Unsaturated Macrocyclic Compounds. XIX.[1] Linear and Cyclic Coupling Products Derived from *trans*-5-Decene-1,9-diyne. Attempted Syntheses of Cycloeicosadecaene and Cyclotriacontapentadecaene

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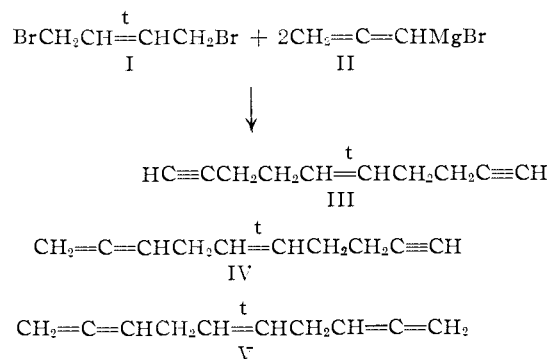
Received November 9, 1960

The reaction between *trans*-1,4-dibromo-2-butene (I) and excess allenylmagnesium bromide (II) yields *trans*-5-decene-1,9-diyne (III) as well as the allenes 1,2,5-decatrien-9-yne (IV) and 1,2,5,8,9-decapentaene (V). Oxidative coupling of the diyne III with oxygen in the presence of cuprous chloride and ammonium chloride in aqueous alcohol leads to the linear dimer VIa, trimer VIb and tetramer VIc, whereas oxidation with cupric acetate in pyridine affords the cyclic dimer VIII, trimer IX, tetramer X and pentamer XI. Attempts have been made to effect the rearrangement of the cyclic dimer VIII and trimer IX by means of potassium *t*-butoxide in *t*-butyl alcohol to the isomeric cycloeicosadecaene (XVI) and cyclotriacontapentadecaene (XVII), respectively, since analogous isomerizations in the acyclic series had been carried out by us previously. Although oily products were obtained which may contain the conjugated cyclopolyenes XVI and XVII (or stereoisomers), no homogeneous substances could be isolated and the yields must be small if XVI and XVII have indeed been formed. This provides the first indication that, the pentadecaene XVII does not represent a stable system.

The completely conjugated cyclic polyenes are an interesting class of compounds of which only two members (benzene and cyclooctatetraene) were known when our work was initiated. It has been predicted that such substances should possess some aromatic character provided they contain $(4n + 2)$ π-electrons[2] and they can take up a planar or near planar configuration.[3,4] The smallest cyclopolyene to comply with both these criteria has been postulated to be cyclotriacontapentadecaene (XVII), containing 30 π-electrons $(n = 7)$,[3] and this substance would therefore be expected to show unusual stability if we accept the view[4] which associates aromaticity with stability as is the case with benzenoid compounds.

It has recently been shown by our group[5] as well as that of Eglinton and Galbraith[6] that large-ring hydrocarbons containing α,γ-diacetylene units can be prepared by the oxidative coupling of aliphatic α,ω-diacetylenes. In addition, we have found that linear 1,5-enyne hydrocarbons can be isomerized to the corresponding conjugated polyenes by means of potassium *t*-butoxide in *t*-butyl alcohol.[7] It appeared that a combination of these two types of reactions might provide a route to certain of the above-mentioned conjugated cyclopolyenes, and in the present paper we describe an attempt thereby to prepare the theoretically non-aromatic cycloeicosadecaene (XVI) and the theoretically aromatic cyclotriacontapentadecaene (XVII). Although the pure substances could

not be obtained, our work is of interest since it provides the first indication that the pentadecaene XVII in fact does *not* represent a stable system.[8] However our findings by no means imply XVII to be nonaromatic, since the association of aromaticity with stability is not necessarily justified when dealing with nonbenzenoid compounds.

In order to introduce 1,5-enyne units into a macrocycle by the acetylene coupling reaction, it was necessary to prepare an α,ω-diacetylene containing the 1,5-enyne grouping. The compound of choice was the previously unknown *trans*-5-decene-1,9-diyne (III), which was obtained by the reaction between *trans*-1,4-dibromo-2-butene (I) and excess allenylmagnesium bromide (II).[9] Under carefully defined conditions (see Experimental) the diyne III was the major product and generally was produced in *ca.* 40% yield, although in certain experiments carried out under apparently identical conditions the yield was as low as 20%. The mono-allene 1,2,5-decatrien-9-yne (IV) and the di-allene 1,2,5,8,9-decapentaene (V) were formed as by-products, but these substances were practically the only ones obtained when small changes in the reaction conditions were made (see

$$BrCH_2\overset{t}{CH}\!=\!CHCH_2Br + 2CH_2\!=\!C\!=\!CHMgBr$$

$$\text{I} \qquad\qquad\qquad \text{II}$$

$$\downarrow$$

$$HC\!\equiv\!CCH_2CH_2\overset{t}{CH}\!=\!CHCH_2CH_2C\!\equiv\!CH$$

$$\text{III}$$

$$CH_2\!=\!C\!=\!CHCH_2\overset{t}{CH}\!=\!CHCH_2CH_2C\!\equiv\!CH$$

$$\text{IV}$$

$$CH_2\!=\!C\!=\!CHCH_2\overset{t}{CH}\!=\!CHCH_2CH\!=\!C\!=\!CH_2$$

$$\text{V}$$

(1) For Part XVIII, see F. Sondheimer, D. A. Ben-Efraim and Y. Gaoni, *J. Am. Chem. Soc.*, **83**, 1682 (1961).

(2) E. Hückel, *Z. Physik*, **70**, 204 (1931); "Grundzüge der Theorie ungesättigter und aromatischer Verbindungen," Verlag Chemie, Berlin, 1938.

(3) K. Mislow, *J. Chem. Phys.*, **20**, 1489 (1952).

(4) For reviews, see W. Baker and J. F. W. McOmie in "Progress in Organic Chemistry," Ed. J. W. Cook, Butterworths Scientific Publications, London, 1955, Vol. 3, Chapter 2; W. Baker in "Perspectives in Organic Chemistry," Ed. Sir A. Todd, Interscience Publishers, Inc., New York, N. Y., 1956, p. 28; W. Baker and J. F. W. McOmie in "Non-benzenoid Aromatic Compounds," Ed. D. Ginsburg, Interscience Publishers, Inc., New York, N. Y., 1959, Chapter 9.

(5) (a) F. Sondheimer and Y. Amiel. *J. Am. Chem. Soc.*, **78**, 4178 (1956); **79**, 5817 (1957); (b) F. Sondheimer, Y. Amiel and R. Wolovsky, *ibid.*, **79**, 6263 (1957); (c) F. Sondheimer, Y. Amiel and R. Wolovsky, *ibid.*, **79**, 4247 (1957); **81**, 4600 (1959).

(6) G. Eglinton and A. R. Galbraith, *Chemistry & Industry*, 737 (1956); *J. Chem. Soc.*, 889 (1959).

(7) F. Sondheimer, D. A. Ben-Efraim and R. Wolovsky, *J. Am. Chem. Soc.*, **83**, 1675 (1961).
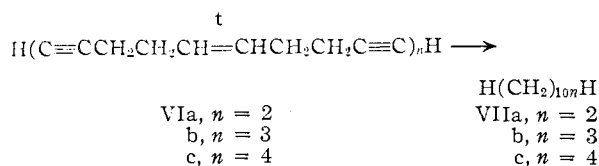
(8) For a preliminary communication, see F. Sondheimer, R. Wolovsky and Y. Gaoni, *ibid.*, **82**, 755 (1960).

(9) This reagent, obtained by the reaction between propargyl bromide and magnesium, catalyzed with mercuric chloride (M. Gaudemar, *Ann. chim. (Paris)*, (13) **1**, 190 (1956)), has been shown to exist in the allene form (C. Prevost, M. Gaudemar, L. Miginiac, F. Bardone-Gaudemar and M. Andrac, *Bull. soc. chim. France*, 679 (1959)). It has previously been condensed with allylic bromides by L. Crombie (*J. Chem. Soc.*, 4338 (1952)) and by L. Groizeleau-Miginiac (*Compt. rend.*, **248**, 1190 (1959)).

Experimental). We have not been able to ascertain the exact factors responsible for these variations in the proportions of the products.

The structures of the three liquid compounds III, IV and V, which were readily separated from each other by chromatography on alumina, follows from their infrared spectra (III showing acetylene but no allene bands, IV showing acetylene as well as allene bands and V showing allene but no acetylene bands), their lack of a high intensity maximum in the ultraviolet and the fact that all three gave *n*-decane on full hydrogenation.

The oxidative coupling of the diyne III was first carried out by means of oxygen in the presence of cuprous chloride and ammonium chloride in aqueous alcohol[5a,b] at 60–65°. When performed in *ca.* 20% aqueous ethanol this reaction gave rise to 44% of the linear dimer[10] *trans-trans*-5,15-eicosadiene-1,9,11,19-tetrayne (VIa) (m.p. 55–56°). In *ca.* 75% aqueous methanol, small quantities of the linear trimer all-*trans*-5,15,25-triacontatriene-1,9,-
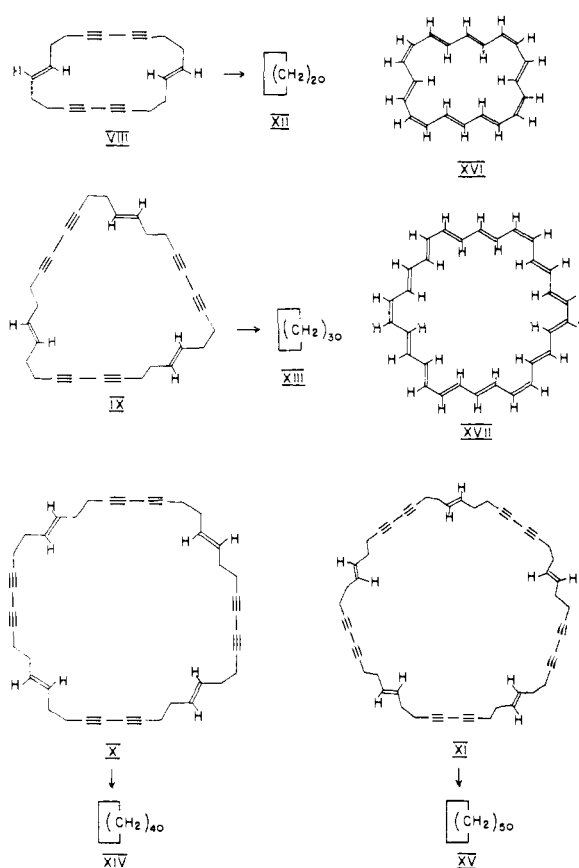
$$\overset{t}{H(C\equiv CCH_2CH_2CH=CHCH_2CH_2C\equiv C)_nH} \longrightarrow$$

	$H(CH_2)_{10n}H$
VIa, $n = 2$	VIIa, $n = 2$
b, $n = 3$	b, $n = 3$
c, $n = 4$	c, $n = 4$

11,19,21,29-hexayne (VIb) (5.6%, m.p. 94–95°) and the linear tetramer all-*trans*-5,15,25,35-tetracontatetraen-1,9,11,19,21,29,31,39-octayne (VIc) (2.6%, m.p. 123–125°) were also produced, presumably for solubility reasons. As in the case of 1,9-decadiyne,[5b] no cyclic products could be detected. The linear tetramer VIc was also obtained by a similar oxidative coupling of the linear dimer VIa, a reaction which again yielded no cyclic products. The structures of VIa, VIb and VIc are based on their infrared spectra (presence of terminal acetylene as well as α,γ-diacetylene groupings), ultraviolet spectra (medium intensity maxima at 226, 240 and 254 mμ due to the α,γ-diacetylene chromophore[11]) and the fact that full hydrogenation yielded *n*-eicosane (VIIa), *n*-triacontane (VIIb) and *n*-tetracontane (VIIc), respectively. The formation of the linear trimer VIb is noteworthy, since this type of coupling of α,ω-diacetylenes had previously given the linear dimers and tetramers, but (rather surprisingly) not the trimers.[5a,b]

The diyne III was then submitted to oxidative coupling with cupric acetate in pyridine[5c,6] at 70°, the dilution (1:100) being the same as used by us previously.[5c] The infrared spectrum of the total product showed only a weak band at 3.02 μ due to terminal acetylene. Careful chromatography on alumina yielded, in order of elution, 7.3% of the cyclic dimer *trans-trans*-1,11-cyclo-eicosadiene-5,7,15,17-tetrayne (VIII) (m.p. 125–126°), 2.5% of the cyclic trimer all-*trans*-1,11,21-cyclotriacontatriene-5,7,15,17,25,27-hexayne (IX) (m.p. 112–113°), 2.3% of the cyclic tetramer all-*trans*-1,11,21,31-cyclotetracontatetraene-5,7,15,17,-

25,27,35,37-octayne (X) (m.p. 150–151°) and 0.9% of the cyclic pentamer all-*trans*-1,11,21,31,-41 - cyclopentacontapentaene - 5,7,15,17,25,27,35,-37,45,47-decayne (XI) (m.p. 156–157°). Each one of these highly crystalline substances was obtained as a separate, analytically pure entity. The infrared spectra showed the presence of α,γ-diacetylene and the absence of terminal acetylene (or allene) groupings, while the ultraviolet spectra exhibited the medium intensity triplet at *ca.* 226, 240 and 254 mμ typical of the α,γ-diacetylene function.[11] Full hydrogenation of the cyclic dimer VIII, trimer IX and tetramer X yielded, respectively, cycloeicosane (XII), cyclotriacontane (XIII) and cyclotetracontane (XIV), identified by direct comparison with these cycloalkanes obtained previously.[5c]

The cyclic pentamer XI is the first example of the hitherto unknown fifty-membered carbocyclic system. Full hydrogenation led to the new cyclopentacontane (XV), the molecular weight of which could not be determined by the Rast method in view of its insolubility in camphene.[5c] However, the structure XV assigned to this cycloalkane (and hence to its unsaturated precursor) follows unequivocally from its melting point (87–88°), which is almost exactly identical with the value 87° predicted for cyclopentacontane (XV) from the curve relating the melting points of cycloalkanes to their ring size.[5c]

The four cyclic compounds VIII, IX, X and XI are isomeric with the completely conjugated cyclopolyenes containing 10, 15, 20 and 25 double bonds, respectively, and might be expected to rear-

(10) As previously[5] we are, for convenience, using the terms "dimer," "trimer," etc., although the empirical formulas of the substances referred to are of course not exact multiples of the "monomer."

(11) See J. B. Armitage, C. L. Cook, N. Entwistle, E. R. H. Jones and M. C. Whiting, *J. Chem. Soc.*, 1998 (1952).

range to these through reaction with potassium *t*-butoxide in *t*-butyl alcohol, especially since in the linear series the monomer III and the dimer VIa have already been isomerized by these means to the corresponding conjugated polyenes.[7]

Treatment of the cyclic dimer VIII with a saturated solution of potassium *t*-butoxide in *t*-butyl alcohol resulted in increased conjugation, as evidenced by the appearance of new ultraviolet maxima above 300 mμ. The reaction was run under a variety of conditions and was followed spectrophotometrically. Careful chromatography of the product, obtained under apparently optimum conditions (involving benzene as well as *t*-butyl alcohol as solvent), yielded material from which only unchanged VIII could be obtained crystalline. Re-chromatography of the mother liquors led to yellow oils with ultraviolet maxima in pentane at *ca.* 240, 253, 270, 284 298, 313, 374 and 395 mμ (for further details see Experimental). Although the product could not be obtained crystalline and is certainly not homogeneous, we believe it probably to contain cycloeicosadecaene (XVI or a stereoisomer) since a different route (involving partial hydrogenation of a cycloeicosaoctaene-diyne) has given material with rather similar ultraviolet properties.[12]

The attempted rearrangement of the cyclic trimer IX to cyclotriacontapentadecaene (XVII) equally gave no clear-cut result. After apparently optimum conditions had been established, a preparative experiment was carried out and the product was submitted to chromatography three times successively. Finally non-homogeneous yellow-brown oils were obtained with ultraviolet maxima or inflections in pentane at *ca.* 320, 340, 352, 370, 390, 410 and 430 mμ, which may contain some of the conjugated pentadecaene XVII (or a stereoisomer).[8] In view of these rather unpromising results, the analogous rearrangements of the cyclic tetramer X and pentamer XI were not investigated.

If the conjugated cyclopolyenes XVI and XVII (or stereoisomers) have indeed been formed in the presently described isomerizations of VIII and IX, the yields must be small and the conditions for their formation appear to be quite critical. These facts, taken together with the observation that in the acyclic series the required type of rearrangement can be carried out,[7] strongly suggest that neither the cyclic decaene XVI *nor* the cyclic pentadecaene XVII represents a stable system.

Experimental[13]

trans-5-Decene-1,9-diyne (III).—A solution of allenylmagnesium bromide (II)[9] was prepared from 60.8 g. (2.5 moles) of magnesium, 297.5 g. (2.5 moles) of propargyl bromide (dried and freshly distilled)[14] and 5 g. of mercuric chloride by covering the magnesium with 150 cc. of dry ether, adding 1 g. of the mercuric chloride and then *ca.* 20 cc. of the propargyl bromide, the mixture being stirred in nitrogen;

a vigorous reaction usually started within a few minutes (if not, outside heat was applied until reaction set in) and the rest of the bromide dissolved in 1 l. of ether then was added as rapidly as possible (*ca.* 1.5 hr.) without cooling, during which time the remaining mercuric chloride was added in several portions to the steadily boiling mixture. The latter was stirred until it reached room temperature, when *ca.* 2–3 g. of magnesium generally remained unchanged. A solution of 107 g. (0.5 mole) of *trans*-1,4-dibromo-2-butene (I)[15] in 250 cc. of ether was then added during 0.5 hr. without cooling and when the temperature again reached room temperature, 2.5 g. of cuprous chloride was added in small portions (exothermic reaction). The mixture was stirred for a further 2 hr., set aside overnight and finally boiled for 1 hr. It was then cooled in ice and carefully decomposed by addition of water. The aqueous layer was acidified with hydrochloric acid, extracted with ether and the combined organic extracts were washed with water, dried and evaporated through a Vigreux column. Rapid distillation of the residue yielded 41.2 g. (62%) of a pale yellow liquid, b.p. 58–67° (9 mm.), n^{21}D 1.4782. The infrared spectrum showed that it consisted mainly of the diyne III with only comparatively little allene, while microanalysis indicated it to be contaminated with bromine-containing material (found: Br, 8.53). It had been found in previous experiments that careful distillation did not result in a pure product. The material was therefore dissolved in 100 cc. of pentane and chromatographed on a column of 2.5 kg. of alumina which was developed with pentane, each fraction being evaporated through a Vigreux column. Infrared examination showed that small quantities of the di-allene V and the allene-acetylene IV (see below) were eluted first, followed by the diyne III. The latter on distillation yielded 26.8 g. (41%) of III as a colorless liquid, b.p. 81–82° (20 mm.), n^{19}D 1.4701; no high-intensity maximum in the ultraviolet; infrared bands (chloroform) at 3.02(s) and 4.70(m) (terminal acetylene) and 10.34(s) μ (*trans*-ethylene), no trace of allene bands at *ca.* 5.09 or 11.76 μ. The compound was reasonably stable and could be kept for some time in light and air without change.

Anal. Calcd. for $C_{10}H_{12}$: C, 90.85; H, 9.15; acetylenic H (2), 1.52. Found: C, 90.55; H, 9.12; acetylenic H (by titration against silver nitrate),[16] 1.50.

Full hydrogenation of III in ethyl acetate over platinum yielded *n*-decane, b.p. 172–173°, identified with an authentic sample (b.p. 173–174°) by infrared comparison.

Repetition of the above experiment several times under apparently identical conditions gave variable yields of the diyne III (20–45%), more of the allene-acetylene IV and the di-allene V being formed in those cases where the yield of III was lower.

1,2,5-Decatrien-9-yne (IV) and 1,2,5,8,9-Decapentaene (V).—The following is a typical experiment in which small changes from the above-described one were made and which resulted mainly in the allenes IV and V. Allenylmagnesium bromide (II) was made as before, on one-fifth the scale, but the mixture was kept at *ca.* 20° by outside cooling during the addition of the propargyl bromide once the reaction had started. Cuprous chloride (0.35 g.) was then added, followed by slow addition of a solution of 21.4 g. (0.1 mole) of *trans*-1,4-dibromo-2-butene in 100 cc. of ether during 1 hr. with continued ice-cooling. The mixture was then stirred for a further 2 hr. during which time it was allowed to reach room temperature, followed by decomposition with water and isolation with ether as previously. Distillation yielded 9.9 g. (75%) of a liquid, b.p. 52–60° (7 mm.), n^{20}D 1.4982; the infrared spectrum showed a strong allene band at 5.09 μ as well as the acetylene bands at 3.02 and 4.70 μ. This material was chromatographed on a column of 1.2 kg. of alumina which was eluted with pentane, 100-cc. fractions being collected.

Fractions 11–30 were combined (on the basis of the infrared spectra of representatives), evaporated through a Vigreux column and then distilled. The resulting di-allene V was obtained as a colorless liquid (3.7 g., 28%), b.p. 81–82° (22 mm.), n^{20}D 1.5090; no high-intensity maximum in the ultraviolet; infrared bands (chloroform) at 5.09(s), 5.86(m)

(12) F. Sondheimer and Y. Gaoni, *J. Am. Chem. Soc.*, in press.

(13) Melting points were taken on a Fisher–Johns apparatus and are uncorrected. All chromatograms were carried out with Alcoa activated alumina, grade F-20 (Aluminum Co. of America, Pittsburgh, Pa.). Ultraviolet spectra were taken on a Unicam model S.P. 500 as well as on a Cary model 14 recording spectrophotometer. Infrared spectra were measured with a Baird double-beam recording spectrophotometer with sodium chloride optics. Analyses were carried out in our microanalytical laboratory under the direction of Mr. Erich Meier.

(14) A. Kirrmann, *Bull. soc. chim. France*, [4] **39**, 698 (1926).

(15) Prepared from butadiene and bromine according to E. M. Shantz, *J. Am. Chem. Soc.*, **68**, 2553 (1946).

(16) R. M. Evans, quoted by G. Eglinton and M. C. Whiting, *J. Chem. Soc.*, 3052 (1953).

and 11.76(s) μ (allene)[17]; 6.09(m), 10.08(m) and 10.88(m) μ (monosubstituted ethylene); and 10.34(s) μ (*trans*-ethylene); no trace of terminal acetylene bands at *ca.* 3.02 or 4.70 μ. The compound was very unstable and even the pentane solutions from the chromatogram deposited an insoluble polymer on being allowed to stand for some hours at room temperature. No satisfactory elemental analysis could be obtained.

Anal. Calcd. for $C_{10}H_{12}$: C, 90.85; H, 9.15. Found: C, 89.25; H, 8.85.

Full hydrogenation of V in ethyl acetate over platinum, followed by filtration in pentane through alumina (to remove some polymer), yielded *n*-decane, b.p. 173°.

Fractions 42–64 on evaporation and distillation yielded 3.0 g. (23%) of the allene-acetylene IV as a colorless liquid, b.p. 82–83° (23 mm.), $n^{20}D$ 1.4879; infrared bands (chloroform) at 3.02(s) and 4.70(m) μ (terminal acetylene); 5.09 (s), 5.85(m) and 11.75(s) μ (allene)[17]; 6.09(m), 10.10(m) and 10.88(m) μ (monosubstituted ethylene); and 10.33(s) μ (*trans*-ethylene). The elemental analysis was unsatisfactory.

Anal. Calcd. for $C_{10}H_{12}$: C, 90.85; H, 9.15. Found: C, 88.37; H, 8.90.

The substance IV was intermediate in stability between III and V; it polymerized on being allowed to stand at room temperature, but was reasonably stable in pentane solution. That IV was a separate entity and not a mixture of III and V was confirmed by the fact that on careful re-chromatography representative fractions showed identical infrared spectra.

Full hydrogenation of IV in petroleum ether (b.p. 70–80°) over platinum once more yielded *n*-decane, b.p. 172–173°.

Fractions 72–80 contained 0.5 g. (4%) of the diyne III, the infrared spectrum of which (no trace of allene bands) was identical with that of the above-described substance.

Preparation of the Linear Dimer VIa from *trans*-5-Decene-1,9-diyne (III).—A solution of 2.5 g. of the diyne III in 5 cc. of ethanol was added to a mixture of 5 g. of cuprous chloride and 8 g. of ammonium chloride in 22 cc. of water containing 0.05 cc. of concd. hydrochloric acid. The mixture was heated to 60° and oxygen then was bubbled in, with vigorous stirring, a condenser cooled with Dry Ice–acetone being used to prevent loss of the diyne. After 4.5 hr. at 60–65°, the mixture was cooled, ether was added and the aqueous layer was diluted with 7.5 N ammonia and extracted with ether and then with benzene. The combined organic extracts were washed with dilute hydrochloric acid, sodium bicarbonate solution and water, and then were dried and evaporated. The resulting brown viscous liquid (1.95 g.) was dissolved in 10 cc. of benzene and chromatographed on 500 g. of alumina. Fractions 95–155 (50 cc. each), eluted with pentane–ether (9:1), yielded 1.09 g. (44%) of the linear dimer *trans-trans*-5,15-eicosadiene-1,9,11,19-tetrayne (VIa), m.p. 49–53°. Crystallization from methanol produced the analytical sample as sparkling colorless plates, m.p. 55–56°; $\lambda_{max}^{isooctane}$ 226, 240 and 254 mμ (ϵ 350, 340 and 200); infrared bands (chloroform) at 3.03(s) and 4.71(w) μ (terminal acetylene); 4.43(w) and 4.63(w) μ (α,γ-diyne); and 10.32-(s) μ (*trans*-ethylene). The compound was reasonably stable, but turned yellow after some weeks of standing in light and air.

Anal. Calcd. for $C_{20}H_{22}$: C, 91.55; H, 8.45. Found: C, 91.56; H, 8.16.

Full hydrogenation of VIa and crystallization from methanol smoothly yielded *n*-eicosane (VIIa), m.p. 36–37°, undepressed on admixture with a previously described sample (m.p. 36–37°).[5b]

No other pure substances could be obtained from earlier or later chromatography fractions.

Preparation of the Linear Dimer VIa, Trimer VIb and Tetramer VIc from *trans*-5-Decene-1,9-diyne (III).—A solution of 7.4 g. of the diyne III in 240 cc. of methanol was added to a mixture of 15 g. of cuprous chloride and 45 g. of ammonium chloride in 80 cc. of water containing 1.1 cc. of concd. hydrochloric acid. The mixture was then shaken in oxygen in a hydrogenation apparatus at room temperature.[11] Gas was absorbed only slowly and the reaction was therefore interrupted after 19 hr. and allowed to proceed for another 3 hr. at 65°, oxygen being passed through

the stirred mixture. The product then was isolated with ether and benzene as described previously and was chromatographed on 1.1 kg. of alumina, 100-cc. fractions being collected.

Fractions 101–119, eluted with pentane–ether (9:1 to 1:3), gave 1.12 g. (15%) of the linear dimer VIa, m.p. 52–54°, undepressed on admixture with the above-described compound.

Fractions 151–165, eluted with pentane–ether (7:3 to 3:2), yielded 0.41 g. (5.6%) of the linear trimer all-*trans*-5,15,25 - triacontatriene - 1,9,11,19,21,29 - hexayne (VIb), which on crystallization from ether–methanol showed m.p. 94–95°; $\lambda_{max}^{isooctane}$ 226, 240 and 254 mμ (ϵ 880, 820 and 510); infrared bands (KBr) at 3.03(s) and 4.71(w) μ (terminal acetylene); 4.44(w) and 4.65(w) μ (α,γ-diyne); and 10.32-(s) μ (*trans*-ethylene). The compound turned pink after several hours on being allowed to stand in light and air.

Anal. Calcd. for $C_{30}H_{32}$: C, 91.78; H, 8.22; acetylenic H, 0.51. Found: C, 91.20; H, 8.40; acetylenic H (by titration against silver nitrate),[16] 0.51.

Full hydrogenation of VIb, followed by distillation at 180–200° (bath temp.) (5 × 10⁻⁴ mm.) and crystallization from ethanol, gave *n*-triacontane (VIIb), m.p. 63–65° (reported[18] m.p. 65.7°).

Fractions 174–186, eluted with pentane–ether (1:1), yielded 0.19 g. (2.6%) of the linear tetramer all-*trans*-5,15,25,35-tetracontatetraen-1,9,11,19,21,29,31,39-octayne (VIc), which on crystallization from ether–methanol had m.p. 123–125°; λ_{max}^{ether} 226, 240 and 254 mμ (ϵ 1400, 1330 and 940); infrared bands (KBr) at 3.03(s) and 4.71(w) μ (terminal acetylene); 4.43(w) and 4.63(w) μ (α,γ-diyne); and 10.31(s) μ (*trans*-ethylene). The substance turned pink on standing in light.

Full hydrogenation of VIc, followed by crystallization from ethanol, yielded *n*-tetracontane (VIIc), m.p. 78–80°, undepressed on admixture with a previously prepared sample (m.p. 80–81°).[19]

Preparation of the Linear Tetramer VIc from the Linear Dimer VIa.—A solution containing 0.55 g. of the linear dimer VIa in 25 cc. of methanol was added to a mixture of 0.55 g. of cuprous chloride, 1.65 g. of ammonium chloride, 5.5 cc. of water and 0.05 cc. of concd. hydrochloric acid, and the mixture was then shaken in oxygen at room temperature until uptake stopped (*ca.* 4 hr.).[11] The product, isolated with ether and benzene as before, was chromatographed on 140 g. of alumina. Pentane–ether (9:1) eluted 0.30 g. (55%) of unchanged starting material, m.p. 51–54°. Pentane–ether (3:2 to 1:1) eluted 0.055 g. (10%) of the linear tetramer VIc, m.p. 120–123°, identified with the above-described compound through non-depression of the m.p. on admixture and infrared comparison.

Preparation of the Cyclic Dimer VIII, Trimer IX, Tetramer X and Pentamer XI from *trans*-5-Decene-1,9-diyne (III).—The diyne III (12 g.) was added to a mixture of 180 g. of finely ground neutral cupric acetate monohydrate in 1.2 l. of pyridine (commercial grade, previously distilled over sodium hydroxide). The mixture was heated to 70° (internal temperature) and stirred vigorously at this temperature under a reflux condenser for 4.5 hr., moisture being excluded. It was then cooled, filtered and the solid was washed well with benzene. The combined filtrates were evaporated to small volume under reduced pressure, diluted with benzene and filtered several times through Celite. They were then washed well with dilute hydrochloric acid and water, and were dried and concentrated to *ca.* 40 cc. (an aliquot on being taken to dryness exhibited only a weak infrared band at 3.02 μ due to terminal acetylene). The solution was chromatographed on a column of 2.3 kg. of alumina, which was washed successively with pentane, various mixtures of pentane–ether and finally pure ether, 100-cc. fractions being collected.

Fractions 118–160, eluted with pentane–ether (37:3 to 9:1), on evaporation to small volume and cooling gave 0.86 g. (7.3%) of the cyclic dimer *trans-trans*-1,11-cyclo-eicosadiene-5,7,15,17-tetrayne (VIII) in three crops (m.p. 124–125°, 118–121° and 115–120°). Recrystallization from ether–pentane or from petroleum ether (b.p. 70–80°) gave the analytical sample as sparkling colorless plates,

(17) See J. H. Wotiz and D. E. Mancuso, *J. Org. Chem.*, **22**, 207 (1957).

(18) W. F. Seyer, R. F. Patterson and J. L. Keays, *J. Am. Chem. Soc.*, **66**, 179 (1944).

(19) See footnote 5b. This substance (formula VIIc also in that paper) was erroneously called tetracosane in the Experimental section).

m.p. 125–126°; $\lambda_{max}^{isooctane}$ 226, 240 and 254 mμ (ϵ 850, 780 and 490); infrared bands (KBr) at 4.43(w) and 4.63(m) μ (α,γ-diyne) and 10.33(s) (trans-ethylene), no terminal acetylene band at ca. 3.03 μ. The compound was reasonably stable, but slowly turned pink on standing in light and air.

Anal. Calcd. for $C_{20}H_{20}$: C, 92.26; H, 7.74. Found: C, 92.45; H, 7.94.

Full hydrogenation of VIII and crystallization from methanol–ethyl acetate gave cycloeicosane (XII), m.p. 62°, undepressed on admixture with an authentic sample (m.p. 61–62°, derived from 1,9-decadiyne[5c]). On admixture with cyclotriacontane (XIII) (m.p. 57–58°),[5c] the m.p. was depressed to 42–46°.

Fractions 232–331, eluted with pentane–ether (17:3) to pure ether, were combined, evaporated, dissolved in pentane–ether (1:1) and rechromatographed on a new column of 540 g. of alumina (chromatogram a), since investigation of representative fractions had shown separation to have been unsatisfactory; 100-cc. fractions were again collected.

Fractions 42a–81a, eluted with pentane–ether (17:3), on evaporation to small volume and cooling gave 0.29 g. (2.5%) of the cyclic trimer all-trans-1,11,21-cyclotriaconta-triene-5,7,15,17,25,27-hexayne (IX), m.p. 100–105°. Further crystallization from ether–pentane gave the pure compound as square colorless plates, m.p. 112–113°; $\lambda_{max}^{isooctane}$ 226, 240 and 254 mμ (ϵ 1040, 1020 and 680); infrared bands (KBr) at 4.42(w) and 4.62(w) μ (α,γ-diyne) and 10.34(s) μ (trans-ethylene), no terminal acetylene band at ca. 3.03 μ. A marked m.p. depression was observed on admixture with the cyclic dimer VIII. On standing in light and air, the substance gradually became pink and then red.

Anal. Calcd. for $C_{30}H_{30}$: C, 92.26; H, 7.74. Found: C, 92.27; H, 7.93.

Full hydrogenation of IX and crystallization from methanol–ethyl acetate yielded cyclotriacontane (XIII), m.p. 56–57°, undepressed on admixture with an authentic sample (m.p. 57–58°).[5c] The m.p. was depressed on admixture with cycloeicosane (XII) (m.p. 61–62°)[5c] as well as with cyclotetracontane (XIV) (m.p. 76–77°).[5c]

Fractions 98a–125a, eluted with pentane–ether (3:1), on concentration to small volume and cooling yielded 0.27 g. (2.3%) of the cyclic tetramer all-trans-1,11,21,31-cyclotetracontatetraen-5,7,15,17,25,27,35,37-octayne (X), m.p. 142–147°. Further crystallization from pentane–ether or from pentane–chloroform gave the analytical sample as colorless needles, m.p. 150–151°; $\lambda_{max}^{isooctane}$ 226, 240 and 254 mμ (ϵ 1460, 1410 and 790); infrared bands at 4.43(w) and 4.62(w) μ (α,γ-diyne) and 10.35(s) μ (trans-ethylene), no terminal acetylene band at ca. 3.03 μ. The compound slowly turned pink and then red on standing in light and air.

Anal. Calcd. for $C_{40}H_{40}$: C, 92.26; H, 7.74. Found: C, 92.27; H, 7.89.

Full hydrogenation of X, followed by crystallization from methanol–ethyl acetate, led to cyclotetracontane (XIV), m.p. 75–76°, undepressed on admixture with an authentic sample (m.p. 76–77°).[5c] A m.p. depression was observed on admixture with cyclotriacontane (XIII) (m.p. 57–58°)[5c] as well as with cyclopentacontane (XV) (m.p. 87–88°, see below).

Fractions 143a–147a, eluted with pentane–ether (3:2), on evaporation and trituration with pentane gave 0.11 g. (0.9%) of the cyclic pentamer all-trans-1,11,21,31,41-cyclopentacontapentaene - 5,7,15,17,25,27,35,37,45,47 - decayne (XI), m.p. 145–150°. Crystallization from ether produced a pure specimen as colorless needles, m.p. 156–157°; λ_{max}^{ether} 225, 239 and 254 mμ (E 0.578, 0.523 and 0.338); infrared bands (KBr) at 4.42(w) and 4.62(w) μ (α,γ-diyne) and 10.33(s) μ (trans-ethylene), no terminal acetylene band at ca. 3.03 μ. On admixture with the cyclic tetramer X, a m.p. depression to 125–135° was observed. The substance XI turned bright red on being allowed to stand in light and air.

Anal. Calcd. for $C_{50}H_{50}$: C, 92.26; H, 7.74. Found: C, 92.50; H, 7.66.

Full hydrogenation of XI and crystallization from ethyl acetate furnished the new cyclopentacontane (XV), m.p. 87–88°. The m.p. was depressed to 60–72° on admixture with cyclotetracontane (XIV) (m.p. 76–77°).[5c] The molecular weight could not be determined by the Rast method in camphene[5c] due to insolubility.

Anal. Calcd. for $C_{50}H_{100}$: C, 85.63; H, 14.37. Found: C, 85.36; H, 14.55.

Attempted Rearrangement of the Cyclic Dimer VIII to Cycloeicosadecaene (XVI).—The following are representative of a number of experiments carried out.

A solution containing 15 mg. of the cyclic dimer VIII, 2.5 cc. of benzene and 10 cc. of a saturated solution of potassium *t*-butoxide in *t*-butyl alcohol was heated at 60–65° (internal temperature) under a reflux condenser in purified nitrogen, moisture being excluded. Aliquots were withdrawn at intervals, diluted with benzene, washed well with water, dried and the ultraviolet spectra (above 300 mμ) were examined. The aliquots taken after 5, 10, 15 and 20 minutes showed rather ill-defined maxima at ca. 375 and 400 mμ (with rising absorption below 350 mμ), which had become inflections after 30 minutes and disappeared after 1 hr. (only steadily rising absorption below 500 mμ). When the same reaction was carried out at 70–75°, the aliquot after 5 minutes showed maxima at 377 and 401 mμ, which had become inflections after 10 minutes and had disappeared after 15 minutes.

A preparative experiment was carried out by heating a solution containing 200 mg. of VIII, 33 cc. of benzene and 133 cc. of a saturated solution of potassium *t*-butoxide in *t*-butyl alcohol at 60–65° for 13 minutes. The product, isolated with benzene as previously, was evaporated to ca. 10 cc. and the resulting dark red solution was chromatographed on 200 g. of alumina, 50-cc. fractions being collected. Fractions 40–72, eluted with pentane–ether (19:1 to 37:3), were combined on the basis of the ultraviolet spectra of representatives. Evaporation yielded 87 mg. of a mixture of a yellow oil and crystals, which on trituration with ether–pentane gave 42 mg. of unchanged starting material in two crops (19 mg. with m.p. 123–125° and 23 mg. with m.p. 116–122°, neither depressed on admixture with VIII). The material recovered from the mother liquors (45 mg. of yellow oil) showed $\lambda_{max}^{pentane}$ 240, 253, 268, 273, 283, 298(infl.), 313, 372 and 395 mμ (ϵ 9,100, 11,500, 18,700, 18,600, 25,800, 11,100, 8,800, 4,700 and 3,900) and was re-chromatographed on 120 g. of alumina.

Typical fractions (25 cc. each), eluted with pentane–ether (49:1), were fraction 40 with $\lambda_{max}^{pentane}$ 240, 253, 268, 284, 298(infl.), 313, 375 and 397 mμ (E 0.405, 0.555, 0.927, 1.087, 0.312, 0.244, 0.166 and 0.123); fraction 50 with $\lambda_{max}^{pentane}$ 239, 253, 268–272, 283, 297, 312, 373 and 394 mμ (E 0.560, 0.645, 1.132, 1.610, 0.865, 0.685, 0.260 and 0.238); and fraction 60 with $\lambda_{max}^{pentane}$ 240(infl.), 254, 272, 283, 297, 312, 372 and 393 mμ (E 0.444, 0.512, 0.880, 1.172, 0.760, 0.616, 0.164 and 0.162). The fractions on evaporation yielded yellow oils which could not be crystallized.

Another preparative experiment was performed under more vigorous conditions (65–70° for 1 hr.) to ensure that no unchanged starting material should be left. Chromatography as before showed that the results were inferior to those described.

Attempted Rearrangement of the Cyclic Trimer IX to Cyclotriacontapentadecaene (XVII).—The following are typical of the various experiments performed.

A solution containing 10 mg. of the cyclic trimer IX, 5 cc. of benzene and 5 cc. of a saturated solution of potassium *t*-butoxide in *t*-butyl alcohol was heated at 60–65° (bath temp.) and aliquots were withdrawn at intervals and worked up into benzene, as described above for the cyclic dimer VIII. After 4 minutes reaction time maxima at 301, 318, 350, 369 and 396 mμ had appeared, which (except for the 369 mμ maximum) were still present after 30 minutes. When the mixture was heated at 90–95° (bath temp.), a maximum at 395 mμ had appeared after 3 minutes, which had become an inflection after 6 minutes and disappeared after 9 minutes.

A preparative experiment was carried out by heating 100 mg. of IX, 50 cc. of benzene and 50 cc. of a saturated solution of potassium *t*-butoxide in *t*-butyl alcohol at 60–65° (bath temp.) for 15 minutes. Isolation with benzene and evaporation to ca. 10 cc. gave a blood-red solution which was chromatographed on 120 g. of alumina. Fractions 26–60 (50 cc. each), eluted with pentane–ether (19:1 to 9:1), which showed maxima in pentane at ca. 352 and 390 mμ (among others), were combined and re-chromatographed on 120 g. of alumina. Fractions 80–93 (50 cc. each), from the new chromatogram, eluted with pentane–ether (23.2 to 4.1) now showed more pronounced maxima in

pentane at *ca.* 320, 340, 352 and 391 mμ with inflections at *ca.* 368, 410 and 430–435 mμ. These were chromatographed once more on 200 g. of alumina.

Typical fractions (50 cc. each), eluted with pentane–ether (4:1), were fraction 35 with $\lambda_{max}^{pentane}$ 319, 340, 352, 367(infl.), 391, 407(infl.) and 430 mμ; fraction 45 with $\lambda_{max}^{pentane}$ 322, 342(infl.), 354, 372, 393, 410(infl.) and 434-(infl.) mμ; and fraction 50 with $\lambda_{max}^{pentane}$ 322, 343, 361-(infl.), 374, 391, 414, 433(infl.) and 458 (infl.). All these fractions on evaporation gave yellow-brown oils which could not be crystallized.

Full Hydrogenations.—All the full hydrogenations of the crystalline polyacetylenes were carried out by shaking the substance dissolved in dioxane (freshly distilled over sodium) in hydrogen over a pre-reduced platinum catalyst at room temperature and atmospheric pressure. When no more gas was absorbed, the catalyst was removed, washed with hot dioxane, and the solvent was evaporated. The crystalline residue was dissolved in a little pentane or petroleum ether (b.p. 70–80°) and filtered through a short column of alumina. The solvent was again evaporated and the residue was crystallized from the specified solvent.

# Ring Closure *via* Aryne Intermediates: A General Principle of Synthesis[1,2]

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RECEIVED SEPTEMBER 8, 1960

A novel general principle of ring closure, conceivably applicable to the synthesis of countless heterocyclic and homocyclic systems, is developed and explored. This principle involves the formation of an aryne (benzyne) intermediate having a side chain bearing a strong nucleophile which can add intramolecularly to the aryne structure. Such an intermediate is formed by treatment of a suitably constituted aryl halide with a strong base such as potassium amide in liquid ammonia. The principle is illustrated by new syntheses of benzothiazole, benzoxazole, phenothiazine and indole systems, mostly in yields of 60–90%. Several observations of interest with respect to reaction mechanisms are discussed.

Most anions having negative charge on carbon, nitrogen or sulfur are effective nucleophiles *versus* arynes (benzyne derivatives).[4–8] Nucleophilic attack initiates an addition to the "triple bond," which is completed by acquisition of a proton from the medium. For example, thiophenoxide ion reacts with benzyne in liquid ammonia to form diphenyl sulfide.[5,6]

It was therefore expected that compounds having (a) a halogenated aromatic ring as an aryne precursor plus (b) the conjugate acid of an active nucleophile in a suitably located side chain would, on treatment with a very strong base, furnish ring closure products representing intramolecular nucleophilic addition to the aryne structure. The principle is represented by the generalized equation
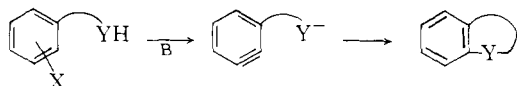
in which X is a halogen atom *ortho* or *meta*[9] to the side chain and YH is a functional group which, upon loss of a proton, forms the nucleophilic group Y^-.

In the laboratory, we discovered several ring closure reactions which fulfill the expectations from theory. These are described in this paper. While this work was in progress, Huisgen and König[10]

described some examples of this principle of ring closure in which YH was a primary or secondary amino group. Additional examples (nearly all involving amine side chains) and experiments bearing on the reaction mechanism are reported in three further papers from Huisgen's laboratory.[11,12]

In our ring closure reactions, summarized in Table I, many classes of side-chain nucleophiles are represented. Intramolecular addition of sulfur anions, nitrogen anions, oxygen anions and a carbanion have been realized. In presenting this work, we first describe the experiments and discuss their significance in regard to reaction mechanism. Applications in synthesis are considered later in the paper.

Benzothiazoles.—Treatment of thiobenz-(*o*-bromo)-anilide (1a) with potassium amide in liquid ammonia gave, in the best experiment,
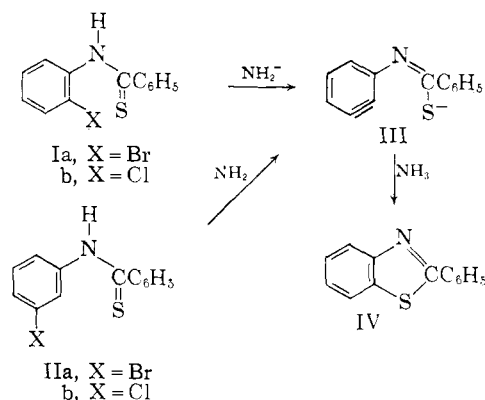
2-phenylbenzothiazole (IV) in 90% yield. A somewhat lower yield (62%) of the same product was obtained from the chlorine analog Ib. The presumed intermediate III should also be formed from the *meta* isomers IIa and IIb and indeed these compounds also gave IV on treatment with potas-

(1) Described in part in preliminary communications: B. F. Hrutfiord and J. F. Bunnett, *J. Am. Chem. Soc.*, **80**, 2021, 4745 (1958). Based on the Ph.D. thesis of B. F. H., April, 1959.

(2) Supported in part by the Office of Ordnance Research, U. S. Army.

(3) Brown University, Providence, Rhode Island.

(4) E. F. Jenny, M. C. Caserio and J. D. Roberts, *Experientia*, **14**, 349 (1958).

(5) F. Scardiglia and J. D. Roberts, *Tetrahedron*, **3**, 197 (1958).

(6) J. F. Bunnett and T. K. Brotherton, *J. Org. Chem.*, **23**, 904 (1958).

(7) W. W. Leake and R. Levine, *J. Am. Chem. Soc.*, **81**, 1169, 1627 (1959).

(8) R. Huisgen and J. Sauer, *Angew. Chem.*, **72**, 91 (1960).

(9) If the side chain is long enough, the halogen may even be *para* to it.[8]

(10) R. Huisgen and H. König, *Angew. Chem.*, **69**, 268 (1957).

(11) R. Huisgen and H. König, *Chem. Ber.*, **92**, 203, 429 (1959).

(12) R. Huisgen, H. König and N. Bleeker, *ibid.*, **92**, 424 (1959).