379. *Chemistry of the Higher Fungi. Part XIII.*[1] *Synthesis of* (a) *a* C_9 *Triacetylenic Epoxy-alcohol, a* Coprinus quadrifidus *Metabolite and* (b) *a* C_9 *Triacetylenic* 1,2-*Diol. The Structure of Biformyne* 1.

By E. R. H. Jones, J. S. Stephenson, W. B. Turner, and M. C. Whiting.

trans- and *cis*-2,3-Epoxynona-4,6,8-triyn-1-ol (XVIIa and b) have been prepared by epoxidation of the synthetic *trans*- and *cis*-non-2-ene-4,6,8-triyn-1-ols (XVIa and b) and it has thereby been proved that a trace polyacetylenic metabolite of *Coprinus quadrifidus* is the *trans*-epoxide (XVIIa). Biformyne 1 from *Polyporus biformis* has the same structure, rather than that of nona-4,6,8-triyne-1,2-diol (XII), a synthesis of which is also described.

In Part IX [2] it was shown that the Basidiomycete fungus *Coprinus quadrifidus* produced, as polyacetylenic metabolites, the C_{10} compounds (I) and (II) and the C_9 compounds (III), (IV), and (VI), containing a free ethynyl group, the triacetylenic triol (VI) being the major product. The structures of compounds (III), (IV), and (VI) have since been confirmed by the elegant synthetic work of Bohlmann, Herbst, and Gleinig.[3] The suggestion that the C_9 compounds arise from C_{10} precursors by ω-oxidation and decarboxylation has been strongly supported by the demonstration [1] that a cell-free extract from the mycelium of *C. quadrifidus* effects the decarboxylation of an acetylenic acid, viz.:

$$\mathrm{HO_2C{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH\overset{t}{=}CH{\cdot}CH_2{\cdot}OH \longrightarrow HC{\equiv}C{\cdot}C{\equiv}C{\cdot}CH\overset{t}{=}CH{\cdot}CH_2{\cdot}OH}$$

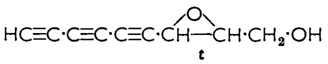
The aldehyde (III) was present in appreciable quantities only in the early stages of growth of the fungus, and the amount of the alcohol (IV) reached a maximum much later. The most plausible mode of biosynthesis of the triol (VI), which has the *erythro*-configuration, would be from the *trans*-alcohol (IV) by oxidation to the epoxide (V) and *trans*-

$$\mathrm{HO{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH\overset{t}{=}CH{\cdot}CH_2{\cdot}OH}\quad\text{(I)}$$

$$\mathrm{OHC{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH\overset{t}{=}CH{\cdot}CH_2{\cdot}OH}\quad\text{(II)}$$

$$\mathrm{HC{\equiv}C{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH\overset{t}{=}CH{\cdot}CHO}\quad\text{(III)}$$

$$\mathrm{HC{\equiv}C{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH\overset{t}{=}CH{\cdot}CH_2{\cdot}OH}\quad\text{(IV)}$$


(V)

$$\mathrm{HC{\equiv}C{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}\underset{t}{\overset{O}{CH{-}CH}}{\cdot}CH_2{\cdot}OH}\quad\text{(V)}$$

$$\underset{erythro}{\mathrm{HC{\equiv}C{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH(OH){\cdot}CH(OH){\cdot}CH_2{\cdot}OH}}\quad\text{(VI)}$$

opening of the ring to the *erythro*-triol (VI). An indication had been obtained of the presence of a relatively non-polar metabolite which might have been the epoxide; this component was slightly more polar than the alcohol (IV), but the ratio of the extinction coefficient at 2095 Å to that at 3095 Å of *ca.* 120 was much less than that ($\varepsilon_{2080}/\varepsilon_{3050} =$ *ca.* 700) for the triol (VI), suggesting the presence of a weakly chromophoric group adjacent to the triyne system. However, the amount of this metabolite was exceedingly small and a synthetic approach seemed to be both more promising and more interesting. Since only biogenetic arguments favoured the *trans*-structure for the epoxy-alcohol, it seemed prudent to synthesise both isomers of compound (V).

Until recently the only good method of obtaining the higher monosubstituted polyacetylenes was the dehydrohalogenation procedure:

$$\mathrm{R{\cdot}CHCl{\cdot}[C{\equiv}C]_{\mathit{n}}{\cdot}CH_2Cl \longrightarrow R{\cdot}[C{\equiv}C]_{\mathit{n}}{\cdot}C{\equiv}CH}$$

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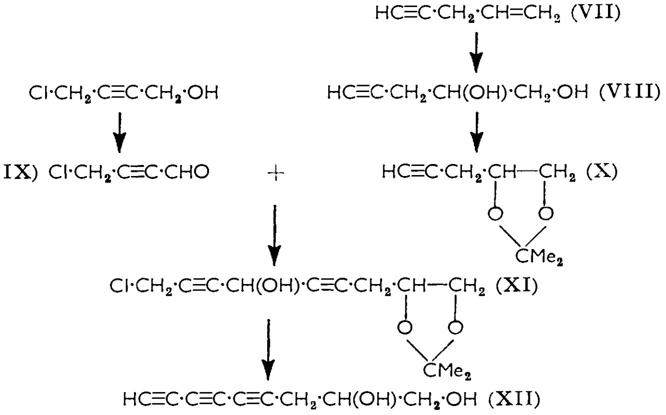
[1] Part XII, Gardner, Lowe, and Read, *J.*, 1961, 1532.

[2] Jones and Stephenson, *J.*, 1959, 2197.

[3] Bohlmann, Herbst, and Gleinig, *Chem. Ber.*, 1961, **94**, 948.

We now describe the application of this approach to the synthesis of nona-4,6,8-triyne-1,2-diol, a structure which had been proposed[4] for an antibiotic biformyne 1 (originally biformin [5]) isolated from *Polyporus biformis*, and subsequently to the preparation of the two stereoisomeric epoxy-alcohols (V). Since this work was completed an alternative route to monosubstituted hexatriynes, involving the coupling [6] of an excess of diacetylene, has been described.[3]

Pent-1-en-4-yne[11] (VII) was oxidised with performic acid to the diol (VIII), in which the hydroxyl groups were then protected as the isopropylidenedioxy-grouping (cf. X) during a Grignard reaction with chlorobutynal (IX). The chlorohydrin (XI) was converted into the 1,4-dichloro-compound with thionyl chloride and this was dehydrochlorinated at −35° with potassium ethoxide.

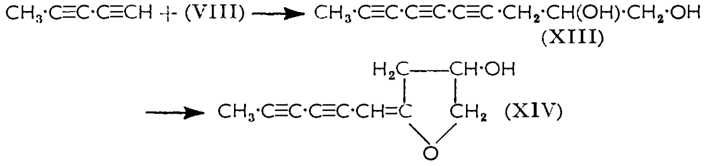


$HC{\equiv}C{\cdot}CH_2{\cdot}CH{=}CH_2$ (VII) $\rightarrow$ $HC{\equiv}C{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2{\cdot}OH$ (VIII) $\rightarrow$ $HC{\equiv}C{\cdot}CH_2{\cdot}\underset{O-CMe_2-O}{CH{-}CH_2}$ (X)

$Cl{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}OH$ $\rightarrow$ (IX) $Cl{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}CHO$ + (X) $\rightarrow$ $Cl{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}CH(OH){\cdot}C{\equiv}C{\cdot}CH_2{\cdot}\underset{O-CMe_2-O}{CH{-}CH_2}$ (XI) $\rightarrow$ $HC{\equiv}C{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2{\cdot}OH$ (XII)

The great instability of triynes with free ethynyl groups rendered the final purification of the triynediol difficult, and ultraviolet absorption had to be employed as the criterion of purity. Countercurrent distribution between ether and 20% methanol, ether–hexane and 20% methanol, and finally ether–hexane and water gave fractions which were spectroscopically pure, two maxima at 3040 and 3080 Å being clearly defined. Low-temperature crystallisation gave the diol (XII) as colourless needles, immediately becoming violet and then black on exposure to light. This synthesis was completed in 1956; a synthesis by the alternative route [3] has been described in the meantime. Differences between this diol and biformyne 1 are discussed below.

Opportunity was taken of the availability of the C_5 diol (VIII) to couple it with penta-1,3-diyne to give the homologous C_{10} diol (XIII). The diol had m. p. 110—113°, rapidly became violet in light, and with alkali gave the crystalline cyclic enol ether (XIV) (cf. ref. 2).



$CH_3{\cdot}C{\equiv}C{\cdot}C{\equiv}CH$ + (VIII) $\longrightarrow$ $CH_3{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2{\cdot}OH$ (XIII)

$\longrightarrow$ $CH_3{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH{=}C\langle\begin{smallmatrix}CH_2{-}CH{\cdot}OH\\ O{-}CH_2\end{smallmatrix}$ (XIV)

Condensation of the chloro-aldehyde (IX) with the tetrahydropyranyl ether (XVa) of *trans*-pentenynol gave a chlorohydrin which on treatment with thionyl chloride, dehydrohalogenation, and hydrolysis gave the *trans*-alcohol (XVIa), identical with the

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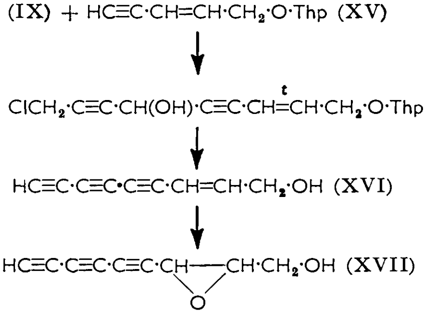
[4] Anchel, quoted by Bohlmann, *Angew. Chem.*, 1955, **67**, 389.

[5] Anchel and Cohen, *J. Biol. Chem.*, 1954, **208**, 319; cf. Anchel, in " Essays in Biochemistry," ed. Graff, 1956, Vol. I.

[6] Chodkiewicz, *Ann. Chim.* (*France*), 1957, **2**, 819.

natural material. (The synthesis of this alcohol by the alternative route[3] has been referred to above.) Treatment of the *trans*-alcohol (XVIa) with 0·3M-trifluoroperacetic acid and countercurrent purification gave the *trans*-epoxide (XVIIa). This proved to be identical with the non-polar metabolite in its infrared and ultraviolet absorption spectra, which are both highly characteristic. Distribution coefficients between light petroleum–benzene and water for the synthetic *trans*-epoxy-alcohol and the metabolite were identical. Both the natural and the synthetic compound reacted with alkali to give a species with the characteristic ultraviolet spectrum of the system $RO{-}\underset{|}{C}{=}CH{-}C{\equiv}C{-}C{\equiv}C{-}$; this cannot have involved direct intramolecular attack, which would give a *trans*-fused 5,3-bicyclic system, and so it must have proceeded *via* the triol (VI), giving the known hydroxy-enol ether (XVIII). In fact apparent rate-constants, identical for the two specimens, were somewhat lower than that for the cyclisation of the triol, as expected. The *trans*-epoxide was extremely unstable in the crystalline state; on two occasions, once in a desiccator and once while a sample was being weighed, the material exploded.

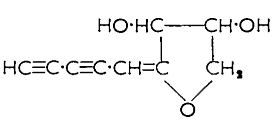


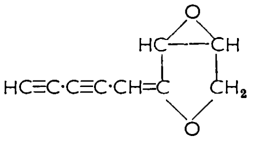
$$\text{(IX)} + HC{\equiv}C{\cdot}CH{=}CH{\cdot}CH_2{\cdot}O{\cdot}Thp \ \text{(XV)}$$
$$\downarrow$$
$$ClCH_2{\cdot}C{\equiv}C{\cdot}CH(OH){\cdot}C{\equiv}C{\cdot}CH\overset{t}{=}CH{\cdot}CH_2{\cdot}O{\cdot}Thp$$
$$\downarrow$$
$$HC{\equiv}C{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH{=}CH{\cdot}CH_2{\cdot}OH \ \text{(XVI)}$$
$$\downarrow$$
$$HC{\equiv}C{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}\underbrace{CH{-}CH}_{O}{\cdot}CH_2{\cdot}OH \ \text{(XVII)}$$

(In XV—XVII, a = *trans*, b = *cis*.) (Thp = tetrahydropyranol)

Use of the much less accessible *cis*-pentenynol[7] in the above synthesis led to the *cis*-alcohol (XVIb), purified with greater difficulty but shown by its infrared absorption to contain none of the *trans*-isomer (no bands at 1090 or 943 cm.$^{-1}$). This alcohol was very sensitive to trifluoroperacetic acid but from dilute solution (0·024M), the epoxide (XVIIb) was obtained in very small quantity. The ultraviolet spectrum of the epoxide was identical with that of the *trans*-isomer, but its infrared spectrum was quite different. It reacted almost instantaneously with alkali, giving a product that had the same ultraviolet spectrum as the ether (XVIII) but was much less polar and so was presumed to have structure (XIX). The identity of the ultraviolet absorption of compounds (XVIII) and (XIX) is not unexpected as the bathochromic effect of the allylic epoxide would be sterically inhibited.

(XVIII)





(XIX)

Biformyne 1.—The crucial properties of biformyne 1 are its biological activity and its ultraviolet absorption spectrum; the latter is clearly defined only on samples purer than those originally described. The authentic spectrum was obtained only after the synthetic work on the diol (XII) was complete and differs unmistakably from that of a simple mono- or di-substituted triyne and from that of the synthetic diol.

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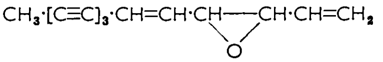
[7] Bell, Jones, and Whiting, *J.*, 1957, 2597

As small quantities of a strongly absorbing impurity can complicate such comparisons, the antibiotic properties of the diol (XII) and those of biformyne 1, against a range of bacteria and fungi, were examined by Dr. Anchel in 1957 and revealed marked differences, the diol exhibiting generally only one-hundredth of the activity of the natural material.

All the evidence available on the chemistry of biformyne 1 is explicable on structure (V), if the hydrogenolysis of the propargylic C–O bond is assumed.[8] The ultraviolet and infrared spectra are identical and the antibiotic activities of biformyne 1 and the (±)-epoxy-alcohol (V) are closely similar. Moreover, treatment of both the natural and the synthetic material with alkali, and with sulphuric and hydrochloric acid brought about identical changes in light absorption. Rates for the reaction with 0·8N-sodium hydroxide were identical within experimental error.

The polyacetylenic epoxide (V) is the first to be established as a fungal metabolite. Bohlmann and his colleagues,[9,10] however, have now isolated five such epoxides from plants of the *Compositae* family and it seems likely that epoxidation of the ethylenic bonds in polyenynes is a standard metabolic process. As with the *trans*-alcohol (IV) and the *trans*-epoxide (V), Bohlmann and Jastrow[10] have demonstrated the co-occurrence of the all-*trans*-hydrocarbon (XX) and the *trans*-pontica epoxide (XXI), the oxidation of the latter to (+)-*trans*-ethylene oxide dicarboxylic acid proving its absolute configuration and suggesting its production from (XX) by enzymic epoxidation.

(XX) $CH_3\cdot[C\equiv C]_3\cdot CH=CH\cdot CH=CH\cdot CH=CH_2$



$CH_3\cdot[C\equiv C]_3\cdot CH=CH\cdot \underbrace{CH—CH}_{O}\cdot CH=CH_2$ (XXI)

EXPERIMENTAL

Ultraviolet absorption spectra were measured for ethanol solutions, unless otherwise stated (chromatographic and distribution fractions were examined directly), on a Cary recording spectrophotometer model 14 M. Infrared absorption spectra were obtained on a Perkin-Elmer model 21 spectrophotometer, and m. p.s (corrected) determined on a Kofler block. Alumina for chromatography was Peter Spence's grade " H," deactivated by treatment with 5% of 10% acetic acid. Light petroleum refers to a fraction with b. p. 60—80°. Evaporations were done under reduced pressure in nitrogen. Crystallisations of poly-ynes were carried out in a cold room (−9°) in red light.

trans-2,3-*Epoxynona*-4,6,8-*triyn*-1-*ol* (V) *from* Coprinus quadrifidus (*with* R. E. Bew).—An accumulated stock of non-polar material in light petroleum (160 c.c.; b. p. 40—60°) was distributed in equal proportions together with an equal volume of water in the first 4 tubes of a 120-plate Craig countercurrent apparatus, and 80 transfers were carried out. Material with triyne absorption was concentrated in tubes 13—27 and when isolated (*ca.* 400 mg. estimated spectrographically) by means of ether showed $\lambda_{max.}$ 2070, 2480, 2540, 2600, 2740, 2905, and 3100 Å. The ethereal solution was concentrated to *ca.* 8 c.c. at −9° in red light and hexane was added just to cloudiness. Cooling to −40° gave colourless crystals which darkened rapidly even under these conditions. The mother-liquors were removed, the crystals were kept at 1 mm. at −9° for 5 min. and then used for the following determinations: partition coefficient between light petroleum–benzene (3 : 1) and water (20°) = 2·0 (cf. ~1·0 quoted earlier[3] on impure material); $\lambda_{max.}$ (after a sample had exploded whilst weighing, concentrations were determined by subsequent evaporation of the ethanolic solution used) 2090 (ε 99,000), 2450 (ε 725), 2585 (ε 730), 2740 (ε 890), 2905 (ε 1000), and 3100 Å (ε 695); $\nu_{max.}$ 3509, 3236, 1087, 1064, 1010, 903, 874, 843, and 752 cm.$^{-1}$.

Pent-4-*yne*-1,2-*diol* (VIII).—To a mixture of pent-1-en-4-yne[11] (28·3 g.; b. p. 41—42°, n_D^{17} 1·4113) and formic acid (220 c.c.) were added 100-vol. hydrogen peroxide (65 g.) and

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[8] For examples see Anet, Lythgoe, Silk, and Trippett, *J.*, 1953, 309; Ashworth, Jones, Mansfield, Schlögl, Thompson, and Whiting, *J.*, 1958, 951.

[9] Bohlmann, Arndt, and Bornowski, *Chem. Ber.*, 1960, **93**, 1937; Bohlmann, Sucrow, Jastrow, and Koch, *ibid.*, 1951, **94**, 3179; Bohlmann, Arndt, Bornowski, Jastrow, and Kleine, *ibid.*, 1962, **95**, 1320, and personal communication from Professor F. Bohlmann.

[10] Bohlmann and Jastrow, *Chem. Ber.*, 1962, **95**, 1742.

[11] Paul and Tchelitcheff, *Compt. rend.*, 1951, **233**, 1116.

sufficient ether to give a homogeneous solution. The temperature was kept at 30° by external cooling and the mixture was then left at 20° overnight. The mixture was made alkaline by the addition, with cooling, of pellets of sodium hydroxide and the product, isolated after 24 hr. by continuous ether-extraction, on distillation gave the *diol* (27·8 g.), b. p. 66—68°/0·2 mm., n_D^{17} 1·4788 (Found: C, 59·9; H, 8·0. $C_5H_8O_2$ requires C, 60·0; H, 8·1%). The *bis*-3,5-*dinitrobenzoate* was obtained as pale yellow plates (from chloroform), m. p. 132—139° (Found: C, 46·7; H, 2·6; N, 11·6. $C_{19}H_{12}N_4O_{12}$ requires C, 46·7; H, 2·5; N, 11·5%).

2,2-*Dimethyl*-4-*prop*-2′-*ynyl*-1,3-*dioxalan* (X).—Pent-4-yne-1,2-diol (34 g.) and toluene-*p*-sulphonic acid (1·4 g.) were dissolved in a mixture of acetone (175 c.c.) and light petroleum (105 c.c.; b. p. 40—60°) and heated under a column packed with glass helices and fitted with a constant-reflux water separator, for 26 hr. Freshly fused sodium acetate (1·4 g.) was added to the cooled solution which was stirred for ½ hr. and filtered. Removal of solvent and distillation gave 2,2-*dimethyl*-4-*prop*-2′-*ynyl*-1,3-*dioxalan* (90%), b. p. 60—62°/20 mm., n_D^{20} 1·4351 (Found: C, 68·6; H, 8·5. $C_8H_{12}O_2$ requires C, 68·5; H, 8·6%).

4-*Chlorobut*-2-*ynal* (IX).—8N-Chromic acid (43 c.c.) was added dropwise with stirring and cooling to 4-chlorobut-2-yn-1-ol [12] (20 g.) in acetone (190 c.c.) and water (10 c.c.). The product was isolated by means of ether, and the neutral portion (after filtration through alumina of a light petroleum–benzene solution) on distillation gave the aldehyde (4·2 g.), b. p. 52—56°/19 mm., n_D^{17} 1·4979, followed by unoxidised alcohol (5·2 g.). Redistillation gave pure 4-*chlorobut*-2-*ynal* as a colourless lachrymatory liquid, b. p. 57°/14 mm., n_D^{15} 1·4981 (Found: C, 46·7; H, 3·4. C_4H_3ClO requires C, 46·9; H, 2·95%), which became yellow on distillation and rapidly darkened unless stored at −40°. Two 2,4-*dinitrophenylhydrazones* were obtained which could be separated by crystallisation from methanol. The *syn*-isomer (more soluble) formed orange plates, m. p. 117—120° (Found: C, 42·7; H, 2·5. $C_{10}H_7ClN_4O_4$ requires C, 42·8; H, 2·5%), $\lambda_{max.}$ 2050, 2450, and 3550 Å. The *anti*-isomer was obtained as orange-brown plates, m. p. 166—170° (decomp.) (Found: C, 43·0; H, 2·6%), $\lambda_{max.}$ 2020, 2270, and 3620 Å.

Nona-4,6,8-*triyne*-1,2-*diol* (XII).—The above dioxalan (8 g.) in anhydrous tetrahydrofuran (10 c.c.) was added dropwise with stirring to a solution of n-propylmagnesium chloride (from magnesium, 1·1 g.) in tetrahydrofuran (20 c.c.). The mixture was stirred for 1½ hr. and 4-chlorobut-2-ynal (4·5 g.) in tetrahydrofuran (5 c.c.) was added dropwise with cooling. After 2 hr. at 0° the complex was decomposed with saturated ammonium chloride solution, the product was isolated by means of ether, and on evaporation a dark oil was obtained. This was extracted thoroughly with light petroleum (b. p. 40—60°) and passed down a column of alumina (150 g.), elution being continued until no more material came off the column. Elution now with benzene yielded an oil (5·25 g.), which rapidly became reddish-brown but showed no infrared bands at 3300 and 1680 cm.$^{-1}$ associated with the starting materials.

A mixture of this chloro-alcohol (5·8 g.) and thionyl chloride (4 c.c.) in ether (20 c.c.) was kept at 0° for 3 hr. The solvent and the excess of thionyl chloride were then removed at 20 mm. and the residue was thoroughly extracted with light petroleum. The solution was filtered through a column of alumina, and elution with the same solvent and evaporation gave an unstable oil (3·2 g.). This was dissolved in ethanol (50 c.c.) and dehydrochlorinated by being added dropwise to a stirred solution of potassium ethoxide (from potassium, 7·5 g.) in ethanol (150 c.c.) at −30° to −40°. After 25 minutes' stirring a 1 : 1 mixture (40 c.c.) of ethanol and concentrated hydrochloric acid was slowly added, the whole was kept at −5° overnight, potassium chloride was removed by filtration and thoroughly washed with ether, and the ethereal washings were combined with the ethanol filtrate.

The crude triynediol was isolated by means of ether and then purified by countercurrent distribution in a 50-tube apparatus (volume of phases, 40 c.c.). In the first distribution between ether and water–methanol (4 : 1), after 50 tranfers spectroscopic examination of the ether layers revealed that the triyne occupied tubes 35—50. After isolation by means of ether and filtration through alumina to remove polymeric material a second distribution was effected between ether–hexane (1 : 1) and water–methanol (1 : 4). 90 transfers were effected and the triyne was found to be concentrated in tubes 22—38, while material with maxima at 2070, 2180, 2400, 2530, 2670, and 2830 Å was present in tubes 16—21. Isolation was again effected in ether, and the product was then distributed between ether–hexane (1 : 1) and water. After 120 transfers, 70 fractions being collected, the triyne was present in tubes 40—50 and

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[12] Bailey and Fujiwara, *J. Amer. Chem. Soc.*, 1955, **77**, 165.

fractions 64—70, some fractions being almost spectroscopically pure with the twin maxima at 3040 and 3080 Å clearly discernible. The triynediol fractions were combined and spectroscopic assay indicated that *ca.* 100 mg. of the desired product were present. Concentrating the solution, in red light in a cold room at −9°, gave needles and these were recrystallised from ether–hexane by cooling in solid carbon dioxide–acetone. The nona-4,6,8-triyne-1,2-diol separated as colourless needles but on filtration became violet almost immediately and rapidly darkened further. Ultimate analysis was not attempted but the triynediol is well characterised by its ultraviolet absorption (the extinction coefficient was measured by evaporating an aliquot part to dryness and weighing the polymeric residue), $\lambda_{\text{max.}}$ 2070 (ε 210,000), 2410 (ε 175), 2540 (ε 275), 2570 (ε 275), 2690 (ε 380), 2780 (ε 280), 2850 (ε 300), 3040 (ε 155), and 3080 Å (ε 150), $\lambda_{\text{infl.}}$ 2710 (ε 360) 2870 (ε 255), and 2950 Å (ε 115).

On treatment of the nonatriynediol (*ca.* 1 mg.) in methanol (10 c.c.) with 5% sodium hydroxide solution (10 c.c.), isomerisation occurred to give material with intense maxima at 2170, 2240, 2660, 2790, and 2940 Å.

Deca-4,6,8-*triyne*-1,2-*diol* (XIII).—To a solution of cuprous chloride (12·5 g.) and ammonium chloride (20 g.) in water (65 c.c.) were added pent-4-yne-1,2-diol (1 g.) and penta-1,3-diyne (2·55 g.) together with enough ethanol for homogeneity. The solution was shaken in oxygen until absorption ceased (20 min.) and the mixture was extracted continuously with ether. The solid product was extracted with ether–benzene (1 : 2), leaving a violet polymeric residue. The solution was passed down a column of alumina, elution was effected with the same solvent mixture, and, after some deca-2,4,6,8-tetrayne, the *glycol* was eluted. Recrystallisation from benzene–light petroleum gave plates, m. p. 110—113°, rapidly becoming violet in light (Found: C, 73·9; H, 6·2. $C_{10}H_{10}O_2$ requires C, 74·05; H, 6·2%), $\lambda_{\text{max.}}$ 2100 (ε 165,000), 2395 (ε 140), 2500 (ε 210), 2520 (ε 280), 2630 (ε 260), 2670 (ε 170), 2790 (ε 235), 2900 (ε 235), and 3100 Å (ε 150), $\lambda_{\text{infl.}}$ 2720 (ε 215), 2870 (ε 195), 2960 (ε 135), and 3070 Å (ε 145).

2-(*Hexa*-2,4-*diynylidene*)*tetrahydro*-4-*hydroxyfuran* (XIV).—A solution of the above triynediol (237 mg.) and sodium hydroxide (1 g.) in an air-free mixture of water (20 c.c.) and methanol (20 c.c.) was kept in nitrogen at 20° for 21 hr. by which time the absorption at 2770 Å had become constant. Isolation by means of ether gave a solid (232 mg.), m. p. 95—109°, which was adsorbed from benzene on a column of grade " H " alumina (15 g.). Elution with ether–benzene (1 : 4) gave fractions containing material, m. p. *ca.* 90—95° and then fractions of material (46 mg.), m. p. 110—113°, which on crystallisation from benzene–light petroleum gave the isomerisation *product* (XIV) as silky needles, m. p. 113—114° (Found: C, 74·0; H, 6·2. $C_{10}H_{10}O_2$ requires C, 74·05; H, 6·2%), $\lambda_{\text{max.}}$ 2170 (ε 22,500), 2240 (ε 30,000), 2650 (ε 13,000), 2780 (ε 18,500), and 2935 Å (ε 15,000), $\nu_{\text{max.}}$ 1650 cm.$^{-1}$ (vinyl ether).

trans-9-*Chloro*-1-*tetrahydropyranyloxynon*-2-*ene*-4,7-*diyn*-6-*ol*.—A solution of *trans*-1-tetrahydropyranyloxypent-2-en-4-yne (5·0 g.; b. p. 47°/0·15 mm., n_D^{18} 1·4889) in tetrahydrofuran (5 c.c.) was added during ½ hr. at 20° to a solution of n-propylmagnesium chloride (from ammonium, 0·8 g.) in tetrahydrofuran (20 c.c.). The mixture was then stirred for 1 hr. after which 4-chlorobut-2-ynal (3·1 g.) in tetrahydrofuran (5 c.c.) was added during ½ hr. at 0°. After being stirred at 0° for a further 2 hr. the mixture was treated with ice-cold saturated ammonium sulphate solution and extracted with ether (4 × 100 c.c.). Evaporation of the dried ethereal solution gave an oil (7·4 g.) which was adsorbed from light petroleum–benzene (1 : 1; 20 c.c.) on deactivated alumina (100 g.). Elution with the same solvent mixture (200 c.c.) afforded starting materials, then benzene–ether (9 : 1; 600 c.c.) gave the *chloro-alcohol* which for analysis was distilled at 135° (bath temp.)/5×10^{-4} mm. (Found: C, 62·7; H, 6·1. $C_{14}H_{17}ClO_3$ requires C, 62·55; H, 6·4%); it had $\lambda_{\text{max.}}$ 2285 Å.

trans-*Non*-2-*ene*-4,6,8-*triyn*-1-*ol* (XVIa).—A solution of the above chloro-alcohol (4·5 g.) in ether (100 c.c.) was treated at 0° with pyridine (1·7 g.) and thionyl chloride (1·25 c.c.) in ether (50 c.c.). The mixture was kept at 20° for 3 hr. with occasional swirling and then poured carefully into sodium hydrogen carbonate solution. The ethereal solution was washed with sodium hydrogen carbonate solution and water, dried, and evaporated at 20 mm. to give the dichloro-compound (4·1 g.) as a yellow oil, which darkened rapidly in light and was not further characterised. Its solution in ethanol (150 c.c.) was added dropwise to potassium ethoxide (potassium, 3 g., in dry ethanol, 150 c.c.) at −40°. After 30 min. the solution exhibited a relatively broad ultraviolet absorption maximum at 2260 Å, presumably due to an intermediate, since when the temperature was allowed to rise to −15° normal enetriyne absorption appeared. After 2 hr. the mixture was poured into water, and the product was extracted with light petroleum and filtered through deactivated alumina (50 g.). Light petroleum (1100 (c.c. eluted material containing the expected tetrahydropyranyl ether (*ca.* 250 mg. according to spectroscopic estimate). The solution was evaporated to 40 c.c., more light petroleum being removed after the addition of methanol (50 c.c.). The mixture was acidified with 25% methanolic sulphuric acid (10 c.c.), kept at 20° in darkness for 1 hr., and then poured into a large volume of water, the alcohol (II) being isolated with ether. The ethereal solution was evaporated to small bulk, water (80 c.c.) and light petroleum (100 c.c.) were added, and the evaporation was continued to remove the remaining ether. The organic phase was made up to 80 c.c. with light petroleum, and the material placed in the first 2 tubes of a 50-tube counter-current apparatus (volume of phases 40 c.c.) and partitioned between light petroleum and water. After 73 transfers the contents of tubes 30—50 were combined to give pure *trans*-non-2-ene-4,6,8-triyn-1-ol (XVIa) (112 mg.), identical (distribution coefficient, infrared, and ultra-violet absorption) with the natural material.

$\lambda_{\text{max.}}$	2280	2400	2570	2710	2870	3060	3270 Å
$10^{-3}\varepsilon$: natural	60·5	86·5	3·05	6·5	13	17	12·5
synthetic......	64	89·5	4·05	8·3	15	19·5	12·5

trans-2,3-*Epoxynona*-4,6,8-*triyn*-1-*ol* (XVIIa).—A solution of trifluoroperacetic acid [from trifluoroacetic anhydride (1·7 c.c.) and 90% hydrogen peroxide (0·28 c.c.) in methylene dichloride (25 c.c.)] was added to a stirred mixture of the above alcohol (94 mg.) and disodium hydrogen phosphate (5 g.) in methylene dichloride (20 c.c.). After 20 min., when the absorption at 3275 Å (starting material) had almost disappeared, water was added and the mixture stirred for a further 5 min. The aqueous layer was extracted with ether and the combined ether and methylene dichloride extracts were dried and evaporated, benzene being added during the evaporation. The product was adsorbed from benzene (50 c.c.) on deactivated alumina. Elution with benzene–ether (19 : 1, 100 c.c.) gave a small amount of starting material. Continued elution with the same solvent mixture (100 c.c.) afforded the *trans*-epoxide (XVIIa; 60 mg. estimated spectroscopically). The solvent was removed under reduced pressure at −9° in red light and the product was crystallised (needles) twice from ether–hexane; it had $\lambda_{\text{max.}}$ 2095 (ε 82,500), 2455 (ε 390), 2590 (ε 630), 2740 (ε 890), 2910 (ε 910), and 3095 Å (ε 580), $\nu_{\text{max.}}$ 3550, 3290, 1085, 1065, 903, 873, 843, and 753 cm.$^{-1}$. With this synthetic material it was observed that, although the pure epoxide is extremely unstable in the crystalline state, larger crystals seemed to be the more stable and these if quickly heated lost their birefringence at *ca.* 40°.

Treatment of the *trans*-epoxide with 2N-aqueous sulphuric acid for 2 hr. at 20° gave (±)-triol (VI), $\lambda_{\text{max.}}$ 2080, 2540, 2695, 2865, and 3050 Å, $E_{2080}/E_{3050} = 550$ [cf. pure (−)-triol $E_{2080}/E_{3050} = 717$). Partition coefficient between ether and water (21°), 1·15 [cf. (−)-triol, 1·2].

cis-1-*Tetrahydropyranyloxypent*-2-*en*-4-*yne* (XVb).—Phosphorus oxychloride (50 mg.) was carefully added to *cis*-pent-2-en-4-yn-1-ol [7] (3·35 g.) and dihydropyran (4·0 g.), the mixture being cooled in ice. After 2·5 hr. at 20° aqueous sodium hydroxide was added, isolation with ether and distillation then giving the *tetrahydropyranyl ether* (5·8 g.), b. p. 73—75°/0·04 mm., n_D^{17} 1·5861 (Found: C, 72·6; H, 8·7. $C_{10}H_{14}O_2$ requires C, 72·3; H, 8·5%), $\lambda_{\text{max.}}$ 2220 Å (ε 12,800), $\nu_{\text{max.}}$ 3290, 2940, and 2100 cm.$^{-1}$.

cis-*Non*-2-*ene*-4,6,8-*triyn*-1-*ol* (XVIb).—A solution of *cis*-1-tetrahydropyranyloxypent-2-en-4-yne (3·4 g.) in tetrahydrofuran (5 c.c.) was added during ½ hr. at 20° to a solution of n-propylmagnesium chloride [from magnesium (0·6 g.) in tetrahydrofuran (20 c.c.)]. After a further 1 hr. 4-chlorobut-2-ynal (2·2 g.) in tetrahydrofuran (5 c.c.) was added during 30 min. at 0°, and the mixture was left at 0° for a further 2 hr. Ice-cold saturated ammonium sulphate was then added, the mixture extracted with ether, and the ethereal solution dried and evaporated. The resulting yellow oil (4 g.) was adsorbed from light petroleum–benzene (2 : 1, 15 c.c.) on to alumina (100 g.). A fraction (2·6 g.), eluted with light petroleum–benzene (1 : 1; 200 c.c.), consisted of starting materials. Ether–benzene (9 : 1; 200 c.c.) eluted the crude *cis*-chloro-alcohol (1 g.), $\lambda_{\text{max.}}$ 2290 Å.

Chlorination of the *cis*-chloro-alcohol (0·9 g.) under the conditions employed for the *trans*-isomer gave a product (550 mg.) which was dissolved in ethanol (20 c.c.) and added at −40° to a solution of potassium (3 g.) in ethanol (100 c.c.). The temperature was then allowed to rise to 20°; after 2 hr. the solution was diluted with water, and the product isolated with ether.

The crude enetriyne was adsorbed from light petroleum (20 c.c.) on to alumina (50 g.). Elution with the same solvent (300 c.c.) gave the *cis*-tetrahydropyranyl ether contaminated with material having strong ultraviolet absorption with $\lambda_{\text{max.}}$ 3200 Å. After removal of the tetrahydropyranyl ether protecting group as before, the material was distributed (50 transfers, volume of phases 40 c.c.) between light petroleum and water. The enetriynol was present in tubes 20—34, but impurities with general ultraviolet absorption were still present (in contrast to the purification of the *trans*-isomer). The material was adsorbed from light petroleum–benzene (1 : 1; 30 c.c.) on alumina (180 g.) and elution with benzene–ether (97 : 3; 250 c.c.) gave the *cis*-non-2-ene-4,6,8-triyn-1-ol (XVIb) (17 mg., estimated spectroscopically), $\lambda_{\text{max.}}$ 2050, 2100, 2285, 2395, 2565, 2710, 2875, 3060, and 3270 Å, $\nu_{\text{max.}}$ 3550, 3250, 3010, 2900, 1025, and 730 cm.$^{-1}$. Distribution coefficient between hexane and water (17°), 1·16.

cis-2,3-*Epoxynona*-4,6,8-*triyn*-1-*ol* (XVIIb).—A solution of *cis*-non-2-ene-4,6,8-triyn-1-ol (15 mg.) in methylene dichloride (50 c.c.) was treated at 20° with a solution of trifluoroperacetic acid [from trifluoroacetic anhydride (0·28 c.c.) and 90% hydrogen peroxide (0·05 c.c.) in methylene dichloride (4 c.c.)]. After 2 hr. the solution ($\lambda_{\text{max.}}$ 2590, 2750, 2930, and 3110 Å) was washed with aqueous sodium thiosulphate and sodium hydrogen carbonate and it now showed strong absorption in the 2800 Å region. The crude epoxide was adsorbed from light petroleum–benzene (1 : 1; 100 c.c.) on alumina (100 g.), and elution with the same solvent gave a fraction with $\lambda_{\text{max.}}$ 2820 Å (probably a cyclisation product). Benzene–ether (9 : 1; 200 c.c.) eluted the expected product (7 mg.; estimated spectroscopically) which was rechromatographed on alumina (30 g.) and eluted with benzene–ether (9 : 1; 100 c.c.) to give the pure *cis*-epoxide as very unstable crystals, $\lambda_{\text{max.}}$ 2095, 2450, 2590, 2745, 2910, and 3105 Å, $E_{2095}/E_{3105} = 134$, $\nu_{\text{max.}}$ 3540, 3270, 1038, 893, 820, and 778 cm.$^{-1}$. Distribution coefficient between light petroleum and water (24°), 0·03. After treatment with base the distribution coefficient (light petroleum–water at 24°) became 1·8.

Comparison of the Cyclisation Rates on Alkali Treatment.—Samples of the (−)-triyne-triol (VI), (±)-triol (VI), synthetic *trans*- and *cis*-epoxide (XVIIa and b), and the natural epoxide were used. Cyclisations were carried out with 0·8N-sodium hydroxide in ethanol–water (1 : 4) at 21°, the rates of the reactions being followed by measuring the high-intensity absorption appearing at 2800 Å. Values of log $E_f/E_f - E_t$ (where E_f = final E_{2800} reached and $E_t = E_{2800}$ after time *t*) were computed.

Values of log $[E_f/(E_f - E_t)]$.

t (min.)	(−)-Triol (VI)	(±)-Triol (VI)	*trans*-Epoxide	*cis*-Epoxide	Natural epoxide
3	0·375	0·33			
4	0·45		0·31	Immeasurably	0·31
5	0·52	0·53	0·35	fast	0·36
6			0·42		0·46
10	0·98	0·93	0·61		0·75
15	1·5	1·6	0·98		1·1
k (min.$^{-1}$)	0·22	0·22	0·145	∞	0·16

When cyclisation was complete the products were isolated with ether and showed identical absorption maxima (2660, 2790, and 2930 Å in ether).

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THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY.

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