Acetylene and Acetylenic Compounds in Organic Synthesis.

THE TILDEN LECTURE, DELIVERED BEFORE THE SOCIETY AT THE IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY, LONDON, ON OCTOBER 20TH, 1949.

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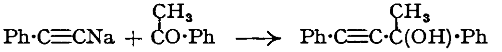
RECENT developments in acetylene chemistry have been many and varied and, as a result, the opportunities for the use of acetylene and acetylenic compounds in synthetic work have been greatly extended. The advantages to be gained by employing these versatile and reactive compounds are not too widely appreciated and consequently when this lecture was first planned, more than two years ago, it had been intended to attempt a broad review of the whole field. In the meantime, however, several aspects of the subject have been admirably dealt with (Johnson, " Some Applications of Acetylenic Compounds in Organic Synthesis," R.I.C., 1948; Bergmann, " Acetylene Chemistry," 1948; Sir Ian Heilbron, Pedler Lecture, *J.*, 1948, 386; Reppe, *Experientia*, 1949, **5**, 93), and this lecture is therefore somewhat more restricted in its scope than would otherwise have been the case. Even with this almost welcome limitation the selection of topics has been by no means easy and to a large extent the examples chosen to illustrate the general theme have been taken from recent work in the laboratories at Imperial College, London, and at Manchester University.

Although the original discovery of acetylene was made by Davy more than a hundred years ago, and many of its reactions and those of simple acetylenic compounds were investigated from 1860 onwards, especially by Berthelot and his school, it was not until the turn of the century that acetylene became readily available with the introduction of a method for the manufacture of calcium carbide. In the first instance, this availability of carbide led to the widespread use of acetylene as an illuminant (1894), to the utilisation of the cyanamide process for nitrogen fixation (1904), and to the employment of the oxy-acetylene flame (1906). The potentialities for organic syntheses, realised by Berthelot as early as 1872, were to remain largely unexploited for many years. It was not until World War I that the conversion of acetylene into acetaldehyde, long studied in the laboratory, was realised commercially, and during World War II many processes based on acetylene, but not competitive under normal conditions, were operated on a large scale in Germany. The remarkable work of Reppe and his collaborators, revealing so many novel and fascinating reactions in the field of acetylene chemistry emanated largely from the need for the utilisation of acetylene as a major starting material for the German organic chemical industry.

At just about the time when carbide became readily available, Nef (*Annalen*, 1899, **308**, 264) discovered a reaction which, probably more than any other, has fostered the employment of acetylenic compounds in synthetic work. Reasoning from analogy with the zinc alkyls he demonstrated that the sodium derivative of phenylacetylene could be condensed with carbonyl compounds to give acetylenic carbinols (*e.g.*, I), previously available only from the corresponding



$$\mathrm{Ph{\cdot}C{\equiv}CNa} + \overset{\mathrm{CH_3}}{\mathrm{CO{\cdot}Ph}} \longrightarrow \mathrm{Ph{\cdot}C{\equiv}C{\cdot}}\overset{\mathrm{CH_3}}{\mathrm{C}}\mathrm{(OH){\cdot}Ph}$$

(I.)

ethylenic carbinols by halogenation and dehydrohalogenation procedures. The Grignard reagents, discovered shortly afterwards, proved to be useful in this connection and in the succeeding fifty years this reaction has been found to be of an extremely general character, occurring between any compound containing a free ethynyl group and a carbonyl compound in the presence of a suitable condensing agent (cf. Johnson, " Acetylenic Compounds," Vol. I). The scope of this addition reaction, especially for large-scale applications, has been greatly extended by the efforts of Reppe and his collaborators, who have developed the use of copper and related acetylides as catalysts. This discovery was applied most successfully to the manufacture of butynediol ($HO{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}OH$) by the condensation of acetylene with formaldehyde, the first stage in the Reppe process for the production of butadiene.

One of the best-known synthetic uses of the ethynylcarbinols arises from their partial hydrogenation, followed by anionotropic rearrangement of the vinylcarbinols to the isomeric primary alcohols or their derivatives. The value of this reaction was early appreciated in the terpene series as is illustrated by the syntheses of linaloöl (Ruzicka and Fornasir, *Helv. Chim. Acta*, 1919, **2**, 182), of farnesol and nerolidol (Ruzicka, *Helv. Chim. Acta*, 1923, **6**, 492), and of phytol (Fischer and Löwenberg, *Annalen*, 1929, **475**, 183). Many more examples of the application of this convenient procedure are on record but some further instances from the steroid series will suffice to indicate its wide applicability. In the ethynylcarbinols prepared

$$\mathrm{Me_2C{=}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}CH_3 + C_2H_2 \xrightarrow{NaNH_2} Me_2C{=}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CMe(OH){\cdot}C{\equiv}CH \xrightarrow{Na\text{-}moist\ Et_2O}}$$

$$\underset{\text{Linaloöl}}{\mathrm{Me_2C{=}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CMe(OH){\cdot}CH{=}CH_2}} \xrightarrow{\mathrm{Ac_2O}} \underset{\text{Geranyl acetate}}{\mathrm{Me_2C{=}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CMe{=}CH{\cdot}CH_2{\cdot}OAc}}$$

from the 17-ketones of the steroid series the hydroxyl group has an orientation (β) different from that of the 17-hydroxylated substances isolated from the adrenal cortex. After partial hydrogenation and rearrangement to the primary alcohol, however, a hydroxyl group with the correct orientation (α) can be introduced by hydroxylation with osmium tetroxide [*cf.* the synthesis of 17-hydroxyprogesterone (Prins and Reichstein, *Helv. Chim. Acta*, 1941, **24**, 945) and the synthesis of Kendall's Compound *E* (Sarett, *J. Biol. Chem.*, 1946, **162**, 601)].

A major extension of the field of application of acetylenic carbinols in organic synthesis arose from the discovery of the ready anionotropic rearrangement undergone by the carbinols and glycols obtained by condensations with αβ-unsaturated carbonyl compounds (*cf. Ann. Reports*,

$$\text{(II.)}\quad \mathrm{CH_3{\cdot}CH{=}CH{\cdot}CH(OH){\cdot}C{\equiv}CH \xrightarrow{acids} CH_3{\cdot}CH(OH){\cdot}CH{=}CH{\cdot}C{\equiv}CH}\quad \text{(III.)}$$

1944, **41**, 175). While examining the properties of the acetylenic carbinol (II) prepared from crotonaldehyde, it was found that on treatment with acids it was isomerised to the conjugated vinylacetylenic alcohol (III). The broad scope of this reaction has been clearly demonstrated, its kinetics have been studied, and the marked influence of substituent groups, which produce variations in rates of isomerisation of 10^9, is a notable feature (Braude and Jones, *J.*, 1944, 436; 1946, 122, 128). Its application in the case of the glycol (IV) from octatrienal points to its potentialities

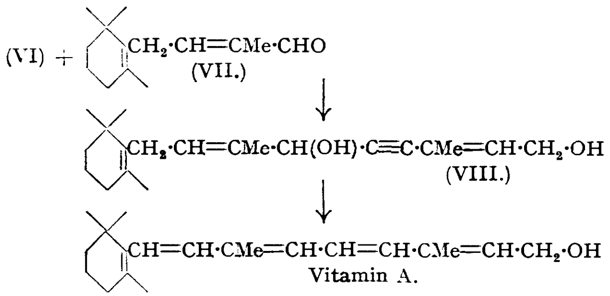
$$\text{(IV.)}\quad \mathrm{CH_3{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}CH(OH){\cdot}C{\equiv}C{\cdot}CH(OH){\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}CH_3}$$

$$\Big\downarrow\ \text{acids}$$

$$\mathrm{CH_3{\cdot}CH(OH){\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}C{\equiv}C{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}CH(OH){\cdot}CH_3}$$

for the synthesis of conjugated polyenynes and it has found valuable use in the synthesis of vitamin A and its analogues (see Sir Ian Heilbron, *J.*, 1948, 386). Isler and his co-workers (Isler, Huber, Ronco, and Kofler, *Helv. Chim. Acta*, 1947, **30**, 1911) utilised the anionotropic rearrangement of the ethynylcarbinol (V) from methyl vinyl ketone to prepare the C_6 alcohol

$$\mathrm{CH_3{\cdot}CO{\cdot}CH{=}CH_2 \longrightarrow HC{\equiv}C{\cdot}CMe(OH){\cdot}CH{=}CH_2}\ \text{(V.)} \longrightarrow \mathrm{HC{\equiv}C{\cdot}CMe{=}CH{\cdot}CH_2{\cdot}OH}\ \text{(VI.)}$$



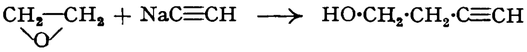
(VI) which, by condensation with the C_{14} aldehyde (VII), furnished the glycol (VIII), ultimately converted into vitamin A.

The vinylcarbinols obtained by partial hydrogenation of the ethynyl compounds rearrange

$$\underset{\text{(IX.)}}{\mathrm{CH_3{\cdot}CH{=}CH{\cdot}CH(OH){\cdot}CH{=}CH_2}} \longrightarrow \underset{\text{(X.)}}{\mathrm{CH_3{\cdot}CH(OH){\cdot}CH{=}CH{\cdot}CH{=}CH_2}} \longrightarrow \underset{\text{(XI.)}}{\mathrm{CH_3{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}CH_2{\cdot}OH}}$$

even more readily and in the simple case of the carbinol (IX) derived from crotonaldehyde it was shown that isomerisation occurred to give the secondary butadienylcarbinol (X) (Jones, Heilbron, McCombie, and Weedon, *J.*, 1945, 84). It appears from recent work (Nazarov and Fisher, *Chem. Abstracts*, 1949, **43**, 112) that the rapid isomerisation to the conjugated secondary carbinol is succeeded by a slow conversion into the primary sorbyl alcohol (XI).

As has already been indicated, a considerable variety of procedures can be utilised for the preparation of the normal acetylenic carbinols, *i.e.*, the αβ-acetylenic carbinols [$>C(OH){\cdot}C{\equiv}C{\cdot}$]. For the βγ-analogues (*e.g.*, XII), however, the only procedure hitherto available employs the reaction between ethylene oxides and sodium acetylide in liquid ammonia (*cf.* Kreimeier, U.S.P. 2,106,182; Macallum, U.S.P. 2,125,284). Its scope is limited by the relative inaccessibility of the oxides and by the poor yields obtained. Even with ethylene oxide it is not easy to achieve yields of more than 50% and with increasing substitution the yields fall appreciably (propylene oxide gives about 35% and *iso*butylene oxide only about 20% yields; Haynes and Jones, unpublished).

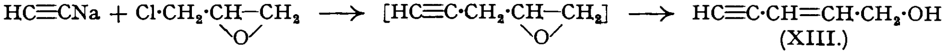


$$\underbrace{CH_2{-}CH_2}_{O} + NaC{\equiv}CH \longrightarrow HO{\cdot}CH_2{\cdot}CH_2{\cdot}C{\equiv}CH \quad \text{(XII.)}$$

It may be noted that it was while searching for new methods of effecting the condensation between ethylene oxide and acetylene, that the remarkable polymerisation of acetylene to *cyclo*octatetraene was revealed (Reppe, Schichting, Klager, and Topel, *Annalen*, 1948, **560**, 1). Seeking a more convenient route to the βγ-acetylenic alcohols it has now been established (Henbest, Jones, and Walls, *J.*, 1949, 2696) that the Reformatsky type of condensation, initially reported by Zeile and Meyer (*Ber.*, 1942, **75**, 356) between *cyclo*hexanone and propargyl bromide, can be extended to include aldehydes, unsaturated aldehydes, and ketones, in reactions with a variety of substituted propargyl bromides.

$$>C{=}O + BrCH_2{\cdot}C{\equiv}CH \xrightarrow{Zn} >C(OH){\cdot}CH_2{\cdot}C{\equiv}CH$$

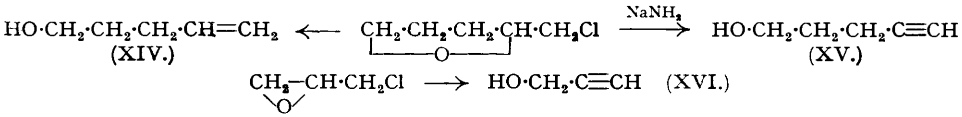
On the basis of our present knowledge it is hardly to be expected that any widely applicable methods can be devised for the preparation of γδ-acetylenic alcohols. However, two novel examples of the formation of these rather inaccessible alcohols have recently been discovered. The condensation between epichlorohydrin and sodium acetylide in liquid ammonia gave, very unexpectedly, the primary alcohol, pentenynol (XIII) in about 40% yield (Haynes, Heilbron, Jones, and Sondheimer, *J.*, 1947, 1583).



$$HC{\equiv}CNa + Cl{\cdot}CH_2{\cdot}\underbrace{CH{-}CH_2}_{O} \longrightarrow [HC{\equiv}C{\cdot}CH_2{\cdot}\underbrace{CH{-}CH_2}_{O}] \longrightarrow HC{\equiv}C{\cdot}CH{=}CH{\cdot}CH_2{\cdot}OH \quad \text{(XIII.)}$$

Unequivocal evidence indicates that the initial step in this reaction is substitution to yield the acetylenic oxide followed by rearrangement to the alcohol, rather than the alternative addition to the oxide ring and subsequent elimination of sodium chloride.

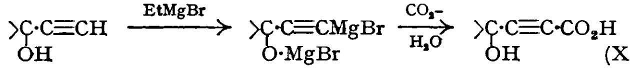
The other example originated from the work of Paul (*Bull. Soc. chim.*, 1935, **2**, 745), who described the formation of the pentenol (XIV) from tetrahydrofurfuryl chloride by treatment with sodium in an inert solvent. It has now been observed that with sodamide in liquid ammonia the corresponding pentynol (XV) is produced directly in over 70% yield. This pentynol, which has many potential synthetic uses, thus becomes one of the most easily accessible acetylenic alcohols. Propargyl alcohol (XVI) is almost certainly the major product resulting from the similar treatment of epichlorohydrin but the optimum conditions for its formation and isolation have yet to be fully elucidated (Eglinton, Jones, and Whiting, unpublished).



$$\underset{\text{(XIV.)}}{HO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH{=}CH_2} \longleftarrow \underbrace{CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH}_{O}{\cdot}CH_2Cl \xrightarrow{NaNH_2} \underset{\text{(XV.)}}{HO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}C{\equiv}CH}$$

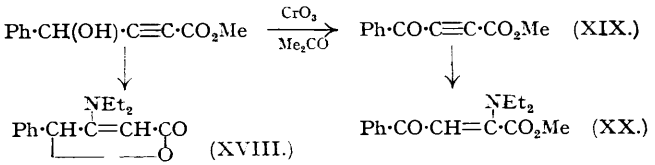
$$\underbrace{CH_2{-}CH}_{O}{\cdot}CH_2Cl \longrightarrow HO{\cdot}CH_2{\cdot}C{\equiv}CH \quad \text{(XVI.)}$$

The experiences of earlier workers on the carboxylation of ethynylcarbinols were not encouraging, but it was found that by careful attention to the reaction conditions, especially to the choice of solvent for the Grignard complex, excellent conversions into the hydroxy-acetylenic acids (XVII) could be obtained (Haynes and Jones, *J.*, 1946, 503).

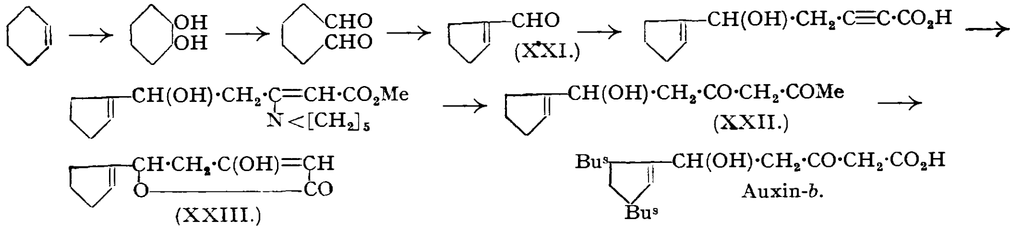


$$>\underset{OH}{C}{\cdot}C{\equiv}CH \xrightarrow{EtMgBr} >\underset{O{\cdot}MgBr}{C}{\cdot}C{\equiv}CMgBr \xrightarrow[H_2O]{CO_2,-} >\underset{OH}{C}{\cdot}C{\equiv}C{\cdot}CO_2H \quad \text{(XVII.)}$$

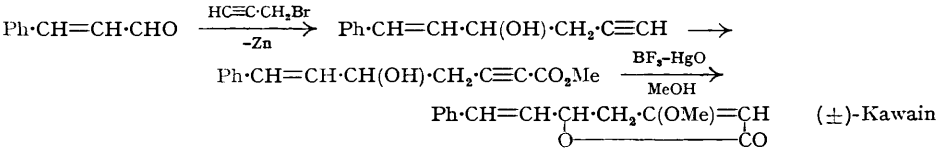
These acids have already found several synthetical applications, for example, by partial hydrogenation, syntheses of αβ-ethylenic lactones are possible (Haynes and Jones, *J.*, 1946, 954). With nucleophilic reagents, addition reactions of the esters lead to β-substituted γ-hydroxyacrylic esters which are spontaneously converted into γ-lactones (XVIII) (Jones and Whiting, *J.*, 1949, 1423). On the other hand, if the esters are first oxidised to the γ-keto-esters (XIX), a simple process, nucleophilic addition reactions occur in the reverse direction with the formation of α-substituted β-acylacrylic esters (XX).



By taking advantage of the nucleophilic addition reactions mentioned above, some progress has been made towards the synthesis of the plant-growth hormone, auxin-*b*, as formulated by Kögl and his collaborators (*Z. physiol. Chem.*, 1934, **225**, 215). The *cyclo*pentenealdehyde (XXI), made by a route capable of extension to the more complex aldehydes required for the final auxin synthesis, is condensed with propargyl bromide by a Reformatsky reaction, and the resulting βγ-acetylenic carbinol is carboxylated. Addition of piperidine to the acetylenic linkage of the ester, followed by mild acid hydrolysis, yields the β-keto-ester (XXII) in excellent yield.



Hydrolysis of this ester with dilute sodium hydroxide solution, followed by acidification, leads to the lactone (XXIII), the conversion of which into the corresponding acid is at present being studied (Jones and Whiting, *J.*, 1949, 1419; Brown, Henbest, and Jones, unpublished). Mention should be made at this stage of Raphael's elegant syntheses of dihydropenicillic acid and of penicillic acid itself (*J.*, 1947, 805; 1948, 1508), both of which are based on reactions of the hydroxy-acetylenic acids. A synthesis of (±)-kawain has recently been achieved (Fowler, Henbest, and Jones, unpublished) by the application of similar reactions according to the accompanying scheme; the relationship of the synthetic material to the naturally-occurring lactone, (+)-kawain (Borsche and Peitzsch, *Ber.*, 1930, **63**, 2414) being established by the identity of their ultra-violet and infra-red spectra.



Ethylenic linkages result from the partial hydrogenation of acetylenic bonds and, since isomerisations are unlikely to occur during hydrogenation, this procedure has distinct advantages over most others for the synthesis of ethylenic compounds containing the –CH=CH– grouping. Moreover, the partial catalytic hydrogenation of an isolated acetylenic linkage is stereo-selective, that is, it gives rise mainly to the *cis*-configuration of the resulting ethylenic bond. This almost exclusive production of the *cis*-isomer and the unequivocal position of the ethylenic bond are valuable advantages accruing from the partial hydrogenation procedure; moreover, in the majority of the naturally occurring unsaturated fatty acids, the *cis*-orientation is found. It is not surprising therefore, to find several examples in which this procedure is utilised. It should be noted that transformation into the *cis*-form is not absolutely quantitative: some complete hydrogenation occurs and traces of the *trans*-isomer may be present. However, the isolation of pure *cis*-forms is relatively simple when crystallisable materials are being employed.

In the synthesis of unsaturated lactones already referred to, lactonisation is possible only as a result of the *cis*-orientation of the double bond; in this case any *trans*-acid is eliminated on distillation. Lauer and Gensler (*J. Amer. Chem. Soc.*, 1945, **67**, 1171) have achieved the synthesis of the *cis*-form of the plant-growth hormone, traumatic acid, by partial hydrogenation of the corresponding acetylenic dicarboxylic acid. The synthesis of *cis*- and *trans*-octadec-11-enoic acids (Akmad, Bumpas, and Strong, *J. Amer. Chem. Soc.*, 1948, **70**, 3391, *cf.* 1699) illustrates

$$\mathrm{HC{\equiv}C{\cdot}[CH_2]_8{\cdot}CO_2H \xrightarrow[+\,CO_2]{\text{Na salt}} HO_2C{\cdot}C{\equiv}C{\cdot}[CH_2]_8{\cdot}CO_2H \xrightarrow[Ni]{H_2-} HO_2C{\cdot}CH{=}CH{\cdot}[CH_2]_8{\cdot}CO_2H} \quad \textit{cis}\text{-Traumatic acid.}$$

clearly the potentialities for syntheses in the fatty acid series. Alkylation of oct-1-yne with a polymethylene chloride iodide leads to the chloro-alkyne and treatment of this with sodium cyanide suffices to provide the required carbon skeleton. Partial hydrogenation produces the *cis*-acid, which, on heating with selenium gives the *trans*-isomer. Mention should also be made

$$\mathrm{C_6H_{13}{\cdot}C{\equiv}CH + I{\cdot}[CH_2]_9{\cdot}Cl \xrightarrow[NH_3]{\text{Na-liq.}} C_6H_{13}{\cdot}C{\equiv}C{\cdot}C{\cdot}[CH_2]_9{\cdot}Cl \xrightarrow[\text{hydrol.}]{\text{NaCN and}}}$$

$$\mathrm{C_6H_{13}{\cdot}C{\equiv}C{\cdot}[CH_2]_9{\cdot}CO_2H \xrightarrow{Ni-H_2} (\textit{cis-})C_6H_{13}{\cdot}CH{=}CH{\cdot}[CH_2]_9{\cdot}CO_2H \xrightarrow{\text{Se, heat}}} \textit{trans-}\ \text{(vaccenic acid)}$$

of the syntheses of geometrical isomerides of the naturally occurring insecticide, pellitorine, and the homologous herculin (Raphael and Sondheimer, *Nature*, 1949, **164**, 707), and of syntheses of alkenylphenols related to the constituents of cashew nut shell liquid and urushiol, the vesicant principle in poison ivy (Sletzinger and Dawson, *J. Org. Chem.*, 1949, **14**, 849; Wasserman and Dawson, *ibid.*, 1943, **8**, 73). An interesting extension of these methods is to be found in the recent work of Raphael and Sondheimer (*Nature*, in the press) on the synthesis of linoleic acid, presumably in the *di-cis*-form. The final product has as yet been obtained only in small

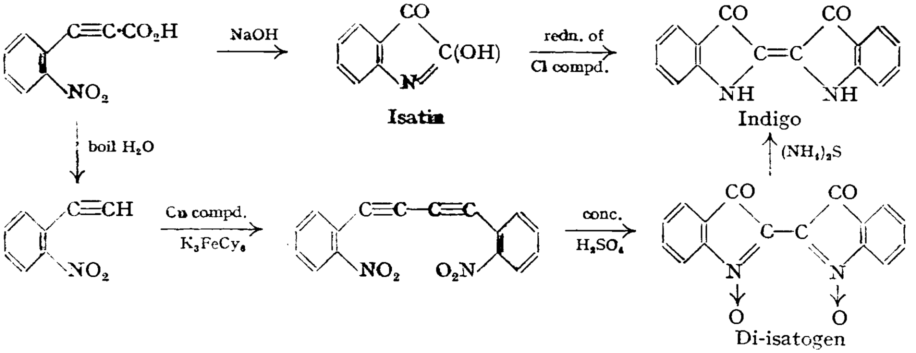
$$\begin{tikzcd}
\mathrm{C_5H_{11}{\cdot}C{\equiv}CH} \arrow[r] & \mathrm{C_5H_{11}{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}OH} \arrow[r] & \mathrm{C_5H_{11}{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}OMs} \arrow[dr, "\mathrm{EtMgBr}"] & \\
\mathrm{Cl{\cdot}[CH_2]_6{\cdot}Cl} \arrow[r] & \mathrm{I{\cdot}[CH_2]_6{\cdot}Cl} \arrow[r] & \mathrm{HC{\equiv}C{\cdot}[CH_2]_6{\cdot}Cl} \arrow[r] & \mathrm{C_5H_{11}{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}[CH_2]_6{\cdot}Cl} \arrow[d, "\mathrm{CH_2(CO_2Et)_2}"] \\
\begin{matrix}\mathrm{C_5H_{11}{\cdot}CH{=}CH{\cdot}CH_2{\cdot}CH{=}CH{\cdot}[CH_2]_7{\cdot}CO_2H}\\ \text{Linoleic acid}\end{matrix} & & & \begin{matrix}\mathrm{C_5H_{11}{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}[CH_2]_6{\cdot}CH_2{\cdot}CO_2H}\\ \text{m. p. } 43^\circ\end{matrix} \arrow[lll, "\mathrm{H_2-Pd}", "\mathrm{-CaCO_3}"']
\end{tikzcd}$$

quantity but it gave a tetrabromide with the correct melting point. In view of the freedom from double-bond migration, procedures of this type may well prove to be particularly suitable for the synthesis of the rather unstable acids of the drying-oil type.

In 1870, Glaser (*Annalen*, **154**, 159) made the surprising observation that, when the copper derivative of phenylacetylene was oxidised with air in ammoniacal alcoholic solution, a smooth

$$\mathrm{Ph{\cdot}C{\equiv}CH \longrightarrow Ph{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}Ph}$$

coupling reaction occurred yielding diphenyldiacetylene. This work was extended by Baeyer in connection with his classical studies in the indigo series. He effected the coupling of the



copper derivative of *o*-nitrophenylacetylene with potassium ferricyanide and converted the di(nitrophenyl)diacetylene with sulphuric acid into di-isatogen and thence produced indigo by reduction with ammonium sulphide. These experiments provided the first real evidence of the nature of the carbon skeleton of indigo (Baeyer, *Ber.*, 1880, **13**, 2254; 1882, **15**, 50).

The coupling reaction has been extensively studied and it has recently been shown, contrary to the experiences of earlier workers, that the coupling of ethynylcarbinols by the convenient procedure of aerial oxidation in the presence of cuprous ammonium chloride is a general reaction, applicable to carbinols of various types (Bowden, Heilbron, Jones, and Sargent, *J.*, 1947, 1579). Furthermore, the function of the cuprous salt appears to be largely catalytic and considerably less than one equivalent can be employed.

The application of this oxidative coupling in the case of pentenynol (XXIV) to give the glycol (XXV) in 70% yield (Heilbron, Jones, and Sondheimer, *J.*, 1947, 1586) gives an indication of the scope of the method. Mixed coupling reactions cannot easily be effected in this way but it is worthy of note that Baeyer and Landsberg (*Ber.*, 1882, **15**, 57) obtained a good yield of *o*-nitrodiphenyldiacetylene by treating a mixture of phenylacetylene and nitrophenylacetylene with ammoniacal cuprous chloride and oxidising the mixed copper salts with potassium ferricyanide. Such mixed coupling reactions are better carried out, however, by interaction of acetylenic Grignard reagents with iodoacetylenes (Grignard and Perichon, *Ann. Chim.*, 1926, **5**, 5; Horn and Weedon, forthcoming communication).

$$\text{(XXIV.)}\quad 2\mathrm{HC{\equiv}C{\cdot}CH{=}CH{\cdot}CH_2{\cdot}OH} \longrightarrow \mathrm{HO{\cdot}CH_2{\cdot}CH{=}CH{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH{=}CH{\cdot}CH_2{\cdot}OH}\quad\text{(XXV.)}$$

By oxidation of secondary ethynylcarbinols in acetone solution with chromic acid, the highly reactive ethynyl ketones (*e.g.*, XXVI) are readily prepared (Bowden, Heilbron, Jones, and Weedon, *J.*, 1946, 39). These substances undergo with notable facility a variety of addition reactions, and those with amines and other nucleophilic reagents, and with dienes, have been studied in some detail (Bowden, Braude, Jones, and Weedon, *J.*, 1946, 45; Bowden and Jones, *J.*, 1946, 52; Bowden, Braude, and Jones, *J.*, 1946, 953). Application of the selective oxidation procedure to primary acetylenic alcohols yields the corresponding acids, and even the unsaturated glycol (XXV) can be oxidised smoothly to the dicarboxylic acid (XXVII) (Heilbron, Jones, and Sondheimer, *J.*, 1949, 604).

$$\mathrm{Ph{\cdot}CH(OH){\cdot}C{\equiv}CH} \longrightarrow \mathrm{Ph{\cdot}CO{\cdot}C{\equiv}CH}\quad\text{(XXVI.)}$$

$$\text{(XXV)} \longrightarrow \mathrm{HO_2C{\cdot}CH{=}CH{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH{=}CH{\cdot}CO_2H}\quad\text{(XXVII.)}$$

Kuhn and Wallenfells (*Ber.*, 1938, **71**, 1510, 1889) achieved conspicuous success in the synthesis of polyenes and cumulenes *via* acetylenic glycols. From the 1 : 4- and 1 : 6-glycols, obtained by condensation of carbonyl compounds with acetylene and diacetylene, partial hydrogenation with palladium catalysts, followed by treatment with phosphorus di-iodide or chromous or vanadous chlorides, gave good yields of diphenylpolyenes (*e.g.*, XXVIII). On the other hand, direct reduction of the glycols with chromous chloride in the presence of hydrogen chloride yielded cumulenes, the scarlet tetraphenylhexapentaene (XXIX) being formed from the diacetylenic glycol from benzophenone in 90% yield.

$$\mathrm{Ph{\cdot}CH{=}CH{\cdot}CH(OH){\cdot}C{\equiv}C{\cdot}CH(OH){\cdot}CH{=}CHPh} \xrightarrow{\mathrm{Pd\text{-}H_2}}$$
$$\mathrm{Ph{\cdot}CH{=}CH{\cdot}CH(OH){\cdot}CH{=}CH{\cdot}CH(OH){\cdot}CH{=}CHPh} \longrightarrow \mathrm{Ph{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}CH{=}CHPh}\quad\text{(XXVIII.)}$$

$$\mathrm{Ph_2C(OH){\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}C(OH)Ph_2} \longrightarrow \mathrm{Ph_2C{=}C{=}C{=}C{=}C{=}CPh_2}\quad\text{(XXIX.)}$$

Not unrelated to these studies are some investigations carried out during the past year on the preparation of the conjugated poly-ynes, compounds containing a series of conjugated acetylenic linkages. The diacetylenes or di-ynes of this type are of course well known, being readily available by the coupling reaction already described. As long ago as 1885, Baeyer (*Ber.*, **18**, 674, 2269) conceived the idea of making a conjugated tetra-acetylenic compound by the coupling of diacetylenecarboxylic acid, $\mathrm{HC{\equiv}C{\cdot}C{\equiv}C{\cdot}CO_2H}$, but the product proved to be extraordinarily unstable although on reduction with sodium amalgam he did obtain a small amount of what might have been sebacic acid.

In seeking general methods we directed our attention to the observation that 1 : 4-dichlorobut-2-yne (XXX), prepared from the easily accessible butynediol with thionyl chloride, yields diacetylene on treatment with alkaline reagents (cf. Keyssner and Eichler, G.P. 750,637; Johnson, *J.*, 1946, 1009, 1014). It has now been found (Armitage, Jones, and Whiting, unpublished) that, when this process is carried out with sodamide in liquid ammonia, either the mono- or the di-sodio-derivative of diacetylene can be obtained at will, practically instantaneously and in quantitative yields. The ready production of the monosodio-derivative is particularly important since by straightforward substitution reactions, carried out subsequently in the liquid ammonia medium, mono-substituted diacetylenes (XXXI) can easily be made. Already we have observed that these substances can be coupled by the standard methods to yield the conjugated tetra-acetylenes or tetra-ynes (XXXII).

$$\underset{\text{(XXX.)}}{\mathrm{ClCH_2{\cdot}C{\equiv}C{\cdot}CH_2Cl}} \xrightarrow[\text{liq. NH}_3]{\mathrm{NaNH_2}} \mathrm{NaC{\equiv}C{\cdot}C{\equiv}CH} \xrightarrow{\mathrm{RHal}} \underset{\text{(XXXI.)}}{\mathrm{R{\cdot}C{\equiv}C{\cdot}C{\equiv}CH}} \xrightarrow{\mathrm{EtMgBr\text{-}I_2}} \underset{\text{(XXXII.)}}{\mathrm{R{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}R}}$$

If the disodio-derivative, in the liquid ammonia in which it is formed, is treated with formaldehyde, then hexadiynediol (XXXIII) is produced in almost 90% yield. This can be

$$\mathrm{NaC{\equiv}C{\cdot}C{\equiv}CNa} \xrightarrow{\mathrm{CH_2O}} \underset{\text{(XXXIII.)}}{\mathrm{HO{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}OH}} \xrightarrow[\mathrm{C_5H_5N}]{\mathrm{SOCl_2\text{-}}}$$

$$\mathrm{ClCH_2{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH_2Cl} \xrightarrow[\text{liq. NH}_3]{\mathrm{NaNH_2}} \mathrm{NaC{\equiv}C{\cdot}C{\equiv}C{\cdot}C{\equiv}CNa} \xrightarrow{\mathrm{MeI}} \mathrm{Me{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}C{\equiv}CMe}$$

converted into the dichloride, and by repetition of the sodamide treatment the sodio-derivatives of triacetylene are obtained, and its mono- and di-alkyl derivatives and other condensation products thus become available.

It is not possible at this stage to give more than a brief description of the properties of these novel substances, the parents of which are the polyacetylene hydrocarbons, C_nH_2. Considerable differences have been observed between individual members and, although in general they appear to be rather unstable under normal conditions, in nitrogen or in a vacuum at $-70°$ they can be kept for reasonable periods. Dimethyltriacetylene (1 : 6-dimethylhexatriyne) crystallises well and has m. p. 128°, and dimethyltetra-acetylene (1 : 8-dimethyloctatetrayne), which is also beautifully crystalline, decomposes when heated above about 80°. The ultra-violet light absorption properties of the tetra-acetylenes have revealed some unexpected features, especially the remarkably high intensity of the absorption in the 2200—2500-A. region. The intensities, $\varepsilon =$ about 270,000, which have been observed in several cases, are amongst the highest ever recorded. Now that methods of synthesis have been developed, it is hoped to examine the physical properties of a wide range of substances of this polyacetylene series, since the enforced linearity of the conjugated poly-yne chain might be expected to endow these predominantly carbon-containing molecules with exceptional properties.

Acetylene has frequently been employed in synthetic work mainly as a convenient and reactive unit for building up the required carbon skeletons. The scope for the use of acetylenic compounds in synthesis is, however, by no means restricted to this purpose, and in many of the cases already discussed due advantage has been taken of the well-known and unique addition reactions of the triple bond in order subsequently to introduce functional groups. No attempt can be made here to summarise these addition reactions, but some recently discovered procedures which break new ground merit special attention.

The first of these concerns the conversion of ethynyl compounds into aldehydes. It has long been known that methyl ketones or their derivatives result from the catalysed hydration of compounds containing an ethynyl group; attempts have been made to obtain aldehydes by reversing the direction of hydration but such successes as have been claimed have been shown

$$\mathrm{R{\cdot}CH_2{\cdot}CHO} \dashleftarrow \mathrm{R{\cdot}C{\equiv}CH} \longrightarrow \mathrm{R{\cdot}CO{\cdot}CH_3}$$

to be largely ill-founded (for summary, cf. Chanley, *J. Amer. Chem. Soc.*, 1948, **70**, 244). It has now been found that when thiolacetic acid reacts with monosubstituted acetylenes, under the influence of organic peroxides or irradiation with ultra-violet light, mono- and di-adducts are produced by "abnormal" addition reactions. The mono-adducts on treatment with the usual carbonyl reagents are converted smoothly into derivatives of the corresponding aldehydes, while,

$$\begin{tikzcd}
 & \mathrm{Bu{\cdot}CH{=}CH{\cdot}SAc} \arrow[r, "\mathrm{NH_2{\cdot}CO{\cdot}NH{\cdot}NH_2}"] & \mathrm{[Bu{\cdot}CH{=}CH{\cdot}SH]} \arrow[r] & \mathrm{Bu{\cdot}CH_2{\cdot}CH{=}N{\cdot}NH{\cdot}CO{\cdot}NH_2} \arrow[dd] \\
\mathrm{Bu{\cdot}C{\equiv}CH} \arrow[ur] \arrow[dr] & + & & \\
 & \mathrm{Bu{\cdot}CH(SAc){\cdot}CH_2{\cdot}SAc} \arrow[r] & \mathrm{Bu{\cdot}CH(SH){\cdot}CH_2{\cdot}SH} & \mathrm{Bu{\cdot}CH_2{\cdot}CHO}
\end{tikzcd}$$

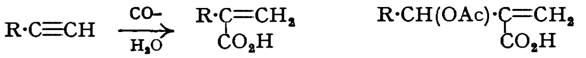
under rather more acidic conditions, the di-adducts yield 1 : 2-dithiols (Bader, Cross, Heilbron, and Jones, *J.*, 1949, 619; cf. Behringer, *Annalen*, 1949, **564**, 219).

Another elegant method of obtaining aldehydes *via* acetylenic compounds has been described by Arens and Van Dorp (*Nature*, 1947, **160**, 189; *Rec. Trav. chim.*, 1948, **67**, 973) in connection with their important synthetic work in the vitamin A series. These authors found that the carbinols arising from condensation of ethoxyacetylene with carbonyl compounds gave, after partial hydrogenation, ethylenic carbinols convertible by mild treatment with dilute acids into

$$>C{=}O \longrightarrow >C(OH)\cdot C{\equiv}C\cdot OEt \xrightarrow{H_2} >C(OH)\cdot CH{=}CH\cdot OEt \xrightarrow{\text{acids}} >C{=}CH\cdot CHO$$

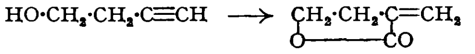
αβ-unsaturated aldehydes. The last stage in this procedure is analogous to the behaviour of certain β-chlorovinylcarbinols under similar conditions (Jones and Weedon, *J.*, 1946, 937).

Finally, the discovery by Reppe and his collaborators (B.I.O.S. Final Reports Nos. 266, 355, and 358; see also *Experientia*, **1949**, 5, 93) of a method of effecting the combination of acetylenic compounds and carbon monoxide provides an outstanding additional rôle to the already extensive repertoire of the acetylenic bond in synthetic operations. Using nickel carbonyl, either stoicheiometrically or, together with carbon monoxide, as a catalyst, in reactions either with acetylene itself or with simple acetylenic hydrocarbons, Reppe succeeded in obtaining acrylic acid and related substances. This novel reaction thus leads to syntheses of branched-chain compounds by addition to the triple bond, a possibility realised hitherto only in a few instances such as the application of the Michael reaction to αβ-acetylenic carbonyl compounds (*e.g.*, Dey, *J.*, 1937, 1057). Much careful study has been necessary in order to find suitable conditions for the extension of this reaction to acetylenic carbinols but, by employing the acetates of the carbinols in reactions with nickel carbonyl in alcohol–acetic acid media, reasonable conversions into analogues (XXXIV) of acrylic acid have been achieved. From the βγ-acetylenic carbinols, the hitherto practically inaccessible methylenebutyrolactone (XXXV), a naturally-



$$R\cdot C{\equiv}CH \xrightarrow[H_2O]{CO-} \begin{array}{l}R\cdot C{=}CH_2\\ \quad CO_2H\end{array} \qquad \begin{array}{l}R\cdot CH(OAc)\cdot C{=}CH_2\\ \qquad\qquad\quad CO_2H\end{array}$$

(XXXIV.)



$$HO\cdot CH_2\cdot CH_2\cdot C{\equiv}CH \longrightarrow \begin{array}{l}CH_2\cdot CH_2\cdot C{=}CH_2\\ O\text{———}CO\end{array}$$

(XXXV.)

occurring antibiotic (Cavallito and Haskell, *J. Amer. Chem. Soc.*, 1946, **68**, 2332), has been synthesised in this way (Jones, Shen, and Whiting, *J.*, in the press).

It is usual at this stage, when so much collaborative work has been described, for some tribute to be paid to those who, by their efforts, have contributed to the development of the subject. Although my remarks must, of necessity, be brief, I do not pay this tribute in any perfunctory spirit, but rather with a deep and sincere feeling of gratitude for the wholehearted co-operation and assistance which it has been my good fortune to receive. It is a source of much pleasure to note that several of our former co-workers are actively engaged in exploring and exploiting new territories in the vast realm which is acetylene chemistry.

To you, Mr. President, in your rôle as teacher, colleague, and friend, and to our many collaborators, both past and present, to whom most of the credit is due, I offer my warmest thanks.