[CONTRIBUTION FROM THE CHEMISTRY DIVISION OF OAK RIDGE NATIONAL LABORATORY]

Molecular Rearrangements. XIII. Additional Evidence for the Mechanism of the Aldehyde–Ketone Rearrangement[1]

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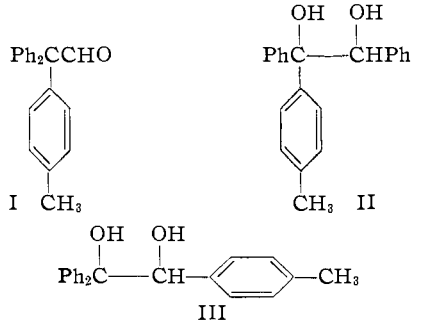
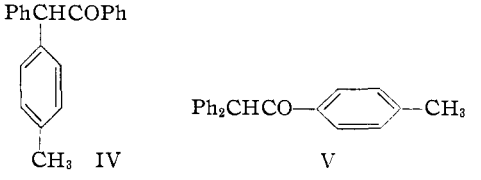
Phenyl-di-*p*-tolylacetaldehyde (VI) and the related system of glycols *threo*-VII, *erythro*-VII and VIII have been subjected to rearrangement in cold, concentrated sulfuric acid. The yields of the ketones (IX and X) produced were obtained in each case by the radioactivity dilution method.[3] The fates 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 Hearon equation,[4] it has been established that the *p*-tolyl/phenyl migration ratio in the rearrangement of VI is not reversed, but is greater than unity. The mechanism[4] proposed in paper VIII and correlating the aldehyde–ketone and pinacol rearrangements is thus supported.

Introduction

In three previous papers[1,3,4] the pinacol rearrangement of triaryl-substituted ethylene glycols and the closely related rearrangement of substituted acetaldehydes to ketones have been considered. A mechanism was proposed to explain the apparently anomalous[5,6] migratory aptitudes observed during the conversion of di- and trisubstituted acetaldehydes to their corresponding ketones. Through an application[4] of this mechanism to the rearrangements of diphenyl-*p*-tolylacetaldehyde (I) and the associated glycols II (both *threo* and *erythro* forms) and III, it was suggested that the migration ratio of the



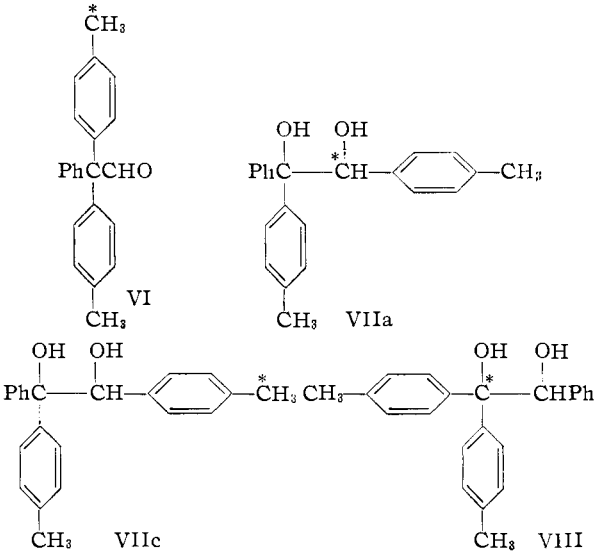
p-tolyl and phenyl groups of aldehyde I during its acid-catalyzed conversion to ketones IV and V was not directly calculable from the ratio of these two



ketones formed during the reaction, but was instead equal to $2k_T/k_P$, the ratio k_T/k_P having been evaluated[4] by means of equation 1. By a combination of double-labeling techniques and radioactivity dilution experiments upon appropriately labelled isotope position isomers of I, II and III, the ratios k_H/k_ϕ and m_e/m_d (m_e = moles of ketone V, m_d = moles of ketone IV) were calculated readily. The ratio k_{Tol}/k'_H, unfortunately, was so large that the error inherent in the experiments precluded its direct experimental determination. It was possible, however, to estimate k_{Tol}/k'_H by an indirect method, and thus to conclude that the *p*-tolyl/phenyl migration ratio in the rearrangement of I in cold, concentrated sulfuric acid was about 3, whereas a direct comparison of the ratio of the ketones IV and V would force the conclusion that, contrary to all previous experience,[7] this ratio was less than 1.

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

In order to establish whether the mechanism proposed[4] for the rearrangement of I to the ketones IV and V is general, several other examples of the



(1) This paper is based upon work performed at Oak Ridge National Laboratory which is operated by Union Carbide Corporation for the Atomic Energy Commission. Paper XII, V. F. Raaen and C. J. Collins, THIS JOURNAL, **80**, 1409 (1958).

(2) Graduate Fellow of the Oak Ridge Institute of Nuclear Studies from the University of Florida, Gainesville. A portion of this paper is taken from the Ph.D. dissertation of L. W. Kendrick, Jr.; senior advisor, University of Florida, Professor W. M. Lauter.

(3) C. J. Collins, THIS JOURNAL, **77**, 5517 (1955).

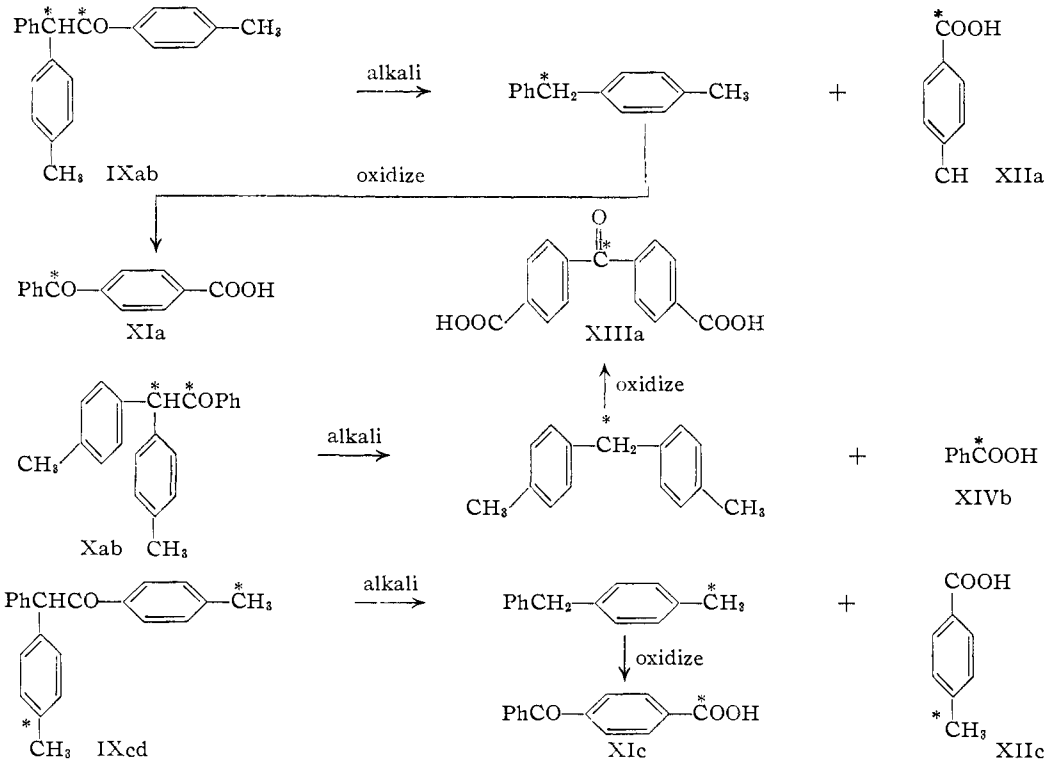
(4) B. M. Benjamin and C. J. Collins, *ibid.*, **78**, 4329 (1956).

(5) G. W. Wheland, "Advanced Organic Chemistry," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1949, pp. 494-495.

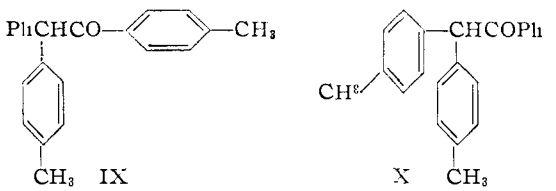
(6) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 479.

(7) Previous experimental determinations of the *p*-tolyl/phenyl migration ratio in diverse reactions are: W. E. Bachmann and R. V. Shankland, THIS JOURNAL, **51**, 306 (1929); W. E. Bachmann and J. W. Ferguson, *ibid.*, 2081 (1934), 16; W. E. McEwen, M. Gilliland and B. I. Sparr, *ibid.*, **72**, 3212 (1950), 5.0; J. G. Burr and L. S. Ciereszko, *ibid.*, **74**, 5426 (1952), 2.0; J. G. Burr, *ibid.*, **75**, 5008 (1955), 2.5; D. Y. Curtin and M. C. Crew, *ibid.*, **76**, 3719 (1954), 1.3; S. N. Ege and K. W. Sherk, *ibid.*, **75**, 354 (1953), 4.0; R. F. Tietz and W. E. McEwen, *ibid.*, **72**, 4011 (1955), 3.44; B. M. Benjamin and C. J. Collins, *ibid.*, **78**, 4952 (1956), 1.2.

CHART I



aldehyde–ketone rearrangement have been studied. In the previous paper[1] the diphenyl-*o*-tolyl system was discussed. In the present paper we report the results of experiments on compounds VI, VII (both *threo* and *erythro* forms) and VIII, in which we used techniques similar to those previously employed[3,4] in analogous systems. These compounds were selected as models for study for the following reasons: (1) It seemed likely from prior work[3,4] that in cold concentrated sulfuric acid VI, VII and VIII should yield the ketones IX and X in approximately equal amounts, thus providing a contrast with the



rearrangements of I, II and III in which the ratio IV/V was 4.7:1, for on a statistical basis alone one could predict that the rearrangement of VI in cold, concentrated sulfuric acid should yield the ketones X and IX in the ratio 4.7:4 corresponding to 54% X and 46% IX; (2) whereas k_{Tol}/k'_H was obtained by an indirect method in the previous study,[4] the present system should allow us to calculate the corresponding ratio directly; and (3) the aryl/hydrogen migration ratios (k_ϕ/k_H, k_{Tol}/k'_H, etc.) for three different carbonium ions in two different solvents (see Table IV of ref. 4) seemed to be related to one another in a predictable manner. Thus the aryl/hydrogen migration ratio increases in acid catalysts of higher ionizing power,[3] and decreases as the stability of the carbonium ion at the migration terminus becomes greater. We were interested in determining whether this correlation would hold for the present system.

Methods and Results

The aldehyde VI, the *threo* and *erythro* forms of the chain-labeled glycol VII (VIIa or VIIb), the *threo* form of the tolyl-labeled glycol VII (VIIc) and the chain-labeled glycol VIII were all subjected to rearrangement in cold, concentrated sulfuric acid at 0° under identical conditions. In each case the yields of ketones IX and X were determined by the carbon-14 dilution method.[8] The results of these yield determinations are given in Table I.

TABLE I

YIELDS OF KETONES IX AND X FROM THE ACTION OF H_2SO_4 AT 0° UPON VI, VIIa, VIIc AND VIII

Reactant	Combined yield,[a] % IX and X	Relative yield, % IX	X
VI	71.3	49.0	51.0
threo-VIIa	87.6	51.6	48.4[b]
erythro-VIIa	65.2	45.4	54.6[b]
VIII	91.4	40.0	60.0

[a] Based on total starting material. Reactants did not completely dissolve in the cold sulfuric acid solutions, thus part of the loss in yield is due to incomplete reaction. [b] The difference in yields of IX and X from the *erythro* and *threo* forms of VII is a consequence of different contributions of paths A and B (see Chart II and Table II).

The fractions of chain label and tolyl label which underwent rearrangement during conversion of the appropriately labeled reactants to the ketones IX and X were determined by: (1) alkaline cleavage of the ketones followed by (2) oxidation of the nonacidic fractions to suitable degradation products.

(8) R. H. Mayor and C. J. Collins, THIS JOURNAL, **73**, 471 (1951).

TABLE II

MOLAR RADIOACTIVITIES OF THE DEGRADATION PRODUCTS OF KETONES IX AND X OBTAINED BY THE ACTION OF H_2SO_4 AT 0° UPON VI, VIIa, VIIc AND VIII

	Molar radioactivity of degradation product[a]			
	From IX		From X	
Reactant	Toluic acid	*p*-Benzoyl-benzoic acid	Benzoic acid	4,4'-Di-carboxyl-benzo-phenone
VI	0.505	...	...	...
threo-VIIa	.971	0.030	0.979	0.021
erythro-VIIb	...	.66	...	.574
		(0.056)[b]		(0.295)[b]
threo-VIIc	.508	...	...	...
VIII	.014[c]	...	.009[c]	...

[a] The molar radioactivities of reactants are taken as 1.000 mc./mole, and of degradation products as fractions thereof. [b] *erythro*-VIIb contained 68.0% of the carbon-14 in the tertiary carbon and 32.0% in the secondary position. The numbers in brackets are the fractions of rearrangement calculated from these data. [c] These values have been neglected in making the calculations of Table III.

TABLE III

SUMMARY OF MOLE FRACTION (m_i) CALCULATIONS FROM THE DATA OF TABLES I AND II

	Calculated by			
	Method 1		Method 2	
m	*threo*-VII	*erythro*-VII	*threo*-VII	*erythro*-VII
m_a	0.010	0.161	0.010	0.161
m_b	.016	.025	.016	.025
m_c	.024	.042	.045	.059
m_d	.474	.385	.474	.385
m_e	.476	.387	.455	.370

For glycol VIII		
	Method 1	Method 2
m_f	0.203	0.184
m'_d	.397	.416
m'_e	.400	.400

The degradation products were then assayed for radioactivity. The degradative sequence are given in Chart I, and the results of the radioactivity assays for each fraction are given in Table II.

In order to have a comparison with the results[4] of the formic acid-catalyzed rearrangements of glycols II and III, the glycols *threo*-VIIc and VIII were subjected to rearrangement conditions in 98% formic acid at 25°. The yields of aldehyde, determined by the radioactivity dilution technique,[8] were 81% (from *threo*-VIIc) and 36% (from VIII). These yields permit calculation of a k_{Tol}/k'_H ratio (in formic acid) of 4.3, and a k_ϕ/k_H ratio of 0.56.

Discussion

Given in Chart II is a mechanism for the rearrangements, in concentrated sulfuric acid at 0°, of aldehyde VI and of *threo*- and *erythro*-VII. If we now define m_a, m_b, m_c, m_d and m_e, respectively, as the mole fractions of *threo*- or *erythro*-VII which proceed to products through paths A to E (Chart II), then from Tables I and II it is possible to calculate values for these mole fractions (m_i). Similarly, if m_f, m'_d and m'_e (also generalized for purposes of later discussion as m_i) represent the mole fractions of VIII which proceed to products through paths F, D' and E' (Chart III), then these values likewise may be determined. In order to calculate the various m_i we have treated the data of Tables I and II by two different methods: (1) In the first method the m_i were calculated directly for *threo*-VII from the yield data (Table I) and double-labeling experiments (Table II), and the value $m_e/m_d = 1.004$ obtained therefrom was used in subsequent m_i calculations for *erythro*-VII and VIII; and (2) in the second method the ratio of the yields of the two ketones IX and X (49:51 = 0.961) observed upon rearrangement of aldehyde VI was used in the same manner as described[1] in a previous paper. The calculations are given in the Experimental section, and the results of these calculations are listed in Table III.

By a method analogous to that previously used,[4] it can be shown that equation 1 applies to the mechanism, outlined in Charts II and III, for the rearrangement of aldehyde VI. The symbols employed in the present instance for the specific rate constants and for the various reaction paths of Charts II and III are the same as those employed in the analogous schemes for the rearrangements of I, II and III. This has been done to permit an easy comparison of the former[4] work with the data presented in this paper. Given in Table IV is a summary of the ratios, calculated from Table III, for use in equation 1. Given also in Table IV are the values for the *p*-tolyl/phenyl migration ratio ($k_T/2k_P$ calculated by means of equation 1.

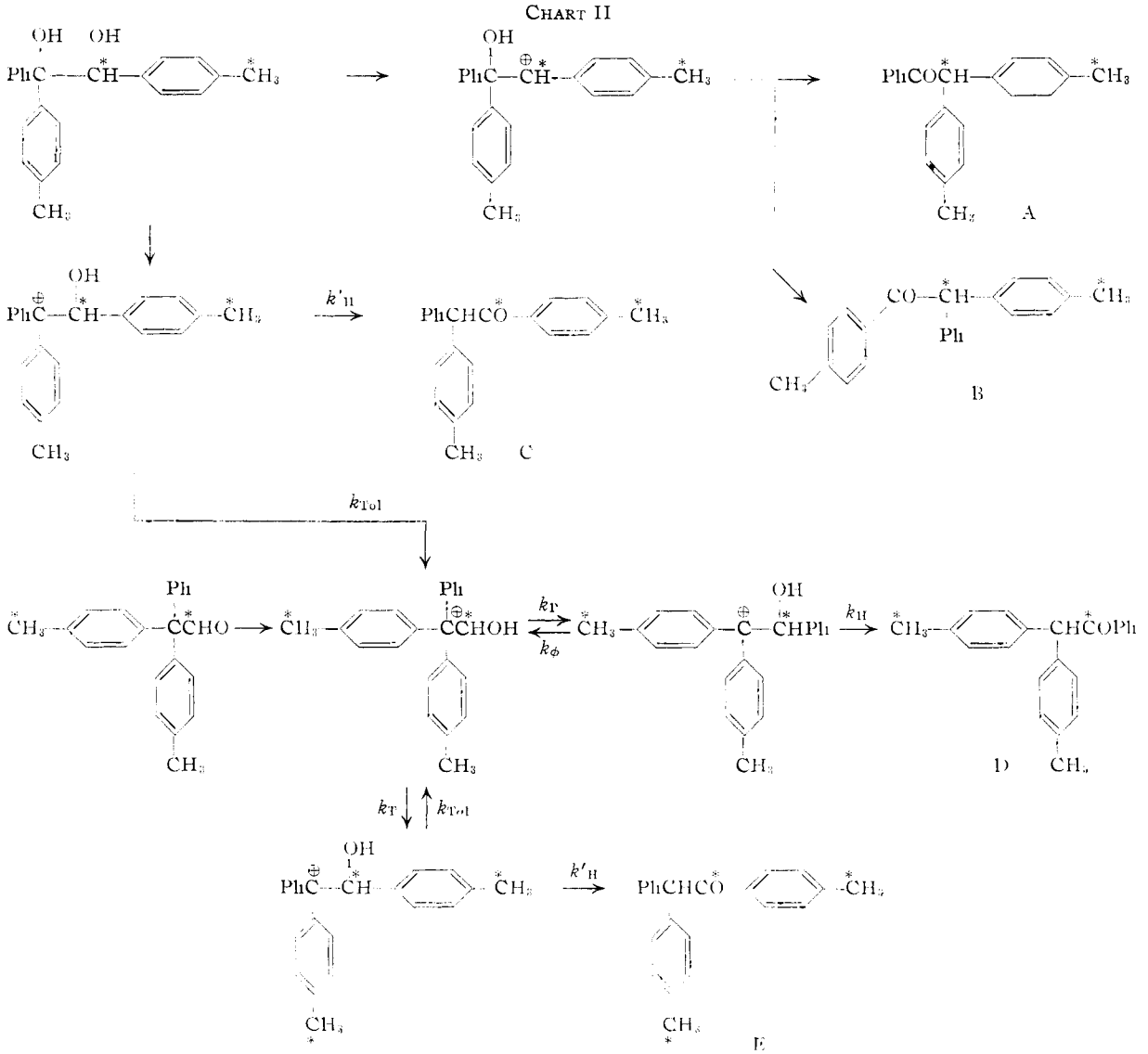
TABLE IV

SUMMARY OF THE RATIOS CALCULATED FOR USE IN OR BY MEANS OF EQUATION 1

	Method of calculation							
	1				2			
Ratio								
m_e/m_d			1.004				0.961	
k_ϕ/k_H			3.95				4.44	
$(m_c + m_e)/m_d$	1.05	*threo*-VII	1.11	*erythro*-VII	1.05	*threo*-VII	1.11	*erythro*-VII
k_{Tol}/k'_H	39.6		18.4		20.6		12.8	
$k_T/2k_P$	4.4		2.1		1.9		1.2	

From Table IV it is apparent that our data support a *p*-tolyl/phenyl migration ratio of greater than one, in agreement with our previously proposed[3,4] mechanism. Although the probable error in these calculations is not so easy to estimate as was the probable error of our former work,[1] a maximum value for m_c and thus a minimum ratio $k_T/2k_P$ can be estimated. This is possible because small changes in m_c will have more effect on the final ratio $k_T/2k_P$ calculated by means of equation 1, than will similar changes in all other m_i. Further, the calculations of m_i by method 1 for the *threo*-glycol are more reliable than those by method 2 for either *threo*- or *erythro*-glycol, for method 2 relies upon the relative yields of products from the rearrangement of aldehyde VI, and relatively small changes in these particular determinations will cause wide fluctuations in m_c. We have, therefore, estimated an upper limit for m_c through the one method of calculation (method 1) by which m_c for *threo*-VII is measured directly, by making the

CHART II



highly improbable assumption that the value (0.508) for the molar radioactivity of the toluic acid obtained from ketone IX upon rearrangement of *threo*-VIIc (Table II) is in error by 6% and possesses a value of 0.538. Thus m_c becomes 0.055, k_{Tol}/k'_H 16.8, and the tolyl/phenyl migration ratio $k_T/2k_P$ 1.7. There is another method available for estimating k_{Tol}/k'_H. Given in Table V is a summary of the k_ϕ/k_H ratios which have been determined for carbonium ions of increasing stability in cold, concentrated sulfuric and in formic acids. It can be seen that as the charge of the carbonium center of the migration terminus becomes more delocalized, the k_ϕ/k_H value decreases.[9] We have recently[10] determined that the k_{Tol}/k_H' value for the rearrangement of tri-*p*-tolylethylene glycol can be no less than 14. From Table V we would infer, therefore, that k_{Tol}/k'_H of the present system could also not be smaller than 14, and that the tolyl/phenyl migration ratios of Charts II and III should therefore not be smaller than 1.55 as an absolute minimum value.

(9) See also S. Winstein and E. Grunwald, THIS JOURNAL, **70**, 830 (1948).

(10) See Experimental section for details.

TABLE V

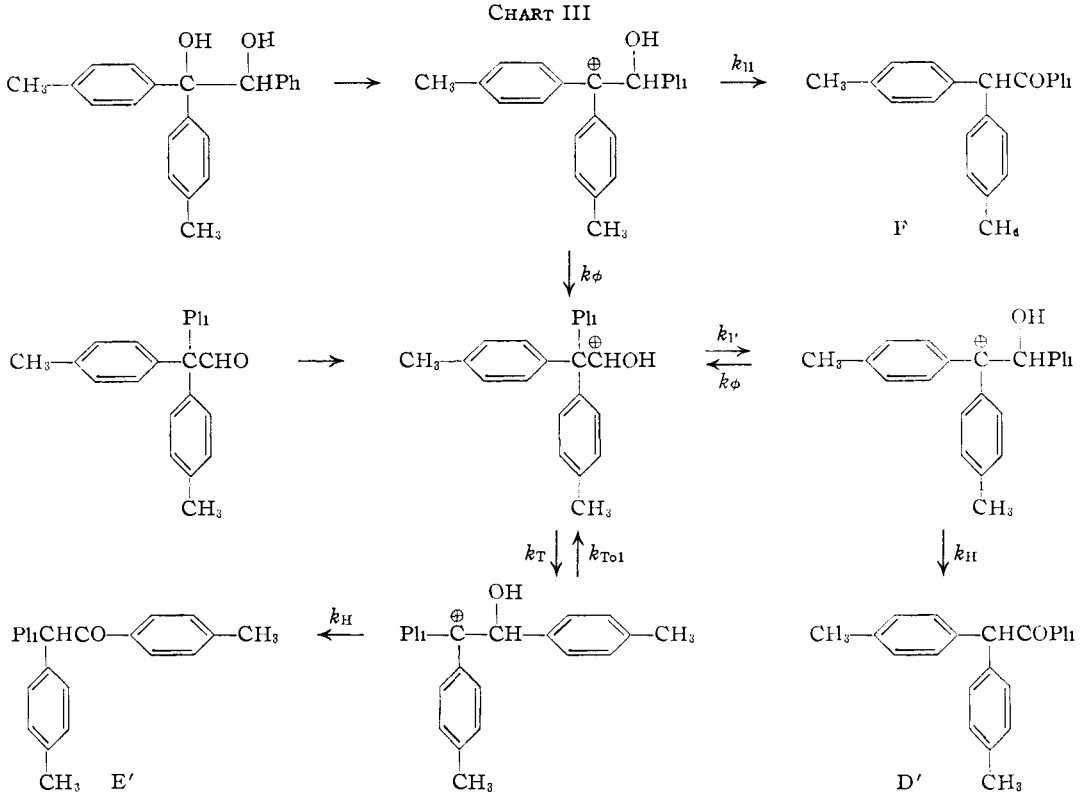
SUMMARY OF $k\phi/k$ RATIOS

Carbonium ion R = *p*-tolyl	Catalyst: Concd. H_2SO_4 at 0°	Catalyst: 99% HCOOH	Reference
$Ph_2\overset{\oplus}{C}CHOHPh$	7.3	1.7[a]	3
$PhC(R)\overset{\oplus}{C}HOHPh$	6.9	1.2	4
$R_2\overset{\oplus}{C}CHOHPh$	3.9–4.4	0.56	This paper

[a] Recalculated from the data of ref. 3 on the basis of unpublished experiments demonstrating 7% scrambling of the chain carbons of triphenylacetaldehyde upon rearrangement of this compound in boiling formic acid.

Three other facts are worthy of mention: (1) The *threo* and *erythro* isomers of glycol VII undergo rearrangement in sulfuric acid to produce different yields of ketones IX and X (see Table I). This is because the two glycols exhibit widely differing proportions of secondary hydroxyl removal. It is

CHART III



important to notice, however, that in each case the material which is funneled through the identical tertiary carbonium ion (Chart II) behaves identically; this can be seen (Table IV) from the values (1.05 and 1.11, respectively) for the ratios $(m_c + m_e)/m_d$; (2) the *erythro*-glycol exhibits secondary hydroxyl removal to the extent of about 20%, with a *p*-tolyl/phenyl migration ratio of about 6:1, whereas the *threo*-glycol exhibits secondary hydroxyl removal to the extent of about 3% with what appears to be a slight preference for phenyl over *p*-tolyl migration. Thus reaction paths A and B (Chart II) proceed with stereospecific migration of the neighboring aryl groups, migration of that group predominating which is presumed to shift to the opposite side of the migration terminus through a *trans* transition state[11,12]; and (3) the ratio (0.961) of the yields of ketones IX and X obtained upon rearrangement of VI in cold, concentrated sulfuric acid is the same, within experimental error, as that calculated (1.004) from the double-labeling experiments upon *threo*-VII (Tables I and II).

In summary, the foregoing data support in every respect the mechanism proposed[4] for the combined pinacol and aldehyde–ketone rearrangements of trisubstituted glycols and their corresponding aldehydes.

Experimental

p-**Methylbenzhydryl** *p*-**Tolyl Ketone (IX).**—Phenyl-*p*-tolylacetyl chloride was prepared through the sequence phenyl *p*-tolyl ketone ($LiAlH_4$) → phenyl-*p*-tolylcarbinol[13] (thionyl chloride) → phenyl-*p*-tolylmethyl chloride[13] (cuprous cyanide) → phenyl-*p*-tolylacetonitrile[14] → phenyl-*p*-tolylacetic acid[15] (thionyl chloride) → phenyl-*p*-tolylacetyl chloride. *p*-Tolylmagnesium bromide was prepared from 151 g. of *p*-bromotoluene and 21.5 g. of magnesium turnings. The ether solution was cooled and then treated with 83 g. 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 was continued until the distillate temperature reached 65°. Dry benzene (150 ml.) was added and the reaction mixture was cooled with ice-water. While the mixture was being stirred vigorously, 100 ml. of acid chloride solution in benzene, prepared from 84 g. of phenyl-*p*-tolylacetic acid, 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 g. (48%) of the ketone, m.p. 67.5–68.5°.

Anal. Calcd. 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 had a m.p. of 210–210.5°.

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

p-**Methylbenzhydryl** *p*-**tolyl ketone-C**^{14} **(IXa)** was prepared in the same manner as was IX, radioactive cuprous cyanide being used in the preparation of the phenyl-*p*-

(11) P. I. Pollak and D. Y. Curtin, THIS JOURNAL, **72**, 961 (1950); D. Y. Curtin and P. I. Pollak, *ibid.*, **73**, 992 (1951); D. Y. Curtin, E. E. Harris and P. I. Pollak, *ibid.*, **73**, 3453 (1951); and D. Y. Curtin and M. C. Crew, *ibid.*, **77**, 355 (1955).

(12) B. M. Benjamin, H. J. Schaeffer and C. J. Collins, *ibid.*, **79**, 6160 (1957).

(13) J. F. Norris and C. Banta, *ibid.*, **50**, 1804 (1928).

(14) J. Hoch, *Compt. rend.*, **197**, 770 (1933).

(15) K. Isimura, *Bull. Chem. Soc. Japan*, **16**, 196, 252 (1911).

tolylacetonitrile. The phenyl-*p*-tolylacetic acid used in the synthesis had a radioactivity assay of 2.193 ± 0.009 mc./mole. The pure ketone had a m.p. of 67–68° and 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.[4] 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 non-radioactive. 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 (VIIa). —*p*-Methylbenzhydryl *p*-tolyl ketone-C^{14} (8 g.) was dissolved in 120 ml. of glacial acetic acid, treated with 20 ml. of concentrated nitric acid, 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 of 1,2-di-*p*-tolyl 1-phenyl ketol was used directly for the reduction without further treatment. A slurry was prepared with 4.5 g. 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 g. of glycol, m.p. 147–150°, radioactivity assay 2.179 mc./mole. The melting point could be raised only by further repeated crystallization. The remaining material had a m.p. of 130–135°, identical with the behavior of an approximately equal mixture of the two diastereomers, prepared as described below.

threo-1,2-Di-*p*-tolyl-1-phenylethylene-1-C^{14} Glycol (VIIa). —Carboxyl-labeled *p*-toluic acid (55.5 g.) was treated with 25 g. 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 g. (98%) of *p*-methylbenzyl-α-C^{14} alcohol. The carbinol was treated with 100 g. 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 g. (98%) of the chloride. *p*-Methylbenzyl-α-C^{14} chloride was treated with sodium cyanide according to the method of Vogel.[16] Upon distillation of the product there was obtained 43.9 g. of the nitrile (85%). *p*-Tolylacetonitrile-α-C^{14} (43.9 g.) was treated with 100 ml. of 50% aqueous sulfuric acid, to which had been added 50 ml. of glacial acetic acid.[16] After being heated at reflux for one hour the mixture was poured over 500 g. 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 solution hydroxide and the solution was filtered through a pad of Celite. Upon acidification of the filtrate and cooling, there was obtained 39.4 g. (78%) of the pure acid, m.p. 90–91°.[17] The glycol was prepared by the identical method as indicated for the tolyl-labeled glycol VIIc, discussed in the following section, 19.4 g. of the above α-labeled *p*-tolyl acetic acid being employed in the synthesis. There was obtained 5.7 g. of the glycol VIIb, m.p. 156–157°, undepressed when mixed with an authentic sample (VIIe). Depression in melting point to 130–135° was observed when VIIb was mixed with approximately equal amounts of the *erythro* isomer; radiochemical assay, 2.121 ± 0.001 mc./mole.

threo-1,2-Di-*p*-tolyl-(2-*p*-methyl-C^{14})-1-phenylethylene Glycol (VIIc).—Benzoic acid-*carboxyl*-C^{14} was prepared by the carbonation of phenylmagnesium bromide with radio active carbon dioxide, using standard vacuum line technique. The carboxyl-labeled benzoic acid was esterified by the method of Acree[18] and then treated with lithium aluminum hydride in dry ether. The resulting benzyl-α-C^{14} alcohol was purified by distillation. Zinc (120 g.) was treated with 12 g. of mercurous chloride and then washed with water. The amalgam, 200 ml. of water, 25 ml. of concentrated hydrochloric acid and 25 g. of radioactive benzyl alcohol, was 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 g. (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 non-radioactive toluene to yield 43 g. of toluene-C^{14} with a radioactivity assay of 22.55 mc./mole. In a modification of the method reported in reference 19, 4 g. of methyl-labeled toluene in 200 ml. of carbon disulfide was first treated with 150 g. of anhydrous aluminum chloride and then, while being refluxed gently over a period of 45 minutes, with 41 g. of acetic anhydride. Refluxing was continued for 1.5 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° being retained (yield 51 g., 83%). *p*-Methyl-C^{14}-acetophenone (55.5 g.) was dissolved in 250 ml. of methanol and to it was added 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 put in until a total of one liter had been added. 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 g. 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 g.[20] (64.5%), m.p. 145–146°. The product was further characterized by preparation of the ethyl ester, m.p. 77°,[17] and reduction with lithium aluminum hydride to *p*-tolylethylene glycol, m.p. 76°,[21] in agreement with the literature. To a solution of 21 g. of the 4-methyl-C^{14}-mandelic acid in 185 ml. of glacial acetic acid was added 20 ml. of concentrated sulfuric acid and 3.2 g. 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 absorbed. 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 g. (84.4%) of the acid, m.p. 88–90°.[22] To 35.6 g. of *p*-tolylacetic acid (from several runs as described above) was added 50 g. of phosphorus 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 g. of anhydrous aluminum chloride and, after the initial vigorous reaction ceased, the mixture was heated under reflux for 1.5 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 were washed with water and evaporated to dryness. There was obtained 31.3 g. (62.6%) of α-(*p*-tolyl-C^{14})-acetophenone, m.p. 98–99°.[23] A solution of 28.3 g. of 4'-methyl-C^{14}-des-

(16) A. I. Vogel, "A Textbook of Practical Organic Chemistry," 2nd ed., Longmans, Green and Co., New York, N. Y., 1951, p. 722.

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

(18) S. F. Acree, *ibid.*, **37**, 2764 (1904).

(19) "Organic Syntheses," John Wiley and Sons, Inc., New York, N. Y., Coll. Vol I, pp. 109–111.

(20) A. M. Van Arendonk and M. E. Cupery, THIS JOURNAL, **53**, 3184 (1931).

(21) K. Isimura, *Bull. Chem. Soc. Japan*, **16**, 196, 252 (1941).

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

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

oxybenzoin 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 g. of bromine, dissolved in 50 ml. of carbon disulfide, was then added slowly while a rapid stream of nitrogen was passed through the solution.[24] 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 distil, 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 α-bromo-4'-methyl-C^{14}-desoxybenzoin was dissolved in 1 l. of 95% ethanol without further purification, and an equivalent amount of 10% ethanolic sodium hydroxide was added. The solution was stirred for 10 minutes and poured into 2 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 g. (95%) of the crude product, from which 26 g. of the pure 4'-methylbenzoin-C^{14} was obtained on crystallization from ethanol, m.p. 118°,[25] radioactivity assay 20.3 mc./mole. This sample was diluted with non-radioactive 4'-methylbenzoin to a tracer level of approximately 5 mc./mole. A Grignard reagent was prepared from 189 g. of *p*-bromotoluene and 26.5 g. of magnesium turnings. To it 100 g. of methyl-labeled 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 was 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. The yield of pure glycol VIIc, of m.p. 156.5–157°, was 45 g. (32%).

Anal. Calcd. 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 (VIIa).**—To 20 g. of *p*-tolyl-(acetic-2-C^{14}) acid, prepared as for *threo*-glycol VIIb above, was added 11 ml. of phosphorus trichloride and 60 ml. of toluene. The toluene solution was decanted onto 30 g. 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 g. (67%) of the desoxybenzoin was obtained, m.p. 101–102°.[26] The α-bromodesoxybenzoin was prepared as described previously for 4'-methyl-α-bromodesoxybenzoin, 19.9 g. of the desoxybenzoin above and 14.8 g. of bromine in 75 ml. of carbon disulfide being employed. Upon evaporation of the solvents, a solid compound separated, which upon crystallization from hexane had a m.p. of 96°, and a radioactivity assay of 2.037 mc./mole. This material was treated with base in alcoholic solution, followed by acidification in a manner described previously for the preparation of 4'-methylbenzoin; 9.9 g. (46%) of pure benzoin was obtained, m.p. 87–88°.[27] To a Grignard solution prepared from 2.74 g. of magnesium turnings and 15.7 g. of bromobenzene in ether, was added 9.9 g. of the 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 g. of the glycol, *erythro*-VIIa, m.p. 160–161°; radiochemical assay, 2,102 mc./mole. Degradation of this glycol disclosed 8.1% of the carbon-14 in the 1-position. In another preparation of the *erythro*-glycol VIIb in which appropriately labeled starting materials were used, there was obtained a product whose radioactivity assay was 3.978 ± 0.003 mc./mole, and whose radioactivity distribution was 68.0% in the 1-position and 32.0% in the 2-position.

Anal. Calcd. 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 (VIII).—Mandelic-*carboxyl*-C^{14} acid was prepared by the method of Vogel[16] from benzaldehyde, radioactive sodium cyanide and sodium bisulfite, with subsequent hydrolysis of the nitrile with concentrated hydrochloric acid. It was converted to the methyl ester by the method of Acree,[18] and thence with *p*-tolylmagnesium bromide to 22 g. (51.5%) of glycol VIII, m.p. 155–157°. Crystallization from 95% ethanol produced the pure glycol,[28] m.p. 158–158.5°, radioactivity assay 2.153 ± 0.015 mc./mole. On oxidation of the glycol with chromium 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 non-radioactive.

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

Di-*p*-tolylphenylacetaldehyde (VI).—A 5.000-g. sample of *threo*-1,2-di-*p*-tolyl-(*2-p-methyl-*C^{14})-1-phenylethylene glycol (VIIc) 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 subsequently filtering, 3.764 g. (79.8%) of the nearly pure aldehyde was obtained, m.p. 93–94°. On recrystallization from 95% ethanol the pure compound was obtained; m.p. 94.5–95°; radioactivity assay, 5.235 ± 0.025 mc./mole.

Anal. Calcd. 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 had a m.p. of 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.

Anal. Calcd. 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 (X).—Di-*p*-tolyl ketone was converted to the carbinol[29] by reduction with lithium aluminum hydride, and thence to di-*p*-tolylchloromethane[29] by treatment with thionyl chloride. The slightly colored product, which on distillation (b.p. 163–168° (0.6 mm.)) gave 108 g. (95.7%) of a water-white oil, crystallized spontaneously on standing. Crystallization from hexane gave the pure compound, m.p. 44–45°.[29] A mixture of 100 g. of di-*p*-tolylchloromethane and 45.5 g. of cuprous cyanide (20% excess) was converted to di-*p*-tolylacetonitrile as described previously for the preparation of diphenylacetonitrile.[30] The product was distilled (b.p. 165–175° (7 mm.)) to yield 69 g. (72%) of a slightly yellow oil which spontaneously crystallized on standing. Crystallization from hexane yields pure white crystals of di-*p*-tolylacetonitrile, m.p. 46.5–47°. Hoch[31] gives b.p. 212° (18 mm.) and does not record the melting point of the compound. A mixture of 65 g. of di-*p*-tolylacetonitrile, 120 ml. of glacial acetic acid and 600 ml. of 50% aqueous sulfuric acid was heated under reflux with vigorous stirring for 3.5 hours. The mixture was then cooled and poured into one liter 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 g. (85%), m.p. 143°.[32] Conversion of 67 g. of di-*p*-tolylacetic acid to the acid chloride was accomplished in 250 ml. of hexane by treatment with 100 ml. of thionyl chloride. Diphenylcadmium was prepared

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(25) A. Weissberger, *ibid.*, 223 (1935).

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

(27) C. D. Shacklett and H. A. Smith, THIS JOURNAL, **75**, 2654 (1953).

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

(29) J. F. Norris and J. T. Blake, THIS JOURNAL, **50**, 1810 (1928).

(30) W. A. Bonner and C. J. Collins, *ibid.*, **75**, 5376 (1953).

(31) J. Hoch, *Compt. rend.*, **197**, 770 (1933).

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

from 131 g. of bromobenzene, 20.3 g. of magnesium turnings and 80 g. of anhydrous cadmium chloride. This reagent was treated with di-*p*-tolylacetyl chloride as described[30] for the preparation of benzhydryl phenyl ketone. The fraction, b.p. 236–242° at 0.5 mm., was a slightly yellow oil weighing 77 g. After three crystallizations from ether–hexane (1:20) at Dry Ice temperature, 66 g. (79%) of the pure ketone X was obtained, m.p. 57–58°.[28]

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

Rearrangements Catalyzed by Sulfuric Acid.—In a typical experiment 3.000 g. of radioactive glycol (VII or VIII) or aldehyde VI was added to 70 ml. of concentrated sulfuric acid, previously cooled to 0° in an ice–salt-bath. Stirring was continued while the temperature was maintained between −2° to 0°. 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 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 was dissolved in chloroform, transferred quantitatively to a 100-ml. volumetric flask and diluted with chloroform to 100 ml. One 50-ml. aliquot was transferred to a flask containing 2.000 g. of non-radioactive ketone IX and the remaining 50-ml. aliquot was transferred to a flask containing 2.000 g. of non-radioactive ketone X. 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. Each fraction was then dissolved in hexane and passed through a column of alumina to remove any unreacted glycol. The eluents were once again taken to dryness. The aliquot to which ketone IX had been added was reduced with lithium aluminum hydride and the corresponding carbinol was recovered in the usual way. To the residue remaining after evaporation of the ether there was added 20 ml. of pyridine and 8 ml. of acetic anhydride. The mixture was boiled for 15 minutes and then poured on ice. The acetyl derivative was recovered and crystallized three times from hexane (Norit) and once from ethanol. The m.p., 144°, was not changed by the last two crystallizations. Although the reduction and subsequent acetylation of IX produces both *erythro*- and *threo*-acetates, the one whose m.p. is 144° is very easily isolated and purified.

Anal. Calcd. for $C_{24}H_{24}O_2$: C, 83.69; H, 7.02. Found: C, 83.73; H, 6.89.

The aliquot to which ketone X had been added was reduced with lithium aluminum hydride. The recovered carbinol was dissolved in 20 ml. of pyridine and 2.5 g. of *p*-nitrobenzoyl chloride was added. After heating the mixture on the steam-bath for two hours, it was poured on ice. The recovered *p*-nitrobenzoate derivative of the carbinol was crystallized twice from ethanol, once from hexane (Norit), again from ethanol and finally from ethanol–ether mixture. The m.p., 152°, was not changed by the last two crystallizations.

Anal. Calcd. for $C_{29}H_{25}NO_4$: C, 77.14; H, 5.58. Found: C, 76.97; H, 5.59.

The conversion of each of the above aliquots to high melting derivatives was absolutely essential in the application of the isotope dilution method of analysis, for in earlier experiments in which the ketones themselves were isolated, repeated crystallization 7–12 times was not sufficient to give reliable results. Following are the data from which the yields given in Table I were calculated: Compound VI (5.274 ± 0.0026 mc./mole), 2.9534 g., treated as above yielded the derivative of IX whose radioactivity assay was 1.079 ± 0.001 mc./mole, and the derivative of X whose radioactivity assay was 1.112 ± 0.004 mc./mole; *threo*-VII, 3.0028 g. (5.429 ± 0.011 mc./mole), derivatives: IX, 1.315 ± 0.002 mc./mole; X, 1.221 ± 0.003 mc./mole, 2.065 g. of X added; *erythro*-VII, 3.1798 g. (3.978 ± 0.003 mc./mole), derivatives: IX, 0.7230 ± 0.0010 mc./mole; X, 0.8383 ± 0.0026 mc./mole; compound VIII, 3.0529 g. (2.257 ± 0.008 mc./mole), derivatives: IX, 0.4705 ± 0.005 mc./mole; X, 0.6367 ± 0.0019 mc./mole.

Rearrangements Catalyzed by Formic Acid.—In a typical experiment 2.000 g. of the glycol was stirred with 100 ml. of 98% 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 quantitatively to a 200-ml. volumetric flask. A 20-ml. aliquot was taken and added to 150 mg. of non-radioactive aldehyde VI, 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, then cooled in an ice-bath and the product was 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. Thus it was shown that the glycol *threo*-VIIc yielded 81% of VI, and the glycol VIII yielded 36% of VI under these conditions. Both results are corrected for 94.1% recovery of VI, as indicated in the following section.

Stability in Formic Acid of the Aldehyde VI.—In order to determine the recovery of the aldehyde under the reaction conditions, the foregoing procedure was repeated with purified, radioactive VI. 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. 93–94°. 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%.

Procedure for the Cleavage of Ketones IX and X.—In a typical experiment 0.5 g. of the ketone IX or X 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 g. 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 and acidified to recover the acid. 4,4′-Dicarboxybenzophenone was crystallized from boiling glacial acetic acid; *p*-benzoylbenzoic acid was purified either by sublimation of the acid or by conversion to the methyl ester by means of diazomethane and subsequent crystallization from methanol. The results of these experiments are summarized in Table II.

Stability of Ketones IX and X in Concentrated Sulfuric Acid.—In separate experiments 1.000 g. of each of the ketones IX and X was stirred with 20 ml. of concentrated sulfuric acid while the temperature was maintained at 4°. After 30 minutes the mixture was poured into ice-water and extracted in a manner identical with that employed in the rearrangements of the glycols and the aldehyde. In the case of 4,4′-dimethylbenzhydryl phenyl ketone (X), the recovery of ketone with m.p. 58° was 98.8% and in the case of 4-methylbenzhydryl *p*-tolyl ketone (IX) the recovery of ketone with m.p. 68° was 99.1%. The fluorescent green coloration and ether-insoluble material, which was always observed in the sulfuric acid rearrangements, was entirely absent during the ketone stability tests.

Calculations of m_i. (a) For *threo*-VII; Method 1

$m_a + m_d = 0.484$; $m_b + m_c + m_e = 0.516$ (Table I)

$m_a = 0.021 \times 0.484 - 0.010$

$m_b = 0.030 \times 0.516 = 0.016$

$m_c + m_e = 0.500$

Let c = fraction IX formed through path C, then (0.97 − c) is the fraction of IX formed through path E.

$$0.508 = c + \frac{0.97}{2} - c \text{ (Table II)}; \quad c = 0.046$$

$m_c = 0.046 \times 0.516 = 0.024$

$m_e = 0.476$ and $m_d = 0.474$

Method 2.—The ratio of IX/X from rearrangement of VI = 0.961 (Table I). Therefore $m_d \times 0.961 = m_e = 0.455$ and $m_c = 0.500 - 0.455 = 0.045$.

(b) For *erythro*-VII; **Method 1.**—The *erythro*-glycol has 68% of its carbon-14 in the 1-position and 32% in the 2-position. From Table II, x = fraction of rearrangement in X. Therefore

$$0.32x \times 0.68\,(1 - x) = 0.574$$
$$x = 0.295$$

y = fraction of rearrangement in IX, then

$$0.32y + 0.68\,(1 - y) = 0.66$$
$$y = 0.056$$

$m_a + m_d = 0.546$; $m_b + m_e = 0.454$

$m_a = 0.295 \times 0.546 = 0.161$;
$m_b = 0.056 \times 0.454 = 0.0254$

$m_d = 0.385$

$m_c + m_e = 0.429$

$m_e = m_d \times 1.004 = 0.387$; thus $m_c = 0.042$

Method 2

$m_e = m_d = 0.961 = 0.370$; thus $m_c = 0.059$

(c) For VIII; **Method 1**

$m_f + m'_d = 0.600$ (Table I)

$$m'_e = 0.400; \quad m'_d = \frac{0.400}{1.004} = 0.397 \text{ and } m_f = 0.203$$

Method 2

$$m'_d = \frac{0.400}{0.961} = 0.416 \text{ and } m_f = 0.184$$

Preparation and Rearrangement of Tri-*p*-tolylethylene Glycol.—In a typical run, 10 g. of 4,4′-dimethylbenzoin[27] in 150 cc. of ether was added to the Grignard reagent prepared from 21.4 g. of *p*-bromotoluene and 3.0 g. of magnesium turnings. After addition was complete the mixture was heated under reflux for 4.5 hours, then poured over ice to which had been added saturated, aqueous ammonium chloride solution. The crude glycol was obtained through ether extraction and weighed 8 g. (61% of theory). Upon crystallization from ethanol followed by crystallization from hexane there was obtained 5.9 g. of white needles, m.p. 161°.

Anal. Calcd. for $C_{23}H_{24}O_2$: C, 83.1; H, 7.29. Found: C, 83.27, 83.48; H, 7.31, 7.29.

In an analogous experiment 9.5 g. of 4,4′-dimethylbenzoin,[27] 2.6 g. magnesium turnings and 16.9 g. of *p*-bromotoluene-*methyl*-C^{14})-tri-*p*-tolylethylene glycol, m.p. 161.5°; radioactivity assay, 3.387 ± 0.017 mc./mole.

For the preparation of chain-labeled 1,1,2-tri-*p*-tolylethylene glycol, chain-labeled 4,4′-dimethylbenzoin and non-radioactive *p*-bromotoluene were employed to yield a product whose m.p. was 161.5°, and whose radioactivity assay was 1.871 ± 0.012 mc./mole. Oxidation of this glycol with chromic acid yielded *p*-toluic acid, 0.1089 ± 0.0002 mc./mole, and di-*p*-tolyl ketone, whose 2,4-dinitrophenylhydrazone had a m.p. of 221° and a radioactivity assay of 1.752 ± 0.003 mc./mole, corresponding to 94.15% carbon-14 in the 1-position and 5.85% carbon-14 in the 2-position.

The foregoing isotope position isomers of 1,1,2-tri-*p*-tolylethylene glycol were subjected to rearrangement in cold concentrated sulfuric acid as described for compounds VI, VII and VIII. The products were dissolved in hexane and passed through alumina to yield 60–80% of α-*p*-tolyl-4,4′-dimethyldesoxybenzoin, a viscous oil which was characterized by alkaline cleavage to *p*-toluic acid and di-*p*-tolylmethane. The latter fractions were oxidized with chromic acid in acetic acid to the di-*p*-tolyl ketones which were converted to 2,4-dinitrophenylhydrazones. The degradation products from oxidation of the tolyl-labeled ketone were: toluic acid, m.p. 176°, 1.145 ± 0.004 mc./mole; di-*p*-tolyl ketones 2,4-dinitrophenylhydrazone, m.p. 220°, 2.188 ± 0.016 mc./mole. The degradation products from oxidation of the chain-labeled ketone were: toluic acid, m.p. 176°, 0.1888 ± 0.0005 mc./mole, and di-*p*-tolyl ketone 2,4-dinitrophenylhydrazone, m.p. 221°.

Calculation of k_{Tol}/k'_H Ratio for the Rearrangement of Tri-*p*-tolylethylene Glycol.—These calculations are carried out in an analogous fashion to those previously reported (ref. 3, Chart I) for the rearrangement of triphenylethylene glycol. Let x be the fraction of secondary hydroxyl removal (corresponding to path 1 in ref. 3), then (1 − x) represents the fraction proceeding through tertiary hydroxyl removal. Then $0.9415x + 0.0585(1 - x) = 0.1015$ and $x = 0.0487$. In order to calculate a *minimum* value for k_{Tol}/k'_H we assume that only the unlabeled tolyl group migrates to the secondary carbonium ion. Thus let y correspond to path 2 (ref. 3) then (0.951 − y) corresponds to path 4 and

$$y + \frac{(0.951 - y)}{3} = 0.656$$

$y = 0.0645$; $(0.951 - y) = 0.887$

and

$$\frac{k_{Tol}}{k'_H} = \frac{0.887}{0.0645} = 14$$

OAK RIDGE, TENNESSEE

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF WAYNE STATE UNIVERSITY]

Nitrogen Analogs of Ketenes. IV.[1] Reactions with Carboxylic Acids

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The nitrogen analogs of ketenes react readily with carboxylic acids to form imides in good yield. The dicarboxylic acids, phthalic and succinic, form the acid anhydride when treated with a ketenimine. The structure of one of the unsymmetrical imides was proved by independent synthesis and infrared analysis. Evidence was obtained that the reaction of ketenimines with carboxylic acids proceeded *via* an intermediate that was a more active acylating agent than the imide. This intermediate is considered to be the isoimide. The imides were shown to be acylating agents for alcohols, aliphatic amines and aromatic amines. The attack of a nucleophilic agent upon an unsymmetrical imide was shown to be subject to steric control.

Staudinger published the first study of nitrogen analogs of ketenes in 1920[4] and 1921.[5] The ketenimines were prepared by reaction of a ketene with a phosphinimine or an isocyanate with a phosphine-

(1) Part III is in THIS JOURNAL, **79**, 6057 (1957).

(2) Abstracted from the dissertation submitted by M. E. Munk in partial fulfillment of the requirement for the degree of Doctor of Philosophy, Wayne State University, 1957.

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(4) H. Staudinger and J. Meyer, *Ber.*, **53B**, 72 (1920).

(5) H. Staudinger and E. Hauser, *Helv. Chim. Acta*, **4**, 887 (1921).