the central GC pairs owing to end-fraying of the duplex. On reaction with **1**, the peak at $\delta = 13$ broadened. The complexity of the spectra can be attributed to binding of **1** to both thymine and guanine with similar affinities, and to binding on each of the two strands leading to a large number of possible products. Titration beyond 4 mol equiv of **1** led to precipitates which did not redissolve.

The conclusion that complex **1** can bind to both thymine and guanine bases with similar affinities is supported by NMR spectroscopic investigations of mixtures containing both 5′-dTMP and 5′-dGMP at pH* 7.19. At a Pt/5′-dTMP/5′-dGMP mol ratio of 0.5:1:1 (20 mM), 35% of the 5′-dGMP and 18% of the 5′-dTMP were bound, and at a mol ratio of 1:1:1 50% of each nucleotide was bound.

There are few precedents for the rapid reaction of Pt complexes with thymine bases. The strong *trans* effect of P in square-planar Pt^{II} complexes[15] is probably important, and indeed Bandoli et al.[16] have reported that the dinuclear complex $[\{(dppf)Pt(\mu\text{-}OH)\}_2]^{2+}$ (dppf = 1,1′-bis(diphenylphosphino)-ferrocene) forms an N3-bonded 1-methylthymine (1-Me-T) complex in dimethylformamide (dmf), dimethyl sulfoxide, or acetonitrile, and determined the X-ray crystal structure of $[(dppf)Pt(1\text{-Me-T-H}_{-1})(dmf)]^+$, but the reactions were slow (complete in about 14 h at ambient temperature). However, they also found[17] that *cis*-$[Pt(PMe_3)_2]^{2+}$ is unreactive towards 1-Me-T in water unless 2 mol equiv of NaOH was added, emphasizing the role of the base in facilitating the removal of the proton at N3. In the present case the dangling arm amino group may play a role in enhancing removal of this proton. Compounds of the type **1** provide significant scope for control of chelate ring-opening, gating of ligand exchange, and base-specificity of attack on DNA or RNA which are being further explored.

Experimental Section

5′-UMP and 5′-dTMP were purchased from Sigma. Complex **1** was prepared and characterized as previously described in ref. [6]. The 8 mer oligonucleotide d(TTGGCCAA) was purchased as an HPLC-purified sodium salt from OSWEL DNA Service (University of Southampton).

Measurements of pH were made using a Corning 145 pH meter equipped with an Aldrich microcombination electrode calibrated with Aldrich buffer solutions of pH 4, 7 and 10. Values of pH* were adjusted with 1 M DNO_3 or NaOD as appropriate.

NMR spectra were recorded on the following instruments: JEOL GSX270, Bruker AM400, Bruker DRX500 and Varian INOVA600 using 5 mm tubes. The chemical shift references were sodium trimethylsilylpropanoate (through internal dioxan at $\delta = 3.744$; ^{1}H NMR), and 85% H_3PO_4 (external; ^{31}P NMR). Typical acquisition conditions for ^{1}H spectra were: 45–60° pulses, 2.5 s relaxation delay, 64–256 transients, final digital resolution 0.2 Hz per point. When necessary the water resonance was suppressed by presaturation, or the WATERGATE pulsed field gradient sequence [18]; for ^{31}P spectra: 50–90° pulses, 512–2048 transients, and a final digital resolution of 3–5 Hz per point.

For the experiments with d(TTGGCCAA), microliter aliquots of a 40 mM solution of complex **1** (in the same solvent as used for the oligonucleotide: H_2O/D_2O 9/1, 4 mM phosphate, 0.1 M $NaClO_4$, pH 7.0) were added in steps to give totals of 0.5, 1, 2, and 4 mol equivalents.

Titration curves were fitted to the Henderson-Hasselbalch equation with the program KaleidaGraph (Synergy Software, Reading, PA, USA) on a Macintosh computer.

Received: December 4, 1996 [Z 9852 IE]
German version: *Angew. Chem.* **1997**, *109*, 1233–1236

Keywords: bioinorganic chemistry · DNA recognition · NMR spectroscopy · nucleobases · platinum

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Formation of Isobenzenes by Thermal Isomerization of 1,3-hexadiene-5-yne Derivatives**

Henning Hopf,* Harald Berger, Gerhard Zimmermann,* Uta Nüchter, Peter G. Jones, and Ina Dix

The cyclization of 1,3-hexadiene-5-yne (**1**) to benzene (**3**),[1] first described in the late 1960s, has proven in recent years to be a useful reaction for preparing bowl-shaped, nonalternating polycyclic arenes (fullerene fragments).[2a–c] The activation parameters for the formation of **3** from **1** were determined, and the electrocyclic formation of 1,2,4-cyclohexatriene (**2**, isobenzene) was suggested as the first step.[3] As this highly reactive benzene isomer has recently been prepared by treatment of the dibromocarbene adduct of 1,3-cyclopentadiene with methyllithium at −30 °C by Christl et al.,[4] the question arises whether **2** and its derivatives are also thermally accessible from **1** and related hydrocarbons. The experiments described here show that this is indeed the case.

When a 1:1 mixture of *cis*- and *trans*-**1** and styrene (**4**) is heated to 200 °C in an ampoule, 70% of the dienyne and 30% of the trapping reagent are consumed after 90 min (GC analysis of the pyrolysate with fluorobenzene as internal standard). The products obtained are **3** (3%), addition products (homo- and codimers and trimers, 68%), polymers (29%), and cracking gases (traces; Scheme 1). The fraction with the addition prod-

[*] Prof. Dr. H. Hopf, Dipl.-Chem. H. Berger
Institut für Organische Chemie der Technischen Universität
Hagenring 30, D-38106 Braunschweig (Germany)
Fax: Int. code +(531)391-5388
e-mail: h.hopf@tu-bs.de
Prof. Dr. G. Zimmermann, Dr. U. Nüchter
Institut für Technische Chemie der Universität
Permoserstrasse 15, D-04303 Leipzig (Germany)
Fax: Int. code +(341)235-2701
e-mail: zimmerma@sonne.tachemie.uni-leipzig.de
Prof. Dr. P. G. Jones, I. Dix
Institut für Anorganische und Analytische Chemie der
Technischen Universität Braunschweig (Germany)

[**] Thermal rearrangements, Part 27. We thank the Volkswagenstiftung and the Fonds der Chemischen Industrie for support of this work in the field of high-temperature chemistry. We also thank Dr. M. Nüchter for supplying data for compounds **9d** and **13d** and Prof. Dr. M. Christl (Würzburg, Germany) for valuable discussions. Part 26: H. Hopf, W. Graf von der Schulenburg, R. Walsh, *Angew. Chem.* **1997**, *109*, 415; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 408.

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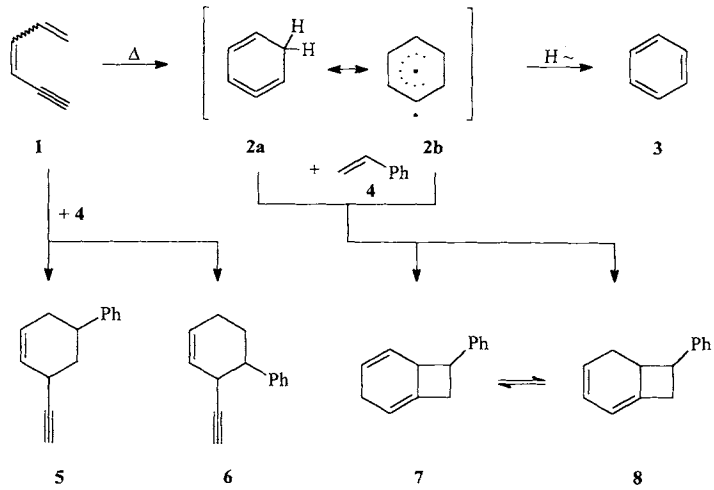


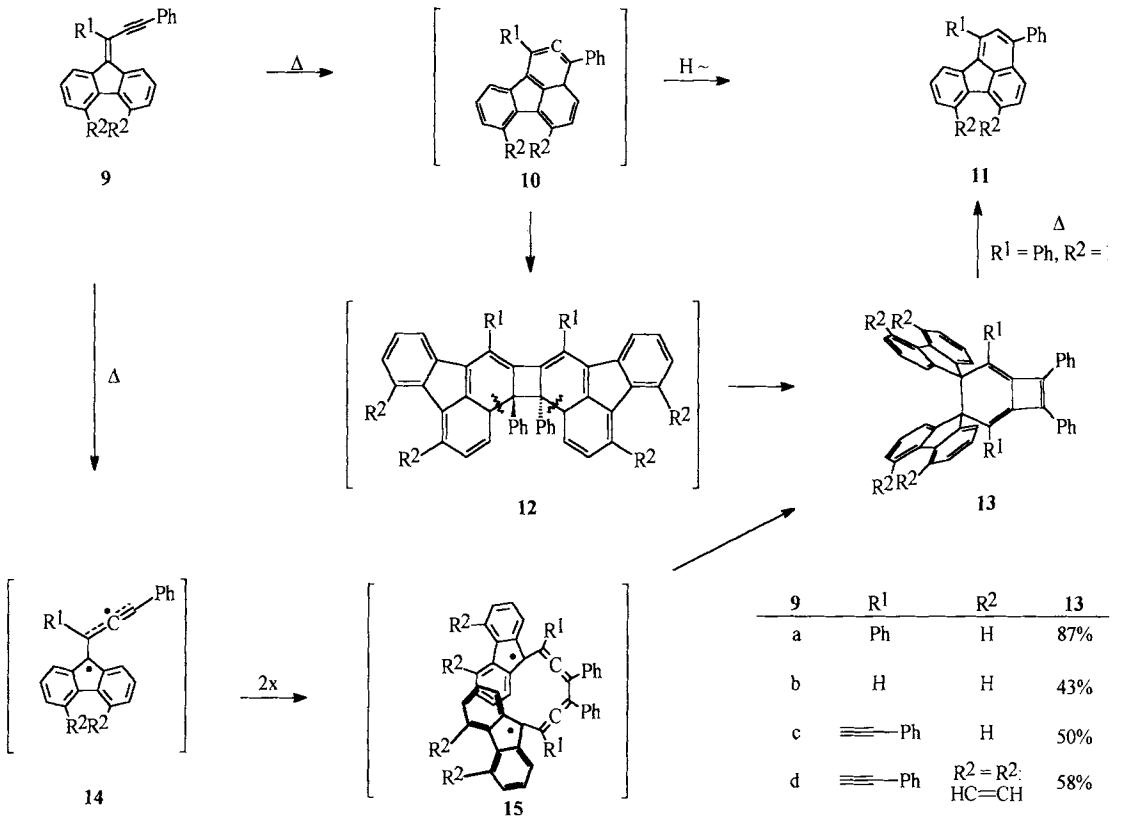
Scheme 1. Thermal isomerization of 1 and trapping experiments with 4.

ucts consists of about 35 compounds, of which 22 are obtained in amounts of less than 1%. The main part of this fraction is made up of the two Diels–Alder regioisomers **5** and **6** (48%, 1:1 ratio) and also the products of the [2+2] cycloaddition of **2** and **4**, 7-phenylbicyclo[4.2.0]octa-1,4-diene (**7**) and 7-phenylbicyclo[4.2.0]octa-1,3-diene (**8**), which are present in a ratio of 7:3 (6%).

The structure of **7** was assigned by comparison with the authentic hydrocarbon, first synthesized by Christl et al.[4] In addition to the 1:1 adducts **5**–**8**, the main fraction contains $C_{20}H_{20}$ hydrocarbons, which are formed from two molecules of **1** and one molecule of **4**, and $C_{22}H_{22}$ compounds, which require one molecule of **1** and two molecules of **4** for their formation (46%). The structures of these compounds have not yet been determined. If **4** is not added to the reaction mixture, **7** and **8** cannot be detected in the pyrolysate. Christl et al. have shown[4] that **7** and **8** are in thermal equilibrium at 130 °C; regioisomers of **7** and **8** are not obtained. At temperatures below 180–190 °C and above 260–270 °C the cycloadducts **7** and **8** are not detectable. In the first case ($T \leq 190$ °C) the available thermal energy is apparently insufficient to overcome the activation barrier of 30 kcal mol^{-1}[3] for the electrocyclization, and in the second ($T \geq 260$ °C) the reaction of **2** to form **3** by a hydrogen shift and the cycloreversion reaction of **7** and **8** are probably so strongly favored that both codimers cannot be detected (by GC/MS analysis). Therefore, only a narrow temperature range remains in which isobenzene formation can be determined by trapping reactions.

After the formation of **2** by thermal isomerization of **1** had been experimentally confirmed, several hydrocarbons containing the hexadienyne structure,[5a–c] including dibenzofulvenes **9a–d**, were synthesized and thermally converted. When **9a**, either neat or dissolved in toluene, is heated to 250 °C, the 1,3-diphenylfluoroanthene **11** expected in analogy to the reaction of **1** → **3** is formed, but only in trace amounts (2%; Scheme 2). The main product is the dimer **13a** (87%), whose structure was established by spectroscopy (see Table 1) and an X-ray structure analysis of the 1,2-dichloroethane bis(solvate) (Figure 1).[6] The elongated C9–C9′ bond (163.8(8) pm) in the cyclohexadiene ring is probably attributable to steric congestion at these carbon atoms.

Heating **13a** to 350 °C results in rearrangement to yield **11** (80%), which is also obtained from **9a** under these drastic conditions (350 °C, 70%).[7] These isomerizations are best explained by the existence of the isobenzene intermediate **10**. After its formation by electrocyclization of **9**, **10** can react in analogy



9	R^1	R^2	13
a	Ph	H	87%
b	H	H	43%
c	≡—Ph	H	50%
d	≡—Ph	$R^2 = R^2$: HC=CH	58%

Scheme 2. Thermal isomerization of the condensed arenes **9a–d** with 1,3-hexadiene-5-yne substructure.

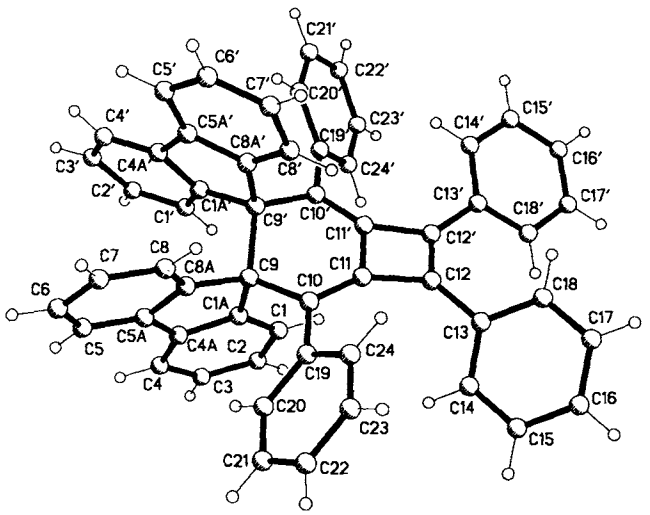


Figure 1. Crystal structure of **13a** (without solvent). Radii are arbitrary. Selected bond lengths [pm]: C9–C9′ 163.8(8), C9–C10 154.5(7), C10–C11 133.3(8), C11–C12 148.7(8), C9′–C10′ 154.3(7), C10′–C11′ 133.2(8), C11′–C12′148.3(7), C11–C11′ 149.2(9), C12–C12′ 138.2(9).

to the well-documented [2 + 2] cycloadditions of allenes to give **12**, which undergoes a stabilizing bond reorganization (cleavage of the weakest bonds in **12**, marked with wavy lines, and C–C bonding at the five-membered ring of the fluorenyl unit) to yield **13a**. Alternatively, a hydrogen shift in **10**, which is favored at higher temperatures, is possible, as was the case with the parent compound (see above). Presumably, the reaction of **13a** → **11** also proceeds via **10**. However, at these temperatures a decoupling of the exocyclic double bond of the starting material is also feasible (thermal *cis–trans* isomerization of **9**). The resonance-stabilized diradical **14** thus formed could dimerize to **15**, which can react to **13a** by cyclization and conversion of the bis(allene) unit to a bis(methylene)cyclobutadiene group.[9] Dimer formation is not restricted to **9a**, as is demonstrated by the isomerization–dimerization of **9b–d** to **13b–d**, whose structures were proven spectroscopically (Table 1) and by comparison with data obtained for **13a**.

These experiments show that isobenzenes are by no means exotic intermediates; they are in fact easily accessible by different routes. It is conceivable that such benzene isomers are also intermediates in the formation of condensed arenes by high-temperature pyrolysis of alkynes. This is particularly likely when ring-closing reactions of 1,3-hexadiene-5-ynes by 1,6-C,H insertion of alkenylidenecarbene intermediates, which dominate at temperatures above 800 °C, are disfavored because of conformational constraints, and it is also probable for the carbene obtained from **9a** by a 1,2-phenyl shift.[12] In the future, dimers of type **13** should systematically be sought when pyrolyzing aromatic hydrocarbons with 1,3-hexadiene-5-yne substructure.[14]

Table 1. Spectroscopic data for **13a–d**.

13a: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16 (m, 1H), 7.47 (m, 1H), 7.40 (m, 2H), 7.16 (m, 1H), 7.11 (d, 1H), 7.04 (m, 4H), 6.87 (dt, 1H), 6.77 (m, 3H), 6.49 (d, 2H), 6.29 (t, 1H), 5.35 (d, 1H); ^{13}C NMR (100.1 MHz, $CDCl_3$): δ = 151.7, 147.9, 145.0, 142.0, 141.5, 139.2, 137.7, 132.9, 128.8, 128.6, 128.3, 128.0, 127.8, 127.0, 126.9, 126.6, 126.5, 126.4, 126.1, 125.0, 124.2, 119.5, 118.0, 66.1; IR (KBr): $\tilde{\nu}$ = 3056 (w), 3029 (w), 1443 (m), 1026 (w), 768 (m), 739 (s), 696 cm^{-1} (s).

13b: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (m, 2H), 7.38 (m, 5H), 7.16 (br. s, 3H), 6.97 (br. s, 3H), 5.71 (s, 1H); ^{13}C NMR (100.1 MHz, $CDCl_3$): δ = 145.5, 141.2, 140.9, 133.3, 129.1, 128.7, 127.7, 127.4, 126.1, 126.0, 118.9, 111.5, 61.3; IR (KBr): $\tilde{\nu}$ = 3060 (w), 3031 (w), 1443 (m), 759 (m), 734 (s), 698 cm^{-1} (m).

13c: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.23 (dd, 2H), 7.94 (br. s, 1H), 7.45 (m, 4H), 7.34 (br. s, 3H), 7.08 (m, 4H), 6.68 (dd, 3H), 6.07 (br. s, 1H); ^{13}C NMR (100.1 MHz, $CDCl_3$): δ = 148.1, 144.5, 141.7, 132.0, 130.9, 129.7, 129.1, 128.4, 127.9, 127.8, 123.2, 106.7, 97.5, 87.6, 63.8; IR (KBr): $\tilde{\nu}$ = 3060 (w), 3031 (w), 3019 (w), 1595 (m), 1488 (s), 1474 (m), 1446 (s), 766 (s), 753 (s), 739 (s), 688 cm^{-1} (s).

13d: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (dd), 7.40 (m), 7.00 (br. m), 7.00–6.90 (m), 6.38 (dd), 5.90 (br. m); ^{13}C NMR (100.1 MHz, $CDCl_3$): δ = 148.6, 144.9, 137.8, 132.2, 130.8, 129.6, 129.1, 128.4, 128.2, 127.8, 127.7, 127.5, 126.9, 124.8, 123.6, 123.2, 122.4, 106.6, 97.4, 87.9, 66.1; MS (70 eV): *m/z* (%) = 804 (100) [M^+], 727 (33) [$M - C_6H_5$], 402 (20) [M^{2+}], 400 (20) [$(M - 2H)^{2+}$], 278 (25) [$C_{22}H_{14}$], 189 (62) [$C_{15}H_9^+$], 78 (95) [$C_6H_6^+$]

Experimental Section

9a–d: Compounds **9a** and **9c** were prepared by reaction of 9-trimethylsilylfluorene-9-yllithium with 1,3-diphenylpropynone and 1,5-diphenyl-1,4-pentadiyne-3-one [10], respectively, in Et_2O at −40 °C (69% and 57%). Derivative **9b** was obtained from fluorene-9-ylidene triphenylphosphane and 3-phenylpropynal in $CHCl_3$ (70%), and **9d** from cyclopenta[*def*]phenanthrenyllithium and 1,5-diphenyl-1,4-pentadiyne-3-one [10] in THF (75%).

9a: m.p. 118 °C (116 °C) [13]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.87 (m, 1H), 7.63 (m, 1H), 7.55 (m, 4H), 7.49 (m, 3H), 7.36 (m, 6H), 7.22 (m, 1H), 6.86 (dt, 1H), 6.46 (d, 1H); ^{13}C NMR (100.1 MHz, $CDCl_3$): δ = 140.7, 140.4, 140.1, 138.2, 137.5, 131.7, 129.0, 128.9, 128.8, 128.5, 128.4, 127.4, 126.6, 125.5, 124.9, 122.5, 122.2, 119.4, 102.4, 92.2; IR (KBr): $\tilde{\nu}$ = 3056 (w), 3030 (w), 2180 (w), 1567 (w), 1488 (w), 1442 (s), 782 (s), 757 (s), 728 (s), 694 (s), 687 cm^{-1} (s).

9b: m.p. 91–92 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.58 (d, 1H), 7.65 (m, 3H), 7.59 (m, 2H), 7.37 (m, 6H), 7.25 (dt, 1H), 6.76 (s, 1H); ^{13}C NMR (100.1 MHz, $CDCl_3$): δ = 144.2, 140.7, 139.4, 138.2, 136.9, 131.6, 129.3, 129.1, 128.8, 128.6, 127.4, 127.2, 124.9, 123.3, 120.3, 119.8, 119.7, 103.7, 100.9, 88.7; IR (KBr): $\tilde{\nu}$ = 3049 (w), 2923 (w), 2183 (w), 1619 (w), 1440 (m), 840 (s), 728 (s), 688 cm^{-1} (s).

9c: m.p. 137 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.70 (d, 2H), 7.65 (m, 6H), 7.41 (dd, 6H), 7.36 (dt, 2H), 7.30 (dt, 2H); ^{13}C NMR (100.1 MHz, $CDCl_3$): δ = 145.2, 140.3, 137.5, 131.8, 129.5, 129.1, 128.6, 127.5, 125.5, 122.9, 119.6, 101.3, 97.9, 88.9; IR (KBr): $\tilde{\nu}$ = 3052 (w), 3029 (w), 2186 (w), 1448 (m), 1442 (s), 779 (w), 752 (s), 720 (s), 683 cm^{-1} (s).

9d: m.p. 210 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.52 (d, 2H), 7.82 (d, 2H), 7.81 (s, 2H), 7.73 (m, 4H), 7.64 (t, 2H), 7.45 (m, 8H); ^{13}C NMR (100.1 MHz, $CDCl_3$): δ = 146.7, 136.4, 135.8, 131.9, 129.6, 128.6, 128.0, 127.4, 125.8, 125.1, 123.2, 122.8, 103.9, 97.3, 88.4; IR (KBr): $\tilde{\nu}$ = 3036 (w), 2186 (w), 1489 (s), 1441 (s), 822 (s), 755 (s), 689 cm^{-1} (s).

Received: November 14, 1996 [Z9771IE]
German version: *Angew. Chem.* **1997**, *109*, 1236–1238

Keywords: arenes · cycloadditions · isomerizations

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[6] Crystal structure data for **13a**·$2C_2H_4Cl_2$: $C_{60}H_{44}Cl_4$, monoclinic, $P2_1/c$, a = 1281.2(2), b = 1937.3(3), c = 1893.4(3) pm, β = 100.674(14)°, V = 4.6181 nm^3, Z = 4, μ = 0.3 mm^{-1}, T = −100 °C. Pale yellow plate, 0.8 × 0.4 × 0.12 mm^3, Siemens P4 diffractometer, 9875 measured reflections ($2\theta_{max}$ = 50°) 8000 independent (R_{int} = 0.059). Structure solved with direct methods and refined on F^2 with anisotropic displacement parameters (SHELXL-93, G. M. Sheldrick, Universität Göttingen (Germany)); a riding model was used for H atoms; $wR(F^2)$ = 0.250, $R(F)$ = 0.082, 577 parameters, 765 restraints; max. $\Delta\rho$ = 1361 e nm^{-3}. Crystallographic data (excluding structure factors) for the structure reported in this Communication have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-179174. Copies of the data can be ordered free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: int. code +(1223)336-033; e-mail: deposit@chemcrys.cam.ac.uk).
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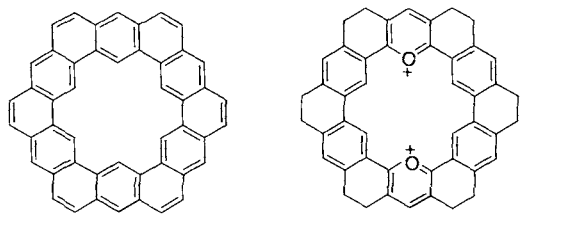
[14] Such a situation occurs in, for example, the case of 7,10-diethynylfluoroanthene, which rearranges to form corannulene under the conditions of flash vacuum pyrolysis [2a].

Synthesis of 3,9,15,19,21,23-Hexaazakekulene

Arnaud Tatibouët, Richard Hancock, Martine Demeunynck,* and Jean Lhomme

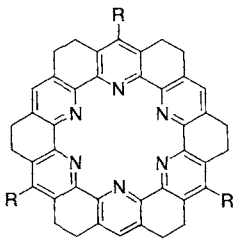
Kekulene (**1**) was synthesized by Diederich and Staab in 1978[1] as the first member of a series of compounds designated as cycloarenes or coronaphenes. The electronic structure (annulenoid or benzenoid) of **1** is intriguing.[2a] ^{1}H NMR results[2b] and a very recent theoretical study[2a] indicate the benzenoid structure. Synthesis of cycloarenes is a challenging problem, and only very few molecules have been described. Dodecahydro-18,21-dioxoniakekulene[3] (**2**) and dodecahydrohexaazakekulenes[4] **3** are the only heteroaromatic analogues of kekulene prepared so far.

In the course of investigating the synthesis of heterocyclic Tröger's bases,[5] we studied the reactivity of 3-aminoacridine with formaldehyde and observed the formation of a new, fully unsaturated heptacycle, acridino[3,4-*j*]benzo[*b*]-1,7-phenanthroline.[6] On the basis of this result, we designed a strategy for preparing 3,9,15,19,21,23-hexaazakekulene (**4**), in which the nitrogen atoms are located alternatively at the inner and outer perimeters of the cycloarene.

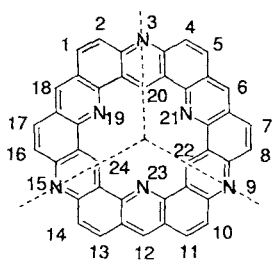


Kekulene **1**

2

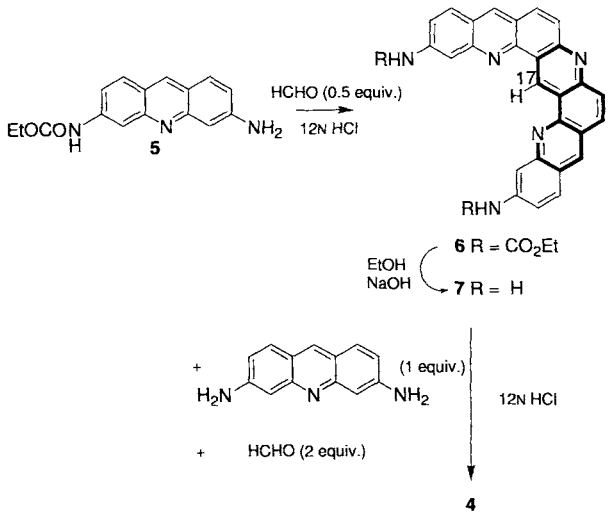


3 R = H, C_4H_9



4

Compound **4** could be constructed by condensation of three molecules of proflavine (3,6-diaminoacridine) with three molecules of formaldehyde. Proflavine has to first be monoprotected to avoid polymerization. We used the ethoxycarbonyl protecting group, since it is stable in the strongly acidic conditions required for the condensation reaction. Monoprotected proflavine (6-amino-3-(ethoxycarbonylamino)acridine, **5**)[7] slowly reacted with paraformaldehyde in 12 N HCl to give 2,14-di(ethoxycarbonylamino)acridino[3,4-*j*]benzo[*b*]-1,7-phenanthroline (**6**) in 84% yield after 3 weeks (Scheme 1). The stoichiometry of the reaction was crucial, as formation of **6** required only one equivalent of formaldehyde for two proflavine molecules. An excess of formaldehyde would lead to different compounds (analogues of Tröger's base, tetrahydroquinazoline, or dihydrooxazine derivatives).[5] The ^{1}H NMR spectrum of **6** is characterized by the strong deshielding of the internal H-17 proton, which appears at $\delta = 11.3$.



Scheme 1. Synthesis of hexaazakekulene **4**.

Removal of the ethoxycarbonyl groups was achieved under basic conditions (EtOH, NaOH) to give 2,14-diaminoacridino[3,4-*j*]benzo[*b*]-1,7-phenanthroline (**7**) in 68% yield. This polar compound was analyzed by ^{1}H NMR spectroscopy in deuteriated trifluoroacetic acid ([D]TFA); the H-17 proton appears as a singlet at $\delta = 12.24$.

To obtain the hexaazakekulene **4**, stoichiometric amounts of **7** and proflavine were allowed to react with two equivalents of paraformaldehyde in 12 N HCl. After the mixture was stirred at 50 °C for one week, there was total disappearance of **7** (HPLC). The mixture was basified, and a dark brown residue, which was analyzed by ^{1}H NMR spectroscopy and mass spectrometry, was obtained. The ^{1}H NMR spectrum ([D]TFA) indicated the presence of one major product, later identified as the desired hexaazakekulene **4**, and several by-products. The mass spectrum confirmed the formation of **4** ($m/z = 606$ [M^+]) along with two compounds of higher mass ($m/z = 815$ and 829).[8] Since **4** is insoluble in most organic solvents, pure product can be obtained by extensive washings of the solid reaction mixture with CH_2Cl_2, MeOH, and DMF. Elemental analysis was performed three times, and the data are in agreement with structure $4 \cdot 10H_2O$ ($C_{42}H_{18}N_6 \cdot 10H_2O$); the water molecules could not be removed by extensive drying in vacuo. High-resolution mass

[*] Dr. M. Demeunynck, A. Tatibouët, R. Hancock, J. Lhomme
LEDSS, CNRS/Université J. Fourier
BP 53, F-38041 Grenoble Cedex (France)
Fax: Int. code +(47) 651-4382
e-mail: martine.demeunynck@ujf-grenoble.fr

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