λ^{EtOH} 255 mμ (ϵ 8700), λ^{KBr} 5.76, 5.93, 6.20 μ. The nuclear magnetic resonance spectrum determined in deuteriochloroform solution did not have a signal characteristic of an olefinic proton.

Anal. Calcd. for $C_{32}H_{50}O_3$: C, 79.62; H, 10.44. Found: C, 79.73; H, 10.79.

Attempted dehydrobromination with lithium bromide and lithium carbonate in dimethylformamide gave a mixture of debrominated and dehydrobrominated product.[19]

Acknowledgment.—We wish to thank Professor Carl Djerassi, Stanford University, for the optical rotatory dispersion spectra reported. The support of the National Institute of Arthritic and Metabolic Diseases, Public Health Service (Grant A-3439), is gratefully acknowledged.

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[19] M. E. Kuehne, *J. Am. Chem. Soc.*, **83**, 1492 (1961), has noted debromination accompanying dehydrobromination with this reagent.

The Pinacol Rearrangement of 1-Phenyl-2-methylpropane-1,2-diol

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Received March 21, 1962

The classical example of the aldehyde–ketone rearrangement, that of 2-phenyl-2-methylpropanal and the related glycol, 1-phenyl-2-methylpropane-1,2-diol, in formic acid has been studied kinetically. The phenyl–methyl migratory ratio has been found to be 24.8 to 1. The rearrangement of the glycol in concentrated sulfuric acid has also been studied, and the results compared with those in formic acid. The results of both reactions are interpreted in the light of the complex equilibria of carbonium ions proposed for reactions of this type.

The pinacol rearrangements of trisubstituted 1,2-glycols, and the closely related aldehyde-ketone rearrangement have long been considered to be an anomalous case of the pinacol rearrangement, where migratory aptitudes are apparently reversed.[1]

Although the apparent anomaly of this reaction has been satisfactorily explained recently by Collins,[2] the classical example of the aldehyde–ketone rearrangement, that of 2-phenyl-2-methylpropanal (I) to 3-phenyl-2-butanone[1,3] (II), has not been reinvestigated since the advent of modern theoretical concepts or experimental methods. Our attention was drawn to this reaction several years ago, when it was found that 2-phenyl-2-methylpropanal prepared from the reaction of 1-phenyl-2-methylpropane-1,2-diol (III) and formic acid[4] showed infrared absorption at 5.94 μ in addition to the expected aldehyde band at 5.78 μ. This band could only be consistent with the formation of isobutyrophenone (IV) in this reaction, whereas it would be expected that any subsequent rearrangement of the aldehyde should give 3-phenyl-2-butanone.[2,3]

It was found early in our work that by increasing the reaction time in the dehydration of 1-phenyl-2-methylpropane-1,2-diol with formic acid, that the percentage of aldehyde produced decreased. It is thus apparent that, since the over-all yield of rearranged product is good even after a relative short reaction time,[4] the pinacol rearranges rapidly, followed by a considerably slower rearrangement of the aldehyde to 3-phenyl-2-butanone, and/or isobutyrophenone.

We have carried out a series of rearrangements at various times and analyzed the products by a combination of gas chromatography and chemical techniques. The results of these rearrangements are summarized in Table I. We have also found that both ketones (II and IV), are recovered unchanged on boiling with formic acid for forty hours, and that at the end of thirty minutes all the glycol is consumed.[5]

TABLE I

SUMMARY OF THE RESULTS OF THE REACTION OF III WITH 97% FORMIC ACID

Time	% I	% II	% IV
15 min.	77	6	17
30 min.	76	7	17
1 hr.	77	6	17
4 hr.	74	6	20
13.5 hr.	56	13	31
20.5 hr.	51	15	34
26 hr.	38	19	43
36 hr.	35	19	46
48.7 hr.	25	19	56
60 hr.	22	21	57
68 hr.	21	19	60
80 hr.	23	19	58
95.5 hr.	21	19	60
209.5 hr.	12	23	65

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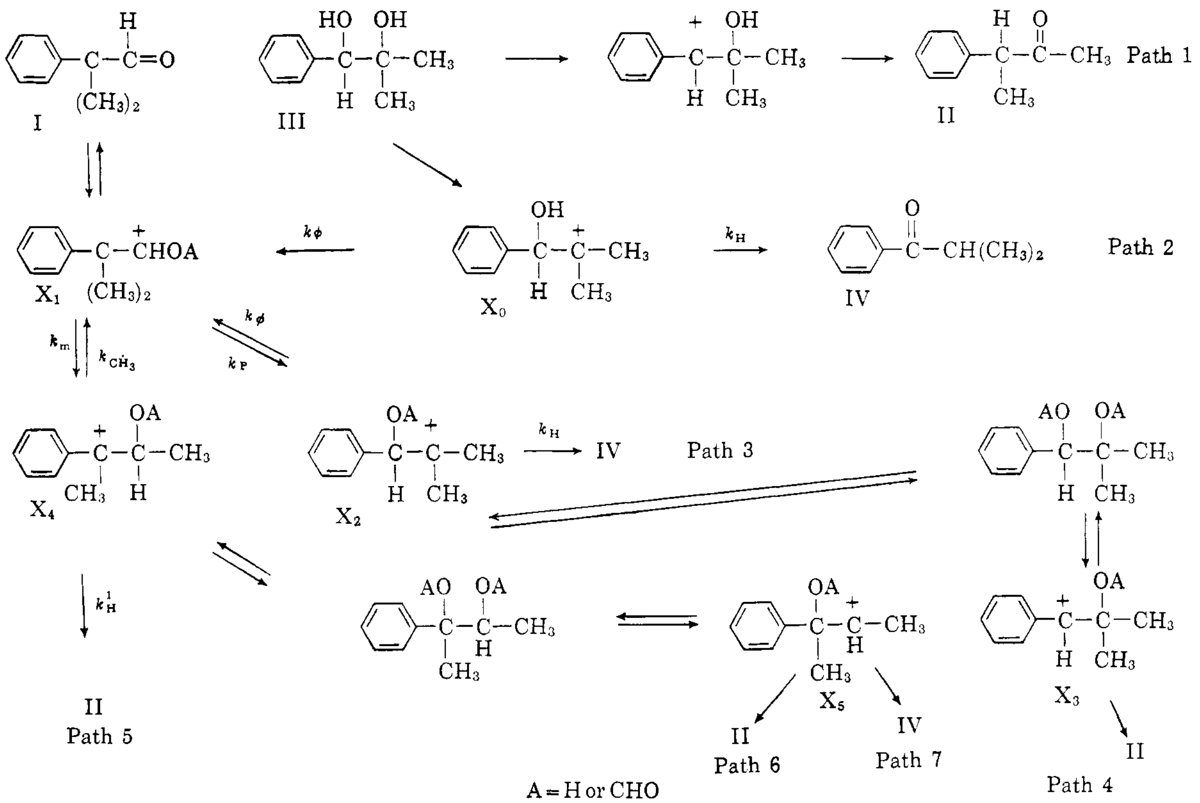
[1] (a) G. W. Wheland, "Advanced Organic Chemistry," 2nd ed., John Wiley and Sons, Inc., New York, 1953, pp. 494–534; (b) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, New York, 1953, p. 479.

[2] (a) C. J. Collins, *Quart. Rev.*, **14**, 357 (1960); (b) B. M. Benjamin and C. J. Collins, *J. Am. Chem. Soc.*, **78**, 4329 (1956).

[3] A. Orekhov and M. Tiffeneau, *Compt. rend.*, **182**, 67 (1926).

[4] N. H. Cromwell and H. H. Eby, *J. Am. Chem. Soc.*, **74**, 4201 (1952).

[5] This was done by carefully weighing the products from a thirty-minute run, diluting with a known weight of acetophenone, and checking the relative percentages of acetophenone and total reaction products by gas chromatography. The diol is not removed from the column under the conditions of temperature and flow rate used in this determination.



It is of course, probable, that the over-all course of this rearrangement follows the same general course of the rearrangement of diphenyl-*p*-tolylacetaldehyde, studied by Collins,[2b] although the principal product is the result of phenyl migration. It will then follow that the rearrangement of 1-phenyl-2-methyl propane-1,2-diol, and the related aldehyde (I) with formic acid will be a series of equilibria as shown in Chart I.

From the data in Table I, it is evident that the relative amounts of aldehyde, and ketones are unchanged during the first hour of the reaction; thus virtually all of the products formed in the first hour are derived from direct reaction of the glycol, rather than from rearrangement of the aldehyde. Consequently all the 3-phenyl-2-butanone present at this time must arise from secondary hydroxyl removal, followed by methyl migration (path 1), while the aldehyde and isobutyrophenone must be derived from tertiary hydroxyl removal followed by either phenyl or hydrogen migration.[6] It is also apparent from the data given in Table I for the runs of one hour and less that the ratio of removal of tertiary to secondary hydroxyl removal for glycol III in formic acid will be given by equation 1.

$$\frac{\text{Removal of } 3^\circ \text{ OH}}{\text{Removal of } 2^\circ \text{ OH}} = \frac{\%\ \text{I}_{1\text{ hr.}} + \%\ \text{IV}_{1\text{ hr.}}}{\%\ \text{II}_{1\text{ hr.}}} = 15.7 \quad (1)$$

In addition the relative rate of hydrogen to phenyl migration for this reaction will be given by equation 2.

$$k_\phi/k_\text{H} = \frac{\%\ \text{I}_{1\text{ hr.}}}{\%\ \text{IV}_{1\text{ hr.}}} = 4.5 \qquad (2)$$

Since all the diol had been consumed after one hour, and it has been shown (*vide supra*) that the ultimate products, II and IV are stable to the conditions of the reaction, it is possible to employ a kinetic approach to this reaction. By correcting the percentages at one hour for II and IV formed from direct dehydration of the glycol, *i.e.*, considering that one hour is t_0 for kinetic purposes, it is found that the rate of disappearance of the aldehyde follows rather good first-order kinetics from one to sixty hours.[7] The rate constant for this reaction in boiling formic acid is found to be 1.59×10^{-2} hr.$^{-1}$.[8] Since the aldehyde decomposes by two paths, to ions X_2 and X_4, and thence to products, and if it be assumed that the various paths resulting from esterification of ions X_2 and X_4 are of negligible importance,[9] then the rate constant for the aldehyde may be treated as that of a simple decomposition *via* two parallel first-order reactions (paths 3 and 5) and it may be

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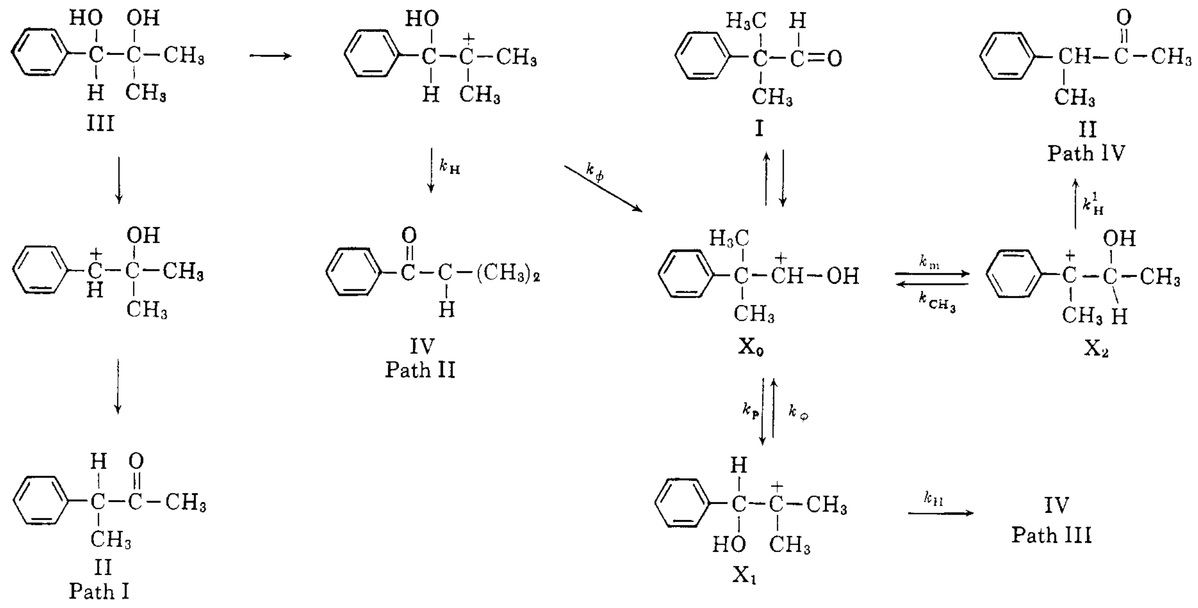
[6] Although it is of course possible to propose a "vinyl dehydration" rather than a hydride shift, there appears to be overwhelming evidence against such a process. This is thoroughly discussed by Collins (ref. 2a and numerous references cited therein).

[7] The reaction is, of course, pseudo-first-order, since the formic acid is involved as a reactant, but is present in many-fold excess. We have no *a priori* explanation for the deviation from good first-order kinetics over sixty hours.

[8] The points used to calculate this rate constant are those from one to 48.7 hours, inclusive.

[9] While these are of definitely minor importance, the change in ratio of the experimentally determined amounts of the ketones indicates they are not completely negligible.



calculated that the rate constant for the decomposition of the aldehyde *via* path 3 (k_1) is 1.10 × 10^{-2} hr.$^{-1}$ and that *via* path 5 (k_2) is 4.86 × 10^{-3}.[10]

By applying the steady-state approximation[11] to ion X_2 the following expression for k_1 may be derived:

$$k_1 = \frac{k_H k_P}{k_\phi + k_H} = 1.10 \times 10^{-2} \qquad (3)$$

Since k_ϕ/k_H has been found (*vide supra*) to be 4.5 it follows that $k_P = 6.05 \times 10^{-2}$. By applying the same approximation to ion X_4, and making the assumption that $k_H >> k_{CH_3}$ then, $k_2 = k_m = 4.86 \times 10^{-3}$.[12]

This method of calculation gives a value of 12.4 for the k_P/k_m ratio and since there are two methyls per phenyl, a phenyl to methyl migratory aptitude of 24.8 to 1.

This rearrangement has been also carried out using sulfuric acid as the catalyst, by Collins[13] using 1-phenyl-2-methylpropane-1,2-diol-1-C^{14} and in our laboratory using unlabeled material. In both cases it was found that after fifteen minutes there was formed 5% of the aldehyde, 63% 3-phenyl-2-butanone, and 32% isobutyrophenone. From the experiments using labeled material it was found that the ratio of tertiary to secondary hydroxyl removal was 15.7:1. Once again it may be assumed that the over-all course of the reaction is the same as that elucidated by Collins, for the general dehydration of trisubstituted glycols in sulfuric acid,[2] and is represented by Chart II. Since there is only 6% secondary hydroxyl removal, it follows that only 6% of the total of 63% of 3-phenyl-2-butanone was formed *via* path 1, and the remaining 57% was from path 4. It has been found[2b] that the k_{aryl}/k_H ratio is increased by a factor of about 5.5 in going from formic to sulfuric acids. In our case this gives a value of k_ϕ/k_H = 25, and shows that 28% of the glycol rearranges by path III, and only 4% by path II. The over-all irreversibility of the sulfuric acid-catalyzed reactions under the conditions used was verified by checking the stability of the products under these conditions. After treatment with cold, concentrated sulfuric acid for fifteen minutes, both isobutyrophenone and 3-methyl-2-butanone were recovered unchanged.

Although it is difficult to compare precisely the results in formic acid, and sulfuric acid it is apparent that 2-methyl-2-phenylpropanal rearranges in formic acid to give approximately a 2:1 ratio of isobutyrophenone to 3-phenyl-2-butanone, while in sulfuric acid this ratio is 1:2. This shift in product ratio is probably due to two factors, the first being the esterification of the various carbonium ions in formic acid. It may be assumed that those paths (6 and 7, Chart I) which would arise *via* a nonconjugated, secondary carbonium ion (X_5) would be negligible. The only path of this sort of any importance should be path 4, which is in reality very similar to that which is involved in the reaction of the original glycol. This would

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[10] A. A. Frost and R. G. Pearson, "Kinetics and Mechanisms," John Wiley and Sons, Inc., New York, 1953, p. 148, outlines the considerations used in calculations of this sort. While it is of course possible to calculate k_1 and k_2 from the data in Table I, the changes in percentages of products are rather small, between any two sets of points, and, although it is possible to draw a smooth curve of per cent aldehyde *vs.* time, there is a considerable scattering of points when one plots percentages of the ketones *vs.* time. This is undoubtedly due to experimental error, since the deviation appears to be purely random.

[11] A. A. Frost and R. G. Pearson, *ibid.*, p. 181.

[12] These rate constants, as well as the over-all rate constant neglect the equilibrium expression for the protonation of the aldehyde by formic acid (I to ion X_1 in Chart I). It may be assumed that since formic acid is present in gross excess that very little of the free aldehyde remains in solution, however whether this is valid or not the term for this equilibrium will ultimately cancel out in the determination of the migration ratio.

[13] C. J. Collins, private communication. We would like to express our gratitude to Dr. Collins for giving us these results, as well as for several helpful discussions about this work.

be expected to shift the product ratio in the direction of isobutyrophenone, and is probably responsible for some of the "drift" in relative percentages of IV and II with time (Table I). The second factor is the relative changes in the values of k_{ϕ}/k_{H} and k_{CH_3}/k^1_{H}.[14] These are summarized in Table II.

TABLE II

	Migration Ratios in:	
	H_2SO_4	HCOOH
k_{ϕ}/k_{H}	25	4.5
k_{CH_3}/k^1_{H}	0.024	0.032

Since in both acids, the value of k_{CH_3}/k^1_{H} is sufficiently small to make methyl migration essentially irreversible, the rather large increase in k_{ϕ}/k_{H} in sulfuric acid would account for the reversal in product ratio, which we observe. It should be pointed out that the values for the migratory aptitudes of phenyl and methyl calculated by the above method are of very limited applicability, and are in fact valid only for the particular rearrangement under discussion.[15]

Experimental[16]

1-Phenyl-2-methylpropane-1,2-diol.—This compound was prepared in 95% yield by the reaction of methylmagnesium bromide and methyl mandelate. The diol was recrystallized from ether–hexane and formed white, hygroscopic crystals, m.p. 62–63°. Tiffeneau reports the diol to melt at 63°.[17]

Isobutyrophenone.—The isobutyrophenone used was Eastman White Label material and was homogeneous by gas chromatography.

3-Phenyl-2-butanone.—This compound was prepared in 84% yield by the chromic acid–pyridine oxidation[18] of the mixture of *erythro-* and *threo*-3-phenyl-2-butanol obtained from 2-phenylpropanal and methylmagnesium bromide.[19] The product boiled at 88–89° at 10 mm. and was homogeneous by gas chromatography. The 2,4-dinitrophenylhydrazone melted at 176° (reported: 175–176[20]).

Rearrangements of 1-Phenyl-2-methylpropane-1,2-diol. a. Formic Acid.—To 10 ml. of 97% formic acid was added 0.4 g. of the diol, and the solution was heated under reflux from 15 min. to 209.5 hr. (see Table I). The reaction mixture was poured over ice and extracted with several portions of ether. The ethereal extracts were washed with saturated sodium bicarbonate solution, water, dried, and the solvent removed at reduced pressure. The residual oil was subjected to qualitative analysis by infrared spectroscopy, and the percentage of isobutyrophenone and 3-phenyl-2-butanone plus 2-phenyl-2-methylpropanal was determined by gas chromatography. The remainder of the sample was then dissolved in 50 ml. of methanol, 50 ml. of water, and 3.0 g. of silver oxide was added.[21] The reaction mixture was heated under reflux for 20 hr., cooled, extracted with ether, washed with saturated sodium bicarbonate solution, water, dried, and the solvent removed at reduced pressure. The residual oil was again analyzed by infrared spectroscopy and gas chromatography, to give the relative amounts of 3-phenyl-2-butanone and isobutyrophenone in the mixture. From the two sets of gas chromatographic data (before and after oxidation) the relative amounts of the three components of the original reaction product could be obtained.

b. Sulfuric Acid.—To 10 ml. of 96% sulfuric acid at 0° was added with constant stirring 0.4 g. of the diol. After 15 min. the reaction mixture was poured over ice, and then extracted with ether and subjected to analysis as described in part a, above.

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(14) These may be approximated by use of Collins' equation,[2] and the assumption that the over-all migratory aptitudes do not change from one acid to another.

(15) M. Stiles and R. P. Mayer, *J. Am. Chem. Soc.*, **81**, 1497 (1959), have discussed in some detail the variation in relative migratory aptitudes, with small changes in structure, for a series of closely related pinacols.

(16) All analytical determinations were made on a Perkin-Elmer Model 154D gas chromatograph with a $^1/_4$-in. × 2-m. column of silicone grease on diatomaceous earth (Perkin-Elmer column O_X). Infrared spectra were taken on a Perkin-Elmer Model 137 spectrophotometer either as liquid films or as potassium bromide pellets. Melting points were determined using a Hershberg melting point apparatus and are uncorrected.

(17) M. Tiffeneau and H. Dorlencort, *Ann. Chem. Phys.* (8), **16**, 248 (1909); *Chem. Abstr.*, **3**, 1277 (1909).

(18) W. A. Bonner and D. D. Tanner, *J. Am. Chem. Soc.*, **80**, 1477 (1958).

(19) D. J. Cram, *ibid.*, **71**, 3863 (1949).

(20) G. M. Badger and W. H. F. Sasse, *J. Chem. Soc.*, 3862 (1957).

(21) Some difficulty was encountered in obtaining silver oxide of the proper activity to oxidize completely the aldehyde, but not the ketones. Commercial silver oxide proved inactive, and freshly prepared silver oxide was used. Each batch was checked against mixtures of known relative amounts of 3-phenyl-2-butanone and isobutyrophenone to ensure that these materials would not be oxidized. In one case silver oxide was obtained which oxidized 3-phenyl-2-butanone readily to acetophenone. (Identified by retention time on the gas chromatograph.) No other batch of silver oxide showed this anomalous behavior.