mmol) and hexamethyl-2,4-cyclohexadienone[7] (6.7 g, 37.6 mmol) in 137 mL of toluene was heated at reflux under nitrogen for 5 h. After cooling, the solvent was evaporated at reduced pressure to give an oil. ^{1}H NMR analysis of the crude reaction mixture showed that the reaction had proceeded with a ca. 40% conversion of the starting dienone to give a quantitative yield of **10**. Most of the dienone was removed by distillation (55 °C, 0.03 mm). Upon extended standing, sulfoxide **10** slowly crystallized from the distillation residue. Repeated recrystallizations from pentane gave **10** as a white, crystalline solid: ν (CCl_4) 2970, 2935, 1738, 1475, 1455, 1435, 1385, 1375, 1290, 1190, 1110, 1100, 1070, and 1005 cm^{-1}.

Anal. Calcd for $C_{12}H_{18}O_2S$: C, 63.68; H, 8.02; S, 14.17. Found: C, 63.69; H, 7.85; S, 13.96.

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Registry No.—**9**, 3854-96-4; *anti*-**10**, 61966-92-5; *syn*-**10**, 61966-93-6; ethylene episulfoxide, 7117-41-1.

Supplementary Material Available. A listing of fractional coordinates for nonhydrogen atoms, anisotropic thermal parameters for nonhydrogen atoms, refined fractional coordinates and isotropic thermal parameters for hydrogen atoms, observed and calculated structure factor amplitudes, and a detailed description of the experimental conditions for the crystallographic study (15 pages). Ordering information is given on any current masthead page.

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(1) (a) University of Delaware; (b) University of Nebraska; (c) Camille and Henry Dreyfus Teacher-Scholar Grant Recipient.
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(19) Tables of fractional coordinates for nonhydrogen atoms, anisotropic thermal parameters for nonhydrogen atoms, refined fractional coordinates and isotropic thermal parameters for hydrogen atoms, and observed and calculated structure factor amplitudes will be found in the microfilm edition.
(20) The first number in parentheses following a given bond length or angle is the root mean square estimated standard deviation of an individual datum. The second and third numbers, when included, are the average and maximum deviations from the average value, respectively.
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Synthesis of Methyl-Substituted Bisdehydro[13]annulenones. Conformational Isomerism and Ring Current Effects in Conjugated 13-Membered Cyclic Ketones[1]

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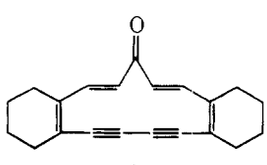
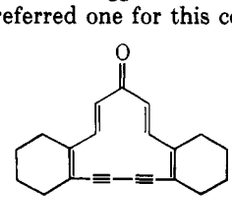
Syntheses of 5,10-dimethyl-6,8-bisdehydro[13]annulenone (**3**) and 2,5,10-trimethyl-6,8-bisdehydro[13]annulenone (**4**) are described. It was found that the extra methyl group in **4** causes a change of conformation as compared with **3**. The ^{1}H NMR spectrum of **4** proved to be temperature dependent, due to rotation of the trans double bond. Both **3** and **4** are weakly paratropic, and the paratropicity is increased by dissolution in deuteriotrifluoroacetic acid.

The synthesis of the bis(cyclohexene)-annelated bisdehydro[13]annulenone **1** in these laboratories has been described previously.[2] Although inspection of models suggested that the conformation **1a** would be the preferred one for this compound, ^{1}H NMR spectrometry [nuclear Overhauser experiments and Eu(fod)$_3$ shifts], combined with selective deuteration, pointed to conformation **1b**.[2]

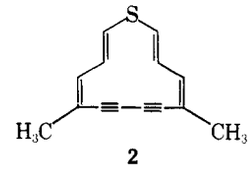


1a



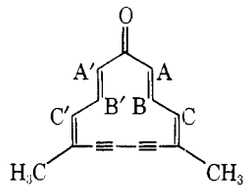
1b

Since this work was carried out, it has been shown that the related dimethylbisdehydrothia[13]annulene **2** is conforma-



2

tionally mobile on the NMR time scale.[3] This suggested that the annulenone **1** might also be conformationally mobile, with **1b** predominating. In order to investigate this possibility, it was decided to synthesize dehydroannulenones related to **1** in which one of the trans double bonds is conformationally fixed. The target compounds were the potentially mobile 5,10-dimethyl-6,8-bisdehydro[13]annulenone (**3**)[4a] and 2,5,10-trimethyl-6,8-bisdehydro[13]annulenone (**4**),[4b] in which



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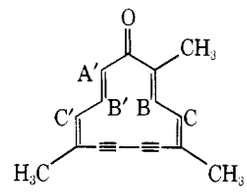
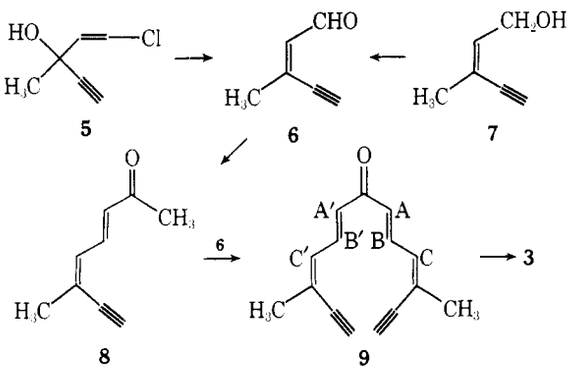


4

the methyl group adjacent to the ketone must be external. This series of compounds was chosen instead of bis(cyclohexene)-annelated compounds of type **1**, since in other cases it has been found that methyl substituted dehydroannulenes are preferable for the study of conformational mobility and ring current effects.[5] We now describe the synthesis of **3**[6] and **4**, the first monocyclic large-ring annulenones to be obtained.[7]

(*Z*)-3-Methyl-2-penten-4-yn-1-al (**6**) has been prepared by acid treatment of 1-chloro-3-methyl-1-penten-4-yn-3-ol (**5**),[8,9] as well as by manganese dioxide oxidation of (*Z*)-3-methyl-2-penten-4-yn-1-ol (**7**).[10] We have found that the aldehyde **6** obtained by the first method is contaminated with ~5–10%



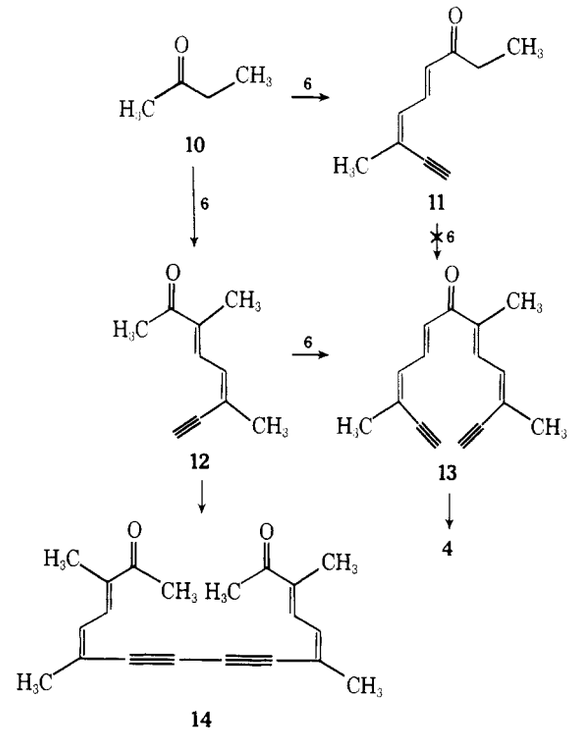
of the *E* isomer (as determined by the ^{1}H NMR spectrum), in agreement with the conclusion of Ojima et al.[8c] The second method was the preferred one, since **6** was obtained stereochemically pure in ~70% yield, and **7** was kindly made available to us by Hoffmann-La Roche, Basel.

Aldol condensation of **6** and acetone in the presence of aqueous ethanolic sodium hydroxide, essentially by the described[8c] modification of the method of Heilbron et al.,[8b] led to 6-methyl-3,5-octadien-7-yn-2-one (**8**) in 58% yield. A second aldol condensation of **8** and **6** in ether with methanolic potassium hydroxide then gave 42% of 3,11-dimethyl-3,5,8,10-tridecatetraene-1,12-diyn-7-one (**9**). The structure and stereochemistry of **9** were confirmed by the ^{1}H NMR spectrum determined in the presence of Eu(fod)$_3$ shift reagent.

Oxidative coupling of **9** with cupric acetate monohydrate in pyridine at 60 °C led to ~25% of the dimethylbisdehydro[13]annulenone **3** as orange needles, mp >170 °C dec. Subsequently it was found that oxidative couplings of this type proceed in higher yield when anhydrous cupric acetate in pyridine–ether at ~50 °C is employed,[11] and the yield of **3** from **9** could be improved to 80% under these conditions. The overall yield in the four-step sequence **7** → **6** → **8** → **9** → **3** is ~15%, and the dehydro[13]annulenone **3** has become a relatively readily available substance.

A suitable precursor of the trimethylbisdehydro[13]annulenone **4** appeared to be 3,6,11-trimethyl-3,5,8,10-tridecatetraene-1,12-diyn-7-one (**13**). It was expected that this ketone could be obtained by the aldol condensation between 2-butanone (**10**) and (*Z*)-3-methyl-2-penten-4-yn-1-al (**6**) to give the ketone **11** or **12**, followed by condensation with another molecule of the aldehyde **6**. In practice, reaction of **10** with **6** in the presence of methanolic sodium methoxide[12] led to 7-methyl-4,6-nonadien-8-yn-3-one (**11**) in 43% yield. Unfortunately, all attempts to condense this ketone with another molecule of the aldehyde **6** to give **13** failed.

The alternative approach to **13** was therefore investigated. Reaction of **10** with **6** under acidic conditions (sulfuric acid–acetic acid)[12] yielded 59% of 3,6-dimethyl-3,5-octadien-7-yn-2-one (**12**). Condensation of this ketone with the aldehyde



6 in the presence of ethanolic potassium hydroxide then gave the required ketone **13**, admixed with unchanged **12**. The separation between **12** and **13** proved to be inefficient, and it was found most convenient to proceed with the mixture.

Oxidative coupling of the mixture of **12** and **13** with cupric acetate monohydrate in dimethylformamide at 60 °C gave rise to a mixture of the diketone **14** (derived from **12**) and the dehydroannulenone **4** (derived from **13**), which were readily separated by chromatography. The dehydroannulenone **4**, isolated in 4% yield (based on **12**), formed orange crystals, mp 83–84 °C.

The electronic absorption maxima (in ether) of the dimethylbisdehydro[13]annulenone **3** and trimethylbisdehydro[13]annulenone **4**, as well as of the bis(cyclohexene)-annelated bisdehydro[13]annulenone **1**,[2] are given in Table I. As expected, the spectra are similar, the maxima exhibiting small bathochromic shifts as the degree of alkyl substitution increases. The electronic absorption maxima of **3**, **4**, and **1** in trifluoroacetic acid are given in Table II, and it is evident that protonation with this acid causes the main maxima to shift to higher wavelengths.

The ^{1}H NMR chemical shifts of the bisdehydro[13]annulenones **3** and **4** are given in Table III. The individual assignments were made on the basis of the multiplicity and coupling constants, given in the Experimental Section. The spectrum

Table I. Electronic Absorption Maxima of Bisdehydro[13]-annulenones in Ether [λ_{max} (ϵ_{max})]

3	4	1[a]
~250 sh (25 800)	~250 sh (24 700)	~250 sh (16 000)
262 (37 900)	265 (48 300)	~270 sh (26 800)
273 (39 900)	276 (50 300)	279 (31 000)
387 (990)	390 sh (1400)	394 (1160)

[a] See ref 2.

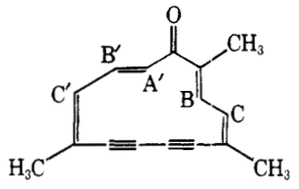
Table II. Electronic Absorption Maxima of Bisdehydro[13]-annulenones in Trifluoroacetic Acid [λ_{max} (Relative Extinction Coefficients)][a]

3	4	1[b]
~269 sh (0.82)	~271 sh (0.90)	~275 sh (0.89)
281 (1.00)	282 (1.00)	288 (1.00)
~350 sh (0.12)	~350 sh (0.12)	~350 sh (0.15)

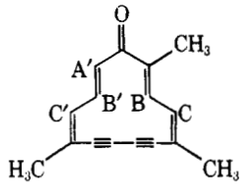
[a] All the spectra showed tailing to ~700 nm. [b] See ref 2.

of the dimethyl compound **3** (Figure 1) proved to be essentially temperature independent in the range −60 to 80 °C. On the other hand, the spectrum of the trimethyl compound **4** was temperature dependent, as indicated in Figure 2. At 27 °C (and above), the $H^{A'}$, $H^{B'}$, and $H^{C'}$ resonances are unresolved multiplets. On cooling, these bands become resolved, and the expected first-order pattern is observed at −60 °C. Further cooling results in increased separation of the $H^{A'}$ and the $H^{B'}$ bands.

Two facts indicate that the trimethylbisdehydro[13]annulenone **4** exists as conformer **4a**, and not **4b**. Firstly, H^{B} and



4a



4b

$H^{B'}$ resonate at very different field (τ 0.27 and 2.60, respectively, at −60 °C), indicative of their different environments. Secondly, the low $J_{B'C'}$ value (6 Hz) points to the s-cis relationship of $H^{B'}$ and $H^{C'}$, and is in contrast to the s-trans $J_{B,C}$ value (11 Hz). The reason for the temperature dependence of the spectrum of **4** must be due to rotation of the $H^{A'}$, $H^{B'}$ double bond.

Comparison of the ^{1}H NMR spectrum of the dimethylbisdehydro[13]annulenone **3** with that of **4** shows that **3** exists essentially in the indicated conformation. This follows from

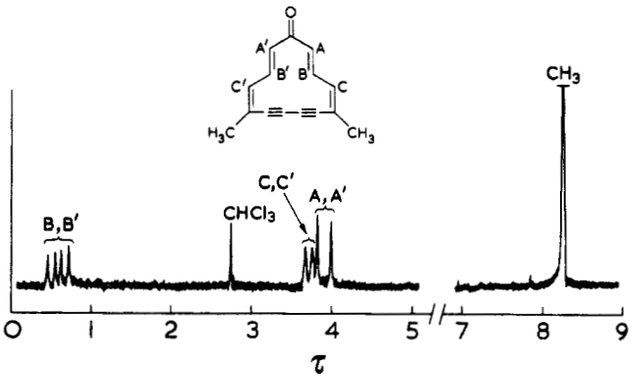
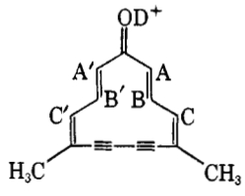


Figure 1. ^{1}H NMR spectrum of the dimethylbisdehydro[13]annulenone **3** in $CDCl_3$ at 27 °C (100 MHz, τ values, internal standard Me_4Si).

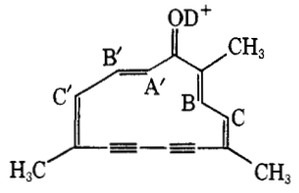
the similarity of the H^{B} resonance in **3** (τ 0.61) to that in **4** (τ 0.45),[13] and the difference of the $H^{A'}$ resonance in **3** (τ 3.90) from that in **4** (τ 2.10, at −60 °C). It is interesting that the perturbation caused by introduction of the extra methyl group into **3** to give **4** is sufficient to effect a conformational change in the other trans double bond.

Comparison of the NMR chemical shifts of the various protons of the bisdehydro[13]annulenones **3** and **4** with those of the corresponding acyclic model **9** (Table III) indicates that **3** and **4** are weakly paratropic, as might be expected of 12π-electron systems. This follows from the fact that essentially all the outer protons in **3** and **4** (especially the methyl protons) resonate at higher field than the corresponding protons in **9**, whereas the inner protons in **3** and **4** resonate at lower field. The bis(cyclohexene)-annelated bisdehydro[13]annulenone **1** is presumably also paratropic, but no conclusion could be made, since the "open" model in this series is even less satisfactory than in the presently described methyl substituted series.

The ^{1}H NMR chemical shifts of the deuteronated species **15** and **16**, obtained by dissolving **3** and **4** in deuteriotrifluo-



15



16

roacetic acid, are also given in Table III. It is evident that the conformations are unchanged. The positive charge is expected to cause a downfield shift of all of the proton resonances (~−0.8 ppm for the olefinic protons if the charge were equally

Table III. ^{1}H NMR Chemical Shifts of 3, 4, 9 (in $CDCl_3$) and 15, 16 (in CF_3COOD) at 100 MHz, Determined at 27 °C Unless Otherwise Stated (τ Values, Internal Standard Me_4Si)

Compd	H^{A}	H^{B}	H^{C}	$H^{A'}$	$H^{B'}$	$H^{C'}$	CH_3
3	3.90	0.61	3.71	3.90	0.61	3.71	8.26
4		0.45	3.46	2.10[a]	2.51[a]	3.82	8.20
9	3.55	2.32	3.54	3.55	2.32	3.54	7.98
Δ (**3** − **9**)	+0.35	−1.71	+0.17	+0.35	−1.71	+0.17	+0.28
Δ (**4** − **9**)		−1.87	−0.08	−1.45	+0.19	+0.28	+0.22
15	3.85	−0.79	3.88	3.85	−0.79	3.88	8.33
16		−0.50	3.50	*b*	*b*	3.84	8.28
Δ (**15** − **3**)	−0.05	−1.40	+0.17	−0.05	−1.40	+0.17	+0.07
Δ (**16** − **4**)		−0.95	+0.04			+0.02	+0.08

[a] At −60 °C. [b] The $H^{A'}$ and $H^{B'}$ chemical shifts of **16** appeared as a multiplet at τ 1.74–2.18, due to conformational mobility.

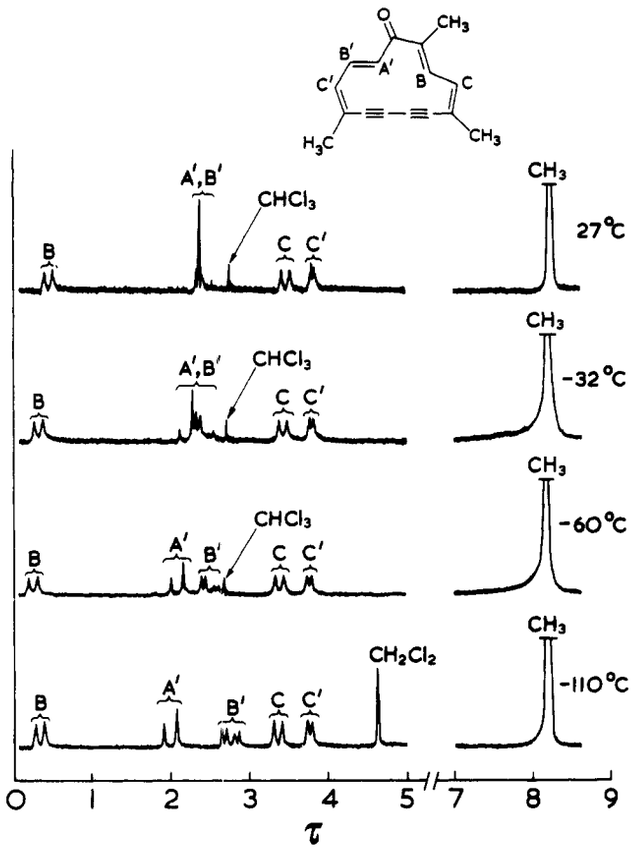


Figure 2. ^{1}H NMR spectra of the trimethylbisdehydro[13]annulenone **4** in $CDCl_3$ or $CDCl_2$–CS_2 (−110 °C) at different temperatures (100 MHz, τ values, internal standard Me_4Si).

distributed over the 13-membered ring). The observation that deuteronation of **3** and **4** caused a considerable downfield shift of the inner proton bands, but only little change of the outer ones (see Table III), indicates **15** and **16** to be more paratropic than **3** and **4**.

Experimental Section

General Procedures. Melting points were determined on a Kofler hot stage apparatus and are uncorrected. Infrared spectra were measured on a Unicam SP 200 spectrophotometer (s = strong, m = medium, w = weak); only significant maxima are reported. Electronic spectra were determined on a Unicam SP 800 spectrophotometer (sh = shoulder). ^{1}H NMR spectra were measured on a Varian T60 (60 MHz) or a Varian HA 100 (100 MHz) spectrometer, tetramethylsilane being used as an internal standard. Assignments were assisted by nuclear Overhauser experiments and Eu(fod)$_3$ shifts where necessary. Proton decoupled ^{13}C NMR spectra were measured on a Varian CFT 20 spectrometer, tetramethylsilane being used as an internal standard. Mass spectra were determined on an AEI MS-12 or (for accurate mass measurements) on an AEI MS-9 spectrometer, both operating at 70 eV. Alumina for column chromatography refers to Woelm neutral alumina activity III. Compounds were preadsorbed from ether or dichloromethane solution onto alumina before being applied to the column. Pyridine and dimethylformamide were Analar grade that had been stored for a prolonged period over 4Å molecular sieves. Petrol refers to light petroleum (bp 40–60 °C) which had been distilled from phosphorus pentoxide. Organic extracts were washed with saturated aqueous sodium chloride and dried over magnesium sulfate immediately prior to solvent removal. All reactions were conducted under a purified nitrogen flow.

(*Z*)-3-Methyl-2-penten-4-yn-1-al (6) from (*Z*)-3-Methyl-2-penten-4-yn-1-ol (7).[10] A solution of the alcohol **7** (20 g) in methylene chloride (300 ml) was stirred with activated manganese dioxide[14] (100 g) at ambient temperature for 3 h. A further quantity of activated manganese dioxide (30 g) was added, and stirring was continued for 2 h. The mixture was filtered, the solid was washed well with methylene chloride, and the solvent was evaporated. Examination of the residue (14.1 g, 72%) by ^{1}H NMR spectrometry showed it to be essentially pure *Z* aldehyde **6**.

6-Methyl-3,5-octadien-7-yn-2-one (8). An ice-cold solution of aqueous sodium hydroxide (0.65 N, 4.1 mL) and ethanol (4.1 mL) was added over 10 min to an ice-cooled stirred solution of the *Z* aldehyde **6** (1.41 g) in acetone (8.1 mL). The solution was stirred for a further 1 h at 0 °C and aqueous sulfuric acid (2 N, 1.6 mL) was then added. The solution was diluted with water (100 mL) and extracted with ether, and the extracts were washed with saturated aqueous sodium bicarbonate. The residue after solvent removal was chromatographed on a column of alumina (5 × 4 cm). Fractions eluted with 5% ether–petrol on evaporation afforded the ketone **8**[8b,c] (1.16 g, 58%) as a pale yellow oil: UV (Et_2O) λ_{max} 288 nm (ϵ 21 400), ~300 sh (18 800); IR (film) 3260 m (C≡CH), 2100 w (C≡C), 1660 s (C=O), 1610 m and 1600 m (C=C), 985 cm^{-1} m (trans HC=CH); ^{1}H NMR (60 MHz, $CDCl_3$) τ 2.50 (dd, $J_{4,3}$ = 16, $J_{4,5}$ = 11 Hz, H-4), 3.62 [d (b), $J_{5,4}$ = 11 Hz, H-5], 3.92 (d, $J_{3,4}$ = 16 Hz, H-3), 6.53 (s, H-8), 7.74 (s, H-1), 8.00 [s (b), CH_3-6].

3,11-Dimethyl-3,5,8,10-tridecatetraene-1,12-diyn-7-one (9). Methanolic potassium hydroxide (3.6 N, 2 mL) was added to a stirred solution of the ketone **8** (2.0 g, 15 mmol) and the aldehyde **6** (1.41 g, 15 mmol) in ether (60 mL, previously passed through basic alumina and flushed with nitrogen). After 1.5 h at ambient temperature, acetic acid (3 mL) was added, followed by stirring for 15 min and then dilution with water (100 mL). The separated aqueous layer was extracted with ether and the combined ethereal extracts were washed with saturated aqueous sodium bicarbonate. The residue after solvent removal was chromatographed on a column of alumina (5 × 4 cm). Fractions eluted with 15% ether–petrol on evaporation yielded the ketone **9** (1.31 g, 42%) as a yellow solid. It formed yellow cubes, mp 100–101 °C dec (sealed and evaporated tube, Buchi melting point apparatus) from ether–petrol: mass spectrum *m/e* 210.104 (M^+, calcd 210.104), 209 ($M^+ - 1$), 195 ($M^+ - 15$), 181 ($M^+ - 29$); UV (Et_2O) λ_{max} 250 nm (ϵ 13 800), 338 (28 300); IR ($CHCl_3$) 3280 m (C≡CH), 2100 w (C≡C), 1640 s (C=O), 1600 s (C=C), 995 cm^{-1} m (trans HC=CH); ^{1}H NMR (100 MHz, $CDCl_3$) τ 2.32 (dd, $J_{5,6}$ = $J_{9,8}$ = 16, $J_{5,4}$ = $J_{9,10}$ = 11 Hz, H-5, H-9), 3.54 (d, $J_{4,5}$ = $J_{10,9}$ = 11 Hz, H-4, H-10), 3.55 (d, $J_{6,5}$ = $J_{8,9}$ = 16 Hz, H-6, H-8), 6.54 (s, H-1, H-13), 7.98 (s, CH_3-3, CH_3-11). Addition of Eu(fod)$_3$ shift reagent effected complete separation of the overlapping bands at τ 3.54 and 3.55.

5,10-Dimethyl-6,8-bisdehydro[13]annulenone[4a] (3) (with L. Lombardo). A solution of the ketone **9** (500 mg) in pyridine and dry ether (3:1, 50 mL) was added dropwise during 4.5 h to a stirred solution of anhydrous cupric acetate[15] (3.0 g) in pyridine and dry ether (3:1, 110 mL) at 45–50 °C (bath). The solution was stirred at 45 °C for a further 1.5 h and was then cooled. The residue after solvent removal was extracted thoroughly with ether, the solid removed by filtration, and the filtrate evaporated. Chromatography on a column of alumina (8 × 4 cm), elution with 25% ether–petrol, evaporation, and trituration with petrol yielded the annulenone **3** as orange needles (395 mg, 80%). The substance could be crystallized from benzene–pentane or from ethanol, mp >170 °C dec: mass spectrum *m/e* 208 (M^+), 180 ($M^+ - 28$), 178 ($M^+ - 30$), 165 ($M^+ - 43$); UV (Et_2O) see Table I; UV (CF_3COOH) see Table II; IR (KBr) 2180 w and 2120 w (C≡C), 1620 s and 1605 s (C=O, C=C), 985 cm^{-1} s (trans HC=CH); ^{1}H NMR (100 MHz, $CDCl_3$, see Figure 1 and Table III) τ 0.61 (dd, $J_{3,2}$ = $J_{12,13}$ = 16.5, $J_{3,4}$ = $J_{12,11}$ = 9.5 Hz, H-3, H-12), 3.71 [d (b), $J_{4,3}$ = $J_{11,12}$ = 9.5 Hz, H-4, H-11], 3.90 (d, $J_{2,3}$ = $J_{13,12}$ = 16.5 Hz, H-2, H-13), 8.26 [s (b), CH_3-5, CH_3-10]; ^{1}H NMR (100 MHz, CF_3COOD, see Table III) τ −0.79 (dd, $J_{3,2}$ = $J_{12,13}$ = 16, $J_{3,4}$ = $J_{12,11}$ = 10 Hz, H-3, H-12), 3.85 (d, $J_{2,3}$ = $J_{13,12}$ = 16 Hz, H-2, H-13), 3.88 (d, $J_{4,3}$ = $J_{11,12}$ = 10 Hz, H-4, H-11), 8.33 (s, CH_3-5, CH_3-10); ^{13}C NMR (20 MHz, $CDCl_3$) δ 194.9 (C-1), 142.5 (C-3, C-12), 140.1, 129.8 (C-4, C-5, C-10, C-11), 127.3 (C-2, C-13), 98.5 (C-6, C-9), 86.0 (C-7, C-8), 20.1 (CH_3-5, CH_3-10).

Anal. Calcd for $C_{15}H_{12}O$: C, 86.51; H, 5.81. Found: C, 86.80; H, 5.84.

The yield of **3** was only ~25% when the coupling of **9** was carried out with cupric acetate monohydrate in pyridine at 60 °C for 3 h.

7-Methyl-4,6-nonadien-8-yn-3-one (11). A solution of the aldehyde **6** (470 mg, 5 mmol) in ether (5 mL) was added dropwise over 30 min to a stirred solution of 2-butanone (**10**, 720 mg, 10 mmol) in dry ether (30 mL) containing methanolic sodium methoxide [from sodium (7.6 mg) and methanol (2 mL)]. After a further 1 h, the reaction was quenched by addition of aqueous oxalic acid. The ethereal layer was evaporated and the residue chromatographed on a column of alumina (6 × 3.5 cm) with 10% ethyl acetate–petrol as eluent. Early fractions afforded the ketone **11** (320 mg, 43%) as a yellow oil: mass spectrum *m/e* 148.088 (M^+, calcd 148.089); UV (Et_2O) λ_{max} 291 nm (ϵ 19 800), ~300 sh (18 700), ~345 sh (1700); ^{1}H NMR (60 MHz, $CDCl_3$) τ 2.40 (dd, $J_{5,4}$ = 16, $J_{5,6}$ = 11 Hz, H-5), 3.58 [d (b), $J_{6,5}$ = 11

Hz, H-6], 3.83 (d, $J_{4,5}$ = 16 Hz, H-4), 6.47 (s, H-9), 7.37 (q, H-2), 7.97 [s (b), CH_3-7], 8.88 (t, H-1).

3,6-Dimethyl-3,5-octadien-7-yn-2-one (12). A solution of the aldehyde **6** (2.43 g, 0.026 mol) in acetic acid (8 mL) was added dropwise over 15 min to a stirred solution of 2-butanone (**10**, 8.0 g, 0.11 mol) and concentrated sulfuric acid (2 mL) in acetic acid (100 mL). The resultant dark solution was stirred for a further 18 h, and then cautiously poured into saturated aqueous potassium carbonate. The residue after solvent removal was chromatographed on a column of alumina (11 × 4 cm) with 5% ethyl acetate–petrol as eluent. Early fractions afforded the ketone **12** (2.24 g, 59%) as a yellow solid. It formed yellow prisms, mp 41–43 °C from pentane: mass spectrum *m/e* 148.089 (M^+, calcd 148.089), 133 ($M^+ - 15$), 119 ($M^+ - 29$), 105 ($M^+ - 43$), 103 ($M^+ - 45$); UV (Et_2O) λ_{max} ~277 nm sh (ϵ 17 000), 295 (26 600), ~307 sh (22 200); IR (CCl_4) 3250 m (C≡CH), 2100 w (C≡C), 1660 s (C=O), 1620 cm^{-1} m (C=C); ^1H NMR (60 MHz, $CDCl_3$) τ 2.47 [d (b), $J_{4,5}$ = 11 Hz, H-4], 3.30 [d (b), $J_{5,4}$ = 11 Hz, H-5], 6.40 (s, H-8), 7.62 (s, H-1), 7.93 [s (b), CH_3-6], 8.10 [s (b), CH_3-3].

2,5,10-Trimethyl-6,8-bisdehydro[13]annulenone[4b] (4) and 3,6,11,14-Tetramethyl-3,5,11,13-hexadecatetraene-7,9-diyne-2,15-dione (14) from 12. A solution of potassium hydroxide (0.4 g) in ethanol (5 mL) was added to a solution of the ketone **12** (2.15 g, 0.015 mol) in dry tetrahydrofuran (45 mL), and a solution of the aldehyde **6** (2.15 g, 0.023 mol) in dry tetrahydrofuran (15 mL) was then added during 30 min, with stirring. After 3 h, the reaction was quenched by the addition of acetic acid (3 mL), the resulting solution was poured into water (500 mL), and the mixture was extracted with ether. Chromatography of the residue after solvent removal on a column of alumina (10 × 4 cm), with 5% ethyl acetate–petrol as eluent, afforded a yellow gum (2.34 g). Spectroscopic examination of this material showed that it was a mixture of **12** and **13**.

A solution of the mixture of **12** and **13** (2.34 g) in dimethylformamide (40 mL) was added dropwise during 1 h to a stirred mixture of cupric acetate monohydrate (18.9 g) in dimethylformamide (100 mL) at 60 °C (bath). After a further 0.5 h at 60 °C, the mixture was cooled, diluted with water (1 L), and extracted with ether, and the extracts were washed with water. The residue after solvent removal was chromatographed on a column of alumina (6 × 4 cm), with 5–15% ethyl acetate–petrol as eluent.

Early fractions gave the annulenone **4** (136 mg, 4% based on **12**) as an orange solid. It formed orange rods, mp 83–84 °C, from petrol: mass spectrum *m/e* 222.105 (M^+, calcd 222.105), 207 ($M^+ - 15$), 194 ($M^+ - 28$), 179 ($M^+ - 43$); UV (Et_2O) see Table I; UV (CF_3COOH) see Table II; IR (KBr) 2165 w and 2100 w (C≡C), 1640 s, 1620 m and 1600 s (C=O, C=C), 980 cm^{-1} m (trans HC=CH); ^1H NMR (100 MHz, $CDCl_3$ 27 °C, see Figure 2 and Table III) τ 0.45 (d, $J_{3,4}$ = 11 Hz, H-3), 2.37 (m, H-12, H-13), 3.46 (d, $J_{4,3}$ = 11 Hz, H-4), 3.82 (m, H-11), 8.20 [s (b) CH_3-2, CH_3-5, CH_3-10]; ^1H NMR (100 MHz, $CDCl_3$ −60 °C, see Figure 2) τ 0.27 (d, $J_{3,4}$ = 11 Hz, H-3), 2.10 (d, $J_{13,12}$ = 16 Hz, H-13), 2.51 (dd, $J_{12,13}$ = 16, $J_{12,11}$ = 6 Hz, H-12), 3.39 [d (b), $J_{4,3}$ = 11 Hz, H-4], 3.76 [d (b), $J_{11,12}$ = 6 Hz, H-11], 8.17 [s (b), CH_3-2, CH_3-5, CH_3-10]; ^1H NMR (100 MHz, CF_3COOD, see Table III) τ −0.50 (d, $J_{3,4}$ = 11 Hz, H-3), 1.74–2.18 (m, H-12, H-13), 3.50 (d, $J_{4,3}$ = 11 Hz, H-4), 3.84 [d (b), $J_{11,12}$ = 7 Hz, H-11], 8.18 [s (b), CH_3-2], 8.28 [s (b), CH_3-5, CH_3-10]; ^{13}C NMR (20 MHz, $CDCl_3$) δ 195.5 (C-1), 139.8, 139.6, 138.6, 138.2, 137.4, 129.2, 127.2, 123.5 (C-2, C-3, C-4, C-5, C-10, C-11, C-12, C-13), 97.6, 97.1 (C-6, C-9), 88.3 (C-7, C-8), 21.2, 20.0 (CH_3-5, CH_3-10), 12.20 (CH_3-2).

Later fractions afforded the diketone **14** (442 mg, 21%) as a yellow solid. It formed yellow needles, mp 110–112 °C, from ethanol: UV (Et_2O) λ_{max} 248 nm sh (ϵ 11 800), 259 (14 000), 286 sh (31 700), 325 sh (30 000), 342 (34 600), 366 (32 100), 393 (22 400); IR (KBr) 2180 w (C≡C), 1660 s (C=O), 1610 m (C=C); ^1H NMR (100 MHz, $CDCl_3$) τ 2.53 [d (b), $J_{4,5}$ = $J_{13,12}$ = 11 Hz, H-4, H-13], 3.23 [d (b), $J_{5,4}$ = $J_{12,13}$ = 11 Hz, H-5, H-12], 7.60 (s, H-1, H-16), 7.90 [s (b), CH_3-6, CH_3-11], 8.10 [s (b), CH_3-3, CH_3-14].

Anal. Calcd for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81.62; H, 7.54.

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Crystal Structure of Tetrahymanol Hemihydrate

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The crystal structure of a hemihydrate of the pentacyclic triterpenoid tetrahymanol, $C_{30}H_{52}O \cdot \frac{1}{2}H_2O$ [monoclinic, $P2_1$, a = 7.417 (1) Å, b = 11.438 (2), c = 30.248 (4), β = 91.95°, Z = 4, R = 0.076] has been determined. Steric overcrowding warps the gross conformation of the two molecules in the asymmetric unit and generates unusually long carbon–carbon single bonds. The observed weakening of the C8–C14 bond, whose average length is 1.61 Å, is consistent with its scission observed in mass spectral experiments. Although the molecular skeleton possesses rotational symmetry, the observed conformations are markedly asymmetric, appear to be independent of the hydroxyl moiety, and suggest the presence of conformational isomers in solution.

The pentacyclic triterpene tetrahymanol (**1**) was first isolated from the protozoan *Tetrahymena pyriformis*.[2] Later, it was also obtained from the fern *Oleandra walichii*.[3] Initially, tetrahymanol (**1**) was thought to be an "isomer of cho-