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The Synthesis of Tetrakisdehydrotetraazaannulenes. Tetramethyl[32]-, [40]-, and Tetrabenzo[32]annulene

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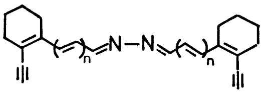
The conjugate aldehydes, containing terminal acetylenes, were converted to the corresponding conjugated azines **6a**—**c** and **8a**—**c**, respectively. Oxidative couplings of these azines were attempted. The azines **6b**, **6c**, and **8b** afforded the corresponding cyclic dimers **9**, **10**, and **11**, respectively. Examination of ^{1}H NMR spectra indicates that the tetraazaannulenes are atropic.

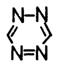
In 1974, Yamamoto and Sondheimer attempted the oxidative couplings of the conjugated azines of type **1** to obtain the corresponding cyclic monomer and/or dimer, which are the macrocyclic analogues of pyridazine **2** and 1,2,4,5-tetrazine **3**, respectively.[1] In attempted oxidative couplings, they obtained the cyclic dimer **4** from the azine **1b** using copper(II) acetate monohydrate in ether and pyridine under relatively dilute concentrations. Also, quite recently, Darby *et al.* found that oxidative coupling of terminal diacetylenes to macrocyclic 1,3-diacetylenes usually proceeds in higher yield when anhydrous copper(II) acetate instead of the monohydrate is employed.[2]



1

1a : n=0
b : n=1
c : n=2

2



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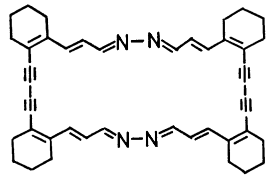

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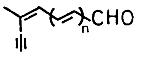
Bearing these results in mind and expecting to obtain the cyclic monomeric compounds using the conditions reported by Darby *et al.*, we undertook to examine oxidative couplings of the conjugated azines of types **6** and **8**. In practice, we obtained no cyclic monomeric compounds, but the respective cyclic dimers **9**, **10**, **11**, from the azines **6b**, **6c**, and **8b**.



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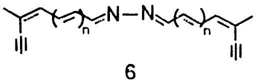
b : n=1
c : n=2



6

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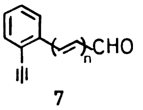
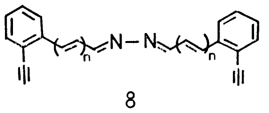
b : n=1
c : n=2



7

7a : n=0
b : n=1
c : n=2



8

8a : n=0
b : n=1
c : n=2

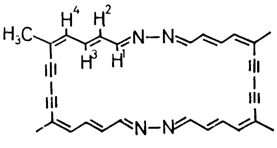
TABLE 1. YIELDS AND MELTING POINTS OF THE AZINES 6 AND 8

	Azines	
	Yield (%)	Mp (°C)
6a	82	110 (dec)
6b	76	160 (dec)
6c	87	110 (dec)
8a	85	140 (dec)
8b	64	169—170
8c	64	199—200

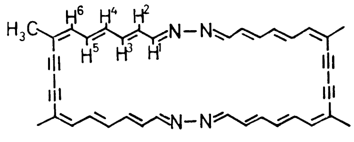
The trienyne aldehyde **5c** was prepared from its lower homologue, the dienyne aldehyde **5b** in 50% yield by condensation with ethyl vinyl ether according to the Isler's method[3,4] or by Wittig condensation with (1,3-dioxolan-2-ylmethyltriphenyl)phosphonium bromide.[5,6]

Treatment of the aldehydes **5a**—**c** and **7a**—**c** in ethanol with aqueous hydrazine, as described by Yamamoto and Sondheimer,[1] yielded the corresponding conjugated azines **6a**—**c** and **8a**—**c**, respectively. The yields and melting points of the azines are summarized in Table 1.

All of attempted oxidative couplings of these azines (**6a**—**c**, **8a**—**c**) were carried out with anhydrous copper(II) acetate in pyridine and ether at 50 °C as reported by Darby *et al.*[2] The azines **6b**, **6c**, and **8b** afforded the corresponding cyclic dimers **9** (14%), **10** (17%), **11** (20%), and they formed red needles (122 °C (dec)), purple needles (*ca.* 95 °C (dec)), yellow needles (170 °C (dec)), respectively; the compound **10** was a rather unstable material. Under the same conditions as above, the yellow crystals were isolated from the azine **8c**, but the structure of the material is not yet established. In the cases of **6a** and **8a**, the oxidative couplings were also investigated under several different conditions (see Experimental), but no desired cyclic product could be obtained.



9



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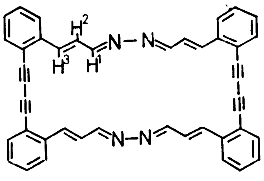
The dimeric structure of the product from **6b**, **6c**, and **8b** was established by the mass spectra. The mass spectral measurement of **10** using direct inlet system were not satisfactory owing to decomposition

Table 2. ^{1}H-NMR parameters of **9**, **10**, and **11** in $CDCl_3$ at 100 MHz
(τ-Values; internal standard, TMS; J values in Hz in parentheses)

Proton	**9**	**10**	**11**
H^1	2.30 (d, 9)	2.03 (d, 9)	1.86 (d, 9)
H^2	3.51 (dd, 15, 9)	2.6—3.6 (m)	2.92 (dd, 16, 9)
H^3	2.86 (dd, 15, 11)		2.51 (d, 16)
H^4	3.45 (d, 11)		
H^5, H^6			
CH_3	7.98 (s)	7.96 (s), 7.99 (s)	
benzenoid H			2.3—2.6 (m)

during measurement. However, the mass spectrum obtained by field desorption technique was satisfactory one, revealing a molecular ion peak (mol wt, 573) clearly. The UV spectra of **9**, **10**, and **11** are illustrated in Fig. 1. These spectra are similar as those of **4**,[1] and shows characteristic feature of [4*n*]annulene.[7] The ^{1}H-NMR data of **9**, **10**, and **11** are given in Table 2. The chemical shifts of the olefinic and methyl protons of these compounds suggest that the compounds **9**, **10**, and **11** are atropic molecules.



11

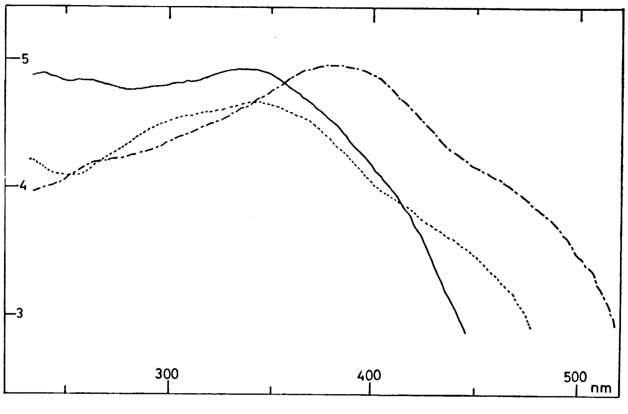


Fig. 1. Electronic spectra of tetrakisdehydrotetraazaannulenes **9** (----), **10** (------), and **11** (——) in THF.

In conclusion, although we expected that the cyclic monomers, which are the macrocyclic analogues of pyridazine **2**, might also result from the azines by using the procedure reported by Darby *et al.*, the compounds obtained are dimeric ones.

Experimental

All melting points are uncorrected. The IR spectra were measured on Hitachi EPI-S2 or Unicam SP 200 spectrophotometer: only significant maxima are reported. The electronic spectra obtained on Hitachi 124 or Unicam SP-800 spectrophotometer were recorded in nm. The ε-values are given in parentheses, the shoulder being denoted by sh. The mass spectra were measured with JEOL JMS-OI-SG-2, AEI MS-12 or JEOL JMS-D equipped with field desorption system. The ^{1}H-NMR spectra were obtained on Varian EM-930, Varian T-60 or Varian XL-100 spectrometer, and refer to solutions in $CDCl_3$, in τ-values with TMS as an internal standard at 90 MHz unless otherwise stated. The coupling constants (J) are given in Hz. The individual assignments are made on the basis of the multiplicity and coupling constants. The number indicated in the by-line starts from the carbon adjacent to nitrogen atom of the azine group, as shown in the formulae of **9**, and in **5c** the number starts from the carbon of the aldehyde group. Alumina (Act. II—III) was used for column chromatography unless otherwise indicated. Progress of most reactions was followed by TLC using Merck precoated alumina. Evaporation of the solvents was carried out at water aspirator pressure.

7-Methyl-2,4,6-nonatrien-8-ynal ***5c***.[4] A 1% soln of *p*-toluenesulfonic acid monohydrate in absolute ethanol (15 drops) was added to a soln of the aldehyde **5b**[3] (6.1 g, 0.05 mol) and ethyl orthoformate (9.2 g, 0.06 mol) in absolute ethanol (10 ml). After being stirred at room temperature overnight, the mixture was treated with pyridine (1 ml) and poured into 2% aqueous $NaHCO_3$ (100 ml). Extraction with ether, drying over $MgSO_4$, and evaporation of the solvents yielded the crude diethyl acetal of **5b** as a red liquid. The liquid was dissolved in ethyl acetate (10 ml) and warmed to 35 °C in a flask equipped with two dropping funnels, a condenser, and a magnetic stirrer. A 10% soln of zinc chloride in ethyl acetate (20 drops) was added, and then the same soln (10 ml) and ethyl vinyl ether (40 ml) were added simultaneously during 5 min under stirring at 35 °C. The mixture was stirred for 2 h at room temperature, stoppered, and allowed to stand overnight. A soln of sodium acetate (15 g) in water (10 ml) and acetic acid (150 ml) was then added, and the mixture was heated to 90 °C for 2 h. Dilution with water (700 ml), extraction with ether, drying over $MgSO_4$, and evaporation gave a residue, which was chromatographed on alumina (200 g, Woelm, Act. III). Elution with pentane-ether (96:4—90:10) and evaporation of the solvents gave the aldehyde **5c** (3.6 g, 50%) as solid. Recrystallization from ether–hexane gave pure **5c** as orange needles, mp 64—65 °C; MS: *m/e* 146 (M^+), 131 (M^+-15), 117 (M^+-29); mol wt, 146.2; IR ($CHCl_3$): 3290 ($-C\equiv CH$), 2100 ($-C\equiv C-$), 1670, 1600 (C=O, C=C), 995 cm^{-1} (*trans* C=C); UV (ether): λ_{max} 234 (14600), 305 sh (32900), 324 (47500), 337 nm (44900); NMR (60 MHz): 0.41 (d, 8, 1H, CH^1O), 2.80 (dd, 15, 11, 1H, H^5), 2.87 (dd, 15, 11, 1H, H^3), 3.41—3.67 (m, 2H, H^4 and H^6), 3.82 (dd, 15, 8, 1H, H^2), 6.54 (s, 1H, $-C\equiv CH$), 7.99 (s, 3H, $-CH_3$).

Found: C, 82.42; H, 6.71%. Calcd for $C_{10}H_{10}O$: C, 2.16; H, 6.90%.

The compound **5c** was also prepared in 42% yield by Wittig condensation with (1,3-dioxolan-2-ylmethyl) triphenylphosphonium bromide as reported for the preparation of **7b**,[6] except the use of lithium ethoxide instead of lithium methoxide as a base.[5]

*Azine **6a**.* A soln of **5a**[8] (2.0 g, 2.1 mmol) in ethanol (20 ml) was added to a soln prepared from hydrazine sulfate (1.5 g), Na_2CO_3 (2.0 g), and H_2O (15 ml), with stirring at ambient temperature. After the reaction was continued for 2 h at the same temperature, the reaction mixture was poured into aqueous $NaHCO_3$ soln (200 ml), and extracted with benzene, washed with aqueous $NaHCO_3$ and dried over K_2CO_3. The residual red liquid, after solvent removal, was chromatographed on alumina (120 g) with light petroleum–ether (80:20) to give **6a** (1.6 g, 82%). Recrystallization from chloroform–ethanol afforded yellow needles, mp *ca.* 110 °C (dec), MS: *m/e* 184 (M^+, 50), 183 (100); mol wt, 184.2; IR (KBr disk): 3200 (–C≡CH), 2100 (–C≡C–), 1610 (N=C); UV (EtOH): λ_{max} 302 sh (19900), 315 (26700), 328 (27100), 344 sh (18200); NMR: 1.38 (d, 10, 2H, H^1), 3.40 (broad d, 10, 2H, H^2), 6.55 (s, 2H, –C≡CH), 7.90 (s, 6H, $-CH_3$).

Found: C, 78.05; H, 6.30; N, 15.00%. Calcd for $C_{12}H_{12}N_2$: C, 78.23; H, 6.57; N, 15.21%.

*Azine **6b**.* In a similar manner, **6b** was prepared from **5b**[3] (1.4 g, 12 mmol) in EtOH (15 ml) and hydrazine sulfate (0.79 g), Na_2CO_3 (0.98 g), and H_2O (8.1 ml). Elution with light petroleum–ether (20:80—5:95) from the column of alumina (130 g) gave **6b** (1.05 g, 76%), obtained as yellow needles from benzene–hexane, mp *ca.* 160 °C (dec), MS: *m/e* 236 (M^+, 44), 193 (100); mol wt, 236.3; IR (KBr disk): 3300 (–C≡CH), 2100 (–C≡C–), 1615 (N=C), 1600 (C=C), 980 cm^{-1} (*trans* C=C); UV (THF): λ_{max} 231 (11400), 239 sh (9710), 247 sh (6380), 280 sh (6420), 292 (7600), 322 sh (22400), 341 sh (42500), 357 (57200), 373(57700), 392(36800); NMR (100 MHz): 1.79 (d, 10, 2H, H^1), 2.84 (dd, 15, 11, 2H, H^3), 3.52 (dd, 15, 11, 2H, H^2), 3.53 (d, 11, 2H, H^4), 6.56 (s, 2H, –C≡CH), 7.99 (s, 6H, $-CH_3$).

Found: C, 81.42; H, 6.86; N, 11.65%. Calcd for $C_{16}H_{16}N_2$: C, 81.32; H, 6.83; N, 11.86%.

*Azine **6c**.* This substance was similarly prepared from **5c** (430 mg, 2.94 mmol) in EtOH (3.8 ml) and hydrazine sulfate (199 mg), Na_2CO_3 (247 mg), and H_2O (2 ml). Elution with ether–chloroform (1:1) from the column of alumina (120 g) gave **6c** (370 mg, 87%), obtained as brownish yellow needles from chloroform, mp *ca.* 110 °C (dec), MS: *m/e* 288 (M^+, 100); mol wt, 288.3; IR (KBr disk): 3280 (–C≡CH), 2100 (–C≡C–), 1620 (N=C), 1590 (C=C), 995 cm^{-1} (*trans* C=C); UV (THF): λ_{max} 260 (6460), 271 sh (5590), 281 sh (4020), 312 sh (5460), 325 sh (7070), 396 (40000), 413 (40900), 434 (25200); NMR: 1.81 (d, 9. 2H, H^1), 3.0—3.7 (m, 10H, olefinic H), 6.63 (s, 2H, –C≡CH), 8.03 (s, 6H, $-CH_3$).

Found: C, 83.27; H, 6.72; N, 9.87%. Calcd for $C_{20}H_{20}N_2$: C, 83.29; H, 6.99; N, 9.71%.

*Azine **8a**.* Similarly, **8a** was prepared from **7a**[9] (3.0 g, 2.3 mol) in EtOH (30 ml) and hydrazine sulfate (1.6 g), Na_2CO_3 (1.9 g), and H_2O (16 ml). Elution with light petroleum–ether (85:15—60:40) from the column of alumina (150 g) gave **8a** (2.5 g, 85%), obtained as yellow needles from benzene–hexane, mp *ca.* 140 °C (dec), MS: *m/e* 256 (M^+, 75), 255 (100); mol wt, 256.2; IR (KBr disk): 3200 (–C≡CH), 2100 (–C≡C–), 1625 cm^{-1} (N=C); UV (THF): λ_{max} 232 (31400), 248 sh (25700), 255 sh (19900), 302 sh (26200), 315 (29200). 332 sh (24500), 349 sh (11300); NMR: 0.83 (s, 2H, H^1), 1.66—1.85 (m, 2H, benzenoid H), 2.36—2.75 (m, 6H, benzenoid H), 6.60 (s, 2H, –C≡CH).

Found: C, 84.27; H, 4.92; N, 10.66%. Calcd for $C_{18}H_{12}N_2$: C, 84.35; H, 4.72; N, 10.93%.

*Azine **8b**.* This material was similarly prepared from **7b**[6] (1.8 g, 0.12 mmol) in EtOH (20 ml) and hydrazine sulfate (0.97 g), Na_2CO_3 (0.98 g), and H_2O (1.1 ml). The resulting precipitates were collected and washed with EtOH, giving **8b** (1.14 g, 64%), obtained as yellow needles from benzene-ethanol, mp 169—170 °C, MS: *m/e* 308 (M^+, 30), 280 (100); mol wt, 308.3; IR (KBr disk): 3250 (–C≡CH), 2100 (–C≡C–), 1635 (N=C), 1590 (C=C), 980 cm^{-1} (*trans* C=C); UV (THF): λ_{max} 290 sh (8260), 339 sh (44600), 353 (52900), 370 sh (47400), 390 sh (24000); NMR: 1.67 (d, 9, 2H, H^1), 2.43 (d, 16, 2H, H^3), 2.97 (dd, 16, 9, 2H, H^2), 2.32—2.90 (m, 8H, benzenoid H), 6.68 (s, 2H, –C≡CH).

Found: C, 86.43; H, 5.33; N, 8.83%. Calcd for $C_{22}H_{16}N_2$: C, 86.69; H, 5.23; N, 9.09%.

*Azine **8c**.* This substance was similarly prepared from **7c**[10] (1.0 g, 5.5 mmol) in EtOH (7.1 ml) and hydrazine sulfate (371 mg), Na_2CO_3 (460 mg), and H_2O (3.7 ml). Fractions eluted with light petroleum–ether (50:50) from the column of alumina (150 g) gave **8c** (623 mg, 64%), obtained as yellow plates from chloroform, mp 199—200 °C. Attempts to obtain a satisfactory elemental analysis were unsuccessful in our hands, but the Mass (*m/e* 360 (M^+, 45), 180 (100); mol wt, 360.4), the IR (KBr disk) (3300 (–C≡CH), 2100 (–C≡C–), 1615 (N=C), 995 cm^{-1} (*trans* C=C)), the UV (THF) λ_{max} 276 sh (14300), 368 sh (54000), 389 (67000), 405 sh (62000), 430 sh (15000)), and the NMR (1.75 (d, 9, 2H, H^1), 2.35—3.48 (m, 16H, benzenoid and olefinic H), 6.65 (s, 2H, –C≡CH)) were found to be consistent with the assigned structure.

*Oxidative Coupling of **6b** to the Tetrakisdehydrotetraaza[32]annulene **9**.* A soln of **6b** (950 mg, 4.02 mmol) in pyridine (63 ml) and dry ether (21 ml) was added dropwise during 4 h to a stirred soln of anhydrous copper(II) acetate (5.1 g) in pyridine (140 ml) and dry ether (47 ml) kept at 50 °C; the mixture was stirred for further 2 h at the same temperature. Then the mixture was chilled, diluted with benzene (100 ml), and filtered through Hyflo Super-Cel. The precipitates formed were washed with benzene (100 ml × 4). The filtrate was washed with H_2O thirteen times to remove pyridine, and dried over K_2CO_3. After solvent removal, the residual red liquid was chromatographed on alumina (200 g). Fractions eluted with light petroleum–ether (65:35)—ether–benzene (30:70) contained **9**. The slightly crude **9** was dissolved in ether and chromatographed on alumina (140 g) with ether to give **9** (129 mg, 14%), obtained as orange needles from benzene–hexane, mp 122 °C (dec); MS: *m/e* 470 (M^+, 8), 324 (100); mol wt, 470.5; IR (KBr disk): 2150 (–C≡C–), 1610 (N=C), 1600 (C=C), 975 cm^{-1} (*trans* C=C); UV (THF): (see Fig. 1) λ_{max} 232 (14000), 269 sh (15700), 312 sh (33000), 339 nm (45000): NMR: see Table 2.

*Oxidative Coupling of **6c** to the Tetrakisdehydrotetraaza[40]annulene **10**.* To a stirred soln of anhydrous copper(II) acetate (1.3 g) in pyridine (36 ml) and dry ether (12 ml) kept at 50 °C was added with stirring a soln of **6c** (300 mg, 1.04 mmol) in pyridine (40 ml) and dry ether (10 ml) during 2.5 h: the mixture was stirred for further 2.5 h at 45—50 °C (bath temp). Then the mixture was worked up as in the preparation of **9**. Elution with benzene from the column of alumina (200 g) gave **10** (50 mg, 17%), obtained as purple microcrystals from chloroform mp *ca.* 95 °C (dec); MS (field desorption method): *m/e* 573 (M^+), 574 ($M^+ + 1$); mol wt, 572.6; IR (KBr disk): 2200 (–C≡C–), 1620 (N=C), 1580 (C=C), 995 cm^{-1} (*trans* C=C), UV (THF): (see Fig. 1) λ_{max} 238 sh (10100), 258 sh (14900), 381 (87500), 468 sh (9630); NMR: see Table 2.

*Oxidative Coupling of **8b** to the Tetrakisdehydrotetraaza[32]annulene **11**.* A soln of azine **8b** (710 mg, 2.30 mmol) in pyridine (42 ml) and dry ether (14 ml) was added during

2 h to a stirred soln of anhydrous copper(II) acetate (2.9 g) in pyridine (80 ml) and dry ether (27 ml) at 50 °C; the mixture was stirred for further 3 h. Then the product was worked up as in the preparation of **9**. The residual liquid, after solvent removal, was chromatographed on alumina (150 g) with ether-benzene (50:50—90:10) to give **11** (144 mg, 20%), obtained as yellow microcrystals from chloroform, mp 168—170 °C (dec): MS: *m/e* 613 (M^+, 27), 307 (100); mol wt, 612.7; IR (KBr disk): 2200, 2150 (-C≡C-), 1635 (N=C), 1595 (C=C), 980 cm^{-1} (*trans* C=C); UV (THF): (see Fig. 1) λ_{max} 287 sh (60200), 303 sh (65400), 333 (83400); NMR: see Table 2.

The yield of **11** was only 8% when the coupling of **8b** was carried out with copper(II) acetate monohydrate in pyridine and ether at 70 °C according to the procedure described for the preparation of **4**.[1)]

*Oxidative Coupling of **6a** and **8a**.* These oxidative couplings were carried out under the following conditions: a) with conditions as described for the preparation of **9**; b) with copper(II) acetate monohydrate in pyridine and ether as reported for the preparation of **4** (Ref. 1); c) with copper(II) acetate monohydrate in pyridine under concentrate conditions.[11)] In all attempted runs, only polymeric products were obtained.

*Oxidative Coupling of **8c**.* In a run performed under similar conditions as the preparation of **9**, the yellow crystals (260 mg) were obtained from the azine **8c** (690 mg, 1.91 mmol) in pyridine (50 ml) and dry ether (16 ml), and anhydrous copper(II) acetate (2.4 g) in pyridine (66 ml) and dry ether (22 ml). After chromatographic purification, they formed yellow microcrystals from chroloform, mp 180 °C (dec). However, the structure of the material is not established.

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