

Syntheses and Properties of Trimethyltetrahydro[19]annulenones and the Benzannulated Derivatives

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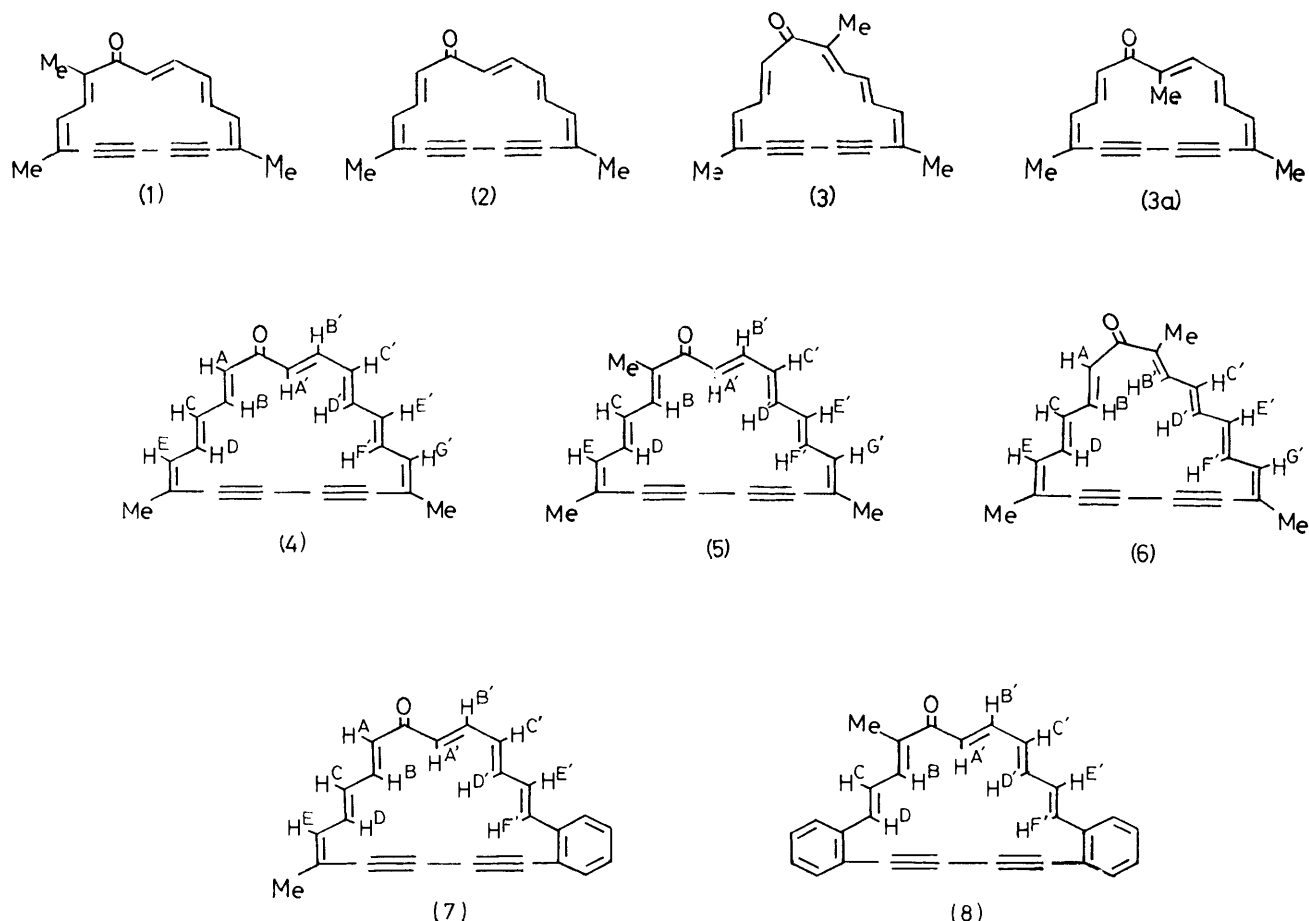
Syntheses of 2,7,12- (5) and 7,12,19-trimethyl-8,9,10,11-tetrahydrocyclonadecenone (6), 17-methyl-18,19,20,21-tetrahydrobenzocyclonadecen-11-one (7), and 8-methyl-20,21,22,23-tetrahydrodibenzo[*a,g*]cyclonadecen-9-one (8) are described. The influence of α -methyl substitution and benzannulation upon the structure and tropicity of the tetrahydro[19]annulenone ring system is discussed in view of the ^1H -n.m.r. and u.v. spectra of these annulenones as well as those of 7,12-dimethyl-8,9,10,11-tetrahydrocyclonadecenone (4).

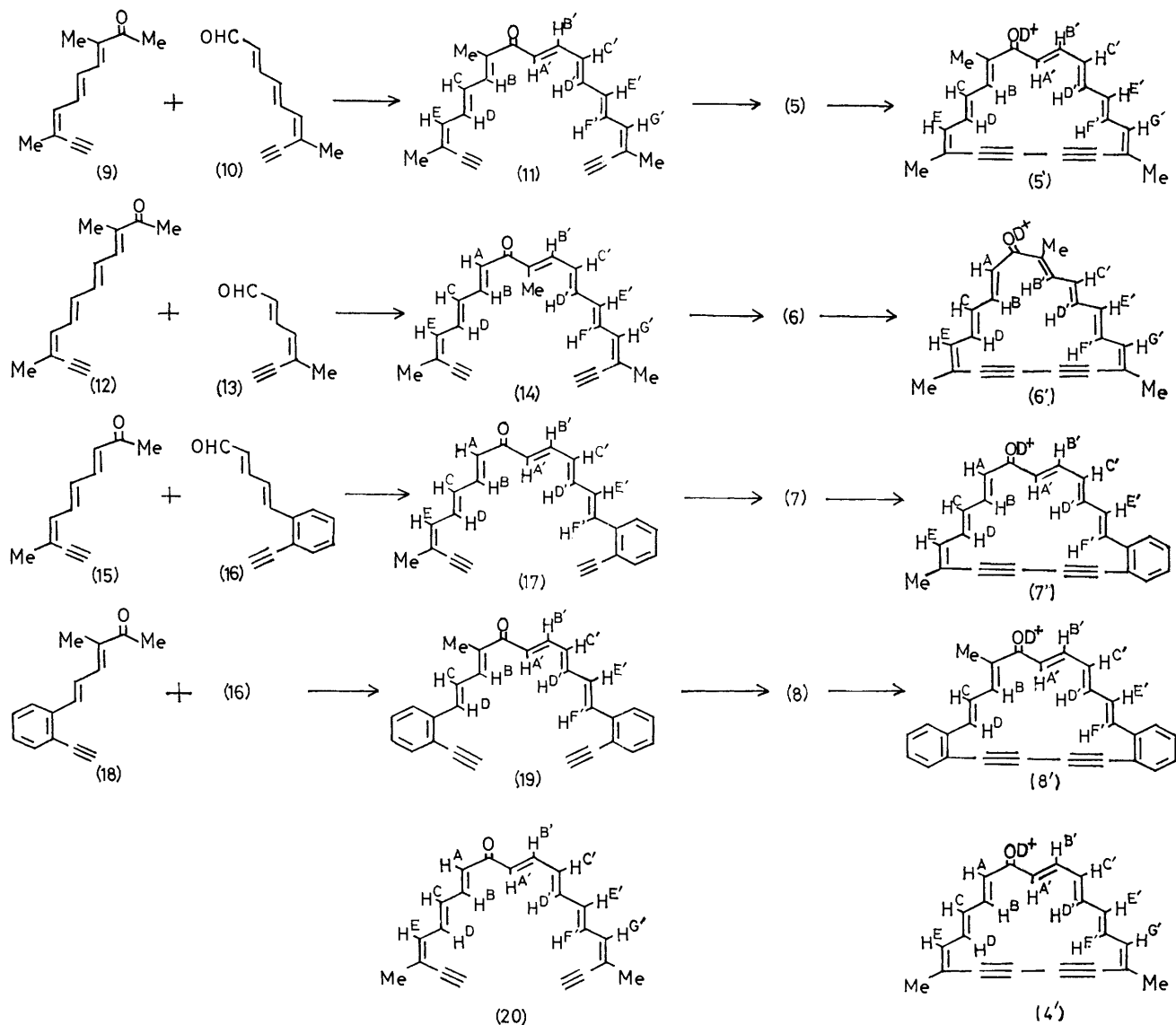
In a previous paper, we reported the syntheses of the tetrahydro[15]annulenones (1)—(3), and showed that the planarity of the [15]annulenone ring system decreases in the sequence of (1) > (2) > (3) on the basis of the chemical shifts of the olefinic protons of the corresponding deuteriated species. It was also shown that the trimethylannulenone (3) [not (3a)] was obtained from the corresponding acyclic ketone by intramolecular oxidative coupling.¹

In view of these results as to effect of benzannulation, we were interested in examining the properties of the higher analogues of the annulenones (1)—(3) and the

benzannulated ones, *i.e.* 7,12-dimethyl- (4),² 2,7,12-trimethyl- (5), and 7,12,19-trimethyl-8,9,10,11-tetrahydrocyclonadecenone (6), 17-methyl-18,19,20,21-tetrahydrobenzocyclonadecenone (7), and 8-methyl-20,21,22,23-tetrahydrodibenzo[*a,g*]cyclonadecen-9-one (8).³

Formation of the trimethyltetrahydro[15]annulenone (3) from the corresponding acyclic ketone led us to expect that the trimethyltetrahydro[19]annulenone (6), with a larger π -electron cloud than (3), might have the α -methyl substituent inside the ring. However, the compound obtained from the corresponding acyclic





ketone (14) proved still to have the configuration (6), with the α -methyl group outside the ring, by an analysis of the $^1\text{H-n.m.r.}$ spectra.

The annulenone (4) was prepared *via* (20) as reported.² The syntheses of the annulenones (5)—(8) were carried out by the same procedure as previously reported.⁴ Condensation of 3,8-dimethyldeca-3,5,7-trien-9-yn-2-one (9)^{4c} with (2*E*,4*E*,6*Z*)-7-methylnona-2,4,6-trien-8-ynal (10)⁵ in ether in the presence of ethanolic sodium ethoxide gave the acyclic ketone (11) in 38% yield. Oxidative coupling of (11) with anhydrous copper(II) acetate in pyridine and ether⁶ for 5 h at 50 °C gave the annulenone in 23% yield. An acid-catalysed aldol condensation of butan-2-one with the trienyne aldehyde (10) afforded the ketone (12) in 39% yield. A second aldol condensation of (12) with (2*E*,4*Z*)-5-methylhepta-2,4-dien-6-ynal (13),⁷ under the conditions described for that between (9) and (10), gave the acyclic ketone (14)

in 43% yield. Oxidative coupling of (14) as before yielded the annulenone (6) (16% yield). Similarly, the reaction of 8-methyldeca-3,5,7-trien-9-yn-2-one (15)² with 5-(*o*-ethynylphenyl)penta-2,4-dienal (16)⁸ afforded the ketone (17) in 70% yield. Oxidation of (17) gave the monobenzannulenone (7) in 5.6% yield. Condensation of 6-(*o*-ethynylphenyl)-3-methylhexa-3,5-dien-2-one (18)^{4c} with (16) in the presence of ethanolic sodium ethoxide in tetrahydrofuran gave the ketone (19) (56% yield), which led to the dibenzannulenone (8) (16% yield).

Treatment of the annulenones (4)—(8) with trifluoroacetic acid or deuteriotrifluoroacetic acid gave the corresponding protonated or deuterated species (4')—(8'): (4') dark green,² (5') dark green, (6') dark blue, (7') purple, and (8') purple. Quenching of (5'), (7'), and (8') with aqueous sodium hydrogencarbonate resulted in regeneration of (5), (7), and (8), respectively. When set

aside (4') and (6') changed irreversibly, and the ketones (4) and (6) were not recovered on quenching (see below).

The electronic absorption maxima of the annulenones (4)—(8) in tetrahydrofuran are given in Table 1. Little difference is observed between these spectra and those of the corresponding tetrahydro[15]annulenones, except that each band shows a bathochromic shift (26—35

between the various protons for the cyclic ketone (annulenone) and the corresponding acyclic model (*i.e.* upfield shift for the inner protons and downfield shift for the outer) (Table 3), annulenones (4), (5), and (6) are seen to be diatropic, while the benzannulated annulenones (7) and (8) are atropic. This is readily seen from Figures 1—3 (centre portion of the spectra) and 4, which

TABLE 1

Electronic absorption maxima of tetrahydro[19]annulenones in tetrahydrofuran [$\lambda_{\text{max.}}$ /nm ($\epsilon_{\text{max.}}$)]

(4) ^a	(5)	(6)	(7)	(8)
248 (15 900)	225 (14 700)	236 (14 300)	220 (28 700)	226 (30 600)
254 (16 800)		247 (13 100)		
260 (17 100)		252 (13 700)		
278 (17 900)	264 (15 800)	258 (14 700)	265sh (25 200)	280sh (29 000)
329 (51 300)	279 (16 000)	266 (15 400)	277 (29 100)	300sh (41 300)
420sh (6 150)	333 (62 500)	280sh (15 000)	320sh (61 900)	320sh (56 700)
	425sh (8 540)	329 (59 500)	332 (68 100)	332 (61 200)
	451sh (6 020)	415sh (6 600)	395sh (13 800)	381sh (13 100)

^a See ref. 2.

nm). However, the bathochromic shifts are small between these [19]annulenones and the corresponding tetrahydro[21]annulenones.⁹ Also, the longest wavelength band of these [19]annulenones exhibits absorption toward longer wavelength in the order (4) \simeq (5) \simeq (6) > (7) > (8), demonstrating the degree of extended conjugation of the π -electron system in the tetrahydro[19]annulenone ring (Table 1 and see ref. 3).

The absorption maxima of the annulenones (4)—(8) in trifluoroacetic acid are given in Table 2. It is evident that the main maxima of these protonated species shift to longer wavelength (25—79 nm) in every case. It is noted that much larger bathochromic shifts of the main

show the ¹H n.m.r. spectra of (4)—(8) at room temperature. In the spectra of (7) and (8) (Figure 4), compared with those of (4)—(6), the high- and low-field shifts of the resonances of the inner and outer protons, respectively, are not observed. In the deuteriated series (4')—(6') are strongly diatropic, (7') is diatropic, and (8') is atropic (Table 3). Thus, the diatropicity of both the annulenones and their deuteriated species decreases in the sequence (4) \simeq (5) \simeq (6), [(4') \simeq (5') \simeq (6')] > (7), [(7')] > (8), [(8')], *i.e.* with increasing number of fused benzene rings on the tetrahydro[19]annulenone ring system, as has been observed for the tetrahydro[15]annulenone system.¹

TABLE 2

Electronic absorption maxima of tetrahydro[19]annulenones in trifluoroacetic acid [$\lambda_{\text{max.}}$ /nm (relative extinction coefficients)]

(4) ^{a,b}	(5)	(6) ^b	(7)	(8)
296sh (0.64)	270 (0.10)	285sh (0.67)	285 (0.67)	295 (0.70)
301 (0.65)	298 (0.61)	293 (0.73)		
408 (1.00)	406 (1.00)	397 (1.00)	374 (1.00)	357 (1.00)
420sh (0.97)	426 (0.84)	444sh (0.27)	435sh (0.22)	
580sh (0.35)	583 (0.31)	583 (0.38)	563 (0.44)	545 (0.32)
610 (0.39)	602 (0.31)	627sh (0.27)	675sh (0.09)	655sh (0.06)
656 (0.26)	661 (0.19)			

^a See ref. 2. ^b The spectra of (4) and (6) in trifluoroacetic acid changed on standing.

maxima, caused by protonation, are observed in the cases of the methylated tetrahydro[19]annulenones (4)—(6) (68—79 nm) than in those of the corresponding methylated tetrahydro[17]annulenones (25 nm).^{2,4c}

The chemical shifts of the olefinic, aromatic, and methyl protons of the annulenones (4)—(8) are listed in Table 3, together with those of the corresponding acyclic ketones (20), (11), (14), (17), and (19). Data for the deuteriated species (4')—(8') are also given in Table 3. Individual assignments, some of which are tentative, were made on the basis of multiplicity and coupling constants (see Experimental section), and by comparison with the data of closely related compounds.¹

From Table 3, if we judge the tropicity of these annulenones from the differences in chemical shifts

Variable-temperature ¹H n.m.r. spectra of (4)—(8) were run at 100 MHz over the range -60 to +60 °C, the results of which, summarized in Table 4, show the spectra of all the annulenones (4)—(8) to be essentially temperature-independent, although with decreasing temperature the resonances of the inner and outer protons of these annulenones move to a slightly higher and lower field, respectively, reflecting the higher planarity of the tetrahydro[19]annulenone ring at low temperatures. The spectra of the trimethyltetrahydro[19]annulenone (6) which is the higher analogue of (3), are shown in Figure 3. On cooling, the resonances of the inner protons (H^B, H^{B'}, H^D, H^{D'}, H^F) of (6) move to a slightly higher field, whereas those of the outer protons (H^A, H^C, H^{C'}, H^E, H^{E'}, H^G) and the methyl protons move to a

TABLE 3

¹H N.m.r. parameters of compounds (4)–(8), (20), (11), (14), (17), (19) (in CDCl₃) and (4')–(8') (in CF₃CO₂D) at 90 MHz, determined at 35 °C (τ-values)

	H ^A	H ^{A'}	H ^B	H ^{B'}	H ^C	H ^{C'}	H ^D	H ^{D'}	H ^E	H ^{E'}	H ^F	H ^{F'}	H ^G	H ^{G'}	Ar-H	Me
(20)	2.43												3.73			7.97
(4)	3.52	3.80	4.10 ^b	2.87	3.22 ^c	3.33 ^c	4.15 ^d	3.98 ^b	2.87	3.22	4.35 ^d		2.87	3.22		7.79, 7.83
Δ[(4)–(20)]	1.2–1.8	8.4–9.1	1.2	1.8	1.8	8.4–9.1	1.2–1.8	8.4–9.1	1.2–1.8				1.2–1.8			6.96, 7.07
Δ[(4')–(20)]																–0.14 to –0.18
Δ[(4')–(20)]																–0.90 to –1.01
(11)		2.49														7.99
(5)		3.87	4.22	2.87	2.90	3.40	4.30 ^e	4.20 ^e	2.97	3.13	4.48 ^e					7.79, 7.83
(5')		7.12	9.47	1.56	1.22	2.90	9.52	9.17	1.16 ^f	1.23	9.54					6.84, 6.94
Δ[(5)–(11)]																–0.16 to –0.20
Δ[(5')–(11)]																–1.05 to –1.15
(14)			2.45													7.99
(6)	2.45–3.70		4.1	4.6	2.8	3.3	4.1	4.6	2.8	3.3	4.1	4.6	2.8	3.3		7.80, 7.87, 7.95
(6')	3.42		7.69	7.43	1.3	1.9	8.12 ^g	8.02 ^g	1.3	1.9	8.42 ^g		1.3	1.9		7.07, 7.18
Δ[(6)–(14)]	1.3–1.9															–0.04 to –0.19
Δ[(6')–(14)]																–0.81 to –0.92
(17)																7.99
(7)	2.27															7.89
(7')	3.03		5.02 ^h	4.87 ^h	1.7	2.7	4.13 ^h	5.15 ^h	1.7	2.7	4.60 ^h					7.42
Δ[(7)–(17)]																–0.10
Δ[(7')–(17)]																–0.57
(19)																7.89
(8)		2.23														7.87
(8')		2.20														7.58
Δ[(8)–(19)]																–0.02
Δ[(8')–(19)]																–0.31

^a At 100 MHz. ^{b–f} Assignments may be reversed in each group (see Experimental section). However, the most probable values are given in Table 3 by referring to the chemical shifts of related compounds (see refs. 1 and 4). ^g The spectra of (4') and (6') changed with time.

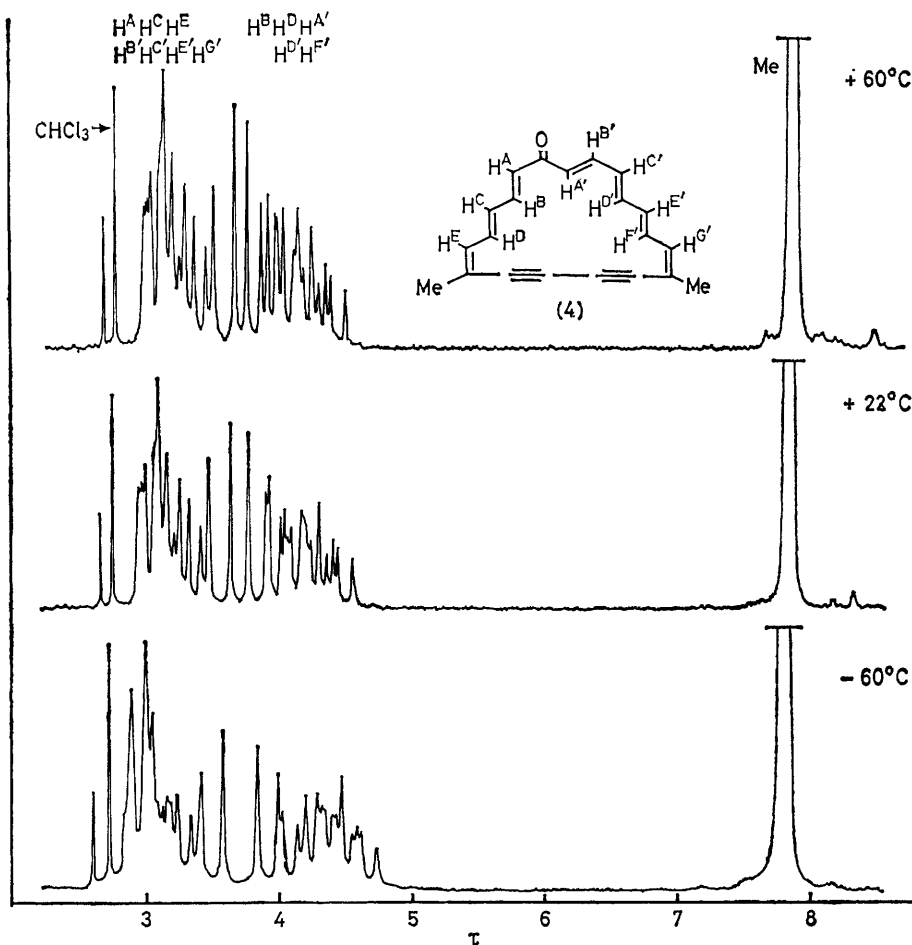
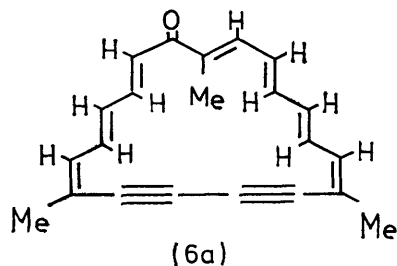


FIGURE 1 100-MHz Fourier-transform ^1H n.m.r. spectra of the [19]annulenone (4) in CDCl_3 .

slightly lower field. However, the $J_{B,C}$ value (11 Hz), indicating an *s-trans* relationship of the H^B and H^C bonds, does not vary from -60 to 60°C , thus excluding a change of conformation of (6) due to a rotation of the $\text{CH}^A=\text{CH}^B$ double bond over this temperature range, in contrast to trimethyltetrahydro[13]annulenone.^{4a} The spectra of the dimethyltetrahydro[19]annulenone (4) and the trimethyltetrahydro[19]annulenone (5) are illustrated in Figures 1 and 2, which show that the signals of both the inner and outer protons of (4) and (5) vary less than those of (6) between -60 and 60°C (see also Table 4), reflecting the greater rigidity of the molecular skeleton. This observation is very apparent in the spectra of (4), (5), and (6) in deuteriotrifluoroacetic acid (Figure 5 and the bottom portion of Figure 6). As can also be seen from Table 3, the inner protons of these annulenones resonate at lower field in the sequence (5') > (4') > (6'), while the outer protons and methyl protons resonate at higher field in the same sequence. This result suggests that the planarity, *i.e.* the rigidity of the molecular skeleton of the tetrahydro[19]annulenone ring system decreases in the sequence (5) > (4) > (6), reflecting the perturbation caused by the introduction of

the α -methyl substituent. This observation is supported by the fact that a bathochromic shift of the main maximum as well as the longest wavelength band is seen in this sequence in the u.v. spectra of these annulenones in both tetrahydrofuran and trifluoroacetic acid (Tables 1 and 2).



In addition, the intramolecular oxidative coupling of (14) gave the trimethylannulenone (6) with the α -methyl substituent outside the ring in the tetrahydro[19]annulenone system, as observed for the formation of the trimethylannulenone (3) in the corresponding tetrahydro[15]annulenone system.¹ This suggests that the

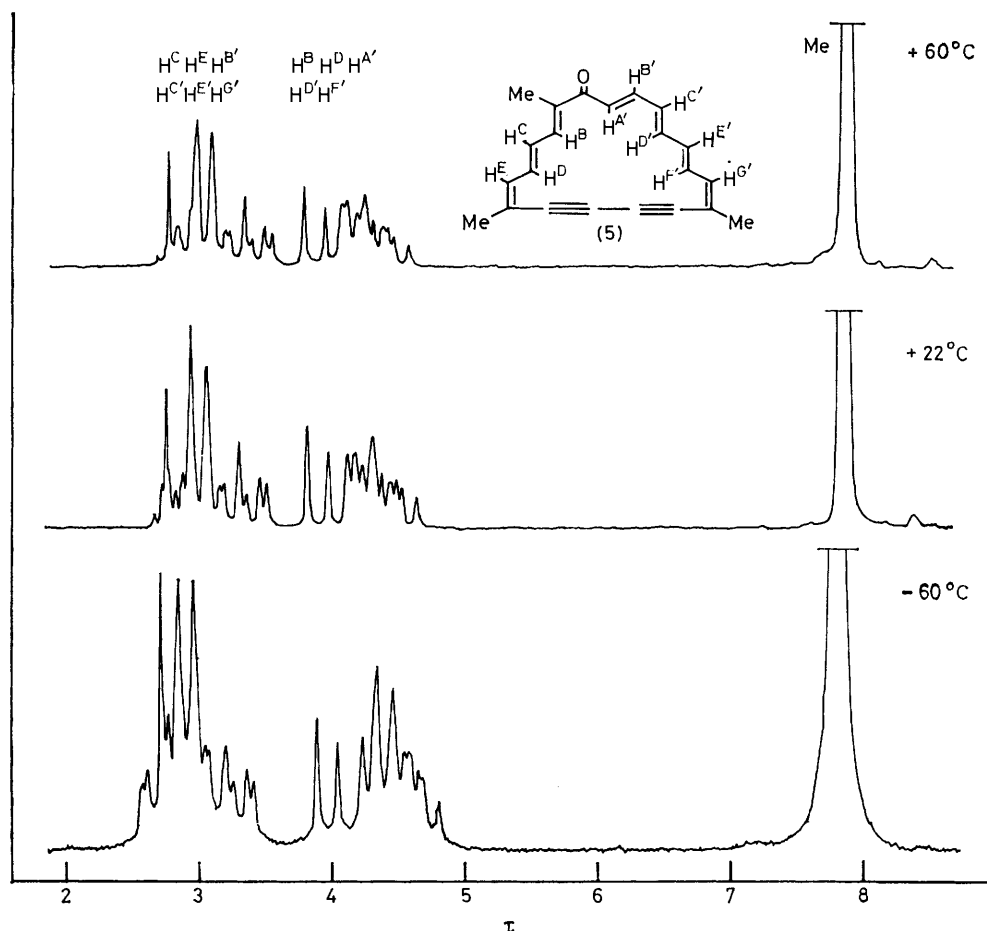


FIGURE 2 100-MHz Fourier-transform ^1H n.m.r. spectra of the [19]annulenone (5) in CDCl_3

TABLE 4

Variable-temperature ^1H n.m.r. parameters for the compounds (4)–(8) at 100 MHz (τ -values)

Compd.	T ($^{\circ}\text{C}$)	H^{A}	$\text{H}^{\text{A}'}$	H^{B}	$\text{H}^{\text{B}'}$	H^{C}	$\text{H}^{\text{C}'}$	H^{D}	$\text{H}^{\text{D}'}$	H^{E}	$\text{H}^{\text{E}'}$	H^{F}	H^{G}	ArH	Me
(4)	+60	3.57	3.83	4.10	2.97–3.24	3.36	4.16	3.98	2.97–3.24	4.36	2.97–3.24				7.85, 7.89
	+22	3.57	3.84	4.17	2.94–3.20	3.34	4.22	4.03	2.94–3.20	4.42	2.94–3.20				7.83, 7.87
	-30	3.50	3.87	4.26	2.83–3.20	3.28	4.33	4.11	2.83–3.20	4.52	2.83–3.20				7.79, 7.83
	-60	3.49	3.89	4.31	2.82–3.18	3.25	4.39	4.15	2.82–3.18	4.57	2.82–3.18				7.77, 7.81
(5)	+60		3.85	4.12	2.88	2.95	3.40	4.24	4.22	3.10	3.20	4.44	3.10		7.84, 7.89
	+22		3.88	4.17	2.84	2.94	3.37	4.31	4.29	2.98	3.16	4.50	2.98		7.82, 7.87
	-30		3.93	4.25	2.73	2.89	3.31	4.43	4.41	2.93	3.10	4.61	2.93		7.79, 7.83, 7.86
	-60		3.96	4.28	2.73	2.89	3.27	4.48	4.46	2.89	3.06	4.67	2.89		7.77, 7.80, 7.84
(6)	+60	3.50		4.07–4.59	2.88–3.34		4.07–4.59	2.88–3.34	4.07–4.59	2.88–3.34					7.85, 7.92, 7.99
	+22	3.48		4.13–4.63	2.85–3.30		4.13–4.63	2.85–3.30	4.13–4.63	2.85–3.30					7.83, 7.90, 7.98
	-30	3.40		4.22–4.69	2.80–3.23		4.22–4.69	2.80–3.23	4.22–4.69	2.80–3.23					7.79, 7.86, 7.95
	-60	3.39		4.39–4.72	2.78–3.19		4.39–4.72	2.78–3.19	4.39–4.72	2.78–3.19					7.77, 7.84, 7.94
(7)	+60	2.30												3.80	7.92
	+22	2.28												3.82	7.89
	-30	2.26												3.84	7.86
	-60	2.24												3.86	7.84
(8)	+60		2.15											3.52	7.90
	+22		2.14											3.53	7.89
	-30		2.14											3.54	7.88
	-60		2.08											3.55	7.87

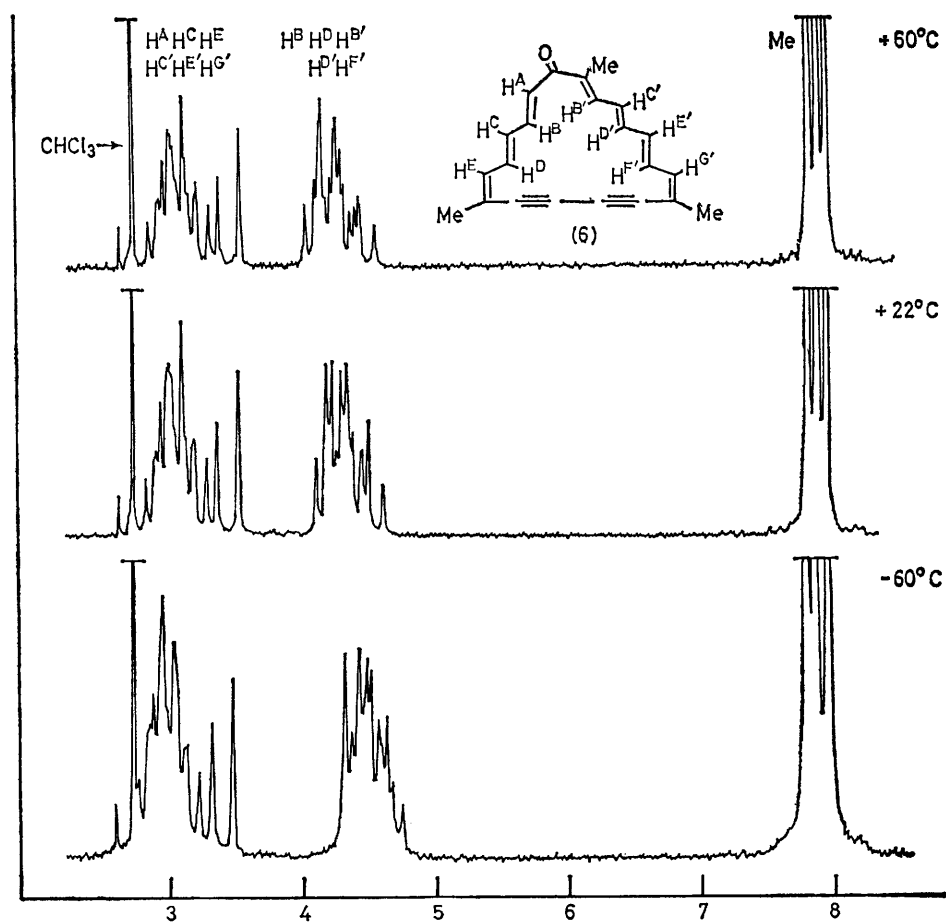


FIGURE 3 100-MHz Fourier-transform ^1H n.m.r. spectra of the [19]annulene (6) in CDCl_3

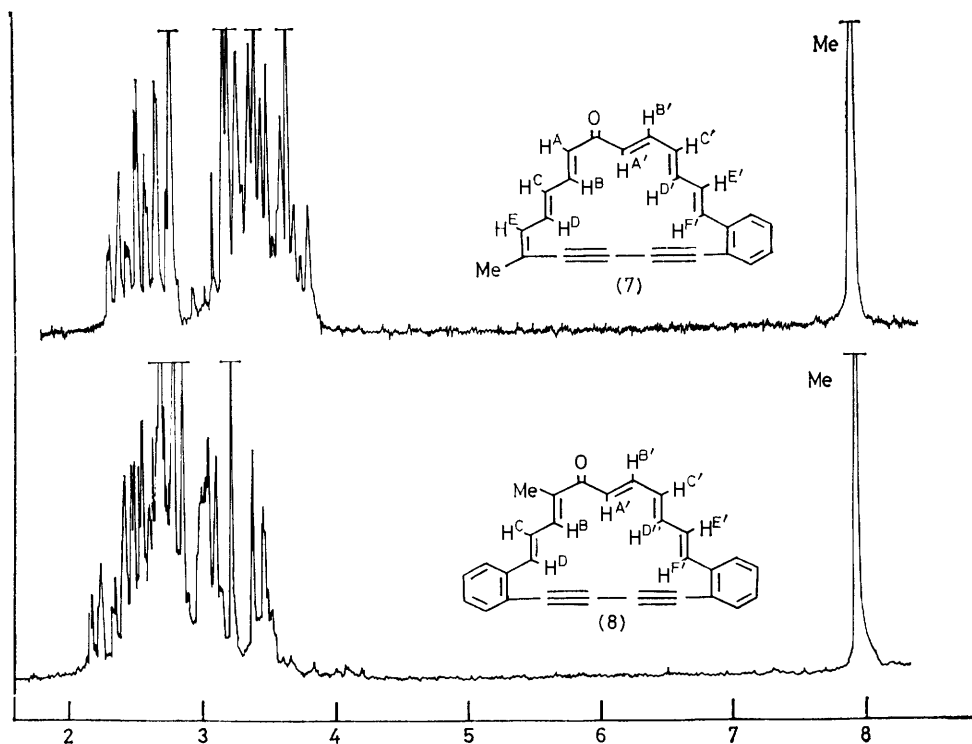


FIGURE 4 100-MHz Fourier-transform ^1H n.m.r. spectra of the [19]annulenes (7) and (8) in CDCl_3 at 22°C

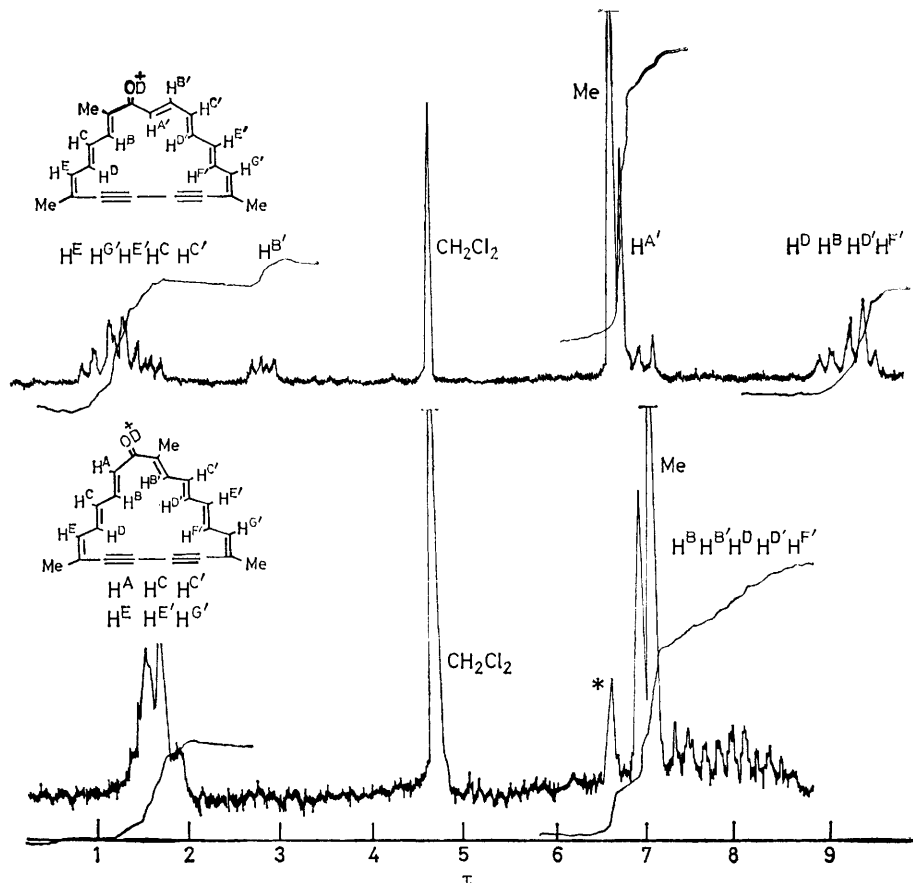


FIGURE 5 90-MHz ^1H N.m.r. spectra of the [19]annulenes (5) and (6) in $\text{CF}_3\text{CO}_2\text{D}$ at 35°C ; peaks marked with an asterisk are due to an unknown compound (see text)

alternative structure (6a) with the α -methyl group inside the tetradecahydro[19]annulenone ring experiences considerable steric hindrance between the internal olefinic protons and methyl protons. Thus it may be concluded that this behaviour is inherent in 1,2,3,4-tetradecahydroannulenone ring systems of this type.

Also, the ^1H n.m.r. and u.v. spectra of compound (4') which are shown in Figures 6 and 7, respectively, change with time, suggesting that a new compound is being formed. A similar observation was made for (6'), but it occurred more slowly. As can be seen from Figure 6, the ^1H n.m.r. spectra of a freshly prepared sample of (4') in deuteriotrifluoroacetic acid (a) already exhibited two singlets at *ca.* τ 6.8, presumably due to methyl protons of another compound. After 5 min (b), these signals became bigger, while the signals assigned to (4') became smaller and new signals appeared at both higher and lower field. After 15 min (c), the signals for (4') had almost disappeared and the new signals dominated the spectrum. After one day (d), only the signals due to the new compound remained. We believe that this new compound is more diatropic than (4'), since the signals observed after one day resonate at unexpectedly high and low field. Examination of the u.v. spectra of (4') supports the interpretation. As seen in Figure 7, all the bands of (4') shift to longer wavelength with the

passage of time. The electronic spectrum taken after standing for one day indicates a bathochromic shift of 15 nm as compared with that of freshly prepared (4'). Since a similar observation was made for (6'), solutions of both (4') and (6') in trifluoroacetic acid were allowed to stand for an appropriate time and then quenched with aqueous sodium hydrogencarbonate. We then isolated new compounds from both (4') and (6') after separation by column chromatography, and examined the spectra (see Experimental section). However, we could not determine their structures.

EXPERIMENTAL

Deoxygenated ether was used, prepared as reported.^{1,4} The ethanolic sodium ethoxide solution used for aldol condensations was prepared from sodium (380 mg) and dry ethanol (50 ml) immediately before use. M.p.s were determined with a hot-stage apparatus and are uncorrected. I.r. spectra were taken as KBr discs with a Hitachi EPI-S2 spectrophotometer. U.v. spectra were measured in tetrahydrofuran solution unless otherwise specified and run with a Hitachi 124 spectrophotometer. Mass spectra were recorded with a JEOL JMS-200 spectrometer at 75 eV using a direct-inlet system. ^1H N.m.r. spectra were run with a Varian EM-390 (90 MHz) or JEOL MH-100 (100 MHz) or JEOL FX-100 (100 MHz) spectrometers (CDCl_3 solution). Merck alumina (activity II-III) was used for column

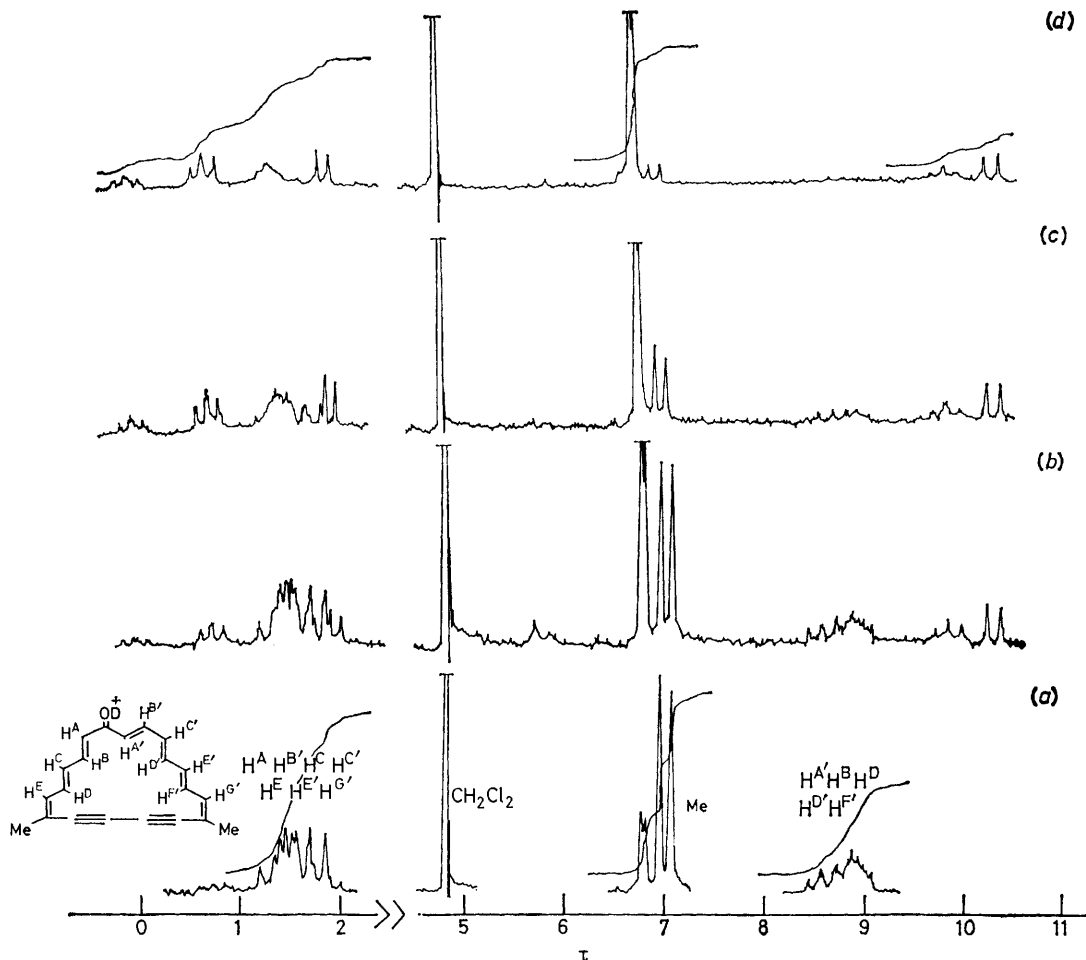


FIGURE 6 100-MHz ^1H n.m.r. spectra of the [19]annulenone (4) in $\text{CF}_3\text{CO}_2\text{D}$ at 35°C ; (a): spectrum taken with freshly prepared (4'); (b): spectrum after 5 min; (c): spectrum after 15 min; (d): spectrum after one day

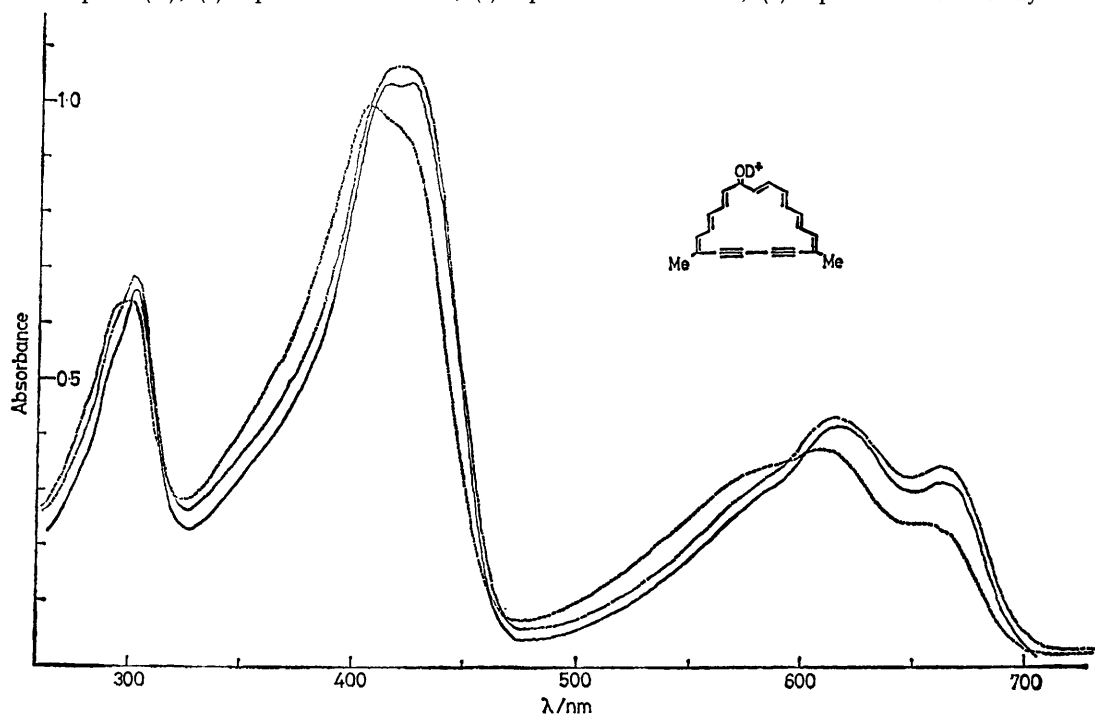


FIGURE 7 U.v. spectra of (4) in $\text{CF}_3\text{CO}_2\text{H}$: (-----), spectrum taken with freshly prepared (4'); (- · - · -), spectrum after 15 min; and (————), spectrum after one day

chromatography, sodium sulphate was used as drying agent, and solvents were evaporated under water-pump pressure.

3,17-Dimethylnonadeca-3,5,7,10,12,14,16-heptaen-1,18-diyn-9-one (20).—This compound was prepared from (15) and (10) as previously reported.²

7,12-Dimethyl-8,9,10,11-tetradehydrocyclononadecenone (4).—This compound was prepared from (20) as previously reported.²

3,8,17-Trimethylnonadeca-3,5,7,10,12,14,16-heptaen-1,18-diyn-9-one (11).—A solution of ethanolic sodium ethoxide (30 ml) was added to a solution of the ketone (9) ^{4c} (1.00 g, 5.7 mmol) in deoxygenated ether (46 ml), and a solution of (2*E*,4*E*,6*Z*)-7-methylnona-2,4,6-trien-8-ynal (10) ⁵ (1.26 g, 8.62 mmol) in deoxygenated ether (13 ml) was added dropwise during 0.5 h with stirring at 2–3 °C. After stirring for a further 4 h at the same temperature, further portions of ethanolic sodium ethoxide (each 2.0 ml) were added after every 2 h. After stirring for a total of 10 h, the reaction was quenched by the addition of aqueous oxalic acid. The mixture was poured into water, extracted with benzene, and the extracts were washed successively with water, aqueous sodium hydrogen-carbonate, and brine, and then dried. The dark red liquid obtained by evaporation of the solvent was chromatographed on alumina (110 g). The initial fractions gave the unchanged ketone (9) (486 mg). Later fractions, eluted with hexane-ether (7 : 3), gave the ketone (11) (665 mg, 38%) as a solid. Recrystallization from hexane-benzene afforded orange *needles*, m.p. 117 °C (decomp.); *m/e* 302 (*M*⁺, 100%); *M*, 302.4; ν_{\max} 3 250 (C=C-H), 2 150 (C≡C), 1 635 (C=O), 1 590 (C=C), and 1 000 cm⁻¹ (*trans*-C=C); λ_{\max} 224 (ϵ 17 500), 298sh (31 100), 308sh (33 300), 325 (36 300), 340 (38 300), 393 (57 900), and 415sh nm (47 900); τ 2.49–3.78 (11 H, m, olefinic H), 6.57 (1 H, s, C≡CH), 6.60 (1 H, s, C≡CH), and 7.99 (9 H, s, Me) (Found: C, 87.4; H, 7.3. C₂₂H₃₂O requires C, 87.4; H, 7.3%).

2,7,12-Trimethyl-8,9,10,11-tetradehydrocyclononadecenone (5).—A solution of the ketone (11) (2.03 g, 6.71 mmol) in pyridine-dry ether (3 : 1, 141 ml) was added dropwise during 4 h to a stirred solution of anhydrous copper(II) acetate (8.3 g) in pyridine-dry ether (3 : 1, 316 ml) at 51–55 °C. The solution was stirred for a further 1 h at the same temperature and cooled. After addition of benzene (100 ml), the mixture was filtered through Hyflo Super-Cel. The precipitates formed were washed with benzene (100 ml × 3), and the filtrate was poured into water. The organic layer, combined with the benzene extracts from the aqueous layer, was washed successively with 3*M*-hydrochloric acid, aqueous sodium hydrogen-carbonate, and brine, and then dried. After removal of solvent, the dark brown liquid obtained was chromatographed on alumina (120 g). Fractions, eluted with hexane-ether (2 : 3), gave the annulene (5) (462 mg, 23%). It formed red *needles* from hexane-benzene, m.p. 201 °C (decomp.); *m/e* 300 (*M*⁺, 73%) and 241 (100); *M*, 300.4; ν_{\max} 2 250 (C≡C), 1 635 (C=O), 1 610 (C=C), 995, and 970 cm⁻¹ (*trans*-C=C); for u.v. data see Tables 1 and 2; τ 2.87 (1 H, dd, *J* 15 and 6 Hz, H^B) 2.90 (1 H, dd, *J* 15 and 11 Hz, H^C), 2.97 (2 H, d, *J* 12 Hz, H^B and H^G), 3.13 (1 H, dd, *J* 15 and 12 Hz, H^E), 3.40 (1 H, dd, *J* 15 and 6 Hz, H^C), 3.87 (1 H, d, *J* 15 Hz, H^A), 4.20 (1 H, dd, *J* 15 and 12 Hz, H^D or H^{D'} or H^F), 4.22 (1 H, d, *J* 11 Hz, H^B), 4.30 (1 H, dd, *J* 15 and 12 Hz, H^D or H^{D'} or H^F), 4.48 (1 H, dd, *J* 15 and 12 Hz, H^D or H^{D'} or H^F), 7.79 (3 H, s, Me), and 7.83 (6 H, s, Me) (see also Figure 2); τ (CF₃CO₂D,

CH₂Cl₂ as internal standard) 0.84 (1 H, d, *J* 12 Hz, H^B or H^G), 1.16 (1 H, d, *J* 12 Hz, H^B or H^G), 1.22 (1 H, dd, *J* 15 and 12 Hz, H^C), 1.23 (1 H, dd, *J* 15 and 12 Hz, H^E), 1.56 (1 H, dd, *J* 15 and 8 Hz, H^B), 2.90 (1 H, dd, *J* 15 and 8 Hz, H^C), 6.84 (6 H, s, Me), 6.94 (3 H, s, Me), 7.12 (1 H, d, *J* 15 Hz, H^A), 9.17 (1 H, dd, *J* 15 and 12 Hz, H^D), 9.47 (1 H, d, *J* 12 Hz, H^B), 9.52 (1 H, dd, *J* 15 and 12 Hz, H^D), 9.54 (1 H, dd, *J* 15 and 12 Hz, H^F) (see also Figure 5) (Found: C, 87.8; H, 6.4. C₂₂H₂₀O requires C, 88.0; H, 6.7%).

3,10-Dimethyldodeca-3,5,7,9-tetraen-11-yn-2-one (12).—A solution of (2*E*,4*E*,6*Z*)-7-methylnona-2,4,6-trien-8-ynal (10) (1.5 g, 10 mmol) in acetic acid (9.4 ml) was added dropwise over 6 min to a stirred solution of butan-2-one (14.8 g, 0.21 mol) and concentrated sulphuric acid (3.2 ml) in acetic acid (40 ml) at 8–9 °C. The reaction was continued for a further 30 min at the same temperature. The mixture was then cautiously poured into saturated aqueous potassium carbonate (75 g, 240 ml), and extracted with benzene. The extracts were washed with brine and dried. Chromatography of the product over alumina (110 g) with hexane-ether (4 : 1) as eluant gave the ketone (12) (795 mg, 39%) as a solid. Recrystallization from hexane-benzene afforded yellow *needles*, m.p. 76–77 °C; *m/e* 200 (*M*⁺, 68%) and 142 (100); *M*, 200.3; ν_{\max} 3 250 (C=C-H), 2 150 (C≡C), 1 650, 1 620, 1 585 (C=O, C=C), and 990 cm⁻¹ (*trans*-C=C); λ_{\max} (EtOH) 250sh (ϵ 2 880), 258 (4 160), 336sh (19 500), 356 (50 900), and 367 nm (51 000); τ 2.83–3.75 (6 H, m, olefinic H), 6.58 (1 H, s, C≡CH), 7.63 (3 H, s, Me), 8.00 (3 H, s, Me), and 8.07 (3 H, s, Me) (Found: C, 83.75; H, 7.8. C₁₄H₁₆O requires C, 84.0; H, 8.05%).

3,10,17-Trimethylnonadeca-3,5,7,10,12,14,16-heptaen-1,18-diyn-9-one (14).—A solution of ethanolic sodium ethoxide (2.4 ml) was added to a solution of the ketone (12) (868 mg, 4.3 mmol) in deoxygenated ether (34 ml), and a solution of (2*E*,4*Z*)-5-methylhepta-2,4-dien-6-ynal (13) ⁷ (780 mg, 6.5 mmol) in deoxygenated ether (10 ml) was added dropwise during 35 min with stirring in an ice-bath. After stirring for a further 1 h at the same temperature, further portions of ethanolic sodium ethoxide (each 1.5 ml) was added after every 30 min. After stirring for a total of 7 h, the reaction was quenched by the addition of aqueous oxalic acid. After work-up as for the isolation of (11), the product was chromatographed on alumina (180 g). Initial fractions gave the unchanged ketone (12) (380 mg). Later fractions, eluted with hexane-ether (7 : 3), gave the ketone (14) (568 mg, 43%) as a solid. Recrystallization from hexane-benzene afforded brown *cubes*, m.p. 187–188 °C; *m/e* 302 (*M*⁺, 8%) and 215 (100); *M*, 302.4; ν_{\max} 3 260 (C=C-H), 2 150 (C≡C), 1 635 (C=O), 1 615 (C=C), 995, and 980 cm⁻¹ (*trans*-C=C); λ_{\max} 233 (ϵ 8 070), 284sh (17 800), 296sh (21 600), 310sh (24 600), 323 (26 800), 338 (26 500), 377sh (37 000), 394 (41 500), and 415sh nm (36 800); τ 2.45–3.70 (11 H, m, olefinic H), 6.57 (2 H, s, C≡CH), and 7.99 (9 H, s, Me) (Found: C, 87.3; H, 7.4. C₂₂H₂₂O requires C, 87.4; H, 7.3%).

7,12,19-Trimethyl-8,9,10,11-tetradehydrocyclononadecenone (6).—A solution of the ketone (14) (188 mg, 0.62 mmol) in pyridine-dry ether (3 : 1, 13 ml) was added dropwise during 40 min to a stirred solution of anhydrous copper(II) acetate (0.77 g) in pyridine-dry ether (3 : 1, 36 ml) at 55–57 °C. The solution was stirred for a further 0.5 h at the same temperature and cooled. After work-up as for the isolation of (5), the product was chromatographed on alumina (80 g). Fractions, eluted with hexane-ether (4 : 1), gave the annulene (6) (30 mg, 16%) as a solid. It formed orange *needles*

from hexane-benzene, m.p. 120–121 °C; m/e 300 (M^+ , 24%) and 165 (100); M , 300.4; ν_{\max} . 2 175 ($C\equiv C$), 1 610, 1 595 ($C=O$, $C=C$), and 980 cm^{-1} (*trans*- $C=C$); for u.v. data see Tables 1 and 2; τ 2.80–3.30 (5 H, m, H^C , H^E , H^F , and $H^{F'}$), 3.42 (1 H, d, J 16 Hz, H^A), 4.06–4.62 (5 H, m, H^B , $H^{B'}$, H^D , $H^{D'}$, and $H^{E'}$), 7.80 (3 H, s, Me), 7.87 (3 H, s, Me), and 7.95 (3 H, s, Me) (see also Figure 3); $\tau(CF_3CO_2D$, CH_2Cl_2 as internal standard) 1.3–1.9 (6 H, m, H^A , H^C , $H^{C'}$, H^E , $H^{E'}$, and $H^{G'}$), 7.07 (3 H, s, Me), 7.18 (6 H, s, Me), and 7.43 (1 H, d, J 12 Hz, $H^{B'}$), 7.69 (1 H, dd, J 15 and 12 Hz, H^B), 8.02 (1 H, dd, J 15 and 12 Hz, H^D or $H^{D'}$ or $H^{E'}$), 8.12 (1 H, dd, J 15 and 12 Hz, H^D or $H^{D'}$ or $H^{E'}$), and 8.42 (1 H, dd, J 15 and 12 Hz, H^D or $H^{D'}$ or $H^{E'}$) (see also Figure 5) (Found: C, 87.7; H, 6.9. $C_{22}H_{20}O$ requires C, 88.0; H, 6.7%).

1-(*o*-Ethynylphenyl)-13-methylpentadeca-1,3,5,8,10,12-hexaen-14-yn-7-one (17).—A solution of ethanolic sodium ethoxide (2.8 ml) was added to a mixture of the ketone (15) ² (1.20 g, 7.5 mmol) and 5-(*o*-ethynylphenyl)penta-2,4-dienal (16) ⁸ (1.36 g, 7.5 mmol) in deoxygenated ether (70 ml) at 2–3 °C. After stirring for 1 h at the same temperature, further portions of ethanolic sodium ethoxide (each 0.5 ml) were added after every 1 h. After stirring for a total 7 h, the reaction was quenched by addition of aqueous oxalic acid. After work-up as for the isolation of (11), the product was chromatographed on alumina (100 g). Initial fractions gave the unchanged ketone (15) (250 mg). Later fractions, eluted with hexane-ether (1 : 1), gave the ketone (17) (1.69 g, 70%) as a solid. Recrystallization from hexane-benzene afforded yellow needles, m.p. 141–142 °C; m/e 324 (M^+ , 70%) and 178 (100); M , 324.4; ν_{\max} . 3 280, 3 230 ($C\equiv C-H$), 2 130 ($C\equiv C$), 1 640 ($C=O$), 1 610, 1 595 ($C=C$), and 1 005 cm^{-1} (*trans*- $C=C$); λ_{\max} . 226 (ϵ 22 000), 235sh (20 900), 267sh (22 100), 276 (24 200), 289 (24 300), 300sh (24 100), and 393 nm (67 200); τ ca. 2.3–3.8 (15 H, m, olefinic and ArH), 6.56 (1 H, s, $C\equiv CH$), 6.60 (1 H, s, $C\equiv CH$), and 7.99 (3 H, s, Me) (Found: C, 88.6; H, 6.2. $C_{24}H_{20}O$ requires C, 88.85; H, 6.2%).

17-Methyl-18,19,20,21-tetradehydrobenzocyclononadecen-11-one (7).—A solution of the ketone (17) (1.61 g, 4.96 mmol) in pyridine-dry ether (3 : 1, 105 ml) was added dropwise during 3.5 h to a stirred solution of anhydrous copper(II) acetate (6.1 g) in pyridine-dry ether (3 : 1, 233 ml) at 50–55 °C. The solution was stirred for a further 30 min at 50–60 °C and cooled. After work-up as for the isolation of (5), the orange semi-solid obtained was chromatographed on alumina (100 g). Fractions, eluted with hexane-ether (3 : 7), gave the annulenone (7) (89 mg, 5.6%) as a solid. It formed orange needles from hexane-benzene, m.p. 135–136 °C; m/e 322 (M^+ , 76%) and 278 (100); M , 322.4; ν_{\max} . 2 160 ($C\equiv C$), 1 635 ($C=O$), 1 585, 1 570 ($C=C$), and 985 cm^{-1} (*trans* $C=C$); for u.v. data see Tables 1 and 2; τ 2.27–3.90 (15 H, m, olefinic and ArH), and 7.89 (3 H, s, Me) (see also Figure 4); $\tau(CF_3COOD)$ 1.72–2.70 (9 H, m, H^B , H^C , $H^{C'}$, H^E , $H^{E'}$, and ArH), 3.03 (1 H, d, J 15 Hz, H^A), 4.13 (1 H, dd, J 15 and 11 Hz, H^B or H^D or $H^{D'}$), 4.60 (1 H, d, J 15 Hz, $H^{A'}$ or $H^{F'}$), 4.87 (1 H, dd, J 15 and 11 Hz, H^B or H^D or $H^{D'}$), 5.02 (1 H, d, J 15 Hz, $H^{A'}$ or $H^{F'}$), 5.15 (1 H, dd, J 15 and 11 Hz, H^B or H^D or $H^{D'}$) and 7.42 (3 H, s, Me) (Found: C, 89.4; H, 5.6. $C_{24}H_{18}O$ requires C, 89.4; H, 5.6%).

1,11-Bis-(*o*-ethynylphenyl)-4-methylundeca-1,3,6,8,10-pentaen-5-one (19).—A solution of ethanolic sodium ethoxide (7.0 ml) was added to a solution of 6-(*o*-ethynylphenyl)-3-methylhexa-3,5-dien-2-one (18) ^{4c} (1.8 g, 8.5 mmol) in

tetrahydrofuran (65 ml, flushed with nitrogen), and a solution of the aldehyde (16) (1.94 g, 11 mmol) in tetrahydrofuran (25 ml, flushed with nitrogen) was added dropwise during 45 min at 5 °C. After stirring for a further 2 h, further portions of ethanolic sodium ethoxide (each 1.5 ml) were added to the solution every 1 h. After stirring for a total of 8 h at 8–10 °C, the reaction was quenched by the addition of aqueous oxalic acid. After work-up as for the isolation of (11), the product was chromatographed on alumina (130 g). Initial fractions gave the unchanged ketone (18) (961 mg). Later fractions, eluted with hexane-ether (3 : 2), gave the ketone (19) (1.78 g, 56%) as a solid. It formed yellow needles from hexane-benzene, m.p. 158–159 °C; m/e 374 (M^+ , 100%); M , 374.5; ν_{\max} . 3 280, 3 220 ($C\equiv C-H$), 2 150 ($C\equiv C$), 1 640 ($C=O$), 1 615, 1 595 ($C=C$), 1 010, and 965 cm^{-1} (*trans*- $C=C$); λ_{\max} . 237 (ϵ 47 200), 258sh (42 700), 267 (44 700), 275sh (41 100), 328sh (54 100), and 385 nm (81 200); τ 2.23–3.42 (17 H, m, olefinic and Ar-H), 6.56 (1 H, s, $C\equiv CH$), 6.61 (1 H, s, $C\equiv CH$), and 7.89 (3 H, s, Me) (Found: C, 89.6; H, 6.1. $C_{28}H_{22}O$ requires C, 89.8; H, 5.9%).

8-Methyl-20,21,22,23-tetradehydrodibenzo[a,g]cyclononadecen-9-one (8).—A solution of the ketone (19) (1.80 g, 4.89 mmol) in pyridine-dry ether (3 : 1, 117 ml) was added dropwise during 3 h to a stirred solution of anhydrous copper(II) acetate (5.90 g) in pyridine-dry ether (3 : 1, 234 ml) at 49–50 °C. After stirring for a further 2 h at 53–54 °C, the solution was cooled. After work-up as for the isolation of (5), the product was chromatographed on alumina (80 g). Fractions, eluted with hexane-ether (1 : 1), gave the annulenone (8) (287 mg, 16%) as a solid. Recrystallization from benzene afforded yellow needles, m.p. 216 °C (decomp.), m/e 372 (M^+ , 55%) and 326 (100); M , 372.4; ν_{\max} . 2 250 ($C\equiv C$), 1 640, 1 620, 1 610 ($C=O$, $C=C$), 985, and 975 cm^{-1} (*trans*- $C=C$); for u.v. data see Tables 1 and 2; τ ca. 2.00–3.36 (17 H, m, olefinic and Ar-H), and 7.87 (3 H, s, Me) (see also Figure 4) (Found: C, 90.4; H, 5.4. $C_{28}H_{20}O$ requires C, 90.3; H, 5.4%).

Isolation of Crystals from (4').—A solution of (4) (60 mg) in trifluoroacetic acid (3 ml) was allowed to stand for 1 h in a refrigerator; the solution was then poured into aqueous sodium hydrogencarbonate and extracted with chloroform. The extracts were washed with aqueous sodium hydrogencarbonate and brine, then dried. The residue obtained after solvent removal was chromatographed on alumina (200 g). The early fractions eluted with hexane-ether (1 : 1) afforded crystals (30 mg), which formed dark red cubes from hexane-benzene, m.p. 111–112 °C: the spectral properties of the crystals are the following, m/e 288 (5%), 287 (8%), 286 (40%), 279 (50%), and 69 (100); ν_{\max} . 1 640, 1 605, 1 600, and 970 cm^{-1} ; λ_{\max} . 266 (ϵ 16 000), 283sh (13 600), 347 (35 100), and 440sh (4 730); τ (200 MHz) ca. 2.15–4.40 (complex multiplet), 7.62 (s), 7.71 (s), and 7.79 (s).

Isolation of (6').—A solution of (6) (98.9 mg) in trifluoroacetic acid (3 ml) was allowed to stand for 2 days in a refrigerator. After work-up as described immediately above, the product was chromatographed on alumina (150 g). The early fractions eluted with hexane-ether (1 : 1) gave a red liquid (19.5 mg). Attempts to crystallize the liquid failed; u.v. data: main band λ_{\max} . 345 (qualitative).

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REFERENCES

¹ J. Ojima, K. Wada, and K. Kanazawa, *Chem. Lett.*, **1979**, 1035; J. Ojima, K. Wada, K. Kanazawa, and Y. Nakagawa, *J. Chem. Soc., Perkin Trans. 1*, **1981**, 947.

² J. Ojima, Y. Shiroishi, K. Wada, and F. Sondheimer, *J. Org. Chem.*, **1980**, **45**, 3564.

³ A portion of this work has appeared in a preliminary communication; J. Ojima, K. Wada, Y. Nakagawa, M. Terasaki, and Y. Juni, *Chem. Lett.*, **1980**, 225.

⁴ (a) T. M. Cresp, J. Ojima, and F. Sondheimer, *J. Org. Chem.*, **1977**, **42**, 2130; (b) J. Ojima and M. Fujiyoshi, *Chem. Lett.*, **1978**, 569; *J. Chem. Soc., Perkin Trans. 1*, **1980**, 466; (c) J. Ojima, K. Kanazawa, K. Kusaki, and K. Wada, *Chem. Lett.*, **1978**, 1009; *J. Chem. Soc., Perkin Trans. 1*, **1980**, 473.

⁵ J. Ojima, Y. Shiroishi, and M. Fujiyoshi, *Bull. Chem. Soc. Jpn.*, **1978**, **51**, 2112.

⁶ N. Darby, T. M. Cresp, and F. Sondheimer, *J. Org. Chem.*, **1977**, **42**, 1960; and see ref. 5.

⁷ J. Ojima, M. Ishiyama, and A. Kimura, *Bull. Chem. Soc. Jpn.*, **1977**, **50**, 1584.

⁸ J. Ojima, M. Enkaku, and M. Ishiyama, *J. Chem. Soc., Perkin Trans. 1*, **1977**, 1548.

⁹ J. Ojima, Y. Nakagawa, K. Wada, and M. Terasaki, following paper; *Chem. Lett.*, **1980**, 1299.