

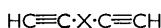
## 182. Macrocyclic Acetylenic Compounds. Part I. cycloTetradeca-1 : 3-diyne and Related Compounds.

By G. EGLINTON and A. R. GALBRAITH.

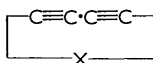
A high-dilution modification of the conventional Glaser procedure for the oxidative coupling of ethynyl compounds has been used in the synthesis of new macrocyclic systems containing the  $\alpha\gamma$ -diyne unit, notably the hydrocarbons *cyclotetradeca-1 : 3-diyne* (IIa;  $n = 10$ ) and *cyclooctacos-1 : 3 : 15 : 17-tetrayne* (IIIa;  $n = 10$ ), and the macrolides (IIb and IIIb).

In a preliminary announcement,<sup>1a</sup> we reported the synthesis of a number of macrocyclic compounds containing the  $\alpha\gamma$ -diyne unit. The present paper gives a full account of this work and of more recent results. Sondheimer and his collaborators<sup>1b</sup> have described independent studies which have also led to cyclic  $\alpha\gamma$ -dienes.

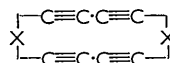
Medium-sized carbocyclic compounds containing an acetylenic linkage are well known,<sup>2</sup> *cyclooctyne* being the smallest so far obtained. However, at the commencement of these researches, no cyclic  $\alpha\gamma$ -diyne had been described, though such compounds would be of particular interest for the study of the correlations of their physical and chemical properties with the degree of ring strain. Further, the presence of other groups within the ring would introduce the possibility of transannular phenomena.



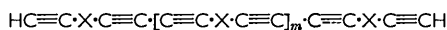
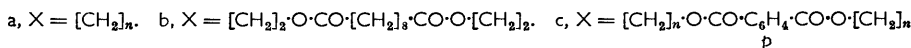
(I)



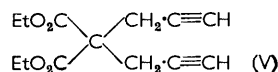
(II)



(III)



(IV)



(V)

Although ethynyl compounds and their derivatives have been coupled in other ways<sup>3,4</sup> the obvious approach to systems of type (II) is clearly the oxidative coupling of  $\alpha\omega$ -diethynyl compounds (I); this reaction has been extensively employed<sup>3</sup> in the synthesis of

<sup>1</sup> (a) Eglinton and Galbraith, *Chem. and Ind.*, 1956, 737; (b) Sondheimer, Amiel, and Wolovsky, *J. Amer. Chem. Soc.*, 1957, **79**, 4247 and preceding papers.

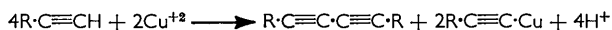
<sup>2</sup> Blomquist *et al.*, *J. Amer. Chem. Soc.*, 1951, **73**, 5510; 1952, **74**, 3636, 3643; 1953, **75**, 2153; Prelog *et al.*, *Helv. Chim. Acta*, 1952, **35**, 1598; 1953, **36**, 471; 1955, **38**, 1776, 1786; Cram *et al.*, *J. Amer. Chem. Soc.*, 1955, **77**, 4090; 1956, **78**, 2518; Epstein and Marszak, *Compt. rend.*, 1956, **243**, 283.

<sup>3</sup> Raphael, "Acetylenic Compounds in Organic Synthesis," Butterworths, London, 1955.

<sup>4</sup> Chodkiewicz, *Ann. Chim. (France)*, 1957, **2**, 819; Cadiot and Chodkiewicz, *Compt. rend.*, 1957, **245**, 1634.

acyclic  $\alpha\gamma$ -diynes,  $2R\cdot C\equiv CH \longrightarrow R\cdot C\equiv C\equiv C\cdot R$ , normally by agitating a suspension of the ethynyl compound in a mixture of cuprous chloride, ammonium chloride, and water in air or oxygen: water-soluble ethynyl compounds, *e.g.*,  $HC\equiv C\cdot CMe_2\cdot OH$ , couple rapidly and almost quantitatively, whereas water-insoluble compounds, *e.g.*, alk-1-yne, frequently do so only with difficulty.<sup>5</sup>

The mechanism of this reaction has received serious attention only recently. In 1955, Baxendale and Westcott<sup>6</sup> showed that cupric ion is the oxidising agent; with stoichiometric quantities of cupric ion in an aqueous medium buffered to pH 6 to avoid inhibition of the reaction by developing acidity, the  $\alpha\gamma$ -diyne was rapidly formed in 50% yield, the remainder of the ethynyl compound being converted into the insoluble cuprous derivative:



The latter is then available for slow oxidation to the  $\alpha\gamma$ -diyne by excess of cupric ion, oxygen, or other oxidising agent, giving the overall reaction:



For successful cyclisation of  $\alpha\omega$ -diynes the coupling should be in homogeneous solution under high-dilution conditions, in order to avoid the formation of much polymer (IV) and of insoluble cuprous salts. The formation of cyclic products might be further assisted by the rigid nature of the four-atom system  $C-C\equiv C-H$ , which would reduce the number of possible molecular conformations.<sup>7</sup>

A solvent capable of retaining in solution the ethynyl compound, some form of cupric ion, and the intermediate cuprous derivative was found with anhydrous cupric acetate in methanol-pyridine. The pyridine-cupric ion complex appeared to be solvated by the methanol, rendering possible extensive dilution with the ether used as the entraining agent in the high-dilution apparatus. The pyridine also served to remove the acetic acid liberated in the coupling reaction. These experiments were conducted with the readily available 2-methylbut-3-yn-2-ol and phenylacetylene. Virtually quantitative yields of the highly crystalline  $\alpha\gamma$ -diynes were obtained by using catalytic quantities of the cupric ion in solution and continuously oxidising the soluble cuprous derivative in a stream of oxygen. However, for general preparative purposes, it was more convenient to use excess of the reagent. Only occasionally was the formation of a small amount of reddish-brown precipitate (presumably cuprous derivative) observed, and the reaction mixtures were otherwise homogeneous. Solutions of ferric and cobaltic salts and of strongly complexed cupric ion (salicylate and ethylenediamine complexes) were ineffective.

The reagent was now employed in the cyclisation of an  $\alpha\omega$ -diyne, the intention being either to add the substance at a rate such that it underwent immediate reaction or, less satisfactorily, to continue reaction until ethynyl groupings would be no longer detectable. The sebacic diester (Ib) proved to be readily accessible, stable and highly crystalline and, from an examination of models, the derived cyclic monomer (IIb) appeared to be strainless. Slow entrainment of the ester in refluxing solvent evidently resulted in satisfactory high-dilution conditions during the oxidative coupling, as the product appeared to consist largely of the cyclic monomer (IIb), m. p. 54-5°, which was readily isolated in 63% yield.\* In another experiment, the cyclic dimer (IIIb), m. p. 109-110°, was also obtained, in about 2% yield. The structures were inferred from the method of preparation, and from analyses, light-absorption characteristics, and Rast molecular-weight determinations. Although suitable reference substances were not available to allow of proof by hydrogenation, it is clear that these colourless, highly crystalline substances provided the first

\* The terms "monomer," "dimer," etc., are here used to denote the cyclic compounds  $\left[ \begin{array}{c} C \\ | \\ C \\ | \\ C \\ | \\ C \end{array} \cdot X \cdot C \equiv C \right]_n$  derived from the true acyclic monomer  $HC\equiv C\cdot X\cdot C\equiv CH$ .

<sup>5</sup> Bowden, Heilbron, Jones, and Sargent, *J.*, 1947, 1579; Salkind and Fundyler, *Ber.*, 1936, 69, 128.

<sup>6</sup> Baxendale and Westcott, personal communication.

<sup>7</sup> Baker, McOmie, and Ollis, *J.*, 1951, 200.

examples of macrocycles containing the  $\alpha\gamma$ -diyne unit. The conventional cuprous chloride-ammonium chloride procedure for coupling gave only starting material and polymer.

The synthesis of a *cycloalka-1:3*-diyne (IIa), the ring size of which would allow of proof by hydrogenation to a known *cycloalkane*, was next attempted. From consideration of "Catalin" models, *cyclotetradeca-1:3*-diyne (IIa;  $n = 10$ ) was chosen in the belief that the chain of ten methylene units would be long enough to allow the ring to be reasonably free from strain. Tetradeca-1:13-diyne (Ia;  $n = 10$ ), m. p. 33—34°, readily obtained from decamethylene dibromide and sodium acetylide in liquid ammonia at 20°, coupled much more slowly than the ester (Ib): it was adequate and convenient to put the substance aside, in a large volume of the reagent for several days. The crude product (*ca.* 50% yield) appeared to be largely cyclic (absence of ethynyl absorption at 3300  $\text{cm}^{-1}$ ) and was separated by chromatography into monomer (IIa;  $n = 10$ ), m. p. 18°, and the dimer (IIIa;  $n = 10$ ), m. p. 101—102°. These structures followed unambiguously from the analytical data and light-absorption characteristics and from the identity of the fully hydrogenated hydrocarbons with *cyclotetradecane* and *cyclooctacosane* respectively. *cycloTetradeca-1:3*-diyne was generally the chief product, though the yield (17—40%) varied according to the degree of dilution. Liquid at room temperature, the hydrocarbon rapidly reddened in air with the simultaneous appearance of carbonyl absorption at 1735  $\text{cm}^{-1}$ . This instability is probably associated with ring strain as the corresponding dimer was much more stable.

Three esters (Ic;  $n = 1, 2$ , and 4) were next prepared and intramolecular couplings attempted. It was hoped that a suitable cyclic monomer might exhibit some abnormalities<sup>1b</sup> resulting from transannular interaction, particularly between the benzene ring and the  $\alpha\gamma$ -diyne unit. The ester linkages proved unexpectedly labile under cyclisation conditions, as even in pyridine alone the esters (Ic;  $n = 1$  or 2) gave complicated tarry mixtures. The dihexynyl ester (Ic;  $n = 4$ ), under high-dilution conditions in pyridine-methanol, was largely converted into dimethyl terephthalate and dodeca-5:7-diyne-1:12-diol, presumably as a result of pyridine-catalysed ester interchange. When the methanol was omitted, a new substance (30% yield), m. p. 210—211°, was isolated which, from the analytical, molecular weight and light absorption data, was clearly the dimer (IIIC;  $n = 4$ ). A few milligrams of another substance, m. p. 145—148°, believed to be the monomer (IIC;  $n = 4$ ), were also isolated, but no support for this supposition is available.

It is surprising that identifiable compounds could not be isolated from the reaction mixtures derived from the esters (Ic;  $n = 1$  and 2) and that the dimer was obtained almost to the exclusion of the monomer in the case of (Ic;  $n = 4$ ). Presumably internal strains resulting from unfavourable dipolar interactions render difficult the formation of the smaller rings and may also occasion their decomposition during the removal of the rather large bulk of solvent necessitated by the high-dilution procedure.

Several attempts to isolate identifiable substances from the coupling of the ester (V) have been frustrated as the resulting red oil, though substantially "coupled" (absence of free ethynyl groups), decomposed rapidly at room temperature and no evidence as to its constitution could be obtained.

The light absorption of the  $\alpha\gamma$ -diyne unit in a cyclic compound (cf. Table 1) might be expected to indicate any molecular abnormalities, for example, ring strain and transannular interaction. However,  $\alpha\gamma$ -dienes are reported<sup>8</sup> as having only weak ultraviolet and infrared<sup>12</sup> absorption ( $\lambda_{\text{max}}$  approx. 228, 238, and 254  $\text{m}\mu$ ,  $\epsilon$  300—400, 300—400, and 180—240;  $\nu_{\text{max}}$  at 2230 and 2140  $\text{cm}^{-1}$ ).

Measurements in the 200—230  $\text{m}\mu$  region are subject to certain instrumental difficulties and are likely to be somewhat inaccurate.<sup>9</sup> Further, the weak diyne absorption is easily interfered with by absorption due to strongly absorbing impurities,

<sup>8</sup> Armitage, Cook, Entwistle, Jones, and Whiting, *J.*, 1952, 1998.

<sup>9</sup> Eglinton, Jones, and Whiting, *J.*, 1952, 2873.

readily formed by oxidation or hydration of the  $\alpha\gamma$ -diyne; enynes ( $\lambda_{\max}$  228  $m\mu$ ,  $\epsilon$  14,000), now obtainable on a preparative scale by dimerisation of ethynyl compounds under conditions rather similar to those employed in the oxidative coupling,<sup>10</sup> probably contaminate  $\alpha\gamma$ -dienes prepared in this way. Variations in  $\epsilon$  values which have been

TABLE 1. *Physical characteristics of macrocyclic  $\alpha\gamma$ -dienes.*

Diyne	M. p.	Yield (%)	$\lambda_{\max}$ ( $m\mu$ )	$\epsilon$ /unit *	$\lambda_{\max}$ ( $m\mu$ )	$\epsilon$ /unit *	$\lambda_{\max}$ ( $m\mu$ )	$\epsilon$ /unit *
(IIa; $n = 10$ )...	18°	17—40	230	690	242	600	257	440
(IIIa; $n = 10$ )	101—102	10—30	226	490	239	465	254	320
(IIb) .....	54—55	63	226	686	238	551	254	225
(IIIb) .....	109—110	2	225	415	240	375	254	190

\* Per diyne unit.

encountered in the present work are probably to be attributed to one or more of the above causes. Previously<sup>1a</sup> we quoted ( $\lambda_{\max}$  226  $m\mu$ ,  $\epsilon$  1357 in hexane) for (IIb), though later material of lower  $\epsilon$  resulted. Chromatography and crystallisation of the highly crystalline cyclic di-yne (IIb) failed markedly to change the  $\epsilon$  values, which are now in reasonable accord with those for an open-chain  $\alpha\gamma$ -diyne. The original values are explicable if the presence of *ca.* 5% of enyne is assumed. The only compound in the present series likely to be subject to ring strain (IIa;  $n = 10$ ) has absorption maxima shifted about 3  $m\mu$  to longer wavelength, though it is doubtful whether this shift has much significance.

In small-ring lactones ring strain raises the carbonyl stretching frequencies (6-, 5-, and 4-membered lactone rings have absorption maxima at 1740, 1765, and 1800  $\text{cm}^{-1}$  respectively<sup>12</sup>), but in larger rings conformational effects and steric interactions may be important and may have the reverse effect. The ester (Ic;  $n = 4$ ) and the large-ring lactone (IIIc;  $n = 4$ ) have virtually the same carbonyl frequency (cf. Table 2), while the values for the compounds (Ib, IIb, and IIIb) differ by only small amounts. It is evident that in (IIb) ring strain if present has had no effect; the "Catalin" model of (IIb) is not strained and several orientations for the ester groupings including the stable *s-trans*-conformation, are possible.

TABLE 2. *Carbonyl stretching frequencies (in  $\text{CCl}_4$ ).*

Compound	$\nu$ ( $\text{cm}^{-1}$ )	$\Delta\nu_{\frac{1}{2}}^{\Delta}$ † ( $\text{cm}^{-1}$ )	$\epsilon_A$ †	Compound	$\nu$ ( $\text{cm}^{-1}$ )	$\Delta\nu_{\frac{1}{2}}^{\Delta}$ † ( $\text{cm}^{-1}$ )	$\epsilon_A$ †
(Ic; $n = 4$ ) ...	1726	16	1140	(IIIb) .....	1743	Not measured	
(IIIc; $n = 4$ )	1727	Very sparingly soluble		* Acetone .....	1719	18	246
(Ib) .....	1745	18	855	* <i>cyclo</i> Pentan- one .....	1751	24	288
(IIb) .....	1742	18	980				

\* Reference standard for calibration.<sup>11</sup>†  $\Delta\nu_{\frac{1}{2}}^{\Delta}$  apparent half band width;  $\epsilon_A$  apparent molecular extinction coefficient =  $(1/cl) \log_{10}(T_0/T)_\nu$ .

The  $\alpha\gamma$ -diyne  $\text{C}\equiv\text{C}$  stretching frequencies seem to be relatively insensitive to the nature of substituent groups and are of such low intensity ( $\epsilon < 10$ ) that they may be masked by overtone and combination bands, particularly in aromatic and oxygenated substances. The cyclic compounds seemed normal (cf. Table 3); for example, the hydrocarbon (IIIa;  $n = 10$ ) has weak bands at 2250 and 2140  $\text{cm}^{-1}$  (in Nujol): Sondheimer and Amiel<sup>13</sup> give 2228 and 2142  $\text{cm}^{-1}$  for dodeca-5 : 7-diyne (in  $\text{CHCl}_3$ ).<sup>14</sup>

After our preliminary communication<sup>1a</sup> Sondheimer and his collaborators described a parallel investigation.<sup>1b</sup> Employing  $\alpha\omega$ -dienes of shorter chain length (Ia;  $n = 3, 4$ , and 5) and the conventional cuprous chloride-ammonium chloride coupling reagent, they

<sup>10</sup> Dr. B. C. L. Weedon, personal communication.<sup>11</sup> Bellamy and Williams, *J.*, 1957, 4294.<sup>12</sup> Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 1958.<sup>13</sup> Sondheimer and Amiel, *J. Amer. Chem. Soc.*, 1957, 79, 5817.<sup>14</sup> Sheppard and Simpson, *Quart. Rev.*, 1952, 6, 1.

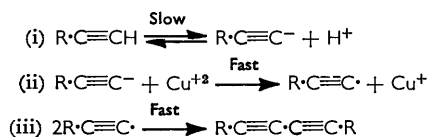
isolated, not only the corresponding acyclic dimers, trimers, and tetramers (IV), but also, though in small yield, the cyclic dimer (IIIa;  $n = 3$ ). The diynes (Ia;  $n = 2$  and 6) failed to give cyclic products. However, our cupric acetate reagent with relatively high concentrations of the diynes (Ia;  $n = 2-5$ ) gave products consisting almost entirely of cyclic polymers ranging from dimers (IIIa;  $n = 4$ ) to hexamers ( $n = 5$ ). The fact that

TABLE 3.  $\nu$  (C≡C) of  $\alpha\gamma$ -diynes.

Compound	In CCl <sub>4</sub>			In Nujol	
	cm. <sup>-1</sup>	$\Delta\nu_{\frac{1}{2}}^A$ cm. <sup>-1</sup>	$\epsilon_A$	cm. <sup>-1</sup>	$\Delta\nu_{\frac{1}{2}}^A$ cm. <sup>-1</sup>
Ph·C≡C·C≡C·Ph .....	2222	35	2.3	Very weak	
	2132	20	3.5	2130	19
Ph·C≡C·C≡C·CMe <sub>2</sub> ·OH .....	2235	16	7.4	—	—
	2132	30	0.7	—	—
HO·CMe <sub>2</sub> ·C≡C·C≡C·CMe <sub>2</sub> ·OH .....	Insoluble			2251	14
				2124	21
HO·[CH <sub>2</sub> ] <sub>4</sub> ·C≡C·C≡C·[CH <sub>2</sub> ] <sub>4</sub> ·OH .....	Insoluble			2171(?)	~50
				2120	~50
AcO·[CH <sub>2</sub> ] <sub>4</sub> ·C≡C·C≡C·[CH <sub>2</sub> ] <sub>4</sub> ·OAc .....	2258	} Complex	2	{ Overtone bands causing confusion	
	2204				
	2150				
(IIb) .....	2256	30	1.3	—	—
	2150	33	1.5	—	—
(IIIa; $n = 10$ ) .....	—	—	—	2250	~60
				2140	~30
CH <sub>2</sub> =CH·CN (liquid) * .....	2228	11	—	—	—

\* Standard for reference (Halverson, Stamm, and Whalen, *J. Chem. Phys.*, 1948, **16**, 808).

the homogeneous reagent favours the formation of cyclic products must have some bearing on the mechanism. Klebanski *et al.*<sup>15</sup> postulated that in aqueous solutions the reaction of ethynyl compounds with cupric ion proceeds as follows:



Stages (i) and (ii) involve complex copper derivatives rather than the simple anion. However, it seems hardly possible that a cyclic cuprous salt could exist during the formation of (IIa;  $n = 10$ ), the cyclisation presumably occurring as a result of the transitory formation of a diradical  $\cdot\text{C}\equiv\text{C}\cdot[\text{CH}_2]_{10}\text{C}\equiv\text{C}\cdot$ . Klebanski *et al.* showed that the more acidic the ethynyl compound the more rapidly it coupled, *e.g.*,  $\text{Ph}\cdot\text{C}\equiv\text{CH} > \text{Me}_2\text{C}(\text{OH})\cdot\text{C}\equiv\text{CH}$ , a fact which we had noted and is in accord with a rate-determining stage (i).

Further work is in progress.<sup>16</sup> The cupric acetate reagent also appears advantageous in the coupling of monoethynyl compounds.<sup>17</sup>

## EXPERIMENTAL

M. p.s were taken on the Kofler block. The alumina for chromatography was acid-washed, neutralised, and standardised according to Brockmann's method; grade 5 was used unless otherwise stated. Light petroleum was of b. p. 40–60°. Molecular weights were obtained by the Rast method [*ca.* 7 mg. in camphor (50 mg.)]. Ultraviolet absorption spectra refer to solutions in hexane determined on the Unicam S.P. 500 spectrophotometer, infrared measurements (Perkin-Elmer, Model 13) to mulls in "Nujol" unless stated to the contrary. Precise frequency and  $\epsilon$  determinations in solution were made with the Unicam S.P. 100 spectrophotometer (sodium chloride prism). Sublimations were performed at  $10^{-4}$  mm.

<sup>15</sup> Klebanski, Grachev, and Kustretsova, *Zhur. obshchei Khim.*, 1957, **27**, 2977.

<sup>16</sup> Eglinton and Galbraith, *Proc. Chem. Soc.*, 1957, 350.

<sup>17</sup> Bohlman *et al.*, *Ber.*, 1957, **90**, 130, 1661.

*Oxidative Coupling of 2-Methylbut-3-yn-2-ol by Cupric Ion.*—(i) *In water at pH 5.6 (conditions suggested by Dr. J. H. BAXENDALE).* The alcohol (5 g.) was added to a stirred solution of cupric sulphate pentahydrate (12.5 g.), sodium acetate trihydrate (34 g.), acetic acid (1.5 g.), and cuprous chloride (0.5 g.) in water (500 c.c.). The mixture was kept at 70° for 30 min., the precipitated cuprous derivative (3.3 g., 36%) was removed, and the green filtrate extracted with ether. After removal of the solvent, crystalline 2 : 7-dimethylocta-3 : 5-diyne-2 : 7-diol (2.9 g., 58%) remained. Recrystallisation from ether–light petroleum gave the pure diol,<sup>18</sup> m. p. 130–131°.

(ii) *In organic solvents.* (a) 2-Methylbut-3-yn-2-ol (400 mg.) was added to a solution of anhydrous cupric acetate<sup>19</sup> (2 g.) in pyridine–methanol–ether (1 : 1 : 4; 200 c.c.) and heated under reflux for 20 min. After removal of the bulk of the solvent under reduced pressure, the residue was acidified and extracted with ether, and the extract evaporated to give the diol, m. p. 128–130° (350 mg., 88%).

(b) A solution of the alcohol (805 mg.) and cupric acetate (10 mg.) in pyridine–methanol–ether (1 : 1 : 3; 50 c.c.) was heated under reflux for 7 hr. in a stream of oxygen. The diol (645 mg., 80%) was isolated in the usual way.

(c) The cupric salts of inorganic acids had low solubilities in pyridine. Cupric butyrate,<sup>20</sup> stearate, naphthenate, and benzoate<sup>20</sup> were soluble in varying degrees in the solvent and in benzene. However, removal of the corresponding acids from the reaction mixtures presented a complication. Cupric salicylate and the ethylenediamine salt proved ineffective.

*Oxidative Coupling of the Cuprous Derivative of Phenylacetylene.*—The cuprous derivative (1 g.) of phenylacetylene was added in pyridine (60 c.c.) to cupric acetate (2 g.) in hot pyridine (60 c.c.). The resulting green solution was heated for 20 min. at 90°, then cooled, and the product isolated in the usual way. Diphenyldiacetylene (350 mg., 70%) separated in prisms, m. p. 84–86° (Glaser<sup>21</sup> gives 88°) (from aqueous ethanol).

*Dibut-3-yn-1-yl Sebacate (Ib).*—Pyridine (10.5 g.) was added dropwise to a stirred solution of sebacyl chloride (13.3 g., freshly prepared; b. p. 128–134°/0.3 mm.) in dry ether (150 c.c.) containing but-3-yn-1-ol (8 g.). After removal of the precipitated pyridine hydrochloride, the neutral fraction was isolated as an ethereal solution and passed down a column of alumina. The ester (11 g., 61%) crystallised from ether in plates, m. p. 65–65.5° (Found: C, 70.5; H, 8.4. C<sub>18</sub>H<sub>26</sub>O<sub>4</sub> requires C, 70.6; H, 8.5%),  $\nu_{\max}$  (in Nujol) 3260 ( $\equiv\text{CH}$ ), 2100 ( $-\text{C}\equiv\text{CH}$ ), and 1740 cm.<sup>-1</sup> (ester).

*High-dilution Oxidative Coupling of Dibut-3-yn-1-yl Sebacate (Ib) (with W. McCRAE).*—A solution of the sebacate (1 g.) in ether–pyridine (1 : 6; 140 c.c.) was added during 2½ hr. to a refluxing solution of anhydrous cupric acetate (3.4 g.) in ether–pyridine (1 : 6; 700 c.c.), the drops of ester solution being continuously entrained by the refluxing solvent in a modified continuous-extraction apparatus. After a further hour the resulting green solution was cooled and slowly added, with stirring, to 0.05N-hydrochloric acid (5 l.) at 0°, and the neutral fraction isolated with ether, and its solution in benzene passed through alumina (grade III; 30 g.), the final elution being with ether–benzene. The solvent was removed and the residual solid recrystallised from light petroleum, giving octa-3 : 5-diyne sebacate (IIb) (630 mg., 63%) as tablets, m. p. 55–56° (Found: C, 71.2; H, 7.9%; *M*, 334. C<sub>18</sub>H<sub>24</sub>O<sub>4</sub> requires C, 71.1; H, 7.9%; *M*, 304),  $\nu_{\max}$  2120 ( $\text{C}\equiv\text{C}$ ) and 1720 cm.<sup>-1</sup> (ester), and  $\lambda_{\max}$  (the characteristic three diyne maxima) 226, 238, and 254  $\mu$  ( $\epsilon$  686, 551, and 225 respectively). A solution of the compound in ethyl acetate absorbed 95% of the calculated volume of hydrogen during 10 min. over Adams platonic oxide, whereupon absorption ceased.

Under conditions of lower dilution a cyclic dimer bisocta-3 : 5-diyne bis-sebacate (IIIb) was also isolated (ca. 9%). After chromatography it crystallised from light petroleum as prisms, m. p. 109–110° (Found: C, 71.0; H, 8.0%; *M*, 653. C<sub>36</sub>H<sub>48</sub>O<sub>8</sub> requires *M*, 608),  $\nu_{\max}$  2140 ( $\text{C}\equiv\text{C}$ ) and 1720, 1740 (doublet; ester) cm.<sup>-1</sup>,  $\lambda_{\max}$  225, 240, and 254  $\mu$  ( $\epsilon$  830, 750, and 380 respectively).

An attempt to effect coupling in aqueous dioxan by cuprous chloride–ammonium chloride in oxygen at room temperature led to the recovery of most of the ester. The remainder of the product was ether-insoluble and presumably polymeric. The same reaction at 70° in a

<sup>18</sup> Straus, Kolle, and Hauptmann, *Ber.*, 1930, **63**, 1886.

<sup>19</sup> Spath, *Sitzungsber. Akad. Wiss. Wien*, 1911, **120**, 1117.

<sup>20</sup> Crawford, *Nature*, 1950, **165**, 728.

<sup>21</sup> Glaser, *Ber.*, 1869, **2**, 422; *Annalen*, 1870, **154**, 159.

predominantly aqueous medium gave a crystalline, probably short-chain polymer (IV), m. p. ca. 100° (ca. 25%),  $\nu_{\max}$ . 3300 cm.<sup>-1</sup> (ethynyl group), which was not examined further.

*Tetradeca-1 : 13-diyne* (Ia;  $n = 10$ ).—1 : 10-Dibromodecane (25 g.) in ether (40 c.c.) was kept with sodium acetylide (from sodium, 6 g.) in liquid ammonia (500 c.c.) in an autoclave for 24 hr. After the ammonia had been allowed to evaporate and ammonium chloride added, the neutral fraction was isolated with ether. The *hydrocarbon* (9 g., 57%) solidified and a sample was obtained as plates, m. p. 33—34°, after low-temperature crystallisation from light petroleum followed by sublimation (Found: C, 88.7; H, 11.3. C<sub>14</sub>H<sub>22</sub> requires C, 88.4; H, 11.6%),  $\nu_{\max}$ . 3274 and 2100 (C≡CH) cm.<sup>-1</sup>. Canonica *et al.*<sup>22</sup> had previously obtained this compound, *via* the corresponding diene, as a liquid.

*Oxidative Coupling of Tetradeca-1 : 13-diyne* (Ia;  $n = 10$ ).—Tetradeca-1 : 13-diyne (1 g.) was heated with cupric acetate (4 g.) in pyridine (100 c.c.), methanol (600 c.c.), and ether (800 c.c.) for 72 hr., with continuous passage of a slow stream of oxygen. A small sample had still the same ethynyl content. The solvent was removed and the residue heated in fresh pyridine (500 c.c.) for 72 hr. (ethynyl content now small). Most of the pyridine was then removed from the brown solution under reduced pressure and the residue carefully acidified with hydrochloric acid and extracted with ether. The neutral red oil was chromatographed in light petroleum on alumina, giving in the early fractions oily *cyclotetradeca-1 : 3-diyne* (IIa;  $n = 10$ ) (170 mg., 17%), which after evaporative distillation formed prisms, m. p. 18° (Found: C, 89.1; H, 10.4. C<sub>14</sub>H<sub>20</sub> requires C, 89.4; H, 10.6%),  $\nu_{\max}$ . 2215 and 2132 cm.<sup>-1</sup> ( $\alpha\gamma$ -diyne),  $\lambda_{\max}$ . 230, 242, and 257 m $\mu$  ( $\epsilon$  690, 600, and 440 respectively). Later fractions gave *cyclooctacos-1 : 3 : 15 : 17-tetrayne* (IIIa;  $n = 10$ ) (300 mg., 30%), needles, m. p. 101—102° (from methanol-ether) (Found: C, 89.1; H, 10.5%;  $M$ , 395. C<sub>28</sub>H<sub>40</sub> requires  $M$ , 376),  $\nu_{\max}$ . 2252 and 2140 cm.<sup>-1</sup> ( $\alpha\gamma$ -diyne),  $\lambda_{\max}$ . 226, 239, and 254 m $\mu$  ( $\epsilon$  980, 930, and 640 respectively).

*cycloTetradeca-1 : 3-diyne* (128 mg.) in ethyl acetate (PtO<sub>2</sub>) absorbed 90% of the calculated volume of hydrogen. On chromatography of the crude product in light petroleum on alumina, *cyclotetradecane* (30 mg., 23%), subliming as plates, m. p. 54—55°, undepressed on admixture with a genuine sample (kindly provided by Professor V. Prelog), was obtained. The residue was a petroleum-insoluble acidic oil. *cycloOctacos-1 : 3 : 15 : 17-tetrayne* (75 mg.) similarly gave *cyclooctacosane* (20 mg., 25%), which sublimed as plates, m. p. 47—48° (Ruzicka *et al.*<sup>23</sup> give 48°).

*Diprop-2-yn-1-yl Terephthalate* (Ic;  $n = 1$ ).—Terephthaloyl chloride (8 g.) was added portionwise to an ice-cold solution of prop-2-yn-1-ol (5.5 g.) in 10% aqueous sodium hydroxide (180 c.c.). After 30 min. the precipitate was collected and dissolved in ether, and the neutral fraction isolated. The *ester* (6 g., 63%), after further purification over alumina, separated from methanol in needles, m. p. 107—108° raised on sublimation to 108—109° (Found: C, 69.6; H, 4.1. C<sub>14</sub>H<sub>10</sub>O<sub>4</sub> requires C, 69.4; H, 4.1%),  $\lambda_{\max}$ . 242, 285, and 295 m $\mu$  ( $\epsilon$  21,000, 1800, and 1500 respectively),  $\nu_{\max}$ . 3230, 2105, and 1710 cm.<sup>-1</sup>.

*Dibut-3-yn-1-yl Terephthalate* (Ic;  $n = 2$ ).—Terephthaloyl chloride (3 g.) and but-3-yn-1-ol (2.4 g.) in aqueous sodium hydroxide (60 c.c.) similarly gave the *ester* (2 g., 48%) as needles, m. p. 114—115° (from methanol) (Found: C, 71.3; H, 5.2. C<sub>18</sub>H<sub>14</sub>O<sub>4</sub> requires C, 71.1; H, 5.2%),  $\lambda_{\max}$ . 242, 285, and 295 ( $\epsilon$  21,000, 1800, and 1500 respectively),  $\nu_{\max}$ . 3240, 2100, and 1710 cm.<sup>-1</sup>.

*Dihex-5-yn-1-yl Terephthalate* (Ic;  $n = 4$ ).—Terephthaloyl chloride (5 g.) and hex-5-yn-1-ol<sup>9</sup> (5 g.) in aqueous sodium hydroxide (100 c.c.) gave, as above, the *ester* (6 g., 80%), needles, m. p. 87—88° (from methanol) (Found: C, 73.7; H, 6.4. C<sub>20</sub>H<sub>22</sub>O<sub>4</sub> requires C, 73.6; H, 6.7%),  $\lambda_{\max}$ . 242, 285, and 295 m $\mu$  ( $\epsilon$  21,000, 1800, and 1500 respectively),  $\nu_{\max}$ . 3240, 2210, 2100, and 1720 cm.<sup>-1</sup>.

*Oxidative Coupling of Diprop-2-yn-1-yl Terephthalate* (Ic;  $n = 1$ ).—A solution of the ester (2 g.) in pyridine-ether (1 : 2; 100 c.c.) was added (3 hr.) under high-dilution, reflux conditions to a solution of cupric acetate (5 g.) in pyridine-ether (7 : 1; 600 c.c.), and refluxing was continued for a further 20 hr. The solution, now free from ethynyl compounds (absence of absorption at 3300 cm.<sup>-1</sup>), was acidified at 0° and extracted with ether. Much black, polymeric, ether-insoluble material remained, while the neutral fraction deposited further quantities of brown polymer. The residual oil was chromatographed (benzene, then chloroform) over alumina and gave only a few mg. of an intractable brown gum.

<sup>22</sup> Canonica, Martinolli, and Bachetti, *Atti Accad. naz. Lincei, Rend. Classe Sci. fis. mat. nat.*, 1952, **13**, 61; *Chem. Abs.*, 1953, **47**, 11131.

<sup>23</sup> Ruzicka, Stoll, Huyser, and Boekenoogen, *Helv. Chim. Acta*, 1930, **13**, 1152.

In another experiment, when refluxing was for a further 1.5 hr., colourless needles (25 mg.), m. p. 135—137° (Found: C, 63.9; H, 6.2%), were isolated. Light-absorption data were in agreement with formulation of this substance as a non-acetylenic terephthalate derivative.

*Oxidative Coupling of Dibut-3-yn-1-yl Terephthalate* (Ic;  $n = 2$ ).—In an experiment similar to that above, dibut-3-yn-1-yl terephthalate (2 g.) was added to a solution of cupric acetate (4 g.) in pyridine (600 c.c.). Some precipitation of yellow cuprous salt was noticed during the reaction. The neutral fraction again yielded a small quantity of crystalline sublimate (20 mg.) as needles, m. p. 107—109° (Found: C, 71.6; H, 6.0%;  $M$ , 244). Light absorption was similar to that of dimethyl terephthalate but in view of the presence of absorption at 3240  $\text{cm}^{-1}$  ( $\equiv\text{CH}$ ) this substance was not further investigated.

*Oxidative Coupling of Dihex-5-yn-1-yl Terephthalate* (Ic;  $n = 4$ ).—A solution of the ester (1 g.) and cupric acetate (3 g.) in pyridine-ether (6 : 1; 700 c.c.) was heated under reflux for 67 hr. The green solution was reduced to small bulk then carefully acidified, and the neutral fraction was chromatographed on alumina. The benzene eluate (350 mg., 35%) proved to be the substantially pure cyclic dimer *bisoceta-3 : 5-diynylene bisterephthalate* (IIc;  $n = 4$ ), m. p. 210—211° (from benzene) (Found: C, 74.1; H, 6.5%;  $M$ , 618.  $\text{C}_{40}\text{H}_{40}\text{O}_8$  requires C, 74.2; H, 6.2%;  $M$ , 648),  $\lambda_{\text{max}}$  242, 285, and 294  $\mu$  ( $\epsilon$  38,000, 3900, and 2900 respectively),  $\nu_{\text{max}}$  2100 and 1720  $\text{cm}^{-1}$ . The early fractions yielded, in addition to the dimer, a few needles, m. p. 145—148°, possibly the cyclic monomer (IIc;  $n = 4$ ) ( $\lambda_{\text{max}}$  244, 250, 256, 286, and 294  $\mu$ ;  $\epsilon$  not determined). The same reaction in pyridine-ether-methanol (3 : 1 : 3) gave a virtually quantitative yield of dimethyl terephthalate, m. p. 142°, together with dodeca-5 : 7-diyne-1 : 12-diol (33% yield), m. p. 47—49°, undepressed on admixture with a genuine specimen (see below).

*Dodeca-5 : 7-diyne-1 : 12-diol*.—A solution of hex-5-yn-1-ol<sup>9</sup> (2 g.) and cupric acetate (3 g.) in pyridine-methanol (1 : 1, 100 c.c.) was heated under reflux for 7 hr., cooled and carefully added to excess of dilute hydrochloric acid. The solid from an ether extract, on crystallisation from ether-light petroleum, gave the *diol*, m. p. 49—50° (Found: C, 74.4; H, 9.4.  $\text{C}_{12}\text{H}_{18}\text{O}_2$  requires C, 74.2; H, 9.3%),  $\lambda_{\text{max}}$  227, 238, and 254  $\mu$  ( $\epsilon$  400, 380, and 230 respectively),  $\nu_{\text{max}}$  2220 and 2130  $\text{cm}^{-1}$ .

*Diethyl Hepta-1 : 6-diyne-4 : 4-dicarboxylate* (V).—Diethyl malonate (27 g.) was added to dry ethanol (150 c.c.) containing sodium ethoxide (from sodium, 7.8 g.). After 5 min., 3-bromoprop-1-yne,  $n_D^{17}$  1.4896 (42 g.), was slowly added to the stirred suspension, and the mixture heated under reflux for 30 min. After removal of the alcohol in a vacuum, the residue was diluted with water, and the neutral fraction isolated and dissolved in light petroleum. The ester (33 g., 82%) slowly separated in octahedra, m. p. 45° (Schulte and Nimke<sup>24</sup> give 45.5°).

*Oxidative Coupling of Diethyl Hepta-1 : 6-diyne-4 : 4-dicarboxylate* (V).—A solution of the ester (2 g.) and cupric acetate (5 g.) in pyridine-ethanol (1 : 1; 700 c.c.) was set aside for one month, by which time the ethynyl group content had become quite small. The neutral fraction was chromatographed on alumina, being eluted first with benzene (appreciable ethynyl absorption at 3300  $\text{cm}^{-1}$ ) and then with chloroform. The chloroform eluate, a red oil (1.2 g.), rapidly polymerised (before polymerisation,  $\lambda_{\text{max}}$  226 and 254  $\mu$ ;  $\epsilon$  1700 and 732). In one experiment the chloroform eluate was immediately subjected to catalytic hydrogenation ( $\text{PtO}_2$ ). 460 c.c. of hydrogen (calc. for the cyclic dimer, 540 c.c.) were taken up during 21 hr.; the product was an intractable gum.

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<sup>24</sup> Schulte and Nimke, *Arch. Pharm.*, 1957, **290**, 597.