The Benzannelated Annulenones. Syntheses and Properties of 12-Methylbenzo[*f*]- and Dibenzo[*f*,*l*]-8,10-bisdehydro[17]annulenone

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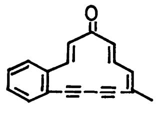
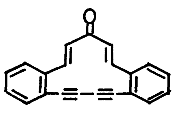
The benzannelated annulenones VII and XI have been synthesized to establish the effect of annelation of benzene ring on the seventeen-membered ring system. An examination of the NMR spectra suggested that both of VII and XI are paratropic and the paratropicities decrease in the order of VII>XI with the number of benzene ring fused to seventeen-membered ring system.

As reported in the previous papers,1) the monobenzo- (I) and dibenzobisdehydro[13]annulenone (II) were prepared by an aldol condensation of an appropriate aldehyde and ketone containing terminal acetylene group, followed by an oxidative coupling of the resulting acyclic ketone. The same approach has been now extended to synthesis of a next higher $(4n+1)$-membered ring system. The present paper deals with the synthesis and properties of the respective vinylogues of I and II, *i.e.*, 12-methylbenzo[*f*]- (VII) and dibenzo[*f*,*l*]-8,10-bisdehydro[17]annulenone (XI).2)



I



II

As outlined in Scheme, the methylbenzo[17]-annulenone (VII) was synthesized as follows. The starting material was the available *cis*-3-methyl-2-penten-4-ynal (III).3) This substance was converted to the vinylogue (IV) in an 88% overall yield by transformation to the diethyl acetal of III followed by condensation with ethyl vinyl ether in the presence of zinc chloride and treatment of the ethoxy acetal of the resulting vinylogue with sodium acetate in acetic acid according to the method of Isler *et al.*4,5) *o*-Ethynylcinnamaldehyde (IX), prepared from *o*-ethynylbenzaldehyde (VIII) as has been reported previously,6) was condensed with acetone in the presence of aqueous sodium hydroxide to afford the ketone (V) in a high yield. Aldol condensation of the dienyne aldehyde (IV) and the ketone (V) by means of methanolic potassium

TABLE 1. ^{1}H-NMR PARAMETERS OF VI AND VII IN $CDCl_3$ AT 100 MHz (τ-values; internal standard, TMS; *J* in Hz in parentheses)

Proton	VIa)	VII	ΔVII−VIi)
H^A	3.53d(15)b)	4.03d(16)e)	+0.50
H^B	2.48dd(15,11)c)	2.28—2.78f,h)	
H^C	3.05dd(15,11)d)	3.51dd(16,11)g)	+0.46
H^D	2.49d(15)	1.94d(16)	−0.55
$H^{A'}$	3.44(15)b)	4.00d(16)e)	+0.56
$H^{B'}$	2.53dd(15,11)c)	2.10dd(16,11)f)	−0.43
$H^{C'}$	3.54dd(15,11)d)	3.76dd(16,11)g)	+0.22
$H^{D'}$	2.45dd(15,11)c)	1.85dd(16,11)f)	−0.60
$H^{E'}$	2.95d(11)	3.50d(11)	+0.55
CH_3	8.10s	8.13s	+0.03
Benzenoid H	2.52—2.78m	2.28—2.78m	

a) In addition, two singlets at 6.57 and 6.61 (–C≡CH). b),c),d),e),f),g) These assignments may be reversed in each group, but most probable values are given by referring to the NMR spectra of the related compounds.1) h) This proton signal is submerged by those of benzenoid protons. i) This exhibits the chemical shift differences for the resonances on passing from IV to V.

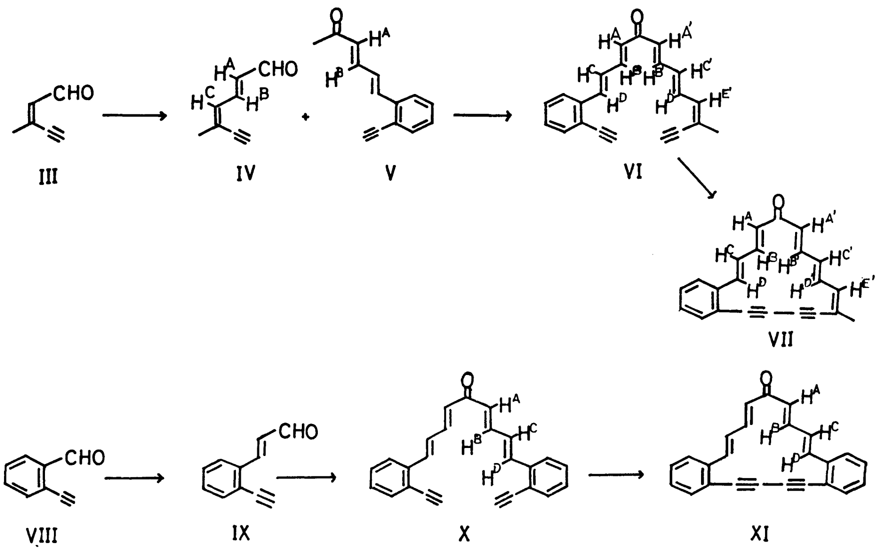


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TABLE 2. ^{1}H-NMR PARAMETERS OF X AND XI AT 90 MHz (τ-values; Internal Standard, TMS; J in Hz in Parentheses)

Proton	X in $CDCl_3$[a)]	XI in $CDCl_3$	XI in CF_3COOD	ΔXI−X
H^A	3.43d(15)	3.92d(16)	3.60d(16)	+0.49
H^B	3.05dd(15,11)	2.28dd(16,11)	1.18dd(16,11)	−0.77
H^C		3.33dd(16,11)	3.20dd(16,11)	(+1.0—+0.53)
H^D		2.08d(16)	1.03d(16)	(−0.72——0.22)
	2.3−2.8m[b)]			
Benzenoid H		2.5—2.8m	2.45—2.70m	

a) In addition, a singlet at 6.63 (–C≡CH).

b) The resonances of H^C and H^D protons are submerged by those of benzenoid protons.

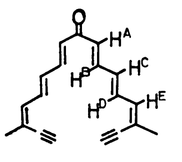
hydroxide gave the acyclic ketone (VI) in a 38% yield. Oxidation of VI with copper(II) acetate in pyridine[7)] afforded the monobenzannelated annulenone (VII) as yellow crystals in a low yield.

While, a condensation of 2 molar equivalents of IX with 1 molar equivalent of acetone, under the same conditions as indicated for the reaction of IV and V, afforded the acyclic ketone (X) in a 28% yield as orange crystals. Oxidation of X as before yielded the dibenzannelated annulenone (XI) as yellow crystals.

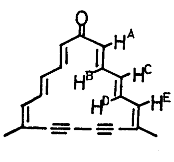
An inspection of the Dreiding molecular model reveals that the title compounds VII and XI should have the assigned conformations corresponding to those for I and II, respectively.

The ^{1}H-NMR parameters of the compounds thus obtained are shown in Tables 1 and 2. The comparison of VI and VII (Table 1) suggests that the compound VII is paratropic, as expected for a potential 16π-electron system due to the polarization of the carbonyl group, since the inner proton (H^B, $H^{B\prime}$, H^D, $H^{D\prime}$) resonances have moved to a lower field, and the outer (H^A, $H^{A\prime}$, H^C, $H^{C\prime}$, $H^{E\prime}$) and methyl ones to a higher field, as compared with those of the corresponding protons of the acyclic analogue (VI), respectively.

The similar result as above is obtained for the comparison of the parameters between X and XI (Table 2),[8)] although the chemical shift differences are smaller than those between VI and VII. Furthermore, the chemical shifts of the olefinic protons of XI in CF_3-COOD (the carbonyl protonated species) also suggest that XI is paratropic, if we consider the small downfield shift of all protons may be caused by introduction of the positive charge.



XII



XIII

In order to obtain an approximate measure of the effect of benzannelation on seventeen-membered ring system, the ^{1}H-NMR parameters of the model compounds (XII and XIII) synthesized by Ojima and Sondheimer,[9)] are listed in Table 3.

TABLE 3. ^{1}H-NMR PARAMETERS OF XII AND XIII AT 60 MHz (τ-values; internal standard, TMS; J in Hz inparentheses)

Proton	XII[a)]	XIII	ΔXIII−XII
H^A	3.57d(16)	4.20d(16)	+0.63
H^B	2.64dd(16,11) or 2.92dd(16,11)	1.37dd(16,11) or 1.40dd(16,11)	−1.24——1.55
H^C	3.61dd(16,11)	3.98dd(16,11)	+0.37
H^D	2.64dd(16,11) or 2.92dd(16,11)	1.37dd(16,11) or 1.40dd(16,11)	−1.24——1.55
H^E	3.60d(11)	3.67d(11)	+0.07
CH_3	8.01s	8.23s	+0.22

a) In addition, a singlet at 6.59 (–C≡CH).

As shown in Tables (1, 2, 3), an examination of the NMR spectra demonstrated that the seventeen-membered ring system in dimethyl compound XIII is paratropic, in monobenzo-fused compound VII, it is less paratropic, and in dibenzo-fused compound XI, it is at most weakly paratropic. The sequence can be seen in particular by the downfield shifts, as compared with the respective models (XIII, VII, XI), of the inner proton (H^B, $H^{B\prime}$, H^D, $H^{D\prime}$) bands [(−1.24——1.55), (−0.43——0.60), (−0.22——0.77) ppm, respectively], and the chemical shifts [(1.37—1.40), (1.85—),[10)] (2.08—2.28) τ, respectively].

The result obtained in the above is accord with that on thirteen-membered ring system obtained by us.[1)]

Experimental

The deoxygenated ether, methanol, and acetone were used to minimize an oxidation of the compounds used for aldol condensation and prepared immediately before use. The ether was freed from a peroxide by passing through a short column of basic alumina (Woelm, Act. I) followed by flushing with nitrogen. The methanol and acetone were flushed by nitrogen immediately prior to use. All 20% methanolic potassium hydroxide solutions were prepared before each use by dissolving 10 g of potassium hydroxide in 50 ml of methanol and flushing the solution with nitrogen. All the melting points are uncorrected. Brockmann alumina (Act. II—III) was used for column chromatography unless otherwise indicated. The IR, UV, and mass spectra were taken on a Hitachi EPI-S2 or a Unicam SP-200, a Hitachi 124 or a Unicam SP-800, and a JEOL-JMS-SG-2 or an AEI MS-12 spectrometers, respectively. Shoulders in UV spectra are denoted by sh, and wavelength of absorption maximum is recorded in nm and ε-values are given in parentheses. NMR spectra were taken on a Varian XL-100, a Varian EM-930, a JEOL-JNM-MH-60 or a Varian T-60 spectrometer. Chemical shifts are given in τ-values with respect to TMS as an internal standard, while the coupling constants (J) are given in Hz.

5-Methyl-2,4-heptadien-6-ynal (IV)[5] A 1% solution of *p*-toluenesulfonic acid monohydrate in absolute ethanol (9 drops) was added to a solution of the aldehyde (III, 3.0 g, 0.032 mol) and ethyl orthoformate (6.0 g, 0.04 mol) in absolute ethanol (5 ml). After being stirred at room temperature for 24 h, the mixture was treated with pyridine (0.5 ml) and poured into 2% aqueous sodium hydrogencarbonate (50 ml). Extraction with ether, drying over magnesium sulfate, and evaporation of the solvent yielded the crude diethyl acetal of III as a red liquid. The liquid was dissolved in ethyl acetate (5 ml) and warmed to 35 °C in a flask equipped with two dropping funnels, a condenser, and a magnetic stirrer. A 10% solution of zinc chloride in ethyl acetate (10 drops) was added, and then simultaneously this solution (5 ml) and ethyl vinyl ether (20 ml) during 15 min with stirring at 35 °C. The mixture was stirred for 2 h at room temperature, stoppered, and allowed to stand for 17 h. A solution of sodium acetate (10 g) in water (7 ml) and acetic acid (100 ml) was then added, and the mixture was heated to 90 °C for 2 h. Dilution with water (500 ml), extraction with ether, drying over magnesium sulfate, and evaporation gave a residue, which was chromatographed on alumina (100 g, Woelm, Act. III). Elution with pentane–ether (96: 4—94: 6) and evaporation of the solvents gave the aldehyde (IV, 3.4 g, 88%) as pale yellow liquid, IR (neat): 3250 (–C≡CH), 2100 (–C≡C–), 1675, 1615 (C=O, C=C), 980 cm^{-1} (*trans* C=C), UV: $\lambda_{\max}^{\text{ether}}$ 290 (24100), 300 sh nm (23100), NMR ($CDCl_3$, 60 MHz): 0.33 (d, J=8, 1H, –CHO), 2.47 (dd, J=15, 11, 1H, H^B), 3.47 (d, J=11, 1H, H^C), 3.83 (dd, J=15, 8, 1H, H^A), 6.32 (s, 1H, –C≡CH), 7.95 (s, 3H, $-CH_3$), MS: *m/e* 120 (M^+), 119 (M^+–1), 105 (M^+–15), 91 (M^+–29); mol wt, 120.14.

*6-(*o*-Ethynylphenyl)-3,5-hexadien-2-one (V).* To a stirred solution of *o*-ethynylcinnamaldehyde (IX, 4.7 g, 0.031 mol) in acetone (250 ml) was added under a nitrogen atmosphere a 5% aqueous sodium hydroxide solution (135 ml) over a period of 15 min at room temperature and stirring was continued for further 2 h at the same temperature. Neutralization with acetic acid and addition of water (250 ml) was followed by extraction with ether. The extracts were washed successively with saturated aqueous sodium hydrogencarbonate and sodium chloride solutions, dried over sodium sulfate and evaporated. The residue was chromatographed on alumina (130 g), eluting with 30% ether in light petroleum to give the ketone (V, 4.8 g, 81%) as crystals. Recrystallization from hexane–benzene afforded pure V as yellow cubes, mp 75.0—76.5 °C, IR (KBr disk): 3250 (–C≡CH), 2100 (–C≡C–), 1655, 1620, 1595 (C=O, C=C), 1000, 970 cm^{-1} (*trans* C=C), MS: *m/e* 196 (M^+, 55), 153 (100); mol wt, 196.24, UV: $\lambda_{\max}^{\text{THF}}$ 246 (11000), 254 (15000), 320 nm (29500), NMR ($CDCl_3$, 60 MHz): 2.47—3.05 (m, 6H, phenyl and olefinic H), 3.25 (dd, J=16, 10, 1H, H^B), 3.85 (d, J=16, 1H, H^A), 6.55 (s, 1H, –C≡CH), 7.82 (s, 3H, Me).

Found: C, 85.42; H, 6.09%. Calcd for $C_{14}H_{12}O$: C, 85.68; H, 6.16%.

*1-(*o*-Ethynylphenyl)-11-methyl-1,3,6,8,10-tridecapentaen-12-yn-5-one (VI).* To a mixture of the dienyne aldehyde (IV, 1.5 g, 0.0125 mol) and the ketone (V, 1.2 g, 0.0061 mol) in deoxygenated ether (80 ml) was added a 20% methanolic potassium hydroxide solution (4.5 ml) with stirring on ice-bath. The mixture was then stirred at room temperature for 90 min. Neutralization with acetic acid (5 ml) followed by pouring into water (1000 ml) and extraction with benzene gave an organic extract which was washed successively with saturated sodium hydrogencarbonate and sodium chloride solutions, and dried over sodium sulfate. The residue obtained by evaporation of the solvent was chromatographed on alumina (100 g) with light petroleum–ether (7: 3) to give the ketone (VI, 0.7 g, 38%) as unstable solids. Recrystallization from hexane–benzene formed yellow-brown needles, mp 121.5—122.5 °C, MS: *m/e* 298 (M^+, 80), 154 (100); mol wt, 198.36, IR (KBr disk): 3300, 3250 (–C≡CH), 2100 (–C≡C–), 1660, 1605, 1600 (C=O, C=C), 1010 cm^{-1} (*trans* C=C), UV: $\lambda_{\max}^{\text{THF}}$ 258 (20200), 267 (21800), 288 sh (18500), 378 nm ((40700), NMR: see Table 1.

12-Methylbenzo[f]*-8,10-bisdehydro*[*17*]*annulenone (VII).* A solution of VI (0.6 g, 0.002 mol) in pyridine (26 ml) was added, drop by drop, with stirring over a period of 10 min into a solution of copper(II) acetate monohydrate (9.0 g) in pyridine (19 ml) kept at 55 °C; the mixture was stirred for further 2 h at 60—65 °C. Then the mixture was chilled, diluted with benzene (200 ml), and poured into 6% hydrochloric acid (1000 ml). The layers were separated, and the aqueous layer was extracted with benzene. The combined benzene layer was washed successively with aqueous sodium hydrogencarbonate and saturated sodium chloride solutions, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on alumina (100 g) with light petroleum–ether (1: 1) to give VII (0.07 g, 12%) as relatively stable solids. Recrystallization from hexane–benzene afforded pure VII as yellow cubes, mp *ca.* 180 °C (dec), MS: *m/e* 296 (M^+, 45), 252 (100); mol wt, 296.35, IR (KBr disk): 2200 (–C≡C–), 1630 (C=O), 1595 (C=C), 995 cm^{-1} (*trans* C=C), UV: $\lambda_{\max}^{\text{THF}}$ 285 sh (28500), 299 (35500), 317 (30400), 400 nm (2760), NMR: see Table 1.

*1,10-Bis(*o*-ethynylphenyl)-1,3,6,8-decatetraen-5-one (X).* A 20% methanolic potassium hydroxide solution (2 ml) was added dropwise to a stirred solution of *o*-ethynylcinnamaldehyde (IX, 5.0 g, 32.0 mmol) and acetone (1.14 g, 19.6 mmol) in deoxygenated ether (103 ml) at room temperature over a period of 15 min. After had been stirred for 2 h at the same temperature, the reaction mixture was neutralized with acetic acid (2 ml) and mixed with water (300 ml). The mixture was extracted with benzene. After work up of the extracts in the standard way, a dark red liquid obtained was chromatographed on alumina (150 g) with light petroleum–ether (75: 25—55: 45) to give X (1.49 g, 28%) as solids. Recrystallization from light petroleum–benzene gave pure X as orange needles, mp 149.0—149.8 °C,[11] MS: *m/e* 334 (M^+, 85), 154 (100); mol wt, 334.39, IR (KBr disk): 3250 (–C≡CH), 2100 (–C≡C–), 1660, 1620, 1595 (C=O, C=C), 995 cm^{-1} (*trans* C=C), UV: $\lambda_{\max}^{\text{THF}}$ 236 (42200), 259 (29500), 267 (29800), 369 nm (57400), NMR: see Table 2.

Found: C, 89.59; H, 5.18%. Calcd for $C_{25}H_{18}O$: C, 89.79; H, 5.43%.

Dibenzo[f,l]*-8,10-bisdehydro*[*17*]*annulenone (XI).* A solution of the ketone (X, 2.08 g, 6.22 mmol) in pyridine (35 ml) was added to a stirred solution of copper(II) acetate monohydrate (17.0 g) in pyridine (56 ml) at 50 °C over a period of 30 min, and the reaction mixture was stirred for further 3 h at 60—65 °C. The precipitate formed on cooling and diluted with benzene (300 ml) was washed with benzene (50 ml × 3). Then the filtrate was washed with 6% hydrochloric acid until it was slightly acidic, and saturated aqueous sodium hydrogencarbonate and sodium chloride solutions successively, and dried over sodium sulfate. The residual dark red liquid obtained after evaporation of the solvent was chromatographed on alumina (130 g) with light petroleum–ether (1: 1) to give the ketone (XI, 348 mg, 17%) as crystals.

Recrystallization from benzene gave pure XI as yellow cubes, mp 209—210.5 °C (dec),[11] MS: *m/e* 332 (M^+, 60), 313 (100); mol wt, 332.38, IR (KBr disk): 2200 (–C≡C–), 1640, 1606, 1594 (C=O, C=C), 1000, 960 cm^{-1} (*trans* C=C), UV: λ_{max}^{THF} 224 (63300), 297 (63300), 313 nm (70000); λ_{max} (CF_3-COOH): 275 sh, 292, 309, 328, 355 sh, 395 sh, 572 nm, NMR: see Table 2.

Found: C, 90.33; H, 4.79%. Calcd for $C_{25}H_{16}O$: C, 90.33; H, 4.85%.

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8) These ^1H-NMR spectra were reexamined by measuring at 90 MHz spectrometer after a preliminary report (Ref. 2a).

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10) It is unable to determine the value because the signal of H^B proton of VII is submerged by those of benzenoid protons.

11) The melting points of X and XI given in the preliminary report (Ref. 2a) were erroneous.