4, }H_3O^+]{\text{1, ether} \;\; \text{2, }H_3O^+} C_6H_5-\underset{\displaystyle O}{\overset{\|}{C}}-\overset{\displaystyle CH_3}{\underset{\displaystyle R_2}{C}}-R_1$$

$R_1 = CH_3$, $R_2 = C_2H_5$ or $R_1 = CH_3$, $R_2 = C_2H_5$ (V)

$R_1 = R_2 = C_2H_5$ $R_1 = R_2 = C_2H_5$ (VI)

TABLE I

OPTICAL DENSITIES OF KETONES AT THOSE WAVE LENGTHS IN THE INFRARED THAT BEST LEND THEMSELVES TO ANALYSES[a]

| Ketone[b] | | Optical densities | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Pin no. | 5 | 6 | 7 | 8 | 9 | 10 | 11 |
| | $\lambda(\mu)$ | 8.21 | 8.51 | 8.87 | 9.22 | 9.80 | 10.60 | 11.00 |
| | Slit (mm.) | 0.291 | 0.291 | 0.315 | 0.315 | 0.360 | 0.590 | 0.540 |
| III | | 0.758 | 0.122 | 0.579 | 0.266 | 0.204 | 0.098 | 0.026 |
| IV | | .191 | .144 | .277 | .599 | .450 | .081 | .026 |
| V | | .293 | 1.08 | .041 | .100 | .186 | .254 | .451 |
| VI | | .456 | 1.10 | .051 | .121 | .074 | .486 | .192 |

[a] Beckman infrared spectrophotometer, Model IR2, NaCl prism, cell thickness = 0.03 mm. [b] Liquid films were employed.

TABLE II

MOLAR EXTINCTION COEFFICIENTS OF KETONES AT THOSE WAVE LENGTHS IN THE ULTRAVIOLET THAT BEST LEND THEMSELVES TO ANALYSES[a]

| Ketone[b] | Molar extinction coefficients $\lambda(m\mu)$ 236 | 272 |
|---|---|---|
| III | 69 | 112 |
| IV | 49 | 109 |
| V | 7460 | 494 |
| VI | 8560 | 575 |

[a] Run on a Cary recording spectrophotometer, Model 11PMS. [b] Solutions of ketones in cyclohexane.

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(3) The differences in ultraviolet absorption spectra between III and IV on the one hand and acetophenone on the other represents another case of steric inhibition of resonance. Coplanarity of the carbonyl function and the benzene ring in III and IV is prohibited by the bulk of the groups on the $\alpha$-carbon and by the ortho-hydrogens of the ring.

TABLE III

RESULTS OF INFRARED AND ULTRAVIOLET ANALYSES OF KETONIC MIXTURES[a]

| | | | | | Infrared analyses corrected to mixtures[c] Pins 7, 8, 10 and 11[d] | | | | | Pins 5, 6 and 9[d] | | | | Ultraviolet analyses[b] λ 236 mμ | | λ 272 mμ | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Run no. | Starting material | Solv. acid | Tm. hr. | Temp., °C. | III, % | IV % | V, % | VI, % | Tot., % | III, % | IV, % | V, % | Tot., % | III, % | V, % | III, % | V, % |
| 1 | (−)-*threo*-II-Bb.[e] | Acetic | 48 | 75 | 70 | 28 | 6 | 0 | 104 | 69 | 27 | 6 | 102 | 94 | 6 | 95 | 5 |
| 2 | (−)-*erythro*-II-Bb.[e] | Acetic | 48 | 75 | 64 | 32 | 6 | 0 | 102 | 65 | 30 | 6 | 101 | 94 | 6 | 95 | 5 |
| 3 | (−)-*threo*-II-Bb.[c] | Formic | 72 | 25 | 22 | 7 | 71 | 2 | 102 | 22 | 6 | 71 | 99 | 29 | 71 | 35 | 65 |
| 4 | (−)-*erythro*-II-Bb.[e] | Formic | 72 | 25 | 21 | 5 | 74 | 2 | 102 | 23 | 5 | 73 | 101 | 14 | 86 | 18 | 82 |
| 5 | Olef. mixt.[f] | Acetic | 48 | 75 | 60 | 36 | 7 | 0 | 103 | 58 | 36 | 9 | 103 | 92 | 8 | 94 | 6 |
| 6 | Olef. mixt.[f] | Formic | 72 | 25 | 50 | 6 | 46 | 0 | 102 | 48 | 7 | 46 | 101 | 38 | 62 | 43 | 57 |

[a] See Tables I and II for the conditions under which the spectral data were gathered. [b] These values are calculated assuming that deviations from Beer's law are negligible. [c] In each case, deviations from Beer's law were compensated for by correcting the unknown mixtures to known mixtures whose compositions differed from the unknown mixtures by less than 3% in any major component, and by less than 1% in any minor component. [d] The wave lengths that correspond to these pin numbers are recorded in Table I. [e] Bb. = *p*-bromobenzoates. These isomeric esters of 3,4-dimethyl-4-phenyl-3-hexanol (II) are reported in Paper XI (ref. 2) of this series. [f] This olefinic mixture was obtained by the treatment of a mixture of optically pure (−)-*threo*-II and (−)-*erythro*-II with phenyl isocyanate at a high temperature (see Experimental).

pounds. Table II records the molar extinction coefficients of the same ketones at those wave lengths in the ultraviolet that best lend themselves to analysis of unknown mixtures of these substances.

Infrared analyses of the mixtures from the ozonolysis experiments were made by solving four simultaneous equations in four unknowns, making use of the optical densities of the unknowns and of the pure components at four different wave lengths. Since ketone VI proved to be virtually absent in the unknown mixtures, an independent set of three simultaneous equations in three unknowns was solved to act as a check on the first set of equations. The values thus obtained were corrected (deviations from Beer's law) to similarly calculated values obtained for known synthetic mixtures whose compositions closely simulated those of the unknown mixtures. The final results are given in Table III.

The values of the molar extinction coefficients at two wave lengths in the ultraviolet of the two conjugated ketones (V and VI) differ enough from the values for the two unconjugated ketones (III and IV) to permit analyses for the sums of the conjugated *vs.* the unconjugated ketones in the unknown mixtures. The results obtained for such analyses are recorded in Table III.

The degree of racemization of ketones III and IV in the final mixtures from the solvolyses was determined through polarimetric analyses of these mixtures, and Table IV reports the results. That the rotations of the active components are almost additive was demonstated through a comparison of the rotations of the unknown and known synthetic mixtures.

The stability of the olefins once formed in those solvolysis experiments conducted in acetic acid at 75° (runs 1 and 2) was demonstrated in run 5. A mixture of optically active olefins (produced by treating a mixture of pure (−)-*threo*-II and (−)-*erythro*-II with phenyl isocyanate at 200°) was subjected to the same conditions that the olefins once formed in runs 1 and 2 had to undergo. The rotations of the olefinic mixtures as well as of the ketonic mixtures prepared from them are the same before and after the acetic acid treatment (compare runs 5 and 7, Table IV). In formic acid, however, the olefins underwent extensive modification in the direction of racemic unconjugated and of conjugated olefins (run 6).

The question of whether any rearrangements occur during the ozonolyses has not been unequivocally decided in this investigation. However, any *rearrangements* that could lead to ketones III, IV and V are extremely unlikely because of the complicated structural requirements for such reactions, and the same is true for any rearrangements that could lead to any further racemization of ketones III and IV. The absence of compounds other than III, IV and V in at least runs 1 and 2 in other than trace amounts is demonstrated by the infrared analyses. The good yields obtained in the ozonolyses and the similarity in structure of the olefins support the assumption that the yields of VII → III, VIII → IV and IX → V are approximately equal.[4]

TABLE IV

OPTICAL PROPERTIES OF THE SOLVOLYSIS AND OZONOLYSIS PRODUCTS

| | | = 1 dm. (homogeneous) | | | |
|---|---|---|---|---|---|
| Run[a] no. | $\alpha^{23}$D olef. mixt. | $\alpha^{23}$D unknown ketonic mixt. | $\alpha^{23}$D model ketonic mixt. | $\alpha^{23}$D ketone / $\alpha^{23}$D olefin | Racemization[b] of unconj. ketone, % |
| 1 | +15.88° | −48.04° | −47.56°[c] | −3.02 | 26 |
| 2 | +17.74 | −53.42 | −52.42[d] | −3.01 | 18 |
| 3 | 0 | 0 | ...... | .... | 100 |
| 4 | 0 | 0 | ...... | .... | 100 |
| 5 | +16.98 | −53.86 | ...... | −3.18 | 0 |
| 6 | + 0.93 | − 2.78 | ...... | −2.99 | 93 |
| 7[e] | +16.98 | −53.88 | ...... | −3.18 | 16 |

[a] Run numbers are carried over from Table III. [b] Rotations of optically pure ketones are $\alpha^{23}$D − 68.32° ($l$ = dm., homo.) for III and $\alpha^{23}$D −70.94° ($l$ = dm., homo.) for IV. The % racemization is calculated utilizing the infrared analytical data of Table III, and assuming that each of the two ketones (III and IV) are racemized to the same degree and that the rotations of the active components are additive. [c] Synthetic mixture made up as follows: 5.9% V, 16.8% rac. III, 52.3% (−)-III, 9.6% rac. IV, 15.4% (−)-IV. If the rotations of the active components had been additive, the rotation would have been $\alpha_D$ −46.6°. [d] Synthetic mixture made up as follows: 6.0% V, 8.6% rac. III, 54.3% (−)-III, 8.3% rac. IV, 22.8% (−)-IV. If the rotations of the active components had been additive, the rotation would have been $\alpha_D$ −53.1°. [e] In this experiment, a mixture of optically pure (−)-*threo*-II and (−)-*erythro*-II were heated to 200° and phenyl isocyanate was added. The olefin produced was carried through to ketone (see Experimental part).

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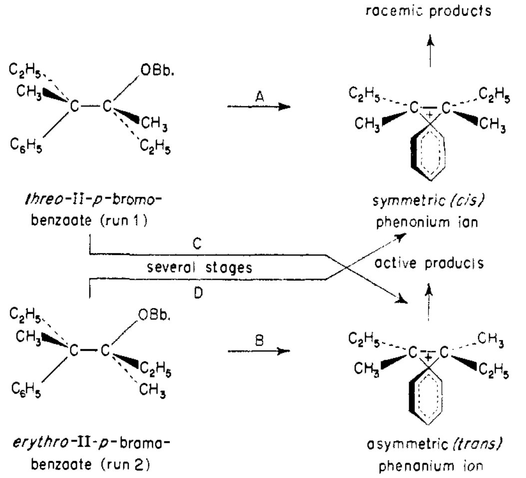
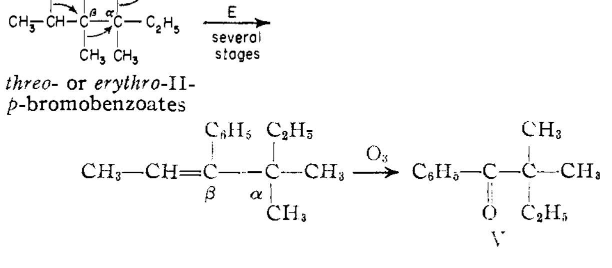
[4] The equality of yields in the two experiments, 2-phenyl-2-pentene → acetophenone and 3-phenyl-2-pentene → propiophenone has been demonstrated [Paper VI of this Series, THIS JOURNAL, **74**, 2137 (1952)].

The absence of aldehydic products in the ketones from runs 1 and 2 was demonstrated by the fact that the infrared analyses of the ketonic mixtures before and after the silver oxide treatment did not change. In runs 3 and 4 however, the silver oxide treatment did remove non-ketonic material.

## Discussion

**The Solvolytic Elimination Reaction in Acetic Acid.**—The relationship between the symmetry properties of the starting materials employed in runs 1 and 2 on the one hand and the differences in the products obtained in these two experiments on the other provide a means of identifying in a general way some of the processes that operate during solvolysis. Thus the production of racemic olefin (and subsequently racemic ketone) is evidence that phenyl migration has occurred, and probably by a path that involves an internally compensated intermediate such as a symmetrical phenonium ion (*i.e.*, process A). Although an analogous process in which asymmetric phenonium ion is produced (*i.e.*, process B) also probably occurs, this process cannot be identified because the same products result regardless of which way the three-membered ring opens. Since racemic ketones (III and IV) were obtained from starting materials of either the *threo* or *erythro* configuration,[2] either starting material must be capable of going to symmetric phenonium ion (*i.e.*, process D or A) and hence to racemic products. By analogy, both starting materials probably go to asymmetric phenonium ion (*i.e.*, processes C and B), although such processes cannot be identified. The presence of ketone V among the ozonolysis products produced by starting material of either configuration is evidence for a reaction in which a methyl group migrated from the β- to the α-carbon atom (process E). The absence of ketone VI among the ozonolysis products in both runs is evidence that no detectable amount of ethyl migration occurred during the acetolysis reactions.





*threo*- or *erythro*-II-*p*-bromobenzoates

$$CH_3{-}CH{=}\underset{\beta}{\overset{C_6H_5}{C}}{-}\underset{\alpha\ CH_3}{\overset{C_2H_5}{C}}{-}CH_3 \xrightarrow{O_3} C_6H_5{-}\underset{O}{\overset{}{C}}{-}\underset{C_2H_5}{\overset{CH_3}{C}}{-}CH_3$$

V

Although the diastereomerically related starting materials in runs 1 and 2 produced the same substances, the balances between the various products in the two runs were different. For instance *threo* starting material produced a larger amount of racemic III and IV than did starting material of the *erythro* configuration, or process A plays a larger role in disposing of starting material of *threo* configuration than process D plays in disposing of starting material of *erythro* configuration. The balances between ketones III and IV in the two runs are also somewhat different, again pointing to a degree of stereospecificity in the solvolysis reactions. Although the same amount of methyl migration was found in each run, the analytical methods were not sensitive enough to detect small differences in the amounts of V produced.

Starting materials of *threo* configuration can produce *cis*-phenonium ions (process A) by a simple inversion of the carbon atom originally carrying the ester function, whereas *erythro* materials can go to this same ion (process D) only by a path involving a frontside displacement of the leaving group by the phenyl, or by processes involving an over-all inversion of the carbon atom carrying the ester function. Since a concerted frontside displacement mechanism is highly unlikely, process D probably occurs in at least two stages, each of which involves a Walden inversion. Since process A probably involves less stages than process D, *threo* starting materials should produce more racemic product than *erythro* starting materials. The fact that the isomer previously assigned[2] the *threo* configuration gave more racemic olefin than the isomer assigned the *erythro* configuration lends considerable support to the validity of these assignments.

No matter how *cis*-phenonium ion is formed the ratio of products which it produces must be the same. Since paths A and D are probably the only ways by which racemic unconjugated olefin can arise, the ratios of racemic ketone III to racemic ketone IV must be the same for runs 1 and 2. Therefore the differences in the ratios of total ketone III to total ketone IV in the two runs must be due entirely to differences in the ratios of active ketone III to active ketone IV. This conclusion makes untenable any mechanism for the simple solvolytic elimination reaction that involves a single precursor common to both runs 1 and 2 through which all optically active olefins arise.

Of the three possible mechanisms for the simple stereospecific $E_1$ reaction presented in Paper VI of this series,[5] the one that involves open (non-bridged) ion-pairs as intermediates provides the most economical explanation of data obtained in the 3,4-dimethyl-4-phenyl-3-hexanol system. The diagram correlates the experimental observations, the stereochemical structures and the mechanisms considered the most applicable to the data. In this mechanistic picture, the stereospecificity associated with the high degree of racemization found

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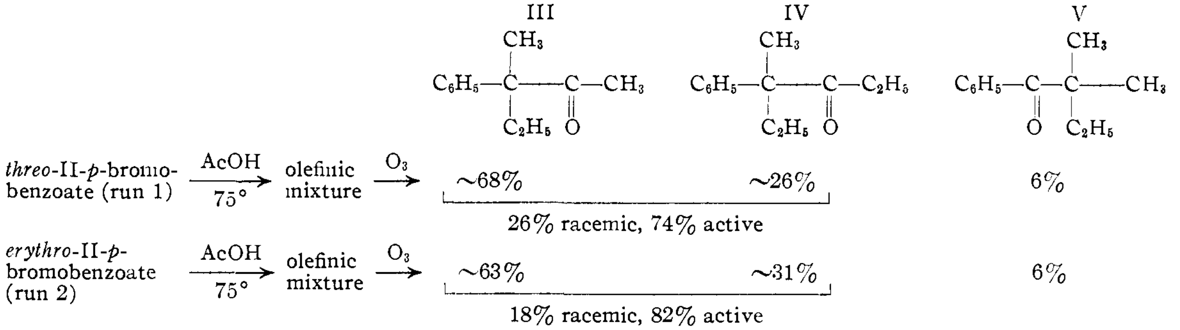
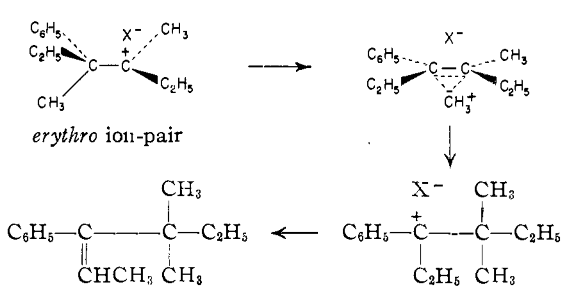
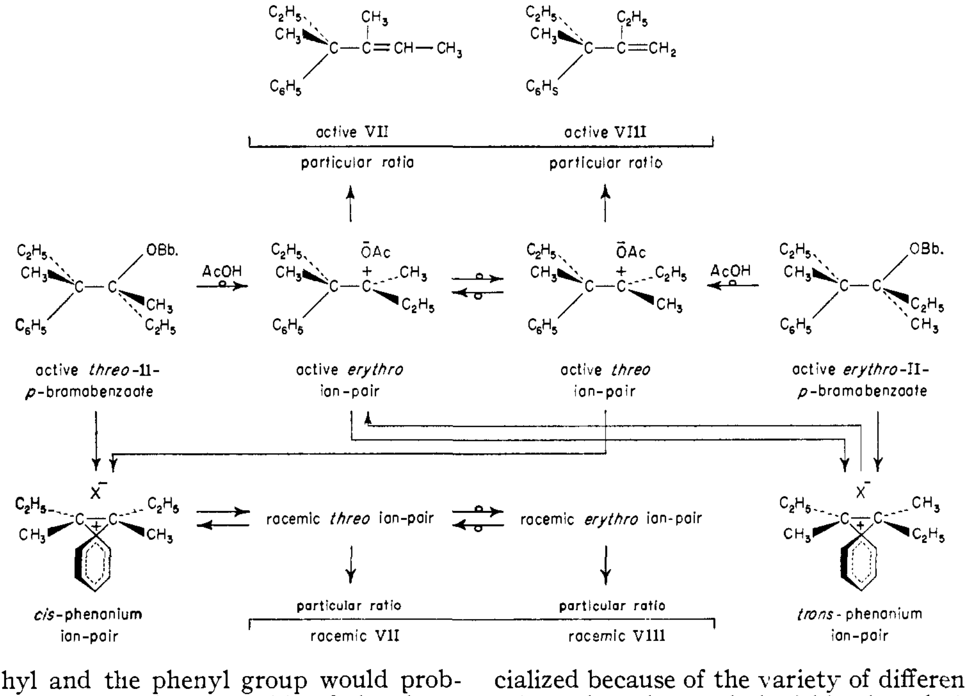
(5) D. J. Cram, This Journal, **74**, 2137 (1952).



in the *threo* series arises out of the direct conversion of starting material to internally compensated (*cis*)-phenonium ion. This process can compete favorably with the two stage process by which *erythro* material goes to *cis*-phenonium ion. The stereospecificity associated with the different balance of optically active non-conjugated olefins (VII and VIII) obtained from the diasteromerically related starting materials is derived from the active *erythro* ion-pair giving a different balance of VII and VIII than the active *threo* ion-pair. The rates of equilibration of the two open ion-pairs would therefore have to be the same order of magnitude as their rates of decomposition to olefin. Although the picture could be complicated further by the intervention of other open ion-pairs that arise by simple ionization of the starting materials, the present data do not demand any such species.

The reaction that involves methyl migration appears to be non-stereospecific, although a small difference in yield of conjugated ketone from the isomeric starting material would have gone undetected. Since during the methyl migration, the second methyl and the phenyl group would probably be distributed on the same side of the three-membered ring,[6] and since methyl migration took place to about the same extent from either *threo* or *erythro* starting materials, the immediate precursor of the bridge (whether ion or transition state) is probably an *erythro* ion-pair. Because of the greatly enhanced stability associated with the resonance of a benzylcarbonium ion, this rearrangement is probably at best only very slowly reversible.





The inability of ethyl to compete with the methyl group in this migration reaction is probably due to both steric and electronic factors. The steric requirements for an ethyl migration are far more specialized because of the variety of different conformations that the methyl-within-the-ethyl-group can assume in the starting species. Furthermore, the methyl group is probably better able to distribute positive charge in the bridge because of the sym-

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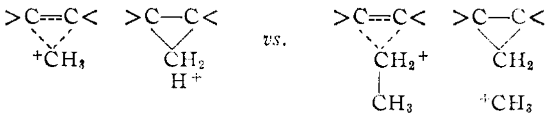
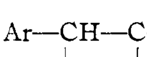
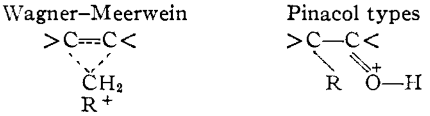
(6) The question of whether this species is another bridged ionic intermediate or a transition state has yet to be answered.

metry and relative stability of its hyperconjugative resonance forms.[7]



The ability of methyl to migrate in the presence of an ethyl group in this Wagner–Meerwein rearrangement is in conflict with the order of migratory aptitudes of alkyl substituents in pinacol and pinacol-like rearrangements. Tiffeneau and Levy[8] have summarized a vast amount of data on the subject as: order of migratory aptitude in the system  $\mathrm{Ar{-}CH{-}C}(\mathrm{R})(\mathrm{R'})$: (1) In the dehydration of glycols, *n*-butyl and benzyl > ethyl > *n*-propyl = methyl > *i*-butyl; (2) In the isomerization of oxides, benzyl > ethyl > methyl >*n*-propyl; (3) in the dehydrohalogenation of iodohydrins, benzyl and ethyl > methyl. In all of these cases and in others involving similar systems, ethyl > methyl in migratory aptitude.[9]

One of the main differences between the Wagner–Meerwein and the pinacol-like rearrangements lies in the probability that in the bridged intermediate (and/or transition state) of the former, hyperconjugative resonance forms are relatively important whereas in the latter the more classical resonance forms dominate the hybrid.



Thus in the pinacol rearrangement, factors other than the ability of the bridging group to enter into hyperconjugation are probably more controlling than in the Wagner–Meerwein rearrangement.

The ability of the methyl to compete with the phenyl group in its migratory ability is surprising, since in the 3-phenyl-2-butanol system no methyl migration was observed.[1a,1b] If one assumes that in system II, *trans*-phenonium ion is formed not more than twice as often as the *cis*-phenonium ion,[10] the migratory ability of the phenyl group is not more than twelve times that of the methyl group.

**The Solvolytic Elimination Reaction in Formic Acid.**—Unfortunately the lack of good agreement between the infrared and ultraviolet methods of analyzing for conjugated and unconjugated olefins in runs 4 and 6 (see Table III) detracts from the conclusions that can be drawn from the data obtained from the solvolyses in formic acid. However, the infrared analyses are internally consistent and the ultraviolet are not, and hence more reliability is associated with the former. Certainly the data are reliable enough to yield general conclusions.

The features that characterize the solvolyses in formic acid are the following: the completely racemized nature of the unconjugated products; the lack of stereospecificity in any of the reactions; the presence of a trace of product in which an ethyl group has migrated; and the preponderance of conjugated over unconjugated products. All of these characteristics are derived either from the ability of the olefins initially formed in formic acid to undergo further transformations, or from the fact that the superior ionizing power of formic acid permits the intermediate ionic species to persist longer and to equilibrate more thoroughly before collapsing to product. Probably both of these effects operate.

In run 6, optically active unconjugated olefin was shown to both racemize and rearrange to conjugated olefin when dissolved in formic acid at room temperature, the rate of the former reaction being the higher by about a factor of four. This factor is about the same as those obtained in runs 1 and 2 in acetic acid where factors of about four from *threo* and of about three from *erythro* starting materials were observed. As would be expected, in run 6 the unconjugated olefin with a terminal ethylene group (VIII) was destroyed faster than the unconjugated olefin without a terminal methylene group (VII), the factor amounting to about three.[11]

The effect of the superior ionizing power of the formic acid in runs 3 and 4 was demonstrated in two ways. First, a distinct pink color developed at the beginning of the reaction in runs 3 and 4, which decreased in intensity as the reaction proceeded and finally faded altogether. Since both the starting materials and products are colorless, this color is probably due to intermediate ionic species, possibly phenonium ions whose partially quinoidal structure should absorb light in the visible region. Apparently the half-lives of at least some of the ionic species are substantial in formic acid. Second, the differences in the balances in products between runs 3 and 4 on the one hand and run 6 on the other demonstrate that the rates at which active unconjugated olefins racemize and isomerize are far too slow to account for more than a fraction of the total isomerization and racemization reactions observed in runs 3 and 4. Therefore, most of these changes must have occurred before olefin was formed, rather than after. If such is the case, then far more extensive rearrangement occurred per molecule of starting ester consumed in formic than in acetic acid.

## Experimental Part

**Preparation of Ketones Used as Standards in the Spectral and Polarimetric Analyses.**—The preparation of the opti-

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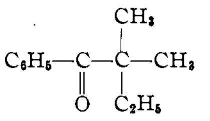
[7] It appears to be established [see F. A. Matsen, W. W. Robertson and R. L. Chuoke, *Chem. Revs.*, **41**, 237 (1947), and V. A. Crawford, *Quart. Revs.* (*London*), **3**, 226 (1949)] that electrons are less localized in the C-H bonds than in the C-C bonds of alkyl groups and as a consequence $CH_3 > C_2H_5 > i\text{-}C_3H_7 > t\text{-}C_4H_9$ in ability to release electrons to other groups.

[8] M. Tiffeneau and J. Levy, *Bull. soc. chim. France*, [4] **49**, 1647, 1676, 1698 (1931).

[9] In much of the data upon which this summary rests, the issue of whether rates or equilibria governed the balance of products was not settled. However, the lack of exception to this order from among a large number of cases suggests that the order persists in either situation.

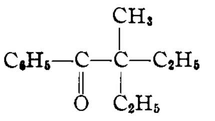
[10] In Paper VIII of this series [THIS JOURNAL, **74**, 2152 (1952)] it was demonstrated that *cis*-phenonium ions formed about half as readily as *trans*- in the 3-phenyl-2-pentanol and the 2-phenyl-3-pentanol systems.

[11] The relative rates at which *cis*- and *trans*-2-phenyl-2-butene and 2-phenyl-1-butene take up protons has been measured in an acetic acid solution of *p*-toluenesulfonic acid at 75° (unpublished results). The last substance with a terminal methylene group reacted at least an order of magnitude faster than the other two.



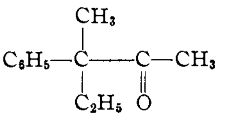
$C_6H_5-C(=O)-C(CH_3)(C_2H_5)-CH_3$

V



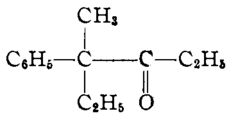
$C_6H_5-C(=O)-C(CH_3)(C_2H_5)-C_2H_5$

VI



$C_6H_5-C(CH_3)(C_2H_5)-C(=O)-CH_3$

III



$C_6H_5-C(CH_3)(C_2H_5)-C(=O)-C_2H_5$

IV

| | V | VI | III | IV |
|---|---|---|---|---|
| (−)-*threo*-II-Bb. (run 3) $\xrightarrow{HCOOH}\xrightarrow{O_3}$ | 70% | ~2% | 22% | 6% |
| (−)-*erythro*-II-Bb. (run 4) $\xrightarrow{HCOOH}\xrightarrow{O_3}$ | 71% | ~2% | 22% | 5% |
| olefinic mixture VII, VIII and IX $\xrightarrow{O_3}$ | 7% | 0% | 58% | 35% |
| | | | 16% racemic | |
| same as above (run 6) $\xrightarrow{HCOOH}\xrightarrow{O_3}$ | 45% | 0% | 49% | 6% |
| | | | 93% racemic | |

cally pure enantiomorphs of 3-methyl-3-phenyl-2-pentanone (III) and of 4-methyl-4-phenyl-3-hexanone (IV) were reported previously.[2] The ketone, 1-phenyl-2,2-dimethyl-1-butanone (V), was prepared by a modification of the method used for the preparation of pivalophenone.[12] Benzonitrile (18 g.) and excess Grignard reagent prepared from 52 g. of 2-methyl-2-chlorobutane were held at reflux temperature in toluene for two hours. The solution was decomposed in the ordinary way and the products submitted to fractional distillation on a fifty-plate center-rod column at reduced pressure. The crude ketone thus obtained (12 g.) was converted to its oxime,[13] which after recrystallization (ethanol) gave 6 g. of material, m.p. 140–141°.[13] This oxime (6 g.) was held at reflux temperature with 30 ml. of concentrated hydrochloric acid for five hours. The ketonic product was extracted into pentane, and separated from unreacted oxime by fractional distillation at reduced pressure to give 3.0 g. of pure V, $n^{25}$D 1.5080.

By a similar procedure, 25 g. of benzonitrile and excess Grignard reagent (prepared from 150 g. of 3-methyl-3-chloropentane) gave 7.6 g. of crude ketone which was oximated,[10] and after three recrystallizations from ethanol, 2.7 g. of oxime was obtained, m.p. 131–132° (Heller and Bauer[13] reported a melting point of 121° for this substance).

*Anal.* Calcd. for $C_{13}H_{19}ON$: C, 76.05; H, 9.33. Found: C, 75.80; H, 9.20.

Hydrolysis of this oxime (1.7 g.) with boiling concentrated hydrochloric acid for five hours gave ketone that was isolated by submitting a pentane (pure) solution of the hydrolysis product to chromatography on alumina and by distilling the column eluates, wt. of VI, 1.0 g., $n^{25}$D 1.5037.

**Solvolyses of the *p*-Bromobenzoate Esters of 3,4-Dimethyl-4-phenyl-3-hexanol in Acetic Acid.**—Pure dry acetic acid and the ester[2] (25 ml. of solvent per g. of solute) were mixed and the resulting solution was allowed to stand at 75° for 48 hours, after which time the solution was diluted threefold with water. The resulting mixture was extracted with pentane (pure) three times, and the combined extracts were washed with water, once with sodium carbonate solution and again with water. The solution was then dried, the solvent was evaporated through a 60-cm. Vigreux column, and the residue was flash distilled at 13 mm. to yield a mixture of olefins. The yields and physical constants of these mixtures are as follows. In run 1, from 2.2 g. of (−)-*threo*-II-*p*-bromobenzoate ($[\alpha]^{23}$D −52.2°; *c* 4% in benzene) was obtained 1.01 g. of olefin (95% yield), $n^{25}$D 1.5132; in run 2 from 3.0 g. of (−)-*erythro*-II-*p*-bromobenzoate ($[\alpha]^{23}$D −12.8°; *c* 10% in benzene) was obtained 1.30 g. of olefin (90% yield), $n^{25}$D 1.5139.

In another experiment, the *p*-bromobenzoate of racemic *threo*-II (0.50 g., m.p. 87–89°) was allowed to stand 60 hours at room temperature in 10 ml. of pure, dry acetic acid. The starting ester (0.46 g., m.p. 87–89°) was recovered from the reaction mixture through the usual pentane extraction and crystallization procedures.

The ozonolyses of the olefinic mixtures to the ketonic mixtures were accomplished by the following procedure. Ozone was led into an ice-cold solution of 1.0 g. of olefinic mixture dissolved in 25 ml. of ethyl acetate until no more ozone was absorbed. The solution was then slowly added to a mixture of 1 g. of zinc dust, a small crystal of silver nitrate and 50 ml. of boiling water. The resulting mixture was extracted three times with ether, and the combined extracts were dried and the solvent was removed through a short column. The residue was flash distilled at 13 mm. pressure. In run 1, from 0.93 g. of the olefinic mixture was obtained 0.60 g. of ketonic mixture, $n^{25}$D 1.5079; and in run 2, from 1.20 g. of olefinic mixture was obtained 0.81 g. of ketonic mixture, $n^{25}$D 1.5078. These mixtures were submitted to polarimetric, infrared and ultraviolet spectral analyses (see Tables III and IV). These mixtures were submitted to the action of silver oxide (see procedure at the end of the next section) to remove possible aldehydic impurities. The analyses before and after this treatment were essentially identical.

**Solvolyses of the *p*-Bromobenzoate Esters of 3,4-Dimethyl-4-phenyl-3-hexanol in Formic Acid.**—Pure dry formic acid and the ester[2] (40 ml. of solvent per gram of ester) were stirred at 25° for six hours. The esters and the reaction products (olefin and *p*-bromobenzoic acid) are only slightly soluble in the reaction solvent. As the reaction proceeded, the mixture turned a pink color which first grew and then faded in intensity. The mixture was finally placed in a bath at 25° and allowed to stand (with occasional shaking) for 66 hours. The procedures for the isolation and ozonolyses of the olefinic mixtures are identical to those employed in the case of the runs carried out in acetic acid. The yields and physical constants of the products are as follows. In run 3, from 2.3 g. of (−)-*threo*-II-*p*-bromobenzoate ($[\alpha]^{23}$D −52.2°; *c* 4% in benzene) was obtained 0.99 g. (89% yield) of olefin, $n^{25}$D 1.5076, 0.89 g. of which produced on ozonolysis 0.62 g. of ketone, $n^{25}$D 1.5053. In run 4, from 3.0 g. of (−)-*erythro*-II-*p*-bromobenzoate ($[\alpha]^{23}$D −12.8°; *c* 10% in benzene) was obtained 1.32 g. (91% yield) of olefin, $n^{25}$D 1.5078, 1.21 g. of which produced on ozonolysis 0.98 g. of ketone, $n^{25}$D 1.5070. These mixtures were both completely optically inactive.

These ketonic mixtures were submitted to the following procedure for purposes of removing aldehydic components. To a mixture of 0.5 g. of silver nitrate dissolved in 10 ml. of water was added with stirring an excess of sodium hydroxide solution. The oxide precipitate was washed well with water and finally with ethanol. The ketonic mixtures were each heated at reflux with 10 ml. of ethanol and the oxide for 30 minutes, and then most of the alcohol was allowed to escape. The residue was diluted with water, and the resulting mixture was extracted several times with pure pentane. The extracts were combined, dried, the pentane was evaporated through a short column, and the residue was flash distilled. The distillate was submitted to ultraviolet and infrared spectral analyses (Table III). The data obtained were somewhat different and more consistent than those obtained before the silver oxide treatment, and some foreign material did appear to be removed by this treatment.

**Control Experiments.**—Olefin for use in control experiments was prepared by the dehydration of 3,4-dimethyl-4-phenyl-3-hexanol (II) by the following method. A mixture of 7.62 g. of (−)-II (this alcohol was a mixture of the two pure

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(12) A. Willemart, *Bull. soc. chim. France*, 867 (1935).

(13) A. Haller and E. Bauer [*Ann. chim. phys.*, **28**, 386 (1913)] reported a melting point of 139° for this substance.

(--)-diastereomers prepared by the addition of methyl lithium to pure (−)-phenyl-4-methyl-3-hexanone[2]) and 5.0 g. of phenyl isocyanate was allowed to react at from 180–220° for 30 minutes. After cooling, the reaction mixture was extracted four times with pure pentane, the extracts were washed with water, dried, and the solvent was evaporated. The residue was distilled at 13 mm. to yield first a forerun of phenyl isocyanate and then 5.0 g. of an impure oil. This material was dissolved in pure pentane and passed through a column of basic alumina. Removal of the solvent from the pentane eluate and distillation of the residue at 13 mm. gave 3.5 g. of olefinic material, $[\alpha]^{22}\text{D}$ +16.98° (homogeneous), $n^{25}\text{D}$ 1.5129. Ozonolysis of this material by the procedure outlined above gave ketone, $n^{25}\text{D}$ 1.5078 (Table IV, run 7). The control runs for the solvolyses in acetic acid were carried out as follows. The olefinic mixture prepared above (1.0 g.) was held at 75° for 48 hours in 50 ml. of dry pure acetic acid. The olefin was isolated by the same procedure recorded for the actual acetolysis, wt. 0.92 g., $n^{25}\text{D}$ 1.5127. Ozonolysis of this material to the ketone gave material whose index of refraction was $n^{25}\text{D}$ 1.5077 (see Table IV, run 5).

That the solvolysis (runs 1 and 2) produced no acetate was demonstrated in the following fashion. A sample of racemic-*threo*-II-*p*-bromobenzoate (0.97 g., m.p. 87–89°) was submitted to the above solvolytic conditions, and the product was extracted into pure pentane as indicated above. The resulting solution was evaporated through a short column (the pot temperature was never allowed to go above 30°) and the residual oil was treated with a solution of 0.5 g. of lithium aluminum hydride in 20 ml. of ether. After the resulting mixture had stood for one hour, water was added, and the mixture was extracted with ether. The ether layer was washed with water, dried, and the solvent was evaporated through a short column. The residue was flash distilled at 13 mm. to give olefin, 0.44 g., $n^{25}\text{D}$ 1.5135. When submitted to chromatographic absorption on a basic alumina column (20 g.) in a pentane solution (any alcohol would remain on the column under these conditions as shown by control experiments), the olefin readily was eluted with pentane, and 0.40 g. of material was recovered (flash distilled), $n^{25}\text{D}$ 1.5137.

The control runs for the formolyses were completely analogous to those carried out for the acetolyses. Thus 1.0 g. of the olefinic mixture (prepared above by the dehydration of II) was submitted to the action of dry pure formic acid for 72 hours (no color developed). The product isolated (0.92 g., $n^{25}\text{D}$ 1.5102) was submitted to ozonolysis to give ketone, $n^{25}\text{D}$ 1.5069, which was submitted to the action of silver oxide, $n^{25}\text{D}$ 1.5070 (see run 6, Tables III and IV).

LOS ANGELES, CALIFORNIA

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

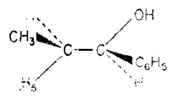
# Studies in Stereochemistry. XIII. The 1,2-Diphenyl-1-propanol System

BY FATHY AHMED ABD ELHAFEZ[1] AND DONALD J. CRAM[2]

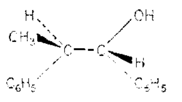
RECEIVED APRIL 25, 1952

Each racemate of 1,2-diphenyl-1-propanol has been shown to react with 3-nitrophthalic anhydride to give substantial amounts of both position isomers of the 3-nitrophthalic acid esters (the anhydride ring can open in either of two directions). The structures of these position isomers were elucidated through the use of spectral techniques. The differences in the balances of the two position isomers from the two racemates is interpreted in terms of the differences in steric requirements for ester formation. The two racemates of 1,2-diphenyl-1-propanol were completely resolved, and the configurations of all of the asymmetric carbon atoms of the system have been related by several unambiguous methods to the configuration of D-glyceraldehyde.

The relative configurations of the two asymmetric carbon atoms in each of the two racemate series of 1,2-diphenyl-1-propanol (I) have been previously determined[3] and were assigned the *erythro* and *threo* configurations. The present investigation reports: (1) the novel behavior of each of the racemates in their reaction with 3-nitrophthalic anhydride; (2) the complete resolution of each of these racemates; (3) a series of reactions that relates the configurations of both carbon atoms of all four isomers to D-glyceraldehyde.

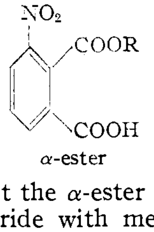


*erythro*-I

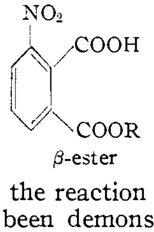


*threo*-I

**The Reaction of the Diastereomeric Alcohols with 3-Nitrophthalic Anhydride.**—The usefulness of 3-nitrophthalic anhydride as a reagent for attaching a handle to a secondary alcohol for purposes of resolution rests in part on the fact that ordinarily the anhydride ring opens predominantly one way.[4] Unlike any previous cases, each racemate of 1,2-diphenyl-1-propanol (I) gives substantial amounts of both the α- and β-position isomers. This observation is rationalized as follows.



α-ester



β-ester

That the α-ester is formed in the reaction of the anhydride with methanol has been demonstrated through a comparison of the conductivities of the α- and β-esters (R = $CH_3$). The β-isomer was formed through the Fischer esterification of the dicarboxylic acid.[4a] The structures of these two isomers were assigned on the basis of their conductivities, the β-ester being the better conductor of the two.[4a] It has been well established that *o*-nitrobenzoic acid is a stronger acid than *m*-nitrobenzoic acid,[5] and therefore this assignment is well founded.

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(1) Predoctoral Fellow of the Egyptian Government. This paper is abstracted from the thesis of this author presented to the Department of Chemistry of the University of California at Los Angeles in partial fulfillment of the rquirements for the Ph.D. Degree.

(2) Requests for reprints should be addressed to this author.

(3) D. J. Cram and F. A. Abd Elhafez, THIS JOURNAL, **74**, 5828 (1952).

(4) (a) R. Wegscheider and A. Lipschitz, *Monatsh.*, **21**, 787 (1900); (b) A. Marckwald and A. McKenzie, *Ber.*, **34**, 485 (1901); (c) G. H. Dickinson, L. H. Crosson and J. E. Copenhaver, THIS JOURNAL, **59**, 1094 (1937).

(5) J. F. J. Dippy and R. H. Lewis, *J. Chem. Soc.*, 1426 (1927).