ANIONOTROPY

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The term *anionotropy* conventionally refers to molecular rearrangements involving the simultaneous transposition of a multiple bond and of groups or atoms such as OH, OR, and Cl which can exist as stable anions. This nomenclature dates from a time when such reactions were generally thought to involve the separation of the migrating group as a free anion, in contrast to *cationotropy*, involving the migration of groups or atoms such as H which can exist as stable cations. It has since become recognised, however, that molecular rearrangements, like other organic reactions, can proceed by homolytic as well as heterolytic bond fission and that heterolytic rearrangement does not necessarily involve the separation of free ions. Moreover, there is no difference in principle between rearrangements involving the simultaneous transposition of two groups, and systems involving the simultaneous migration of one group and of an electron pair belonging to a multiple bond. Also, the description in classical terms of rearrangements resulting in the migration of groups such as alkyl which do not form stable ions is ambiguous. For these reasons, it will be convenient to re-define anionotropy to include all *rearrangements in which the migrating or departing group or groups retain the electron pairs by which they were originally linked to the rest of the molecule.*

An account of some of the early work in this field was given by J. W. Baker [1] in 1934. At that time the subject was still one of mainly academic interest, but during the last ten years many new anionotropic reactions have been discovered and have found numerous synthetic applications. Much progress has also been made in the elucidation of the mechanism of anionotropy, and anionotropic systems have been shown to provide a useful basis for the study of other problems in theoretical organic chemistry, such as the influence of substituents on reactivity.

Diad Anionotropy

According to the generally accepted ideas of Lowry,[2] Whitmore,[3] and others, diad rearrangements such as the pinacol–pinacone and oxime–amide (Beckmann) rearrangements involve a retention of complete electron octets by the migrating hydroxyl and alkyl or aryl groups and therefore represent anionotropic changes within the wider meaning of the term. It is not intended here to discuss in detail the numerous and well-known reactions

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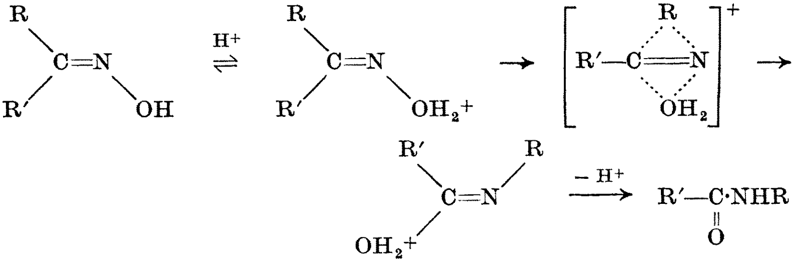
[1] " Tautomerism ", London, 1934.

[2] Institut de Chimie Solvay, IIme Conseil de Chimie, Paris, 1926, p. 150.

[3] *J. Amer. Chem. Soc.*, 1932, **54**, 3274.

of this type,[4, 5] but rather to draw attention to certain features common to diad and higher anionotropic systems.

The most fully investigated example is the Beckmann rearrangement.[6] This has been studied under widely varied conditions, generally giving rise to complicated catalytic influences, but in aqueous solution the rearrangement of an oxime is a simple, acid-catalysed, first-order process and the rate constants are dependent on the acidity function of the medium.[7] There is no evidence for the intermediate formation of oxime esters under these conditions.[8] The other main facts concerning the reaction are: (i) it is facilitated by electron-donating substituents in the aryl or alkyl groups, (ii) the migrating groups originally occupy *trans*-positions about the C:N link, and (iii) a migrating alkyl group retains its optical configuration.[9] These facts are in accord with the mechanism (1):



(1)

The first step is the reversible addition of a proton to the $:N\cdot OH$ group. The protons will be mostly attached to the more basic nitrogen atom to give the imonium ion $:^+NH\cdot OH$, but this will be in equilibrium with the oxonium ion $:N\cdot OH_2^+$, formation of which will weaken the N–O link and facilitate the separation of the hydroxyl group as a neutral water molecule. The second and rate-determining step is a double nucleophilic substitution in which the R and OH groups (the latter in the form of OH_2) exchange positions, each carrying their own electron pairs. The migration of R must be intramolecular; the migration of OH, on the other hand, may be intramolecular as shown, or it may be intermolecular and take place by an attack of a solvent water molecule at the carbon atom. The third step is the fast reversible loss of a proton followed by enol–keto prototropy to give the amide or anilide.

The characteristic features of the pinacol–pinacone rearrangement are very similar. The reaction is facilitated by electron-donating substituents and the rearrangement of benzpinacol in aqueous media is a first-order reaction and the rate-constants are dependent on the acidity function.[10] Mechanism (2), which is analogous to (1), is in accord with all the facts at

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[4] Watson, *Ann. Reports*, 1939, **36**, 191; 1941, **38**, 121.

[5] Wallis and Gilman, "Organic Chemistry", New York, 1943, p. 965.

[6] Blatt, *Chem. Reviews*, 1933, **12**, 215; Chapman, *J.*, 1935, 1223; B. Jones, *Chem. Reviews*, 1944, **35**, 335; *Nature*, 1946, **157**, 519.

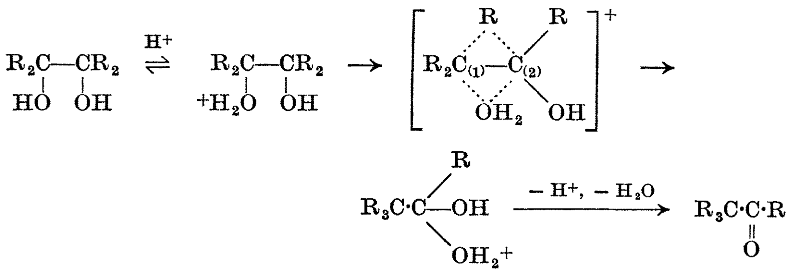
[7] Hammett, *Chem. Reviews*, 1935, **16**, 67.

[8] Pearson and Ball, *J. Org. Chem.*, 1949, **14**, 118.

[9] Campbell and Kenyon, *J.*, 1946, 25.

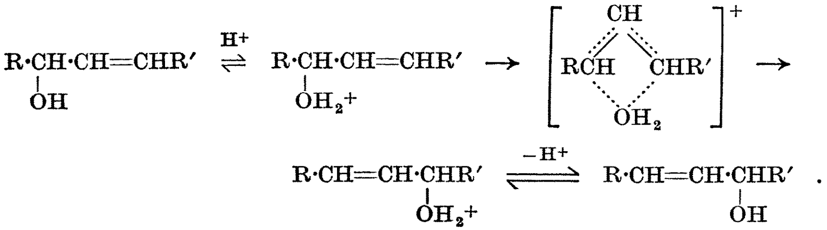
[10] Braude, unpublished.

present known, but as before the rate-determining migration may be intermolecular with regard to the OH group instead of intramolecular, as shown :


(2)

The rearrangement again takes place in the oxonium ion formed by addition of a proton to one of the hydroxyl groups ; the $C_{(1)}$–O and $C_{(2)}$–R links undergo simultaneous fission and during this process the positive charge travels continuously from O to $C_{(1)}$, from $C_{(1)}$ to $C_{(2)}$, and from $C_{(2)}$ back to O. The centre of location of the positive charge in the transition state will be approximately midway between carbon atoms $C_{(1)}$ and $C_{(2)}$, but the above method of representation is adopted in order to indicate the process of migration and to distinguish mechanism (2) from those [4] postulating free mesomeric carbonium ions as intermediates. In an asymmetrical glycol, the direction of the rearrangement will be determined both by the relative " basicities " of the two hydroxyl groups and by the ease of separation of the migrating group R and it is therefore not surprising that no simple generalisations can be made concerning the " relative migratory aptitudes " of different groups.[11]

There is a close resemblance between these diad systems and triad anionotropy, in which a hydroxyl or similar group exchanges positions with an electron pair (3) :


(3)

Such reactions are discussed in detail in the following section. If R′ is an ethoxyl group, rearrangement is followed by loss of ethanol to give [12] the aldehyde R·CH:CH·CHO and the analogy to changes of the pinacol–pinacone type is even more complete.

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[11] Bennett and Chapman, *Ann. Reports,* 1930, **27,** 114 ; cf. Hatt, Pilgrim, and Stephenson, *J.,* 1941, 478.

[12] Arens and van Dorp, *Nature,* 1947, **160,** 189 ; *Rec. Trav. chim.,* 1948, **67,** 973 ; Heilbron, E. R. H. Jones, Julia, and Weedon, *J.,* 1949, 1823.

Triad Anionotropy

Rearrangements of Allyl Alcohols (Three-carbon Oxotropy).—The only type of triad anionotropic system at present known is the so-called three-carbon system and the majority of examples are rearrangements of unsymmetrically substituted allyl alcohols. The special term *oxotropy* [13] is used for such anionotropic rearrangements involving only the migration of a hydroxyl group, corresponding to the term *prototropy* [2] for cationotropic rearrangements in which the migrating group is a hydrogen atom. Whereas triad prototropy is one of the commonest and longest-known types of molecular rearrangement, triad oxotropy has been studied in detail only during the last two decades.

Oxotropic changes are invariably brought about by acidic reagents (proton-donors), in contrast to prototropic changes which are catalysed by either acids or bases, or by both. Initially neutral reagents, such as acetic anhydride or acid chlorides, have occasionally been employed, but under these conditions partial or complete acylation takes place and rearrangement occurs in virtue of the free acid produced; if the reaction mixture is kept neutral, *e.g.*, by working in pyridine solution at low temperatures, only the derivative of the original alcohol is obtained. With simple allyl alcohols containing only alkyl substituents, oxotropic mobility is relatively low and isomerisation to the equilibrium mixture requires acid treatment at elevated temperatures or for prolonged periods. Thus, 1-methylallyl alcohol (I) and 3-methylallyl alcohol (crotyl alcohol) (II) are interconverted by 1% sulphuric acid at 95° (5 hours) to a mixture containing about 30% of the primary alcohol.[14] The next higher homologues, 1 : 1-dimethylallyl alcohol and 3 : 3-dimethylallyl alcohol, are similarly interconverted by treatment with 1% sulphuric acid at room temperature for 60 hours,[15, 16] the equilibrium mixture containing nearly equal proportions of the two isomers. Although caution must be exercised in interpreting data obtained under non-homogeneous conditions in view of the large effect of solubility differences, these two examples clearly show that alkyl substituents increase anionotropic mobility, but have little influence on the relative stability of the two isomers. This conclusion is amply confirmed by kinetic studies in more complex systems (cf. below). In the presence of a chloro- or ethoxyl group in position 3, however, rearrangement is followed by elimination of hydrogen chloride or ethanol and the equilibrium is disturbed.[12, 17] This provides a useful method for the synthesis of unsaturated aldehydes; thus, 3-chloro-1 : 1-dimethylallyl alcohol (III), obtained by condensing

$$\text{(I.)}\quad \mathrm{OH{\cdot}CHMe{\cdot}CH{:}CH_2} \overset{\mathrm{H_2SO_4}}{\rightleftharpoons} \mathrm{CHMe{:}CH{\cdot}CH_2{\cdot}OH}\quad \text{(II.)}$$

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[13] Braude and E. R. H. Jones, *J.*, 1944, 436; Braude, *ibid.*, p. 443.

[14] Hearne and La France, U.S.P. 2,373,956; *Chem. Abstr.*, 1945, **39**, 4081.

[15] Locquin and Sung Wouseng, *Compt. rend.*, 1922, **174**, 1711; **175**, 100; Sung Wouseng, *Ann. Chim.*, 1924, **1**, 386.

[16] Nazarov, Azerbaev, and Rakcheeva, *Bull. Acad. Sci.*, *U.S.S.R.*, 1946, 419.

[17] E. R. H. Jones and Weedon, *J.*, 1946, 937; Toogood and Weedon, *J.*, 1949, 3123; Bruun, Heilbron, Weedon, and Woods, *J.*, 1950, 633.

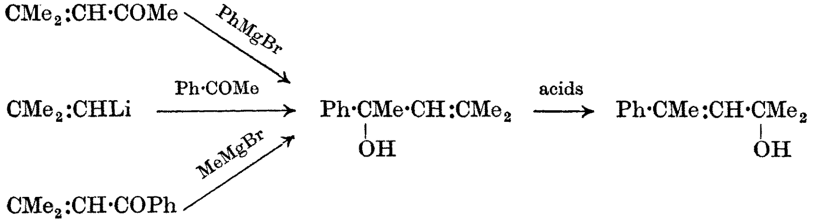
2-chlorovinyl methyl ketone with methylmagnesium bromide, is converted into β-methylcrotonaldehyde (IV) when shaken with 10% sulphuric acid in ether.[17]

$$\text{(III.)}\quad \mathrm{OH{\cdot}CMe_2{\cdot}CH{:}CHCl} \overset{\mathrm{H_2SO_4}}{\rightleftharpoons} \mathrm{CMe_2{:}CH{\cdot}CHCl{\cdot}OH} \xrightarrow{-\,\mathrm{HCl}} \mathrm{CMe_2{:}CH{\cdot}CHO}\quad\text{(IV.)}$$

In aryl-substituted allyl alcohols, oxotropic mobility is considerably enhanced and the equilibrium is displaced in favour of the more highly conjugated arylvinyl isomer. The first example of this type was described by Valeur and Luce[18] who showed that 1-phenylallyl alcohol (V) is converted into cinnamyl alcohol (VI) on treatment with dilute sulphuric acid, whereas 1-*cyclo*hexylallyl alcohol remains unchanged under these conditions. The rearrangement of 1-phenylallyl alcohol into cinnamyl alcohol has

$$\text{(V.)}\quad \mathrm{OH{\cdot}CHPh{\cdot}CH{:}CH_2} \xrightarrow{\text{acid}} \mathrm{CHPh{:}CH{\cdot}CH_2{\cdot}OH}\quad\text{(VI.)}$$

recently been studied in more detail by Braude, Jones, and Stern,[19] who found that the isomerisation goes practically to completion in homogeneous aqueous-dioxan solution in the presence of dilute mineral acid. If aqueous ethanol is employed as a solvent, a mixture of cinnamyl alcohol and cinnamyl ethyl ether is formed, although cinnamyl alcohol is not etherified under these conditions. Detailed analysis shows that ether formation occurs mainly during, and simultaneously with, rearrangement, but that 1-phenylallyl alcohol also undergoes some etherification before rearrangement and that ethyl 1-phenylallyl ether rearranges less readily than the alcohol. Numerous other examples of this type have been described.[19–22] The 1-arylallyl alcohols can be obtained by the condensation of an arylmagnesium halide with an αβ-ethylenic aldehyde or ketone, by the condensation of an aryl aldehyde or ketone with an alkenylmagnesium halide or alkenyl-lithium derivative, or by the selective reduction or Grignard condensation of an alkenyl aryl ketone, as illustrated below for 1 : 3 : 3-trimethyl-1-phenylallyl alcohol.[21, 22] The 3-arylallyl alcohols obtained on rearrangement can be independently synthesised by similar methods.



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[18] *Bull. Soc. chim.*, 1920, **27**, 611.

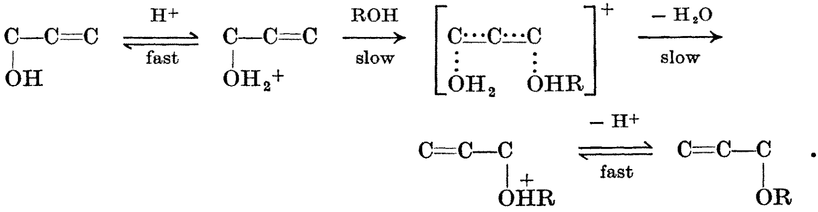
[19] Braude, E. R. H. Jones, and Stern, *J.*, 1946, 396; 1947, 1087; Braude and Stern, *J.*, 1947, 1096; Braude, Fawcett, and Newman, *J.*, 1950, 793; Braude and Fawcett, *J.*, 1950, 800, and unpublished work.

[20] Burton and Ingold, *J.*, 1928, 904; Burton, *J.*, 1928, 1650; 1929, 455; 1930, 248; 1931, 759.

[21] Braude and Timmons, *J.*, 1950, 2000, 2007, and unpublished work.

[22] Braude and Coles, *J.*, 1950, 2012, 2014, and unpublished work.

The rearrangement of 1-arylallyl to 3-arylallyl alcohols, and similar reactions, can be followed conveniently and quantitatively by taking advantage of the accompanying change in ultra-violet light absorption ;[13, 19] thus, cinnamyl derivatives exhibit an intense absorption band near 2510 A. associated with the conjugated (styryl) system, whereas 1-phenylallyl derivatives show only weak absorption in this region. By measuring the change in intensity of the 2510-A. band, the rate of isomerisation can readily be determined. Hardly any kinetic data concerning three-carbon anionotropy were available before the introduction of the spectrometric technique, but during the last few years detailed investigations have been carried out by this means. Oxotropic rearrangements in solution are invariably found to be simple first-order reactions and the rate constants (k) are dependent on Hammett's acidity function H which is a measure of the tendency of the medium to convert a neutral base (B) into its conjugate acid (BH^+).[7, 23] At low acid concentrations and for a given solvent H is proportional to the hydrogen-ion concentration, but at high acid concentration H increases more rapidly, and both H and k also show a characteristic non-linear dependence on solvent composition in organic solvent–water mixtures which can be explained in terms of the changes in solvent " structure " and the mode of solvation of the hydrogen ions.[13, 23] The proportionality between log k and H means that the rate of rearrangement depends on the fraction of the allyl alcohol (ROH) which is converted into its conjugate acid, and that the actual rearrangement is preceded by a fast, reversible formation of the oxonium ion (ROH_2^+). The subsequent migration may be intramolecular as represented in (3) (p. 406), or it may take place intermolecularly through an attack by a water or similar molecule at $C_{(3)}$ as shown in (4).



(4)

Competition between different solvent molecules thus leads to partial etherification in alcoholic solvents and under such conditions the inter- and intra-molecular reactions probably occur side by side. In other solvents, *e.g.*, anhydrous dioxan, on the other hand, the migration must be largely intramolecular. The function of the hydrogen-ion catalyst is to weaken the existing carbon–oxygen bond ;[13] instead of the separation of a charged hydroxyl anion, the migration involves the energetically much more favourable separation of a neutral water molecule. In the rate-determining step, the positive charge undergoes a continuous transfer from the departing oxygen atom *via* the allyl group to the entering oxygen atom, while a continuous electron displacement takes place simultaneously in the

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[23] Braude, *J.*, 1948, 1971 ; Braude and Stern, *J.*, 1948, 1976, 1982 ; *Nature*, 1948, **161**, 169.

opposite direction. Both the formation of the oxonium ion and the fission of the carbon–oxygen bond are facilitated by electron accession at the reaction centre, and oxotropic mobility is therefore increased by electron-donating substituents, and decreased by electron-attracting substituents in the allyl and phenyl groups (Tables I and II). The effect of substituents is exerted mainly through changes in the energy of activation. For nuclear substituents, the first-order rate constants (k) at one temperature vary in the sequence p-Br < p-Cl < p-F < H < m-Me < o-Me < p-Me < p-MeO and show the usual linear relation to the dissociation constants of the corresponding substituted benzoic acids.[19] The result for the halogen derivatives also confirm the " reversed " order of electromeric effects F > Cl > Br frequently encountered in other reactions. The ready accessibility of arylallyl alcohols, the mild conditions under which isomerisation takes place, the absence of side-reactions, and the comparatively high sensitivity of the reaction towards structural changes, combine to render oxotropic rearrangement of this type an excellent basis for investigating the electronic properties of substituents which have been little studied in this respect because of a lack of suitable reactions. In polycyclic arylallyl alcohols, k increases in the order 9-phenanthryl < phenyl < 2-naphthyl $\sim$ 1-naphthyl < 9-anthryl and, except for the phenanthryl derivative which is anomalous, a linear relation holds between k and the expected number of polar resonance forms contributing to the electronic effect of the polynuclear substituent.[19] The

TABLE I

Rate constants and energies of activation in three-carbon oxotropic systems, $\mathrm{HO{\cdot}CHX{\cdot}CH{:}CHMe \rightleftharpoons CHX{:}CH{\cdot}CHMe{\cdot}OH}$ [13, 19, 21, 30]

X.	k_{30} [a] (min.$^{-1}$).	$E_{\mathrm{Arr.}}$ [b] (kcals./g.-mol.).
Phenyl	1·84	19·5
o-Tolyl	3·59	19·5
m-Tolyl	2·17	20·4
p-Tolyl	16·1	19·6
p-Fluorophenyl	1·50	19·4
p-Chlorophenyl	0·43	20·3
p-Bromophenyl	0·34	20·4
p-Methoxyphenyl	189	17·9
1-Naphthyl	3·45	19·9
2-Naphthyl	3·20	20·2
9-Anthryl	8·05	19·5
9-Phenanthryl	1·46	20·3
2-Furyl	166	16·8
2-Thienyl	63·6	17·4
Vinyl	1·75	19·9
Ethynyl	0·00036	26·9
Acetyl [c]	$0{\cdot}15 \times 10^{-6}$	—

[a] First-order rate constants divided by acid concn. for 60% aqueous-dioxan hydrochloric acid solutions at 30°.

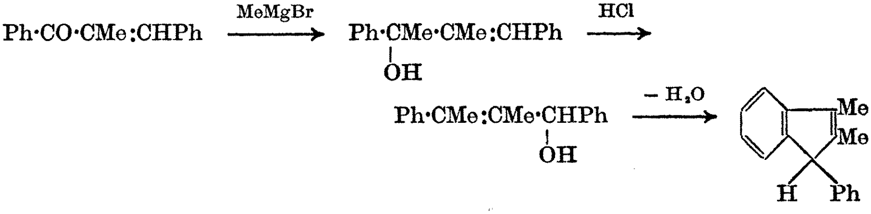
[b] Arrhenius energies of activation.

[c] Extrapolated from measurements on 1-acetyl-1 : 3 : 3-trimethylallyl alcohol (XXIX, p. 416).

large increase in k observed with 1-furyl and 1-thienyl substituents can be discussed in similar terms.[19]

The greater stability of the 3-arylallyl as compared with the 1-arylallyl alcohols indicated by the almost complete displacement of the oxotropic equilibrium must clearly be ascribed to the additional resonance energy associated with the conjugated styryl or arylvinyl system. If aryl groups are present in both the 1- and the 3-position, the difference in thermodynamic stability between the two isomers is much reduced and the equilibrium is again restored. Reversible systems of this type were first investigated by Burton and Ingold,[20] who found that the equilibrium mixture obtained by heating the phenyl-*p*-tolylallyl alcohols (VII, VIII; X = *p*-tolyl) with acetic anhydride contained about equal proportions of the two acetates, while with the phenyl-*p*-chlorophenylallyl alcohols the *p*-chlorostyryl isomer (VIII; X = *p*-C_6H_4Cl) predominated. The phenyl-*p*-nitrophenylallyl alcohols (VII, VIII; X = *p*-NO_2·C_6H_4) and phenylnaphthylallyl alcohols (VII, VIII; X = naphthyl) are similarly interconverted in the presence of dilute mineral acids.[19, 24] By means of the change of equilibrium with temperature, the heat of rearrangement, which should be approximately equal to the difference in resonance energy of the styryl system in (VII) and the arylallyl system in (VIII), can be determined and, since the resonance energy of the styryl system is known from thermal data, this provides a promising method for estimating resonance energies of other conjugated systems. A case of oxotropy in a 1 : 3-diarylallyl system in which one of the isomers undergoes further reaction occurs in the formation of 2 : 3-dimethyl-1-phenylindene from α-benzylidenepropiophenone : [25]

$$\text{(VII.)} \quad \text{HO·CHX·CH:CHPh} \rightleftharpoons \text{CHX:CH·CHPh·OH} \quad \text{(VIII.)}$$



$$\text{Ph·CO·CMe:CHPh} \xrightarrow{\text{MeMgBr}} \underset{\text{OH}}{\text{Ph·CMe}}\text{·CMe:CHPh} \xrightarrow{\text{HCl}} \text{Ph·CMe:CMe·}\underset{\text{OH}}{\text{CHPh}} \xrightarrow{-\,H_2O}$$

In the 1 : 1 : 3-triphenylallyl alcohol system, the equilibrium again lies entirely on one side, and only the diphenylvinyl derivatives are isolated under acidic conditions : [26]

$$\text{Ph·CH:CH·MgBr} \xrightarrow{Ph_2CO} \text{OH·CPh}_2\text{·CH:CHPh} \xrightarrow{\text{HCl–MeOH}} \text{CPh}_2\text{:CH·CHPh·OMe}$$

A displacement of oxotropic equilibrium similar to that shown by arylallyl alcohols might be expected in allyl alcohols containing other types of unsaturated substituents. Hardly any such systems were known, however,

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[24] Braude and Waight, unpublished.

[25] Smith and Hanson, *J. Amer. Chem. Soc.*, 1935, **57**, 1326.

[26] K. H. Meyer and Schuster, *Ber.*, 1922, **55**, 815; Straus and Ehrenstein, *Annalen*, 1925, **442**, 93; K. Ziegler, *Ber.*, 1925, **58**, 359.

until the discovery by E. R. H. Jones and McCombie [27] of the acid-catalysed rearrangement of 1-ethynylallyl alcohols (*e.g.*, IX) to 3-ethynylallyl alcohols (*e.g.*, X):

$$\mathrm{CHMe{:}CH{\cdot}CHO} \xrightarrow{\mathrm{HC{\vdots}CNa}} \underset{\text{(IX.)}}{\mathrm{CH{\vdots}C{\cdot}CH(OH)CH{:}CHMe}} \xrightarrow{\text{acids}} \underset{\text{(X.)}}{\mathrm{CH{\vdots}C{\cdot}CH{:}CH{\cdot}CHMe{\cdot}OH}}$$

This reaction proved to be quite general and has found many important applications, particularly in the synthesis of vitamin A and of vitamin A analogues from acetylenic precursors.[28, 29] The 1-alkynylallyl alcohols are readily accessible by the condensation of acetylenic Grignard or alkali-metal derivatives with ethylenic aldehydes or ketones. Isomerisation to the 3-alkynylallyl alcohols, which are characterised by high-intensity light absorption near 2200 A. associated with the conjugated vinylacetylene chromophore, can usually be effected in high yield by treatment with dilute mineral acids. Although the oxotropic equilibria again lie far on the side of the conjugated isomers, oxotropic mobility in the alkynylallyl system is much lower [30] than in the corresponding arylallyl system (Table I), as might be expected in view of the strong electron-attracting properties of acetylenic groups. As before, rearrangement is greatly facilitated by alkyl

TABLE II

The effect of methyl substituents on the mobility of three-carbon oxotropic systems, $\mathrm{HO{\cdot}CXR^1{\cdot}CR^2{:}CR^3R^4 \rightleftharpoons CXR^1{:}CR^2{\cdot}CR^3R^4{\cdot}OH}$ [18, 21, 30]

X.	R^1.	R^2.	R^3.	R^4.	k_{30}[a] (min.$^{-1}$).	X.	R^1.	R^2.	R^3.	R^4.	k_{30}[a] (min.$^{-1}$).
$\mathrm{C{\vdots}CH}$	H	H	H	H	0·00000015	$\mathrm{CH{:}CH_2}$	H	H	H	H	0·0018
,,	Me	H	H	H	0·00009	,,	H	Me	H	H	0·0033
,,	H	Me	H	H	0·0000011	,,	H	H	Me	H	1·73
,,	H	H	Me	H	0·00058	,,	Me	H	Me	H	22
,,	H	H	Me	Me	0·133	,,	H	H	Me	Me	150
,,	Me	H	Me	Me	4·5						
$\mathrm{C{\vdots}CBu^n}$	H	H	H	H	0·000054	Ph	H	H	H	H	0·0043
,,	Me	H	H	H	0·0164	,,	H	H	Me	H	2·21
,,	H	H	Me	H	0·81	,,	H	H	Me	Me	79
,,	Me	H	Me	H	5·60						
,,	Me	H	Me	Me	354						

[a] First-order rate constants divided by acid concentration for 60% aqueous-ethanolic hydrochloric acid solutions at 30°.

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[27] *J.*, 1943, 261.

[28] Heilbron, E. R. H. Jones, and Raphael, *J.*, 1943, 264; Heilbron, Johnson, E. R. H. Jones, and Raphael, *ibid.*, p. 265; Heilbron, E. R. H. Jones, and Weedon, *J.*, 1944, 140; Cymerman, Heilbron, and E. R. H. Jones, *J.*, 1944, 144.

[29] For summaries, see Sir Ian Heilbron, *J.*, 1948, 386; Johnson, *Ann. Reports*, 1949, **46**, 168; E. R. H. Jones, *J.*, 1950, 754.

[30] Braude and E. R. H. Jones, *J.*, 1946, 122, 128.

substituents, and the relative rates of isomerisation of alkynylallyl alcohols containing up to four such substituents cover a range of over 10^9 (see Table II). The differences in reactivity can be analysed into rate factors which are of the order of 10^2, 10, and 10^3 for methyl substituents attached to the 1- and 2- and 3-allyl positions, respectively.[30] The results clearly demonstrate the operation of two different substituent effects, the inductive effect which rapidly decreases with increasing distance between the substituent and the reacting centre, and the much larger tautomeric effect which comes into play only on the interposition of the highly polarisable ethylenic group.

By partial catalytic hydrogenation, alkynylallyl alcohols can be converted into the corresponding alkenylallyl alcohols (dialkenylcarbinols) and it was shown by Heilbron, E. R. H. Jones, McCombie, and Weedon [31] that the latter undergo oxotropic rearrangement with much greater ease than their acetylenic analogues, in accordance with the weaker electron-attracting properties of ethylenic as compared with acetylenic groups. Thus, vinylethynylcarbinol, obtained by condensing acraldehyde with sodium acetylide, is selectively hydrogenated to divinylcarbinol, which rearranges to butadienylcarbinol (XI).

$$CH{\vdots}C{\cdot}CH(OH){\cdot}CH{:}CH_2 \xrightarrow{H_2\text{–}Pd} CH_2{:}CH{\cdot}CH(OH){\cdot}CH{:}CH_2 \xrightarrow{\text{acids}} CH_2{:}CH{\cdot}CH{:}CH{\cdot}CH_2{\cdot}OH \qquad \text{(XI.)}$$

Dialkenylcarbinols can also be prepared from dialkenyl ketones, but this method is rather limited in scope as the required ketones themselves are not usually accessible. However, di*iso*butenylmethylcarbinol (XII) can be obtained from the readily available di*iso*butenyl ketone (phorone) and methylmagnesium bromide. The rearrangement of highly substituted dialkenylcarbinols such as (XII) occurs so readily that, unless careful precautions are taken to exclude all traces of acids during their preparation and isolation, only the isomeric butadienylcarbinols are obtained. The latter easily undergo dehydration to the corresponding substituted hexa-1 : 3 : 5-trienes (*e.g.*, XIV).[21, 22]

$$(CMe_2{:}CH)_2CO \longrightarrow \underset{\text{(XII.)}}{(CMe_2{:}CH)_2{\cdot}CMe{\cdot}OH} \longrightarrow \underset{\text{(XIII.)}}{CMe_2{:}CH{\cdot}CMe{:}CH{\cdot}CMe_2{\cdot}OH} \longrightarrow \underset{\text{(XIV.)}}{CMe_2{:}CH{\cdot}CMe{:}CH{\cdot}CMe{:}CH_2}$$

A more direct and, in some respects, more general route to dialkenylcarbinols as well as to other anionotropic systems which has recently been developed [21, 22] consists of the condensation of alkenyl organometallic derivatives with carbonyl compounds. With the exception of 2-arylated vinyl bromides, such as β-bromostyrene, vinyl halides do not usually form Grignard derivatives, but the corresponding lithium alkenyls can be obtained in good yields under appropriate conditions. Thus, *iso*butenyl bromide with lithium in ether gives *iso*butenyl-lithium which with acraldehyde

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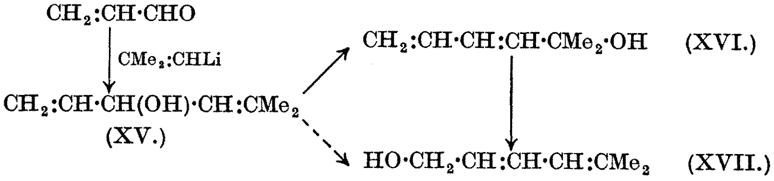
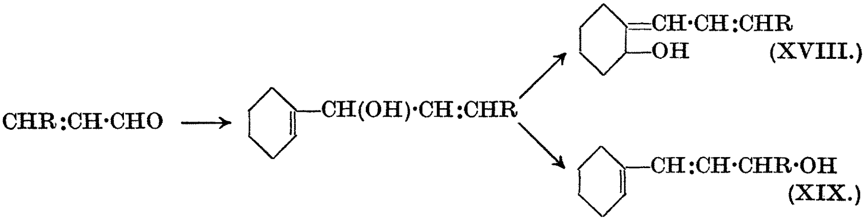
[31] *J.*, 1945, 84, 88.

yields *iso*butenylvinylcarbinol (XV). Rearrangement of such unsymmetrical dialkenylcarbinols could theoretically proceed in two directions, but it is found [21, 31] that the hydroxyl group always migrates initially to



the more alkyl-substituted $C_{(3)}$ and that the resulting butadienylcarbinols (*e.g.*, XVI) then undergo a much slower, reversible further rearrangement to the other conjugated isomer (*e.g.*, XVII). The final equilibrium mixture contains approximately equal proportions of the tertiary and the primary carbinol and it may therefore at first sight appear surprising that the initial rearrangement should proceed exclusively in one direction. However, the influence of alkyl substituents on the relative rates of two possible rearrangements of the same carbinol will be similar to their effect on the relative rates of rearrangement in two different carbinols. Since a 3-methyl substituent increases the rate of rearrangement by a factor of about 10^3, (XVI) will be formed from (XV) at least 1000 times faster than (XVII) and, in conditions leading to the rearrangement into (XVI) at a measurable rate, the amount of (XVII) formed will be indetectably small. The equilibrium position in the subsequent five-carbon oxotropy, on the other hand, is governed by the almost equal stability of the two conjugated isomers (cf. below). The carbinols (XVI) and (XVII) can be distinguished by their high-intensity absorption maxima at 2235 and 2360 A., respectively, characteristic of a mono- and a tri-alkylated butadiene chromophore, and their structures are rigidly proved by complete catalytic hydrogenation to the saturated alcohols. The effect of alkyl substituents in determining the direction of three-carbon oxotropy is also clearly shown [22] in the *cyclo*hexenylcarbinols, rearrangement of which gives exclusively the allylidene*cyclo*hexanol (XVIII) when R = H, but the *cyclo*hexenylbutenol (XIX) when R = Me.



In substituted butadienylvinylcarbinols such as (XX) which represent potential three- as well as five-carbon oxotropic systems, triad rearrangement takes place preferentially. Reactions of this type form a key step in one of the methods successfully employed for the synthesis of vitamin A

(XXI) and vitamin A analogues.[32] Rearrangement and simultaneous dehydration of the glycol (XX) (in the form of its primary acetate) can be effected in high yield by treatment with a trace of iodine in boiling xylene, a method which probably depends on the formation of a small amount of hydrogen iodide which acts as a catalyst.

$$\begin{array}{cl}
\mathrm{CH_2R{\cdot}CH{:}CMe{\cdot}CHO + CH{\vdots}C{\cdot}CMe{:}CH{\cdot}CH_2{\cdot}OH} & \\
\downarrow & \\
\mathrm{CH_2R{\cdot}CH{:}CMe{\cdot}CH(OH){\cdot}C{\vdots}C{\cdot}CMe{:}CH{\cdot}CH_2{\cdot}OH} & \\
\downarrow{\scriptstyle H_2} & \\
\mathrm{CH_2R{\cdot}CH{:}CMe{\cdot}CH(OH){\cdot}CH{:}CHCMe{:}CH{\cdot}CH_2{\cdot}OH} & \text{(XX.)} \\
\downarrow & \\
\mathrm{[CH_2R{\cdot}CH(OH){\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CH_2{\cdot}OH]} & \\
\downarrow{\scriptstyle -\,H_2O} & \\
\mathrm{CHR{:}CH{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CH_2{\cdot}OH} & \text{(XXI.)}
\end{array}$$

(R = 2 : 6 : 6-trimethyl*cyclo*hex-1-enyl.)

The systems so far discussed demonstrate that unsaturated substituents such as aryl, alkynyl, and alkenyl groups invariably displace the oxotropic equilibrium towards one side, but increase or decrease mobility depending on their electron-donating or electron-attracting properties. Low oxotropic mobility would therefore be expected for allylic systems terminated by carbonyl, carboxyl, or nitrile groups. Probably the first example of three-carbon anionotropy to be found in the literature occurs in the conversion of crotonaldehyde cyanohydrin into lævulic acid :[33]

$$\begin{tikzcd}
 & & \mathrm{CHMe{:}CH{\cdot}CH(OH){\cdot}CN} \arrow[dl, "HCl"'] \arrow[dr, "PBr_3"] & & \\
\text{(XXII.)} & \mathrm{CHMe{:}CH{\cdot}CH(OH){\cdot}CO_2H} \arrow[d] & & \mathrm{[CH_2Me{\cdot}CH{:}C(OH){\cdot}CN]} \arrow[d] & \\
\text{(XXIII.)} & \mathrm{HO{\cdot}CHMe{\cdot}CH{:}CH{\cdot}CO_2H} \arrow[d] & & \mathrm{CH_2Me{\cdot}CH_2{\cdot}CO{\cdot}CN} \arrow[d] & \\
 & \mathrm{[HO{\cdot}CMe{:}CH{\cdot}CH_2{\cdot}CO_2H]} \arrow[d] & & \mathrm{CH_2Me{\cdot}CH_2{\cdot}CO{\cdot}CO_2H} & \text{(XXV.)} \\
\text{(XXIV.)} & \mathrm{Me{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H} & & &
\end{tikzcd}$$

Hydrolysis of the cyanohydrin with concentrated hydrochloric acid yields 1-hydroxybut-2-ene-1-carboxylic acid (XXII), which undergoes oxotropic

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[32] Isler, Huber, Ronco, and Kofler, *Helv. Chim. Acta*, 1947, **30**, 1911 ; Cheeseman, Sir Ian Heilbron, E. R. H. Jones, Sondheimer, and Weedon, *J.*, 1949, 1516.

[33] Fittig, *Annalen*, 1898, **299**, 37 ; Bougault, *Compt. rend.*, 1913, **156**, 1469 ; **157**, 377, 403 ; *J. Pharm. Chim.*, 1913, **8**, 393, 406.

rearrangement to 3-hydroxybut-1-ene-1-carboxylic acid (XXIII). The latter can be isolated in the form of its lactone, but easily undergoes further double prototropic rearrangement to lævulic acid (XXIV) *via* the unstable enolic form. Similar, but reversible, oxotropy takes place in 1-hydroxy-3-phenylprop-2-ene-1-carboxylic acid obtained by hydrolysis of cinnamaldehyde cyanohydrin.[33] In the crotonaldehyde cyanohydrin itself, migration of a hydrogen atom occurs in preference to that of the hydroxyl group. Thus, treatment with phosphorus tribromide followed by water yields, not the conjugated nitrile corresponding to the acid (XXIII), but butyroyl cyanide and α-ketovaleric acid (XXV).[34]

The fact that oxotropy is retarded, while prototropy is facilitated by electron-attracting groups is illustrated even more clearly by the corresponding hydroxy-ketones. 4-Hydroxyhept-5-en-3-one (XXVI ; R = Et), obtained by the interaction of crotonaldehyde cyanohydrin with ethylmagnesium bromide, undergoes prototropy to heptane-3 : 4-dione (XXVII ; R = Et),[21] and hydration of 1-ethynyl-3-methylallyl alcohol (IX) leads to hexane-2 : 3-dione (XXVII ; R = Me), the intermediate hydroxy-ketone (XXVI ; R = Me) undergoing immediate rearrangement under the acidic conditions employed :[35]

$$\underset{\text{(XXVI.)}}{\mathrm{CHMe{:}CH{\cdot}CH(OH){\cdot}COR}} \xrightarrow{\text{acid}} [\mathrm{CH_2Me{\cdot}CH{:}C(OH){\cdot}COR}] \longrightarrow \underset{\text{(XXVII.)}}{\mathrm{CH_2Me{\cdot}CH_2{\cdot}CO{\cdot}COR}}$$

Oxotropic rearrangement in systems of this type can, however, be realised if prototropy is precluded by replacing the hydrogen atoms concerned by alkyl groups. 3-Hydroxy-3 : 5-dimethylhex-4-en-2-one (XXIX), obtained by the condensation of *iso*butenyl-lithium with diacetyl dimethyl monoketal (3 : 3-dimethoxybutan-2-one) followed by careful hydrolysis of the ketal (XXVIII), is converted by 1% sulphuric acid at 60° into the isomeric 5-hydroxy-3 : 5-dimethylhex-3-en-2-one (XXX), the constitution of which is proved by oxidative degradation to diacetyl and α-hydroxy*iso*butyraldehyde.[21]

$$\mathrm{(MeO)_2CMe{\cdot}CO{\cdot}Me} \longrightarrow \underset{\text{(XXVIII.)}}{\mathrm{(MeO)_2CMe{\cdot}CMe(OH){\cdot}CH{:}CMe_2}} \longrightarrow$$

$$\underset{\text{(XXIX.)}}{\mathrm{Me{\cdot}CO{\cdot}CMe(OH){\cdot}CH{:}CMe_2}} \longrightarrow \underset{\text{(XXX.)}}{\mathrm{Me{\cdot}CO{\cdot}CMe{:}CH{\cdot}CMe_2{\cdot}OH}}$$

Rearrangements of Propargyl Alcohols.—A type of three-carbon oxotropy less common than that so far discussed occurs in substituted propargyl (α-acetylenic) alcohols. If an allyl group is also present, as in 1-ethynyl-3-methylallyl alcohol (IX) ordinary allylic rearrangement takes place, but in other cases the hydroxyl group can exchange positions with one of the electron pairs of the triple bond, resulting in the formation of an allene

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[34] Rambaud, *Compt. rend.*, 1933, **197**, 689.

[35] Heilbron, E. R. H. Jones, Smith, and Weedon, *J.*, 1946, 54.

alcohol, which immediately undergoes further prototropic rearrangement to an unsaturated aldehyde or ketone.[36, 37, 38] As might be expected in view of the lack of electron accession at the hydroxyl group and in view of the steric strain associated with the formation of the allene system, such rearrangements take place much less readily and much less smoothly than allylic oxotropy. Thus, whereas 1-phenylallyl alcohol is almost quantitatively converted into cinnamyl alcohol by dilute mineral acid, the isomerisation of 1-phenylpropargyl alcohol (XXXI) into cinnamaldehyde (XXXII) requires prolonged treatment with moderately concentrated sulphuric acid and is accompanied by side-reactions :[37]

$$\underset{\text{(XXXI.)}}{\mathrm{HO{\cdot}CHPh{\cdot}C{\vdots}CH}} \longrightarrow [\mathrm{CHPh{:}C{:}CH{\cdot}OH}] \longrightarrow \underset{\text{(XXXII.)}}{\mathrm{CHPh{:}CH{\cdot}CHO}}$$

Rearrangements of Allyl Esters.—Esterification of allylic alcohols usually yields a mixture of the isomeric allyl esters, unless special precautions are taken to neutralise the acid produced in the replacement reaction (cf. p. 407). Numerous examples of this kind are to be found in the earlier literature. In a well-known group of papers,[20] Burton and Ingold reported some qualitative experiments on the degree of rearrangement accompanying replacement–acetylation, –*p*-nitrobenzoylation, and –bromination of arylallyl alcohols, and concluded that the ease of rearrangement increases in the order alcohol < acetate < *p*-nitrobenzoate < bromide, *i.e.*, in the order of the stability of the anions OH^-, OAc^-, $NO_2{\cdot}C_6H_4{\cdot}CO_2^-$, and Br^-. These authors also examined the isomerisation of 1-phenylallyl *p*-nitrobenzoate in different solvents and observed that the rate of rearrangement increases in the sequence *p*-xylene < chlorobenzene < acetic anhydride < benzonitrile, *i.e.*, in the order of increasing dielectric constants and ionising properties of the media. Mainly on the basis of this evidence, Burton and Ingold suggested that anionotropic rearrangement proceeds by way of a rate-determining ionisation into a carbonium ion and a fully dissociated anion, and that the mesomeric carbonium ion then rapidly undergoes further reaction (5) :

$$\mathrm{A{\cdot}C{-}C{=}C} \rightleftharpoons \mathrm{A^-} + \overset{+}{\overbrace{\mathrm{C{\cdots}C{\cdots}C}}} \xrightarrow{\mathrm{A'^-}} \mathrm{A^-} + \mathrm{C{=}C{-}CA'} \quad . \quad (5)$$

Further support for this view has been adduced in later papers by Hughes, Ingold, and their collaborators.[39] More recent investigations, however, have shown that Burton and Ingold's observations receive a more complex explanation than could perhaps at first have been surmised and make it unlikely that mechanism (5) plays any significant part in the anionotropic rearrangement of allyl esters. (For a more detailed discussion, see reference 40.)

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[36] K. H. Meyer and Schuster, *Ber.*, 1922, **55**, 819 ; Rio, *Compt. rend.*, 1949, **228**, 690.

[37] MacGregor, *J. Amer. Chem. Soc.*, 1948, **70**, 3953 ; 1950, **72**, 2501.

[38] Chanley, *ibid.*, p. 244 ; Hennion *et al.*, *ibid.*, 1949, **71**, 2813 ; 1950, **72**, 3542.

[39] Catchpole and Hughes, *J.*, 1948, 1, 4 ; Catchpole, Hughes, and Ingold, *J.*, 1948, 8 ; cf. de la Mare, England, Fowden, Hughes, and Ingold, *J. Chim. physique*, 1948, **45**, 236.

[40] Braude, *Ann. Reports*, 1949, **46**, 125.

A careful study of the rearrangement of allyl esters in various solvents was carried out by Meisenheimer and his co-workers,[41] who made the important observation that the rearrangement of 1-phenylallyl *p*-nitrobenzoate is " autocatalytic " and is accompanied by the formation of *p*-nitrobenzoic acid. Later, Kenyon, Partridge, and Phillips [42] found that the rearrangement of allyl esters is catalysed by dilute acids and that the hydrogen phthalates of phenylallyl alcohols undergo self-rearrangement, whereas the corresponding sodium salts or neutral esters are quite stable. These facts clearly suggest that the rearrangements of allyl esters, like those of allyl alcohols, are hydrogen-ion catalysed and take place by mechanisms analogous to (3) or (4). This has been confirmed by recent investigations. The rates and energies of activation of the rearrangement of 1-ethynylallyl acetate in aqueous acid media are very similar to those of the alcohol ; [43] rearrangement of the acetate is accompanied by hydrolysis, and a detailed analysis indicates that the following reactions occur side by side : (i) intramolecular rearrangement followed by hydrolysis, (ii) simultaneous intermolecular rearrangement and hydrolysis through attack by solvent water molecules at $C_{(3)}$, and (iii) hydrolysis of the acetate, without rearrangement, followed by rearrangement of the alcohol produced. Similar results have been obtained with 1-phenylallyl esters and ethers [24] (see Table III). Contrary to the requirements of mechanism (5), the relative mobilities clearly bear no relation to the anionic stabilities of the migrating groups, but they are fully in accord with mechanism (6) in which relative mobility will be a complex function of the combined effects of the ester group on the proton-addition equilibrium and on the ease of fission of the carbon–oxygen bond in the oxonium ion. In the intramolecular rearrangement of the esters, the transition state may involve a six-membered ring with the acyl-oxygen atom becoming attached to $C_{(3)}$ (6*a*).[42]

TABLE III

Rearrangements of 1-*phenylallyl derivatives by* 0·01M-*hydrochloric acid in* 60% *aqueous dioxan at* 90°.[24]

	k_{90} [a] (min.$^{-1}$).	E_{Arr} (kcals./g.-mol.).		k_{90} [a] (min.$^{-1}$).	E_{Arr} (kcals./g.-mol.).
Alcohol . .	2·97	24·5 ± 0·5	*p*-Nitrobenzoate	0·79	26·5
Acetate . .	1·39	25·5	Methyl ether	1·28	27·0
Benzoate . .	0·27	26·5			

[a] First-order rate constants divided by acid concentration.

The slow rearrangement of allyl esters in neutral solvents is due to the formation of carboxylic acid which then catalyses the rearrangement. In aqueous or alcoholic solvents, the carboxylic acid is produced by hydrolysis or alcoholysis ; thus, 3-methyl-1-phenylallyl *p*-nitrobenzoate is converted

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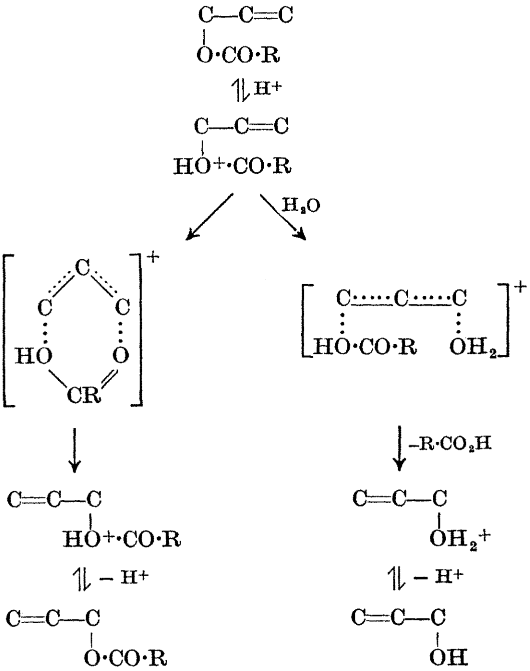
[41] Meisenheimer, Schmidt, and Schäfer, *Annalen*, 1933, **501**, 131.

[42] *J.*, 1937, 207.

[43] Braude, *J.*, 1948, 794.

in methanol solution into methyl 1-methyl-3-phenylallyl ether and *p*-nitrobenzoic acid.[42] In non-hydroxylic solvents such as chlorobenzene the carboxylic acid is produced [24] by a side-reaction the nature of which has not



(6*a*) (6*b*)

yet been established with certainty ; in the case of 1-phenylallyl esters it may be a direct 1 : 2-elimination to give the unstable phenylallene (*e.g.*, XXXIII) :

$$\text{R·CO·O·CHPh·CH:CH}_2 \longrightarrow \underset{\text{(XXXIII.)}}{\text{CHPh:C:CH}_2} + \text{R·CO}_2\text{H}$$

Definite proof that the rearrangement under these conditions is acid-catalysed and not spontaneous is provided by the fact that the values of the rate constants in the absence of added acid fall on the straight lines obtained by plotting the rate constants in the presence of added acid against the total acid concentration.[24] Comparisons of anionotropic mobility in neutral solvents thus have little significance and some of the earlier observations of Burton and Ingold (see above) arise from the fact that the amount of carboxylic acid eliminated varies with the ester and with the solvent and that *p*-nitrobenzoic acid is a better catalyst for rearrangement than is the weaker acetic acid.

Rearrangements of Allyl Halides.—The preparation of allyl halides by replacement reactions of allyl alcohols with hydrogen halides, phosphorus halides, or similar reagents,[44–47] by addition reactions of conjugated dienes,[48] or by substitution reactions of olefins with *N*-halogen compounds [49] generally gives rise to a mixture of the two isomers. Recent work has shown that, contrary to earlier suggestions,[20] the formation of mixtures in the case of allyl chlorides is not caused by the lability of the halogen derivatives, but rather by rearrangement of the allyl alcohol under the influence of the acid reagent, or by simultaneous occurrence of 1 : 2- and 1 : 4-addition. The chlorides can be separated by fractionation and undergo rearrangement in solution rather *less* readily than do the corresponding alcohols or esters. The isomeric rearrangement of allyl chlorides has been little studied, but methylallyl and ethylallyl chlorides have been found to isomerise slowly in boiling acetic acid [44] or under the influence of hydrochloric acid.[45] It thus appears that anionotropy in allyl halides is subject to hydrogen-ion catalysis and may possibly involve the intermediate formation of halonium ions $RHalH^+$ analogous to oxonium ions ROH_2^+. The possible occurrence of another mode of heterolytic catalysis is indicated by the interesting observation [45, 50] that the isomerisation of ethylallyl chlorides in the presence of hydrochloric acid is accelerated by ferric chloride, zinc chloride, and other multivalent metal chlorides. The effect of the metal chloride may well be due to co-ordination with the allylic chloride atom and to an ionisation process $RCl + MCl_3 \rightleftharpoons R^+ + MCl_4^-$, analogous to that believed to be operative in Friedel–Crafts reactions.

In contrast to allyl chlorides, isomeric allyl bromides are difficult to separate and readily undergo interconversion.[45, 47] Here rearrangement is accelerated by peroxides and similar agents [45] and is probably, at least in part, a free radical process involving homolytic fission of the C–Br bond and migration of bromine atoms.

Non-isomeric rearrangement in allyl halides has been more fully investigated. Whereas replacement reactions of allyl esters under basic conditions invariably yield only the unrearranged derivatives,[40] alkaline hydrolysis, alcoholysis, and similar reactions of allyl halides are often accompanied by partial or complete rearrangement. The first observation in this field was made by Charon,[51] who found that the treatment of cinnamyl chloride

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[44] Meisenheimer and Link, *Annalen*, 1930, **479,** 211 ; Meisenheimer and Beutter, *ibid.*, 1934, **508,** 58.

[45] Kharash, Margolis, and Mayo, *J. Org. Chem.*, 1936, **1,** 393 ; Kharash, Kritchevsky, and Mayo, *ibid.*, 1937, **2,** 489.

[46] Martin and Trinh, *Compt. rend.*, 1949, **228,** 688.

[47] Winstein and Young, *J. Amer. Chem. Soc.*, 1936, **58,** 104 ; Young and Lane, *ibid.*, 1937, **59,** 2051 ; 1938, **60,** 847 ; Young and Nozaki, *ibid.*, 1940, **62,** 311.

[48] Petrov, *J. Gen. Chem. Russia*, 1943, **13,** 741 ; Ultée, *J.*, 1948, 530 ; *Rec. Trav. chim.*, 1949, **68,** 125, 352, 483.

[49] Karrer and Ringli, *Helv. Chim. Acta*, 1947, **30,** 863, 1776 ; Braude and Waight, *Nature*, 1949, **164,** 241 ; Bateman, Cuneen, and Koch, *ibid.*, p. 242.

[50] Pudovik and Arbuzov, *Bull. Soc. chim., U.R.S.S., Cl. Sci. Chim.*, 1946, 427 ; Pudovik, Nikitina, and Aigistova, *J. Gen. Chem. Russia*, 1949, **19,** 67, 279 ; Pudovik, *ibid.*, p. 1179.

[51] Charon, *Bull. Soc. chim.*, 1910, **7,** 86 ; Dupont and Labaume, *Chem. Zentr.*, 1910, **11,** 734.

with methanol in the presence of sodium carbonate yielded mainly the methyl ether of 1-phenylallyl alcohol (V). Some of the more important reactions which have been examined in this respect are summarised in Table IV.

TABLE IV

Replacement reactions of allyl chlorides

$$\mathrm{Cl{\cdot}CHR{\cdot}CH{:}CHR'} \begin{array}{l} \nearrow \ \mathrm{Y{\cdot}CHR{\cdot}CH{:}CHR'}\ (\alpha\text{-substitution}) \\ \searrow \ \mathrm{CHR{:}CH{\cdot}CHR'Y}\ (\gamma\text{-substitution}) \end{array}$$

Reaction.	R.	R′.	Product.	Ref.
Hydrolysis (H_2O–EtOH–Na_2CO_3) .	Me	H	$\alpha + \gamma$	44, 52
	H	Me	$\alpha + \gamma$	44, 52
	H	Ph	Mainly γ	44
Ethanolysis (EtOH–NaOEt) . .	Me	H	$\alpha + \gamma$	39, 52
	H	Me	Mainly α	39, 52
	H	Ph	Mainly α	44
	Cl	Ph	Mainly γ	53
Acetolysis (AcOH–KOAc) . . .	Me	H	$\alpha + \gamma$	44, 52
	H	Me	$\alpha + \gamma$	44, 52
	H	Ph	$\alpha + \gamma$	44
Amination ($NHEt_2$)	Et	H	γ	44
	H	Et	α	44
	H	$\mathrm{C{\vdots}CH}$	α	54
	Me	$\mathrm{C{\vdots}CH}$	γ	54

The extent of rearrangement accompanying substitution is intimately dependent both on the structure of the allyl halide and on the reagent. Few valid generalisations can be made, but " abnormal " or γ-substitution is usually favoured by neutral rather than strongly alkaline conditions [39, 47, 55] and kinetic investigations [39, 51] on the hydrolysis, alcoholysis, and acetolysis of the methyl- and ethyl-allyl chlorides indicate that second-order reaction with charged anions proceeds in the normal manner and that γ-substitution is associated with first-order reaction with the solvent. Hughes, Ingold, and their collaborators [39] have concluded that γ-substitution takes place exclusively by mechanism (5) and involves a unimolecular ionisation of the halide to give the mesomeric carbonium ion which then undergoes reaction at the α- and the γ-position at comparable speeds. This view does not readily account for the fact, however, that the thermodynamically less stable, deconjugated products are obtained from cinnamyl and other conjugated halides ; if the mesomeric carbonium ion were formed, the positive charge would be expected to remain concentrated at $C_{(\alpha)}$. For these and other reasons, it appears much more likely [40, 52] that γ-substitution in allyl

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[52] Roberts, Young, and Winstein, *J. Amer. Chem. Soc.*, 1942, **64**, 2157 ; Young and Andrews, *ibid.*, 1944, **66**, 421 ; Kepner, Winstein, and Young, *ibid.*, 1949, **71**, 115.

[53] Andrews, *ibid.*, 1946, **68**, 2584 ; 1947, **69**, 3062 ; Andrews and Linden, *ibid.*, p. 2091.

[54] E. R. H. Jones, Lacey, and Smith, *J.*, 1946, 940.

[55] Owen and Sultanbawa, *Nature*, 1949, **163**, 997 ; *J.*, 1949, 3089.

halides is analogous to intermolecular isomeric rearrangement in allyl alcohols and esters (reactions 4 and 6*b*) and usually involves attack by a *neutral* reagent at $C_{(\gamma)}$. In alcohols and esters this type of substitution is successful under acidic conditions only when the carbon–oxygen link is weakened by the formation of the oxonium ion, whereas fission of the carbon–halogen bond occurs sufficiently readily in neutral solution. Conclusive evidence for this mode of reaction has been obtained by Kepner, Winstein, and Young,[52] who found that the reaction of 1-ethylallyl chloride with diethyl sodiomalonate in ethanol is strictly of the second order, *i.e.*, bimolecular, and yet gives 23% of the 3-ethylallyl derivative. As would be expected, the effectiveness of neutral reagents for γ-attack increases with their basicity in the order $EtOH < H_2O$ and $NH_3 < NH_2Et < NHEt_2$.[54]

Pentad Anionotropy

Five-carbon Anionotropy.—It has already been mentioned (p. 415) that asymmetrical butadienylcarbinols, formed by three-carbon oxotropy of alkenylallyl alcohols, can subsequently undergo further five-carbon oxotropy.[21, 56] If saturated (*e.g.*, methyl) substituents only are present, the stability of the two conjugated isomers differs only by the relatively small hyperconjugation energy of the groups directly attached to the butadiene system, and such rearrangements, like the corresponding three-carbon rearrangements, are therefore reversible. If, on the other hand, an unsaturated substituent is present in one of the terminal positions, the equilibrium is displaced entirely in favour of the triply conjugated derivative. The first example of this type was described by Heilbron, Jones, and McCombie,[57] who showed that 1-ethynylpentadienyl carbinol (XXXIII; $X = CH{\vdots}C$, $R = Me$), obtained by condensing sorbaldehyde with sodium acetylide, is readily converted into octa-3 : 5-dien-7-yn-2-ol (XXXIV; $X = CH{\vdots}C$, $R = Me$) on treatment with dilute mineral acids. Analogous rearrangements have been carried out with several other substituted acetylenic pentadienylcarbinols[58] as well as with butadienylphenylcarbinol (XXXIII; $X = Ph$, $R = H$)[59] and pentadienylphenylcarbinol (XXXIII; $X = Ph$, $R = Me$).[60] Such poly-carbon rearrangements might conceivably take place by two consecutive allylic rearrangements, and it has been claimed[56] that the partly rearranged styrylvinylcarbinol $CHPh{:}CH{\cdot}CH(OH){\cdot}CH{:}CH_2$ is an isolatable intermediate in the isomerisation of butadienylphenylcarbinol.

$$\underset{\text{(XXXIII.)}}{\mathrm{HO{\cdot}CHX{\cdot}CH{:}CH{\cdot}CH{:}CHR}} \xrightarrow{\text{acids}} \underset{\text{(XXXIV.)}}{\mathrm{CHX{:}CH{\cdot}CH{:}CH{\cdot}CHR{\cdot}OH}}$$

[56] Nazarov and Fischer, *Bull. Acad. Sci., U.R.S.S., Cl. Sci. Chim.*, 1945, 631; 1948, 311, 427; 1949, 112.

[57] *J.*, 1944, 134.

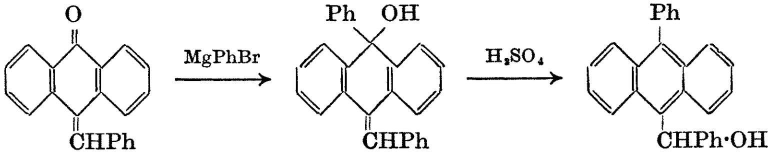
[58] Sir Ian Heilbron, E. R. H. Jones, and Richardson, *J.*, 1949, 287; *idem*, Lewis and Weedon, *J.*, 1949, 742, 2023.

[59] Salkind and Kulikov, *J. Gen. Chem. Russia*, 1945, **15**, 643; Woods and Sanders, *J. Amer. Chem. Soc.*, 1947, **69**, 2926; Nazarov and Fischer, *Bull. Acad. Sci., U.R.S.S., Cl. Sci. Chim.*, 1948, 436.

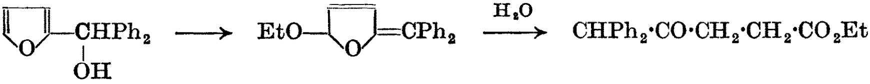
[60] Barany, Braude, and Coles, unpublished.

Other investigations [22, 60] have failed, however, to reveal any measurable concentration of partly rearranged intermediates and it is very probable that the double bond migration takes place in one step by an intermolecular mechanism analogous to (4) (p. 409).

A few isolated examples of five-carbon anionotropy in cyclic systems are also known.[61] Thus, 10-benzylidene-9 : 10-dihydro-9-phenylanthran-9-ol (XXXV), obtained by condensing benzylideneanthrone with phenylmagnesium bromide, undergoes rearrangement to the isomer (XXXVI). A somewhat similar transformation occurs with tertiary furyl carbinols.[62] On treatment with hydrogen chloride in ethanol, furyldiphenylcarbinol (XXXVII) is converted into 2-diphenylmethylene-5-ethoxy-2 : 5-dihydrofuran which undergoes ring opening to give ethyl δδ-diphenyl-lævulate (XXXVIII) :



(XXXV.) (XXXVI.)



(XXXVII.) (XXXVIII.)

These rearrangements are of interest in that they involve the participation of double bonds belonging to an aromatic or a heterocyclic ring.

Replacement reactions of butadienyl halides can give rise to non-isomeric five-carbon anionotropy analogous to the three-carbon rearrangements accompanying replacement reactions in allylic halides. Thus, the action of aqueous potassium cyanide on sorbyl chloride gives 1-methylpenta-2 : 4-dienyl cyanide : [63]

$$\mathrm{CHMe{:}CH{\cdot}CH{:}CH{\cdot}CH_2Cl \xrightarrow{KCN} CN{\cdot}CHMe{\cdot}CH{:}CH{\cdot}CH{:}CH_2 \xrightarrow{H_2SO_4} HO_2C{\cdot}CHMe{\cdot}CH{:}CH{\cdot}CH{:}CH_2}$$

Other Anionotropic Pentad Systems.—Whereas triad and higher-membered prototropic systems involving nitrogen atoms are well known, none of the corresponding open-chain oxotropic systems has yet been described. It is very probable, however, that the acid-catalysed rearrangement of phenylhydroxylamine, and allied reactions, proceed by way of successive

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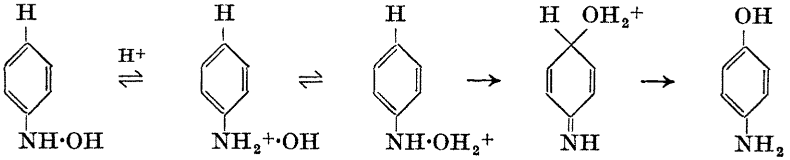
[61] J. W. Cook, *J.*, 1928, 2798 ; Julian, Cole, Diemer, and Schafer, *J. Amer. Chem. Soc.*, 1949, **71**, 2058 ; Badger and Pearce, *J.*, 1950, 2311, 2314.

[62] Ushakov and Kutscherov, *J. Gen. Chem. Russia*, 1944, **14**, 1073, 1080, 1087.

[63] Reichstein and Trivelli, *Helv. Chim. Acta*, 1932, **15**, 254.

pentad anionotropic and prototropic changes in the $C{=}C{-}C{=}C{-}N$ skeleton, as originally suggested by Bamberger.[64] The rearrangement may occur in two steps, with the migrating group first becoming attached to the *ortho*-carbon atom ; in the presence of certain *p*-substituents, the rearrangement, in fact, stops at this point. On the other hand, in the case of *p*-tolylhydroxylamine, the *p*-methyl substituent does not prevent *para*-migration which is followed by migration of the methyl group to the *meta*-position or by loss of water to give the *p*-methyleneimine.



A different mechanism has been put forward by Dewar,[65] who has postulated that the phenylhydroxylamine and similar rearrangements are entirely cationotropic and involve migration of .the hydroxyl or similar group as a positive ion which remains attached to the rest of the molecule in the form of a π-complex. The main argument in favour of this theory is the unproven assumption that such reactions are mainly intramolecular. Even if this assumption should prove to be correct, it would not necessarily conflict with the anionotropic mechanism, and any final decision will have to await kinetic investigations of these reactions.

Heptad and Higher Anionotropic Systems

By condensing sodium acetylide with octatrienal, Heilbron, Jones, and McCombie [57] obtained the acetylenic carbinol (XXXIX) which readily undergoes heptad oxotropy to give the fully conjugated trienyne (XL). This type of reaction has recently been employed in the synthesis of vitamin A homologues from 1-ethynyl*cyclo*hexenes : [66]

$$\underset{\text{(XXXIX.)}}{CH{\vdots}C\cdot CH(OH)\cdot[CH{:}CH]_3\cdot Me} \xrightarrow{\text{acids}} \underset{\text{(XL.)}}{CH{\vdots}C\cdot[CH{:}CH]_3\cdot CHMe\cdot OH}$$

The corresponding glycol (XLI ; $n = 3$), obtained from acetylenebismagnesium bromide, similarly undergoes the interesting double heptad rearrangement to the hexenyne glycol (XLII).[67] This elegant method of polyene synthesis has also been applied to the two lower vinylogues (XLI ; $n = 1$ and 2) and to β-ionone analogues,[68] with a view to the total synthesis of carotenoids (which has since been achieved) : [68]

$$\text{(XLI.)}\quad Me\cdot[CH{:}CH]_n\cdot CH(OH)\cdot C{\vdots}C\cdot CH(OH)\cdot[CH{:}CH]_n\cdot Me \xrightarrow{\text{acids}}$$
$$HO\cdot CHMe\cdot[CH{:}CH]_n\cdot C{\vdots}C\cdot[CH{:}CH]_n\cdot CHMe\cdot OH \quad \text{(XLII.)}$$

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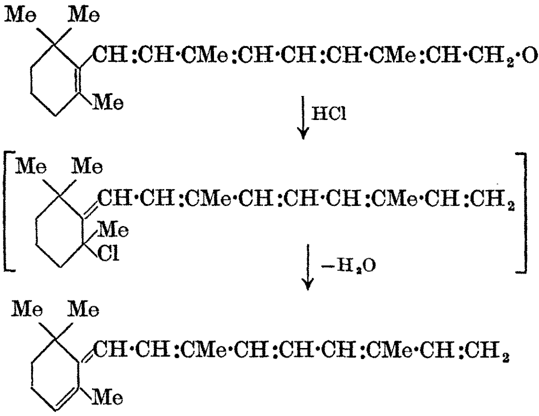
[64] *Ber.*, 1900, **33**, 3600 ; 1901, **34**, 61. [65] *J.*, 1946, 406.

[66] Cheeseman, Sir Ian Heilbron, E. R. H. Jones, and Weedon, *J.*, 1949, 3120.

[67] Heilbron, E. R. H. Jones, and Raphael, *J.*, 1943, 268 ; 1944, 136.

[68] Inhoffen, Pommer, and Bohlmann, *Annalen*, 1948, **561**, 26 ; 1950, **569**, 237.

An example of undecad anionotropy, involving simultaneous migration of five double bonds, probably occurs in the conversion of vitamin A (XLIII) into anhydrovitamin A (XLV) by hydrochloric acid.[69] The structure of anhydrovitamin A has not, however, been rigidly proved and the intermediate (XLIV) has not been isolated.



(XLIII.)

(XLIV.)

(XLV.)

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[69] Shantz, Embree, and Cawley, *J. Amer. Chem. Soc.*, 1943, **65**, 901 ; Meunier, *Compt. rend.*, 1943, **216**, 907 ; 1948, **226**, 128.