THE PINACOL REARRANGEMENT

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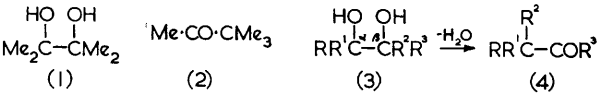
1. Historical

(a) Scope of the Pinacol and Related Rearrangements.—In 1860 Fittig[1] reported that when pinacol (1) was treated with cold, concentrated



sulphuric acid, pinacolin (methyl t-butyl ketone) (2) was produced. Evidently a molecule of water has been lost during the reaction, and a methyl group had shifted from one of the central carbons to another. Since Fittig's original observation, many other examples of the acid-catalysed rearrangement of α-glycols to ketones or aldehydes have been reported, and several reviews on this topic have appeared.[2] In the reacting glycol each hydroxyl-bearing carbon may be primary, secondary, or tertiary, and the substituent groups aryl or alkyl in nature—that is, R, R^1, R^2, and R^3 of structure (3) may be hydrogen, aryl, or alkyl—further, the two adjacent carbon atoms bearing the functional groups may be part of a cyclic system.[3] Although concentrated or dilute sulphuric acid has been most commonly used, many other acids (such as phosphoric, perchloric, formic, and oxalic) will also catalyse the rearrangement. Moreover, in some cases the presence of an acid catalyst is apparently not required. For example, triphenylethylene glycol (3; R = H, $R^1 = R^2 = R^3$ = Ph), when heated above its melting point, has been reported[4] to yield diphenylmethyl phenyl ketone (4; R = H; $R^1 = R^2 = R^3$ = Ph).

α-Amino-alcohols (5; X = NH_2) and α-halogeno-alcohols (5; X = Cl, Br, or I) also undergo rearrangement to produce ketones (6 and 7), usually with one of the two possible products formed in much greater yield.[5] The rearrangement of amino-alcohols is brought about through the action of sodium or potassium nitrite in acid solution, whereas that of the α-halogeno-alcohols is effected by the action of salts of the heavy metals.[5] Oxides (8) are sometimes formed during rearrangement of the

[1] Fittig, *Annalen*, 1859, **110**, 17, 23; 1860, **114**, 54; Stadeler, *ibid.*, 1859, **111**, 277.

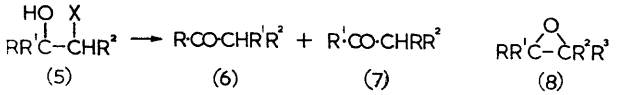
[2] (*a*) Bennett and Chapman, *Ann. Reports*, 1930, **27**, 114—120; 1923, **20**, 115; 1925, **22**, 116; 1928, **25**, 134; (*b*) Wheland, "Advanced Organic Chemistry," Wiley, New York, 1949, Chap. 12; (*c*) Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, Ithaca, N.Y., 1953, Chap. IX.

[3] Meerwein and Unkel, *Annalen*, 1910, **376**, 152; Meerwein, *ibid.*, 1913, **396**, 200; Nametkin and Delektorski, *Ber.*, 1924, **57**, 583.

[4] Danilov, *J. Russ. Phys. Chem. Soc.*, 1929, **61**, 723.

[5] McKenzie and Richardson, *J.*, 1923, **123**, 79; Luce, *Compt. rend.*, 1925, **180**, 145; Tiffeneau, *Ann. Chim. Phys.*, 1907, **10**, 322.

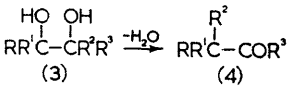
more highly sterically hindered glycols (3), and are often convertible into the same products (4) as are the glycols (3) themselves. In the present



(5) (6) (7) (8)

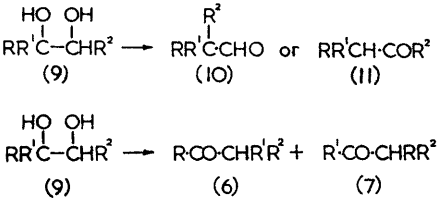
Review the rearrangements of α-glycols alone will be considered; the related rearrangements will be discussed only insofar as they bear upon the α-glycol rearrangement itself.

No serious attempt has been made to classify the pinacol rearrangement except incompletely according to the number of substituents borne by the reacting α-glycol. By this principle there should be six kinds of α-glycol, since each methyl-carbon atom can be primary, secondary, or tertiary in the nature of its substituents. Further, every unsymmetrically substituted glycol can rearrange in two conceivable ways, depending upon which of two hydroxyl groups is lost during reaction. It is thus possible to recognise at least seventeen separate sub-classes of rearrangements, based solely upon the structures of the reactant α-glycols. In practice, however, several of these types are unimportant, and there seems little reason to discuss the sub-classification except for the historical interest involved. Thus in 1930 Bennett and Chapman[2a] grouped the rearrangements of pinacols under three main headings: (i) the "pinacolinic change proper" of tetrasubsti-



(3) (4)

tuted (tertiary-tertiary) glycols (3)→(4), (ii) the "semihydrobenzoinic change"[6] of trisubstituted (tertiary-secondary) glycols "in which the tertiary hydroxyl is lost", and (iii) the "semipinacolinic change"[6] of



(9) (10) (11)

(9) (6) (7)

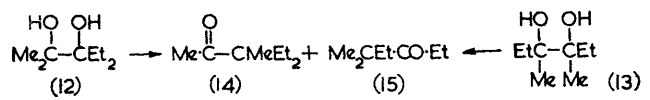
trisubstituted (tertiary-secondary) glycols "in which the secondary hydroxyl is lost": (9)→(6) + (7).

(b) Problems in understanding the Mechanism.—The pinacol rearrangement can be considered as a complicated Wagner–Meerwein reaction[2b,c] in which either one or both of two adjacent hydroxyl groups [α or β of

[6] Originally named by Tiffeneau and Levy, *Bull. Soc. chim.*, 1923, **33**, 758.

structure (3)] can be lost during rearrangement, and in which any one or all of four substituents [R, R^1, R^2, R^3 of structure (3)] can undergo 1,2-shifts. If one of the substituents is hydrogen (*e.g.*, R = H), and an aldehyde is produced, the aldehyde itself may suffer further rearrangement. These uncertainties are the factors which differentiate the pinacol from the Wagner–Meerwein rearrangement, and which have made it difficult to study.[7] In the following paragraphs of this section we shall illustrate these factors, considering the tetrasubstituted and trisubstituted glycols separately. In a subsequent section (p. 364) we shall give a mechanistic rationalisation of these factors.

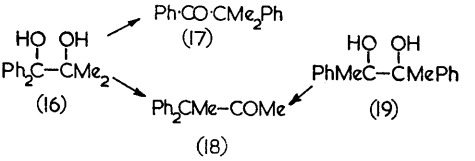
(i) *Tetrasubstituted glycols.* In order that the rearrangements of the tetrasubstituted glycols be understood, the following problems have required study: (1) the direction of rearrangement as determined by which of two hydroxyl groups is initially removed; (2) the "migratory aptitudes" of the substituent groups; (3) the effect of steric properties of the glycol upon the course of the reaction; (4) the role of oxides as intermediates during rearrangement; (5) the stability of the products themselves under reaction conditions; and (6) the effect of reaction media. Bennett and Chapman[2a] pointed out that the general direction of rearrangement is dependent upon which of two hydroxyl groups is removed, and that this in turn is decided by which pair of groups is the more effective in electron release. Thus Meerwein[8a] referred to the "affinity demands" exerted by adjacent substituents upon a hydroxyl in tetra-alkyl-substituted glycols such as (12). He concluded that alkyl groups possessing odd numbers of carbon atoms exerted greater "affinity demands" than do alkyl groups possessing even numbers of carbon atoms, and also that the "affinity demands" of the ethyl, isopropyl, and t-butyl groups diminished in that order. Nybergh[8b] studied the rearrangements, in cold, concentrated sulphuric acid, of glycols (12) and (13) to ketones (14) and (15), and found that glycol (13) (whether *meso* or *dl* was unspecified) was converted into ketones (14) and (15) in the ratio of 4:1, and that glycol (12) under identical conditions was converted into these same ketones in the ratio 1:20. The conclusion was that under the specified conditions of reaction, whereas the ethyl group has a greater "migratory aptitude" than methyl, two methyl groups are better able to release an adjacent hydroxyl group



[7] The formal similarity between the pinacol and Wagner–Meerwein rearrangements has been well established (see ref. 2*b* and 2*c*). That the migrating group in specific cases proceeds to the migration terminus with inversion as in the Wagner–Meerwein reaction, has been established by Bartlett and Brown, *J. Amer. Chem Soc.*, 1940, **62**, 2927. See also Brown, *ibid.*, 1952, **74**, 428; Brown, Nardmann, and Madoft, *ibid.*, 1952, **74**, 432; Brown, *ibid.*, 1954, **76**, 1279.

[8] (*a*) Meerwein, *Annalen*, 1919, **419**, 121—175; (*b*) Nybergh, *Ber.*, 1922, **55**, 1960; (*c*) Stiles and Meyer, *J. Amer. Chem. Soc.*, 1959, **81**, 1497.

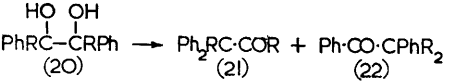
than are two ethyl groups. The effect of changing the acidic medium is illustrated by the observation[9] that glycol (16) in cold, concentrated sulphuric acid yielded the ketone (18), although the same glycol when



subjected to the influence of a trace of sulphuric acid in acetic anhydride yielded ketone (17). These same investigators[9] report that under the influence of either of the foregoing catalysts, the symmetrical glycol (19) is converted exclusively into ketone (18).

Initial attempts[2a] to assign relative "migratory aptitudes", or a mobility sequence representative of the ease with which various groups move to an adjacent carbon during the "pinacolinic change proper", were reasonably successful, although the probability was early recognised[10] that such aptitudes might depend upon the relative positions of the groups in a given molecule; that is, whether such glycols as (13) and (19), for example, were *meso* or DL in configuration. Other difficulties attending both the assignment of migratory aptitudes[2a] and the order in which certain pairs of groups "facilitate the fission of the adjacent hydroxyl group"[2a] had to do with the possibility that often the compound isolable as a result of rearrangement was simply the least soluble, and not the most abundant product.[11]

Bailar and Bachmann,[12] as a result of their studies of the rearrangements of symmetrical pinacols of general structure (20) to the ketones (21) and



(22) (in which R is substituted phenyl), were able to assign specific numbers to a series of substituted phenyl groups representing the "migratory aptitudes" of those groups with respect to phenyl. For example, Bachmann

[9] Ramart-Lucas and Salmon-Legagneur, *Compt. rend.*, 1928, **188**, 1301; Montagne, *Rec. Trav. chim.*, 1901, **21**, 6.

[10] Montagne, *Rec. Trav. chim.*, 1906, **26**, 253.

[11] Such must be the explanation for the observation by Roger and McKay, *J.*, 1931, 2229, that the "β-form" (*erythro*) of 1,2-diphenyl-1-*m*-tolylethylene glycol, when treated with cold concentrated sulphuric acid, yields a mixture of *m*-methyldiphenylmethyl phenyl ketone and diphenylmethyl *m*-tolyl ketone, with the latter "preponderating", whereas Collins and Bowman, *J. Amer. Chem. Soc.*, 1959, **81**, 3614, showed by the isotope-dilution technique that *m*-methyldiphenylmethyl phenyl ketone was the predominant product, actually produced in 70% yield.

[12] Bailar, *J. Amer. Chem. Soc.*, 1930, **52**, 3596; Bachmann and Ferguson, *ibid.*, 1934, **56**, 2081; Bachmann and Sternberger, *ibid.*, 1934, **56**, 170; Bachmann, *ibid.*, 1932, **54**, 2112.

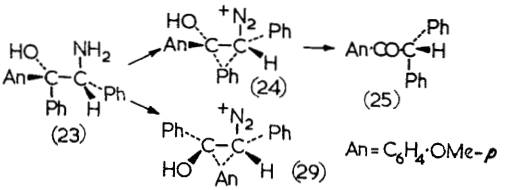
and Moser[13] have shown that when R in glycol (20) is *p*-tolyl, rearrangement of the glycol in a mixture of acetyl chloride, glacial acetic acid, and benzene (4:2:8 by vol.) produces ketone (22) in 94% yield, and ketone (21) in 6% yield. From this experiment they concluded that the migratory aptitude of *p*-tolyl with respect to phenyl is 94:6, or 15·7. Some other migratory aptitudes, obtained in a similar fashion, are: *p*-anisyl (500); *p*-phenetyl (500); *p*-biphenylyl (11·5); *p*-isopropylphenyl (9); *m*-tolyl (2); *m*-methoxyphenyl (1·6); phenyl (1·0); *p*-bromobiphenyl (0·7); *o*-methoxyphenyl (0·3); *o*-chlorophenyl (0).

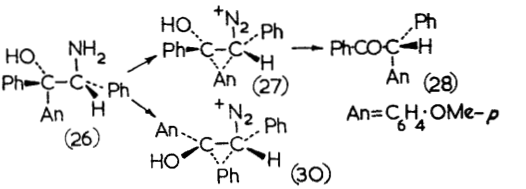
Most of the foregoing data were obtained, however, without any knowledge of whether the configurations of the glycols (20) were *meso* or racemic. As predicted by Montagne,[10] this configuration can influence the course of the rearrangement, at least in the case of the two 1,2-di-α-naphthyl-1,2-diphenylethylene glycols (20; R = α-naphthyl). One form, of m.p. 220°, has been shown[14] to yield only ketone (22; R = α-naphthyl), when treated with glacial acetic acid and iodine or acetyl chloride. The other form, m.p. 159°, produces only ketone (21) upon similar treatment.[14,15]

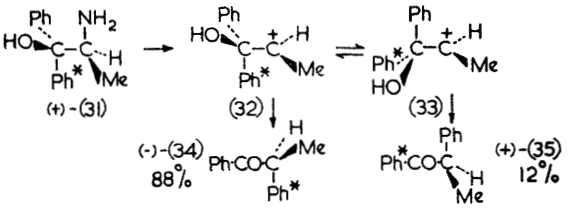
The influence of configuration upon the course of rearrangement has been studied rather exhaustively by Curtin and his co-workers[16] in the closely related semipinacolinic deamination. For example, *erythro*-2-amino-1-*p*-methoxyphenyl-1,2-diphenylethanol (23) yields, upon treatment with potassium nitrite in acid solution, approximately 90% of diphenylmethyl *p*-methoxyphenyl ketone (25), through migration of a *phenyl* group, whereas the *threo*-isomer (26), when similarly treated, yields approximately 90% of ketone (28), through migration of the *methoxyphenyl* group. Curtin explained these results by postulating that the *trans*-transition states (24) and (27) are more easily formed than the corresponding *cis*-transition states (29) and (30). It was shown later[17] that in the deamination-rearrangement of stereospecifically labelled [the carbon-14 label is denoted by an asterisk] 2-amino-1,1-diphenylpropanol [(+)-(31)], both of the products, (−)-(34) and (+)-(35), are formed nearly exclusively through the *trans*-transition states expected by migration of the labelled phenyl group in ion (32), and of the unlabelled phenyl group in ion (33). Oxidative degradation of the products followed by radioactivity assay demonstrated that the ketone (−)-(34) possessed essentially all of its carbon-14 in the phenyl group attached to the asymmetric carbon atom, whereas the ketone (+)-(35) possessed essentially all of its carbon-14 in the phenyl adjacent to the carbonyl group.

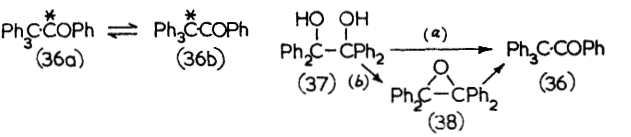
[13] Bachmann and Moser, *J. Amer. Chem. Soc.*, 1932, **54**, 1124.
[14] Bachmann and Shankland, *J. Amer. Chem. Soc.*, 1929, **51**, 306.
[15] Bergmann and Schuchardt, *Annalen*, 1931, **487**, 234.
[16] Pollak and Curtin, *J. Amer. Chem. Soc.*, 1950, **72**, 961; Curtin and Pollak, *ibid.*, 1951, **73**, 992; Curtin, Harris, and Pollak, *ibid.*, 1951, **73**, 3453; Curtin and Crew, *ibid.*, 1955, **77**, 355.
[17] Benjamin, Schaeffer, and Collins, *J. Amer. Chem. Soc.*, 1957, **79**, 6160.

Concerning the questions of product stability and of the role of oxides as intermediates, Fry[18] and his co-workers have shown that benzpinacolone, labelled with carbon-14 in the carbonyl group (36a), undergoes isotope position isomerisation to (36b) when treated with strong acids at high temperatures. Gebhart and Adams[19] studied the rearrangement of







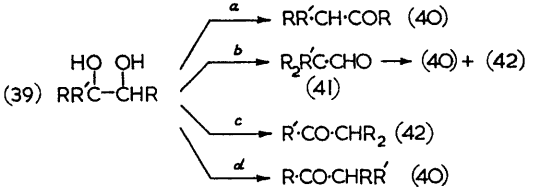


benzpinacol (37) to benzpinacolone (36) in mixtures of perchloric and acetic acid (0·12M in perchloric acid), and demonstrated that the reaction takes place through two routes, route (*a*) being direct rearrangement of the pinacol, and route (*b*) involving the intermediate formation of the oxide (33).*

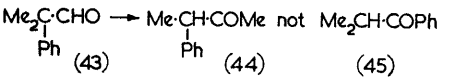
(ii) *Trisubstituted glycols.* The rearrangements of trisubstituted glycols present, in addition to difficulties discussed in the preceding sections, some very special problems of their own. These special problems are related to

[18] Fry, Carrick, and Adams, *J. Amer. Chem. Soc.*, 1958, **80**, 4743.
[19] Gebhart and Adams, *J. Amer. Chem. Soc.*, 1954, **76**, 3925.
* At 75° approximately 80% of the ketone is formed through the oxide. The authors (ref. 19) suggest that oxide intermediates are important where "serious steric retardation" exists [such as in the rearrangement of 37], and unimportant in the rearrangement of, for example, triphenylethylene glycol.

the multiplicity of paths through which trisubstituted glycols can rearrange, to the anomalous aldehyde–ketone rearrangement, and to the role of hydrogen during the reaction. Consider, for example, the structure (39) which could conceivably rearrange through paths (*a*) and (*b*) corresponding to the "semihydrobenzoinic change",[2a,b] and paths (*c*) and (*d*) corresponding to the "semipinacolinic change".[2a,b] Ketone (40) could be formed through paths (*a*) and (*d*), indistinguishable without isotopic tracer studies, or through path (*b*) by further rearrangement of the aldehyde (41). Ketone (42) can conceivably arise through paths (*b*) or (*c*). The rearrangements of trisubstituted aldehydes (41) have long been considered anomalous.[2] For example, dimethylphenylacetaldehyde (43) in cold, concentrated sulphuric acid yields 3-phenylbutan-2-one (44), and not isopropyl phenyl ketone (45).[20] This result is in contrast to the well-established[9] conversion of (19) into (18) with exclusive migration of phenyl rather than of methyl under conditions of both strong and mildly acid medium.[21,22]



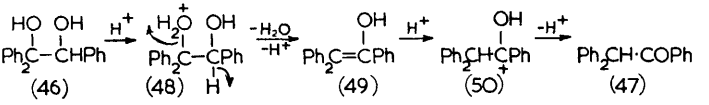
(*a*) loss of tertiary hydroxyl group; hydrogen migrates
(*b*) loss of tertiary hydroxyl group; R migrates
(*c*) loss of secondary hydroxyl group; R migrates
(*d*) loss of secondary hydroxyl group; R′ migrates



In the rearrangements of α-glycols containing less than four substituents, hydrogen itself often undergoes a 1,2-shift from one carbon atom to another[2b] [path (*a*), (39→40)]. This shift can conceivably be either an intermolecular or an intramolecular process. One intermolecular mechanism which has received much attention is the so-called process of "vinyl dehydration",[23–25] through which triphenylethylene glycol (46), for

[20] Orékhov and Tiffeneau, *Compt. rend.*, 1926, **182**, 67.
[21] See also Tiffeneau and Cahnmann, *Bull. Soc. chim.*, 1935, 1876, and Curtin and Schmukler, *J. Amer. Chem. Soc.*, 1955, **77**, 1107, who state that even in deamination reactions "10 is a conservative estimate for the phenyl/alkyl migration ratio. . . ."
[22] The apparent reversal of migratory aptitudes in the aldehyde–ketone rearrangement is quite general.[2] For a discussion of this phenomenon see also Collins and Benjamin, *J. Amer. Chem. Soc.*, 1956, **78**, 4329.
[23] Tiffeneau, *Bull. Soc. chim.*, 1923, **33**, 759.
[24] McKenzie and Roger, *J.*, 1924, **125**, 844.
[25] As recently as 1959 the theory of "vinyl dehydration" was seriously considered as a possibility for the rearrangement of (46). See Gould, "Mechanism and Structure in Organic Chemistry", Henry Holt and Company, New York, 1959, p. 602.

example, would supposedly form diphenylmethyl phenyl ketone (47) through the intermediates (48), (49), and (50).



2. Recent Progress with the Mechanism

(a) Enumeration of Problems.—In the preceding sections were outlined the main problems which must be resolved before our understanding of the mechanism of the pinacol rearrangement can be on the same basis as that of the Wagner–Meerwein rearrangement. These problems are: (i) Which of two hydroxyl groups is initially removed during reaction? (ii) How is the course of the rearrangement altered by changing the acid catalyst? (iii) How does the stereochemistry of the glycol affect the products of rearrangement? (iv) Under what conditions do the products themselves rearrange? (v) To what extent are oxides involved in the rearrangements? (vi) To what extent are aldehydes involved in the rearrangement of other than tetrasubstituted glycols? (vii) What is the reason for the anomalous migratory aptitudes in the aldehyde–ketone rearrangement? (viii) Does hydrogen migrate intermolecularly or intramolecularly (*i.e.*, does "vinyl dehydration"[23–25] occur)?

During the past five years considerable progress has been made towards answering these questions, chiefly through the application of isotopic-tracer techniques. In the present section a review and evaluation of that recent work is presented.

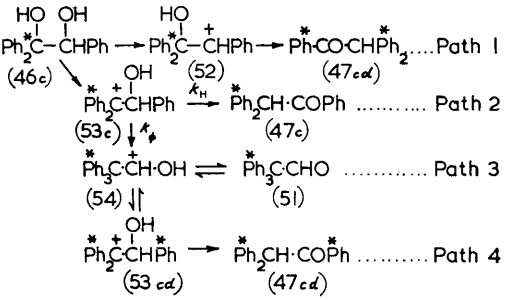
(b) The Rearrangement of Triphenylethylene Glycol (46).—(i) *Multiplicity of paths of rearrangement.* The rearrangement of triphenylethylene glycol (46) under the influence of various acid catalysts to produce, in quantitative yields, diphenylmethyl phenyl ketone (47) or a mixture of (47) and triphenylacetaldehyde (51) has received much attention.[26] An interpretation of the mechanism of this rearrangement, however, was frustrated by the difficulties mentioned in Section 1. By labelling triphenylethylene glycol in one of the methyl carbon atoms (46a) and, alternatively, in the phenyl group (46c) with carbon-14, and then subjecting these isotope-position isomers to rearrangement, it has been possible to determine the fate of each label under the influence of a specific catalyst.[27] The possible paths for rearrangement of (46) are outlined in Chart 1. The phenyl-labelled isomer (46c) alone is illustrated, although similar charts could be drawn for two different chain-labelled isomers and the alternative ring-

[26] Gardeur, *Bull. Acad. roy. Belg.*, 1897, **34**, 67; *Chem. Zentr.*, 1897, **68**, II, 622; Tiffeneau, *Compt. rend.*, 1908, **146**, 29; Legrave, *Ann. Chim.*, 1927, **8**, 416; Danilov, *J. Russ. Phys. Chem. Soc.*, 1917, **49**, 282; Danilov and Venus-Danilova, *Ber.*, 1926, **59**, 377.

[27] Collins, *J. Amer. Chem. Soc.*, 1955, **77**, 5517.

labelled isomer, since each was synthesised and studied.[27,29] The scheme outlined in Chart 1 represents all possibilities mentioned by previous investigators[19,26,28] with the hypothetical intermediates expressed as carbonium ions.[27] Hydrogen has been shown[29] as having undergone

CHART 1



intramolecular migration rather than "vinyl dehydration";[23–25] the evidence[29] for such intramolecularity is discussed later. As explained by Collins,[27] a determination of the yields of the products (47) and (51) through the isotope-dilution method, plus a knowledge (gained through appropriate degradation techniques) of the fraction of rearrangement undergone by the carbon-14 labels of (46a) and (46c), are sufficient to allow calculation of the contribution of each path (1,2,3,4) to the overall reaction under the influence of a given acid catalyst. Table 1 gives the results of such experiments for five different catalysts, and we can draw these important conclusions: (1) the contributions of paths 2, 3, and 4 vary considerably, depending upon the acid catalyst employed: (2) the phenyl/hydrogen "migratory aptitude" (k_ϕ/k_H) varies by a factor of approximately 180:1 within the range of catalysts employed,* and (3) with the exception of the rearrangement in dioxan–hydrochloric acid–water, the interconversion of the intermediates (53⇌54) is reversible.

(ii) *Conditions for secondary hydroxyl loss.* In cold, concentrated sulphuric acid the tertiary hydroxyl group of triphenylethylene glycol (46) is removed in preference to the secondary hydroxyl group by a factor of at least 30:1. Thus it can be concluded that two phenyl groups are better able to stabilise the carbonium ion (53) than one phenyl is able to stabilise carbonium ion (52). It is interesting, however, that if the 2-phenyl

[28] McKenzie, Mills, and Myles, *Ber.*, 1930, **63**, 904· McKenzie, Roger, and McKay, *J.*, 1932, 2597; Roger and McKay, *J.*, 1933, 332.

[29] Collins, Rainey, Smith, and Kaye, *J. Amer. Chem. Soc.*, 1959, **81**, 460.

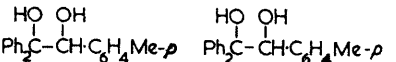
* The evaluation of k_ϕ/k_H depends upon (*a*) the fact that the two chemically identical carbonium ions (53c) and (53cd) can be distinguished isotopically and (*b*) the assumption that the rate of free rotation about the C–C bonds of the intermediates of Chart 1 is much faster than the rates of phenyl or hydrogen migration during the interconversion of these same intermediates.

TABLE 1. *Ratios of* k_ϕ/k_H *in the rearrangement of triphenylethylene glycol (46, Chart 1)*[a]

	% *Contribution of path*				
Catalyst	1	2	3	4	*Ratio* k_ϕ/k_H
Conc. H_2SO_4	2·5	11·7	0	85·8	7·33
Formic acid	4·7	39·0	0	56·3	1·44—1·70[b]
Oxalic acid	2·7	45·3	12·6	39·4	0·85[c]
Dilute H_2SO_4	3·2	67·4	16·5	12·9	0·44
Dioxan–H_2O–HCl	0	96·1	3·9	0	0·041

(*a*) Taken from ref. 27; (*b*) the value 1·70 is from ref. 29, and was recalculated on the basis of 6·9% rearrangement of the chain label of (51) when converted, in boiling formic acid, into (47); (*c*) taken from data of ref. 29—the value for k_ϕ/k_H of 1·13 given therein is in error.

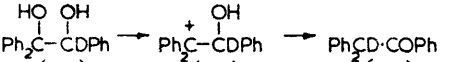
group of (46) is replaced by *p*-tolyl, as in 1,1-diphenyl-2-*p*-tolylethylene glycol (55), the ratio of tertiary to secondary hydroxyl group removal, with cold, concentrated sulphuric acid as the catalyst, is 3·3:1, whereas the same glycol (55) when treated with boiling formic acid exhibits no more than 5% removal of its secondary hydroxyl group.[22] A similar large variation in percentage removal of the two hydroxyl groups of (56) was noted.[30]



(55) (56)

Unfortunately, the action of cold, concentrated sulphuric acid on (56) yielded no isolable products; the action of boiling formic acid, however, caused preferential removal of secondary hydroxyl groups in the ratio of 1·3:1, whereas the action of perchloric–acetic acid mixtures (0·005—0·82M in perchloric acid) at 50° favoured secondary hydroxyl group removal in the ratio of approximately 6:1.

(iii) *The question of "vinyl dehydration"*. In 1953 Mislow and Siegel[31] obtained the first evidence for the intramolecular nature of hydrogen migration through the conversion, in boiling, dilute sulphuric acid, of

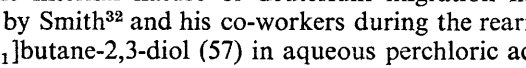


(46e) (53e) (47e)

(+)-1-phenyl-1-*o*-tolylethylene glycol into optically active phenyl-*o*-tolylacetaldehyde. More recently, the rearrangement of the deuterium-containing 1,1,2-triphenyl[2-$^2H_1$]ethylene glycol (46e) to diphenyl[$^2H_1$]-methyl phenyl ketone (47e) was studied.[29] In cold, concentrated sulphuric acid the ketone (47e) was formed from (46e) without loss of deuterium. When (46e) was heated with dilute sulphuric acid (47e) was produced

[30] Collins and Krauth, unpublished work.
[31] Mislow and Siegel, *J. Amer. Chem. Soc.*, 1952, **74**, 1060.

with partial loss of deuterium, whereas boiling formic acid or boiling oxalic acid solution caused the formation of ketone (47) completely devoid of deuterium. It should not necessarily be inferred from the latter experiments, however, that deuterium does not, under these conditions, migrate intramolecularly, for the deuterium-containing ketone (47e), when boiled with formic acid, suffers complete exchange of hydrogen for deuterium. The internal nature of deuterium migration has also been demonstrated by Smith[32] and his co-workers during the rearrangement of 2-methyl[3-$^2H_1$]butane-2,3-diol (57) in aqueous perchloric acid solutions.



(57) (58) (59)

Earlier, Ley and Vernon[33] had obtained presumptive evidence for intramolecular hydrogen migration in the rearrangement of 1,2-dimethoxy-2-methylpropane (58) in deuterated methanolic hydrochloric acid, for they determined that the product, 1,1-dimethoxy-2-methylpropane (59), possessed less than the statistical amount of deuterium. "Vinyl dehydration"[23–25] has thus been refuted[29,32,33] as a mechanism for several pinacol-type rearrangements. Further, under those conditions in which compound (46e) leads to (47) devoid of deuterium, it has been shown[29] that diphenyl-[$^2H_1$]methyl phenyl ketone (47e) itself suffers complete loss of deuterium. It thus seems unlikely that "vinyl dehydration" can be of any great general importance.

(c) Anomalous Migratory Aptitudes in the Rearrangements of Aldehydes.—The apparent reversal of the usual migratory aptitudes in the rearrangements of aldehydes to ketones was discussed in section 1. This anomaly has now been cleared up[22,34–36] through a study of the rearrangement of diphenyl-*p*-tolylacetaldehyde (60) and closely related compounds. Benjamin and Collins demonstrated[22] through the isotopic-dilution tech-

(60) (61) (62)

nique that in cold, concentrated sulphuric acid the aldehyde (60) yielded that ketone (61) formed through phenyl migration in greater yield than the ketone (62) formed by *p*-tolyl migration in the ratio of 4·7:1. When the statistical factor of two phenyls and only one *p*-tolyl was allowed for, it thus appeared that the *p*-tolyl/phenyl migration ratio was 0·43, or *less* than unity. Never before had a *p*-tolyl/phenyl migration ratio or "migratory

[32] Smith, Bowman, and Kmet, *J. Amer., Chem. Soc.*, 1959, **81**, 997.
[33] Ley and Vernon, *J.*, 1957, 2987.
[34] Raaen and Collins, *J. Amer. Chem. Soc.*, 1958, **80**, 1409.
[35] Kendrick, Benjamin, and Collins, *J. Amer. Chem. Soc.*, 1958, **80**, 4057.
[36] Collins and Bowman, *J. Amer. Chem. Soc.*, 1959, **81**, 3614.

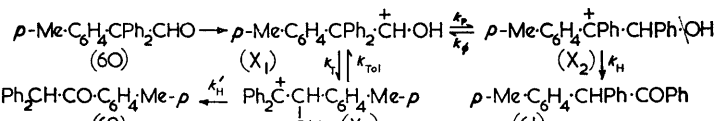
aptitude" of less than unity been observed,[21,37] so it was concluded that the ratio of the two ketones was not a proper measure of the "migratory aptitude".

The reversibility of the carbonium-ion transformation (53⇌54) (Chart 1) indicated that the rearrangement of diphenyl-*p*-tolylacetaldehyde (60) to the two ketones (61) and (62) could best be interpreted through the scheme outlined in Chart 2, which shows the three ions (X_1), (X_2,) and (X_3) in a *dynamic equilibrium*. If the mechanism shown in Chart 2 is correct, then the quantity $2k_T/k_P$ [and *not* the value 0·43 calculated from the product ratio of compounds (61) and (62)] is the true value of the *p*-tolyl/phenyl migration ratio. An exact solution[22] to the mechanism shown in Chart 2 is given by equation (1), in which m_{62} and m_{61} are the mole fractions of the

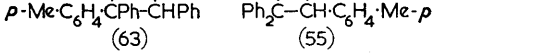
$$\frac{k_T}{k_P} = \frac{k_H}{k_\phi} \cdot \frac{k_{Tol}}{k'_H} \cdot \frac{m_{62}}{m_{61}} \cdot \left[\frac{1 + k'_H/k_{Tol}}{1 + k_H/k_\phi}\right] \quad . \; . \; . \quad (1)$$

two ketones formed during reaction. After experimental determinations of the two ratios k_H/k_ϕ and k_{Tol}/k'_H, by use of equation (1) it was possible to calculate that the quantity $2k_T/k_P$ is about 3, a normal *p*-tolyl/phenyl migration ratio.[37]

CHART 2



The two quantities k_H/k_ϕ and k_{Tol}/k'_H can be determined in principle by subjecting the glycols (63) and (55) to the same conditions of rearrangement in cold, concentrated sulphuric acid as was the aldehyde (60), for both of these glycols should generate the same equilibrating ions (X_1), (X_2), and (X_3). Through the same type of isotope-dilution double-labelling experiments as those performed[27] with triphenylethylene glycol (46) (see Chart 1), it was possible to determine[22] the contributions of each of five possible paths to the over-all reaction of the glycol (63) (both *threo-* and *erythro*-forms were studied). Since the glycol (63), labelled with carbon-14 in the 1-phenyl position, proceeds to the two ketonic products as shown*

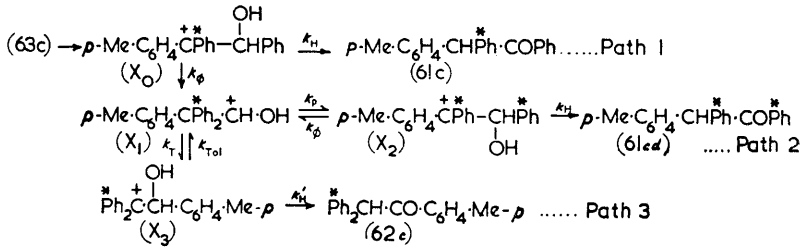


[37] Burr, *J. Amer. Chem. Soc.*, 1953, **75**, 5008; Burr and Ciereszko, *ibid.*, 1952, **74**, 5426; Tietz and McEwen, *ibid.*, 1955, **77**, 4011; McEwen, Gilliland, and Sparr, *ibid.*, 1950, **72**, 3212; Ege and Sherk, *ibid.*, 1953, **75**, 354; Curtin and Crew, *ibid.*, 1954, **76**, 3719; Benjamin and Collins, *ibid.*, 1956, **78**, 4952; Bachmann and Moser, *ibid.*, 1932, **54**, 1124.

* The unimportant paths owing to removal of secondary hydroxyl groups have been neglected in Chart 3 to simplify the discussion.

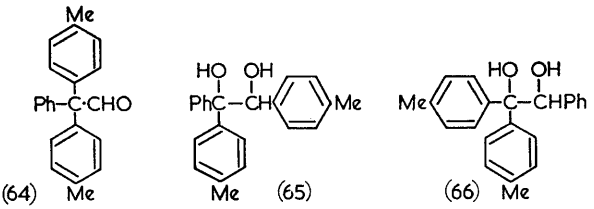
in Chart 3, it was necessary only to divide the contribution of path 1 by the sum of the contributions of paths 2 and 3 to evaluate the ratio k_H/k_ϕ. Evaluation of k_{Tol}/k'_H was also possible through a less direct method.[22] Additional verification for the general validity of the mechanistic schemes

CHART 3

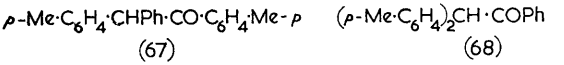


of Charts 2 and 3 can be seen from the fact that the ratio of the contribution of path 2 to that of path 3 (Chart 3) is 4·8, in excellent agreement with the observed ratio (4·7) of the two ketone products during the rearrangement of the aldehyde (60).

In order that supporting evidence could be gained for the mechanism of the aldehyde–ketone rearrangement outlined in Charts 2 and 3, experiments similar to those performed with (60), (63), and (55) were carried out[35] upon the analogous compounds (64), (65), and (66), each of which undergoes rearrangement in cold, concentrated sulphuric acid to mixtures



of the ketones (67) and (68). The aldehyde (64) under these conditions is converted into the ketones (67) and (68) essentially in equal quantities. Once again a "reversed" *p*-tolyl/phenyl migration ratio of 1:2 can be calculated from the product ratio. Application of the same mechanistic



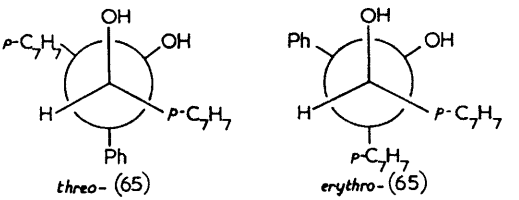
concepts (Charts 2 and 3)[22] to the experimental data obtained[35] during the rearrangements of (65), (66), and (64), when coupled with a mathematical solution similar to equation (1), led to the conclusion that again the true *p*-tolyl/phenyl migration was greater than unity.

Analogous tracer experiments have been carried out with diphenyl-*o*-tolylacetaldehyde and with the three diphenyl-*o*-tolylethylene glycols,[34] as well as with the corresponding *m*-tolyl derivatives.[36] In all cases the mechanism outlined in Chart 2 for the aldehyde–ketone rearrangement was supported. The so-called anomaly of "reversal" of the normal "migratory aptitudes" in the rearrangement of aldehydes to ketones has therefore been solved.

(d) Effect of Steric Properties upon Course of Rearrangement of Glycol.—

(i) *Tetrasubstituted glycols.* Very little progress has been made in understanding how the steric properties of tetrasubstituted diastereoisomeric glycols [*e.g.*, the *meso* and racemic forms of (13), (19), and (20)] affect the course of rearrangement. It has been pointed out [Section (1)] that the *meso* and racemic forms of (20; R = α-naphthyl) undergo rearrangement with the same catalyst to yield different products.[14,15] Since the α-naphthyl group possesses an *ortho*-substituent, however, it is not clear that *meso* and racemic glycols of general structure (20), in which the R groups are *para*-substituted phenyl radicals should necessarily always rearrange with different consequences.[38]

(ii) *Trisubstituted glycols. threo-* and *erythro*-1-Phenyl-1,2-di-*p*-tolylethylene glycol (65), when subjected to rearrangement in cold, concentrated



threo- (65) *erythro*- (65)

sulphuric acid, produce different yields of the two ketones (67) and (68). This has been shown to be a consequence of different fractions of secondary hydroxyl removal.[35] Whereas the glycol, *erythro*-(65), undergoes reaction with 18% of secondary hydroxyl loss accompanied by *p*-tolyl migration, the *threo*-glycol *threo*-(65) exhibits a maximum secondary hydroxyl loss of 3%. It is interesting that those portions of the reactions of both *threo*- and *erythro*-isomers of (65) which take place with tertiary hydroxyl removal, do so with identical consequences. This fact must be a result of the similar effective bulks of the phenyl and *p*-tolyl groups[38] occupying the tertiary position, whereas the large variation in secondary hydroxyl removal is most probably caused by the greater anchimeric assistance[39] provided by the tolyl group on the tertiary carbon atom of *erythro*-(65)

[38] It is well established that in certain Grignard additions and lithium aluminium hydride reductions the "effective bulks" of phenyl and *para*-substituted phenyl groups are identical. See, for example, Stocker, Sidisunthorn, Benjamin, and Collins, *J. Amer. Chem. Soc.*, 1960, **82**, 3913; Cram and Kopecky, *ibid.*, 1959, **81**, 2748.

[39] Winstein, Lindegren, Marshall, and Ingraham, *J. Amer. Chem. Soc.*, 1953, **75**, 147.

than by the phenyl group on the tertiary carbon atom of *threo*-(65), as they undergo migration through their respective *trans*-transition states.[16]

(e) Stability of Ketonic Products and Role of Oxides as Intermediates.— The observations by Fry and his co-workers[18] on the carbon-14 rearrangement which takes place when carbonyl-labelled benzpinacolone (36a) is subjected to catalysis by strong acids under conditions often used to bring about the pinacol rearrangement have already been mentioned. This example is remarkable in that the product (36a,b) has actually been formed with a shift of the carbonyl-oxygen from one carbon atom to another. Another type of acid-catalysed ketonic rearrangement is exemplified by the interconversion of [$^{14}C_1$]methyl t-butyl ketone (2a) with its isotope-position isomer (2b).[40] This interconversion was explained[40] through the rapid, reversible protonation of the carbonyl group, followed by reversible 1,2-shift of methyl to the carbonium centre. A similar mechanism must obtain in the conversion, catalysed by concentrated sulphuric acid, of 2,2,4,4-tetramethyl[3-^{14}C]pentan-2-one (69) into 3,3,4,4-tetramethyl[2-^{14}C]pentan-2-one (70).[41]

$$\underset{(2a)}{CMe_3CO\cdot\overset{*}{M}e} \rightleftharpoons \underset{(2b)}{\overset{*}{M}e\cdot CMe_2\cdot CO\cdot Me} \qquad \underset{(69)}{CMe_3\cdot\overset{*}{C}O\cdot CMe_3} \longrightarrow \underset{(70)}{CH_3\cdot\overset{*}{C}O\cdot CMe_2\cdot CMe_3}$$

The foregoing rearrangements are in contrast to the lack of rearrangement of the isotope-position isomers (47a) and (47c) of ^{14}C-labelled diphenylmethyl phenyl ketone in the presence of cold, concentrated sulphuric acid, or of boiling formic acid,[27,29] for neither Fry's "oxygen function rearrangement"[18] nor the rearrangement[40,41] accompanied by aryl shift was exhibited. The ketones (61), (62), (67), and (68) were similarly resistant to rearrangement in cold, concentrated sulphuric acid.[35,36] Even more remarkably, diphenyl[$^2H_1$]methyl phenyl ketone (47) did not lose

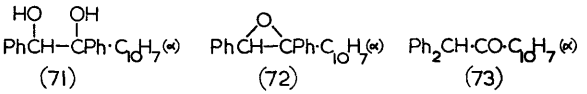
$$\underset{(47\alpha)}{Ph_2CH\cdot\overset{*}{C}OPh} \qquad \underset{(47\varepsilon)}{Ph_2CH\cdot COP\overset{*}{h}} \qquad \underset{(+)\text{-}(61)}{Ph\cdot CO\cdot CHPh\cdot C_6H_4Me\text{-}p}$$

deuterium,[29] and optically active *p*-tolyldeoxybenzoin [(+)-(61)] was not racemised by treatment for 15 minutes with concentrated sulphuric acid at 0°.[42] Only partial racemisation occurred even under the action of cold, concentrated sulphuric acid for 16 hr. At higher temperatures the ketone (47e) does lose deuterium, however, in formic acid.[29] It thus appears that, although ketones such as (36), (2), and (69) which can be formed by rearrangement of tetrasubstituted glycols are themselves often prone to

[40] Rothrock and Fry, *J. Amer. Chem. Soc.*, 1958, **80**, 4349. Pertinent references to other examples of ketonic rearrangements are listed therein.
[41] Barton and Porter, *J.*, 1956, 2483.
[42] Raaen and Collins, unpublished work.

further rearrangement under conditions of the pinacol reaction, such is not generally the case for those ketones which are obtainable from unhindered trisubstituted glycols.

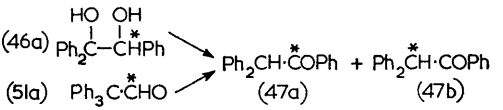
There is no proof that oxides are intermediates in the acid-catalysed ketone interconversion.[40] Tetrasubstituted glycols, on treatment with acid, often form oxides, however, in addition to the usual ketonic products.[19] Also, some hindered trisubstituted glycols yield oxides on treatment with dilute acid. For example, *erythro*-1-α-naphthyl-1,2-diphenylethylene glycol (71) upon treatment with dilute sulphuric acid is reported[43] to yield an



(71) (72) (73)

oxide (72) which, when dissolved in cold, concentrated sulphuric acid, is converted into diphenylmethyl α-naphthyl ketone (73). In studies of the rearrangements in concentrated or dilute sulphuric acid of *threo*- and *erythro*-1,2-diphenyl-1-*o*-tolylethylene glycols,[34,44] however, no mention is made of the isolation of an oxide. Also, Brown[4] failed to find evidence of oxide formation in his studies of the highly hindered *cis*- and *trans*-1,2-di-*o*-tolylacenaphthene-1,2-diols. Oxide formation does not seem to be, therefore, a general reaction of hindered glycols.

In the rearrangement of triphenylethylene glycol (46a), ^{14}C-labelling



experiments have shown[27,29] a measurable amount of rearrangement of the chain label in the product [about 5% of (47b) is formed] when the reaction is catalysed by boiling formic acid. This rearrangement of the chain label is undoubtedly not a consequence of secondary hydroxyl removal followed by phenyl migration (path 1 of Chart 1), for later experiments[29] have shown that carbonyl-labelled triphenylacetaldehyde (51a) on similar treatment yields 8% of (47b). It is possible that triphenylethylene oxide could be an intermediate in the transformation (51a)⇌(47b), although the rapid, reversible formation from (51a) of triphenylethylene diformate followed by migration of one of the tertiary phenyl groups has also been suggested[22] as a mechanism.

It is clear, therefore, that much more information will be required before the role of oxides in the pinacol rearrangement and the interconversions of ketones will be understood.

[43] McKenzie and Roger, *J.*, 1924, **125**, 853; McKenzie and Dennler, *ibid.*, 2105, Tiffeneau and Orékhoff, *Compt. rend.*, 1924, **178**, 1619.
[44] Roger and McKay, *J.*, 1933, 332.

(f) Kinetic Studies; Deuterium Isotope Effect.—Several kinetic studies pertain to the mechanism of the pinacol rearrangement.[7,19,29,32,33,45,46,47] Bunton and his co-workers[45] showed that pinacol, when subjected to rearrangement in aqueous acid enriched with oxygen-18, undergoes oxygen exchange at a measurable rate. Collins *et al.*[29] showed that both *threo*- and *erythro*-1,2-diphenyl-1-*p*-tolylethylene glycol (63) were converted into the same (1:1) mixture of *threo*- and *erythro*-glycol (63) in aqueous-ethanolic sulphuric acid at a rate faster than the rearrangement itself took place. The mechanism suggested by Bunton *et al.*[45] applied[32] to the rearrangement of 2-methyl[3-$^2H_1$]butane-2,3-diol (57) (Chart 4) leads to the kinetic equation (2) in which k_{exp} is the experimental rate constant, and h_0 is the

$$k_{exp} = Kk_2k_3h_0/(k_{-2} + k_3) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

antilog of the Hammett acidity function[48] H_0. The experimental rate constant (k_{exp}) is, therefore, not a simple function of the slow or "rate-determining" step. Both Smith,[32] who studied the kinetics of rearrangement of normal and deuterated 2-methylbutane-2,3-diol (57), and Duncan and Lynn,[46] working with pinacol (1), found plots of log k_{exp} *versus* H_0, and of (log k_{exp})/[H^+] *versus* [H^+] to be linear. The isotope effect (k_H/k_D) in the rearrangement of (57), however, was independent of the acidity of the medium and fairly constant at about 1·6—1·8. Smith[32] cited reasonable evidence to show that the term [$k_3/(k_{-2} + k_3)$] in equation (2) is constant for the rearrangement of deuterated and non-deuterated diols (57), and concluded that the observed isotope effect arose primarily in the loss of water from (74) to produce (75) [k_2]. Because the observed isotope effect was so much larger than any yet observed attributable to hyperconjugation, Smith[49] postulated participation of hydrogen during the slow step.

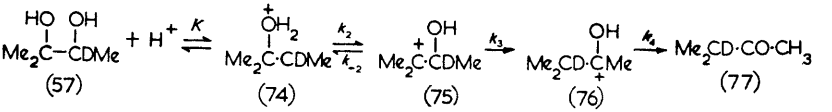
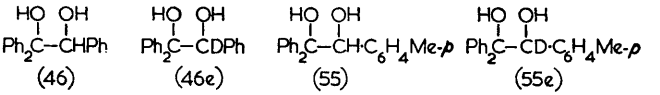


CHART 4

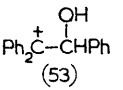


With the aid of multiple carbon-14 labels, Collins *et al.*[29] studied the kinetics of the rearrangements of the glycols (46), (46e), (55), and (55e) in aqueous ethanolic sulphuric acid at 43·3°. All four compounds rearranged under these conditions with almost complete loss of tertiary hydroxyl

[45] Bunton, Hardwick, Llewellyn, and Pocker, *J.*, 1958, 403.
[46] Duncan and Lynn, *J.*, 1956, 3512.
[47] Deno and Perizzolo, *J. Org. Chem.*, 1957, **22**, 836.
[48] Hammett, "Physical Organic Chemistry", McGraw-Hill, New York, 1940, p. 267.
[49] Winstein and Takahaski, *Tetrahedron*, 1958, **2**, 316.

group. The relative rates of reaction were, respectively, 1·00, 0·588, 3·31, and 2·75. It was further shown that (*a*) removal of tertiary hydroxyl group is rapid and reversible; (*b*) hydrogen migration takes place at a nearly constant rate, despite the substitution of *p*-tolyl for phenyl at position 2 of the glycol; (*c*) the rate of aryl migration is essentially independent of the substitution of deuterium for hydrogen; (*d*) the decreased rate of rearrangement of the deuterated glycols is due only to that portion of the reaction proceeding with deuterium migration; (*e*) the mechanism of the rearrangement in dilute aqueous-ethanolic sulphuric acid involves a rapid and reversible removal of hydroxyl ion followed by a rate-determining 1,2-shift of hydrogen, deuterium, or aryl; and (*f*) the most reasonable explanation for the large variation of k_ϕ/k_H with catalyst is control of these phenyl/hydrogen migration ratios by the relative populations of particular ionic conformations. Although Collins *et al.*[29] suggested the same general mechanism as Bunton,[45] Duncan and Lynn,[46] and Smith *et al.*,[32] they believed that in the reactions they studied the two equilibrium steps (corresponding to K and k_2/k_{-2} of Chart 4) are extremely fast, and that the isotope effect is due almost completely to a rate-determining shift of deuterium or of hydrogen (corresponding to k_4 of Chart 4).

It was shown[29] also, through a study of product ratios (or carbon-14 distributions) during the rearrangements of ^{14}C-labelled isotope-position isomers of (46) and (46e), that the k_H/k_D isotope effect was approximately constant at a value of about 3, and independent of the acid catalyst used to effect the rearrangements. Since it had been shown[27] that the ratio of phenyl to hydrogen migration (k_ϕ/k_H, Chart 1 and Table 1) could vary by nearly 200-fold, depending upon the catalyst employed, it was suggested[29] that under all the conditions studied the highly stable, tertiary carbonium ion (53) was formed without assistance (participation) by neighbouring

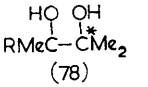


(53)

phenyl or hydrogen, and then destroyed by phenyl or by hydrogen migration followed by loss of a proton as illustrated in Chart 1.

(g) Relation Between Migratory Aptitude and Loss of Adjacent Hydroxyl Groups.—It appears that there is some conflict amongst the published data concerning the relation between the migratory aptitudes exhibited by aryl and alkyl groups and the abilities of these same groups to facilitate the loss of an adjacent hydroxyl group. Nybergh[8b] and Meerwein[8a] showed that in the rearrangement of the glycol (12) in cold, concentrated sulphuric acid, the hydroxyl group adjacent to the two methyl groups was removed in preference to that adjacent to the two ethyl groups by a factor of 20:1. In the rearrangement of glycol (13) under identical conditions, however, migration of the ethyl group predominated over migration of the methyl

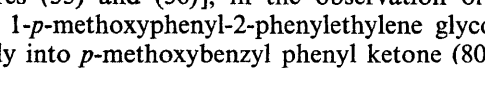
group by a factor of 4:1. A quite different situation exists in the rearrangements,[9] in cold, concentrated sulphuric acid, of glycols (16) and (19). The unsymmetrical dimethyldiphenylethylene glycol (16) rearranges exclusively with methyl migration, meaning that the two phenyl groups facilitate exclusive loss of their adjacent hydroxyl group, whereas the symmetrical glycol (19) undergoes exclusively phenyl migration. With glycols (12) and (13), although two methyl groups are better able to facilitate loss of hydroxyl than are two ethyl groups, the ethyl group possesses the greater migratory aptitude, whereas in the examples (16) and (19) the same groups —phenyl—possess the greater migratory aptitude and the greater ability to facilitate loss of adjacent hydroxyl group. That this apparent anomaly is not necessarily a consequence of different steric properties of glycols (13) and (19) (that is, whether *meso* or racemic) follows from the work of Stiles and Meyer[8c] on ^{14}C-labelled compounds of the general structure (78;



(78)

R = Me, Et, Bu^t). These authors[8c] demonstrated that when R = ethyl the hydroxyl group adjacent to two methyl groups was removed 74% of the time (to 26% for the other), whereas the migratory aptitude of ethyl with respect to methyl was 3·35:1; when R was t-butyl the product was formed with almost exclusive t-butyl migration, signifying that there was no loss of hydroxyl adjacent to the t-butyl group.

The apparent anomaly in certain of these examples is a consequence of the presumption that the same property of a group—namely, the electron-releasing ability—which facilitates migration should also facilitate removal of an adjacent hydroxyl group. There is ample evidence for this presumption in work already cited[22,30] with respect to the abilities of *p*-tolyl and *p*-methoxyphenyl to compete with two phenyl groups in hydroxyl release [structures (55) and (56)], in the observation of Orékhof and Tiffeneau[50] that 1-*p*-methoxyphenyl-2-phenylethylene glycol (79) is converted exclusively into *p*-methoxybenzyl phenyl ketone (80),[51] and in the



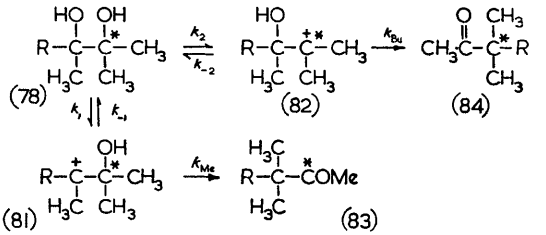
(79) (80)

observation[52] that both *threo*- and *erythro*-1-phenyl-2-*p*-tolylethylene glycol undergo rearrangement in perchloric–acetic acid mixtures of varying molarity with preferential removal of the hydroxyl group adjacent to *p*-tolyl in the ratio of about 9:1.

[50] Orekhof and Tiffeneau, *Bull Soc. chim.*, 1925, **37**, 1410.
[51] See the discussion by Curtin and Crew, ref. 16, concerning the greater migratory aptitudes of *p*-anisyl than of phenyl.
[52] Benjamin and Collins, unpublished data.

A rationalisation of the anomaly posed in this section is to be found in the work of Bunton[45] and others[29,46,47] who demonstrated rapid and reversible exchange of the tertiary hydroxyl group under conditions of the pinacol rearrangement, and in the work of Collins *et al.*,[29] who showed the rates of rearrangement and racemisation in aqueous-ethanolic sulphuric acid of glycol (46) to be identical. If tertiary-hydroxyl group exchange in (46) is rapid and reversible,[29] the identity of the rearrangement and racemisation rates indicates that secondary-hydroxyl exchange, if it takes place at all, must be very much slower than tertiary-hydroxyl exchange. It is therefore reasonable to postulate that the rearrangement[8c] of the tetrasubstituted glycol (78; R = Bu^t) takes place through a mechanism such as outlined in Chart 5. If such be the case, then, although $k_1 > k_2$, if $k_{Bu} \gg k_{Me}$, the yield of ketone (84) could predominate over that of ketone (83).

CHART 5



3. Summary

During the past five years much progress has been made in understanding the mechanism of the hitherto mysterious pinacol rearrangement. Through the use of ^{14}C-labelling it has been possible to determine for several cases the relative fractions of removal of the two hydroxyl groups, and to conclude from these data that the groups with the greater electron-donating abilities also possess the greater abilities to facilitate ionisation of adjacent hydroxyl-bearing carbon atoms. Whenever such ionisation is rapidly reversible, the migratory aptitudes of the moving groups can then become important in determining the course of reaction. The effect of change of acid catalyst on the course of reaction has been demonstrated in the rearrangement of triphenylethylene glycol, and has been explained as being a consequence of changes in the ionic conformations of the intermediates with changes in the surrounding reaction media. The importance of aldehydes or of their conjugate acids as intermediates in the rearrangements of trisubstituted glycols also has been clarified. Within the range of catalysts and reactants employed, it has been shown that in cold, concentrated sulphuric acid the aldehyde intermediate reaches a maximum importance, becoming less important under the influence of the weaker acid catalysts. In this connection the question of the anomalous migratory

aptitudes in the aldehyde–ketone rearrangement has been solved, for it has been shown that these migratory aptitudes cannot be calculated directly from the product ratios, but are obtainable only through a consideration of the several ionic intermediates which are present in a dynamic equilibrium. Glycols labelled with deuterium have been subjected to the conditions of the pinacol rearrangement, and it has thus been established that the ketonic products can be formed with complete retention of deuterium; in such cases it has been concluded that the theory of "vinyl dehydration" is invalid.

Although some slight progress has been made with respect to the influence of steric properties of reactants upon the course of the rearrangement, this problem, particularly in the case of tetrasubstituted glycols, is still not well understood. The role of oxides in the pinacol and related aldehyde–ketone rearrangements also remains unsolved.

The impact of the isotopic method upon the pinacol rearrangement has thus provided a solution to the primary mysteries of the pinacol rearrangement such that our state of knowledge of this interesting and historical reaction is now equal, or nearly so, to our knowledge of the Wagner–Meerwein rearrangement.

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