The First 1,10-Diaza[2.2]metacyclophanes − Strained Medium Membered Heterocycles☆

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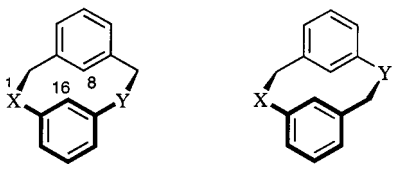
The *N*-protected 1,10-diaza[2.2]metacyclo- and 1,10-diaza-[2]metacyclo[2](2,6)-pyridinophanes **4** and **5** have been synthesized for the first time using high dilution conditions. The free secondary diamine **7** was obtained from **4** by alkaline hydrolysis. – Quantum chemical calculations support the hypothesis that **7** is one of the most strained *anti*-hetera[2.2]metacyclophanes known. This is also evident from the ^{1}H-NMR spectrum of **7**, which shows one of the strongest high field shifts for the intraannular protons in comparison to other *anti*-[2.2]metacyclophanes.

Introduction

During the last decade we have synthesized an increasing number of strained ten-membered heterocyclic [2.2]metacyclophanes of type **I** and **II**, the heteroatoms of which are located in the 1,10- and 1,9-positions, respectively (Figure 1). The challenge is to find the maximum deformation of the benzene ring in this type of molecule that can be synthesized using known and optimized or newly developed synthetic methods. The transannularly strained [2.2]metacyclophanes are well suited as model compounds for spectroscopic and theoretical investigations.[1] Chiral representatives have proven to be suitable species for the calculation of circular dichroism.[2] Since these molecules are not additionally functionalized, they also provide a challenge in terms of the separation of racemates with chiral column materials.

Figure 1. Miscellaneous hetera[2.2]metacyclophanes



I **II**

a: X = Y = NR
b: X = O, Y= NR
c: X = S, Y = NR
d: X = S, Y = CH_2
e: X = NR, Y = CH_2
f: X = O, Y = CH_2
g: X = Y = S
h: X = S; Y = O
i: X = Y = CH_2

a: X = S, Y = O

With this philosophy in mind we have synthesized many achiral and chiral representatives with a variety of heteroatoms X, Y (in **I**, **II**), separated the racemates into the enantiomers, and compared the measured circular dichroism values with the calculated ones.[3] X-ray crystal structure analysis proved that in these ring systems the benzene rings are deformed, usually in a quantitatively different extent to a "boat" shaped conformation due to steric interactions between the 8- and 16-positions of the carbon skeleton.[4] Thereby shorter CH_2-X and CH_2-Y distances in the ten-membered ring of the [2.2]metacyclophane **I** and **II**, respectively, lead to an increase in ring strain in the ten-membered cycles.

In this sense the hitherto unknown 1,10-diaza[2.2]metacyclophane (**7**) and 1-oxa-10-aza[2.2]metacyclophane (**Ib**) should be particularly strongly deformed because of the short clamping of the two *meta*-phenylene rings.

Whereas the oxaza[2.2]metacyclophane **Ib** has so far eluded our synthetic efforts, we here report for the first time the successful synthesis of 1,10-diaza[2.2]metacyclophane (**7**) and the 1,10-diaza[2]metacyclo[2](2,6)pyridinophane skeleton (**5**), compounds that we had previously tried to synthesize without success for many years.[5]

Synthesis of the Diaza[2.2]phanes

The first diaza[2.2]metacyclophane and -pyridinophane representatives **4** and **5** were obtained by reaction of the bis(bromomethyl) compounds **1** and **2**, respectively, with the *N,N′*-bis(trifluoroacetyl)-substituted *meta*-phenylenediamine **3** under high-dilution conditions in yields of <1%. Despite many optimization experiments on the basis of earlier experiences (high dilution, variation of solvents and sol-

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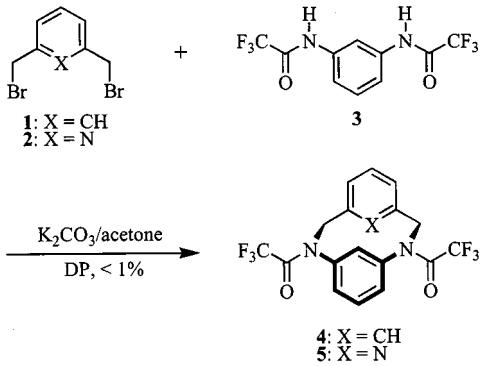
vent mixtures, caesium effect[6]) we did not succeed in increasing these low yields significantly. Similar attempts also failed in the case of the pyridinophane **5**, a system that should be less strained than **4** because an intraannular hydrogen atom is formally replaced by a free electron pair at the pyridine nitrogen, thus requiring less space.[7]

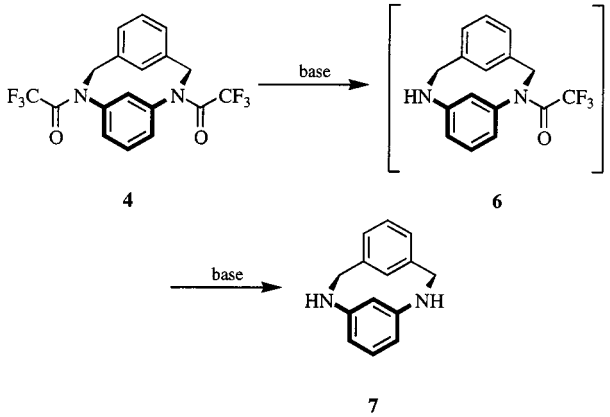
Scheme 1. Synthesis of diazaphanes **4** and **5**



The trifluoroacetyl group activates the amino function of the *meta*-phenylenediamine building block **3** and hence enables the nucleophilic substitution at the bis(bromomethyl) compounds **1** and **2**, respectively. The tosyl group used previously[8] was replaced by the trifluoroacetyl group in the heteracylophane synthesis, as the tosyl group has several major disadvantages: it is not easily removed from the product and its absorption bands and Cotton effects overlap those of the metacyclophane skeleton in UV and CD spectra, respectively.

In contrast to the *N*-tosyl analogues, the new trifluoroacetyl-metacyclophanes **4** and **5** can be detected easily by GC-MS. The isolation and characterization of the new [2.2]phanes **4** and **5** was therefore significantly easier. The trifluoroacetyl groups have already proved worthwhile in the synthesis of the 1-thia-10-aza[2.2]metacyclophanes **Ic** and 1-aza[2.2]metacyclophanes **Ie**.[3f][3g][3h][3i] Since they are easily cleaved off, their use allows the synthesis of the corresponding free amines **7**, **Ic** and **Ie** (R = H).

Scheme 2. Synthesis of the free secondary amine **7**



Removal of the trifluoroacetyl protecting groups under mild alkaline conditions (methanol/K_2CO_3) leads to the hitherto unknown unsubstituted diaza[2.2]metacyclophane **7**. According to GC-MS studies the semi-protected diazaphane **6** is formed first. This allows the preparation of unsymmetrically substituted and planar chiral diaza[2.2]phanes in the future. Compound **4** requires a remarkably long time (7 h) for the completion of its hydrolysis. Steric hindrance and electronic effects may be responsible for this due to the unique geometry and rigidity of the molecule.

^{1}H-NMR Spectroscopy

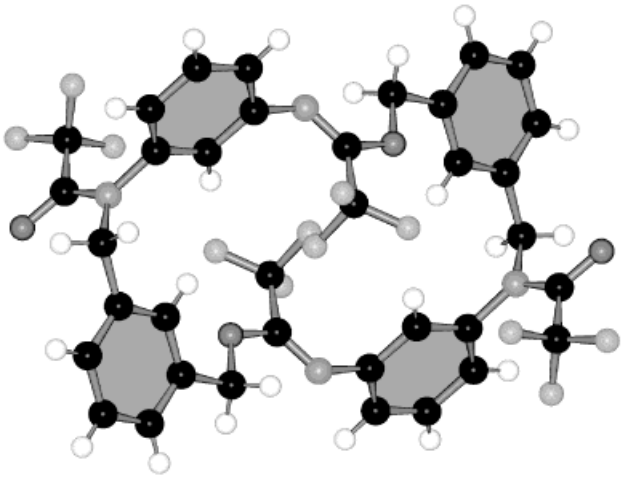
The ^{1}H-NMR spectrum of **7** shows one of the strongest high field shifts for intraannular aromatic protons in the [2.2]metacyclophane system **I**: $\delta(H_i)$ = 3.81 and 4.41. For comparison: the [2.2]metacyclophane hydrocarbon **Ii** shows $\delta(H_i)$ = 4.25. Only the bridged ("tethered") [2.2]metacyclophanes described by Bodwell et al. exhibit [with $\delta(H_i)$ = 4.83 and 3.3, respectively] even stronger high field shifts than **7**.[9]

The strength of the high field shift indicates a tighter clamping of the two *meta*-phenylene rings and a shorter intraannular C8−C16 distance in the diaza[2.2]metacyclophane (**7**) than in other hetera[2.2]metacyclophanes. We therefore consider **7** to be one of the most strained *anti*-hetera[2.2]metacyclophanes.

X-ray Crystal Structure Analysis

During the work-up of the cyclization reaction yielding **4**, single crystals from a solvent mixture of dichloromethane/methylcyclohexane were obtained. In the subsequent X-ray crystal structure analysis it was found that these crystals were not composed of the monomeric cycle **4**, but of tetraaza[4.2.4.2]metacyclophane **8**, a dimer of **4**.

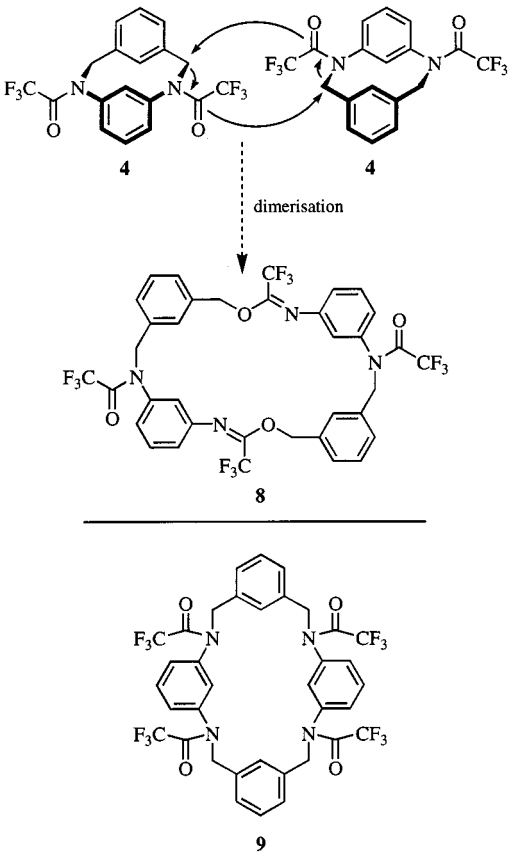
Figure 2. X-ray crystal structure analysis of the macrocycle **8**. This drawing is plotted with SCHAKAL 97



The 24-membered macrocycle **8** can be formed in two different ways: firstly in the reaction of **3** and **1** as a byproduct of the desired compound **4**. A second possibility is the subsequent dimerization of **4** to macrocycle **8**, either during the column chromatographic work-up as a result of the acidic column material, or during the crystalization process, which takes several weeks. As the [4.2.4.2]metacyclophane

8 contains two four-membered iminol bridges, the first hypothesis seems unlikely: the formation of such bridges is energetically unfavorable as the stable carbonyl group no longer exists. Usually a dimer would prefer to adopt the more favorable constitution of a [2_4]metacyclophane **9**. In fact the formation of a dimer analogous to **9** could be observed during our first attempts to synthesize diaza[2.2]metacyclophanes.[5]

Scheme 3. Possible course of the dimerisation of **4** to dimer **8**



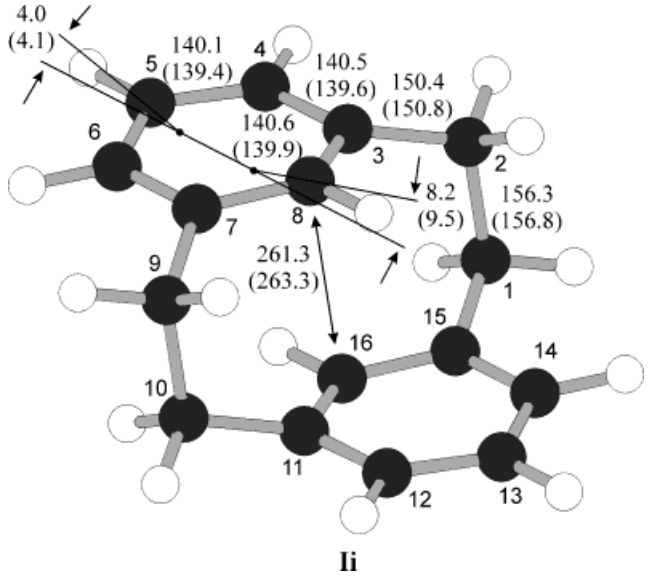
A possible reaction mechanism for the formation of dimer **8** is depicted in Scheme 3.

Theoretical Results for Geometries and Strain Energies of 7

Geometry: Since it was not possible to obtain X-ray crystal structure analyses of the diaza[2.2]metacyclophanes **4** and **7**, respectively, the molecular geometry of **7** has been optimized at different levels of theory to examine the structure of this new family of hetera[2.2]metacyclophanes.

Test calculations for the geometry of parent compound [2.2]metacyclophane **Ii**, obtained with semiempirical methods (AM1, PM3), showed, that the distances between the two *meta*-phenylene rings (esp. the intraannular C8−C16 distance) are too short in comparison with those obtained from X-ray crystal structure analysis of **Ii**.[11] On the other hand, the interring distances calculated with the ab initio Hartree-Fock (HF) method are too long in comparison with the experimental data. The HF method probably overestimates the repulsive non-bonding interactions due to the missing dispersion forces between the two *meta*-phenylene rings. In order to show which theoretical level provides accurate [2.2]metacyclophane geometries, we have also performed density-functional (DFT/B3-LYP) and correlated ab initio (RI-MP2) calculations.[10]

Figure 3. Comparison of experimental and calculated bond distances and deformation angles in [2.2]metacyclophane **Ii**. The angles given indicate the "boat" shaped deformation of the *meta*-phenylene rings. The numbers without brackets refer to the RI-MP2/VDZP geometry, the numbers in brackets refer to experimental data.[11b] Bond lengths are given in pm and angles in deg.



Ii

Table 1. Comparison of the calculated structures of **Ii** with experimental data.[11b] The numbering of the atoms refers to Figure 3. Bond lengths are given in pm and angles in deg. (for the theoretical methods, see ref.[10])

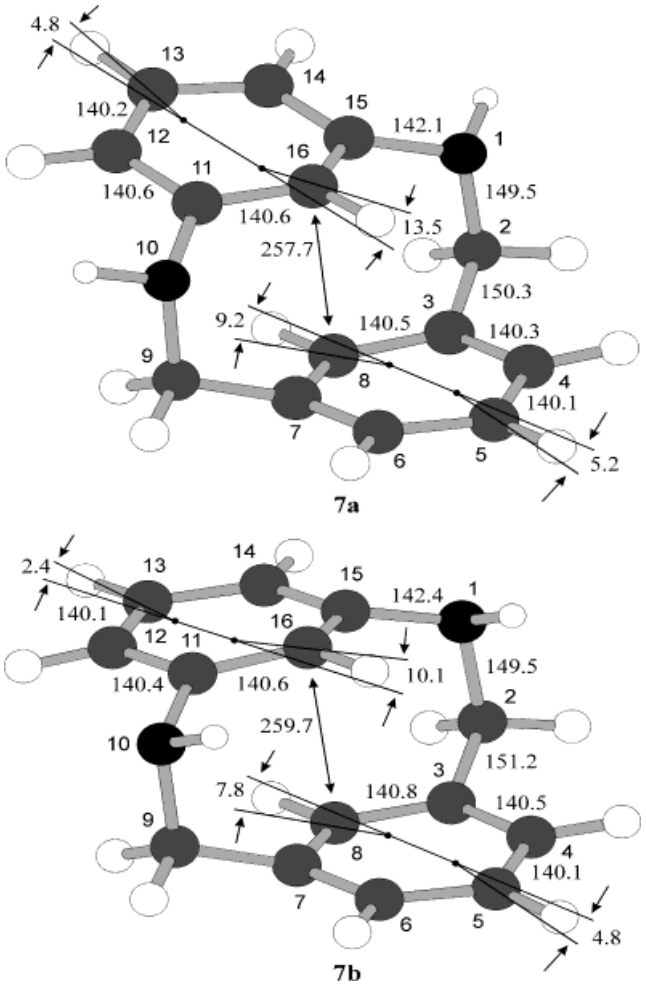
	HF/VDZP	B3-LYP/VDZP	RI-MP2/VDZP	exp.
Bond lengths				
C1−C2	156.8	157.9	156.3	156.8
C2−C3	151.6	151.4	150.4	150.8
C3−C8	139.2	140.4	140.6	139.9
C3−C4	139.3	140.4	140.5	139.6
C4−C5	139.0	140.0	140.1	139.4
C8−C16	269.3	266.9	261.3	263.3
Bond angles				
C1−C2−C3	112.0	111.9	110.0	110.5
"Boat" type deformation angles				
α	11.2	10.0	8.2	9.5
α′	4.3	4.3	4.0	4.1

The calculated geometries of **Ii** are compared with its X-ray data in Figure 3 and Table 1.

As mentioned above, the distances between the two *meta*-phenylene rings of **Ii** are too large at the HF/VDZP and also at the B3-LYP/VDZP level of theory in comparison with the experimental data: the shortest inter-ring distance C8−C16 is too large by 6.0 pm and by 3.6 pm, respectively. The RI-MP2/VDZP structure of **Ii**, on the other hand, agrees well with the X-ray structure of **Ii** (the C8−C16 distance is too short by 2.0 pm). Therefore we expect the RI-

MP2/VDZP structure of the diaza[2.2]metacyclophane **7** to be of similar quality.

Figure 4. Comparison of calculated bond distances and deformation angles in the two conformers **7a** and **7b**. The angles given indicate the "boat" shaped deformation of the *meta*-phenylene rings. The numbers refer to the RI-MP2/VDZP geometry. Bond lengths are given in pm and angles in deg.



The structures of the two conformers of 1,10-diaza[2.2]-metacyclophane (**7a** and **7b**) with C_s symmetry (inverted configuration at both N atoms), calculated with the RI-MP2/VDZP[10] method, are shown in Figure 4 and Table 2. The conformers **7a** and **7b** are of almost equal energy: an energy difference $\Delta E = E(\mathbf{7b}) - E(\mathbf{7a})$ of +0.5 kJ/mol at the B3-LYP/VDZP[10] level of theory and of −6.3 kJ/mol at the RI-MP2/VDZP[10] level is obtained [cf. ref.[3h] for a discussion of the two conformers in the case of **Ic** (R = H)]. These energy differences are too small to allow a conclusive answer to be obtained regarding which of the two conformers is more stable.

Structure **7a** shows significantly larger "boat" type deformation angles of both *meta*-phenylene rings and a significantly smaller intraannular C8−C16 distance than its parent compound **Ii** (cf. Table 1 and Table 2). This difference is a result of the tighter clamping of both *meta*-phenylene rings by shorter bridges [bond length C1−C2 in **Ii**: 156.3 pm (RI-MP2/VDZP value) vs. bond length N1−C2 in **7a**: 149.5 pm (RI-MP2/VDZP value)] and of the inclination of the two *meta*-phenylene rings against each other in **7a** (C_s symmetry), which is not present in **Ii** (C_{2h} symmetry). Since the inclination of the two *meta*-phenylene rings in **7b** is in the opposite direction to that in **7a**, the C8−C16 distance in **7b** is larger than in **7a** and the "boat" type deformation angles are smaller.

Strain energy: Since we expect the diaza[2.2]metacyclophanes to be one of the most strained *anti*-[2.2]metacyclophanes, we have performed calculations at different levels of theory of the strain energy of **7** and its parent compound **Ii** in order to compare these values.

The strain energy of a molecule is usually defined as the energy difference between the molecule and arbitrarily chosen unstrained reference systems. Since the conformers **7a** and **7b** are of almost equal energy, their strain energies are also almost equal in comparison with the same reference system. For this reason only the strain energy of **7a** has been calculated.

We have chosen the following approach[12] to determine the strain energy of **7a** and **Ii**: the Ar−C bonds of the metacyclophane bridges of **7a** and **Ii** are broken and the free valences are saturated with H-atoms at a typical C−H distance and in the same direction as the formerly bonded C atoms. The two fragments that are obtained in this way (benzene and *N,N′*-dimethyl-1,3-diaminobenzene for **7a**; benzene and 1,3-diethylbenzene for **Ii**) have the same conformation as in the corresponding cyclophanes. The strain energy is the difference between the energy of these fragments and the corresponding fully optimized fragments. A drawback of this method is that the part of the strain energy due to the repulsive interaction of the two benzene rings is not taken into account.

The calculations were carried out at the HF/SV and at the RI-MP2/VDZP level of theory.[10]

Table 3 shows the strain energies obtained with these two methods. The strain energies for [2.2]metacyclophane **Ii** agree well with values reported in the literature (49.8 kJ/mol to 87.4 kJ/mol).[13] These values may be compared to the strain energies of the [*n*]metacyclophanes calculated in ref.[14]: 61.1 kJ/mol for [7]metacyclophane and 117.6 kJ/mol for [6]metacyclophane.

Both levels of theory show an increase of strain energy from **Ii** to **7a** by 80−90%. Compared with its parent compound, the diaza analogue **7a** can therefore be considered as highly strained.

Conclusions

The diaza[2.2]metacyclophane compounds **4**, **5**, and **7** have been prepared successfully for the first time. Despite the use of high dilution technologies the yields of compounds **4** and **5** are very low, showing that a limit has been reached in one step nucleophilic substititution reactions yielding strained hetera[2.2]cyclophanes.

Quantum chemical calculations and ^{1}H-NMR spectra indicate high ring strain in the structure of diaza[2.2]metacyclophanes. One consequence of this could be the forma-

Table 2. Comparison of the calculated structures of **7a** and **7b**. The numbering of the atoms refers to Figure 4. Bond lengths are given in pm and angles in deg. (for the theoretical methods, see ref.[10])

	7a			**7b**
	HF/VDZP	B3-LYP/VDZP	RI-MP2/VDZP	RI-MP2/VDZP
Bond lengths				
N1−C2	148.7	150.4	149.5	149.5
C2−C3	151.5	151.3	150.3	151.2
C3−C8	139.2	140.4	140.5	140.8
C3−C4	139.1	140.2	140.3	140.5
C4−C5	139.0	140.0	140.1	140.1
N1−C15	141.9	142.0	142.1	142.4
C11−C16	139.1	140.5	140.6	140.6
C11−C12	139.4	140.7	140.6	140.4
C12−C13	139.0	140.1	140.2	140.1
C8−C16	264.5	261.1	257.7	259.7
Bond angles				
N1−C2−C3	111.0	111.6	109.4	111.1
C2−N1−C15	115.4	116.0	112.2	110.0
"Boat" type deformation angles				
Ring C11–C16				
α	14.6	14.8	13.5	10.1
α′	5.5	5.8	4.8	2.4
Ring C3–C8				
α	12.3	11.3	9.2	7.8
α′	5.3	5.3	5.2	4.8
Inclination angle between the two *meta*-phenylene rings[a]				
	10.2	14.3	12.1	−4.9

[a] Angle between the lines C3−C4 and C14−C15, projected on the C_s plane. A negative angle corresponds to an inclination that increases the C8−C16 distance.

Table 3. Calculated strain energies of 1,10-diaza[2.2]metacyclophane **7a** and [2.2]metacyclophane **Ii** in kJ/mol

Method	Calcd. strain energy of **7a**	Calcd. strain energy of **Ii**
HF/SV	131.8	70.5
RI-MP2/VDZP	85.9	48.4

tion of dimer **8**: the steric strain in the 10-membered ring in **4** is possibly compensated by ring enlargement.

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Experimental Section

General: ^{1}H-NMR and ^{13}C-NMR spectra: Bruker AM-250 (^{13}C: 62.9 MHz) and Bruker AM-400 (^{13}C: 100.64 MHz). The chemical shifts refer to the solvent used ($CDCl_3$, ^{1}H: δ_H = 7.24, ^{13}C: δ_C = 77) or tetramethylsilane (^{1}H, ^{13}C: $\delta_{H,C}$ = 0) as internal standard. − Capillary GC-MS: Hewlett-Packard HP 5890 Series II (column type: HP-1, crosslinked methyl silicone gum, 12 m × 0.2 mm × 0.33 μm) coupled to a Hewlett-Packard HP 5989-A EI mass spectrometer. − Mass spectra: A.E.I. MS-50 spectrometer (EI mode, 70 eV). − Melting points: Kofler Mikroskop-Heiztisch Reichert apparatus. The melting points given are not corrected. Melting points of compounds **5** and **7** were not available because of their very low yields. − Elemental analyses were not available because of the presence of fluorine in the molecules and because of their low yields. − Elution chromatography: Macherey, Nagel & Co. silica gel 60 (40−63 μm). − Thin-layer chromatography: Merck silica gel 60 F_{254}. − Solvents were distilled from an appropriate drying agent before use.

N,N′-Bis(trifluoroacetyl)-1,3-diaminobenzene (**3**): A solution of 38.0 ml (0.28 mol) of trifluoroacetic anhydride in 100 ml of diethyl ether was added dropwise over a period of 1 h to a solution of 15.0 g (0.14 mol) of 1,3-diaminobenzene in 1 l diethyl ether cooled with ice. The reaction mixture was then stirred for 2 h at room temperature or was left to stand overnight. The mixture was washed with water and saturated $NaHCO_3$ solution and the organic phase dried over Na_2SO_4. The solvent was removed in vacuo and the residue washed with chloroform. 35.4 g (84%) of a colorless solid was obtained with a m.p. of 195°C. − ^{1}H NMR (250 MHz, [D$_8$]acetone): δ_H = 7.45 (t, 1 H, $^3J_{HH}$ = 8.4 Hz, Ar−H), 7.61 (dd, 2 H, $^4J_{HH}$ = 2 Hz, $^3J_{HH}$ = 8.4, Ar−H), 8.21 (t, 1 H, $^4J_{HH}$ = 2 Hz, Ar−H), 10.41 (s, 2 H, N−H). − ^{13}C NMR (62.9 MHz, [D$_8$]acetone): δ_C = 114.61, 119.43, 131.22, 138.74 ($C_{ar.}$), signals of CO and CF_3 are not visible because of the low accumulation of the FIDs. − GC-MS: t_{ret} = 4.8 min; *m/z* (%) = 300 (100) [M^+], 231 (55) [$M^+ - CF_3$], 203 (22) [$M^+ - COCF_3$].

N,N′-Bis(trifluoroacetyl)-1,10-diaza[2.2]metacyclophane (**4**): 4.5 g (0.015 mol) of *N,N′*-bis(trifluoroacetyl)-1,3-diaminobenzene (**3**) and 3.95 g (0.015 mol) of 1,3-bis(bromomethyl)benzene[15] (**1**), each dissolved in 50 ml of acetone, were dropped synchronously under an argon atmosphere by use of a perfusion pump to a boiling dispersion of 5.0 g (0.036 mol) of K_2CO_3 in 2 l acetone (prior use degassed in an ultrasound bath) over 17 h. The reaction was performed in an high dilution apparatus according to Vögtle.[16] The reaction mixture was heated under reflux for additional 3 h. The solvent was removed in vacuo to yield a yellow oil. This reaction was repeated an additional three times and the resulting oils were combined and redissolved in 50 ml of chloroform. After filtration the organic phase was washed with water and saturated NaCl solution, dried over Na_2SO_4, evaporated and purified four times by elution chromatography (silica gel, chloroform), yielding 76.0 mg (0.3%, calculated for four reactions) of a white solid with a m.p. of

145°C. – ^{1}H NMR: (400 MHz, $CDCl_3$); δ_H = 3.49 (d, 2 H, $^2J_{HH}$ = 12.75 Hz, N–CH), 4.05 (t, 1 H, $^4J_{HH}$ = 1.6 Hz, Ar–H_i), 4.84 (t, 1 H, Ar–H_i), 6.0 (d, 2 H, $^2J_{HH}$ = 12.75 Hz, N–CH), 7.38 (dd, 2 H; $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 8 Hz, Ar–H), 7.48 (m, 3 H, Ar–H), 7.65 (t, 1 H, $^3J_{HH}$ = 8 Hz, Ar–H). – ^{13}C NMR: (100.64 MHz, DEPT, $CDCl_3$); δ_C = 57.4 ($N–CH_2$), 116.3 (q, $^1J_{CF}$ = 288.9 Hz, CF_3), 155.7 (q, $^2J_{CF}$ = 35 Hz, CO) 129.17, 130.18, 131.52, 131.59, 139.26, 139.65 ($C_{t.\ ar.}$), 134.46, 136.39 ($C_{q.\ ar.}$). – HR-MS: *m/z* (%) = 402.0806 (58) [M^+, calculated for $^{12}C_{18}{}^1H_{12}{}^{29}F_6{}^{14}N_2{}^{16}O_2$: 402.0803], 333 (100) [$M^+ - CF_3$], 305 (37) [$M^+ - CF_3CO$], 104 (69) [$C_8H_8{}^+$]. – TLC (silica gel, chloroform): R_f = 0.45.

N,N′-Bis(trifluoroacetyl)-1,10-diaza[2]metacyclo-[2](2,6)pyridinophane (**5**): 4.5 g (0.015 mol) of *N,N′*-bis(trifluoroacetyl)-1,3-diaminobenzene (**3**) and 3.96 g (0.015 mol) of 2,6-bis-(bromomethyl)pyridine[17] (**2**), each dissolved in 50 ml of acetone, were dropped synchronously under an argon atmosphere by use of a perfusion pump to a boiling dispersion of 5.0 g (0.036 mol) of K_2CO_3 in 2 l of acetone (prior use degassed in an ultrasound bath) over 17 h. The reaction was performed in an high dilution apparatus according to Vögtle.[16] The reaction mixture was heated under reflux for additional 3 h. The solvent was removed in vacuo and the resulting yellow oil redissolved in 50 ml of chloroform. After filtration the organic phase was washed with water and saturated NaCl solution, dried over Na_2SO_4, evaporated, and purified three times by elution chromatography (silica gel, chloroform), yielding 24.0 mg (0.4%) of a colorless solid. – ^{1}H NMR: (250 MHz, $CDCl_3$): δ_H = 3.64 (d, 2 H, $^2J_{HH}$ = 12.55 Hz, N–CH), 4.3 (t, 1 H, $^4J_{HH}$ = 1.7 Hz, Ar–H_i), 6.0 (d, 2 H, $^2J_{HH}$ = 12.55 Hz, N–CH), 7.38 (dd, 2 H; $^4J_{HH}$ = 1.7 Hz, $^3J_{HH}$ = 7.95 Hz, Ar–H), 7.52 (d, 2 H, $^3J_{HH}$ = 7.6 Hz, Ar–H), 7.64 (t, 1 H, $^3J_{HH}$ = 7.95 Hz, Ar–H), 7.84 (t, 1 H, $^3J_{HH}$ = 7.6 Hz, Ar–H). – ^{13}C NMR (62.9 MHz, DEPT, $CDCl_3$): δ_C = 6.57 ($N–CH_2$), 117.6 (q, $^1J_{CF}$ = 280.5 Hz, CF_3), 155 (q, CO), 124.72, 128.6, 131.68, 139.96, 140.14 ($C_{ar.t.}$), 136.51 137.5 ($C_{ar.q.}$). – HR-MS: *m/z* (%) = 403.0731 (46) [M^+, calculated for $^{12}C_{17}{}^1H_{11}{}^{29}F_6{}^{14}N_3{}^{16}O_2$: 403.0755], 334 (100) [$M^+ - CF_3$], 306 (37) [$M^+ - CF_3CO$], 104 (66) [$C_8H_8{}^+$]. – TLC (silica gel, chloroform): R_f = 0.1.

1,10-Diaza[2.2]metacyclophane (**7**): To a solution of 39.0 mg (0.1 mmol) of *N,N′*-bis(trifluoroacetyl)-1,10-diaza[2.2]metacyclophane (**7**) in 20 ml of methanol was added 30.0 mg (0.21 mmol) of K_2CO_3 and the resulting reaction mixture was heated under reflux for 7 h. The solvent was removed in vacuo. The resulting solid was redissolved in dichloromethane and filtered off from the insoluble residue. The filtrate was washed with saturated $NaHCO_3$ solution and water, dried over Na_2SO_4 and purified by elution chromatography (silica gel, dichloromethane/methanol = 10:1), yielding 14.0 mg (31%) of a yellow solid. – ^{1}H NMR (250 MHz, $CDCl_3$): δ_H = 3.45 (d, 2 H, $^2J_{HH}$ = 12.1 Hz, N–CH), 3.71 (bs, 2 H, N–H), 3.81 (t, 1 H, $^4J_{HH}$ = 1.8 Hz, Ar–H_i), 4.41 (d, 2 H, $^2J_{HH}$ = 12.1 Hz, N–CH), 4.41 (1 H, Ar–H_i), 7.02 (dd, 2 H, $^4J_{HH}$ = 1.8 Hz, $^3J_{HH}$ = 7.7 Hz, Ar–H), 7.35 (s, 3 H, Ar–H), 7.41 (t, 2 H, $^3J_{HH}$ = 7.7 Hz, Ar–H). – ^{13}C NMR: (62.9 MHz, DEPT, $CDCl_3$); δ_C = 561.3 ($N–CH_2$), 121.32, 128.22, 130.11, 131.24, 133.87, 136, 137.1 (C_{ar}). – HR-MS: *m/z* (%) = 210.1120 (23) [M^+, calculated for $^{12}C_{14}{}^1H_{14}{}^{14}N_2$: 210.1157]. – TLC (silica gel, dichloromethane/methanol = 10:1): R_f = 0.49.

X-ray Crystal Structure Analysis: X-ray data of **8**: $C_{36}H_{24}F_{12}N_4O_4$; 804.59; colorless plates; 0.25 × 0.15 × 0.10 mm; triclinic; space group: *P*1 (no. 2); *a* = 8.622(5) A, *b* = 9.715(5) A, *c* = 11.296(6) A, α = 90.50(4)°, β = 104.34(4)°, γ = 108.76(4)°; *V* = 864.0(8) A^3; *Z* = 1; $d_{calc.}$ = 1.546 Mg/m^3; absorption coefficient: 0.145 mm^{-1}; *F*(000) = 408; Nicolet R3m diffractometer; wavelength: 0.71073 Å (Mo-K_α); temperature: 293(2) K; monochromator: graphite; θ range for data collection: 1.87 to 22.55°; ω-scans; number of standards: 3; interval of standards: every 147 refl; index ranges: $-9 \le h \le 9$, $-10 \le k \le 10$, $0 \le l \le 12$; reflections collected: 2407; independent reflections: 2267 (R_{int} = 0.0243); refinement method: full-matrix least-squares on F^2; data/restraints/parameter: 2267/0/253; goodness-of-fit on F^2: 0.95; final *R* indices [$I > 2\sigma(I)$]: *R*1 = 0.044, *R*2 = 0.103; *R* indices (all data): *R*1 = 0.076, *R*2 = 0.113, largest diff. peak and hole: 0.324 and −0.193 A^{-3}.

Further details of the crystal-structure investigation can be obtained free of charge from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK (Phone: internat. +44-1223/336-408; Fax: internat. +44-1223/336-033; E-mail: deposit@chemcrys.cam.ac.uk) on quoting the depository number CCDC-100774.

☆ Dedicated to Prof. Dr. *Achim Müller* on the occasion of his 60th birthday.

[1] [1a] F. Vögtle, *Cyclophan-Chemie*, Teubner, Stuttgart **1990**, *Cyclophane Chemistry*, Wiley, Chichester **1993**. – [1b] L. Ernst, V. Boekelheide, H. Hopf, *J. Magn. Reson.* **1993**, *31*, 669–676. – [1c] T. Ishi-i, T. Sawada, S. Mataka, M. Tashiro, T. Thiemann, *Chem. Ber.* **1996**, *129*, 289–296. – [1d] T. Ishi-i, T. Sawada, S. Mataka, M. Tashiro, *J. Chem. Soc., Perkin Trans. 1* **1996**, 1887–1891. – [1e] G. J. Bodwell, *Angew. Chem.* **1996**, *108*, 2221–2224; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2085–2088. – [1f] S. de la Moya Cerero, M. Böhme, M. Nieger, F. Vögtle, *Liebigs Ann./Recueil* **1997**, 1221–1225.

[2] S. Grimme, S. D. Peyerimhoff, S. Bartram, F. Vögtle, A. Breest, J. Hormes, *Chem. Phys. Lett.* **1993**, *213*, 32–40.

[3] [3a] F. Vögtle, *Tetrahedron Lett.* **1968**, *9*, 3623–3626. – [3b] F. Vögtle, J. Struck, H. Puff, P. Woller, H. Reuter, *J. Chem. Soc., Chem. Commun*. **1986**, 1248–1250. – [3c] A. Ostrowicki, F. Vögtle, *Synthesis* **1988**, 1003–1004. – [3d] F. Vögtle, A. Ostrowicki, B. Begemann, M. Jansen, M. Nieger, E. Niecke, *Chem. Ber.* **1990**, *123*, 169–176. – [3e] P. Knops, P.-M. Windscheif, F. Vögtle, A. Rolof, M. Jansen, M. Nieger, E. Niecke, Y. Okamoto, *Chem. Ber.* **1991**, *124*, 1585–1590. – [3f] D. Müller, M. Nieger, F. Vögtle, *J. Chem. Soc., Chem. Commun.* **1994**, 1361–1362. – [3g] D. Müller, F. Vögtle, *Synthesis* **1995**, 759–760. – [3h] D. Wortmann-Saleh, S. Grimme, B. Engels, D. Müller, F. Vögtle, *J. Chem. Soc., Perkin Trans. 2* **1995**, 1185–1189. – [3i] D. Müller, M. Böhme, M. Nieger, K. Rissanen, F. Vögtle, *J. Chem. Soc, Perkin Trans. 1* **1996**, 2937–2943.

[4] [4a] K. Meurer, F. Vögtle, A. Mannschreck, G. Stühler, H. Puff, A. Roloff, *J. Org. Chem.* **1984**, *49*, 3484–3489. – [4b] K.-J. Przybilla, F. Vögtle, M. Nieger, S. Franken, *Angew. Chem.* **1988**, *100*, 987–988; *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 976–977. – [4c] J. Schulz, M. Nieger, F. Vögtle, *Chem. Ber.* **1991**, *124*, 2797–2810.

[5] [5a] F. Vögtle, P. Neumann, *Tetrahedron Lett.* **1970**, *2*, 115–118. – [5b] F. Vögtle, P. Neumann, *Synthesis* **1973**, 85–103.

[6] A. Ostrowicki, E. Koepp, F. Vögtle, *Top. Curr. Chem*, **1992**, *161*, 37–68.

[7] [7a] I. Gault, B. J. Price, I.O. Sutherland, *J. Chem. Soc., Chem. Commun.* **1967**, 540–541. – [7b] J. R. Fletcher, I. O. Sutherland, *J. Chem. Soc., Chem. Commun.* **1969**, 1504–1505. – [7c] F. Vögtle, A. H. Effler, *Chem. Ber.* **1969 102**, 3071–3076.

[8] [8a] F. Vögtle, K.-J. Przybilla, A. Mannschreck, N. Pustet, P. Büllesbach, H. Reuter, H. Puff, *Chem. Ber.* **1988**, *121*, 823–828. – [8b] F. Vögtle, P. Knops, A. Ostrowicki, *Chem. Ber.* **1990**, *123*, 1859–1868. – [8c] E. Kleinpeter, J. Hartmann, W. Schroth, O. Hofer, A. Kalchhauser, *Monatsh. Chem.* **1992**, *123*, 823–836.

[9] [9a] G. J. Bodwell, J. N. Bridson, J. W. J. Kennedy, M. R. Mannion, *Angew. Chem.* **1996**, *108*, 1418–1419; *Angew. Chem. Int. Ed. Eng.* **1996**, *35*, 1320–1321. – [9b] G. J. Bodwell, T. J. Houghton, J. W. J. Kennedy, M. R. Mannion, *Angew. Chem.* **1996**, *108*, 2280–2281; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2121–2123.

[10] *Theoretical Methods:* Geometries and energies were calculated with the ab initio Hartree-Fock (HF) method, with density-functional theory (DFT), whereby the B3-LYP exchange-correlation function[10a] was employed, and with the ab initio RI-MP2 method. In the RI-MP2 method an approximate resolu-

tion of identity (RI) is used to calculate the MP2 energy and its first derivatives. The auxiliary basis set used was the same as in ref.[10b]. From the work of Weigand and Häser[10b] we expect errors introduced by the RI approximation of 0.2 pm or less in the bond lengths. Compared with RI-MP2, single point MP2 calculations (with RI-MP2 geometries) yield higher total energies by 2.12 and 2.17 kJ/mol for **7a** and **7b**, repectively. The error introduced by the RI approximation for ΔE is thus insignificant. The following basis sets were used: a VDZP basis set [valence double-ζ basis[10c], which was augmented with polarization d-functions at the carbon ($\alpha_d = 0.8$) and nitrogen atoms ($\alpha_d = 1.0$) and with polarization p-functions at the hydrogen atoms ($\alpha_p = 0.8$)] and a SV (split-valence) basis set.[10c] All these calculations were performed with the TURBOMOLE[10d] suite of programs. – [10a] A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648–5652. – [10b] F. Weigend, M. Häser, *Theor. Chem. Acc.* **1997**, *97*, 331–340. – [10c] A. Schäfer, H. Horn, R. Ahlrichs, *J. Chem. Phys.* **1992**, *97*, 2571–2577. – [10d] R. Ahlrichs, M. Bär, M. Häser, H. Horn, C. Kölmel, *Chem. Phys. Lett.* **1989**, *162*, 165–169.

[11] [11a] C. J. Brown, *J. Chem. Soc.* **1953**, 3278–3285. – [11b] Y. Kai, N. Yasuoka, N. Kasai, *Acta Crystalogr., Sect. B* **1977**, *B33*, 754–762.

[12] [12a] H. Schmidt, A. Schweig, W. Thiel, M. Jones, Jr., *Chem. Ber.* **1978**, *111*, 1958–1961. – [12b] F. Bokisch, J. C. Rayez, D. Liotard, B. Duguay, *J. Comp. Chem.* **1992**, *13*, 1047–1056.

[13] [13a] C. F. Shieh, D. McNally, R. H. Boyd, *Tetrahedron* **1969**, *25*, 3653–3665. – [13b] H. J. Lindner, *Tetrahedron* **1976**, *32*, 753–757

[14] L. Carballeira, A. J. Pereiras, M. A. Rios, *J. Chem. Phys.* **1984**, *80*, 4387–4395.

[15] [15a] W. Wenner, *J. Org. Chem.* **1953**, *17*, 523–528. – [15b] W. Offermann, F. Vögtle, *Synthesis* **1977**, 272–273. – [15c] W. Offermann, F. Vögtle, *J. Org. Chem.* **1979**, *44*, 710–713.

[16] [16a] F. Vögtle, *Chem. Ind.* (London) **1972**, 346. – [16b] F. Vögtle, *J. Chem. Educ.* **1973**, 650. – [16c] Catalog *Normag Labortechnik*, **1995**, 209–211.

[17] [17a] W. Baker, K. M. Buggle, J. W. F. McOmie, D. A. M. Watson, *J. Chem. Soc.* **1958**, 3594–3603. – [17b] B. Kaptein, G. Barf, R. M. Kellogg, F. V. Bolhuis, *J. Org. Chem.* **1990**, *55*, 1890–1901.

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