to a stirred solution of 4.84 g. (0.018 mole) of glyoxal–sodium bisulfite in 80 ml. of water at 40°. After removal of the ether the temperature was raised to 100° and maintained there for one hour. The mixture was cooled, made basic with 50% potassium hydroxide and the solid that separated was extracted with chloroform. The solvent was removed in a stream of nitrogen and the residue crystallized from benzene–petroleum ether, after decolorizing, to give 1.70 g. (51.3%) of 4,7-diaza-1,10-phenanthroline, m.p. 242° (sealed tube). An analytical sample was prepared by sublimation at 190° (1–2 mm.) and then recrystallization from benzene–petroleum ether.

Anal. Calcd. for $C_{10}H_6N_4$: C, 65.93; H, 3.29. Found: C, 66.19; H, 3.22.

PHILADELPHIA 22, PENNA.

[CONTRIBUTION FROM THE DANIEL SIEFF RESEARCH INSTITUTE, THE WEIZMANN INSTITUTE OF SCIENCE]

Unsaturated Macrocyclic Compounds. X.[1] Poly-oxygenated Macrocyclic Compounds from Hepta-1,6-diyn-4-ol

BY FRANZ SONDHEIMER AND YEHIEL GAONI

RECEIVED MAY 28, 1959

The oxidative coupling of the readily available hepta-1,6-diyn-4-ol (dipropargylcarbinol) (Ia) with oxygen in the presence of cuprous chloride and ammonium chloride has been studied. Acetylation followed by direct crystallization yielded a pure stereoisomer of the cyclic dimer II, while chromatography gave a mixture of the two possible stereoisomers of II, the cyclic trimer V and the cyclic tetramer VIII. Successive hydrogenation, saponification and oxidation of II, V and VIII yielded cyclotetradecane-1,8-dione (IV), cycloheneicosane-1,8,15-trione (VI) and cycloöctacosane-1,8,15,22-tetrone (IX), respectively. The structures of VI and IX were confirmed through their conversion *via* the thioketals to cycloheneicosane (VII) and cycloöctacosane (X), respectively. The coupling of hepta-1,6-diyn-4-ol acetate (Ib) by the oxygen, cuprous chloride, ammonium chloride method yielded the cyclic dimers II as sole cyclic products, whereas oxidation with cupric acetate in pyridine led only to the cyclic trimer V. The ultraviolet spectra of the cyclic poly-acetylenes are discussed and it is shown that the spectra of both isomers of the cyclic dimer II are anomalous.

It has been found recently that macrocyclic poly-acetylenes can be prepared simply by the oxidative coupling of linear terminal diacetylenes under either of two types of reaction conditions.[2] Oxidation with oxygen in the presence of cuprous chloride and ammonium chloride in aqueous ethanol yielded the cyclic dimers besides linear products.[2a,b] On the other hand when the oxidation was carried out with cupric acetate in pyridine (without using a high dilution technique, *cf.*[2c]), the reaction was more complex and cyclic trimers, tetramers, etc., were obtained besides (in some cases) the cyclic dimers.[2d]

When we undertook the work described below, the only carbocyclic poly-acetylenes obtained by either of the above techniques were hydrocarbons. In order to determine whether acetylenic carbocycles containing functional groups could be prepared, we decided to study the oxidative coupling of hepta-1,6-diyn-4-ol (Ia). The corresponding hydrocarbon, hepta-1,6-diyne, had given the cyclic dimer by the oxygen–cuprous chloride method[2b] and the cyclic trimer and tetramer by the cupric acetate–pyridine technique.[2d] It has now been found that poly-oxygenated poly-acetylenic macrocycles can in fact be obtained from the carbinol Ia, as described in the present paper.

Hepta-1,6-diyn-4-ol (dipropargylcarbinol) (Ia) was prepared readily in quantity by the condensation between propargyl aluminum bromide and ethyl formate.[3] The coupling of the carbinol Ia was carried out by means of oxygen in the presence of cuprous chloride and ammonium chloride in aqueous ethanol acidified with hydrochloric acid.[2a,b] The total reaction mixture then was acetylated.

A highly crystalline insoluble substance (explosion point *ca.* 235°) could be obtained by direct crystallization in *ca.* 1% yield. It was clearly cyclic in view of the empirical formula $[(C_9H_8O_2)_n]$ and since the infrared spectrum showed it to contain α-diacetylene but no terminal acetylene groupings. This substance proved to be one of the two possible stereoisomers of the cyclic dimer, cyclotetradeca-1,3,8,10-tetrayne-6,13-diol diacetate (II), as evidenced by the abnormal ultraviolet spectrum (see below) and by the full hydrogenation results. Thus, the corresponding saturated compound (cyclotetradecane-1,8-diol diacetate) (III) on saponification and oxidation yielded cyclotetradecane-1,8-dione (IV), the melting point of which (148°) agreed well with that reported.[4] The corresponding dioxime also exhibited the expected melting point.[4] It is of interest to note that the saturated diol diacetate III appeared to be homogeneous and showed a sharp melting point at 109–110°. This fact gives support that the acetylenic diacetate II from which it was derived is one pure stereoisomer, although it has not been determined whether it is the *cis*- or the *trans*-glycol diacetate.

Chromatography on alumina of the total acetylated material after removal of the above-described cyclic dimer II gave three different crystalline products. The first of these in order of polarity was obtained in *ca.* 1.5% yield and showed an explosion point at *ca.* 195°. The infrared spectrum was similar to that of the insoluble cyclic dimer II, but showed several new bands in the 10–14 μ

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[1] For Part IX, see F. Sondheimer and R. Wolovsky, *Tetrahedron Letters*, No. 3, 3 (1959).

[2] (a) F. Sondheimer and Y. Amiel, THIS JOURNAL, **78**, 4178 (1956); **79**, 5817 (1957); (b) F. Sondheimer, Y. Amiel and R. Wolovsky, *Proc. Chem. Soc.*, 22 (1957); THIS JOURNAL, **79**, 6263 (1957); (c) G. Eglinton and A. R. Galbraith, *Chemistry & Industry*, 737 (1956); *J. Chem. Soc.*, 889 (1959); (d) F. Sondheimer, Y. Amiel and R. Wolovsky, THIS JOURNAL, **79**, 4247 (1957); **81**, 4600 (1959); (e) G. Eglinton and A. R. Galbraith, *Proc. Chem. Soc.*, 350 (1957).

[3] M. Gaudemar, *Compt. rend.*, **239**, 1303 (1954); *Ann. chim. (Paris)*, [1] **13**, 205 (1956).

[4] A. T. Blomquist and R. D. Spencer, THIS JOURNAL, **70**, 30 (1948). Prof. Blomquist informed us that unfortunately he no longer possessed a sample for comparison.

TABLE I

ULTRAVIOLET SPECTRA OF POLY-ACETOXY MACROCYCLIC POLY-ACETYLENES (IN METHANOL)

	λ_{max}, mμ[a]				λ_{min}, mμ[a]		
II (pure isomer)	225 (330)	237 (360)	247 (300)	262 (220)	230 (290)	243 (290)	257 (200)
II (mixt. of isomers)	225 (300)	237 (330)	246 (280)	262 (200)	230 (270)	243 (270)	258 (180)
Cyclotetradeca-1,3,8,10-tetrayne[2b]	226 (310)	238 (300)	246[b] (250)	263[c] (190)	231 (270)	......	258[c] (180)
V	229 (300)	242 (300)	......	255 (210)	235 (260)	......	251 (160)
VIII	228 (350)	241 (360)	......	254 (290)	235 (290)	......	249 (250)
Tetradeca-6,8-diyne[2b]	227 (360)	240 (350)	......	253[c] (200)	233 (280)	......	250[c] (130)

[a] The molecular extinction coefficient (ε) values have been calculated per α-diacetylene unit and are given in parentheses. [b] Inflection. [c] In isoöctane.

region. This material proved to be inhomogeneous and small quantities of the insoluble dimer II could be separated. The material is undoubtedly a mixture of the two possible stereoisomers of II, since successive full hydrogenation, saponification and oxidation smoothly yielded the same cyclotetradecane-1,8-dione (IV) obtained from the pure isomer. The second isomer of II, however, could not be obtained in the pure state.

The second substance to be eluted from the column was obtained in 2–3% yield and showed m.p. 165–168° dec. The infrared spectrum showed it to be cyclic and to be different from the previously described products. Successive full hydrogenation, saponification and oxidation yielded a saturated poly-ketone, m.p. 62°. This must be cycloheneicosane-1,8,15-trione (VI) as evidenced by a molecular weight determination and since conversion to the corresponding tri-ethylenethioketal and subsequent Raney nickel reduction smoothly yielded cycloheneicosane (VII), m.p. 63–64°, identified with an authentic specimen.[2d] The original compound is therefore the cyclic trimer, cycloheneicosa-1,3,8,10,15,17-hexayne-6,13,-20-triol triacetate (V), probably again a mixture of the two possible stereoisomers.

The last crystalline compound to be eluted from the chromatogram was obtained in *ca.* 1.5% yield and showed m.p. 180–183° dec. It proved to be the cyclic tetramer, cyclooctacosa-1,3,8,10,15,17,-22,24-octayne-6,13,20,27-tetrol tetraacetate (VIII), again presumably a mixture of stereoisomers. Full hydrogenation, saponification and oxidation led to cyclooctacosane-1,8,15,22-tetrone (IX), m.p. 95°, with the expected molecular weight. Conversion to the tetra-ethylenethioketal, followed by Raney nickel reduction, yielded cyclooctacosane (X), m.p. 48°, identical with an authentic sample.[2d]

In addition to the above-described crystalline cyclic products, a considerable amount of non-crystalline material was obtained from the chromatogram. This material was not investigated further, since the infrared spectrum showed it to be linear in nature as indicated by the presence of terminal acetylenic groups.

The ultraviolet spectra of the new poly-acetoxy cyclic α-diacetylenes are recorded in Table I. α-Diacetylenes usually show ultraviolet maxima at *ca.* 227, 240 and 253 mμ and minima at *ca.* 233 and 250 mμ.[2b,5] It has been found[2b] previously that cyclotetradeca-1,3,8,10-tetrayne (II, H instead of OAc) shows an anomalous ultraviolet spectrum presumably due to the proximity of the α-diacetylene chromophores, the highest wave length maximum being displaced to 263 mμ and the highest wave length minimum to 258 mμ; in addition an inflection appears at 246 mμ. As anticipated, the same effect is apparent in the ultraviolet spectra of both isomers of II, and this observation gives additional support for the structural assignments. No such proximity effect would be expected for the cyclic trimer V or tetramer VIII, nor was found in the corresponding hydrocarbons.[2d] In fact the spectra of V and VIII are comparatively normal, in harmony with the assigned structures.

The presently described cyclic compounds further parallel the corresponding hydrocarbons[2b] in that the pure cyclic dimer II as well as the mixture of isomers explode on being heated (presumably again due to the proximity of the α-diacetylene groupings), whereas the cyclic trimer V and tetramer VIII show melting points (with decomposition).

It is noteworthy that hepta-1,6-diyn-4-ol (Ia) is the first terminal diacetylene which under the oxygen–cuprous chloride–ammonium chloride–aqueous ethanol coupling conditions has been found to yield cyclic products more complex than the cyclic dimer. This result indicates that there is no fundamental difference in the mode of formation of cyclic compounds by the two types of oxidation conditions referred to in the introduction. The carbinol Ia is of course considerably more soluble in aqueous ethanol than the hydrocarbons studied previously[2a,b] and the question of solubility appears to be an important one in determining the products of the coupling reaction.

The importance of solubility is further borne out by a coupling experiment in which hepta-1,6-diyn-4-ol acetate (Ib) instead of the free carbinol Ia was subjected to the oxygen–cuprous chloride–ammonium chloride–aqueous ethanol oxidation conditions. Direct chromatography gave in *ca.* 3% yield the cyclic dimer II (as the mixture of stereoisomers), but no trace of more complex cyclic products. This result probably is due to the fact that the acetate Ib considerably is less soluble in aqueous ethanol than the carbinol Ia.

In order to compare the two different types of coupling conditions, hepta-1,6-diyn-4-ol acetate (Ib) was oxidized also by the cupric acetate–pyridine technique.[2c,d] The only crystalline product to be isolated was the cyclic trimer V (1.5% yield), none of the cyclic dimers II being detected. The behavior of the acetate Ib, unlike that of the

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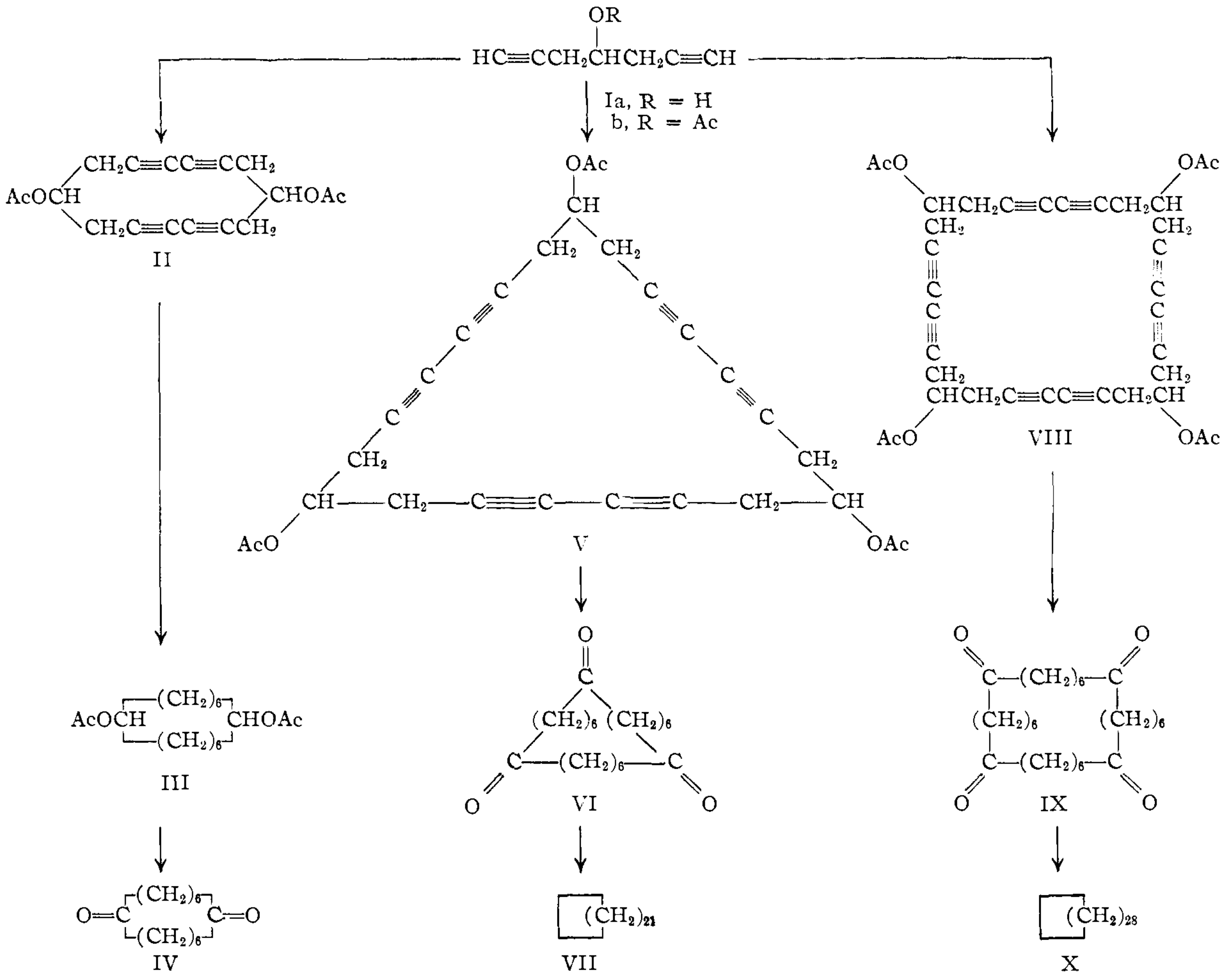
(5) J. B. Armitage, C. L. Cook, N. Entwistle, E. R. H. Jones and M. C. Whiting, *J. Chem. Soc.*, 1998 (1952).



corresponding carbinol Ia, therefore parallels that of the corresponding hydrocarbon, hepta-1,6-diyne.[2b,d]

Although the yields of cyclic products described in this paper are not high, this method for obtaining poly-oxygenated highly unsaturated carbocyclic compounds is of synthetic interest in view of the ready availability in quantity of the starting material Ia and the simplicity of the operation. Since the above-described work on hepta-1,6-diyn-4-ol (Ia) was carried out, we have shown that the coupling of hexa-1,5-diyn-3-ol (a lower homolog of Ia) with cupric acetate in pyridine also yields cyclic products.[6]

Experimental[7]

Oxidation of Hepta-1,6-diyn-4-ol (Ia) with Oxygen in Presence of Cuprous Chloride–Ammonium Chloride.—A solution of 20 g. of hepta-1,6-diyn-4-ol[3] in 40 cc. of ethanol was added to a mixture of 40 g. of cuprous chloride and 64 g. of ammonium chloride in 170 cc. of water containing 0.4 cc. of concd. hydrochloric acid. The mixture was stirred, and most of the precipitate dissolved after a few minutes. Oxygen then was bubbled in for 1 hr., with vigorous stirring, whereby the temperature of the mixture rose to *ca.* 45° and a solid mass separated. The liquid was decanted off, diluted with aqueous ammonia and extracted with ethyl acetate. The solid mass was extracted separately with ethyl acetate and the combined extracts were washed with ammonia solution and water and then were dried and evaporated.

The residual red-brown poly-ol (19.5 g.) was dissolved in 80 cc. of dry pyridine and was acetylated by means of 40 cc. of acetic anhydride at room temperature for 16 hr. Most of the pyridine now was evaporated at room temperature under reduced pressure and the residue was diluted with benzene. The solution on being washed with water, dried and evaporated yielded 23 g. of crude acetylated material as a brown viscous mass.

The above crude poly-acetate was dissolved in benzene, the solution was evaporated to *ca.* 80 cc. and then allowed to stand for 48 hr. at room temperature. The resulting crystalline precipitate was collected and washed with cold benzene. The substance thus obtained as small needles (0.22 g., 0.8%) proved to be one pure isomer of the cyclic dimer II. It showed no melting point, but decomposed explosively at *ca.* 235° when placed on a block at this temperature.[8] The ultraviolet spectral data are recorded in Table I. In the infrared the substance showed bands at 3.39(m), 4.44(w), 4.66(w), 5.79(s), 6.73(w), 7.01(m),

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[6] F. Sondheimer, Y. Amiel and Y. Gaoni, THIS JOURNAL, **81**, 1771 (1959).

[7] Melting points were taken on a Fisher–Johns apparatus and are uncorrected. The alumina used for all chromatograms was Merck acid-washed material. Ultraviolet spectra were taken on a Unicam model S.P. 500 spectrophotometer. Infrared spectra were measured on potassium bromide pellets (except for non-crystalline products, which were measured in chloroform solution) on a Baird double-beam recording spectrophotometer with sodium chloride prism. Full infrared spectra are given only for the cyclic poly-acetylenes (s = strong, m = medium, w = weak); only bands characteristic of functional groups are given for other compounds. Analyses were carried out in our microanalytical laboratory under the direction of Mr. Erich Meier.

[8] This was the lowest temperature at which this phenomenon occurred. Only polymerization took place when the sample was placed on the block at lower temperatures.

7.27(s), 8.00–8.18(s), 8.53(m), 9.12(m), 9.67(s), 10.14(m), 11.03(m) and 11.85(m) μ. Crystallization from benzene furnished the analytical sample with unchanged physical properties.

Anal. Calcd. for $C_{18}H_{16}O_4$: C, 72.96; H, 5.44. Found: C, 72.98; H, 5.47.

The mother liquors, after removal of the above-described crystalline II, were concentrated and poured onto a column containing 1 kg. of alumina. The column was developed with pentane and then with pentane containing increasing amounts of ether. Pentane–ether (1:1) eluted 0.38 g. (1.4%) of a solid material which proved to be a mixture of the two possible isomers of the cyclic dimer II. It did not show a melting point, but decomposed explosively at *ca.* 195°.[8] The ultraviolet spectral data are recorded in Table I. In the infrared, the material showed bands at 3.40(m), 4.45(w), 4.66(w), 5.79(s), 7.00(m), 7.27(s), 8.00–8.20(s), 8.54(w), 9.12(m), 9.72(s), 10.21(m), 10.54(m), 11.02(w), 11.85(m), 12.25(w) and 13.32(m) μ.

Anal. Calcd. for $C_{15}H_{16}O_4$: C, 72.96; H, 5.44. Found: C, 73.46; H, 5.59.

A benzene or dioxane solution of this stereoisomeric mixture of II on being allowed to stand, deposited small amounts of the above-described insoluble isomer, explosion point 235°, but the other isomer could not be obtained in the pure state from the mother liquors.

Further elution of the chromatogram with pentane–ether (1:1) yielded a solid material which after trituration with methanol gave 0.62 g. (2.3%) of the cyclic trimer V, probably as a mixture of isomers, m.p. 165–167° (dec., sample placed on block at 162°), with ultraviolet spectral data given in Table I. In the infrared, the substance showed bands at 3.39(m), 4.44(w), 4.65(w), 5.79(s), 7.01-(m), 7.27(s), 8.00–8.25(s), 9.06(m), 9.68(s), 10.54(m), 11.83(w), 12.41(w) and 13.27(w) μ.

Anal. Calcd. for $C_{17}H_{24}O_6$: C, 72.96; H, 5.44. Found: C, 72.74; H, 5.74.

Further elution with pentane–ether (1:1) gave 0.41 g. (1.5%) of the cyclic tetramer VIII, probably again as a stereoisomeric mixture, with m.p. 182–183° (dec., sample placed on block at 180°) and with ultraviolet spectral data given in Table I. In the infrared, the compound showed bands at 3.38(m), 4.44(w), 4.64(w), 5.79(s), 7.00(m), 7.28(s), 8.00–8.25(s), 9.72(s), 10.54(m), 10.77(m), 11.68-(m) and 12.26(w) μ. The analytical sample, showing unchanged properties, was obtained after crystallization from benzene–petroleum ether.

Anal. Calcd. for $C_{36}H_{32}O_8$: C, 72.96; H, 5.44. Found: C, 72.98; H, 5.32.

Further elution with pentane–ether (1:1) and (1:2) as well as with ether gave a considerable amount of non-crystalline linear material (strong band at 3.02 μ), which was not investigated further.

Cyclotetradecane-1,8-diol Diacetate (III).—A solution of 50 mg. of the pure isomer of II (explosion point 235°) in 20 cc. of dioxane was shaken over 50 mg. of platinum oxide in hydrogen at atmospheric pressure and room temperature until the uptake of gas stopped. One crystallization of the product from aqueous ethanol yielded 38 mg. (72%) of the saturated diacetate III, m.p. 109–110°, unchanged on further crystallization, λ_{max} 5.79 and 8.00–8.15 μ.

Anal. Calcd. for $C_{18}H_{32}O_4$: C, 69.19; H, 10.32. Found: C, 69.23; H, 10.23.

Cyclotetradecane-1,8-dione (IV).—A solution containing 30 mg. of the saturated diacetate III and 200 mg. of potassium hydroxide in 9 cc. of methanol and 1 cc. of water was boiled under reflux for 1 hr. The resulting diol, isolated with ether in the usual way, was oxidized by means of 40 mg. of chromic acid in 4 cc. of 90% acetic acid at room temperature for 12 hr. Water and ether were added and the organic layer was washed with water, dried and evaporated. Crystallization of the residue from pentane gave 16 mg. (74%) of cyclotetradecane-1,8-dione, m.p. 148°, λ_{max} 5.83 μ; reported[4] m.p. 147.5–148°. The dioxime after crystallization from ethanol showed m.p. 234–235°, reported[4] m.p. 234–235°.

The mixture of stereoisomers of II (explosion point 195°) was similarly subjected to successive full hydrogenation, saponification and oxidation. In this case the saturated dione IV, m.p. 146–147° (undepressed on admixture with the above-described sample), was obtained in 55% over-all yield.

Cycloheneicosane-1,8,15-trione (VI).—The cyclic trimer V (200 mg.) was fully hydrogenated in dioxane solution over platinum oxide and the oily saturated product thus obtained now was successively saponified and oxidized, exactly as described above for the cyclic dimer II. Chromatography of the resulting material on 10 g. of alumina, elution with pentane–ether (1:1) and crystallization from pentane then gave 86 mg. (57%) of the trione VI as large shiny plates, m.p. 62°, λ_{max} 5.83 μ.

Anal. Calcd. for $C_{21}H_{36}O_3$: C, 74.95; H, 10.78; mol. wt., 336.5. Found: C, 74.94; H, 10.51; mol. wt., 342 (Rast method, in camphor).

Cycloheneicosane (VII).—The saturated cyclic triketone VI (37 mg.) was dissolved in 1 cc. of ethanedithiol and 3 drops of boron trifluoride etherate were added. The crystalline tri-thioketal, which separated almost immediately, was collected after 10 minutes and was washed with cold methanol. It weighed 60 mg. (97%) and was treated directly with *ca.* 1 g. of Raney nickel in 100 cc. of boiling ethanol for 40 hr. The metal was removed, the filtrate was concentrated and the product was isolated with ether in the usual way. Crystallization from methanol then yielded 29 mg. (90% from VI) of cycloheneicosane, m.p. 63–64°, undepressed on admixture with an authentic sample with m.p. 63–64°.[2d]

Cycloöctacosane-1,8,15,22-tetrone (IX).—The cyclic tetramer VIII (150 mg.) was successively hydrogenated, saponified and oxidized as described above for the pure isomer of II. Chromatography of the product on 5 g. of alumina, followed by elution with benzene–ether (3:1) and crystallization from pentane, gave 63 mg. (55%) of the tetrone IX as fine needles, m.p. 95°, λ_{max} 5.84 μ.

Anal. Calcd. for $C_{28}H_{48}O_4$: C, 74.95; H, 10.78; mol. wt., 449. Found: C, 74.92; H, 10.71; mol. wt., 437 (Rast method, in camphor).

Cycloöctacosane (X).—The tetra-thioketal was prepared from 20 mg. of the tetrone IX and then reduced with Raney nickel, exactly as described above for the trione VI. Crystallization of the product from ethyl acetate then yielded 12 mg. (70% from IX) of cycloöctacosane, m.p. 47–48°, undepressed on admixture with an authentic sample with m.p. 47–48°.[2d]

Hepta-1,6-diyn-4-ol Acetate (Ib).—A solution containing 6 g. of the carbinol Ia[3] and 25 cc. of acetic anhydride in 50 cc. of pyridine was allowed to stand at 23° for 16 hr. Isolation with ether in the usual way then yielded 8.1 g. (97%) of the acetate Ib, b.p. 93–94° (22 mm.), $n^{24}D$ 1.4555; λ_{max} 3.03, 4.72, 5.79 and 7.95–8.10 μ.

Anal. Calcd. for $C_9H_{10}O_2$: C, 71.98; H, 6.71; acetylenic H, 1.34. Found: C, 71.96; H, 6.95; acetylenic H, 1.26.[9]

Oxidation of Hepta-1,6-diyn-4-ol Acetate (Ib) with Oxygen in Presence of Cuprous Chloride–Ammonium Chloride.—The coupling of 3 g. of the acetate Ib was performed exactly as described above for the carbinol Ia, except that the reaction was carried out for 45 minutes without heating and then for 15 minutes at 55° (internal temperature). Extraction with benzene and ethyl acetate yielded 2.9 g. of a product which was chromatographed on 300 g. of alumina. The only crystalline material obtained, eluted with pentane–ether (1:1), proved to be the mixture of isomers of the cyclic dimer II (92 mg., 3.1%), explosion point *ca.* 195°, the infrared and ultraviolet spectra of which were identical with those of the previously obtained material. Again a considerable amount of non-crystalline material was obtained, the infrared spectrum of which showed it to be linear (strong band at 3.02 μ).

Oxidation of Hepta-1,6-diyn-4-ol Acetate (Ib) with Cupric Acetate in Pyridine.—Pyridine (300 cc., commercial grade, distilled from sodium hydroxide) was added to 45 g. of finely ground neutral cupric acetate monohydrate. The mixture was allowed to cool to room temperature and 3 g. of the acetate Ib was added. The mixture then was heated to 55° and stirred vigorously at this temperature under a reflux condenser for 3 hr. It was cooled, filtered and the

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(9) The ethynyl group estimation was carried out by the method of R. M. Evans, as described by G. Eglinton and M. C. Whiting, *J. Chem. Soc.*, 3052 (1953).

solid was washed with hot benzene. The filtrate was evaporated to small volume under reduced pressure and the product then was isolated with chloroform (with benzene, intractable emulsions were formed). The resulting product (2.5 g.) (only weak band at 3.02 μ) was chromatographed on 250 g. of alumina. The only crystalline material was eluted with pentane–ether (1:1). Trituration of this product with methanol yielded 45 mg. (1.5%) of the cyclic trimer V, the infrared and ultraviolet spectra of which were identical with those of the previously obtained substance.

REHOVOTH, ISRAEL

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

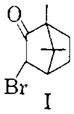
Acid-catalyzed Cleavage of π-Substituted Tricyclenes. Synthesis of 3,8-Cyclocamphor[1]

BY E. J. COREY, MASAJI OHNO, S. W. CHOW AND ROBERT A. SCHERRER

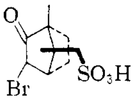
RECEIVED MAY 25, 1959

Syntheses of several *cis*-π-substituted camphor derivatives are described including *cis*-π-bromocamphor, *cis*-π-cyanocamphor, *cis*-isoketopinic acid and 3,8-cyclocamphor.

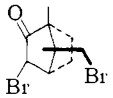
The introduction of substituents on one of the π-positions (C_8 or C_9) of camphor by reaction with certain electrophiles in strongly acidic media is one of the most interesting aspects of camphor chemistry. Exemplary of this process are the sulfonation and bromination of α-bromocamphor (I) to the corresponding π-substituted derivatives II and III.[2-4] These reactions are now understood to involve multi-stage rearrangement *via* cations rather than direct substitution[3] and it is clear from data in the literature[5-7] that the substituent is located exclusively at the π-position which is distal (*trans*) to the carbonyl group.



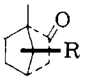
I



II



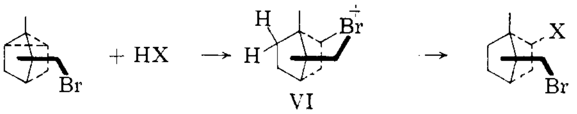
III



IV, R = COOH
V, R = CH₂OH

Consequently, most of the studies with π-substituted camphors have been concerned with the *trans* rather than the *cis* derivatives. Indeed, the only *cis*-π-substituted camphors previously described in the literature are *cis*-isoketopinic acid (IV),[6] and *cis*-π-hydroxycamphor (V) which has been prepared from IV by reduction.[3]

Since *cis*-π-substituted camphors are of considerable chemical interest and are potentially useful intermediates in terpene synthesis, we have investigated the preparation of these compounds from the readily available *trans*-π-substituted camphors. The present paper describes some of our findings on the utility of *tricyclene* intermediates in the *trans*-π → *cis*-π conversion (see ref. 6 for a previous example). An efficient preparation has already been described[8] for π-bromotricyclene from *trans*-π-bromocamphor and this seemed a good starting point because of the replaceability of bromine by other groups. In addition the presence of bromine creates the possibility of directing acid-catalyzed ring cleavage specifically to the desired *cis*-substituted system. Participation by bromine in the ring-cleavage step to form the intermediate VI, a plausible pathway, would provide such direction.



VI

Despite considerable experimentation on acid-catalyzed ring opening of π-bromotricyclene, no indication of selectivity was discernible. Two acids were employed for ring cleavage, formic and trifluoroacetic. In the former case *ca.* 20 hours at 60° was required for completion of the reaction, whereas with the latter acid cleavage was complete after only *ca.* 15 minutes at room temperature. Since the extent of participation by bromine should be greater with the less reactive acid, most of the data obtained relate to the formic acid system.

Formolysis of π-bromotricyclene at 50–60° yielded after distillation *ca.* 90% yield of a mixture of formate esters which was converted to bromoketone directly by oxidation with chromic acid–acetic acid–water in excellent yield. The direct oxidation procedure circumvents serious difficulties which are encountered with the two-step hydrolysis-oxidation sequence and is highly recommended.[9] The product of oxidation was shown by vapor phase chromatography (v.p.c.) to be a mixture of essentially equal amounts of *cis*-π-bromocamphor and *trans*-π-bromocamphor. The *trans* isomer was identified by comparison of infrared and v.p.c. measurements on the mixture with data on authentic material and by actual isolation from the mixture. The *cis* isomer, which could not be separated readily from the mixture, was obtained in pure form and characterized *via* 3,8-cyclocamphor as described below. It was shown

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[1] We are indebted to the Alfred P. Sloan Foundation for generous financial support.

[2] J. L. Simonsen and L. N. Owen, "The Terpenes," Vol. II, 2nd ed., Cambridge University Press, Cambridge, 1949, pp. 386–432.

[3] D. H. R. Barton and S. W. Harper in Rodd, "Chemistry of Carbon Compounds," Vol. IIB, Elsevier Publishing Corp., Houston, Tex., 1953, Chapter XIII, pp. 602–618.

[4] H. Nishimitsu, M. Nishikawa and M. Hagiwara, *Proc. Japan Acad.*, **27**, 285 (1951).

[5] E. Wedekind and R. Stüsser, *Ber.*, **56**, 1557 (1923).

[6] T. Hasselström, THIS JOURNAL, **53**, 1097 (1931).

[7] Y. Sahashi and T. Iki, *Sci. Papers Inst. Phys. Chem. Research, Tokyo*, **25**, 54 (1934).

[8] E. J. Corey, S. W. Chow and R. A. Scherrer, THIS JOURNAL, **79**, 5773 (1957).

[9] The oxidation of the formate of a secondary alcohol to a ketone may occur directly without prior hydrolysis in two stages: (1) oxidation of the formyl group *via* the chromate ester formed by carbonyl addition and (2) oxidation of the resulting secondary alcohol.