Base-catalysed Isomerisation of Acetylenes

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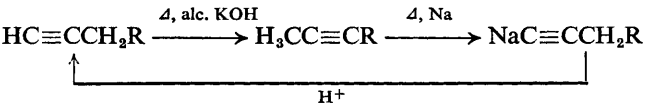
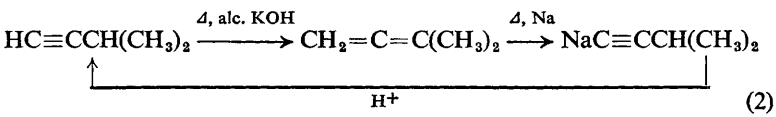
1 Introduction

A. J. Favorskii discovered the base-catalysed isomerisation of acetylenes by accident while working on dehydrohalogenation reactions. His discovery was first reported in '*Correspondance Russe de la Société Chimique de Paris*' in 1886,[1] and the details of his work were published over the next two years.[2] He found that when but-1-yne or pent-1-yne was heated with alcoholic potassium hydroxide the corresponding alk-2-yne was formed (reaction 1, R = Me or Et). This reaction may be formally visualised as the transfer of two protons from the 3-position to the 1-position, and Favorskii argued that an allene intermediate (formed by a one-proton transfer) was probably involved. In support of this hypothesis he was able to show that the isomerisation of 3-methyl-but-1-yne stopped at the allene stage (reaction 2). He was further able to show that the reactions were reversible, for when the products were heated with metallic sodium the sodium salts of the corresponding alk-1-ynes were formed and on acidification the starting materials were recovered.



(1)



(2)

These simple experiments dictated the pattern of work in this field for the next sixty years. During this time many workers repeated Favorskii's reactions with small variations in base and chain length, but little which was fundamentally new was added.[3] Over the last twenty years, however, work has diversified in several ways. In particular, many functionally substituted acetylenes have been studied. Some of these isomerise cleanly under mild conditions, rendering the reactions synthetically attractive. Increasing interest has also been shown in

[1] A. Thillot, *Bull. Soc. chim. Paris*, 1886, **45**, 247.
[2] A. Favorskii, *J. Russ. Phys. Chem. Soc.*, 1887, **19**, 414; 553: *J. prakt. Chem.*, 1888, **37**, 382: *Chem Zentr.*, 1887, (3) **18**, 1539; 242: (3) **19**, 242; 828.
[3] This work is comprehensively reviewed in 'Isomerisation of Pure Hydrocarbons' by Egloff *et al.*, Reinhold, New York, 1942.

the isomerisation of more highly unsaturated systems, particularly conjugated 'ene-ynes', diacetylenes, and triacetylenes and it has become clear that there is a whole family of prototropic rearrangements of which the isomerisations of monoacetylenes and mono-olefins are but the simplest examples. One such 'family' of reactions is seen in the prototropic rearrangements of unsaturated thioethers where there are obvious parallels between the isomerisations of the olefin,[4] monoacetylene,[5] conjugated ene-yne,[6] and conjugated diacetylene[7] (reactions 3—6). As might be expected, in passing down this series from the olefin to the diacetylene, isomerisation becomes increasingly facile.

$$CH_2{=}CHCH_2SMe \longrightarrow CH_3CH{=}CHSMe \qquad (3)$$

$$HC{\equiv}CCH_2SPh \longrightarrow CH_3C{\equiv}CSPh \qquad (4)$$

$$CH_2{=}CHC{\equiv}CCH_2SMe \longrightarrow CH_3CH{=}CHC{\equiv}CSMe \qquad (5)$$

$$HC{\equiv}CC{\equiv}CCH_2SPh \longrightarrow CH_3C{\equiv}CC{\equiv}CSPh \qquad (6)$$

After a brief discussion of the mechanisms of these rearrangements and of the more recent work on acetylenic hydrocarbons, the main part of this review will be concerned with the behaviour of functionally substituted monoacetylenes and of the more highly unsaturated systems.

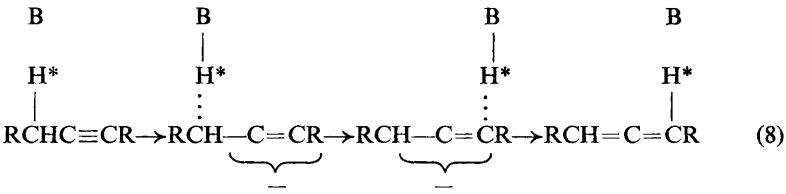
2 Mechanisms of Acetylene Isomerisation

Like similar prototropic rearrangements, the base-catalysed isomerisation of acetylenes is probably best represented by a simple carbanion mechanism.[8,9]

$$RCH_2C{\equiv}CR \underset{+H^+}{\overset{-H^+}{\rightleftharpoons}} [R\bar{C}HC{\equiv}CR \longleftrightarrow RCH{=}C{=}\bar{C}R] \underset{-H^+}{\overset{+H^+}{\rightleftharpoons}} RCH{=}C{=}CHR \rightleftharpoons \textit{etc.} \qquad (7)$$

Removal of a proton from the α-position of the acetylene leads to a mesomeric carbanion, protonation of which then gives the allene. When the isomerisation is carried out in proton-rich solvents the proton supplied in this second step normally comes from the solvent itself. However, under suitable circumstances, the reactions show a high degree of intramolecularity; that is to say that the proton captured by the carbanion is the same as that earlier removed by the base. In these cases it is envisaged that the proton never really becomes free but remains continuously hydrogen bonded to the substrate.

[4] D. E. O'Connor and W. I. Lyness, *J. Amer. Chem. Soc.*, 1964, **86**, 3840.
[5] L. Brandsma, H. E. Wijers, and J. F. Arens, *Rec. Trav. chim.*, 1963, **82**, 1040.
[6] J. H. Van Boom, L. Brandsma, and J. F. Arens, *Rec. Trav. chim.*, 1968, **87**, 97.
[7] G. Pourcelot, *Compt. rend.*, 1965, **260**, 2847.
[8] R. J. Bushby and G. H. Whitham, *J. Chem. Soc.* (*B*), 1969, 67.
[9] R. J. Bushby and G. H. Whitham, *J. Chem. Soc.* (*B*), 1970, 563.



(8)

Cram, who calls this a 'conducted tour' mechanism, has studied the intramolecular aspects of the isomerisation of 1,3,3-triphenyl-prop-1-yne (reaction 9).[10] The methoxide-catalysed isomerisation in methanol and the t-butoxide-catalysed isomerisation in t-butanol show only 20% intramolecularity. However, when the isomerisation is carried out using DABCO in 10% methanol–dimethyl sulphoxide, up to 88% intramolecularity is obtained showing that under these conditions, with both a proton-deficient solvent and also the possibility of ion pair formation, something like a 'conducted tour' mechanism is operative.

$$Ph_2CHC{\equiv}CPh \longrightarrow Ph_2C{=}C{=}CHPh \qquad (9)$$

3 Monoacetylene Hydrocarbons

Figure 1, which is based on thermochemical data given by Benson,[11] shows that

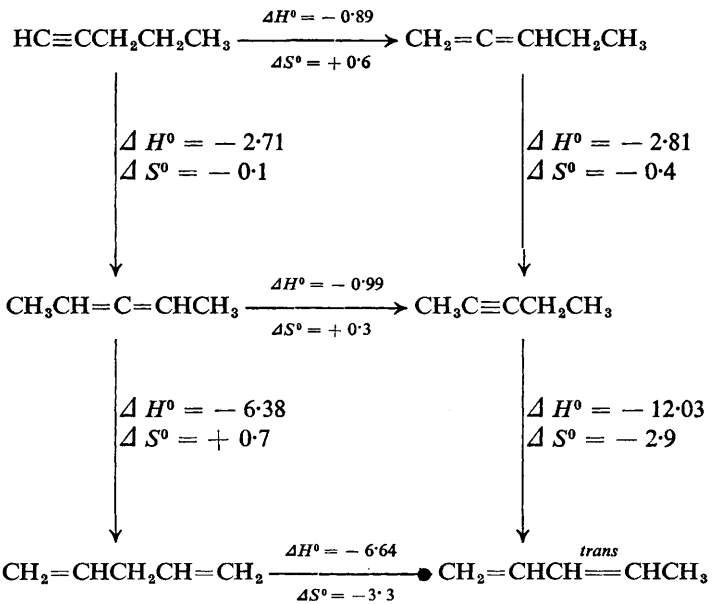


Figure 1 *Standard enthalpy $\Delta H°$ (kcal mol^{-1}) and entropy $\Delta S°$ (cal mol^{-1} deg^{-1}) changes in the vapour phase interconversion of isomers of pentyne.*[11]

[10] D. J. Cram *et al.*, *J. Amer. Chem. Soc.*, 1964, **86**, 5370; 1966, **88**, 2759.
[11] S. W. Benson, F. R. Cruickshank, D. M. Golden, G. R. Haugen, H. E. O'Neal, A. S. Rodgers, R. Shaw, and R. Walsh, *Chem. Rev.*, 1969, **69**, 279.

the six straight-chain isomers of pentyne can be arranged in order of increasing stability as follows: pent-1-yne < penta-1,2-diene < penta-2,3-diene < pent-2-yne < penta-1,4-diene < penta-1,3-diene. The fact that pent-1-yne is less stable than pent-2-yne and the fact that penta-1,2-diene is less stable than penta-2,3-diene may be explained in terms of the preference of the electron-deficient acetylene and allene units for two rather than one electron-donating alkyl substituents. In this series the most stable isomer is penta-1,3-diene and in fact it is found that, in general, conjugated dienes are more stable than either acetylenes or allenes. However, they are kinetically disfavoured and are only formed under extreme conditions. Indeed, in the isomerisation of acetylenes kinetic factors are often of prime importance and the product obtained depends on both the quantity and nature of the base used. For example, when alk-1-ynes are treated with 4N alcoholic potassium hydroxide at 170 °C isomerisation stops at the alk-2-yne stage. Stronger bases, such as potassium t-butoxide in dimethyl sulphoxide, are needed to isomerise alk-2-ynes to alk-3-ynes, alk-4-ynes, *etc.*, and formation of conjugated dienes requires the most forcing conditions of all.

Although it was long understood that the isomerisation of alk-1-ynes to alk-2-ynes was reversible and never quite went to completion, the first reliable measurement of the position of equilibrium was not made until 1957, when Jacobs and co-workers[12] reinvestigated the pentyne system. They showed that exhaustive treatment of pent-1-yne, pent-2-yne, or penta-1,2-diene with *ca.* 4N alcoholic potassium hydroxide at 175 °C gave an equilibrium mixture containing 1·3% pent-1-yne, 95·2% pent-2-yne, and 3·5% penta-1,2-diene. Since

Table 1 *Position of equilibrium in straight-chain acetylenic hydrocarbons*

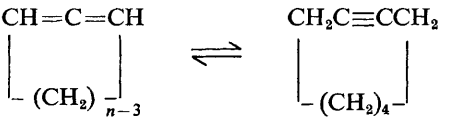
Substrate	*Conditions*	*alk-1-yne*	*alka-1,2-diene*	*alk-2-yne*	*alka-2,3-diene*	*alk-3-yne*	*alka-3,4-diene*
Pentyne[a]	4N-KOH–EtOH, 175 °C	1·3%	3·5%	95·2%	[b]		
Hexyne[c]	0·06% $NaNH_2$–$NH_2CH_2CH_2NH_2$, 25 °C	6%[d]	0%	80%	3%	11%	
Heptyne[e]	Bu^tOK–Bu^tOH, 196 °C	0%	0·5%	46%	7·5%	42%	4%
Octyne[f]	1—4N-KOH–EtOH, 125—175 °C	0·2%	2·3%	97·5%	[b]	[b]	[b]

[a] Ref. 12; [b] Isomer not formed under the reaction conditions; [c] J. H. Wotiz, W. E. Billups, and D. T. Christian, *J. Org. Chem.*, 1966, **31**, 2069; [d] Value anomalously high because of sodium salt formation; [e] W. Smadja, *Compt. rend.*, 1964, **258**, 5461; *Ann. Chim.* (*France*), 1965, **10**, 105; [f] B. Wojtkowiak and R. Romanet, *Bull. Soc. chim.* (*France*), 1962, 805.

[12] T. L. Jacobs, R. Akawie, and R. C. Cooper, *J. Amer. Chem. Soc.*, 1951, **73**, 1273.

that time similar studies have been made of the isomerisations of hexyne, heptyne, and octyne and the results are summarised in Table 1.

Cyclo-undecyne, decyne, and nonyne have been studied by Moore and Ward.[13] These show, rather nicely, the effects of ring strain on the position of equilibrium. The values given in scheme (10) were obtained using potassium t-butoxide in t-butanol at 100·3 °C and it may be seen that the percentage of allene increased with decreasing ring size. In the acetylene, four carbon atoms must be arranged in a straight line, but in the allene only three, with the result that the allene unit is more easily accommodated in a small ring.



(10)

$n = 11$	26%	74%
$n = 10$	65%	35%
$n = 9$	93%	7%

4 Substituted Monoacetylenes

(11)

Since acetylene isomerisations are reversible, the net result is always to convert a less to a more stable isomer. Simple monoacetylene isomerisations may be represented by the general equation (11), and Table 2 summarises the effect of various substituents X and Y on the relative stabilities of the three isomers (and hence which isomer is formed on treatment with base). Broadly speaking, the effects follow the expected pattern. As the acetylene group is relatively electron-deficient, it is stabilised by adjacent electron-donating groups and conversely destabilised by adjacent electron-withdrawing groups. This latter effect is seen in the isomerisation of the diethyl acetal of but-2-yn-1-al (*4*), which with potassium t-butoxide in dimethyl sulphoxide at 25 °C gives the terminal acetylene (*5*)[14], the acetylene group migrating away from the electron-withdrawing acetal group.

(12)

The acetylene group may also be stabilised by conjugation. For example,

[13] W. R. Moore and H. R. Ward, *J. Amer. Chem. Soc.*, 1963, **85**, 86.
[14] R. Mantione, M. L. Martin, G. J. Martin, and H. Normant, *Bull. Soc. chim. France*, 1967, 2912.

Table 2 *Effect of substituents on the relative stabilities of isomers in three-centre monoacetylene systems*

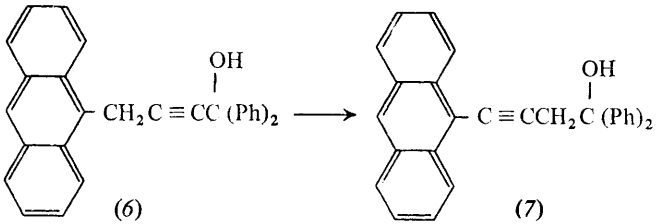
$XC{\equiv}CCH_2Y \rightleftharpoons XCH{=}C{=}CHY \rightleftharpoons XCH_2C{\equiv}CY$

(*1*) (*2*) (*3*)

	X	Y	*1*	*2*	*3*	Ref.
1.	H	alkyl			+	*a*
2.	H	$(CH_2)_nCO_2^-$, $n = 3, 4$			+	*b*
3.	H	CH_2NH_2			+	*c*
4.	H	aryl			+	*d*
5.	H	CO_2^-			+	*b*, *e*
6.	H	CO_2^-	0%	31%	69%	*f*
7.	H	NR_2			+	*g*
8.	H	SR			+	*h*
9.	H	SeC_6H_5	1%	10%	89%	*i*
10.	H	$SO_2C_6H_5$		+		*j*
11.	H	$CH(OEt)_2$	+			*k*
12.	H	CO_2Et		+	?	*e*
13.	H	COR		+	?	*l*
14.	H	OR		+	?	*i*
15.	alkyl	alkyl	+		+	*m*
16.	alkyl	CO_2^-	+			*b*, *n*
17.	CH_3	CO_2^-	82·2%	16·5%	1·3%	*o*
18.	alkyl	$CH(OEt)_2$	+			*k*
19.	alkyl	CH_2OEt	+			*p*
20.	CH_3	CO_2Me	50%	50%	?	*q*
21.	$^-O_2C(CH_2)_7$	COR		+	?	*r*
22.	alkyl	CN		+	?	*s*
23.	alkyl	NR_2		+	?	*t*
24.	s- or t-alkyl	OR		+	?	*u*
25.	aryl	$C(OH)R_2$	+			*v*
26.	C_6H_5	CO_2^-	40%	60%	?	*w*
27.	aryl	aryl		+		*x*
28.	C_6H_5CO	COC_6H_5		+		*y*
29.	^-O_2C	CO_2^-		+		*z*

Where figures for the position of equilibrium are not available '+' indicates the most stable isomer. A '?' indicates that the stability of this isomer, relative to the others, is not clear. [a] Refs. 1—3. [b] Ref. 16. [c] V. A. Engelhardt, *J. Amer. Chem. Soc.*, 1956, **78**, 107. [d] Refs. 15, 22. [e] Ref. 23. [f] 18% K_2CO_3 in H_2O at 90°C. Ref. 35. [g] Refs. 24, 42; U.S. Patent, 3439038, *Chem. Abs.*, 1969, **71**, 13131*j*. [h] Refs. 5, 19, 20, 25. [i] 0·1N EtONa in EtOH at 72°C; Ref. 25. [j] Ref. 20. [k] Ref. 14. [l] Ref. 26. [m] W. Smadja, *Compt. rend.*, 1964, **258**, 5461. [n] J. Cymerman Craig and M. Moyle, *J. Chem. Soc.*, 1963, 4402. [o] 6·25N NaOH in H_2O at 65°C; Ref. 8. [p] R. Mantione, *Compt. rend.*, 1968, **267**, *C*, 90. [q] 4% Et_3N in THF at 40°C; Ref. 8. [r] L. Crombie and A. G. Jacklin, *J. Chem. Soc.*, 1955, 1740. [s] Ref. 35. [t] Ref. 24. [u] J. H. Van Boom, P. P. Montijn, L. Brandsma, and J. F. Arens, *Rec. Trav. chim.*, 1965, **84**, 31. [v] Ref. 15. [w] 18% K_2CO_3 in H_2O at 40°C; Ref. 35. [x] T. L. Jacobs and D. Dankner, *J. Org. Chem.*, 1957, **22**, 1424. [y] F. Gaudemar-Bardone, *Ann. Chim.* (*France*), 1958, **3**[13], 52. [z] Ref. 30.

treatment of the acetylenic alcohol (*6*) with 0·5N ethanolic sodium hydroxide gives the conjugated acetylene (*7*).[15]



(*6*) (*7*) (13)

In most systems more than one of these effects is at work at once and when they are working in opposition the net result is not always easy to predict. For example, in the case of $\alpha\beta$- and $\beta\gamma$-acetylenic acids (reaction 14, R = alkyl) it is found that the non-conjugated isomer is the more stable.[8,16] In this isomer the acetylene group has two electron-donating 'alkyl' substituents and this seems to provide greater stabilisation than that gained by conjugation. It is interesting to compare these acetylenes with the corresponding olefinic acids (reaction 15, R = alkyl), where equilibrium between the $\alpha\beta$- and $\beta\gamma$-unsaturated forms is more evenly balanced but normally slightly favours the conjugated isomer.[17] The difference between the two systems is presumably that the olefin group, being less electron-deficient than the acetylene group, gains less stabilisation by seeking the $\beta\gamma$-position.

$$RCH_2C{\equiv}CCO_2^- \rightleftharpoons RC{\equiv}CCH_2CO_2^- \quad (14)$$

$$RCH_2CH{=}CHCO_2^- \rightleftharpoons RCH{=}CHCH_2CO_2^- \quad (15)$$

Interesting comparisons between acetylene and olefin isomerisations may also be made in the thioether and sulphone systems. O'Connor and Lyness[18] have shown that methyl (prop-1-enyl) thioether (*8*) is more stable than methyl (prop-2-enyl) thioether (*9*) by a factor of at least 99 to 1 (reaction 16). In the corresponding sulphones, however, the equilibrium is more evenly balanced and, at room temperature, the equilibrium mixture comprises 44% methyl (prop-2-enyl) sulphone (*10*) and 56% methyl (prop-1-enyl) sulphone (*11*) (reaction 17).[18] The shift towards the prop-2-enyl derivative was attributed to inductive effects, the olefin group being destabilised by the more electron-withdrawing $-SO_2Me$ group. The behaviour of the acetylenic thioethers is analogous to that of the olefinic thioethers, the prop-1-ynyl derivative (*12*) being

[15] M. R. Skowrouski, *Compt. rend.*, 1967, **265**, *C*, 263; 606.
[16] E. R. H. Jones, G. H. Whitham, and M. C. Whiting, *J. Chem. Soc.*, 1954, 3201.
[17] R. P. Linstead and E. G. Noble, *J. Chem. Soc.*, 1934, 614.
[18] See ref. 4, page 586. This paper also contains a useful summary of the isomerisations of substituted mono-olefins.

much more stable than the prop-2-ynyl derivative (*13*) (reaction 18).[19] In the acetylenic sulphones, however, it is found that the allene is more stable than either of the acetylenes (reaction 19).[20]

$$\underset{(9,\ <1\%)}{CH_2{=}CHCH_2SMe} \rightleftharpoons \underset{(8,\ >99\%)}{CH_3CH{=}CHSMe} \qquad (16)$$

$$\underset{(10,\ 44\%)}{CH_2{=}CHCH_2SO_2Me} \rightleftharpoons \underset{(11,\ 56\%)}{CH_3CH{=}CHSO_2Me} \qquad (17)$$

$$\underset{(13)}{HC{\equiv}CCH_2SPh} \rightleftharpoons CH_2{=}C{=}CHSPh \rightleftharpoons \underset{(12)}{CH_3C{\equiv}CSPh} \qquad (18)$$

$$HC{\equiv}CCH_2SO_2Ph \text{ or } CH_3C{\equiv}CSO_2Ph \rightleftharpoons CH_2{=}C{=}CHSO_2Ph \qquad (19)$$

Most functionally substituted monoacetylenes isomerise under much milder conditions than those required by acetylenic hydrocarbons. For example, whilst the isomerisation of alk-1-ynes to alk-2-ynes requires *ca.* 4N alcoholic potassium hydroxide at 160—170 °C, the isomerisation of the thioether (*13*) proceeds smoothly in 0·1N sodium methoxide–methanol at 40 °C.[18] Also, in the isomerisation of alk-1-ynes to alk-2-ynes (reaction scheme 20, Y = alkyl) formation of the allene is the slow step. Once formed this rapidly isomerises to product and does not accumulate to any appreciable extent.[21] In most other reactions of the type shown in scheme (20) however, the allene is rapidly formed and this is only slowly isomerised to the prop-1-ynyl derivative, with the result that the isomerisation can be stopped at the allene stage. This type of behaviour is shown in those systems where Y is aryl,[22] $\cdot CO_2^-$,[16,23] $\cdot NR_2$,[24] $\cdot SePh$,[25] and $\cdot SR$.[19,25] In other systems, for example those where Y is $\cdot CO_2Et$,[23] $\cdot COR$,[26] and $\cdot OR$,[25] isomerisation has not been shown to proceed appreciably beyond the allene stage. This may be because the second step is very slow or possibly, in some of these systems, the allene is the most stable isomer.

$$HC{\equiv}CCH_2Y \rightarrow CH_2{=}C{=}CHY \rightarrow CH_3C{\equiv}CY \qquad (20)$$

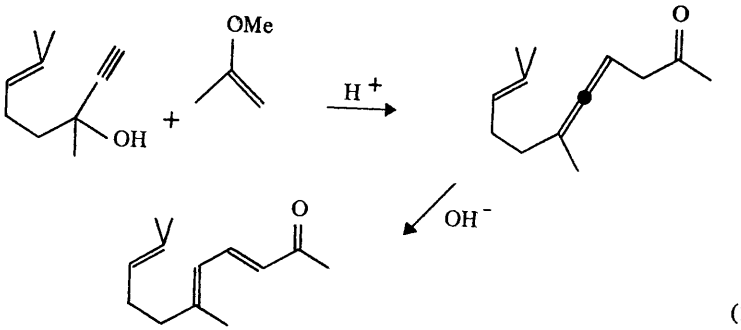
Another important difference between the substituted acetylenes and the acetylenic hydrocarbons is the ease with which some, especially those with an

[19] G. Pourcelot and C. Georgoulis, *Bull. Soc. chim. France*, 1964, 866.
[20] C. J. M. Stirling, *J. Chem. Soc.*, 1964, 5856.
[21] J. H. Wotiz, W. E. Billups, and D. T. Christian, *J. Org. Chem.*, 1966, **31**, 2069.
[22] M. Bourguel, *Compt. rend.*, 1928, **186**, 1211; 1931, **192**, 686; *cf.* ref. 15.
[23] G. Eglington, E. R. H. Jones, G. H. Mansfield, and M. C. Whiting, *J. Chem. Soc.*, 1954, 3197.
[24] A. J. Hubert and H. G. Viehe, *J. Chem. Soc.* (*C*), 1968, 228; A. J. Hubert and H. Reimlinger, *J. Chem. Soc.* (*C*), 1968, 606.
[25] G. Pourcelot and P. Cadiot, *Bull. Soc. chim. France*, 1966, 3016.
[26] G. Le Gras, doctoral thesis, Aix-Marseille, 1966.

aryl,[27] ·COMe,[28] or $\cdot CO_2^-$ [16,29,30] substituent in the β-position, isomerise to conjugated dienes. The general reaction is shown in scheme (21) where R is H or alkyl and Z is aryl, ·COMe, or $\cdot CO_2^-$. The first step gives an allene in which the acidity of the proton in the α-position is greatly enhanced by the presence of the substituent. Removal of this proton then leads through to the conjugated diene.

$$RC{\equiv}CCH_2CH_2Z \rightarrow [RCH{=}C{=}CHCH_2Z] \rightarrow RCH{=}CHCH{=}CHZ \quad (21)$$

This type of reaction has found a number of interesting applications in the synthesis of dienes such as pseudoionone:[28]

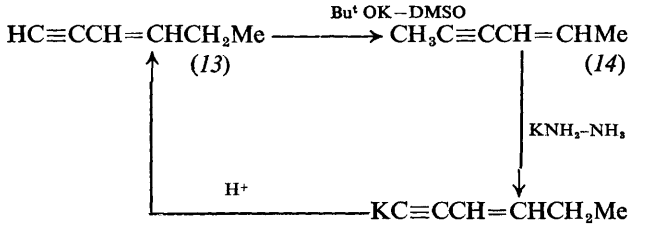


(22)

5 Ene-ynes

As was pointed out in the introduction, the isomerisations of conjugated ene-ynes and diacetylenes often closely parallel those of simple monoacetylenes. Treatment of hex-3-en-1-yne (*13*) with potassium t-butoxide in dimethyl sulphoxide gives hex-4-en-2-yne (*14*).[31] Further treatment of (*14*) with excess potassamide in liquid ammonia gives the potassium salt of hex-3-en-1-yne and on acidification the starting material is recovered (reaction 23).[32] This cycle of reactions is essentially the same as that which Favorskii carried out on but-1-yne[33] except that in these systems an ene-yne unit is shifted by one carbon atom instead of a monoacetylene unit. Similarly, the isomerisation of methyl (pent-2-en-4-ynyl) thioether (*15*) in dilute sodium ethoxide–liquid ammonia (reaction 24)[6] directly parallels the isomerisation of phenyl (prop-2-ynyl) thioether discussed above.[34]

[27] A. J. Hubert and A. J. Anciaux, *Bull. Soc. chim. belges*, 1968, **77**, 518.
[28] G. Saucy and R. Marbet, *Helv. Chim. Acta*, 1967, **50**, 1158.
[29] M. Julia and C. Descoins, *Bull. Soc. chim. France*, 1964, 2541.
[30] E. R. H. Jones *et al.*, *J. Chem. Soc.*, 1954, 3208, 3212.
[31] J. P. C. M. Van Dongen, A. J. De Jong, H. A. Selling, P. P. Montijn, J. H. Van Boom, and L. Brandsma, *Rec. Trav. chim.*, 1967, **86**, 1077.
[32] J. H. Van Boom, P. P. Montijin, M. H. Ber, L. Brandsma, and J. F. Arens, *Rec. Trav. chim.*, 1965, **84**, 813.
[33] Reaction (1), page 585.
[34] Reaction (18), page 592.



(23)

$$HC{\equiv}CCH{=}CHCH_2SMe \longrightarrow CH_3C{\equiv}CCH{=}CHSMe \quad (24)$$

(15)

Although these isomerisations are formally quite simple, the question of what intermediates they involve is exceedingly complex. For most conjugated ene-yne isomerisations there are eight possible intermediates and reference to Figure 2 shows that these may be combined in many different ways. Information

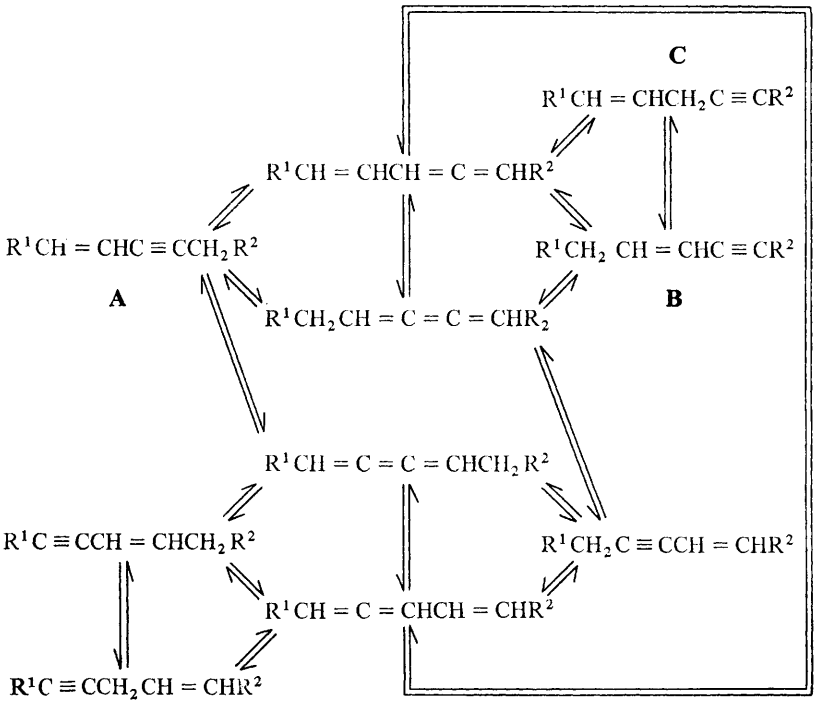


Figure 2 *Possible intermediates in the isomerisations of conjugated ene-ynes* (**A** → **B** *or* **B** → **A**) *and skipped ene-ynes* (**C** → **A** *or* **C** → **B**).

as to what intermediates are normally involved is limited and fragmentary, but in two cases there is direct evidence for the intermediary of an allene-ene. Arens *et al.* showed that when the ene-yne thioether (*16*) was treated with dilute sodium ethoxide in liquid ammonia it isomerised first to the allene-ene (*17*) and then further (incompletely) to the ene-yne (*18*) (reaction 25).[6] Similarly, Mansfield showed that treatment of hex-5-en-3-ynoic acid (*19*) with 18% potassium carbonate at 40 °C gave hexa-2,3,5-trienoic acid (*20*). Further treatment of this acid with 9% aqueous potassium hydroxide gave hex-4-en-2-ynoic acid (*21*) (reaction 26).[35]

$$\underset{(16)}{MeCH_2CEt{=}CHC{\equiv}CSEt} \longrightarrow \underset{(17)}{MeCH{=}CEtCH{=}C{=}CHSEt} \rightleftharpoons \underset{(18)}{MeCH{=}CEtC{\equiv}CCH_2SEt} \quad (25)$$

$$\underset{(19)}{CH_2{=}CHC{\equiv}CCH_2CO_2^-} \xrightarrow{\text{fast}} \underset{(20)}{CH_2{=}CHCH{=}C{=}CHCO_2^-} \xrightarrow{\text{slow}} \underset{(21)}{CH_3CH{=}CHC{\equiv}CCO_2^-} \quad (26)$$

Whether the allene-ene is the only intermediate in these and similar conjugated ene-yne isomerisations, or whether some of the other possible intermediates are involved, remains unclear. Similar uncertainties surround the question of what intermediates are involved in the isomerisation of 'skipped' (1,4)-ene-ynes to conjugated ene-ynes.[36] Again there is some evidence in favour of an intermediate allene-ene. One case where this is seen quite nicely is in the isomerisation of the skipped ene-yne alcohol (*22*), which is first rapidly isomerised to the allene-ene (*23*) and then more slowly to the conjugated ene-yne (*24*).[37]

$$\underset{(22)}{MeEtC(OH)C{\equiv}CCH_2\,CH{=}CH_2} \xrightarrow{\text{fast}} \underset{(23)}{MeEtC(OH)CH{=}C{=}CHCH{=}CH_2} \xrightarrow{\text{slow}} \underset{(24)}{MeEtC(OH)C{\equiv}CCH{=}CHCH_3} \quad (27)$$

Isomerisation of 1,5-ene-ynes leads to conjugated trienes.[38,39] For example, treatment of hex-1-en-5-yne with potassium t-butoxide in t-butanol at 65—70 °C gives hexa-1,3,5-triene (reaction 28).[38] Isomerisations of this type and the isomerisation of 1,5-diacetylenes to conjugated diene-ynes[40] have been used extensively by Sondheimer in the synthesis of annulenes.[39]

[35] G. H. Mansfield, Ph.D. thesis, Manchester, 1954.
[36] W. Oroshnick, A. D. Mebane, and G. Karmas, *J. Amer. Chem. Soc.*, 1952, **74**, 295; 1953, **75**, 1050; L. Skattebøl, *Tetrahedron*, 1969, **25**, 4933.
[37] J. Blanc-Guénée, M. D. d'Engenière, and M. Miocque, *Bull. Soc. chim. France*, 1964, 603.
[38] F. Sondheimer, D. A. Ben-Efraim, and R. Wolovsky, *J. Amer. Chem. Soc.*, 1961, **83**, 1675.
[39] F. Sondheimer, *Pure Appl. Chem.*, 1963, **7**, (2—3), 363.
[40] F. Sondheimer, D. A. Ben-Efraim, and Y. Gaoni, *J. Amer. Chem. Soc.*, 1961, **83**, 1682.

$$HC{\equiv}CCH_2CH_2CH{=}CH_2 \rightarrow [CH_2{=}C{=}CHCH_2CH{=}CH_2] \rightarrow CH_2{=}CHCH{=}CHCH{=}CH_2 \quad (28)$$

Several workers have shown that under forcing conditions 1-(alkynyl)-cyclohexenes give benzenoid products.[31] For example, when the ene-yne acetal (*25*) is heated with potassium t-butoxide in dimethyl sulphoxide it is converted to the benzenoid acetal (*26*).[14]

$C{\equiv}CCH(OEt)_2$
(*25*)

$CH_2CH_2CH(OEt)_2$
(*26*) (29)

6 Diacetylenes

All known isomerisations of conjugated diacetylenes have direct parallels in the monoacetylene series. Hence, the rearrangement of hexa-3,5-diynoic acid (*27*) in 0·2N aqueous sodium hydroxide at 25°C (reaction 30)[41] parallels the rearrangement of but-3-ynoic acid in 10% potassium carbonate at 76 °C (reaction 31).[16,23] Similarly, the isomerisation of the penta-2,4-diynyl-amine (*28*) (reaction 32)[42] parallels that of the corresponding prop-2-ynyl-amine[42] (reaction 33), and the isomerisation of phenyl (penta-2,4-diynyl) thioether (*29*)[7] that of phenyl (prop-2-ynyl) thioether.[43]

$$HC{\equiv}CC{\equiv}CCH_2CO_2^- \longrightarrow CH_3C{\equiv}CC{\equiv}CCO_2^- \quad (30)$$
(*27*)

$$HC{\equiv}CCH_2CO_2^- \xrightarrow{\text{fast}} CH_2{=}C{=}CHCO_2^- \xrightarrow{\text{slow}} CH_3C{\equiv}CCO_2^- \quad (31)$$

$$HC{\equiv}CC{\equiv}CCH_2NPh_2 \longrightarrow CH_3C{\equiv}CC{\equiv}CNPh_2 \quad (32)$$
(*28*)

$$HC{\equiv}CCH_2NPh_2 \longrightarrow CH_3C{\equiv}CNPh_2 \quad (33)$$

$$HC{\equiv}CC{\equiv}CCH_2SPh \longrightarrow CH_3C{\equiv}CC{\equiv}CSPh \quad (34)$$
(*29*)

It is interesting to note that whilst reaction (31) can be stopped at the allene stage, in the corresponding diacetylene isomerisation (reaction 30) no intermediates could be detected at all by normal kinetic, chromatographic, or spectroscopic methods.[41] For this and most other conjugated diacetylene isomerisations there are four possible intermediates, a cumulated tetraene, two allene-ynes, and a skipped diacetylene. The relationship between these is shown

[41] R. J. Bushby, D.Phil. thesis, Oxford, 1968.
[42] J. L. Dumont, W. Chodkiewicz, and P. Cadiot, *Bull. Soc. chim. France*, 1967, 1197.
[43] Reaction (18), page 592.

in Figure 3. One system which has been studied in detail is the isomerisation of hepta-2,4-diynoic acid to hepta-3,5-diynoic acid in aqueous sodium hydroxide

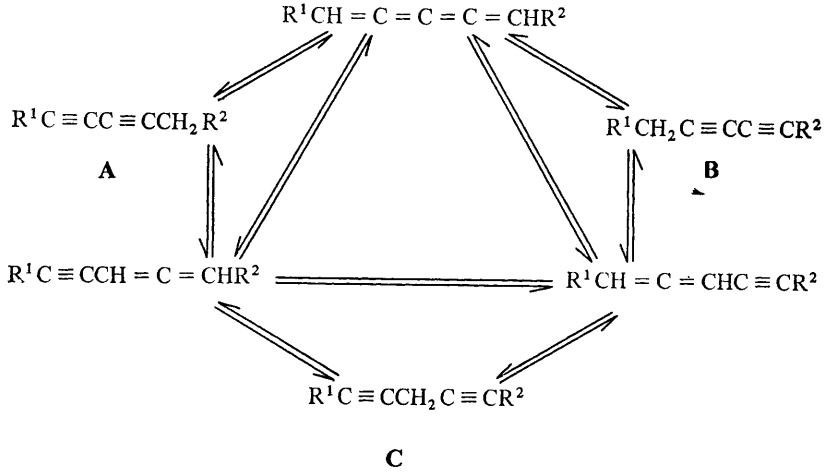


Figure 3 *Possible intermediates in the isomerisations of conjugated diacetylenes* (**A** → **B**) *and skipped diacetylenes* (**C** → **B**).

(reaction 35). In this case the intermediates are hepta-4,5-diene-2-ynoic acid and hepta-2,3,4,5-tetraenoic acid.[9]

$$MeCH_2C{\equiv}CC{\equiv}CCO_2^- \rightarrow [MeCH{=}C{=}CHC{\equiv}CCO_2^-] \rightarrow [MeCH{=}C{=}C{=}C{=}CHCO_2^-] \rightarrow MeC{\equiv}CC{\equiv}CCH_2CO_2^- \quad (35)$$

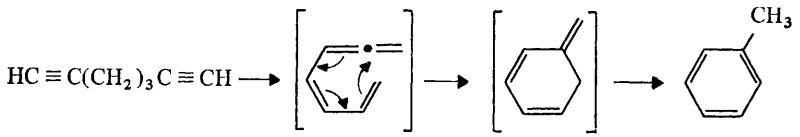
As might be expected, skipped (1,4) diacetylenes can be isomerised to conjugated diacetylenes[44] and the kinetics of these reactions have been studied in some detail by Miller and co-workers.[45] Presumably they simply involve an allene-yne intermediate. Such intermediates can be detected in the isomerisation of alka-1,4-diynes. For example, on treating nona-1,4-diyne with 'mild alcoholic alkali' at room temperature, nona-1,2-diene-4-yne is rapidly formed and then this slowly isomerises to nona-2,4-diyne.[46]

$$Bu^nC{\equiv}CCH_2C{\equiv}CH \xrightarrow{\text{fast}} Bu^nC{\equiv}CCH{=}C{=}CH_2 \xrightarrow{\text{slow}} Bu^nC{\equiv}CC{\equiv}CCH_3 \quad (36)$$

The isomerisation of diacetylenes under forcing conditions often gives aromatic products.[47] Raphael and co-workers have shown that for straight-

[44] H. Taniguchi, I. M. Mathai, and S. I. Miller, *Tetrahedron*, 1966, **22**, 868.
[45] H. Taniguchi, I. M. Mathai, and S. I. Miller, *J. Amer. Chem. Soc.*, 1967, **89**, 115.
[46] W. J. Gensler and J. Casella, *J. Amer. Chem. Soc.*, 1958, **80**, 1376.
[47] G. Eglinton, I. A. Lardy, R. A. Raphael, and G. A. Sim, *J. Chem. Soc.*, 1964, 1154; R. Wolovsky and F. Sondheimer, *J. Amer. Chem. Soc.*, 1962, **84**, 2844; P. P. Montijn, A. Kupecz, L. Brandsma, and J. F. Arens, *Rec. Trav. chim.*, 1969, **88**, 958.

chain diacetylenes the minimum chain length for this reaction is seven carbon atoms.[48] Whereas hepta-1,6-diyne can be isomerised to toluene by treatment with potassium t-butoxide in refluxing diglyme, under comparable conditions hexa-1,5-diyne cannot be isomerised to benzene. This may be explained by invoking a diene-allene intermediate which undergoes electrocyclisation and subsequent isomerisation to the aromatic product, as shown in scheme (37). Such an intermediate clearly cannot be formed in the C_6 system.



(37)

7 Triacetylenes

The only clear-cut examples of triacetylene rearrangements are the isomerisations of 2,4,6-triynoic acids to 3,5,7-triynoic acids [reaction 38, R = Me[9,49] and $^{-}O_2C(CH_2)_3CH{=}CH\cdot$[50]], reactions which clearly parallel those of $\alpha\beta$-acetylenic acids discussed above.[51]

$$RCH_2C{\equiv}CC{\equiv}CC{\equiv}CCO_2^- \longrightarrow RC{\equiv}CC{\equiv}CC{\equiv}CCH_2CO_2^- \qquad (38)$$

8 Naturally Occurring Polyacetylenes

Most work on the rearrangement of naturally occurring polyacetylenes has been concerned with those containing a terminal diyne-allene. The reactions fall into two groups. The first of these involves the conversion of the diyne-allene into a terminal triacetylene[52,53] and is exemplified by the isomerisation of nemotin (*30*) in 0·1N aqueous sodium hydroxide at room temperature (reaction 39).[53] The second group involves formation of a methyl-substituted triacetylene.[52,54] A typical case is the isomerisation of mycomycin (*31*) in N aqueous potassium hydroxide at 27 °C (reaction 40).[54] It is tempting to speculate that this isomerisation and others like it proceed through the terminal triacetylene but there is no direct evidence to support this.

$$HC{\equiv}CC{\equiv}CCH{=}C{=}CHCH(OH)CH_2CH_2CO_2H \longrightarrow$$
(*30*)
$$HC{\equiv}CC{\equiv}CC{\equiv}CCH_2CH(OH)CH_2CH_2CO_2H \qquad (39)$$

[48] G. Eglinton, R. A. Raphael, R. G. Willis, and J. A. Zabkiecvicz, *J. Chem. Soc.*, 1964, 2597.
[49] J. M. Thompson, Ph.D. thesis, Manchester, 1954.
[50] R. C. Cambie, J. N. Gardner, E. R. H. Jones, G. Lowe, and G. Read, *J. Chem. Soc.*, 1963, 5056.
[51] Reaction (14), page 591. See also reaction (35), page 597.
[52] R. E. Bew, J. R. Chapman, E. R. H. Jones, B. E. Lowe, and G. Lowe, *J. Chem. Soc.* (*C*), 1966, 129.
[53] J. D. Bu'Lock, E. R. H. Jones, P. R. Leeming, and J. M. Thompson, *J. Chem. Soc.*, 1956, 3767.
[54] W. D. Celmer and I. A. Solomons, *J. Amer. Chem. Soc.*, 1952, **74**, 3838; 1953, **75**, 1372.

$$HC{\equiv}CC{\equiv}CCH{=}C{=}CHCH\overset{cis}{=\!=}CHCH\overset{trans}{=\!=}CH(CH_2)_2CO_2H \longrightarrow$$
(*31*)

$$CH_3C{\equiv}CC{\equiv}CC{\equiv}CCH\overset{trans}{=\!=}CHCH\overset{trans}{=\!=}CH(CH_2)_2CO_2H \quad (40)$$

Bu'Lock[55] has suggested that the biosynthesis of some naturally occurring allenes itself involves a prototropic rearrangement. The general sequence is shown in scheme (41). The idea is that degradation of crepenynic acid (*32*) leads to a compound, such as (*33*), containing a skipped ene-yne unit, isomerisation of which gives an allene. Further modification of this would quite simply give known allenes such as (*30*), (*31*), and (*34*). This suggestion seems reasonable, both as an explanation of the frequency with which the conjugated diyne-allene unit, often next to a *cis* olefin, is found in these compounds and also in view of the key role played by crepenynic acid in the biosynthesis of polyacetylenes in general, but it still awaits experimental confirmation.

$$CH_3(CH_2)_4C{\equiv}CCH_2CH\overset{cis}{=}CH(CH_2)_7CO_2H$$
(*32*) ↓

$$[CH_3C{\equiv}CC{\equiv}CC{\equiv}CCH_2CH\overset{cis}{=}CH(CH_2)_3CO_2H]$$
(*33*) ↓

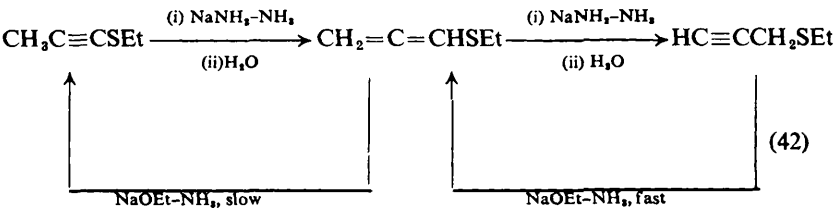
$$[CH_3C{\equiv}CC{\equiv}CCH{=}C{=}CHCH\overset{cis}{=}CH(CH_2)_3CO_2H]$$
↓

$$HO_2CC{\equiv}CC{\equiv}CCH{=}C{=}CHCH\overset{cis}{=}CH(CH_2)_3CO_2H \textit{ etc.} \quad (41)$$
(*34*)

9 'Two Step' Isomerisation Reactions

Many of the recent publications of Arens, Brandsma, and co-workers[56,57] have been concerned with 'two step' isomerisation reactions in which an allene or an acetylene is treated with excess butyl-lithium, lithamide, sodamide, or potassamide to give an organometallic derivative which is then hydrolysed. Such reactions do not necessarily give the most stable end product. For example, when ethyl (prop-1-ynyl) thioether is treated for one and a half minutes with excess sodamide in liquid ammonia, and the sodium salt formed is then hydrolysed with water, ethyl (propa-1,2-dienyl) thioether is obtained. When the process is repeated ethyl (prop-2-ynyl) thioether is formed (reaction 42). These reactions may be reversed by treatment with sodium ethoxide in liquid ammonia and in this way the original starting material is eventually reformed.[57] The intermediate organometallic derivatives will also react with alkyl halides, ketones, ethylene oxide, *etc.* in the normal way.

[55] J. D. Bu'Lock in 'Comparative Phyto-chemistry', Academic Press, London, 1966, p. 79.
[56] J. F. Arens, L. Brandsma, *et al.*, *Rec. Trav. chim.*, 1967, **86**, 393; 1968, **87**, 916; 1447; 1179; 1969, **88**, 609. *Tetrahedron Letters*, 1968, 2483.
[57] L. Brandsma, H. E. Wijers, and J. F. Arens, *Rec. Trav. chim.*, 1963, **82**, 1040.



(42)

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