Multiple Diamine–Dialdehyde Condensations. Synthesis of Heterocyclic Dodecalenes

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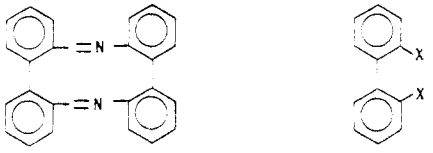
The diamine–dialdehyde condensation of biphenyl-2,6,2′,6′-tetracarbaldehyde (**6**) and 2,2′-diaminobiphenyl (**3**) in benzene (TsOH catalyst) gave the tetra Schiff base 9,15,24,30-tetraazahexabenzo[*d,f,jk,o,q,uv*]dodecalene (**4**). 10,14,25,29-Tetraaza[*d,f,jk,o,q,uv*]dodecalene (**5**) was prepared analogously from 2,6,2′,6′-tetraaminobiphenyl (**7**) and biphenyl-2,2′-dicarbaldehyde (**2**). The condensation of **6** with *o*-phenylenediamine and with 2,3-diaminonaphthalene afforded "hydride shift" products **10** and **13**. The geometries of **4** and **5** are briefly discussed.

Annulenoannulenes result from the fusion of two annulene rings to form a π system with one or more bonds in common.[1] These polycyclic conjugated systems are currently serving as a major focus of activity in nonbenzenoid aromatic chemistry.[2-4] We have recently reported the synthesis of hexabenzo[*d,f,jk,o,q,uv*]dodecalene, a polycyclic [12]annuleno[12]annulene,[1] by multiple Horner–Emmons cyclizations, using 2,6,2′,6′-tetrasubstituted biphenyl synthons.[5] A logical extension seemed to be the application of such synthons for the preparation of *heterocyclic* dodecalenes.

One of the valuable entries into the heteroannulene series in the bis diamine–dialdehyde condensation. The reaction involves double intermolecular reaction between 1 mol of a diamine and 1 mol of a dialdehyde to give a bis Schiff base cyclic product. The method may be illustrated in the synthesis of 9,20-diazatetrabenzo[*a,c,g,i*]cyclododecene (**1**) by the double condensation of biphenyl-2,2′-dicarbaldehyde (**2**) and 2,2′-diaminobiphenyl (**3**).[6,7]



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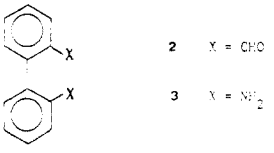
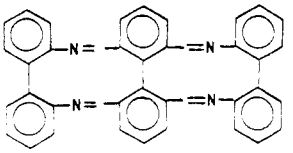


2 X = CHO

3 X = NH_2

The diamine–dialdehyde condensation method has been studied in terms of bis Schiff base vs. bicyclic "hydride shift" products. Thus, **2** and *o*-phenylenediamine gave 15*H*-dibenzo[*c,e*]benzimidazo[1,2-*a*]azepine rather than the annelated 1,4-diaza[10]annulene.[8] It appears that the course and effectiveness of the reaction are governed by the size of the diazannulene and by the conformations of the synthons. Diphenylamine-2,2′-dicarbaldehyde reacted with **3** to give a hetero[26]annulene derivative, a 2:2 cyclization product, to the exclusion of the corresponding 13-membered 1:1 cyclization product.[9] Such a duality (2:2 vs. 1:1 cyclization product) has been observed in the diamine–dialdehyde condensation of bifunctional 1,2-distyrylbenzenes and attributed to kinetically vs. thermodynamically controlled reactions.[10]

The present article describes the synthesis of 9,15,24,30-tetraazahexabenzo[*d,f,jk,o,q,uv*]dodecalene (**4**) and its 10,14-25,29-tetraaza isomer (**5**) by multiple diamine–dialdehyde condensations, using tetrafunctional and bifunctional biphenyl synthons.[11,12] An entry into new heterocyclic systems by the "hydride shift" pathway is included.



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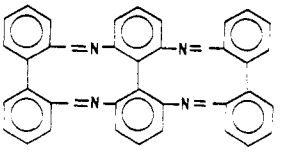

5

Two variants of the diamine–dialdehyde condensations were adopted: a tetra Schiff base reaction between biphenyl-2,6,2′,6′-tetracarbaldehyde (**6**) and **3** leading to **4**, and a tetra Schiff base reaction between 2,6,2′,6′-tetraaminobiphenyl (**7**) and **2**, leading to **5**.

Tetracarbaldehyde **6** was prepared by ozonolysis of pyrene in 50% yield.[5,13] Tetraamine **7** was prepared by reduction of 2,6,2′,6′-tetranitrobiphenyl (**8**).[14] The condensations (**6** + **3** and **7** + **2**) were performed in boiling benzene in the presence of *p*-TsOH. The heterocyclic dodecalenes **4** and **5** were obtained in 46% yields. Their structures were established by elemental analysis, the molecular ions in the mass spectra, and the ^{1}H NMR spectra. For comparison, *N,N′,N″,N‴*-([1,1′-biphenyl]-2,2′,6,6′-tetrayltetramethylidyne)tetrakis[benzenamine] (**9**) was prepared by a 1:4 condensation between **2** and aniline. The bis Schiff base structures of **4** and **5** were confirmed by the low-field azomethine singlets and the absence of any aliphatic absorptions in the ^{1}H NMR spectra.[15] These singlets appear at δ 7.95 (**4**), 7.87 (**5**), 8.09 (**9**), 7.87 (**1**), 8.47 (PhCH=NPh), and 8.35 ppm (2,6-bis[(phenylimino)-methyl]biphenyl). They are shifted to high field in **4**, **5** and **1** as compared with **9**, indicating that each azomethine proton adopts a spatial orientation within the shielding region of the other CH=N linkage within the 12-mem-

(1) Cresp, T. M.; Sondheimer, F. *J. Am. Chem. Soc.* **1977** *99*, 194-204.
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(3) (a) Hess, B. A., Jr.; Schaad, L. J.; Agranat, I. *J. Am. Chem. Soc.* **1978**, *100*, 5268-5271. (b) Agranat, I.; Hess, B. A., Jr.; Schaad, L. J. *Pure Appl. Chem.* **1980**, *52*, 1399-1407.
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(6) Bergmann, E. D.; Agranat, I.; Kraus, M. A. *J. Org. Chem.* **1967**, *32*, 600-602.
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(9) Agranat, I. *Tetrahedron* **1973**, *29*, 1399-1400.
(10) (a) Skrabal, P.; Zollinger, H. *Heterocycles* **1978**, *11*, 363-369. (b) Ehrensperger, C.-P.; Heberlein, M.; Skrabal, P. *Helv. Chim. Acta* **1978**, *61*, 2813-2822.
(11) The *Chemical Abstracts* names are dibenzo[*c,e*]dibenzo-[3,4:5,6][2,7]benzodiazacyclododecino[11,10,9-*ijk*][2,7]benzodiazacyclododecine (**4**) and dibenzo[*c,e*]dibenzo[3,4:5,6][1,8]benzodiazacyclododecino[11,10,9-*ijk*][1,8]benzodiazacyclododecine (**5**).
(12) Preliminary report: Agranat, I.; Rabinovitz, M.; Shaw, W.-C. Abstracts, 6th International Congress of Heterocyclic Chemistry, July 9-13, 1977, Teheran, PIIB, pp 199-200.
(13) Agarwal, S. C.; Van Duuren, B. L. *J. Org. Chem.* **1975**, *40*, 2307-2310.
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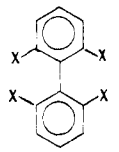
0022-3263/81/1946-3018$01.25/0



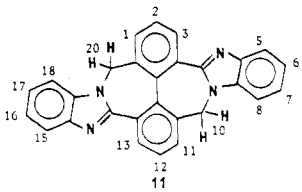
6 X = CHO
7 X = NH_2
8 X = NO_2
9 X = CH=N-Ph

bered ring. The geometrical configurations of **4** and **5** are probably *E,E,E,E* but must await confirmation, e.g., by X-ray determinations.[15,16] The absorptions of the central biphenyl protons ortho to the azomethine groups differ significantly in **4**, **5**, and **9**, appearing at 7.79, 6.50, and 8.48 ppm, respectively. In comparison, the corresponding absorption in **1** appears at 6.56 ppm. The upfield shift in **5** and **1** is obviously due to the ortho nitrogens. The shielding (ca. 0.7 ppm) in **4** relative to **9** is noteworthy. The rigidity in **4** forces the above ortho protons into the shielding region of the nitrogen lone pairs.

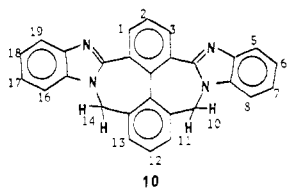
The UV spectrum of **5** is similar to that of **1** with a shoulder at 300 nm (ϵ 18700),[15] while in **4** the corresponding absorption appears as a shoulder at 333 nm (ϵ7700). These would seem to indicate a more extended conjugation through the central biphenyl moiety of the N=CH—Ar—CH=N chromophore in **4**, as compared with the CH=N—Ar—N=CH chromophore in **5**.

This synthesis of the multiple Schiff bases **4** and **5** prompted an investigation of the reaction of the tetracarbaldehyde **6** with *o*-phenylenediamine and 2,3-diaminonaphthalene. Neither the condensation of **2** with *o*-phenylenediamine[8] nor of **3** with *o*-phthalaldehyde afforded a bis Schiff base product.[17]

The reaction of **6** with *o*-phenylenediamine (1:2 mole ratio) gave a product, whose ^{1}H NMR spectra contained an aliphatic AB quarter at 4.89 and 5.69 ppm (J = 14.2 Hz, 4 H), indicating a hydrogen-shift product due to two benzimidazobenzazepine systems. The following two structures were considered: 10*H*,14*H*-benzimidazo[2,1-*a*]benzimidazo[1′,2′:2,3]benzazepino[6,5,6-*def*][2]benzazepine (**10**), and 10*H*,20*H*-benzimidazo[2,1-*a*]benzimidazo[2′,1′:1,2]benzazepino[6,5,4-*def*][2]benzazepine (**11**).



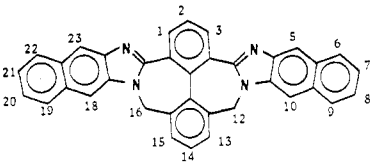
11



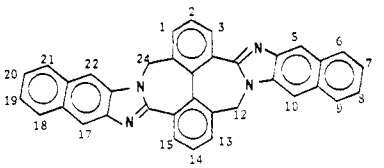
10

The choice between **10** and **11** was based on the ^{1}H NMR absorptions of the protons of the central biphenyl moiety and their different symmetry characteristics. Compound **10** possesses a σ plane bisecting the central biphenyl moiety along its biphenyl linkage. Compound **11** possesses a center of symmetry. In **10**, proton 1 should be magnetically equivalent to proton 3 and proton 11 to proton 13, each appearing as a doublet with an ortho coupling constant. On the other hand, protons 2 and 12 should appear as triplets (not necessarily equivalent). In **11**, proton 1 should be equivalent to proton 11, proton 3 to proton 13, and proton 2 to proton 12. However, proton 1 need not be equivalent to 3 and proton 11 need not be equivalent to 13. Each should appear as a quartet. The ^{1}H NMR spectrum of the product rules out structure **11** and establishes structure **10** as the condensation product. Double irradiation at the δ 7.45 triplet renders the doublet at δ 8.01 into a singlet. It is reasonable to assume that 15*H*-dibenzo[*c*,*e*]benzimidazo[1,2-*a*]azepine-4,5-dialdehyde is an intermediate in the double hydride-shift condensation. The relative conformation of the two formyl groups in this intermediate is much more favorable to the diamine–dialdehyde condensation than that of the two formyl groups of **2**. Assuming that the dialdehyde intermediate condenses with *o*-phenylenediamine, following the mechanism of Bindra and Elix,[8] the formation of **10** supports the contention that the formyl group at position 14 reacts prior to the formyl group at position 5.

The condensation of **2** and 2,3-diaminonaphthalene (1:2 mol ratio) in boiling acetic acid gave **12** in 46% yield. The structure of **12** was established by elemental analysis, the molecular ion in the mass spectrum, and the ^{1}H NMR evidence which rule out strcuture **13**.



12



13

In conclusion, the diamine–dialdehyde condensation of tetrafunctional biphenyl synthons afforded tetrakis Schiff bases as well as "hydride shift" products. No evidence for significant aromatic charater of **4** and **5** due to the dodecalene systems was revealed. Aspects of chirality[15] or **4** and **5** deserve a special study.

Experimental Section

Melting points were taken on a Thomas-Hoover Unimelt capillary melting poing apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 457 spectrometer in Nujol and KBr disks. Ultraviolet spectra were recorded on Unicam Model SP800A and Varian Techtron 635 spectrophotometers. The ^{1}H NMR spectra were taken on a Varian HA-100D spectrometer at 100 MHz (Me_4Si internal reference) and on a Bruker WH-270 spectrometer (with deuterium lock). ^{1}H chemical shifts are reported in parts per million downfield from Me_4Si (δ units). Mass spectra were measured on a Varian MAT-311 double-focusing instrument operating at 70 eV, employing the direct-insertion technique. Analytical TLC separations were carried out at 24 °C on precoated plastic sheets (layer thickness 0.2 mm) of Polygram Sil M-HR/UV_{254} and Polygram Alox N/UV_{254} (Machery-Nagel and Co.). Preparative layer chromatography (PLC) separations were carried out at 24 °C on glass plates (20 × 20 cm) precoated with silica gel F_{254} (layer thickness 2 mm) and aluminum oxide F_{254} (Type T, layer thickness 1.5 mm, E. Merck). DMF was dried by refluxing over calcium hydride under nitrogen and distillation and was used immediately.

***N,N′,N″,N‴*-([1,1′-Biphenyl]-2,2′,6,6′-tetrayltetramethylidyne)tetrakis[benzamine] (9).** A solution of 2,6,2′,6′-biphenyltetracarbaldehyde[5] (0.266 g, 1 mmol) and aniline (0.372 g, 4 mmol, freshly distilled from zinc dust) in methanol (60 mL) was magnetically stirred under a nitrogen atmosphere for 24 h. The precipitated product was filtered off and washed with methanol (10 mL). Recrystallization of the crude product (0.470 g, mp 180–184 °C) from hexane gave **9** as light yellow needles: mp 213–214 °C; yield 39% (0.220 g); UV (CH_2Cl_2) λ_{max} 244 nm (s, ϵ 42500), 269 (49500), 313 (22400); mass spectrum,

(16) For a recent NMR study of the aromatic imine stereochemistry, see: Buchanan, G. W.; Dawson, B. A. *Org. Magn. Reson.* **1980**, *13*, 293–298.
(17) Bindra, A. P.; Elix, J. A. *Tetrahedron* **1969**, *25*, 5465–5473.

m/e 566 (M^+); ^1H NMR ($CDCl_3$) δ 6.88–7.40 (m, 20 H, benzenoid), 7.70 (t, J = 8 Hz, 2 H, benzenoid, biphenyl, H-4, H-4'), 8.09 (s, 4 H, azomethine), 8.48 (d, J = 8 Hz, benzenoid, biphenyl, H-3, H-5, H-3', H-5').

9,15,24,30-Tetraazahexabenzo[*d,f,jk,o,q,uv*]dodecalene (4). Biphenyl-2,6,2',6'-tetracarbaldehyde[5] (0.67 g, 25 mmol),2,2'-diaminobiphenyl[18] (0.92 g, 5 mmol), and *p*-toluenesulfonic acid (0.03 g) were dissolved in benzene (60 mL) in a 100-mL flask equipped with a Dean–Stark trap, a reflux condenser, a drying tube, and a magnetic stirrer. The stirred mixture was refluxed for 24 h. During the reaction, water was removed, benzene (20 mL) was added, and the solid product precipitated from the mixture. After the mixture cooled to room temperature, the solid was filtered off and worked up with warm benzene (200 mL). Thus, **4** was obtained as colorless solid: mp 300 °C; yield 46% (0.650 g); IR (KBr) ν_{max} 1620, 1470, 1430, 1350, 1200, 1090, 950, 790, 760, 750, 730 cm^{-1}; UV (CH_2Cl_2) λ_{max} 242 nm (s, ε 71400), 256 (s, 68900), 333 (s, 17700); mass spectrum, m/e 562 (M^+); ^1H NMR ($CDBr_3$) δ 6.50–6.70 (m, 4 H, benzenoid ortho to N , H-1, H-8, H-16, H-23), 7.20–7.55 (m, 14H, benzenoid, H-2, H-3, H-4, H-5, H-6, H-7, H-12, H-17, H-18, H-19, H-20, H-21, H-22, H-27), 7.79 (d, J = 8 Hz, 4 H, benzenoid, H-11, H-13, H-26, H-28), 7.95 (s, 4 H, azomethine). Anal. Calcd for $C_{40}H_{26}N_4$: C, 85.4; H, 4.60, N, 9.96. Found: C, 85.66; H, 4.68; N, 9.55.

10,14,25,29-Tetraazahexabenzo[*d,f,jk,o,q,uv*]dodecalene (5). Biphenyl-2,2'-dicarbaldehyde[5] (0.210 g, 1 mmol), 2,6,2',6'-tetraaminobiphenyl[14] (0.107 g, 0.5 mmol), and *p*-toluenesulfonic acid (0.01 g) were dissolved in benzene (30 mL) in a 50-mL flask equipped with a Dean–Stark trap, a magnetic stirrer, and a reflux condenser with a drying tube. The stirred mixture was refluxed for 24 h. During the reaction, water was removed, benzene (20 mL) was added, and the solid product precipitated from the mixture. After the mixture cooled to room temperature, the solid was filtered off and washed with warm benzene (100 mL). Thus **5** was obtained as a colorless solid: mp >300 °C; yield 44% (0.125 g); IV (Nujol) ν_{max} 1620, 1510, 985, 970, 750 cm^{-1}; UV (CH_2Cl_2) λ_{max} 262 nm (s, ε 49400), 300 (s, 18700); mass spectrum, m/e 562 (M^+); ^1H NMR ($CDBr_3$) δ 6.46 (d, J = 8 Hz, 4 H, benzenoid, H-11, H-13, H-26, H-28), 7.18 (t, J = 8 Hz, 2 H, benzenoid, H-12, H-27), 7.40–7.74 (m, 16 H, benzenoid, H-1, H-2, H-3, H-4, H-5, H-6, H-7, H-8, H-16, H-17, H-18, H-19, H-20, H-21, H-22, H-23), 7.84 (s, 4 H, azomethine). Anal. Calcd for $C_{40}H_{28}N_4$: C, 85.41; H, 4.62; N, 9.96. Found: C, 85.60; H, 4.88; N, 9.55.

10*H*,14*H*-Benzimidazo[2,1-*a*]benzimidazo[1',2':2,3]benzazepino[6,5,4-*def*][2]benzazepine (10). A mixture of biphenyl-2,6,2',6'-tetracarbaldehyde[5] (0.532 g, 2 mmol) and *o*-phenylenediamine (0.432 g, 4 mmol) in glacial acetic acid (60 mL) was refluxed with magnetic stirring for 24 h. After the mixture cooled, the solvent was evaporated in vacuo and the residue was column chromatographed on alumina (150 g), using CH_2Cl_2–$CHCl_3$ (1:10) as eluent. The fraction free of the starting diamine was rechromatographed on alumina (150 g), using $CHCl_3$–ethyl acetate (1:1) as eluent. Thus, 0.300 g of a colorless solid was obtained. Recrystallization from benzene gave **10** as colorless crystals: mp >300 °C; yield 20% (0.170 g); UV(CH_2Cl_2) λ_{max} 296 nm (ε 32500); IR (Nujol) ν_{max} 1615, 1585, 1425, 1405, 1290, 1165, 910, 870, 840, 820, 790, 765, 760, 740 cm^{-1}; ^1H NMR (270 MHz, Me_2SO-d_6) δ 4.89, 5.69 (AB q, J = 14.2 Hz, 4 H, CH_2), 7.62–7.37 (m, 4 H, H-6, H-7, H-17, H-18) 7.45 (t, J = 7.5 Hz, 1 H, H-12), 7.70, 7.74 (AB q, J = 2.5 Hz, 4 H, H-5, H-8, H-16, H-19), 7.91 (t, J = 7.5 Hz, 1 H, H-2), 8.10 (d, J = 7.5 Hz, 2H, H-11, H-13), 8.28 (d, J = 7.5 Hz, 2 H, H-1, H-3). Anal. Calcd for $C_{28}H_{18}N_4$: C, 81.95; H, 4.39; N, 13.65. Found: C, 81.87; H, 4.62; N, 13.85.

12*H*,16*H*-Naphth[2',2':4,5]imidazo[2,1-*a*]naphth[2'',3'':4',5']imidazo[1',2':2,3][2]benzazepino[6,5,4-*def*]benzazepine (12). This was prepared analogously to **10** from the 2,6,2',6'-tetracarbaldehyde (0.67 g, 25 mmol), 2,3-diaminonaphthalene (0.8 g, 50 mmol), and glacial acetic acid (60 mL). After evaporation of the solvent in vacuo, the residue was dissolved in dichloromethane and filtered through alumina (100 g). The filtrate was evaporated to dryness and the residue was chromatographed on PLC alumina plates, using dichloromethane–chloroform (1:1) as eluent. The yellow band having R_f 0.71 gave 0.120 g of light yellow solid, mp 300 °C. Recrystallization from benzene–petroleum ether (bp 60–80 °C) gave **12** as colorless solid; mp >300 °C; yield 46% (0.08 g); UV (CH_2Cl_2) λ_{max} 249 nm (ε 125400), 273 (s, 80800), 338 (49900); IV (Nujol) ν_{max} 1635, 1615, 1590, 1410, 1320, 1270, 1250, 1205, 1005, 920, 910, 880, 855, 825, 805, 740 cm^{-1}; ^1H NMR (270 MHz, Me_2SO-d_6) δ 5.10, 5.99 (AB q, J = 14.0 Hz, 4 H, CH_2), 7.41 (dt, J = 1.5 Hz, 2 H, H-8, H-20), 7.48 (dt, J = 1.5 Hz, 2 H, H-7, H-21), 7.71 (t, J = 7.0 Hz, 2 H, H-2, H-14), 8.02 (d, J = 7.0 Hz, 2 H, H-13, H-15), 8.06 (d, J = 7.0 Hz, 2 H, H-1, H-3), 8.13, 8.16 (AB q, J = 1.5 Hz, 4 H, H-6, H-9, H-19, H-22), 8.23 (s, 2 H, H-10, H-18), 8.54 (s, 2 H, H-5, H-23). Anal. Calcd for $C_{36}H_{22}N_4$: C, 84.70; H, 4.31; N, 10.98. Found: C, 84.9; H, 4.5; N, 10.7.

Acknowledgment. The 270-MHz proton spectra were run on the Bruker WH-270 spectrometer of the Weizmann Institute of Science, Rehovoth, Israel.

Registry No. 2, 1210-05-5; 3, 1454-80-4; 4, 77097-03-1; 5, 77097-04-2; 6, 4371-26-0; 7, 51640-64-3; 9, 77097-05-3; 10, 23628-98-0; 12, 77097-06-4; aniline, 62-53-3; *o*-phenylenediamine, 95-54-5; 2,3-diaminonaphthalene, 771-97-1.

(18) St. von Niementowsky, *Chem. Ber.* 1901, *34*, 3325–3337.