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Chemistry-General

AN INVESTIGATION OF THE RELATIVE MIGRATORY TENDENCIES OF THE PHENYL AND p-TOLYL GROUPS IN THE PINACOL REARRANGEMENT OF THE 1,1,2-TRIARYLETHYLENE GLYCOL SYSTEM

L. W. Kendrick, Jr.

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By

Lawrence W. Kendrick, Jr.

Date Issued

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INTRODUCTION

A mechanistic correlation of the aldehyde-ketone and the pinacol rearrangements was reported in 1956 by Benjamin and Collins. (1) In an earlier paper Collins (2) had evaluated the importance of the conjugate acid of triphenylacetaldehyde as an intermediate in the pinacol rearrangement of triphenylethylene glycol and had proposed a mechanism to explain the observed fates of the carbon-14 labels for different isotope position isomers of this glycol when it was subjected to rearrangement. The extension of these proposals to the rearrangements of diphenyl-p-tolylacetaldehyde and the two glycols, 1,2-diphenyl-1-p-tolylethylene glycol and 1,1-diphenyl-2-p-tolylethylene glycol, led the authors (1) to propose a general mechanism for the rearrangements.

It was found by Benjamin and Collins that through a mathematical treatment of the mechanism they proposed, the p-tolyl/phenyl migration ratio, during the acid-catalyzed rearrangement of the aldehyde to ketones, was equal to $\frac{2k_T}{k_P}$, where the ratio k_T/k_P was evaluated by means of equation 1. By a combination of double-labeling techniques and

$$1) \quad \frac{k_T}{k_P} = \frac{k_H}{k_\phi} \cdot \frac{k_{Tol}}{k'_H} \cdot \frac{m_e}{m_d}^* \left[\frac{1 + \frac{k'_H}{k_{Tol}}}{1 + \frac{k_H}{k_\phi}} \right]$$

---

*The letter, m, with subscript, d, e, etc., represents the mole fraction of starting material giving product via path, D, E, etc. Similar usage is employed in the construction of Charts I and II of the present research. These charts were drawn to represent the rearrangement of glycols I and II, and aldehyde III, in a manner predictable from the postulations of Benjamin and Collins. (1)

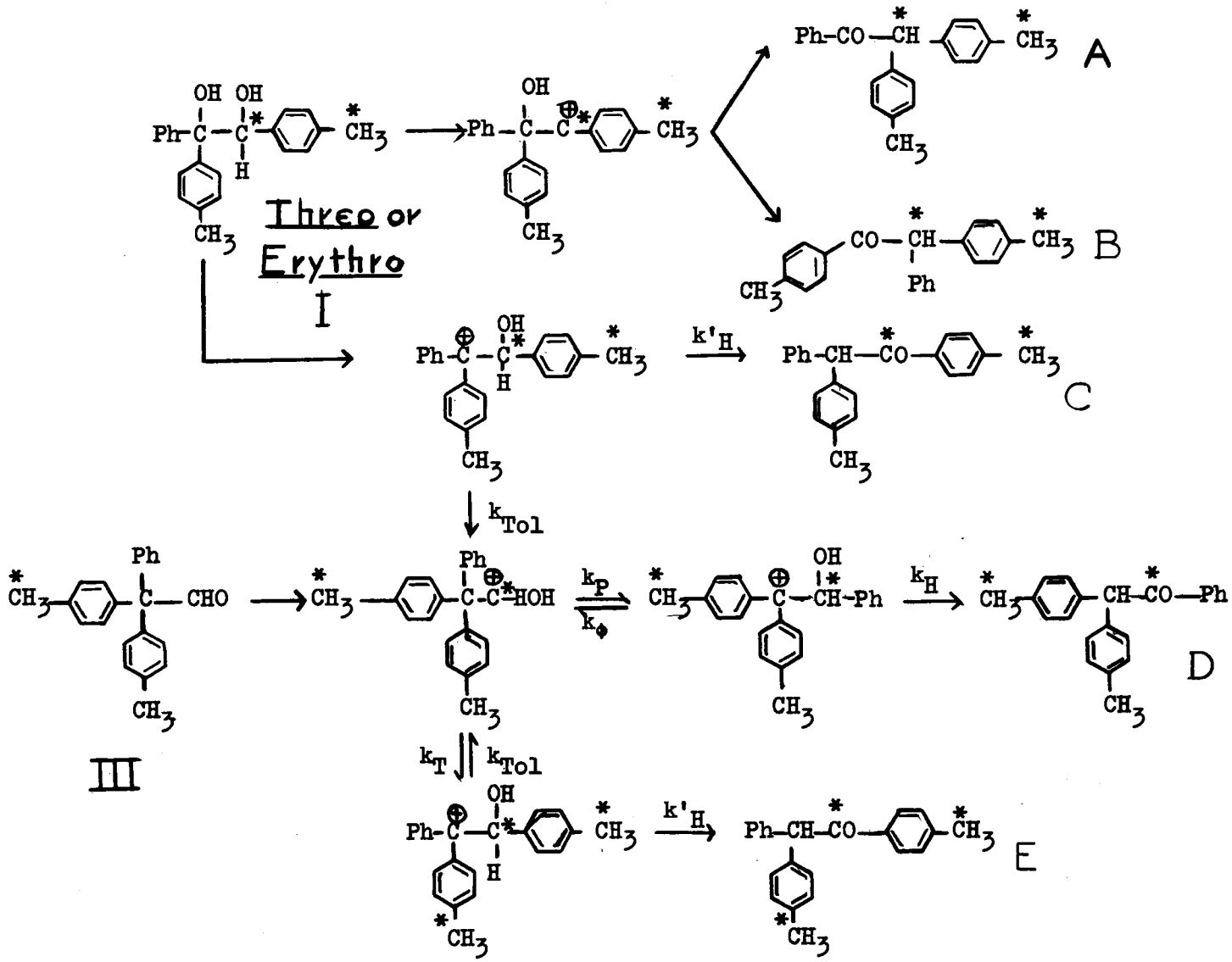


CHART I. Rearrangement of Threo- and Erythro-I, and III.

radioactivity dilution experiments upon appropriately labeled isotope position isomers, these authors were able to show that the p-tolyl/phenyl migration ratio was greater than one, in agreement with other observations, (3-10) but in contradiction to the conclusion to be drawn from a simple product ratio of the ketones obtained. It was necessary, however, for Benjamin and Collins (1) to estimate the k_{Tol}/k'_H ratio in the rearrangement catalyzed by sulfuric acid by means of the proportion,

$$k_{Tol}/k'_H(H_2SO_4):k_{Tol}/k'_H(HCOOH)::k_\phi/k_H(H_2SO_4):k_\phi/k'_H(HCOOH)$$

since the value was so large as to preclude an accurate experimental determination.

The values for the ratios of the specific rate constants found by Benjamin and Collins can be used to calculate similar ratios in closely related systems by taking into account what is apparently a decrease in the values for k_ϕ/k_H when the carbonium ion at the migration terminus is made more stable (Table I). (11) The values then, for k_ϕ/k_H and k_{Tol}/k'_H in concentrated sulfuric acid and in formic acid, may be estimated for the system in which I, II and III* undergo rearrangement

---

*In this dissertation Roman numerals have been used to designate the names of the various compounds when repetition of their names would be cumbersome. In the case of radioactive compounds, a letter has been appended to the Roman numeral to indicate the position of labeling, thus Ia would represent 1,2-di-p-tolyl-1-phenylethylene-1-C^{14} glycol, discretely labeled in the 1-position of the ethylene glycol chain and Ib, the same glycol discretely labeled in the 2-position of the glycol chain and Ic, this glycol discretely labeled in the p-methyl group of the p-tolyl group attached to the 2-position of the chain. More than one letter (e.g., Iab) represents mixtures of the carbon-14 label between the indicated positions. See page 5.

TABLE I

Comparison of k_{Ar}/k_H Ratios for Various Systems in Formic and Sulfuric Acids

	H_2SO_4		HCOOH	
	k_ϕ/k_H	k_{Tol}/k'_H	k_ϕ/k_H	k_{Tol}/k'_H
C. J. C. (2)	7.33		1.7[a]	-
B. M. B. and C. J. C. (1)	6.9	48[b]	1.15	9.3
Estimated for present research	6.5[c]	32[d]	0.78[e]	6.3[f]

[a]Recalculated value, based upon the observation that 7% scrambling of the chain label occurs in the aldehyde rearrangement. (20)

[b]Midpoint of two extremes, calculated by method of B. M. B. and C. J. C., using 1.7 for k_ϕ/k_H in HCOOH.

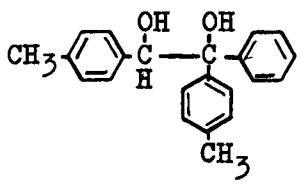
[c]6.9/7.33 x 6.9 = 6.5.

[d]6.3/9.3 = x/48.

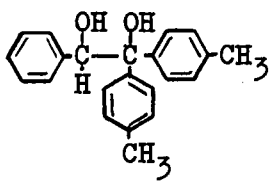
[e]1.15/1.7 x 1.15 = 0.78

[f]1.7/1.15 = 9.3/x.

(Chart I). If the contributions of paths A and B are neglected and the p-tolyl/phenyl migration ratio is assumed to be ca. 3.0 (1) then by use of equation 1 the ratio m_e/m_d may be calculated. From a knowledge of the m_e/m_d ratio and the k_{Tol}/k'_H ratio the yield of ketones IV and V in the ketonic product may then be estimated.



I



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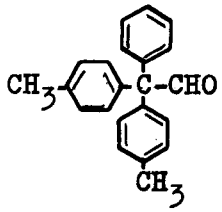

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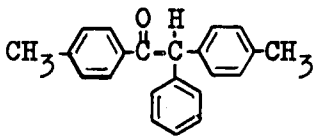

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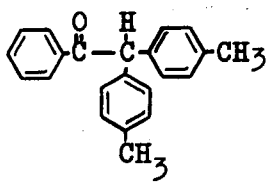


V

2) 2 x p-tolyl/phenyl migration ratio* =

$$\frac{k_T}{k_P} = \frac{k_H}{k_\phi} \cdot \frac{k_{Tol}}{k'_H} \cdot \frac{m_e}{m_d} \left[\frac{1 + \frac{k'_H}{k_{Tol}}}{1 + \frac{k_H}{k_\phi}} \right]$$

$$2 \times 3 = \frac{1}{6.5} \times 32 \times \frac{m_e}{m_d} \left[\frac{1 + \frac{1}{32}}{1 + \frac{1}{6.5}} \right]$$

$$\frac{m_e}{m_d} = 1.36$$

3) Now since

$$k_{Tol}/k'_H = \frac{m_d + m_e}{m_c} = 32 \quad \text{or} \quad m_d + m_e = 32\, m_c$$

---

*The ratio must be multiplied by 2 since there are two p-tolyl groups and only one phenyl in the molecule.

4) $m_c + m_d + m_e = 1.00$

5) Substituting 3) in 4)

$$m_c + 32\, m_c = 1.00$$

$$m_c = 0.03$$

$$m_d + m_e = 0.97$$

Since the ratio $m_e/m_d = 1.36$ or $m_e = 1.36\, m_d$, then,

$$m_d + (1.36\, m_d) = 0.97$$

$$m_d = 0.41$$

$$\text{and } m_e = 0.56$$

The ketones formed from I, through paths C and E, are chemically identical (IV), thus, $m_c + m_e$ (0.59) will represent the expected yield of IV in the ketone product, whereas ketone V is represented by m_d (0.41). Similarly the yields of ketones formed from II (Chart II) and III may be calculated. These are:

for II - $m_f = 0.13$, $m_{d'} = 0.37$, $m_{e'} = 0.50$, V = 50%, IV = 50%;

for III - m_d = IV = 0.43 or 43%, m_e = V = 0.57 or 57%.

It is possible also to predict from Table I the yield of aldehyde (III) formed when the glycol (I) is subjected to rearrangement in formic acid at room temperature. Thus, from Table I, $\frac{k_{Tol}}{k'_H}$ (formic acid)=6.3= $\frac{\text{moles aldehyde formed}}{\text{moles ketone formed}}$. Since the only two products are aldehyde (III) and ketone (IV), and since the aldehyde itself is stable in formic acid for short periods of time, it follows that the yields of aldehyde and

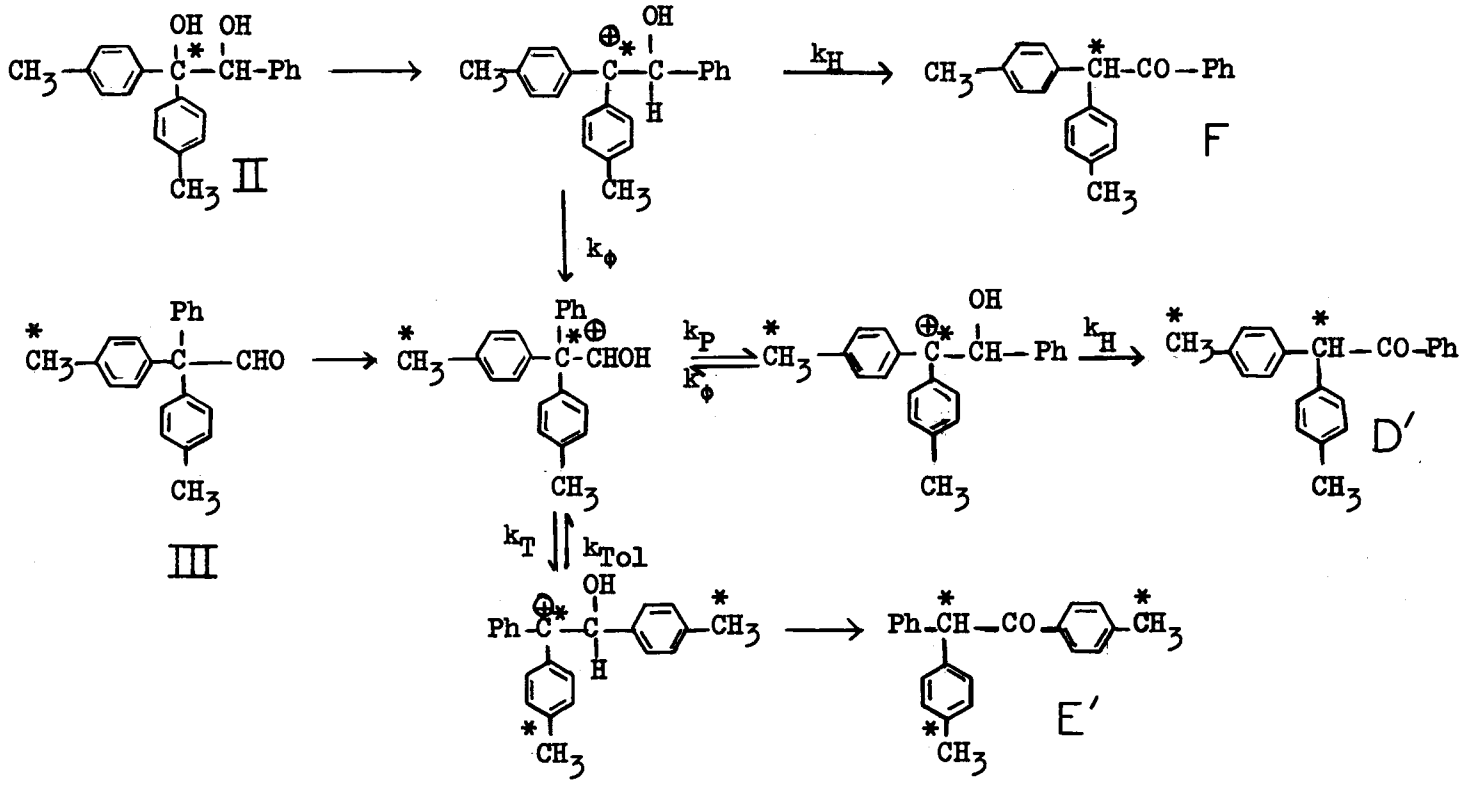


CHART II. Rearrangement of IIa

ketone, respectively, should be 87% and 13%.

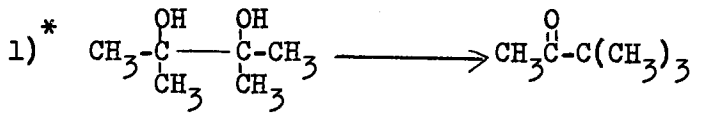
It should be emphasized that although values for the various ratios discussed are recorded, for example, as 9.3 for k_{Tol}/k'_H in formic acid, it is not intended that the precision of such values be interpreted as being better than $\pm$ 10%; for the values of the larger ratios, the uncertainty may be considerably greater. The reason for this will be made clear in the treatment of the data for this research. The ratios are carried through the discussion in this way as an aid to the reader in identifying them as they occur. Despite these uncertainties, it was believed the system involving the rearrangements of I, II and III should offer near optimum conditions for testing the generality of the mechanism proposed by Benjamin and Collins because from the foregoing calculations it appeared the ratio of the two ketones produced from the glycols (I and II) and the aldehyde (III) should be near enough to unity to provide a minimum error. It was for this reason that the rearrangements of compounds I, II and III were chosen as the subject of the present research.

Examination of equation 1 reveals that because of its magnitude k_{Tol}/k'_H is perhaps the most crucial term involved in establishing an accurate k_T/k_P ratio. A minimum value for this ratio must be established, then, if we are to test the conclusion of Benjamin and Collins (1) that the migratory ability of the p-tolyl group is greater than that of phenyl. Benjamin and Collins (1) were unable to do this directly, and found it necessary to estimate the value by the indirect method mentioned in the foregoing discussion.

The purposes for which this research were undertaken have been achieved, in that 1) the p-tolyl/phenyl migration ratio in the rearrangement of aldehyde III in sulfuric acid has been shown to be greater than unity and 2) the general mechanism (1) for the aldehyde-ketone rearrangement has been supported for the system of compounds (I, II, III, IV and V) studied.

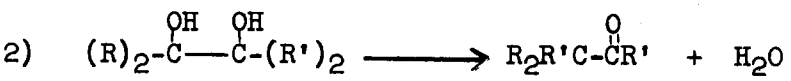
HISTORY

The pinacol rearrangement was discovered by Fittig in 1860. (12) Fittig had synthesized pinacol the previous year and found that upon treatment of the compound with sulfuric acid, the ketone, pinacolone, was produced. The feature of the reaction which was considered unusual at the time was the migration of a methyl group from one carbon atom to an adjacent one:



1)* $CH_3\text{-}\underset{\underset{CH_3}{|}}{\overset{\overset{OH}{|}}{C}}\text{—}\underset{\underset{CH_3}{|}}{\overset{\overset{OH}{|}}{C}}\text{-}CH_3 \longrightarrow CH_3\overset{\overset{O}{\|}}{C}\text{-}C(CH_3)_3$

Since the initial work of Fittig, numerous related conversions have been observed, under a wide variety of acidic conditions. The reaction is quite general for the 1,2 glycols (commonly called "pinacols" after the compound of Fittig), as evidenced by the following discussion, which is concerned with a selected few of the many such



2) $(R)_2\text{-}\overset{\overset{OH}{|}}{C}\text{—}\overset{\overset{OH}{|}}{C}\text{-}(R')_2 \longrightarrow R_2R'C\text{-}\overset{\overset{O}{\|}}{C}R' + H_2O$

rearrangements reported in the literature. On treatment of the glycol with acid, the product formed may be an aldehyde or a ketone, depending upon the nature of the groups, R, and the acid strength of the reaction medium. The reaction takes place when R is alkyl, aryl, part of an

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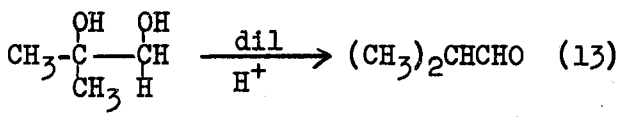
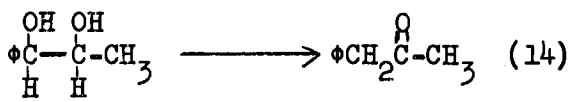
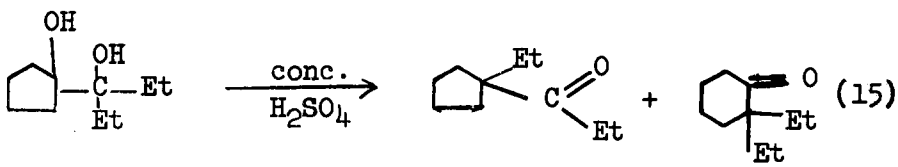
*The equations in this, and other sections are numbered independently; that is, the first equation in each section is numbered 1).

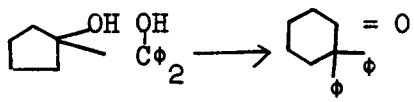
alicyclic structure, or hydrogen.

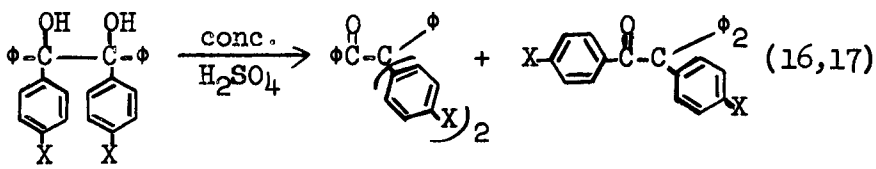
Examples of the generality of the rearrangement may be seen from the following examples:

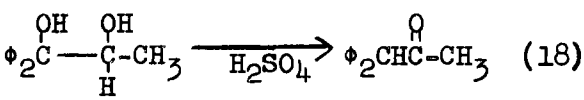
3)  (13)

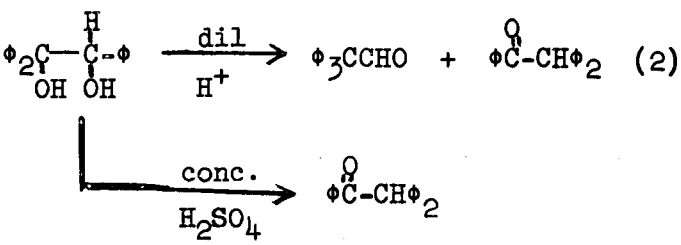
4)  (14)

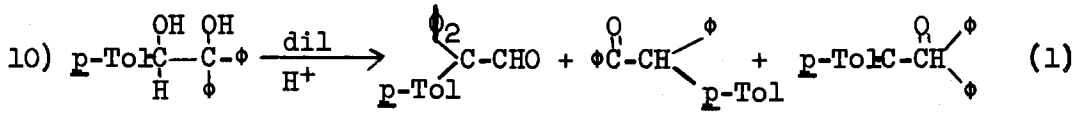
5)  (15)

6)  (15)

7)  (16,17)

8)  (18)

9)  (2)

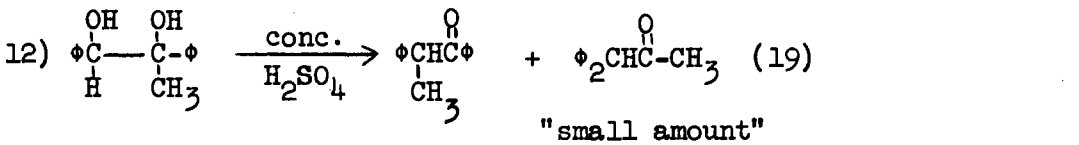


10) p-Tol(OH)C(H)—C(OH)(φ)-φ —dil, H+→ φ2C(p-Tol)-CHO + φC(=O)-CH(φ)(p-Tol) + p-TolC(=O)-CH(φ)2 (1)

" —conc. H2SO4→ " "

11) φC(OH)(H)—C(OH)(p-Tol)-φ —dil, H+→ " " " (1)

" —conc. H2SO4→ " "

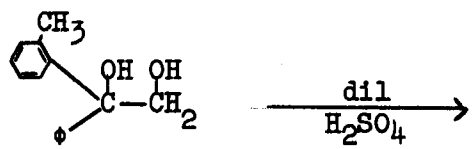


12) φC(OH)(H)—C(OH)(CH3)-φ —conc. H2SO4→ φCH(CH3)C(=O)φ + φ2CHC(=O)-CH3 (19)

"small amount"

The products of the rearrangement of glycols which are incompletely substituted may be aldehydes and/or ketones. Aldehydes are often produced when the reaction is catalyzed by weak acids or by dilute mineral acids and ketones alone are usually produced under strongly acid conditions or at high temperatures. In much of the early work the yields of the ketones produced were not accurately determined. In some reactions in which two ketones were produced, only one was isolated; often, because of its insolubility, that ketone formed in lesser yield was the only product identified. (1, 21) The aldehydes formed during these rearrangements are themselves convertible to ketones under the influence of strong acids, or of dilute or weak acids at elevated

temperatures, (1, 22-25) and thus the aldehyde-ketone rearrangement is known to be intimately related to that of the pinacols. Examples of the production of aldehydes (or aldehydes and ketones) in the presence of dilute or weak acids are seen in equations 3, 9, 10 and 11 and in the following cases:

13)  (26)

d — optically active

14) $\phi_2C(OH)-CH_2(OH) \longrightarrow \phi_2CHCHO$ (27)

15) $\phi-CH(OH)-C(CH_3)_2(OH) \xrightarrow[H_2SO_4]{dil} (CH_3)_2-C(\phi)-CHO$ (28)

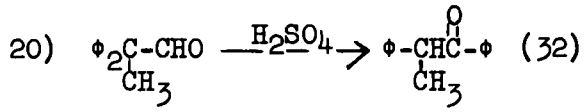
16) $\phi-CH(OH)-CH(OH)-H \longrightarrow \phi CH_2CHO$ (29)

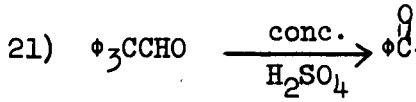
17) $\phi-CH(OH)-C(OH)(\phi)-H \longrightarrow \phi_2CHCHO$ (30)

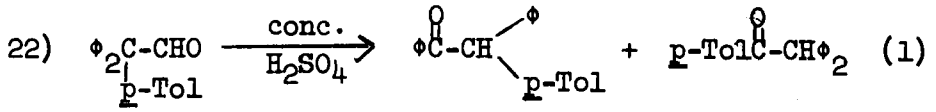
18) $(CH_3)_2C(OH)-CH_2(OH) \xrightarrow[180\text{-}200]{H_2O} (CH_3)_2CHCHO$ (31)

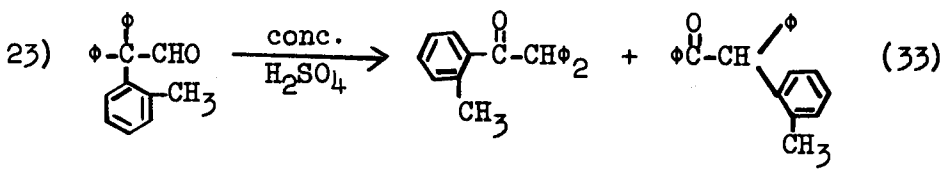
The conversion of aldehydes to ketones in the presence of strong acids may be illustrated by the following examples:

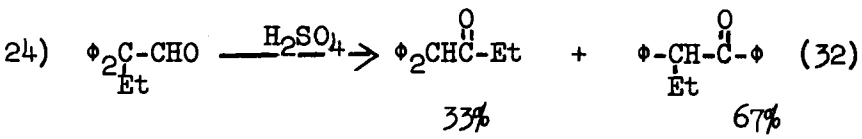
19) $(CH_3)_2-C(\phi)-CHO \longrightarrow (CH_3)CH(\phi)C(=O)-CH_3$ (32)

20)  (32)

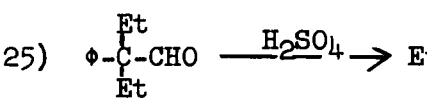
21)  (2)

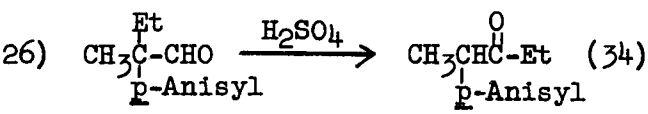
22)  (1)

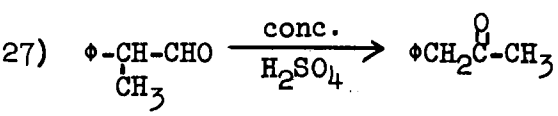
23)  (33)

24)  (32)

33% 67%

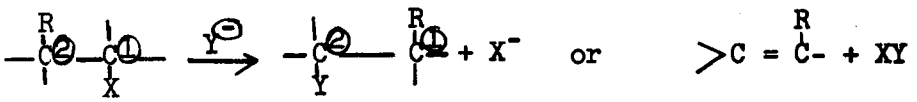
25)  (32)

26)  (34)

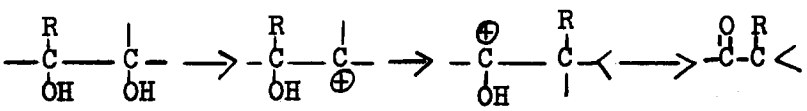
27)  (25)

Although discovered first, the pinacol rearrangement is in reality a Wagner-Meerwin type transformation. Wagner's (35) first example involved the transformation of isoborneol into camphene (equation 30). Wagner's correct interpretation of the course of the dehydration furnished the basis for the explanation of a variety of "1,2 shifts,"

as they are commonly named. (24) These reactions, historically classified under such names as Wagner, Meerwein, Nametkin, Demjanow, Pinacol and Tiffeneau, have recently been discussed by Ingold, Bartlett, Eliel and Cram. (23, 36-38) The Wagner-Meerwein type reaction may be formulated as:

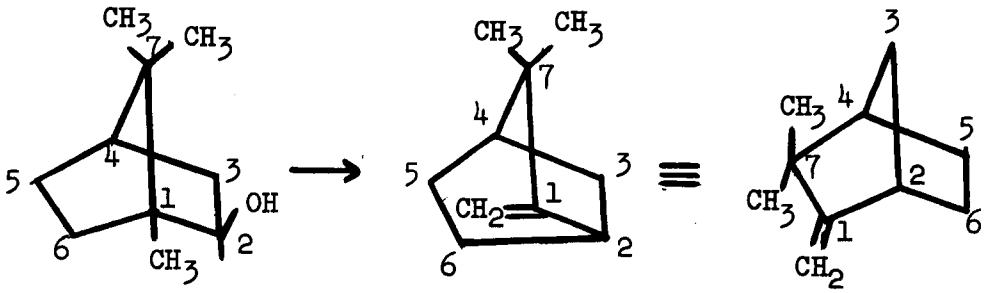
28)  or

where Y^- is the entering group or causative agent, X is the leaving group and R the group migrating during rearrangement. The relation of the pinacol rearrangement may be seen by a like formulation:

29) 

In order to understand the mechanism of this reaction, the effects of solvent, and of changing Y^- and X must be established. The stereochemistry about carbon-1, carbon-2 and R must also be known, as well as the electrical effects within the molecule. These factors will be considered at a later point in this discussion.

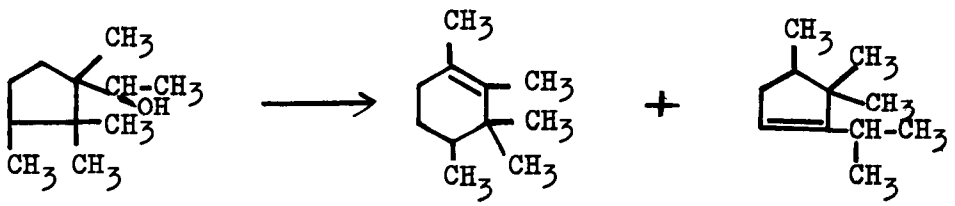
In the transformation of isoborneol to camphene, Wagner correctly interpreted the course of the dehydration to involve the breaking of the 1-6 carbon bond (equation 30) and the subsequent formation of a new bond between the 2 and 6 positions. Such a transformation requires that the 2-carbon position undergo a Walden inversion.(39)

30) 

isoborneol camphene

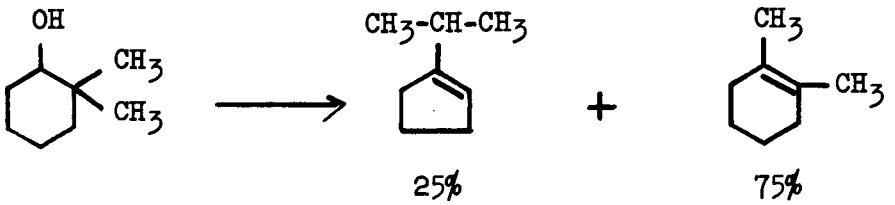
Further light was thrown on the problem some years after Wagner's observations by Meerwein, who observed that ring expansion (40) or

31) 

32) 

ring expansion methyl migration

ring contraction could occur during such dehydrations. (41)

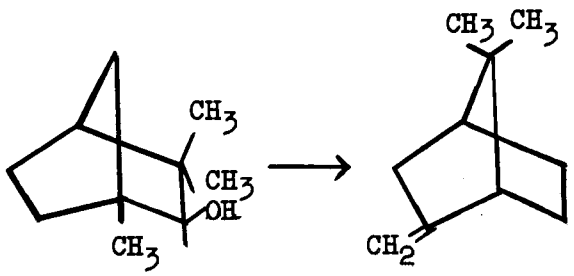
33) 

25% 75%

Nametkin, in a series of papers in 1915, (42-44) reported his

observations of a reaction quite similar to that reported by Wagner. For example, fenchyl alcohol, upon dehydration, was converted into α-fenchane, with bond migration analogous to that observed by Wagner.

34)

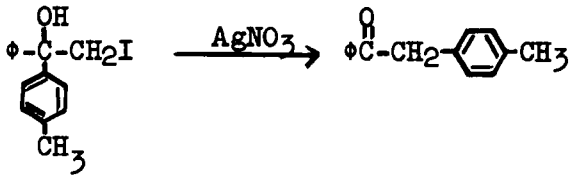


fenchyl alcohol α-fenchane

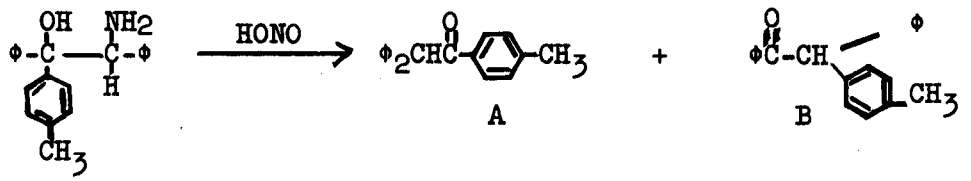
Demjanow, in the years 1902 to 1907, published a series of papers describing the results of his studies upon deamination reactions involving ring expansions. Thus cyclobutylmethylamine, when treated with nitrous acid, was observed to produce, in addition to the expected cyclobutylcarbinol, a considerable amount of the ring expansion product, cyclopentylalcohol. (45) Cyclohexylmethylamine gave cycloheptyl alcohol (46) and cyclopropylmethylamine gave a mixture of cyclobutyl alcohol and cyclopropylcarbinol (47) under similar conditions.

Of the other variations of the Wagner-Meerwein and pinacol transformations, the dehydrohalogenation reaction and the "semipinacol deamination," have been most studied. The dehydrohalogenation reaction may be illustrated by a transformation observed by Tiffeneau. (48) As can be seen in equation 35, the reaction proceeds through the elimination of the elements of hydrogen iodide and the migration of the

p-tolyl group.

35) 

The "semipinacol deamination" may be characterized by the reaction of 1,2-diphenyl-1-p-tolyl-2-aminoethanol when treated with nitrous acid. McKenzie (49) treated the optically active amine with nitrous

36) 

acid and obtained two products, one of which (B) was optically active, indicating that the reaction, in part at least, followed a stereo-specific course.

The mechanism of the pinacol rearrangement has been studied for many years. Erlenmeyer (50) suggested a cyclopropane intermediate, which required loss of a hydrogen atom from the migrating group. This mechanism was shown not to be possible in the case of aryl migration, by the work of Montagne, (51, 52) since loss of hydrogen from the ortho-position in a group with a para-substituent would yield a meta-substituent as the result of the shift. It was found that the para-substituent remained intact. In a more general way, Meerwein and van Emster (53) were able to disprove the cyclopropane intermediate idea in the Wagner-Meerwein rearrangement of isobornyl esters to

camphene--a case in which Erlenmeyer's proposition appeared to have a better chance of success. It was found that tricyclene, which is a cyclopropane derivative corresponding to the presumed cyclopropane intermediate for this reaction, could not be converted into camphene under conditions which isoborneol yields camphene smoothly.

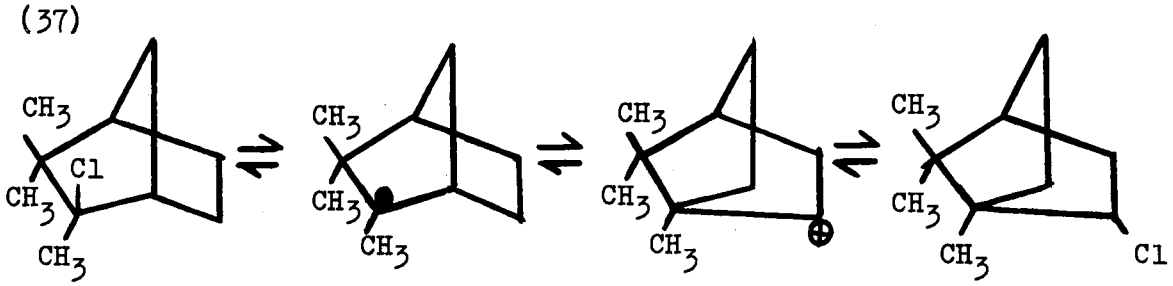
Breuer and Zincke in 1879 (30) proposed ethylene oxides as intermediates in the rearrangement. This mechanism has been disproved for the most part by Tiffeneau (54) and McKenzie (55) and their co-workers who found, in the dehydration of glycols, deamination of 2-amino-alcohols and dehydrohalogenation of 2-iodo-alcohols, that the oxide could not be isolated from an incomplete reaction, and yet the oxide was found to be sufficiently stable under the same conditions to have permitted its recovery, had it been formed. Moreover, Lane and Walters (56) observed that triphenylethylene oxide is easily convertible to the glycol under mildly acidic conditions. Gebhart and Adams (57) support this view but found that tetraphenylethylene glycol, in acetic acid catalyzed by perchloric acid, underwent rearrangement to the oxide to the extent of about 80%. This oxide, however, is not converted to the glycol under conditions which readily cause formation of triphenylethylene glycol from its oxide.

The free-radical hypothesis, as introduced by Tiffeneau (58) and used by McKenzie in the 1920's, (23) was proposed prior to the accumulation of much knowledge as to the properties of free radicals. Subsequently the theory has fallen into disuse, largely for two reasons. The first is the absence of chain reaction and polymerization products

characteristic of free radical reactions; and the second, the appearance of a much better theory due to Meerwein and van Emster in 1922.(53, 59)

Dependence upon ionization of the isobornyl chloride to camphene hydrochloride rearrangement was the key to Meerwein and van Emster's

(37)



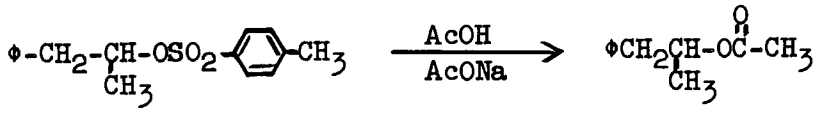
camphene-hydrochloride

isobornyl chloride

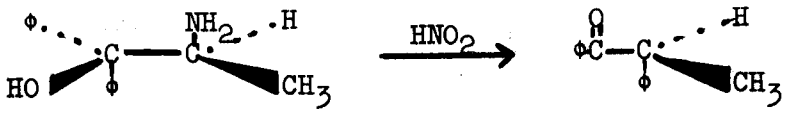
effort. This was strongly supported by these facts: 1) the kinetic rates depended upon the ionizing power of the solvent, 2) the relative rate orders in a number of solvents were essentially the same as had been found for the ionizing capacity of triphenylmethyl chloride, 3) the rate increased as the stability of the anion increased, and 4) compounds such as $HgCl_2$, $SbCl_5$, $SbCl_3$, $FeCl_3$, and $SnCl_4$, all known to form additive compounds with the triphenylmethyl chloride, were powerful catalysts for the rearrangement, whereas halides such as PCl_3 and $SiCl_4$, which do not yield such additive compounds, had no catalytic activity. This evidence leaves little doubt that the intermediate is ionic.

From the foregoing discussion it can be seen that a large number of the "1,2 shifts" which have been discovered are Wagner-Meerwein or pinacol rearrangements. Since elucidation of the Wagner-Meerwein

rearrangement has met with considerable success in recent years, the information obtained in these studies will be relied upon heavily in gaining an insight into the mechanism of the pinacol rearrangement.(60) Recent studies of the Wagner-Meerwein rearrangement have been conducted under conditions in which a specific type of ester interchange occurs. Although the hydrolysis and solvolysis of the esters of carboxylic acids generally involve the rupture of the acyl-oxygen bond, (61, 62) it has been shown by Cohen and Schneider that esters of the tertiary alcohol may undergo acid-catalyzed scission of the alkyl-oxygen bond, while the acyl-oxygen bond remains intact. Also Phillips (63) showed that the p-toluenesulfonate ester of 1-phenylpropanol-2 undergoes acetolysis to produce acetate which has undergone Walden inversion.(39) That both carbons 1 and 2 (equation 28) are normally inverted during

38) 

rearrangement, was shown by experiments such as the deamination of 1,1-diphenyl-2-aminopropanol (equation 39). (64, 65) Examples of similar

39) 

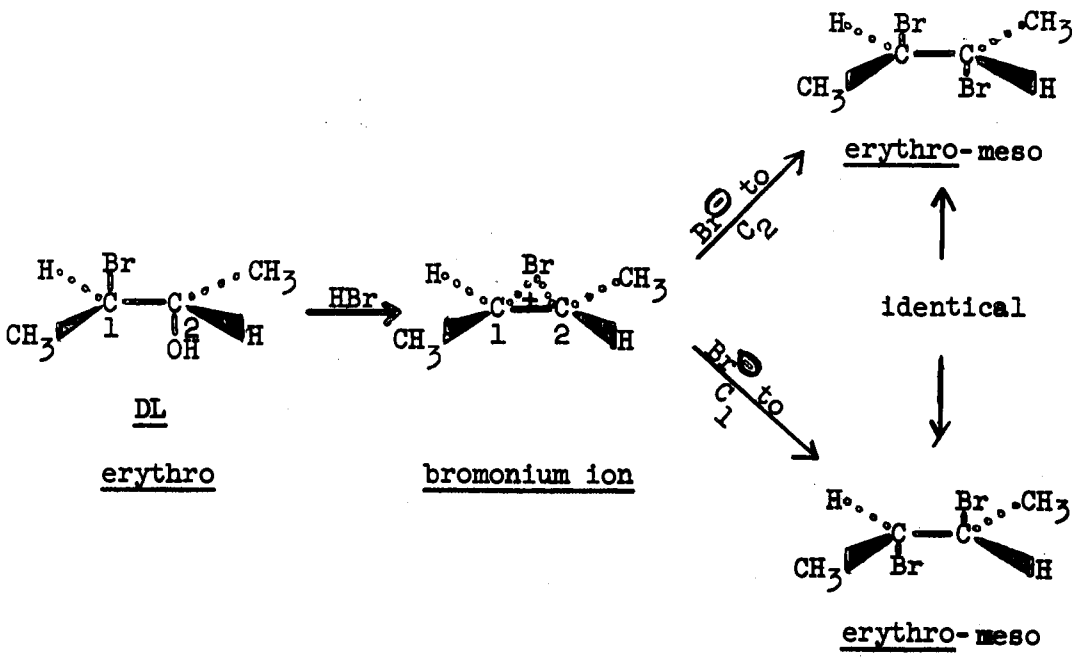
behavior in the pinacol rearrangement may be seen in the rearrangement of levo-1,1-dibenzyl-2-(1'-naphthyl) ethylene glycol to the optically-active 1,4-diphenyl-3-(1'-naphthyl) butanone-2 (66) in dilute sulfuric

acid, (26) and in the formation of optically-active 1,2-diphenyl-1,2-epoxypropane from levo-1,2-diphenyl-1,2-propanediol. (64) In each of these cases, however, the racemic ketones were obtained when concentrated sulfuric acid was used as catalyst.

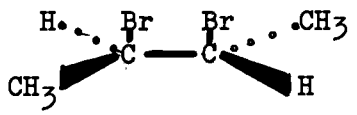
The migrating group itself retains its original configuration. This has been shown in the case of aryl groups many times, since the relative positions of substituents on the ring remains unchanged. Moreover, Lane and Wallis (67) have shown that in the related Wolff reaction a migrating group such as 2-phenylhexyl retains its original configuration.

A stereochemical method of investigating the Wagner-Meerwein reaction was proposed by Roberts and Kimball (68) and illustrated by Winstein and Lucas (69) in the treatment of racemic erythro-3-bromobutanol-2 with hydrogen bromide. Because the product was the erythro

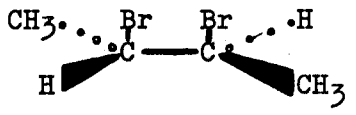
40)



compound and not the threo racemate, the bromonium ion was postulated.



threo-D

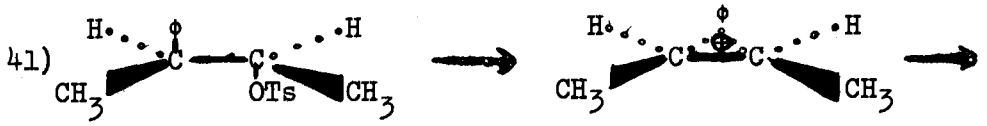


threo-L

This ion could then suffer attack by bromide ion on the back side of either of the two central carbon atoms to yield the erythro compound. If the planar carbonium ion had been the intermediate, it would have been expected that some of the threo racemate should be formed. In like manner, the racemate of threo-3-bromobutanol-2 gave only the DL dibromide.

Cram (70, 71) applied this principle to the acetolysis of the tosylates of the isomeric 3-phenyl-2-butanols. Since the threo

41)

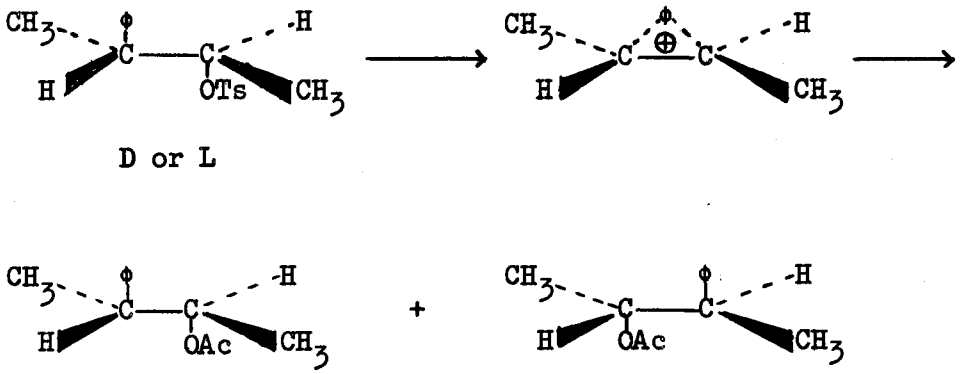


D or L

DL pair

threo

tosylate was not converted to any significant amount of the products of

42) 

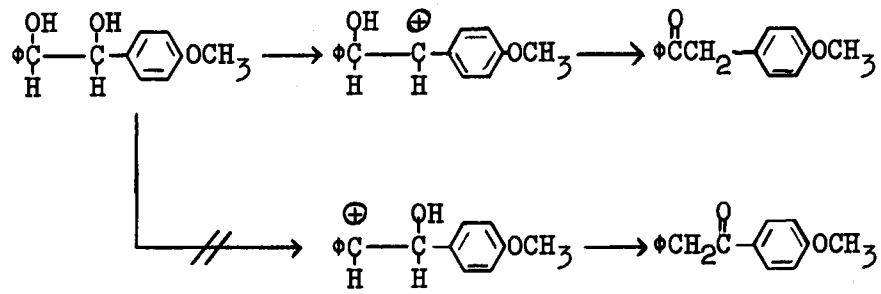
D or L

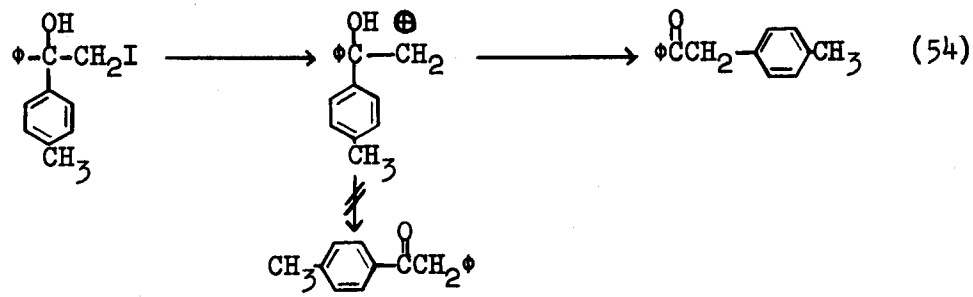
identical

erythro

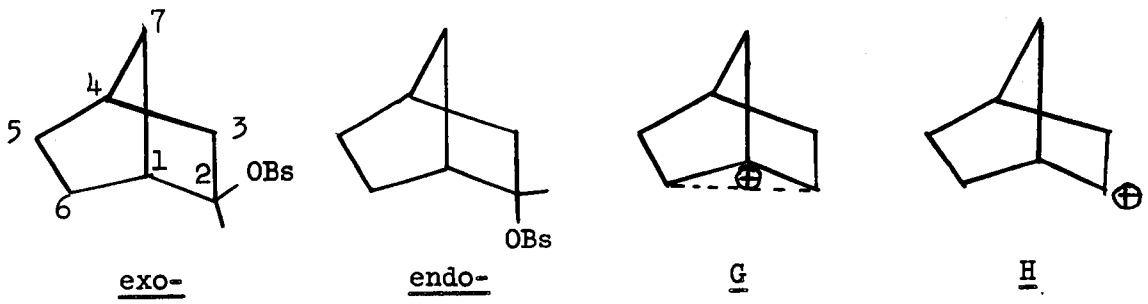
the erythro tosylate and the erythro tosylate was not converted to the products of the threo tosylate, Cram reasoned that rotation about the two central atoms was restricted, and thus that classical, planar, open carbonium ions could not be intermediates in these reactions. In order to account for the results, Cram postulated the bridged phenonium ion as the configuration-holding intermediate in the reaction sequence. Similar bridged-type ions had been suggested on theoretical grounds by Nevell, deSalas and Wilson (72) and others. (73-77)

The electrical effects of the groups within the reactant may control the course of the reaction and determine which of two groups will migrate (equations 43 and 44). (11, 78) These effects may also accelerate the reaction rate. Winstein, et al., (79) has shown that the exo-p-bromobenzene sulfonate of norborneol undergoes acetolysis at

43)  (78)

44)  (54)

a rate 350 times greater than the rate at which the endo-isomer acetolyzes. This fact, plus the fact that both exo- and endo-esters



exo- endo- G H

norbornyl-
p-bromobenzene sulfonate

yielded, upon solvolysis, exclusively exo-products, seemed to indicate that ion G could be an important intermediate in the solvolysis of the exo-form, since carbon-6 is conveniently situated for participation in the rate-determining loss of p-bromobenzenesulfonate ion. Such direct

participation does not appear possible in the case of the endo isomer, although it is possible, of course, that ion G could be formed in this instance subsequent to formation of ion H.

The most striking example of "Neighboring Group Participation," as this phenomenon is known, is to be seen in the rate enhancement in the acetolysis of a series of substituted ethanol tosylates. (80) That the

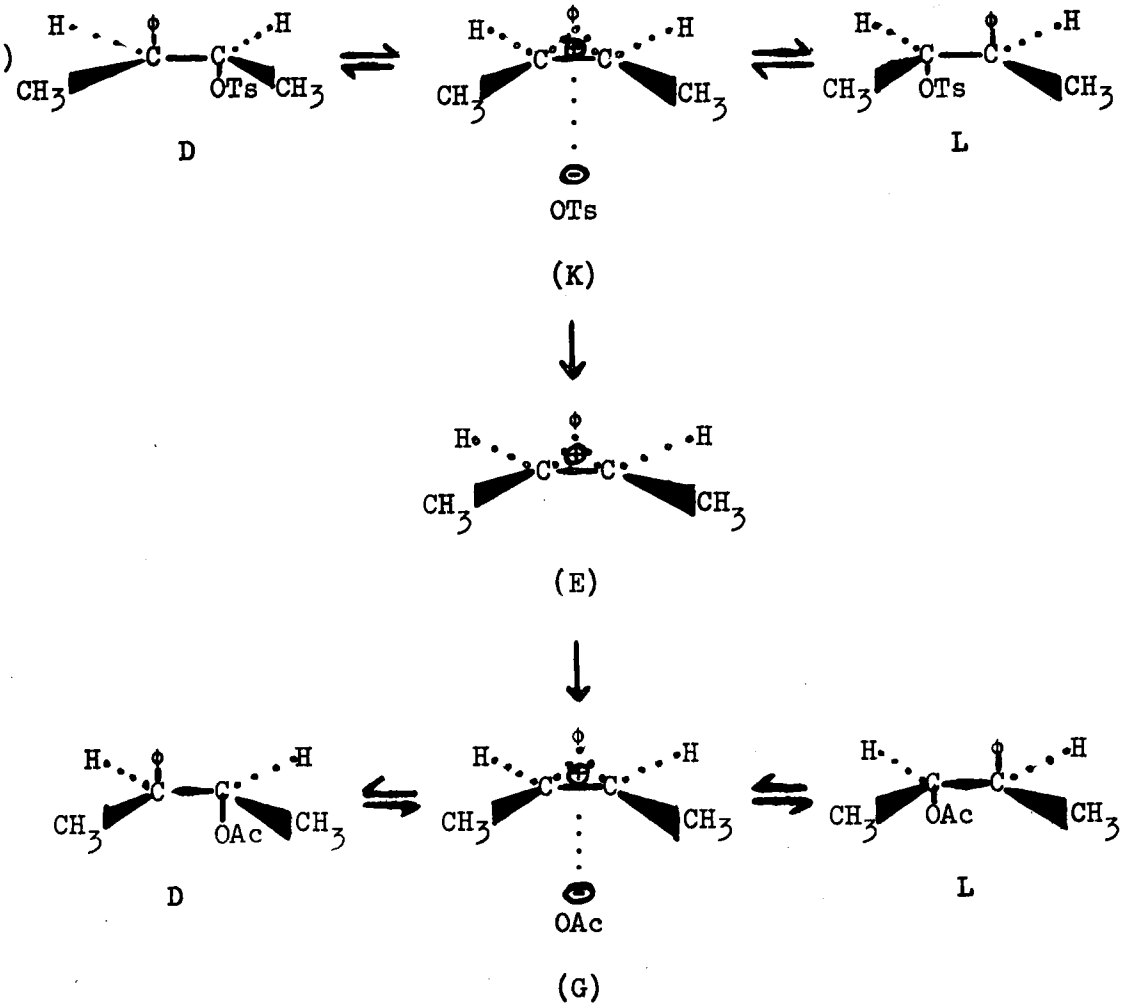
Ethanol tosylate	Relative k
$(CH_3)_2C\text{-}CH_2OTs$	1
ϕ_2CHCH_2OTs	53
$(CH_3)_2\overset{\phi}{\overset{\vert}{C}}\text{-}CH_2OTs$	460
ϕ_3CCH_2OTs	7.7×10^3

participation of an adjacent group may, at times, control the stereochemical course of a reaction is illustrated by the bridged ion concept, discussed previously.

In an extension of his study of the acetolysis rates of the exo- and endo-p-bromobenzenesulfonates of norborneol, Winstein (81) observed that the optically active exo-ester exhibited a racemization rate which was faster than the acetolysis rate. This phenomenon was later found to occur also in the solvolysis of 3-phenyl-2-butyl-p-toluenesulfonate (82, 83) and of 2-phenyl-1-propyl-p-bromobenzenesulfonate. (84, 85) This phenomenon is called "internal return" and can be illustrated with the acetolysis 3-phenyl-2-butyl-p-toluenesulfonate. The ion pair (K),

postulated to explain internal return in this system can collapse

45)



reversibly to give the D or L tosylate, or irreversibly to give ion-pair (G). If then, internal return is faster than the rate of formation of ion-pair (G) and subsequent irreversible collapse to D or L acetate, then the racemization rate will be greater than the solvolysis rate.

When 2-phenyl-2-(p-tolyl)ethylamine is deaminated, the product is

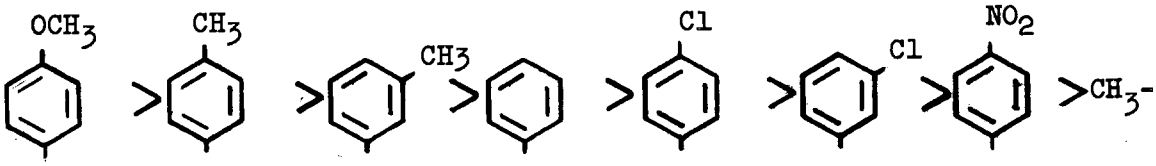
found to consist primarily of two carbinols, 1-phenyl-2-(p-tolyl)-ethanol and 2-phenyl-1-(p-tolyl)ethanol; (86) the former, due to p-tolyl migration, is present in larger amount. In this case the ratio of the yields of products is a ratio of the relative abilities of the two groups to migrate during the rearrangement. Such ratios are termed variously, "migratory abilities," "migratory tendencies," or "migratory aptitudes," and imply a ratio of the ability for the group under discussion to migrate, compared to the ability of some reference group to migrate, given the same environment, the phenyl group being most often used as the reference group.

An enormous amount of work has been performed in attempts to place the more commonly observed migrating groups into some relative order, and to assign some approximate value for the migratory aptitude of each. Such a compilation would have the obvious utility of allowing some prediction to be made regarding the relative yields of products, when several may be anticipated. Among the early investigations carried out with this object in mind, was that of P. J. Montagne, who reviewed the work to 1920 that had been performed in the field of intramolecular migrations. (87) Working with the symmetrical pinacols of the type RΦC(OH)C(OH)ΦR, Montagne found the ratio of ketone formed by phenyl migration to that with R migration, to be, when R was p-chlorophenyl, 60:40; when R was p-bromophenyl, 57:43.

That some progress has been made in this direction can be illustrated, for example, in the controversy which occurred subsequent to the publication of the results for the deamination of 2-phenyl-2-

(p-tolyl)ethylamine. (88, 89) It was soon pointed out by Curtin (10) that the p-tolyl/phenyl migration ratio of approximately 0.9 reported was probably incorrect. A re-examination of the course of the reaction (86) showed that this was the case and that the p-tolyl/phenyl migration ratio was greater than one. This was a result predictable on the basis of values found previously, for example, for the symmetrical pinacols, 16; (3, 4) for the acetolysis of 2-phenyl-2-(p-tolyl)ethyl tosylate, 2.5; (5) for the dehydration of 2-phenyl-2-(p-tolylethanol, 2.0; (6) for the Schmidt reaction, 3.4 to 5.0; (7-9) for the deamination of 2-amino-1-phenyl-1-p-tolylethanol, 1.3. (10)

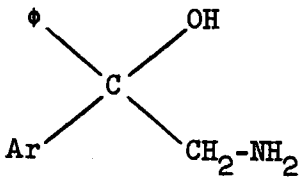
Assignment of relative migratory aptitudes of a number of migrating groups may be compiled. When steric requirements are not determining, this order always holds for rearrangements other than the pinacol



and aldehyde-ketone. (4, 16, 90)

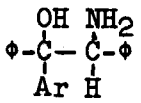
Evidence for the relegation of the electronic nature of the migrating group to a position of secondary importance in certain reactions, has been presented by Curtin and his co-workers, for reactions involving the deamination of the triarylethanolamines. (10, 91-95)

In studies (10, 96-99) of the rearrangement during deamination of aminoalcohols of the type,



ketones of the type $\phi C(=O)-CH_2Ar$ were found to be formed. The ratios of products were qualitatively in the order of the migratory aptitudes for these groups as found by Bachmann, Moser and Ferguson (4, 16) in their studies of the tetra-substituted, symmetrical ethylene glycols.

When, however, Curtin deaminated the diasteromers of the amino-alcohols of the type,



(there are now <u>two</u> asymetric centers--hence two <u>dl</u> pairs), it was found that the migratory aptitudes for the groups in different diastereomeric pairs were not the same. Thus, the <u>erythro</u> pair rearranged to give the ketone with Ar migration, while the <u>threo</u> pair gave the ketone formed by phenyl migration. That the electronic nature of the migrating group was of secondary importance was indicated by the observation that the aryl group, in the <u>erythro</u> pair always migrated whether it was <u>p</u>-tolyl, <u>p</u>-anisyl, <u>p</u>-chlorophenyl or <u>α</u>-naphthyl. (100, 101) The <u>threo</u> pair in all cases gave phenyl migration. Curtin accounts for these observations by suggesting that there is a back-side attack by the migrating group upon the carbon atom from which the amino group is being removed

through a transition state or bridged ion in which the large, bulky, non-migrating groups are in a trans-configuration.

In a series of papers beginning in 1953, Collins and Bonner, (102, 103) in a study of the Wagner-Meerwein Reaction for the 1,2,2-triphenylethyl system, showed that the bridged phenonium ion could not be the intermediate in the transformations observed. The data required the postulation of open-equilibrating carbonium ions, or their equivalent, to explain the distribution of the carbon-14 labels that was observed.

The observations which forced this conclusion may be summarized in this way:

1) Formic acid, to which a catalytic amount of p-toluenesulfonic acid had been added, caused statistical distribution in both the discretely chain- and ring-labeled 1,2,2-triphenylethanol and its acetate (the bridged ion requires 50:50 distribution of the carbon-14 in the ring-labeled compounds, whereas statistical, 2/3-1/3 distribution was observed).

2) Carbon-14 distribution in the p-toluenesulfonate esters of the alcohol, which was not statistical in either the chain- or ring-labeled compounds, could be exactly calculated, one from the other, by means of the rate expressions in a mechanism involving competition between the initial ion formed and its direct conversion to product on the one hand, and its equilibration, with subsequent conversion to product on the other.

3) Examination of the rates of chain- and ring-label equilibration and the rate of labeled acetoxyl loss from the 1,2,2-triphenylethyl acetate, proved that in each instance of acetoxyl loss, a molar equilvalent amount of chain- and ring-label equilibration occurred. These observations indicate, a) that no internal return (74, 81) occurs since this would require a slower rate for acetoxyl loss than for chain- and ring-label equilibration; b) that bridged ions cannot be intermediates since this would require that the rate of chain-label equilibration be faster than the rate of ring equilibration; and c) that completely concerted migration of the phenyl group is excluded since this would require that the rate of loss of acetoxyl be half the equilibration rate of the chain-labeled acetate and the rate of equilibration of the ring-labeled acetate be 3/2 the rate of acetoxyl exchange, whereas the three rates observed are the same.

As has already been noted, the conversion of substituted acetaldehydes into ketones through the agency of dilute acids at elevated temperatures or by means of concentrated mineral acids, has been taken as evidence of the relationship of this rearrangement to that of the pinacol rearrangement. The nature of the relationship, however, has been quite obscure in view of the migratory aptitudes exhibited by the substituent groups in the related rearrangements, discussed earlier in this presentation. Some of the anomalous observations may be illustrated with the following examples:

Equation No.	19	Me > φ
	20	φ > Me
	22	φ > p-Tol
	24	φ/Et = 4/1
	25	Et exclusively
	26	Et > p-anisyl

For additional examples of the apparently quite general phenomenon, see references 23, 24, 32 and 104 through 107.

In an effort to obtain sufficient information to allow correlation between the pinacol and aldehyde-ketone rearrangements, Collins (2) has investigated the rearrangements of triphenylethylene glycol and triphenylacetaldehyde, variously labeled with C^{14}. Using the general mechanism formulated by previous investigators (33, 49, 97, 108, 109) and applying the idea of open carbonium ions, Collins was led to propose a mechanism involving 4 reaction paths, which included the conjugate acid of triphenylacetaldehyde and which adequately explained the distribution of the C^{14} label which was observed. In an extension of this work, Benjamin and Collins (1) were able to link the pinacol rearrangements of 1,1-diphenyl-2-p-tolylethylene glycol, 1,2-diphenyl-1-p-tolylethylene glycol and the aldehyde-ketone rearrangement of diphenyl-p-tolylacetaldehyde through the conjugate acid of the aldehyde. These authors were able to show that the true p-tolyl/phenyl migration ratio was not given by the ratio of ketonic products (these indicate phenyl migration in preference to p-tolyl), but rather was given by the

ratio of the specific rate constants as defined in the equation

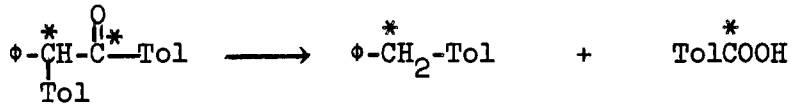
$$\frac{k_T}{k_P} = \frac{k_H}{k_\phi} \cdot \frac{k_{Tol}}{k'_H} \cdot \frac{m_e}{m_d} \quad \frac{1 + \frac{k'_H}{k_{Tol}}}{1 + \frac{k_H}{k_\phi}}$$

The significance of this relation is developed in the Discussion Section of this presentation where these ideas are applied in an identical manner in the explanation of the results obtained in this research.

METHODS AND RESULTS

The syntheses of the carbon-14 labeled compounds were accomplished as shown in Charts III, IV, V, and VI. The nonradioactive ketones IV and V were prepared by adding the diarylcadmium reagent to the appropriate diarylacetyl chloride; the aldehyde, III, was formed upon stirring threo-Ic in 90% formic acid for three days. Each of the glycols used in this research was subjected to cleavage with lead tetraacetate and the fragments were examined for radioactivity, in order to prove the position of the carbon-14 label. All were found to be discretely labeled in the positions indicated except for erythro-Ib, which contained 8.1% of the label in the tertiary carbon. Appropriate corrections have been made in the tables for this small but significant percent of carbon-14 in the number 1 chain position of erythro-Ib.

The aldehyde, III, and the glycols, erythro-Ib, threo-Ib, threo-Ic and IIa, were subjected to rearrangement in concentrated sulfuric acid at 0° C. Glycols Ic and IIa also were subjected to rearrangement in formic acid at room temperature. The yields of IV and V, and in the case of the formic acid rearrangements, III, were determined by the radioactivity dilution method. The results of these experiments are given in Tables II and III. The crystalline ketones obtained as a result of the sulfuric acid rearrangements were cleaved with alkali:



IVab Vb

CHART III

Preparation of threo-1,2-di-p-tolyl (2-p-methyl-C^{14})-1-phenylethylene Glycol (Ic)

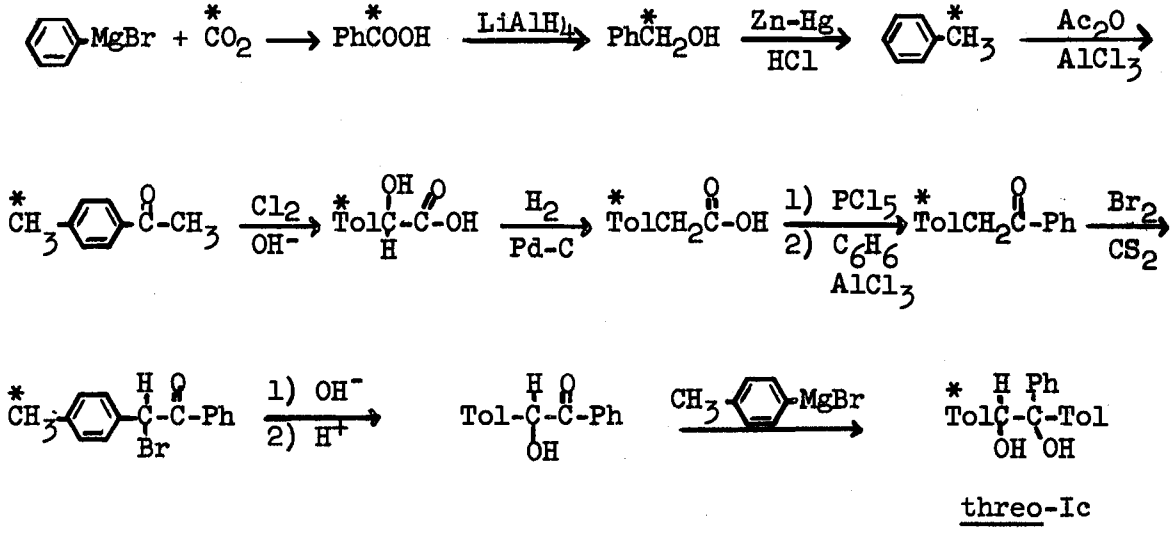


CHART IV

Preparation of threo-1,2-di-p-tolyl-1-phenylethylene-2-C^{14} Glycol (Ib)

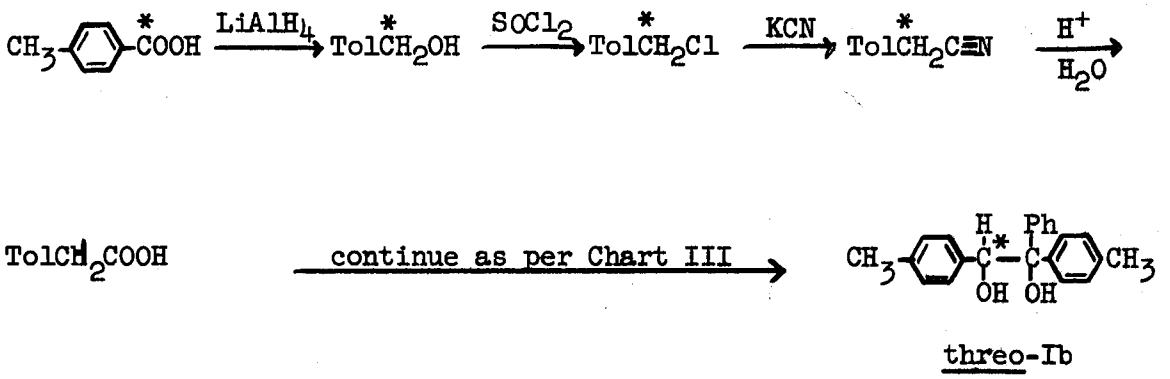
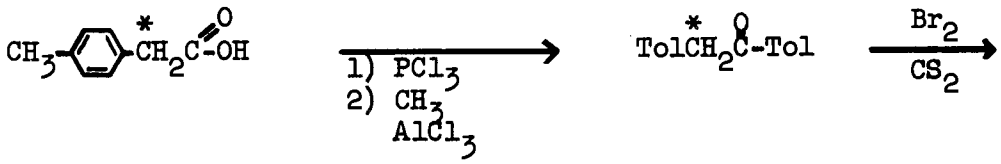
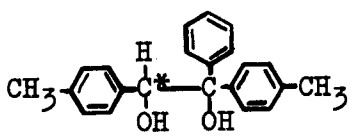


CHART V

Preparation of erythro-1,2-di-p-tolyl-1-phenylethylene-2-C^{14} Glycol (Ib)

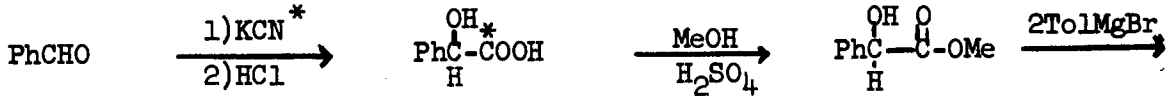


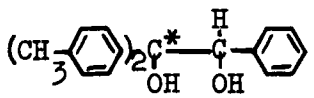


erythro-Ib

CHART VI

Preparation of 1,1-di-p-tolyl-2-phenylethylene-1-C^{14} Glycol (IIa)





IIa

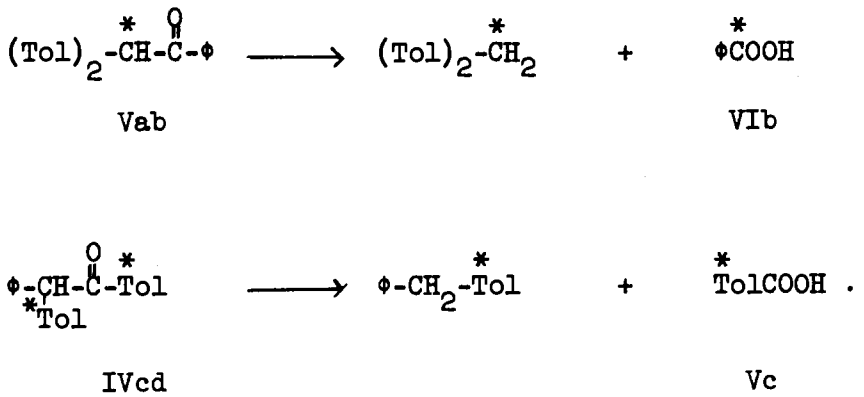
TABLE II

Yields of Ketones IV and V Produced by the Action of Sulfuric Acid Upon I, II, and III

Run No.	Reactant	Yield of Ketone (%) IV	V
1	threo-Ib	58.0	42.0
2	threo-Ic	59.6	40.4
3	threo-Ic	58.3	41.7[a]
4	threo-Ic	58.4	41.6
5	threo-Ic	57.3	42.7
Average		58.3	41.7
6	IIa	49.6	50.4[a]
7	IIa	47.1	52.9
8	IIa	48.0	52.0[b]
Average		47.6	52.4
9	III	53.5	46.5
10	III	53.2	46.8
Average		53.4	46.6
11	erythro-Ib	53.4	46.6

[a]Reactions performed at 10° C. Results not included in averages.

[b]IV determined by dilution technique, total ketone by weight and V by difference.



Vab VIb

IVcd Vc

The benzoic and p-toluic acid fractions obtained upon cleavage were in all cases carefully purified by crystallization and sublimation.

TABLE III

Yield of Aldehyde III, Produced by the Action of Formic Acid Upon Glycols I and II

Run No.	Reactant	Actual Yield (%) III	Yield of III Corrected for 94.1% Recovery
12	threo-Ic	75.9	80.6
13	IIa	33.9	36.0
14	III	94.1	

The neutral, diarylmethane fractions from the cleavages of IVab and Vab were oxidized with chromic acid:

$$\phi\text{-}\overset{*}{C}H_2\text{-Tol} \xrightarrow[HOAc]{CrO_3} \phi\text{-}\overset{O}{\overset{\|}{C}}\overset{*}{}\text{-}\phi\text{-COOH}$$

VIIa

$$\text{Tol-}\overset{*}{C}H_2\text{-Tol} \xrightarrow[HOAc]{CrO_3} \text{HOOC-}\phi\text{-}\overset{O}{\overset{\|}{C}}\overset{*}{}\text{-}\phi\text{-COOH} .$$

VIIIa

The acidic products VIIa and VIIIa were purified carefully by crystallization. The acid degradation products V, VI, VII, and VIII were assayed for carbon-14 content, the results of these being recorded in Tables IV and V.

TABLE IV

Fraction of Radioactivity Found in Vc from Cleavage of IVcd Derived From the Rearrangement of threo-Ic

Run No.	Activity in Vc
2	0.478
2	0.476
3	0.483
4	0.492
5	0.512
5	0.496
Average	0.490

TABLE V

Fraction of Radioactivity in Fragments From Cleavage of IVab and Vab Resulting from Rearrangements of Threo-Ib, Erythro-Ib, and IIa

		From IVab		From Vab	
Run No.	Reactant	Vb	VIIa	VIb	VIIIa
1	threo-Ib	0.961	0.039	0.973	0.026
9	IIa	0.018	0.980	0.008	0.955
10	IIa	0.010	-	0.009	-
11	erythro-Ib	-	0.010	-	0.139
16	threo-Ib	0.980	0.021	0.986	0.014

DISCUSSION

The equation (equation 1) given in the Introduction was developed (1) in an effort to correlate the observed fates of the various carbon-14 labels during the acid-catalyzed rearrangements of several triarylsubstituted ethylene glycols and acetaldehydes. The reasons for extending the investigation to the compounds treated in this research have been discussed in the Introduction and are concerned with a determination of the generality of equation 1 when applied to closely-related systems. Accordingly, Charts I and II represent the rearrangement mechanism for compounds I, II and III as postulated by Benjamin and Collins for the system of compounds they studied. (1) Similar symbols for the various specific rate constants have been used so that equation 1 retains its original form. The derivation of equation 1, as applied to this research, is to be found in the Experimental Section. No steady state assumption (110) is necessary in the derivation.

It should be pointed out that equation 1 is applicable only to that portion of the pinacol rearrangement which proceeds through tertiary hydroxyl removal (paths C through E), and the aldehyde-ketone rearrangement.

The determination of the components for equation 1 may be deduced from an examination of Charts I and II. For the ratio, k_{Tol}/k'_H, the sum of the yields by paths D and E is divided by the yield of path C. If we now define m_a, m_b, m_c, m_d, and m_e, respectively, as the mole frations of threo- and erythro-Ic which proceed to products through

paths A to E (Chart I), k_{Tol}/k'_H then is equal to $m_d + m_e/m_c$. In like manner, the ratio k_H/k_ϕ is obtained by the relation $m_{e'} + m_{d'}/m_f$ (Chart II). The ratio m_e/m_d may be obtained in two ways: 1) From the double-labeling results in the rearrangement of threo-I, the total $m_c + m_e$ is determined by the yield of $Tol\overset{*}{C}OOH$ from threo-Ib, while the total $m + 1/2m_e$ is determined from the yield of $\overset{*}{Tol}COOH$ from threo-Ic. Solution of the simultaneous equations can give the value for m_e. Since the yield of V gives the total $m_a + m_d$, then subtraction of the yield of m_a, as determined by the activity in $O{=}\overset{*}{C}(\phi COOH)_2$, gives m_d; 2) The ratio of the yields IV/V from the rearrangement of aldehyde III, also gives m_e/m_d. Both methods should give the same ratio within the experimental error, if the mechanism of Chart I is to explain the observed carbon-14 distribution during rearrangement. In order to obtain the p-tolyl/phenyl migration ratio upon solution of equation 1, it is necessary to divide k_T/k_P by 2, since the rearranging system under study involves two p-tolyl groups and only one phenyl group.

The implications of the pertinent data of the preceding section may now be considered. Tables II through V reveal the yield of each ketone produced from the different reactants, as well as the fates of the various carbon-14 labels. The mechanism given in Charts I and II accounts for these facts. The consequences of both p-tolyl and of chain labeling are indicated.

For the threo-I glycol may now be calculated the contributions of each of the reaction paths. There are several different methods, some of which are nearly independent one of the other, by which these

calculations may be made. Since it is the purpose of this research to determine, by use of equation 1 (see Introduction), whether, in the rearrangements of I, II, and III the p-tolyl/phenyl migration ratio is greater than one, we have, for this purpose, treated the data of Tables II through V in two different ways: 1) in the first method the yields of IV and V from the rearrangement of di-p-tolylphenylacetaldehyde (III) have been ignored, and the averages of the measurements pertaining to the three glycols have been employed to calculate the various path yields; 2) in the second method the same data were used as in the first. We have taken account, however, of the errors probable in each of the measurements of Tables II through V, and have made the assumption that all of the errors accumulate in m_c, since the determination of a maximum value for m_c is crucial in estimating, from equation 1, a minimum p-tolyl/phenyl migration ratio.*

The results of the foregoing calculations are given in Table VI, and the values for k_H/k_ϕ, k_{Tol}/k'_H and the p-tolyl/phenyl migration ratio ($k_T/2k_P$) estimated from each set of calculations are given in Table VII. Actual sample calculations of the type used in obtaining the results in the tables are given in the Experimental Section.

It is interesting to observe that the threo- and erythro- configurational isomers of I rearrange to give slightly different yields of IV

---

*There is another general method by which the path yields and rate-constant ratios may be calculated, namely through the use of the ratio (1.15) of ketones IV:V produced from the rearrangement of aldehyde III (Table II). This method is much inferior to methods 1 and 2 for it involves subtraction of large numbers in determining the very small m_c and is thus extremely sensitive to small changes in the percentages of ketones produced. This is not true for methods 1 and 2.

TABLE VI

Summary of Mole-Fraction Calculations From the Data of Tables II Through V

Mole Fraction	Method of Calculation 1 threo-I	1 erythro-I	2 threo-I	2 erythro-I
m_a	0.008	0.065	0.011	0.065
m_b	0.018	0.005	0.023	0.005
m_c	0.005	(-) value	0.046	0.020
m_d	0.409	0.401	0.406	0.401
m_e	0.560	0.541	0.514	0.509
	For Glycol II			
m_f	0.177		0.169	
m'_d	0.347		0.355	
m'_e	0.476		0.476	

TABLE VII

Summary of the Ratios Calculated for use in or by Equation 1

Ratio	Method of Calculation 1	2
m_e/m_d	1.37	1.27
k_ϕ/k_H	4.7	4.9
k_{Tol}/k'_H from threo-I	190	20
$k_T/2k_P$ from threo-I	25	2.25
k_{Tol}/k'_H from erythro-I	∞	45
$k_T/2k_P$ from erythro-I	∞	5

and V. That this result is due mostly, if not entirely, to different contributions of paths A and B in the two cases may be demonstrated by comparing the ratios of $(m_c + m_e)/m_d$, for the rearrangements of threo- and erythro-Ib, in which the total $(m_c + m_e)$, is determined by the yield of Tol$\overset{*}{C}$OOH (Vb) in each case. From the threo isomer this is 0.566/0.408 = 1.385, whereas for the erythro isomer it is 0.529/0.401 = 1.32. These ratios are the same within experimental error. Additional support for this explanation is the reversal in relative contributions of paths A and B in the threo and erythro isomers. These values are sufficiently large to preclude their reversal by experimental error

alone. It then is apparent that the aryl group added by means of the Grignard reagent to the appropriate benzoin is not the predominantly migrating group when the rearrangement proceeds through secondary hydroxyl removal, i.e., insofar as the reaction proceeds through paths A and B, it is stereospecific. (91-95) Benjamin and Collins (1) were not able to observe this phenomenon because with the isomers of 1,2-diphenyl-1-p-tolylethylene glycol, there was too little secondary hydroxyl removal to allow them to differentiate paths A and B.

Examination of the p-tolyl/phenyl migration ratios listed in Table VII makes it clear that an exact value for the ratio cannot be given for the reactions under study. The significant point is, however, that when even extreme values, deliberately chosen, are used as the components of equation 1, the minimum value for the p-tolyl/phenyl migration ratio is found to be greater than one, and the most probable value, based upon average values for the components is in the range of three to five.

Additional support for a somewhat higher value for k_{Tol}/k'_H, than the minimum of 20, is found in the rearrangement of tri-p-tolylethylene glycol, (111) where it is found, if the assumption is made that the contribution to the product through secondary hydroxyl removal is of the same order of magnitude as found for the erythro-Ib above, that the k_{Tol}/k'_H must be at least 25. Moreover in the rearrangements of threo-Ic and IIa in formic acid, when the k_{Tol}/k'_H and k_ϕ/k_H values are treated in the same way as previously reported, (1) it is found that k_{Tol}/k'_H in concentrated sulfuric acid is 37.5.

In view of the experimental errors that have been discussed, the values for the ratios and the yields of ketones produced in both sulfuric and formic acids agree with those predicted in the Introduction better than expected. In addition, even though the simple ratio of ketones obtained from aldehyde III indicates the p-tolyl/phenyl migration ratio to be less than one, solution of equation 1 for this system shows that the most probable value is significantly greater than one, in agreement with previous observations. (3-10) It is important also to note that the variations in the relative amounts of ketones from the glycols and aldehyde are successfully predicted by equation 1. The results of this research, therefore, provide strong evidence in support of the mechanism for the pinacol rearrangement proposed by Benjamin and Collins, (1) and in addition provide a possible explanation for the occasionally observed, partially stereospecific course of the rearrangement. (26, 49, 100, 101, 66)

EXPERIMENTAL

Radioactivity Determinations and the Radioactivity Dilution Method of Yield Determinations.

The radioactivity assays reported in this dissertation were performed on a vibrating reed electrometer, using the wet combustion procedure which was described by Neville (112) and modified by Bonner and Collins. (113) This method has also been described by Raaen and Ropp. (114)

The calculation of the yields of the reaction products by the carbon-14 dilution method was performed by means of the equation: $A_1 (D_1 + X) = A_0X$: where

A_0 = molar activity of the starting material = molar activity of undiluted product for which calculation is to be made.

A_1 = measured molar activity of purified, diluted product.

D_1 = weight of nonradioactive analog added.

X = weight of radioactive product with molar radioactivity equal to A_0.

This technique was discussed by Mayor and Collins. (115) The mechanics of the actual dilutions were performed in the manner described in the section next below.

Sulfuric Acid Catalyzed Rearrangements.

In a typical experiment 3.082 gm. of glycol or aldehyde was added to 70 ml. of concentrated sulfuric acid, previously cooled to 0° C. in an ice-salt bath. Stirring was continued while the temperature was

maintained between -2° to 0° C. At the end of 30 minutes, the reaction mixture was poured into 700 ml. of ice-water mixture with vigorous stirring. The mixture was extracted five times with 100 ml. portions of ether in a separatory funnel and the combined ether extracts were washed twice with 100 ml. portions of water, once with 50 ml. of saturated aqueous sodium bicarbonate and again with 100 ml. of water. The ether solution was then evaporated to dryness on the steam bath, the residue dissolved in chloroform, transferred quantitatively to a 100 ml. volumetric flask and dilution to 100 ml. made with chloroform. One 50 ml. aliquot was transferred to a flask containing 2.000 gm. of nonradioactive ketone IV and the remaining 50 ml. aliquot was transferred to a flask containing 2.000 gm. of nonradioactive ketone V. The contents of each flask were stirred until complete solution was effected, and the solvent was removed in an air stream on the steam bath. The residue in each case was dissolved in 95% ethanol, treated with Norit and filtered through a talc pad. On seeding the solutions with the appropriate ketones and cooling with an ice bath, the ketones crystallized. After crystallizing each sample five times from ethanol, 50 mg. of the nonradioactive ketone corresponding to the contaminating ketone was added and each sample was again crystallized five times from ethanol. Melting points of ketone V were always 56.5-57.5°, while those of ketone IV were in the range 65-67°, and were considered to be sufficiently pure for C-14 assay. See Table VIII.

Formic Acid Rearrangements.

In a typical experiment, 2.000 gm. of the glycol was stirred with

TABLE VIII

SUMMARY OF YIELD DETERMINATION EXPERIMENTS FOR H_2SO_4 REARRANGEMENTS

Run No.	Starting[a] Compound	Wt. of Starting Compound	Ketone Yield Theory	Aliquot Taken	Theory of Ketone in Aliquot	Wt. of IV Added to Aliquot	Assay of Recovered IV	Wt. of V Added to Aliquot	Assay of Recovered V
1	Threo-Ib	3.0815	2.908	1/2	1.454	2.000	0.5995	2.000	0.4705
2	Threo-Ic	10.610	10.000	1/4	2.500	2.500	1.758	2.500	1.279
3	Threo-Ic	1.049	0.988	1/2	0.495	1.000	0.937	1.000	0.669
4	Threo-Ic	2.000	1.885	1/2	0.943	2.000	1.069	2.000	0.766
5	Threo-Ic	5.225	4.930	1/10	0.493	1.450	0.786	0.955	0.8313
6	IIa	1.059	1.000	1/2	0.500	1.000	0.3915	1.000	0.3975
7	IIa	5.100	4.811	1/2	2.405	2.500	0.6523	2.500	0.7077
8	IIa	1.0606	1.000	1	1.000	1.500	0.5055	See Table II	
9	III	2.0592	2.0592	1/2	1.0296	2.000	0.954	2.000	0.807
10	III	3.090	3.090	2/5	1.236	2.000	1.2185	2.000	1.050
11	Erythro-Ib	4.6586	4.420	1/2	2.210	3.000	0.4793	3.000	0.4505

[a]Molar activities in millicuries per mole of starting compounds: Threo-Ib, 2.124; Threo-Ic, 5.221; IIa, 2.153; III, 5.221; Erythro-Ib, 2.112.

TABLE IX

SUMMARY OF YIELD DETERMINATION EXPERIMENTS FOR FORMIC ACID REARRANGEMENTS

Run No.	Starting Compound	Wt. of Starting Material	Ketone-Aldehyde Yield Theory	Aliquot Taken	Theory of Ald. and Ketone in Aliquot	Wt. of III Added to Aliquot	Assay of 2,4-DNPH	Actual Yield of IIIcd, %	Cal'd Yield of III on 94.1% Recovery Basis
12	Threo-Ic	2.000	1.886	1/10	0.1886	0.150	2.553	75.9	80.6
13	IIa	2.000	1.886	1/5	0.3772	0.200	0.839	33.9	36.0
14	III	1.000	1.000	1/5	0.200	0.200	2.531	94.1	-

100 ml. of 90% formic acid for three days. The mixture was then poured into 500 ml. of water and extracted five times with chloroform. The combined chloroform extracts were washed twice with water, once with saturated aqueous sodium bicarbonate and again with water. The chloroform solution, after concentration on the steam bath, was transferred quantatively to a 200 ml. volumetric flask. A 20 ml. aliquot was taken and added to 150 mg. of nonradioactive aldehyde, III, stirred until the solution was homogeneous, and evaporated to dryness. The residue was dissolved in 95% ethanol, treated with Norit and filtered through a talc pad. The ethanolic solution was then treated while boiling, with a mixture consisting of 300 mg. of 2,4-dinitrophenylhydrazine, 2 ml. of concentrated sulfuric acid, and sufficient water to make a clear solution. The mixture was boiled for 15 minutes (during which time the oily globules which first separate, solidify), then cooled in an ice bath and the product removed by filtration. The product was purified by crystallization from 95% ethanol (large volume, ca. 300 ml. required). The product had a melting point of 190° and was bright yellow in color. See Table IX.

Aldehyde Stability in Formic Acid.

In order to determine the recovery of the aldehyde under the reaction conditions, the foregoing procedure was repeated with purified, radioactive III. At the end of the three-day reaction time, the formic acid-aldehyde mixture was cooled in ice and the crystalline aldehyde was removed by filtration, to yield 93% of the aldehyde, m. p. 93-4°. The mother liquor (formic acid) was poured into 500 ml.

of water, extracted with chloroform as in the above procedure, and the aldehyde, obtained by filtration, was added to the chloroform extract. The extract was transferred to a volumetric flask and the yield was determined by the radioactivity dilution method. In this way the yield was determined to be 94.1% (Table IX).

Ketone Cleavage for Carbon-14 Distribution.

In a typical experiment 0.5 gm. of the ketone was heated under reflux in an atmosphere of nitrogen with 30 ml. of 25% methanolic potassium hydroxide for 24 hours. (1) The methanol was removed by distillation under nitrogen and the residue was dissolved in 200 ml. of water. The aqueous solution was extracted five times with ether and acidified. The liberated acid was then extracted with ether and the solvent was removed by distillation. The acid was purified by crystallization from water, followed by sublimation.

The ether extract, containing the diarylmethane fragment, was evaporated to dryness and the residue was heated under reflux with a mixture of 20 ml. of glacial acetic acid, 2.0 gm. of chromium trioxide in 2 ml. of water, and 3 ml. of concentrated sulfuric acid. After 45 minutes, the reaction mixture was poured into 100 ml. of ice water and the precipitated acid was filtered from the mixture, washed with water and dissolved in aqueous sodium bicarbonate. The aqueous solution was treated with Norit, filtered through a talc pad and acidified to recover the acid. When the acid was 4,4'-dicarboxybenzophenone the product was crystallized from boiling glacial acetic acid; when p-benzoyl benzoic acid, purification was accomplished either by

sublimation of the acid or conversion to the methyl ester by means of diazomethane and subsequent crystallization from methanol. See Table X.

Ketone Stability in Concentrated Sulfuric Acid.

In separate experiments, 1.000 gm. of each of the product ketones was stirred with 20 ml. of concentrated sulfuric acid while the temperature was maintained at 4° C. After 30 minutes the mixture was poured into ice water and extracted in a manner identical with that employed in the glycol and aldehyde rearrangements. In the case of 4,4'-dimethylbenzhydrylphenyl ketone (V), the recovery of ketone with m. p. 58° C., was 98.8%, and in the case of 4-methylbenzhydryl-p-tolyl ketone (IV), the recovery of ketone with m. p. 68° C. was 99.1%. The fluorescent green coloration and ether insoluble material which was always observed in the sulfuric acid rearrangements, was entirely absent in the ketone stability tests.

p-Methylbenzhydryl p-Tolyl Ketone (IV).

a) Phenyl-p-Tolylcarbinol.

An ether solution of 100 gm. of phenyl-p-tolyl ketone was treated with 14 gm. of lithium aluminum hydride in dry ether in the usual manner. After hydrolysis with water and dilute hydrochloric acid, the ether layer was separated and the aqueous layer was extracted twice with ether. The combined ether extracts were washed with water and dried over anhydrous sodium sulfate, then evaporated to dryness. There resulted 97.1 gm. of the desired carbinol; m. p. 54°. (116)

b) Phenyl-p-Tolylmethyl Chloride.

A hexane solution of 97.1 gm. of the carbinol was treated with

TABLE X

SUMMARY OF RADIOACTIVITY DISTRIBUTION DETERMINATIONS

Run No.[a]	Fragments from IV		Fragments from V		Assay of IV Used	Assay of V Used	Remarks
	V	VII	VI	VIII			
1	0.5727	0.0235	0.4695	0.0125	0.5995	0.4705	m_a and m_b computed from VII and VIII.
2	0.7918	-	-	-	1.758	-	
2	0.4749	-	-	-	1.059	-	
3	0.4256	-	-	-	0.937	-	
4	0.4959	-	-	-	1.069	-	
5	0.3785	-	-	-	0.7863	-	
5	2.575	-	-	-	5.221	-	
6	0.007	-	0.003	-	0.3915	0.3975	
7	0.007	-	0.0065	-	0.6523	0.7077	
9	0.4307	-	-	-	0.954	-	
10	0.5955	-	-	-	1.2185	-	
11	-	0.0451	-	0.0997	0.4793	0.4505	Correct for 8.1% scramble for Table V.
15	2.640	-	-	-	5.221	-	From rearrangement of III.
16	2.094	0.0456	2.045	0.0289	2.124	2.124	From rearrangement of threo-Ia.

[a]Run numbers correspond to those used in Table VIII.

80 ml. of thionyl chloride dissolved in 200 ml. of hexane. After the initial vigorous reaction has subsided, the mixture was heated on the steam bath under reflux for 1-1/2 hours. After the reaction was complete, the hexane and excess thionyl chloride were removed under reduced pressure and the product was distilled, to yield 104 gm. (98%) of water-white oil; b. p. 158-163°/1 mm. (116)

c) Phenyl-p-Tolylacetonitrile.

A mixture of 104 gm. of phenyl p-tolylmethyl chloride and 50 gm. of cuprous cyanide were placed in a round-bottomed flask and a short air condenser was attached. The flask was immersed in a Wood's metal bath and heated to 215°. After 4 hours the flask was removed, cooled and the contents extracted with acetone. The acetone solution was allowed to stand overnight and filtered through a Celite pad. The acetone was removed by distillation and the product was distilled under reduced pressure. There was obtained 85 gm. (85.5%) of the nitrile. On crystallization from hexane the product separated as white crystals; m. p. 61-62°. (117)

d) Phenyl-p-Tolylacetic Acid.

A mixture of 85 gm. of the nitrile, 600 ml. of 50% aqueous sulfuric acid and 200 ml. of glacial acetic acid was refluxed overnight. The reaction mixture was cooled, poured into one l. of ice-water mixture and stirred until the acid solidified. The product was filtered and washed with water. The solid was digested with saturated sodium bicarbonate solution on the steam bath for 30 minutes, treated with Norit and filtered. On acidification there was obtained 84.5 gm.

(91.5%) of the acid; m. p. 116-116.5°. (107)

e) Phenyl-p-Tolylacetyl Chloride.

To a solution of 84 gm. of phenyl p-tolylacetic acid in 100 ml. of benzene was added 54 ml. of thionyl chloride. After the addition was completed, the solution was allowed to reflux on the steam bath for 1 hour. The benzene and excess thionyl chloride was removed by distillation under reduced pressure. An additional 50 ml. of benzene was added and distilled to remove the last traces of thionyl chloride. The residue was then dissolved in 100 ml. of dry benzene and used directly for the following preparation. (102a)

f) p-Methylbenzhydryl p-Tolyl Ketone (IV).

p-Tolyl magnesium bromide was prepared from 151 gm. of p-bromotoluene and 21.5 gm. of magnesium turnings. The ether solution was cooled and then treated with 83 gm. of anhydrous cadmium chloride, while being stirred vigorously. After the cadmium chloride had been added, the reaction mixture was heated under reflux for 1 hour. Most of the ether was removed by distillation, 600 ml. of dry benzene was added and the distillation continued until the distillate temperature reached 65°. Dry benzene (150 ml.) was added and the reaction mixture cooled with ice water. While the mixture was being stirred vigorously, the acid chloride solution, as described above, was added slowly. After the acid chloride solution had been added, the reaction mixture was stirred for 1 hour at room temperature, then 30 minutes under gentle reflux. The reaction mixture was decomposed with ice, followed by addition of sufficient concentrated hydrochloric acid to dissolve

the metal salts, and the benzene layer was separated. The aqueous layer was extracted twice with an ether-benzene mixture (2:1). The combined extracts were washed with water, 5% aqueous sodium hydroxide and again with water, dried with anhydrous sodium sulfate and the solvents distilled. The brown, oily residue was steam distilled to remove di-p-tolyl, and the dried oil was distilled under reduced pressure. The fraction boiling 215-240° at 0.5 mm was collected, dissolved in hexane and allowed to crystallize. There was obtained 53.6 gm. (48%) of the ketone; m. p. 67.5-68.5°.

Anal. Calc'd for $C_{22}H_{20}O$; C, 88.00; H, 6.71; Found: C, 88.09, 88.01; H, 6.69, 6.80.

The oxime was prepared by treating 1 gm. of the ketone in 5 ml. of pyridine and 5 ml. of 95% ethanol with 1.4 gm. of hydroxylamine hydrochloride. The mixture was heated under reflux for 4-1/2 hours and the alcohol and pyridine removed under reduced pressure. The residue was stirred with 120 ml. of water and extracted with ether. Upon evaporation of the ether solution and crystallization twice from 95% ethanol, there resulted 0.2 gm. of the oxime; m. p. 210-210.5° C.

Anal. Calc'd for $C_{22}H_{21}NO$; C, 83.8%; H, 6.67%; Found: C, 83.96; H, 6.78.

g) p-Methylbenzhydryl p-Tolyl Ketone-C^{14} (IVb).

This ketone was prepared in the same manner as that above, radioactive cuprous cyanide ($Cu\overset{*}{C}N$ was prepared by a modification of the method of Barber) (118) being used in the preparation of the phenyl p-tolylacetonitrile. The phenyl p-tolylacetic acid had a radioactivity

assay of 2.193 ± 0.009 mc/mole. The pure ketone melted at 67-68°, and had a radioactivity assay of 2.205 ± 0.011. Structure and radiochemical label position determinations were accomplished by subjecting a sample of the ketone to cleavage with 25% potassium hydroxide in methanol in an atmosphere of nitrogen. (1) On oxidation of the neutral fraction with chromic acid in acetic acid, p-benzoylbenzoic acid was obtained in 87% yield, m. p. 198-199°, and was nonradioactive. The p-toluic acid was obtained by acidification of the aqueous solution from the cleavage reaction, yielding 100% of air-dried crude product; m. p. 174-176°. One crystallization from water sufficed to yield the pure acid, m. p. 178-179°, with a radioactivity assay of 2.167 ± 0.001 mc/mole.

Threo-1,2-di-p-tolyl-1-phenylethylene-2-C^{14} Glycol (Ib), Method I.

p-Methylbenzhydryl p-tolyl ketone-C^{14} (8 gm.) was dissolved in 120 ml. of glacial acetic acid was treated with 20 ml. of concentrated nitric acid (119) and allowed to reflux for 25 minutes. The mixture was then poured into ice water, and extracted with ether, which was, in turn, washed with water, saturated aqueous sodium bicarbonate solution, and again with water. After being dried over anhydrous sodium sulfate, the solution was used directly for the reduction without further treatment.

A slurry was prepared with 4.5 gm. of lithium aluminum hydride in dry ether and the solution of the ketol was added slowly. The mixture was stirred for an additional hour, water added to decompose the excess hydride and to completely hydrate the metal hydroxides. The ether

solution was removed by filtration and evaporated to dryness. The slightly oily, brown residue was washed with petroleum ether and crystallized from ethanol. Repeated crystallization from ethanol gave 1 gm. of glycol; m. p. 147-150°, radioactivity assay 2.179 mc/mole. The remaining material had a m. p. of 130-135°, identical with the behavior of an approximately equal mixture of the two diasteriomers, prepared as described below.

Threo-1,2-di-p-tolyl-1-phenylethylene-2-C^{14} Glycol (Ib), Method II.

a) p-Methylbenzyl-α-C^{14} Alcohol.

Carboxyl-labeled p-toluic acid (55.5 gm.) was treated with 25 gm. of lithium aluminum hydride in ether solution in the usual way. After the excess hydride was destroyed by the cautious addition of water and separation of the ether solution, there was obtained 48.8 gm. (98%) of the carbinol.

b) p-Methylbenzyl-α-C^{14} Chloride.

The above carbinol was treated with 100 gm. of thionyl chloride in 150 ml. of hexane. Upon removal of the excess thionyl chloride and hexane under reduced pressure, there was obtained 55.1 gm. (98%) of the chloride.

c) p-Tolylacetonitrile-α-C^{14}.

The p-methylbenzyl-α-C^{14} chloride was treated with sodium cyanide according to the method of Vogel. (120) Upon distillation of the product there was obtained 43.9 gm. of the nitrile (85.5%).

d) p-Tolylacetic Acid (Carboxyl-labeled with carbon-14).

p-Tolylacetonitrile-α-C^{14} (43.9 gm.) was treated with 100 ml. of

50% aqueous sulfuric acid, to which had been added 50 ml. of glacial acetic acid. (120) After heating at reflux for one hour, the mixture was poured over 500 gm. of ice and the precipitated acid was removed by filtration. The crude acid was melted under water, with stirring, the flask was then cooled in an ice bath and the acid was removed by filtration. The acid was then dissolved in dilute sodium hydroxide and the solution was filtered through a pad of Celite. Upon acidification of the filtrate and cooling, there was obtained 39.4 gm. (78%) of the pure acid; m. p. 90-91°. (121)

e) Preparation of the Glycol (Ib).

The glycol was prepared by identical methods as indicated for the tolyl-labeled glycol discussed below, 19.4 gm. of the above α-labeled p-tolyl acetic acid being employed. There was obtained 5.7 gm. of the glycol; m. p. 156-157°. The melting point was undepressed when mixed with an authentic sample of the tolyl-labeled glycol. Depression in melting point to 130-135° was observed when mixed with approximately equal amounts of the threo-isomer prepared as described below. Radiochamical assay, 2.121 ± 0.001 mc/mole.

Threo-1,2-di-p-tolyl(2-p-methyl-C^{14})-1-phenylethylene Glycol (Ic).

a) Benzoic Acid-carboxyl-C^{14}.

This compound was prepared by the carbonation of phenyl magnesium bromide with radioactive carbon dioxide, using standard vacuum line technique. (122)

b) Toluene-methyl-C^{14}.

The carboxyl-labeled benzoic acid was esterified by the method of

Acree (123) and then treated with lithium aluminum hydride in dry ether. The resulting benzyl-α-C^{14} alcohol was purified by distillation. Zinc amalgam was prepared as directed in "Organic Synthesis." (124) Zinc (120 gm.) was treated with 12 gm. of mercurous chloride, and then washed with water. The amalgam, 200 ml. of water, 25 ml. of concentrated hydrochloric acid, and 25 gm. of radioactive benzyl alcohol, were heated under reflux for 30 hours. Additional 25 ml. portions of hydrochloric acid were added at 8-hour intervals. The mixture was then steam distilled and the toluene was separated, washed with water and dried over anhydrous calcium chloride. Upon filtration and distillation there was obtained 9.22 gm. (44%) of toluene; b. p. 111-115°, refractive index 1.4945, compared with 1.4935 for an authentic sample. Products from several such preparations were diluted with nonradioactive toluene to yield 43 gm. of toluene-C^{14} with a radioactivity assay of 22.55 mc/mole.

c) 4-Methyl-C^{14}-acetophenone.

In a modification of the method reported in "Organic Synthesis," (139) 42 gm. of methyl-labeled toluene in 200 ml. of carbon disulfide was first treated with 150 gm. of anhydrous aluminum chloride and then, while being refluxed gently over a period of 45 minutes, with 41 gm. of acetic anhydride. Refluxing was continued for 1-1/2 hours after which the carbon disulfide was removed by distillation and the residue was poured onto ice to which had been added sufficient concentrated hydrochloric acid to dissolve the aluminum salts. This mixture was extracted with ether, the ether was washed twice with water, once

with 10% NaOH and again with water. The ether solution was then dried over anhydrous calcium chloride, filtered, and the ether was removed by distillation. The residue was fractionated, the fraction b. p. 80-85° at 5 mm. (Feist, F. (125) gives b. p. 111-114/13 mm.) being retained (yield, 51 gm., 83%).

d) 4-Methyl-C^{14}-mandelic Acid.

This compound was prepared by dissolving 56.47 gm. of p-methylacetophenone in 250 ml. of methanol and adding 500 ml. of 20% aqueous sodium hydroxide. Chlorine gas was bubbled through the solution slowly while it was vigorously stirred. The solution gradually became almost clear while the temperature rose to 60°. From time to time additional sodium hydroxide solution was added until a total of one l. was present. Stirring was continued for an additional 20 minutes, and a small quantity of acetone was added to remove the excess chlorine. The mixture was treated with Norit and filtered. Upon acidification of the filtrate with concentrated hydrochloric acid, the precipitate was removed. The yield of p-toluic acid, methyl labeled, was 7 gm. The aqueous solution was then extracted with ether in a continuous extraction apparatus and the ether was removed by distillation. The yield of 4-methylmandelic acid was 45 gm. (64.5%); m. p. 145-146° (this is the method of VanArendouk and Cupery for the preparation of p-toluic acid, except that the chlorine is added slowly and the temperature does not rise as high).(126, 127) The product was further characterized by preparation of the ethyl ester, m. p. 77°; (121) and reduction with lithium aluminum hydride to p-tolylethylene glycol, m. p. 76°, (107)

in agreement with the literature.

e) 4-Methyl-C^{14}-phenylacetic Acid.

To a solution of 21 gm. of the 4-methylmandelic acid in 185 ml. of glacial acetic acid was added 20 ml. of concentrated sulfuric acid and 3.2 gm. of 30% palladium on charcoal catalyst. The mixture was hydrogenated at atmospheric pressure, while being stirred vigorously. After 20 hours, the theoretical quantity of hydrogen had been adsorbed. The catalyst was then removed by filtration. The filtrate was diluted with water and extracted with chloroform. The chloroform solution was washed with water and evaporated to dryness, to yield 16 gm. (84.4%) of the acid; m. p. 88-90°. (128)

f) 4'-Methyl-C^{14}-desoxybenzoin.

To 35.6 gm. of p-tolylacetic acid was added 50 gm. of phosphorous pentachloride. After the vigorous reaction ceased, the mixture was warmed on a water bath for 30 minutes, cooled, and 150 ml. of dry benzene was added. The mixture was then treated with 65 gm. of anhydrous aluminum chloride, and, after the initial vigorous reaction ceased, the mixture was heated under reflux for 1-1/2 hours and was poured onto an ice-hydrochloric acid mixture. The product was extracted three times with a benzene-ether mixture (1:4), the combined extracts washed with water and evaporated to dryness. There was obtained 31.3 gm. (62.6%) of the desoxybenzoin; m. p. 98-99°. (129)

g) α-Bromo-4'-methyl-C^{14}-desoxybenzoin.

A solution of 28.3 gm. of 4'-methyl-C^{14}-desoxybenzoin was prepared in 100 ml. of carbon disulfide and was placed in a flask fitted with an

efficient reflux condenser and an inlet tube for nitrogen. 21.8 gm. of bromine, dissolved in 50 ml. of carbon disulfide, was then added slowly while a rapid stream of nitrogen was passed through the solution (adapted from method of Ward). (130) After all of the bromine had been added and the evolution of hydrobromic acid gas slackened, the solvent was removed by distillation under reduced pressure, in an atmosphere of nitrogen. When the carbon disulfide ceased to distill, 30 ml. of hexane was added and distilled. The product was again treated with hexane in the same fashion and then warmed on the steam bath under reduced pressure in order to remove the last traces of the carbon disulfide solvent. The residue was used directly for the preparation of 4'-methyl-C^{14}-benzoin, described below.

h) 4'-Methyl-C^{14}-benzoin.

The α-bromo-4'-methyl-C^{14}-desoxybenzoin from the above preparation was dissolved in one l. of 95% ethanol and an equivalent amount of 10% ethanolic sodium hydroxide was added. The solution was stirred for 10 minutes and poured into two l. of water. Aqueous hydrochloric acid (20%) was added until the solution was just acid. The mixture was allowed to stand for 10 minutes, the precipitate was filtered, yielding 29 gm. (95%) of the crude product, from which 26 gm. of the pure material was obtained on crystallization from ethanol, m. p. 118°.(131) This material was found to have a radioactivity assay of 20.3 mc/mole and was diluted with nonradioactive 4'-methylbenzoin to a tracer level of approximately 5 mc/mole.

i) Threo-1,2-di-p-tolyl-1-phenylethylene(2-p-methyl-C^{14}) Glycol (Ic).

A Grignard reagent was prepared from 189 gm. of p-bromotoluene and 26.5 gm. of magnesium turnings. To it 100 gm. of the above 4'-methylbenzoin was added slowly over a 30-minute period, and the mixture was heated under gentle reflux for 1 hour. The mixture was hydrolyzed with an aqueous ammonium chloride solution and the ether layer separated. The aqueous layer was extracted three times with ether, the ether extracts were combined and washed with water, dried over anhydrous sodium sulfate and concentrated to approximately 150 ml. Then 500 ml. of hexane was added and the mixture allowed to stand overnight. The solid was filtered and crystallized from 85% ethanol. Yield of pure glycol, m. p. 156.5-157°, was 45 gm. (32%).

Anal. Calc'd for $C_{22}H_{22}O_2$: C, 83.0; H, 6.97; Found: C, 82.92, 83.06; H, 6.99, 7.00. Radioactivity assay, 5.221 mc/mole.

Erythro-1,2-di-p-tolyl-1-phenylethylene-2-C^{14}-Glycol (Ib).

a) 4,4'-Dimethyldesoxybenzoin.

To 20 gm. of the p-tolylacetic acid, prepared as for the threo-glycol (Ib) above, was added 11 ml. of phosphorous trichloride and (132) 60 ml. of toluene. The toluene solution was decanted onto 30 gm. of anhydrous aluminum chloride and after the initial vigorous reaction subsided, the mixture was heated on a steam bath for 1 hour. The reaction mixture was poured over an ice-concentrated hydrochloric acid mixture and the toluene layer separated. The aqueous layer was extracted three times with a benzene-ether mixture (4:1) and the

combined organic extracts were washed twice with water. On evaporation of the solvents there resulted a yellow oily solid which was washed once with a little cold hexane and then dissolved in hot 95% ethanol. Following treatment of the ethanolic solution with Norit and filtration, 19.9 gm. (67%) of the desoxybenzoin was obtained; m. p. 101-102°. (133)

b) 4,4'-Dimethyl-α-bromodesoxybenzoin.

The α-bromodesoxybenzoin was prepared as described previously for 4'-methyl-α-bromodesoxybenzoin, using 19.9 gm. of the desoxybenzoin above, and 14.8 gm. of bromine in 75 ml. of carbon disulfide. Upon evaporation of the solvents, a solid compound separates, which upon crystallization from hexane has a m. p. of 96°, and a radioactivity assay of 2.037 mc/mole (calculation based on molecular weight of 303).

c) 4,4'-Dimethylbenzoin.

The bromodesoxybenzoin from above was treated with base in alcoholic solution, followed by acidification in a manner described previously for the preparation of 4'-methylbenzoin. 9.9 gm. (46%) of pure benzoin was obtained; m. p. 87-88°. (134)

d) Preparation of the Glycol, Erythro-Ib.

To a Grignard solution prepared from 2.74 gm. of magnesium turnings and 15.7 gm. of bromobenzene in ether, was added 9.9 gm. of 4,4'-dimethylbenzoin. After the addition was complete, the mixture was allowed to reflux gently for 4 hours. The reaction mixture was poured into ice water and ammonium chloride was then added to dissolve the magnesium hydroxide. The ether layer was separated and the reaction mixture was extracted three times with 100 ml. portions of ether. The

combined ether solutions were washed with water and evaporated to dryness. Crystallization from 95% ethanol gave 7.4 gms. of the glycol; m. p. 160-161°. Radiochemical assay, 2.102 mc/mole.

Anal. Calc'd for $C_{22}H_{22}O_2$; C, 83.0; H, 6.97. Found: C, 82.72; H, 7.08.

1,1-Di-p-tolyl-2-phenylethylene-1-C^{14} Glycol (IIa).

a) Mandelic-carbonyl-C^{14} Acid.

This compound was prepared by the method of Vogel (135) from benzaldehyde, radioactive sodium cyanide, and sodium bisulfite, with subsequent hydrolysis of the nitrile with concentrated hydrochloric acid.

b) Methyl Mandelate-carbonyl-C^{14}.

This compound was prepared by the method of Acree (123) by refluxing the acid in anhydrous methanol in the presence of concentrated sulfuric acid, followed by distillation of the product.

c) 1,1-Di-p-tolyl-2-phenylethylene-1-C^{14} Glycol (IIa).

A Grignard reagent was prepared in ether solution with 84 gm. of p-bromotoluene and 14 gm. of magnesium turnings. To this solution was added 22.5 gm. of methyl mandelate-carbonyl-C^{14} and the mixture refluxed for 4 hours. The reaction mixture was decomposed with a solution of ammonium chloride, the ether layer was separated, washed with water, dried over anhydrous sodium sulfate and evaporated to dryness. The semisolid residue which remained was dissolved in a small amount of benzene and hexane was added. 22 gm. (51.5%) of glycol separated; m. p. 155-157°. Crystallization from 95% ethanol produced

the pure glycol; m. p. 158-158.5°, radioactivity assay 2.153 ± 0.015 mc/mole. (21) On oxidation of the glycol with chronium trioxide in 50% aqueous acetic acid, the neutral fraction yielded di-p-tolyl ketone with radioactivity assay of 2.140 mc/mole. The benzoic acid fraction was nonradioactive.

Anal. Calc'd for $C_{22}H_{22}O_2$: C, 83.0; H, 6.97; Found: C, 83.27; H, 7.11.

Di-p-tolylphenylacetaldehyde.

A 5.000 gm. sample of 1,2-di-p-tolyl(2-p-methyl-C^{14})-1-phenyl-ethylene glycol (Ic) was stirred at room temperature with 350 ml. of 90% formic acid for 96 hours. On cooling the reaction mixture in an ice bath and subsequent filtration, 3.764 gm. (79.8%) of the nearly pure aldehyde was obtained; m. p. 93-94°. On crystallization from 95% ethanol gave the pure compound; m. p. 94.5-95°. Radiochemical assay, 5.235 ± 0.025 mc/mole.

Anal. Calc'd for $C_{22}H_{20}O$; C, 88.10; H, 6.73; Found: C, 88.10; 87.83; H = 6.59, 6.52.

The 2,4-dinitrophenylhydrazone was prepared by treating 20 ml. of a hot ethanolic solution of 500 mg. of the aldehyde with a solution of 500 mg. of 2,4-dinitrophenylhydrazine, 1 ml. of concentrated sulfuric acid and 5 ml. of water. After boiling the solution for 20 minutes, it was cooled and the precipitate was removed by filtration. In several preparations the crude 2,4-dinitrophenylhydrazone had a low and broad melting point. Boiling for 10 minutes with a large volume of hexane or crystallization from a large volume of ethanol gave the bright yellow

product with sharp melting point; 190.5-191°. Radioactivity assay, 5.205 mc/mole. Further proof of the identity of the aldehyde was obtained by comparison of its ultraviolet spectrum with that of the known aldehyde, diphenyl-p-tolylacetaldehyde. Both curves have identical characteristics.

Anal. Calc'd for $C_{28}H_{25}O_4N_4$; C, 69.85; H, 5.24; Found: C, 70.66; H, 5.07.

4,4'-Dimethylbenzhydrylphenyl Ketone (V).

a) Di-p-tolylcarbinol.

An ether solution of 40 gm. of di-p-tolyl ketone was added slowly to a stirred slurry of 7.3 gm. of lithium aluminum hydride in 300 ml. of ether. After the addition was completed the solution was allowed to stir for an additional 15 minutes, after which 50% ethyl acetate in ether was added slowly in sufficient quantity to destroy the excess hydride. Water was then added, followed by sufficient concentrated hydrochloric acid to dissolve the metal hydroxides. The ether layer was separated and the aqueous layer was extracted with ether. The combined ether extracts were washed once with water and evaporated to dryness. The product crystallized on cooling and several different runs gave yields of 98% or better of the theory. Crystallization from hexane yields the pure carbinol; m. p. 70°. (136)

b) Di-p-tolylchloromethane.

A solution of 40 gm. of di-p-tolyl carbinol in 100 ml. hexane was heated under gentle reflux while 38 ml. of thionyl chloride was added dropwise. Reflux was continued for 1-1/2 hours, after which the hexane

and the excess thionyl chloride was removed under reduced pressure. The slightly colored product, which on distillation (b. p. 163-168°/ 0.6 mm.) gave 108 gm. (95.7%) of a water white oil, crystallized spontaneously on standing. Crystallization from hexane gave the pure compound; m. p. 44-45°. (136)

c) Di-p-tolylacetonitrile.

A mixture of 100 gm. of di-p-tolylchloromethane and 45.5 gm. of cuprous cyanide (20% excess) were placed in a flask with an air condenser attached and immersed in a Wood's metal bath, preheated to 180°. The mixture was heated for 5-1/2 hrs. with occasional mixing, while the temperature was slowly increased to 220°. The product was removed from the bath, cooled and 250 ml. of acetone was added. The acetone solution was filtered to remove the copper halide cake, which was washed on the filter with an additional 100 ml. of acetone. The acetone solution was allowed to stand overnight in the refrigerator after which it was again filtered to remove the fine sediment of copper halide which had settled out. The acetone was removed under reduced pressure and the product was distilled (b. p. 165-175°/7 mm.) to yield 69 gm. (72%) of a slighly yellow oil which spontaneously crystallized on standing. Crystallization from hexane yields pure white crystals; m. p. 46.5-47°. Hoch (117) gives b. p. 212°/18 mm. and does not record the melting point of the compound.

d) Di-p-tolylacetic Acid.

A mixture of 65 gm. of di-p-tolylacetonitrile, 120 ml. of glacial acetic acid and 600 ml. of 50% aqueous sulfuric acid were heated under

reflux with vigorous stirring for 3-1/2 hours. The mixture was then cooled and poured into one l. of ice water and stirred for 1 hour, during which time the acid, which first separated as an oil, solidified. The product was removed by filtration and washed with cold water. The air-dried product weighed 60 gm. (85%); m. p. 143°. (137)

e) Di-p-tolylacetyl Chloride.

This compound was prepared from 67.1 gm. of di-p-tolylacetic acid in 250 ml. of hexane, by treatment with 100 ml. of thionyl chloride. After the reaction had almost ceased at room temperature, the mixture was warmed to not more than 40° under reduced pressure to remove the hexane and excess thionyl chloride. After distillation ceased, 50 ml. of dry benzene was added and distillation continued. This process was repeated to remove the last traces of thionyl chloride. After the thionyl chloride was removed the residue was dissolved in 100 ml. of dry benzene and used without further purification in the preparation of the ketone below.

f) 4,4'-Dimethylbenzhydryl Phenyl Ketone.

A Grignard reagent was prepared in the usual way from 131 gm. of bromobenzene and 20.3 gm. of magnesium turnings. To the cooled solution was added, in small portions, 80 gm. of anhydrous cadmium chloride, vigorous stirring being maintained. After the addition was complete, the mixture was stirred at room temperature for 30 minutes, then under gentle reflux for an additional 30 minutes. Almost all of the ether was removed by distillation, 100 ml. of dry benzene was added and distillation continued. When 100 ml. of distillate had been

collected, an additional 200 ml. of benzene was added and the distillation was continued until the condensing vapor had a temperature of 68°. Then 500 ml. of dry benzene was added and the mixture was cooled to 10-15°. While vigorous stirring was maintained, the solution of di-p-tolylacetyl chloride was added slowly. Stirring was continued at room temperature for 30 minutes and then under gentle reflux for 1 hour. The reaction mixture was poured into water, sufficient concentrated hydrochloric acid was added to dissolve the magnesium and cadmium salts, and the benzene layer was separated. The aqueous layer was extracted with 200 ml. of an ether-benzene mixture (4:1) and the combined organic layers were washed three times with water. The solutions were dried over anhydrous sodium sulfate and the solvents removed by distillation. The brown oily residue was then steam distilled to remove di-phenyl, dried and distilled under reduced pressure. The fraction, b. p. 236-242° at 0.5 mm., was a slightly yellow oil weighing 77 gm. After three crystallizations from ether-hexane (1:20) at dry ice temperature, 66 gm. (79%) of the pure ketone was obtained; m. p. 57-58°. (21)

Anal. Calc'd for $C_{22}H_{20}O$: C, 88.00; H, 6.71: Found: C, 88.06; H, 6.71.

Sample Calculations for Ketone Yields, Reaction Path Yields and Carbon-14 Label Distribution.

a) Correction Factor for Ketone Yields from Threo-Ic and III, and Cleavage Products of IVcd.

It may be seen from Table X for Runs 2-5 and 9, 10, 15, that

cleavage of the ketone IV from the dilution yield determinations gives a slightly lower value for p-tolyl label scrambling than does the cleavage of the undiluted ketone. Since in the case of the aldehyde 50:50 distribution is demanded (and observed for the undiluted ketone) it is apparent that a correction is necessary for this observation. Since this behavior is probably due to a minute quantity of highly radioactive contaminate in the glycol, threo-Ic, because of the method of synthesis, we have applied the correction factor 47/50 in the following manner: 47/50 X uncorrected ketone yield = corrected ketone yield and, since the p-tolyl scrambling recorded in Table IV is also affected, 50/47 X uncorrected p-tolyl scrambling = corrected p-tolyl scrambling. This correction factor is, of course, only approximate, being derived from the average of the two values for V_c (47%; Table X, Runs 9 and 10) and the fact that 50% is required and observed (Table X, Run 15). Since, however, the factor is close to unity, rather wide limits are allowable in its accuracy without introducing significant error by its use. Substantially the same correction is arrived at by plotting the observed percentages of p-tolyl scrambling against the ratio by which the ketone was diluted, and extrapolating to zero dilution. This correction is required only in the calculations of data derived from the rearrangements conducted with threo-Ic or the aldehyde III. Moreover, no correction was needed for the ketone V because these dilutions were consistantly more readily purified, and upon cleavage, in control experiments, the ketone fragments did not indicate any contamination, as was found for ketone IV.

b) Ketone Yield Calculations.

Application of the equation $A_1 (D_1 + X) = A_o X$, mentioned earlier in this section, gives, for Run 2 (Table VIII), the uncorrected values of 51.1% for the yield of IV and 32.6% for the yield of V. The corrected yield of IV (47/50 x 51.1) is 48%. The yields of IV and V were then normalized to show the relative yields of IV and V in the ketonic product, giving values of 59.6% and 40.4% for IV and V, respectively (Table II).

c) Reaction Path Yields.

Consideration of Chart I and the degradation schemes on pages 35, 36 and 40, shows that when threo-Ib undergoes rearrangement only path B yields p-benzoylbenzoic acid which contains the carbon-14 label. Therefore the molar activity (Table V) of this compound (VIIa), together with the yield of IV (Table II) is a measure of the yield by path B. Thus $m_b = 0.039 \times 0.583 = 0.023$ as one value (Table VI). Calculation of m_a is performed in like manner using the yield of Vab and VIIIa.

The total contribution to product via paths A and D is given by the yield of V (Table II), hence $m_a + m_d = 0.417$ and from Table VI the average value for m_a is 0.008, giving a value for m_d of 0.409.

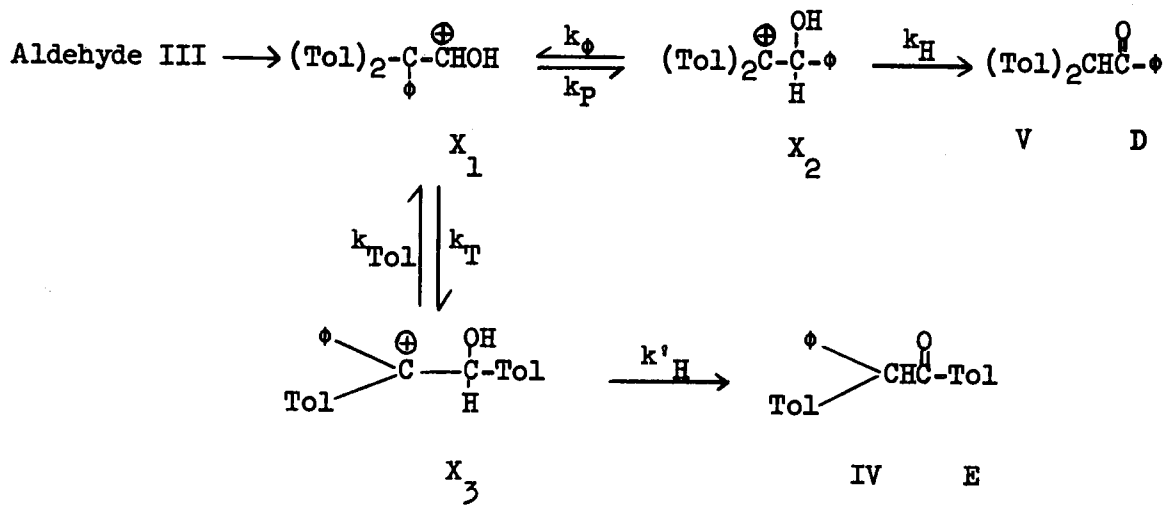
Methods for calculating the ratio m_e/m_d have been given previously (page 43). From a knowledge of this ratio, e. g., 1.37 (Table VII, Method 1), and m_d, the value for m_e may be calculated, thus $1.37 \times 0.409 = 0.560$ (Table VI).

Calculations for m_c may be performed in several ways, one of which is described here. The yield of IV (Table II) gives $m_b + m_c + m_e$ which

is 0.583. From this is subtracted the sum $m_b + m_e$ calculated as described above, thus 0.583 - (0.018 + 0.560) = 0.005 (Table VI).

Derivation of Equation 1 of the Introduction.

In the following scheme, X_1, X_2, and X_3 represent three ionic species in a dynamic equilibrium. If then this scheme is correct, the specific rate-constant ratio k_T/k_p, rather than the product ratio IV/V,



represents the relative migratory abilities of the one phenyl and the two p-tolyl groups of aldehyde III, when this aldehyde is subjected to acid catalysis. Now if x_1, x_2, and x_3 are the instantaneous, time-variable concentrations of the ions X_1, X_2, and X_3, respectively, then from the above scheme

2) $dx_2(t)/dt = k_p\, x_1(t) - k_\phi\, x_2(t) - k_H\, x_2(t)$

3) $dx_3(t)/dt = k_T\, x_1(t) - k_{Tol}\, x_3(t) - k'_H\, x_3(t)$.

Since all reactions were allowed to go to completion, equations 2 and 3 are now integrated between the limits zero and infinity.

$$4)\quad x_2\Big|_0^\infty = k_P\int_0^\infty x_1(t)dt - k_\phi\int_0^\infty x_2(t)dt - k_H\int_0^\infty x_2(t)dt$$

$$5)\quad x_3\Big|_0^\infty = k_T\int_0^\infty x_1(t)dt - k_{Tol}\int_0^\infty x_3(t)dt - k'_H\int_0^\infty x_3(t)dt.$$

The values $\int_0^\infty x_1(t)dt$, $\int_0^\infty x_2(t)dt$, and $\int_0^\infty x_3(t)dt$ are now replaced with the "integration areas" S_1, S_2, and S_3, and then since at $t = 0$ and $t = \infty$, the concentration of all intermediates are zero, equations 4 and 5 become:

$$6)\quad k_P S_1 - k_\phi S_2 - k_H S_2 = 0$$

$$7)\quad k_T S_1 - k_{Tol} S_3 - k'_H S_3 = 0$$

or:

$$6)\quad S_2 = \frac{k_P S_1}{k_\phi + k_H}$$

$$7)\quad S_3 = \frac{k_T S_1}{k_{Tol} + k'_H}$$

and at complete reaction, since S_1, S_2 and S_3 represent the total moles of X_1, X_2, and X_3 formed during period t = 0 and t = ∞, and m_d and m_e represent the moles of product formed through paths D and E (Chart I), respectively;

$$8) \quad \frac{m_d}{m_e} = \frac{k_H S_2}{k'_H S_3} .$$

Substitution of equation 6 and 7 for S_2 and S_3, respectively, in equation 8 and simplifying gives equation 1.

The derivation of equation 1 is made possible by use of the "area theorem" of Hearon, (138) who pointed out the utility of this theorem in chemical kinetics.

Analytical Determinations.

The carbon and hydrogen analyses for this dissertation were performed by the Huffman Microanalytical Laboratories, Wheatridge, Colorado.

SUMMARY

Phenyl-di-p-tolylacetaldehyde and the related system of glycols; threo-1,2-di-p-tolyl(2-p-methyl C^{14})-1-phenylethylene glycol, threo-1,2-di-p-tolyl-1-phenylethylene-2-C^{14} glycol and 1,1-di-p-tolyl-2-phenylethylene glycol, have been subjected to rearrangement in cold, concentrated sulfuric acid. The yields of the ketones (4-methylbenzhydryl p-tolyl ketone and 4,4'-dimethylbenzhydryl phenyl ketone) produced were obtained in each case by the radioactivity dilution method. The fates of the carbon-14 labels of suitably labeled reactants were determined by appropriate degradation methods, followed by radioactivity assay of the degradation products. By means of the equation,

$$\frac{k_T}{k_P} = \frac{k_H}{k_\phi} \cdot \frac{k_{Tol}}{k'_H} \cdot \frac{m_e}{m_d} \left[\frac{1 + \frac{k'_H}{k_{Tol}}}{1 + \frac{k_H}{k_\phi}} \right]$$

and a mechanism involving open, equilibrating carbonium ions, it has been established that the p-tolyl/phenyl migration ratio in the rearrangement of the aldehyde is not reversed, but is almost certainly greater than unity. The mechanism correlating the aldehyde-ketone and pinacol rearrangements, proposed by B. M. Benjamin and C. J. Collins (1) in 1956, is thus supported.

BIBLIOGRAPHY

1. Benjamin, B. M. and Collins, C. J., J. Am. Chem. Soc., 78, 4329 (1956).

2. Collins, C. J., J. Am. Chem. Soc., 77, 5517 (1955).

3. Bachmann, W. E. and Shankland, R. V., J. Am. Chem. Soc., 51, 306 (1929).

4. Bachmann, W. E. and Ferguson, J. W., J. Am. Chem. Soc., 56, 2081 (1934).

5. Burr, J. G., Jr., J. Am. Chem. Soc., 75, 5008 (1953).

6. Burr, J. G., Jr., and Ciereszko, L. S., J. Am. Chem. Soc., 74, 5426 (1952).

7. Tietz, R. F. and McEwen, W. F., J. Am. Chem. Soc., 77, 4007 (1955).

8. McEwen, W. E., Gilliland, M. and Sparr, B. I., J. Am. Chem. Soc., 72, 3212 (1950).

9. Ege, S. N. and Sherk, K. W., J. Am. Chem. Soc., 75, 354 (1953).

10. Curtin, D. Y. and Crew, M. C., J. Am. Chem. Soc., 76, 3719 (1954).

11. Winstein, S. and Grunwald, E., J. Am. Chem. Soc., 70, 830 (1948).

12. Fittig, R., Ann., 110, 17 (1859); ibid., 114, 54 (1860).

13. Tiffeneau, M. and Levy, J., Bull. soc. chim. IV , 33, 735 (1923).

14. Zincke, Th., Ber., 43, 849 (1910).

15. Meerwein, H., Ann., 396, 200 (1913).

16. Bachmann, W. E. and Moser, F. H., J. Am. Chem. Soc., 54, 1124 (1932).

17. Bachmann, W. E., J. Am. Chem. Soc., 54, 2112 (1932).

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

19. McKenzie, A. and Widdows, S. T., J. Chem. Soc., 107, 702 (1915).

20. Collins, C. J., unpublished results.

21. Danilov, S., J. Russ. Phys. Chem. Soc., 58, 148 (1926).

22. Royals, E. E., "Advanced Organic Chemistry," Prentice-Hall, Inc., Englewood Cliffs, N. J., 1954, p. 253.

23. Ingold, C. K., "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, Chapter IX, pp. 474-528.

24. Wheland, G. W., "Advanced Organic Chemistry," 2d Ed., John Wiley and Sons, Inc., New York, N. Y., 1949, pp. 494-534.

25. Danilov, S. and Venus-Danilova, E., Ber., 60, 1050 (1927).

26. Mislow, K. and Siegel, M., J. Am. Chem. Soc., 74, 1060 (1952).

27. Stoermer, R., Ber., 2288 (1906).

28. Tiffeneau, M. and Orekhov, A., Compt. rend., 172, 387 (1921).

29. Zincke, Th., Ann., 216, 286 (1883); ibid., 199, 115 (1879).

30. Breuer, A. and Zincke, Th., Ann., 199, 141 (1879).

31. Nevole, M., Ber., 9, 448 (1876).

32. Orekhov, A. and Tiffeneau, M., Compt. rend., 182, 67 (1926).

33. Roger, R. and McKay, W. B., J. Chem. Soc., 332 (1933).

34. Levy, J. and Weill, P., Compt. rend., 185, 135 (1927).

35. Wagner, G., J. Russ. Phys. Chem. Soc., 31, 680 (1899).

36. Bartlett, P. D. in Gilman's, "Organic Chemistry," John Wiley and Sons, N. Y., 1953, Volume III, Chapter I.

37. Eliel, E. L., "Steric Effects in Organic Chemistry" edited by Newman, M. S., John Wiley and Sons, Inc., N. Y., 1956, Chapter I.

38. Cram, D. J., ibid., Chapters 5 and 6.

39. Walden, P., Ber., 26, 210 (1893); ibid., 29, 133 (1896).

40. Meerwein, H., Ann., 417, 255-77 (1918).

41. Meerwein, H., Ann., 405, 129 (1914).

42. Nametkin, S. S., J. Russ. Phys. Chem. Soc., 47, 1590 (1915).

43. Nametkin, S. S., J. Chem. Soc., 110 (1) 269 (1916).

44. Nametkin, S. S. and Chochrjakova, V. A., J. Russ. Phys. Chem. Soc., 47, 1611 (1915).

45. Demjanow, N. J. and Luschnikow, S. N., J. Russ. Phys. Chem. Soc., 35, 26 (1903).

46. Demjanow, N. J., J. Russ. Phys. Chem. Soc., 36, 166 (1904).

47. Demjanow, N. J., Ber., 40, 4393 (1907).

48. Tiffeneau, M., Ann. chim. Phys., [8], 10, 322 (1907).

49. McKenzie, A., Roger, R. and McKay, W. B., J. Chem. Soc., 2597 (1932).

50. Erlenmeyer, E., Ber., 14, 322 (1881).

51. Montague, P. J., Rec. trav. chim., 24, 105 (1905); ibid., 25, 411 (1906); ibid., 29, 150 (1910).

52. Acree, S. F., Am. Chem. J., 33, 180 (1905).

53. Meerwein, H. and vanEmster, K., Ber., 55, 2500 (1922).

54. Tiffeneau, M., Ann. chim., [8], 10, 322 (1907).

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

56. Lane, J. F. and Walters, D. R., J. Am. Chem. Soc., 73, 4234 (1951).

57. Gebhart, H. J. and Adams, K. H., J. Am. Chem. Soc., 76, 3925 (1954).

58. Tiffeneau, M., Bull. soc. chim. (Fr.), 1, 1221 (1907).

59. Bartlett, P. D. and Pöckel, I., J. Am. Chem. Soc., 60, 1585 (1938).

60. Whitmore, F. C., J. Am. Chem. Soc., 54, 3274 (1932).

61. Ann. Repts. Chem. Soc., London, 38, 229 (1941).

62. Cohen, S. G. and Schneider, A., J. Am. Chem. Soc., 63, 3382 (1941).

63. Phillips, H., J. Chem. Soc., 123, 44 (1923).

64. McKenzie, A., Roger, R. and Wills, G. O., J. Chem. Soc., 779 (1926).

65. Bernstein, H. I. and Whitmore, F. C., J. Am. Chem. Soc., 61, 1324 (1939).

66. McKenzie, A. and Dennler, W. S., Ber., 60, 220 (1927).

67. Lane, J. F. and Wallis, E. S., J. Am. Chem. Soc., 63, 1674 (1941).

68. Roberts, I. and Kimball, G. E., J. Am. Chem. Soc., 59, 947 (1937).

69. Winstein, S. and Lucas, H. J., J. Am. Chem. Soc., 61, 1576 (1939).

70. Cram, D. J., J. Am. Chem. Soc., 71, 3863, 3875 (1949).

71. Cram, D. J. and Davis, R., J. Am. Chem. Soc., 71, 3871 (1949).

72. Nevell, T. P., deSalas, E. and Wilson, C. L., J. Chem. Soc., 1188 (1939).

73. Eyring, H., Ind. Eng. Chem., 35, 511 (1943).

74. Dewar, M. J. S., J. Chem. Soc., 777 (1946).

75. Price, C. C., "Mechanisms of Reaction at Carbon-Carbon Double Bonds," Interscience Publishers, Inc., N. Y., 1946, pp. 39-43.

76. Walsh, A. D., J. Chem. Soc., 89 (1947).

77. Arcus, C. L., Chem. and Ind., 442 (1947).

78. Orekhoff, A. and Tiffeneau, M., Bull. soc. chim., [iv], 37, 1410 (1925).

79. Winstein, S., Morse, B. K., Grunwald, E., Jones, N. W., Corse, J., Trifan, D. and Marshall, H., J. Am. Chem. Soc., 74, 1127 (1952).

80. Winstein, S., Morse, B. K., Grunwald, E., Schreiber, K. C. and Corse, J., J. Am. Chem. Soc., 74, 1113 (1952).

81. Winstein, S. and Trifan, D., J. Am. Chem. Soc., 74, 1154 (1952).

82. Cram. D. J., J. Am. Chem. Soc., 74, 2129, 2137, 2159 (1952).

83. Winstein, S. and Schreiber, K. C., J. Am. Chem. Soc., 74, 2165 (1952).

84. Winstein, S. and Schreiber, K. C., J. Am. Chem. Soc., 74, 2171 (1952).

85. Winstein, S. and Heck, R., J. Am. Chem. Soc., 74, 5584 (1952).

86. Benjamin, B. M. and Collins, C. J., J. Am. Chem. Soc., 78, 4952 (1956).

87. Montague, P. J., Chem. Week blad., 17, 378 (1920).

88. Ciereszko, L. S. and Burr, J. G., Jr., J. Am. Chem. Soc., 74, 5431 (1952).

89. Bailey, P. S. and Burr, J. G., Jr., J. Am. Chem. Soc., 75, 2951 (1953).

90. Jaffe, H. H., Chem. Rev., 53, 191 (1953).

91. Pollak, P. I. and Curtin, D. Y., J. Am. Chem. Soc., 72, 961 (1950).

92. Curtin, D. Y. and Pollak, P. I., J. Am. Chem. Soc., 73, 992 (1951).

93. Curtin, D. Y., Harris, E. E. and Pollak, P. I., J. Am. Chem. Soc., 73, 3453 (1951).

94. Curtin, D. Y. and Meislich, E. K., J. Am. Chem. Soc., 74, 5905 (1952).

95. Curtin, D. Y. and Kellow, D. B., J. Am. Chem. Soc., 75, 6011 (1953).

96. Luce, L., Compt. rend., 180, 145 (1925).

97. McKenzie, A., Mills, A. K. and Myles, R. J., Ber., 63, 904 (1930).

98. Orekhoff, A. and Roger, R., Compt. rend., 180, 70 (1925).

99. Tiffeneau, M., Orekhoff, A. and Roger, R., Bull soc. chim. Fr., 49, 1757 (1931).

100. McKenzie, A. and Richardson, A. C., J. Chem. Soc., 123, 79 (1923).

101. McKenzie, A. and Dennler, W. S., J. Chem. Soc., 2105 (1924).

102. Bonner, W. A. and Collins, C. J., a) J. Am. Chem. Soc., 75, 5372 (1953); b) ibid., 77, 99 (1955).

103. Collins, C. J. and Bonner, W. A., J. Am. Chem. Soc., 75, 5379 (1953); ibid., 77, 92 (1955).

104. Danilov, S. N., J. Russ. Phys. Chem. Soc., 51, 109 (1919); ibid., 57, 347 (1925); ibid., 58, 129 (1926); ibid., 59, 196, 210 (1927); ibid., 61, 723 (1929).

105. Danilov, S. N., J. Gen. Chem., 18, 200 (1948).

106. Lucas, R. and Guerlain, J., Bull. soc. chim., 49, 1860 (1931).

107. Isimura, K., Bull. chim. soc., Japan, 16, 196, 252 (1941).

108. Danilov, S., J. Russ. Phys. Chem. Soc., 49, 282 (1917).

109. Danilov, S. and Venus-Danilova, E., Ber., 59, 377 (1926).

110. Laidler, K. J., "Chemical Kinetics," McGraw-Hill Book Co., Inc., N. Y., 1950, p. 183.

111. Kendrick, L. W. and Collins, C. J., unpublished results.

112. Neville, O. K., J. Am. Chem. Soc., 70, 3501 (1948).

113. Bonner, W. A. and Collins, C. J., J. Am. Chem. Soc., 75, 3693 (1953).

114. Raaen, V. F. and Ropp, G. A., Anal. Chem., 25, 174 (1953).

115. Mayor, R. H. and Collins, C. J., J. Am. Chem. Soc., 73, 471 (1951).

116. Norris, J. F. and Banta, C., J. Am. Chem. Soc., 50, 1804 (1928).

117. Hoch, J., Compt. rend., 197, 770 (1933).

118. Barber, H. J., J. Chem. Soc., 79 (1943).

119. Biltz, H., Ber., 32, 650 (1899).

120. Vogel, A. I., "A Textbook of Practical Organic Chemistry," 2d Ed., Longmans, Green and Co., New York, N. Y., 1951, p. 722.

121. Kindler, K., Metzerdorf, W. and Dschi-yin-Kwok, Ber., 76, 308 (1943).

122. Collins, C. J., J. Am. Chem. Soc., 73, 1038 (1951).

123. Acree, S. F., Ber., 37, 2764 (1904).

124. Organic Syntheses, John Wiley and Sons, Inc., New York, N. Y., Vol. II, p. 499.

125. Feist, F., Ber., 67B, 938 (1934).

126. Van Arendouk, A. M. and Cupery, M. E., J. Am. Chem. Soc., 53, 3184 (1931).

127. Riebsomer, J. L., Irvine, J. and Andrews, R., J. Am. Chem. Soc., 60, 1015 (1938).

128. Kindler, K. and Dschi-yin-Kwok, Ann., 554, 9 (1943).

129. Tiffeneau, M. and Levy, J., Bull. soc. chim., 49, 1738 (1931).

130. Ward, A. M., J. Chem. Soc., 1549 (1929).

131. Weissberger, A., J. Chem. Soc., 223 (1935).

132. Reference 124, p. 156.

133. Danilov, S. and E. Venus-Danilova, J. Russ. Phys. Chem. Soc., 57, 428 (1925).

134. Shacklett, C. D. and Smith, H. A., J. Am. Chem. Soc., 75, 2654 (1953).

135. Reference 120, p. 734.

136. Norris, J. F. and Blake, J. T., J. Am. Chem. Soc., 50, 1810 (1928).

137. Danilov, S. and E. Venus-Danilova, Ber., 59B, 1032 (1926).

138. Hearon, J. Z., unpublished work. See footnote 14, reference 1.

139. "Organic Syntheses," John Wiley and Sons, Inc., New York, N. Y., Vol. I, pp. 109-111.

BIOGRAPHICAL ITEMS

The author, Lawrence "W" Kendrick, Jr., was born in Underwood, Alabama, on September 16, 1925. He completed his elementary and secondary education in the Shelby County schools, and was graduated from Thompson High School in 1943. He attended Howard College, Birmingham, Alabama, for one term prior to entering the United States Navy in 1943. During his Naval Service, he was commissioned a Naval Aviator and served in that capacity until his release from active duty in 1949. While on active service in the Navy he attended Carson-Newman College, Jefferson City, Tennessee, for one year.

In January 1950, Mr. Kendrick entered the School of Pharmacy at Howard College and received the degree of Bachelor of Science in Pharmacy in June, 1953. After having completed the requirements for his degree from Howard College, Mr. Kendrick transferred to the College of Pharmacy at the University of Florida in September, 1952, where he is still in attendance.

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