[2.2](2,6)- and [2.2](2,5)Pyrazinophanes: Synthesis and Molecular Structure

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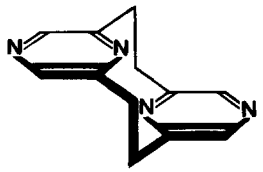
The title compounds **1**–**3** and their methyl derivatives **4**–**7** were synthesized either by photolytic sulfur extrusion from the corresponding 2,11-dithia[3.3]pyrazinophanes **24**–**26** or by Hofmann 1,6-elimination of the appropriate [(5-methyl-2-pyrazinyl)methyl]trimethylammonium hydroxides followed by dimerization of the generated 2,5-dihydro-2,5-dimethylenepyrazines. α-Chlorination of the methylpyrazines **8**–**10** with *N*-chlorosuccinimide gave the required precursors **11**, **12**, **14**, **17**, and **18**. The results of the X-ray structure determinations for **1**–**4** and **7** which indicate an unequivocal isomer assignment are discussed with regard to steric strain in these molecules. The electronic spectra of the pyrazinophanes **1**–**7** are reported and compared with those of the parent methylpyrazines.

[2.2]Cyclophanes are intriguing models for exploring how the forced proximity and the mutual orientation of two π systems influence their chemical and physical properties. Previous studies of transannular interactions in N-heterocyclic [2.2]paracyclophanes[1–3] directed our interest to [2.2]-pyrazinophanes. We now report the syntheses and molecular structures of [2.2](2,6)pyrazinophane (**1**), the two isomeric [2.2](2,5)pyrazinophanes **2** (pseudo-ortho) and **3** (pseudo-geminal), and the methyl-substituted derivatives (**4**–**7**). Some preliminary results have already been published[4].



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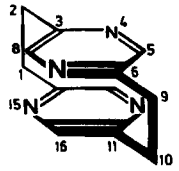

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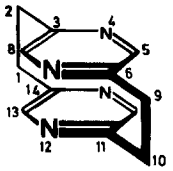

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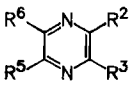
4: 5,8-$(CH_3)_2$
6: 5,8,13,16-$(CH_3)_4$

5: 5,8-$(CH_3)_2$
7: 5,8,13,16-$(CH_3)_4$

Syntheses

The [2.2]pyrazinophanes were prepared either by Hofmann 1,6-elimination or by photochemical sulfur extrusion of the corresponding precursors.

Substituted Pyrazines: The syntheses of [2.2]pyrazinophanes require α-methyl-functionalized pyrazines as precursors, i.e. mono- or bis(halomethyl)pyrazines. Bromomethyl derivatives of 2,5-dimethylpyrazine (**8**) have been obtained by reaction with *N*-bromosuccinimide[1]; the yields, however, were very low, and the compounds decomposed rapidly. Side-chain chlorinations of methyl-substituted pyrazines with *N*-chlorosuccinimide (NCS) gave better results[5–8]. NCS chlorination of **8**, for example, affords 2-chloromethyl-5-methylpyrazine (**11**) in reasonable yield[5,7,8]. By using two equivalents of NCS, we prepared 2,5-bis(chloromethyl)pyrazine (**12**) (21%). Besides **11** and **12**, 2-chloromethyl-5-dichloromethylpyrazine (**13**) was also isolated and characterized. Treatment of 2,3,5,6-tetramethylpyrazine (**9**) under similar conditions yielded **14** (49%), **15**, **16**, and a mixture of three isomeric bis(chloromethyl)dimethylpyrazines. Simi-



	R^2	R^3	R^5	R^6
8	CH_3	H	CH_3	H
9	CH_3	CH_3	CH_3	CH_3
10	CH_3	H	H	CH_3
11	CH_2Cl	H	CH_3	H
12	CH_2Cl	H	CH_2Cl	H
13	CH_2Cl	H	$CHCl_2$	H
14	CH_2Cl	CH_3	CH_3	CH_3
15	CH_2Cl	CH_2Cl	CH_2Cl	CH_2Cl
16	CH_2Cl	CH_2Cl	CH_2Cl	CH_3
17	CH_2Cl	H	H	CH_3
18	CH_2Cl	H	H	CH_2Cl
19	CH_2Cl	H	H	$CHCl_2$
20	$CH_2N(CH_3)_3]Cl$	H	CH_3	H
21	$CH_2N(CH_3)_3]Cl$	CH_3	CH_3	CH_3
22	$CH_2SC(NH_2)_2]Cl$	H	$CH_2SC(NH_2)_2]Cl$	H
23	$CH_2SC(NH_2)_2]Cl$	H	H	$CH_2SC(NH_2)_2]Cl$

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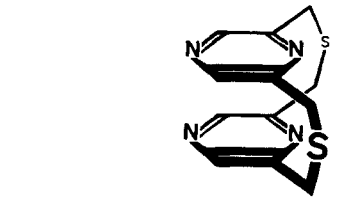
larly, side-chain chlorination of 2,6-dimethylpyrazine (**10**) afforded **17**[7,8] (1 equivalent of NCS, 63%), **18**[5,8,9] (2 equivalents of NCS, 38%), and **19** as by-product. All chloromethyl-substituted pyrazines, especially the "monohalogenated" species, are highly lachrymatory and skin irritants.

The (chloromethyl)pyrazines **11** and **14** reacted with trimethylamine to give the corresponding (2-pyrazinylmethyl)-trimethylammonium chlorides **20** and **21**, respectively. Treatment of the bis(chloromethyl)pyrazines **12** and **18** with thiourea afforded the bis(isothiouronium) salts **22** (82%) and **23** (84%) readily.

2,11-Dithia[3.3]pyrazinophanes **24**–**26**: The bis(isothiouronium) salts were directly used for the cyclization performed by dropping constantly during ca. 8 h a 1:1 solution of **22** and **12** (or **23** and **18**) in methanol/water (99:1) into boiling methanol/water (99:1) in the presence of excess of cesium hydroxide or carbonate. By this procedure the reaction of **23** with **18** gave 2,11-dithia[3.3](2,6)pyrazinophane (**24**) in reasonable yield (42%). The molecular structure of **24** (Figure 4) shows the pyrazine rings in a nearly parallel *syn* orientation. In $CDCl_3$ (303 K) the ^{1}H-NMR spectrum displays the methylene protons as a sharp singlet at δ = 4.02. This averaging of the methylene protons is probably due to a rapid *syn* ⇌ (*anti*) ⇌ *syn* interconversion accompanied by simultaneous "wobbling processes" of the CH_2-S-CH_2 bridges in the *syn* conformer[10–12]. The related 2,11-dithia[3.3]metacyclophane[10] and 2,11-dithia[3.3](2,6)pyridinophane[12], which crystallize in a *syn* conformation, also exist in solution predominantly as the *syn* conformer according to NMR studies. Cyclization of **22** with **12** yielded the two isomeric 2,11-dithia[3.3](2,5)pyrazinophanes (**25** and **26**) and 2,11,20,29-tetrathia[3.3.3.3](2,5)pyrazinophane (**27**), which were separated by flash chromatography [**25**: m.p. 280–281 °C (dec.) (pseudo-ortho, 13.7%); **26**: m.p. >310 °C (pseudo-geminal, 2.8%); **27**: m.p. 184–185 °C (0.25%); the assignments of the isomers based on the m.p.s and the ratio of yields are tentative].



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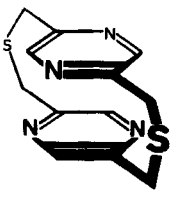

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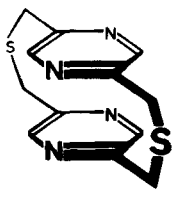

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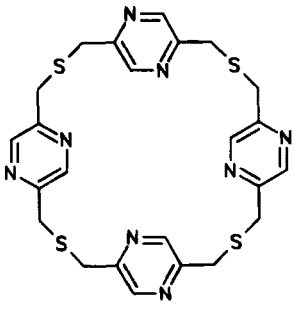

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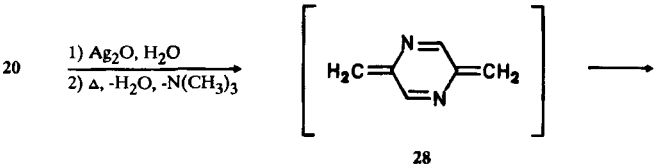

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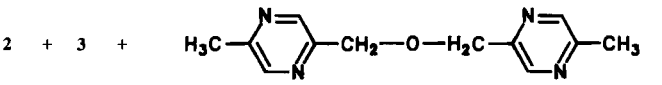

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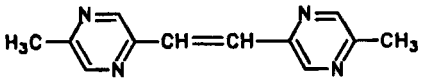

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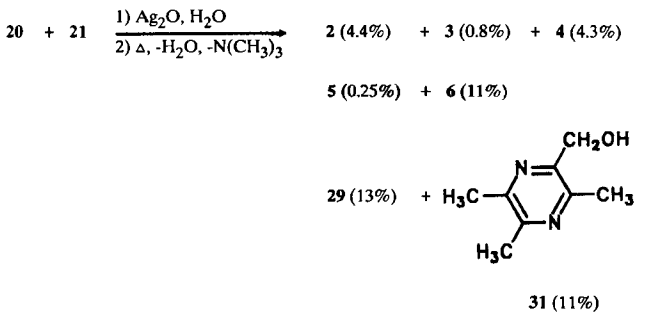
[2.2](2,6)- and [2.2](2,5)Pyrazinophanes **1**–**7**: UV photolysis of **24** in trimethyl phosphite led to extrusion of sulfur and yielded after separation by flash chromatography [2.2]-(2,6)pyrazinophane (**1**) (16%, m.p. 231 °C). The X-ray structure determination (Figure 1) shows **1** to possess a nonplanar chair-like *anti* conformation. In the ^{1}H-NMR spectrum of **1** in CD_2Cl_2 at 263 K a clear AA'BB' pattern for the axial and equatorial protons at the ethylene bridges ($\nu_A - \nu_B$ = 442 Hz; 500 MHz) is observed. At higher temperatures ($CDCl_2CDCl_2$) the signals of the AA'BB' system collapse and coalesce to a broad singlet at 327 K, which becomes increasingly sharper as the temperature is further raised. These observations indicate an exchange between the A and B proton environments resulting from rapid interconversion of the chair-like conformation[13].

Similarly, sulfur extrusion of the mixture of **25** and **26** in trimethyl phosphite resulted in the formation of both [2.2]-(2,5)pyrazinophanes [**2**: m.p. 258 °C (25%); **3**: m.p. 297 to 298 °C (6%); the isomers are unequivocally assigned by X-ray structure determinations (Figures 2 and 3)].

A better and shorter approach leading to **2** and **3** is by dimerization of the intermediate 2,5-dihydro-2,5-dimethylenepyrazine (**28**) generated by Hofmann 1,6-elimination of the free base derived from **20**. This route provides **2** and **3** in larger quantities, although, with 8.7% and 1.5%, respectively, the yields are lower. Further products isolated were the ether **29** (28%) and the ethylene derivative **30** (0.5%).

Similarly, the two 5,8,13,16-tetramethyl[2.2](2,5)pyrazinophanes were obtained from **21** [**6**: m.p. 114 °C (pseudo-ortho, 51%); **7**: m.p. 258 °C (pseudo-geminal, 1.9%); the isomer assignment based on m.p. and ratio of yields was

confirmed by the X-ray structure determination of **7** (Figures 2 and 3)]. A "crossed" Hofmann 1,6-elimination of a 1:1 mixture of **20** and **21** led among other products to the formation of the two 5,8-dimethyl[2.2](2,5)pyrazinophanes [**4**: m.p. 103–104°C (4.3%); **5**: m.p. 159–160°C (0.25%); again, X-ray structure determination of **4** (Figures 2 and 3) proved the isomer assignment].



Molecular Structures of 1–4, 7, and 24

The X-ray structure determinations of the [2.2](2,5)pyrazinophanes **2**–**4** and **7** establish an unequivocal structural assignment for the isomers. These studies also provide some insight into the stress and strain of these molecules which led to deformation from planarity of the aromatic rings and distortion of the ethylene bridges. In the case of the (2,6)pyrazinophanes **1** and **24** molecular structure determinations disclose the preferred conformation in the crystalline state.

The crystallographic data and the parameters of structure refinement for the studied compounds are given in Table 1[17]. The numbering of atoms follows the "phane" nomenclature. Bond lengths and bond angles with standard deviations are shown in Figures 1A (**1**) and 2 (**2**, **3**, **7**). Corresponding data of **4** and **24** are listed in Tables 2 and 3, respectively. The bond lengths and angles in the pyrazine moieties are very similar to those of pyrazine itself (C–C 138.8, C–N 133.3 pm; C–N–C 116.2, C–C–N 121.9°)[18,19] and 2,3,5,6-tetramethylpyrazine (C–C 137.8, C–N 133.1 pm; C–N–C 118.0, C–C–N 121.0°)[20,21].

Table 2. Bond distances [pm] and angles [°] of **4** with standard deviations in parentheses

C(1)-C(11i)	149.9(3)	C(11i)-C(1)-C(2)	111.2(2)
C(1)-C(2)	157.0(3)	C(1)-C(2)-C(3)	111.3(2)
C(2)-C(3)	149.9(3)	C(2)-C(3)-N(4)	115.9(2)
C(3)-N(4)	133.9(2)	C(2)-C(3)-C(5i)	123.5(2)
C(3)-C(5i)	138.1(3)	N(4)-C(3)-C(5i)	119.8(2)
N(4)-C(5)	134.1(2)	C(3)-N(4)-C(5)	118.0(2)
C(5)-C(5')	150.8(3)	N(4)-C(5)-C(3i)	120.0(2)
C(11)-N(12)	133.4(3)	N(4)-C(5)-C(5')	117.0(2)
N(12)-C(13)	132.9(2)	C(3i)-C(5)-C(5')	122.7(2)
C(13)-C(11i)	138.1(3)	C(1)-C(11i)-C(13)	122.6(2)
		C(1)-C(11i)-N(12i)	117.5(2)
		C(13)-C(11i)-N(12i)	119.0(2)
		C(11i)-C(13)-N(12)	122.3(2)
		C(13)-N(12)-C(11)	116.5(2)

Molecular Structure of **1**: Figure 1 shows the molecular structure of **1** in a projection onto the planes of the pyrazine moieties (A) and in side-views (B and C) across the pyrazine rings. As in the case of [2.2]metacyclophane[22] or [2.2](2,6)pyridinophane[23] crystalline **1** exists in a step-like *anti* conformation (Figure 1B). The step-like structure is characterized by the distance of 224 pm between the basis planes passing through C(3), C(4), C(6), C(7) and C(3i), C(4i), C(6i), C(7i), the "inclination" angle of 130° between the basis plane and the plane passing through the four bridgehead carbons [C(3), C(7), C(3i), C(7i)], and the transannular distance between the bridgehead carbons of 295 pm. As indicated by the torsion angle of 60.1° around the $-CH_2-CH_2-$ bonds the ethyl-

Table 1. Crystallographic data and refinement parameters of **1**–**4**, **7**, and **24**

	1	**2**	**3**	**4**	**7**	**24**
Formula	$C_{12}H_{12}N_4$	$C_{12}H_{12}N_4$	$C_{12}H_{12}N_4$	$C_{14}H_{16}N_4$	$C_{16}H_{20}N_4$	$C_{12}H_{12}N_4S_2$
Molecular mass	212.3(1)	212.3(1)	212.3(1)	240.3(1)	268.4(1)	276.4(1)
Crystallized from	ethyl acetate	ethyl acetate	ethyl acetate	hexane	ethyl acetate	trichloromethane/acetone
Crystal size [mm]	0.1 × 0.1 × 0.2	0.2 × 0.2 × 0.4	0.1 × 0.2 × 0.3	0.2 × 0.2 × 0.35	0.15 × 0.25 × 0.35	0.2 × 0.25 × 0.4
Crystal system	monoclinic	orthorhombic	monoclinic	monoclinic	monoclinic	monoclinic
Space group	$P2_1/a$	$Ccca$	$P2_1/n$	$C2/c$	$P2_1/n$	$P2_1/n$
a [pm]	738.5(2)	1131.4(1)	726.3(1)	1231.2(2)	686.8(1)	701.3(2)
b [pm]	997.8(3)	912.0(1)	912.0(2)	1160.3(2)	919.7(2)	2103.0(4)
c [pm]	761.5(2)	974.1(1)	773.3(2)	912.7(2)	1129.1(2)	875.4(3)
β [°]	113.36(1)		99.09(1)	107.42(1)	100.96(1)	110.28(1)
Z	2	4	2	4	2	4
Symmetry of molecule in crystal	C_i	D_2	C_i	C_2	C_i	C_1
$F(000)$	224	448	224	512	288	288
D_X [g cm^{-3}]	1.368	1.403	1.394	1.283	1.272	1.517
μ [cm^{-1}] (MoK_α)	0.812	0.832	0.827	0.749	0.733	4.078
Measured reflections	999	673	1275	1515	2034	3336
max. $\sin\Theta/\lambda$ [nm^{-1}]	6.20	6.82	6.82	6.82	7.20	6.82
Observed reflections [$I \geq 3\sigma(I)$]	638	489	948	796	1507	2757
Refinement R	0.042	0.038	0.051	0.052	0.057	0.030
max. Δϱ/e [nm^{-3}]	120	70	110	90	70	160

ene bridges adopt a nearly gauche conformation. The pyrazine rings are slightly distorted from planarity towards an asymmetric boat conformation, the inner nitrogen N(8) being more displaced above the basis plane C(3), C(4), C(6), C(7) than the outer N(5) (Figure 1B). Due to the ethylene bridges the inner C–N bonds [C(3)–N(8), C(7)–N(8); 133.9(2) pm] and the inner C(3)–N(8)–C(7) angle (116.9°) are a little larger than the corresponding outer ones [C(4)–N(5), C(6)–N(5), mean value 132.6(3) pm; C(4)–N(5)–C(6) 115.0°]. The transannular distance between the inner nitrogens N(8) and N(8i) of 251 pm is quite similar to that of 254.5 pm found for [2.2](2,6)pyridinophane[23].

Table 3. Bond distances [pm] and angles [°] of **24** with standard deviations in parentheses

C(1)-S(2)	180.7(1)	S(2)-C(1)-C(17)	113.9(1)
C(1)-C(17)	149.9(1)	C(1)-S(2)-C(3)	102.3(1)
S(2)-C(3)	181.9(1)	S(2)-C(3)-C(4)	113.7(1)
C(3)-C(4)	149.6(1)	C(3)-C(4)-C(5)	121.9(1)
C(4)-C(5)	138.8(1)	C(3)-C(4)-N(9)	117.5(1)
C(4)-N(9)	133.2(1)	C(5)-C(4)-N(9)	120.6(1)
C(5)-N(6)	132.6(1)	C(4)-C(5)-N(6)	123.0(1)
N(6)-C(7)	132.6(1)	C(5)-N(6)-C(7)	115.6(1)
C(7)-C(8)	138.2(1)	N(6)-C(7)-C(8)	122.9(1)
C(8)-N(9)	133.9(1)	C(7)-C(8)-N(9)	120.8(1)
C(8)-C(10)	151.3(1)	C(7)-C(8)-C(10)	120.0(1)
C(10)-S(11)	179.4(1)	N(9)-C(8)-C(10)	119.1(1)
S(11)-C(12)	181.4(1)	C(4)-N(9)-C(8)	117.1(1)
C(12)-C(13)	149.8(1)	C(8)-C(10)-S(11)	116.2(1)
C(13)-C(14)	137.7(1)	C(10)-S(11)-C(12)	103.3(1)
C(13)-N(18)	134.2(1)	S(11)-C(12)-C(13)	113.9(1)
C(14)-N(15)	133.6(1)	C(12)-C(13)-C(14)	121.5(1)
N(15)-C(16)	132.3(1)	C(12)-C(13)-N(18)	117.3(1)
C(16)-C(17)	138.9(1)	C(14)-C(13)-N(18)	121.1(1)
C(17)-N(18)	133.1(1)	C(13)-C(14)-N(15)	122.9(1)
		C(14)-N(15)-C(16)	115.2(1)
		N(15)-C(16)-C(17)	123.2(1)
		C(1)-C(17)-C(16)	121.9(1)
		C(1)-C(17)-N(18)	117.2(1)
		C(16)-C(17)-N(18)	120.8(1)
		C(13)-N(18)-C(17)	116.8(1)

Molecular Structures of **2**–**4** *and* **7**: Figure 2 shows the structures in top-views perpendicular to the least-squares planes through the four nonbridgehead atoms of the pyrazine moieties. Due to the alkyl substitution the (H)C–N and (C_{sp^3})C–N bond lengths and (H)C–N–C(CH_2) and (CH_3)C–N–C(CH_2) angles are slightly different. The molecular structures of the pseudo-geminal phanes **3** and **7**, which exhibit C_i symmetry, avoid an ecliptic arrangement of the pyrazine rings by a slight shift (ca. 25 pm) parallel to the mean ring plane and perpendicular to the C(3)···C(3i) axis. For the pseudo-ortho isomers **2** and **4**, on the other hand, deviations are observed corresponding to twist angles of ca. 10° [angle between the C(2)···C(2i) and C(2j)···C(2k) (**2**) or (C1)···C(1i) and C(2)···C(2i) axes (**4**)].

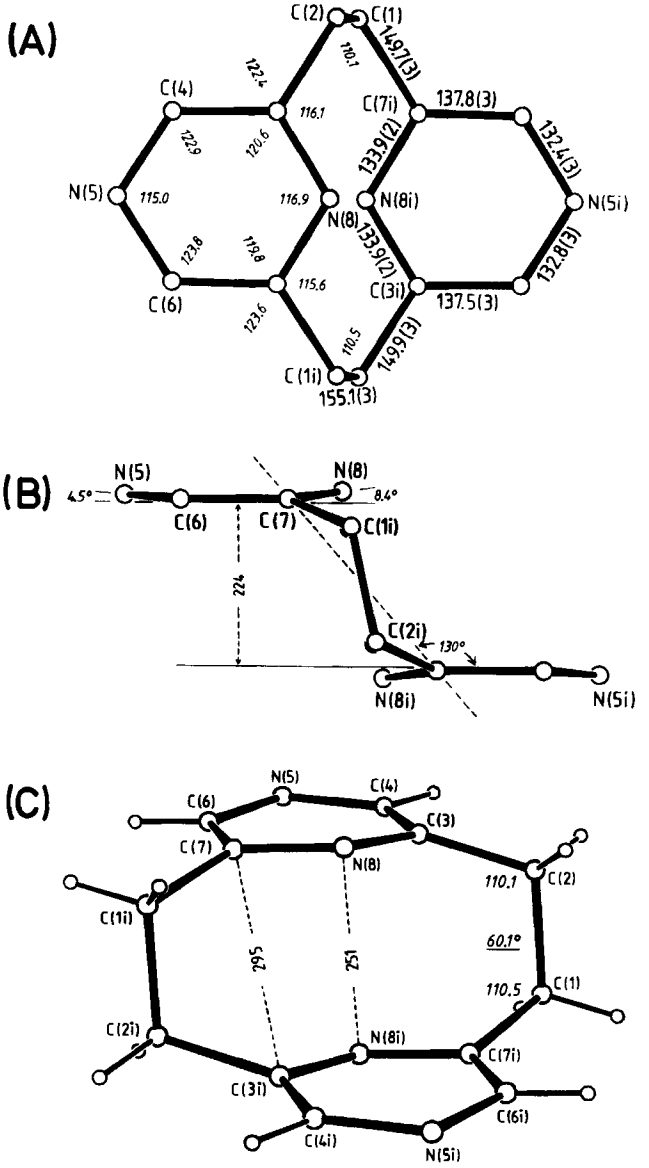


Figure 1. Molecular structure of **1**: (A) Top-view showing bond distances [pm] and angles [°], (B) side-view across pyrazine rings, (C) side-view showing transannular distances [pm]

Figure 3 shows the molecular structures of **2**–**4** and **7** in side-views along the pyrazine rings. These side-views clearly display the twist boat-like deformation of the pyrazine rings. As compared to the aromatic rings of [2.2]paracyclophane (interplanar angle $\alpha = 12.6°$)[24] the pyrazine rings are significantly more bent. The interplanar angles α of **2**–**4** and **7** [e.g. **2**: between the N(4), C(5), N(4i), C(5i) and the C(3), N(4), C(5i) planes] lie in the range of 14.3–15.8°, the largest being found for the tetramethyl-substituted phane **7**. As a consequence, the exocyclic bonds at the bridgehead carbons of the pyrazine rings are less bent than in [2.2]paracyclophane ($\beta = 11.2°$). The β angles [e.g. **2**: between the C(3), N(4), C(5i) plane and the C(3)–C(2) vector] decrease in the order 9.4° (**2**), 9.1° (**4**), 8.5° (**3**, mean value), and 7.9° (**7**, mean value). The more pronounced boat-like deformation of the pyrazine moieties shows that the inherent strain of the [2.2]-

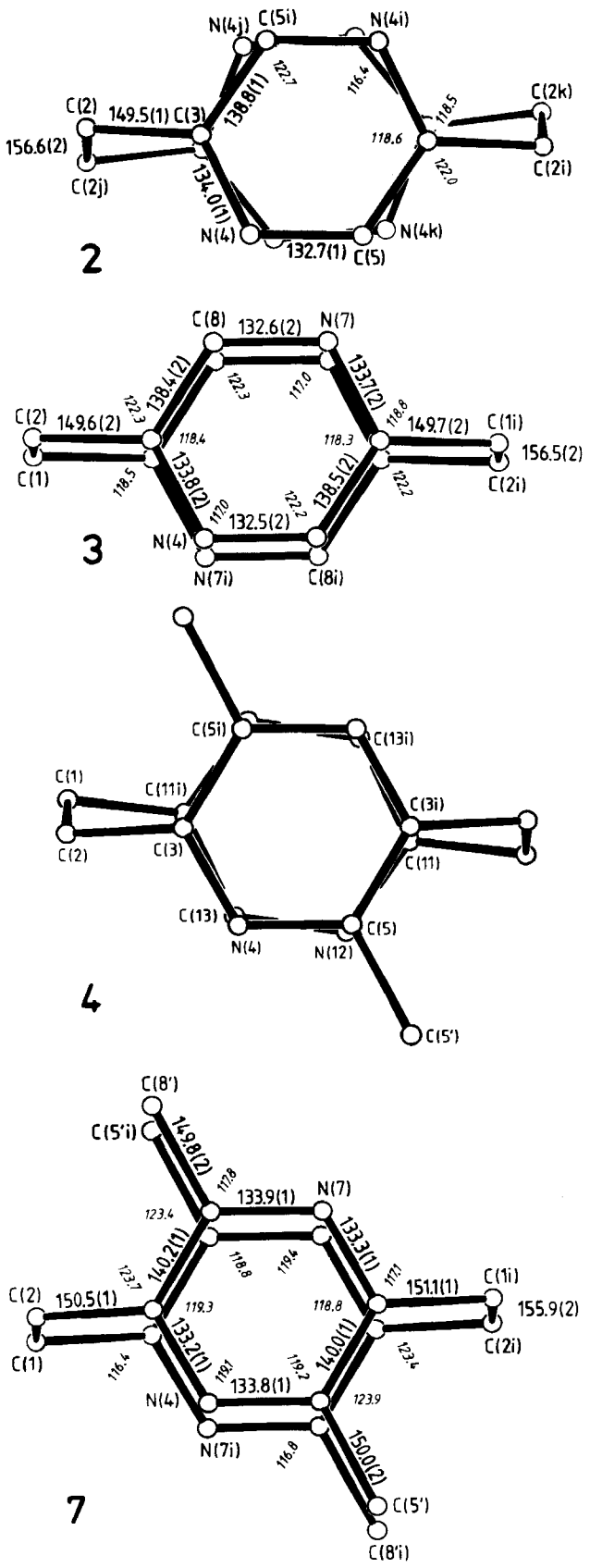


Figure 2. Molecular structures of **2**, **3**, **4**, and **7** in top-views perpendicular to the least-squares planes through the four nonbridged atoms of the pyrazine rings showing bond distances [pm] and angles [°]; the data of **4** are given in Table 2

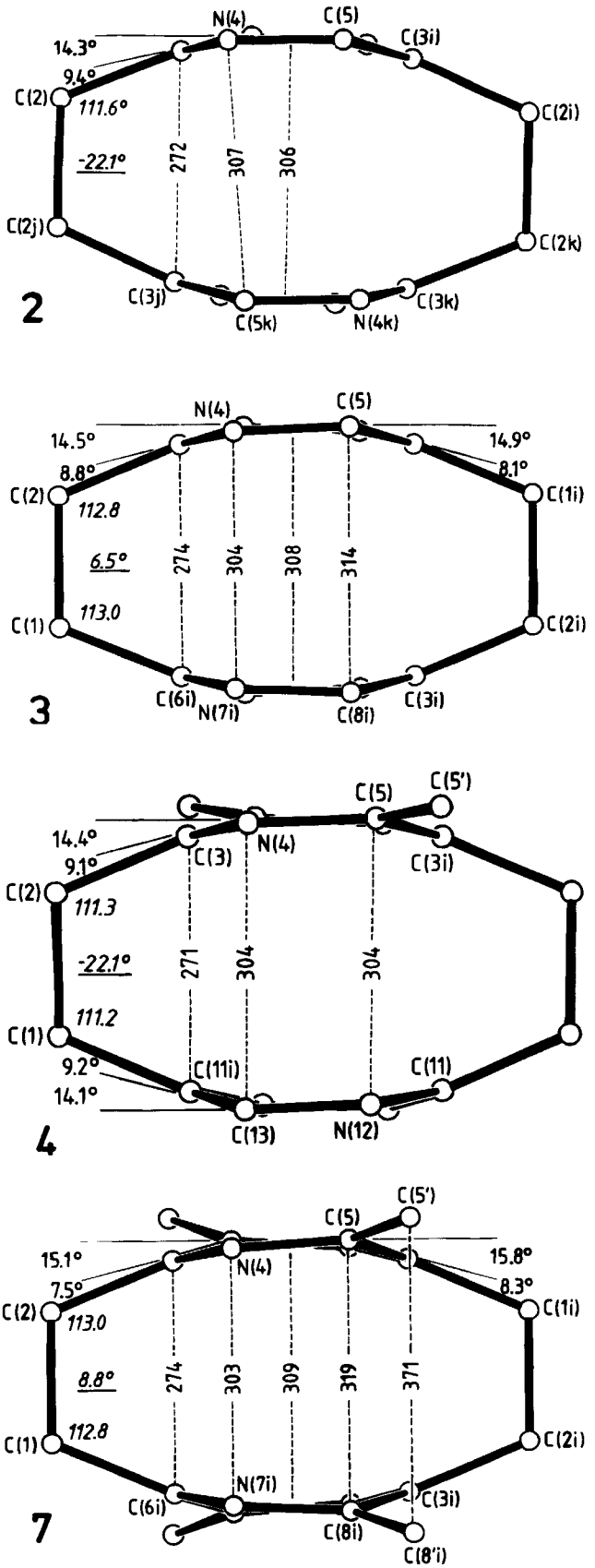


Figure 3. Molecular structures of **2**, **3**, **4**, and **7** in side-views along the pyrazine rings with transannular distances [pm] and bending angles [°] of the pyrazine rings

(2,5)pyrazinophanes is mainly taken up by the "softer" pyrazine rings. For **7** the additional steric interaction of the "ecliptic" methyl groups force the pyrazine rings to adopt a more distinct twist boat-like geometry. In the pseudo-geminal **3** and **7** the transannular distances N(4)···N(7i) (**3**: 304 pm; **7**: 303 pm) and C(5)···C(8i) (**3**: 314 pm; **7**: 319 pm) are different and, on the whole, a little larger than the corresponding transannular distances for the pseudo-ortho isomers [**2**: N(4)···C(5k) 307 pm; **4**: N(4)···C(13) 304 pm]. The same holds for the mean transannular distances defined as the vertical distance between the centers of the pyrazine moieties: 304 (**4**), 306 (**2**), 308 (**3**), and 309 pm (**7**). Apparently, the mutual twist (ca. 10°) of the pyrazine rings in the pseudo-ortho isomers **2** and **4** leads to some reduction of the mean transannular distance. The values for **3** and **7** are similar to those in [2.2]paracyclophane (309 pm)[24].

Molecular Structure of **24**: Figure 4 shows the molecular structure of **24** in a top-view (A) and in a side-view (B). The pyrazine rings are oriented *syn* to each other and are nearly planar. The C(4), N(9), C(8) and C(13), N(18), C(17) planes deviate from the ring basis planes C(4), C(5), C(7), C(8) and C(13), C(14), C(16), C(17), respectively, only by an angle of 2°. In this conformation, however, the atoms of each pyrazine ring do not eclipse the atoms of the other ring. The rings are slightly twisted (6°) about the axis passing through N(9) and N(18). An asymmetrical arrangement is found for the bridges, one sulfur atom, S(2), is folded towards the inner nitrogens N(9) and N(18), the other, S(11), away from them. N(9) and N(18) are directed to each other and are 303 pm apart. This is the shortest transannular distance. The dihedral (inclination) angle between the planes of the two pyrazines is found to be 15.8°. The structural features of **24** are similar to those of *syn*-2,11-dithia[3.3]metacyclophane[10] (twist angle 7°, transannular distance between the inner carbon atoms 305 pm, inclination angle 20.6°) and of *syn*-2,11-dithia[3.3](2,6)pyridinophane[12] with one exception: In these

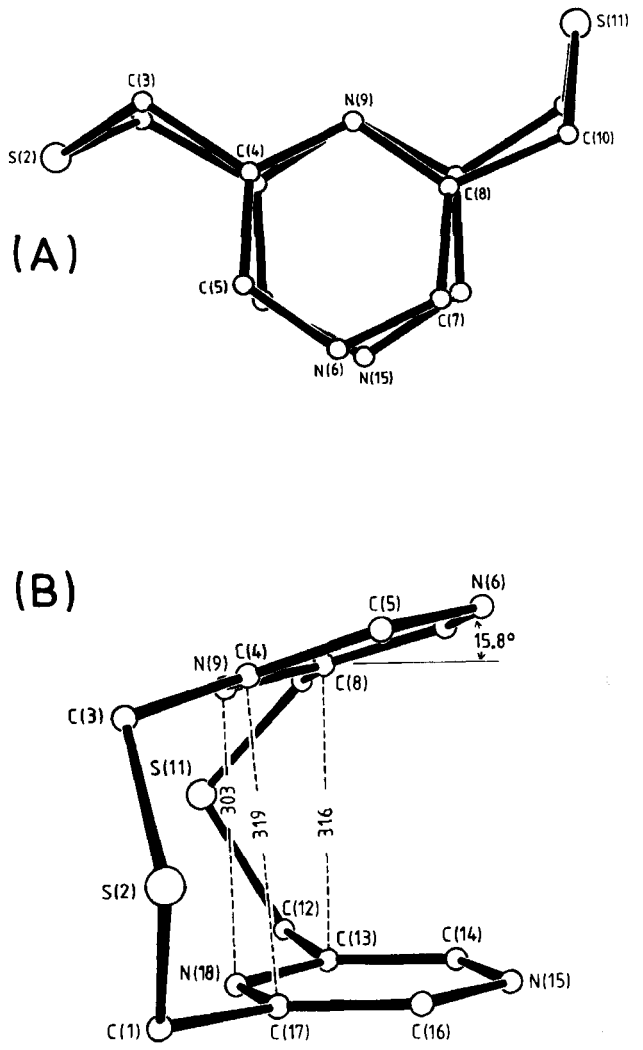


Figure 4. Molecular structure of **24**: (A) Top-view, (B) side-view showing transannular distances [pm]

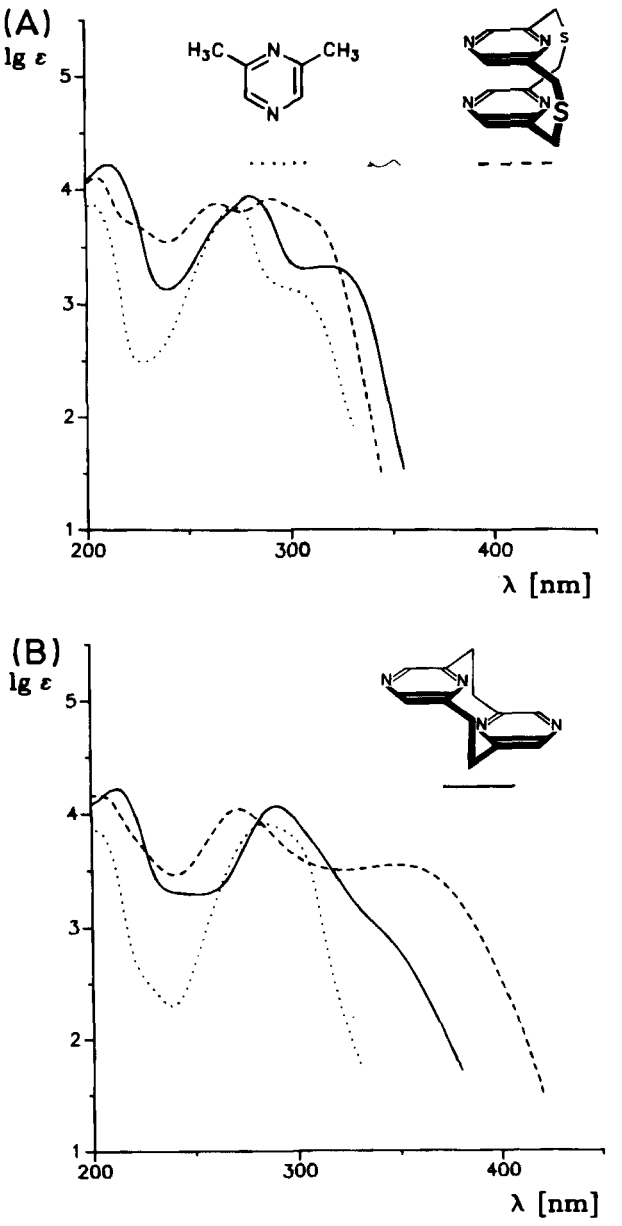


Figure 5. Electronic spectra of **1** (——), **24** (----), and **10** (·····) in ethanol (A) and in 5 N sulfuric acid (B)

phanes[10,12] the sulfur atoms of the bridges are *syn*-oriented with respect to one another and with respect to the rings corresponding to a crown-like configuration. The different conformations of the bridges observed in these compounds and in **24** are probably related to general packing effects.

Electronic Spectra

A comparison of the electronic spectra of the [2.2]pyrazinophanes **1**–**7** with those of the parent 2,6-dimethyl- (**10**), 2,5-dimethyl- (**8**), and 2,3,5,6-tetramethylpyrazines (**9**)[25] shows in all cases a bathochromic shift of the pyrazinophane bands. In the pseudo-ortho (**2**, **4**, **6**) and in the pseudo-geminal series (**3**, **5**, **7**) the spectra are very similar. Furthermore, the long-wavelength band patterns of **1** (Figure 5) and the pseudo-geminal isomers **3** (see Figure 1 in ref.[4]), **5**, and **7** (Figure 6), dissolved in trichloromethane or ethanol, resemble those of the parent pyrazines. For the pseudo-ortho isomers, on the other hand, a distinct first absorption band is observed at a wavelength which coincides with the position of the first shoulder in the electronic spectra of the pseudo-geminal isomers. Similar features are found in the electronic spectra of [2.2](2,5)pyridinophanes[26]. The electronic spectra of the [2.2]pyrazinophanes are not significantly affected when different organic solvents are used, see for example the absorption data of **2** and **3** in Table 4. A clear bathochromic shift, however, is observed in 5 N sulfuric acid which protonates the pyrazine moieties (Figures 5 and 6; Table 4). This effect is even more pronounced in the case of **24**, probably due to multiple protonation. Statements concerning the nature of the electronic transitions in [2.2]pyrazinophanes require a detailed theoretical investigation which, in combination with further experimental data provided by phosphorescence spectra, could also reveal the origin of the transitions.

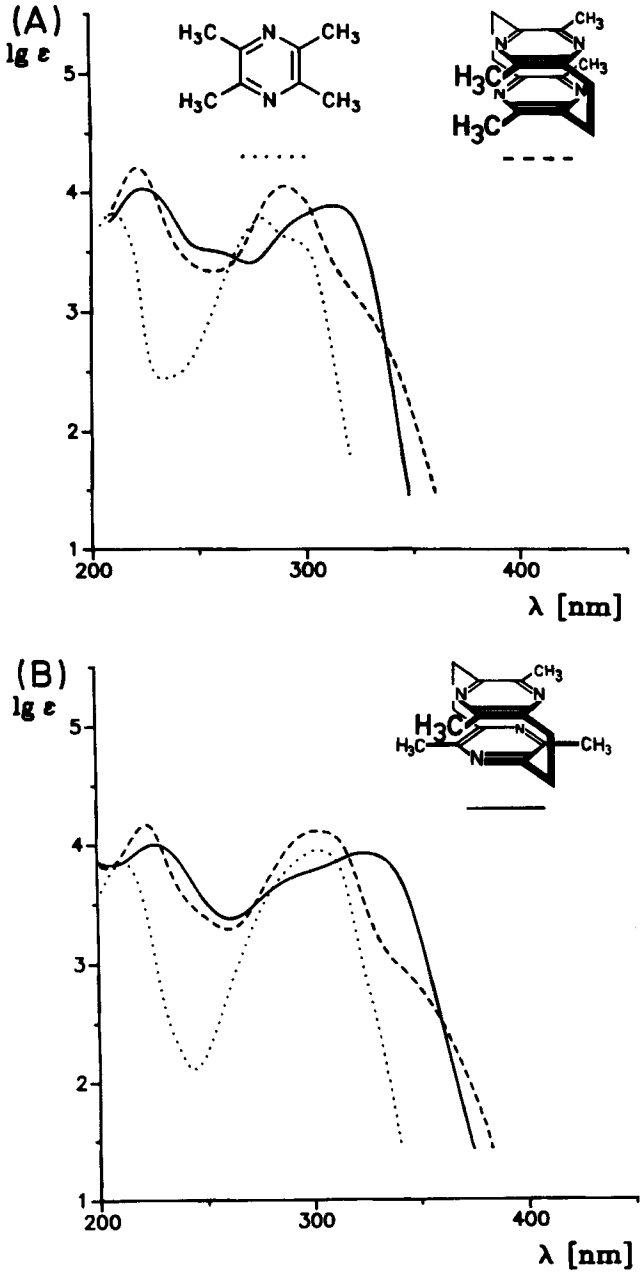


Figure 6. Electronic spectra of **6** (——), **7** (----), and **9** (·····) in ethanol (A) and in 5 N sulfuric acid (B)

Table 4. UV data for **2**, **3**, and **8**: λ_{max} [nm] (lg ε)

	Cyclohexane λ_{max} (lg ε)	Ethanol λ_{max} (lg ε)	5 N H_2SO_4 λ_{max} (lg ε)
8	205 (3.95)	203 (3.96)	204 (3.93)
	271 (3.80)		
	277 (3.77)	277 (3.83)	284 (3.89)
	305 (2.86)	300 sh (3.12)	
	308 (2.96)		
	314 (3.00)		
	319 (2.93)		
	326 (2.70)		
2	212 (4.05)	211 (4.09)	211 (4.05)
	240 sh (3.57)	240 sh (3.62)	
	302 (3.67)	306 (3.70)	313 (3.67)
3	214 (4.20)	212 (4.21)	212 (4.13)
	281 (4.00)	**282** (4.01)	**288** (3.96)
	320 sh (3.07)	320 sh (3.13)	

Experimental

M. p.s were measured with a Büchi apparatus and are uncorrected. UV: Cary 2300 spectrophotometer. ^{1}H- and ^{13}C-NMR: Bruker HX-360 or WM-500 spectrometer at 303 K unless otherwise stated (with tetramethylsilane as internal standard). Mass spectra: Dupont CEC 21-492 (70 eV), or Finnigan MAT 212 (70 eV) spectrometer. To monitor the progress of reactions and the separation of the products, TLC on silica gel (Macherey-Nagel G/UV_{254} plates) was used. Flash chromatography was done on Amicon matrex silica Si (particle size 35–70 μm).

X-ray Structure Analyses of **1**–**4**, **7**, *and* **24**: Intensity data were measured with an Enraf-Nonius CAD-4 four-circle diffractometer, using graphite-monochromated Mo-K_α radiation (λ = 7.1069 pm, Θ/2Θ scanning technique). The structures of **1**, **3**, **4**, **7**, and **24** were solved by direct methods (MULTAN) and were refined by full matrix technique of F^2 using anisotropic temperature factors for non-hydrogen atoms and isotropic temperature factors for hydrogen[27]. In the case of **2** the structure was solved by analysis of a Patterson map. Atomic scattering factors and anomalous dispersion corrections were taken from "International Tables for X-ray Crystallo-

graphy"[28]. The crystallographic data and the parameters of structure refinement are given in Table 1[17].

UV Data of **9** *and* **10** *for Comparison:* **9** ($CHCl_3$): λ_{max} (lg ε) = 280 nm (3.79), 298 sh (3.50); (ethanol): λ_{max} (lg ε) = 210 nm (3.82), 279 (3.78), 294 sh (3.60); (5 N H_2SO_4): λ_{max} (lg ε) = 212 nm (3.85), 303 (3.95). **10** ($CHCl_3$): λ_{max} (lg ε) = 271 nm (3.82), 276 (3.83), 306 (3.07); (ethanol): λ_{max} (lg ε) = 272 nm (3.88), 275 (3.84), 300 sh (3.13); (5 N H_2SO_4): λ_{max} (lg ε) = 202 nm (3.85), 283 (3.91)[25].

2-Chloromethyl-5-methylpyrazine (**11**): To a stirred suspension of 10.80 g (0.1 mol) 2,5-dimethylpyrazine (**8**) and 13.35 g (0.1 mol) finely divided *N*-chlorosuccinimide in 250 ml of boiling anhydrous tetrachloromethane 0.50 g of dibenzoyl peroxide was added. The stirred mixture was heated at reflux for 1 d, and after cooling to 0–5°C the precipitated succinimide was filtered off and washed with tetrachloromethane (2 × 50 ml). The combined filtrates were distilled under reduced pressure to leave a yellow oil. Flash chromatography of this residue [silica gel, dichloromethane/ethyl acetate (10:1)] yielded besides the starting compound (R_f = 0.2) three products:

2-Chloromethyl-5-dichloromethylpyrazine (**13**): R_f = 0.8; ca. 0.10 g (≤1%) of a yellow, decomposing oil. – ^{1}H NMR ($CDCl_3$): δ = 4.73 (s, 2H, CH_2), 6.77 (s, 1H, $CHCl_2$), 8.69 (d, ^5J = 1.3 Hz, 1H, 3-H), 8.98 (d, 1H, 6-H).

2,5-Bis(chloromethyl)pyrazine (**12**): R_f = 0.65; ca. 0.30 g (≤3%) of colorless decomposing crystals; for data see **12** below.

11: R_f = 0.4; ca. 7.00 g (ca. 50%) of a colorless, slowly decomposing oil. – ^{1}H NMR ($CDCl_3$): δ = 2.58 (s, 3H, CH_3), 4.69 (s, 2H, CH_2), 8.43 (d, ^5J = 1.3 Hz, 1H, 6-H; assignment confirmed by NOE), 8.61 (d, 1H, 3-H). – MS: *m/z* (%) = 144 (31), 142 (100) [M^+], 108 (20), 107 (95) [M^+ – Cl], 81 (8), 80 (46).

2,5-Bis(chloromethyl)pyrazine (**12**): 16.2 g (0.15 mol) of 2,5-dimethylpyrazine (**8**), 1.0 g of dibenzoyl peroxide, and 40.0 g (0.3 mol) of finely divided N-chlorosuccinimide, added in 4 portions to 500 ml of anhydrous tetrachloromethane, were treated as described above yielding 5.5 g (21%) of **12**, colorless crystals from hexane, m.p. 65–66°C. – ^{1}H NMR ($CDCl_3$): δ = 4.71 (s, 4H, CH_2), 8.70 (s, 2H, 3,6-H). – MS: *m/z* (%) = 180 (10), 178 (64), 176 (100) [M^+], 143 (31), 141 (94) [M^+ – Cl], 114 (17), 106 (5), 87 (11), 78 (5), 58 (8).

$C_6H_6Cl_2N_2$ (177.0) Calcd. C 40.71 H 3.42 Cl 40.05 N 15.82
Found C 40.53 H 3.29 Cl 39.90 N 15.55

2-Chloromethyl-3,5,6-trimethylpyrazine (**14**): 13.60 g (0.1 mol) of 2,3,5,6-tetramethylpyrazine (**9**), 13.35 g (0.1 mol) of finely divided *N*-chlorosuccinimide, and 0.5 g of dibenzoyl peroxide in 500 ml of anhydrous tetrachloromethane were treated as described above yielding six products, separated by flash chromatography (silica gel, dichloromethane):

2,3,5,6-Tetrakis(chloromethyl)pyrazine (**15**): R_f = 0.7; ca. 0.05 g (≤1%) of colorless prisms from tetrachloromethane, m.p. 148–149°C. – ^{1}H NMR ($CDCl_3$): δ = 4.84 (s, 8H, CH_2). – MS: *m/z* (%) = 278 (8), 276 (37), 274 (73), 272 (55) [M^+], 242 (8), 240 (40), 238 (90), 236 (85), 205 (9), 203 (20), 201 (25), 169 (6), 167 (20), 162 (10), 128 (15), 126 (37), 89 (20), 87 (50), 78 (16), 76 (20), 52 (48), 51 (100).

$C_8H_8Cl_4N_2$ (274.0) Calcd. C 35.07 H 2.94 Cl 51.76 N 10.23
Found C 35.32 H 2.92 Cl 51.58 N 10.19

6-Methyl-2,3,5-tris(chloromethyl)pyrazine (**16**): R_f = 0.5; ca. 0.10 g (≤1%) of colorless crystals from petroleum ether (b.p. 60–95°C), m.p. 74–77°C. – ^{1}H NMR ($CDCl_3$): δ = 2.70 (s, 3H, CH_3), 4.70 (s, 2H, CH_2), 4.81 (s, 4H, CH_2). – MS: *m/z* (%) = 242 (29), 240 (100), 238 (95) [M^+], 207 (7), 205 (40), 203 (68) [M^+ – Cl], 167 (9), 164 (4), 162 (7), 133 (4), 128 (12), 126 (11), 89 (13), 87 (21).

$C_8H_9Cl_3N_2$ (239.5) Calcd. C 40.11 H 3.79 Cl 44.41 N 11.70
Found C 40.34 H 3.69 Cl 44.55 N 11.56

Mixture of Three Isomeric Bis(chloromethyl)dimethylpyrazines: R_f = 0.2; 3.10 g (15%) of a yellow oil. – ^{1}H NMR ($CDCl_3$): δ = 2.56 (s, 6H, CH_3), 4.78 (s, 4H, CH_2) (22%), according to the chemical shifts probably *2,3-bis(chloromethyl)-5,6-dimethylpyrazine;* δ = 2.64 (s, 6H, CH_3), 4.67 (s, 4H, CH_2) (40%); δ = 2.66 (s, 6H, CH_3), 4.68 (s, 4H, CH_2) (38%). – Several crystallizations from petroleum ether (b.p. 60–95°C) afforded one isomer, *2,5-bis(chloromethyl)-3,6-dimethyl-* or *2,6-bis(chloromethyl)-3,5-dimethylpyrazine* as colorless crystals, m.p. 94–95°C. – ^{1}H NMR ($CDCl_3$): δ = 2.64 (s, 6H, CH_3), 4.67 (s, 4H, CH_2). – MS: *m/z* (%) = 208 (12), 206 (80), 204 (100) [M^+], 171 (34), 169 (90) [M^+ – Cl], 133 (12), 130 (5), 128 (15), 93 (5), 87 (6).

$C_8H_{10}Cl_2N_2$ (205.1) Calcd. C 46.85 H 4.91 Cl 34.58 N 13.66
Found C 46.58 H 4.83 Cl 34.84 N 13.43

2-Chloromethyl-3,5,6-trimethylpyrazine (**14**): R_f = 0.1; 8.40 g (49%) of colorless crystals from pentane, m.p. 31–32°C. – ^{1}H NMR ($CDCl_3$): δ = 2.50 (s, 3H, CH_3), 2.51 (s, 3H, CH_3), 260 (s, 3H, 3-CH_3, assignment confirmed by NOE), 4.66 (s, 2H, CH_2). – MS: *m/z* (%) = 172 (35), 170 (100) [M^+], 135 (100) [M^+ – Cl], 107 (6), 94 (24).

$C_8H_{11}ClN_2$ (170.6) Calcd. C 56.31 H 6.50 Cl 20.78 N 16.42
Found C 56.03 H 6.44 Cl 20.73 N 16.28

2-Chloromethyl-6-methylpyrazine (**17**): 10.80 g (0.1 mol) of 2,6-dimethylpyrazine (**10**), 13.35 g (0.1 mol) of finely divided *N*-chlorosuccinimide, and 0.5 g of dibenzoyl peroxide in 300 ml of anhydrous tetrachloromethane were treated as described above yielding three main products, separated by flash chromatography [silica gel, dichloromethane/ethyl acetate (10:1)].

2-Chloromethyl-6-dichloromethylpyrazine (**19**): R_f = 0.75; 0.80 g (4%) of a yellow, decomposing oil. – ^{1}H NMR ($CDCl_3$): δ = 4.73 (s, 2H, CH_2), 6.78 (s, 1H, $CHCl_2$), 8.81 (s, 1H, 3-H), 9.01 (s, 1H, 5-H). – MS: *m/z* (%) = 214 (11), 212 (30), 210 (30) [M^+], 179 (13), 177 (71), 175 (100), 143 (16), 141 (47), 102 (5), 100 (15).

2,6-Bis(chloromethyl)pyrazine (**18**): R_f = 0.55; 3.50 g (20%) of a yellow, decomposing oil. – ^{1}H NMR ($CDCl_3$): δ = 4.71 (s, 4H, CH_2), 8.72 (s, 2H, 3,5-H). – MS: *m/z* (%) = 180 (11), 178 (65), 176 (100) [M^+], 143 (29), 141 (83) [M^+ – Cl], 121 (25), 119 (65), 117 (65).

17: R_f = 0.3; 9.00 g (63%) of a yellow, decomposing oil. – ^{1}H NMR ($CDCl_3$): δ = 2.58 (s, 3H, CH_3), 4.65 (s, 2H, CH_2), 8.42 (s, 1H, 5-H), 8.54 (s, 1H, 3-H). – MS: *m/z* (%) = 144 (34), 142 (100) [M^+], 107 (30) [M^+ – Cl], 80 (20), 66 (25).

2,6-Bis(chloromethyl)pyrazine (**18**): 16.2 g (0.15 mol) of 2,6-dimethylpyrazine (**10**), 1.0 g of dibenzoyl peroxide, and 40.0 g (0.30 mol) of finely divided *N*-chlorosuccinimide, added in 4 portions to 500 ml of anhydrous tetrachloromethane, were treated as described above: R_f = 0.55; 10.2 g (38%) of a yellow, decomposing oil.

Trimethyl[(5-methyl-2-pyrazinyl)methyl]ammonium Chloride (**20**): Into 100 ml of dimethylformamide (DMF), cooled to 0°C, 15.0 g (0.25 mol) trimethylamine were passed. Then a solution of 7.0 g of **11** (crude product) in 30 ml of DMF was added, and the reaction mixture was stirred at room temp. for 12 h. The precipitation of the product was completed by adding 50 ml of diethyl ether. The collected product was recrystallized twice from ethanol/ethyl acetate to yield 7.2 g [36%, related to 0.1 mol of 2,5-dimethylpyrazine (**8**)] of colorless needles, m.p. 223°C (dec.). – ^{1}H NMR

([D$_6$]DMSO, 323 K): δ = 2.56 (s, 3H, CH_3), 3.17 [s, 9H, $N(CH_3)_3$], 4.76 (s, 2H, CH_2), 8.67 (d, ^5J = 1.3 Hz, 1H, 6-H, assignment confirmed by NOE), 8.78 (d, 1H, 3-H). – MS: *m/z* (%) = 144 (7), 142 (21), 108 (100), 107 (44), 80 (19), 58 (54).

$C_9H_{16}ClN_3$ (201.7) Calcd. C 53.59 H 8.00 Cl 17.58 N 20.83
Found C 53.72 H 8.02 Cl 17.55 N 20.63

Trimethyl[(3,5,6-trimethyl-2-pyrazinyl)methyl]ammonium Chloride (**21**): 21 g (0.35 mol) of trimethylamine in 150 ml of DMF and 8.4 g (0.05 mol) of **14** in 30 ml of DMF were treated as described above; from ethanol/ethyl acetate 10.5 g (93%) of colorless crystals, m.p. 232–233°C. – ^{1}H NMR (CD_3CN): δ = 2.48 (s, 3H, CH_3), 2.49 (s, 3H, CH_3), 2.60 (s, 3H, CH_3), 3.24 [s, 9H, $N(CH_3)_3$], 4.68 (s, 2H, CH_2). – MS: *m/z* (%) = 172 (29), 171 (9), 170 (90), 165 (5), 137 (8), 136 (90), 135 (100), 134 (5), 94 (20), 88 (5), 59 (25), 58 (70), 57 (6), 54 (10), 53 (40), 52 (14), 51 (8), 50 (13).

$C_{11}H_{20}ClN_3$ (229.8) Calcd. C 57.50 H 8.77 Cl 15.43 N 18.29
Found C 57.56 H 8.79 Cl 15.63 N 18.36

2,5-Bis(isothiouroniomethyl)pyrazine Dichloride (**22**): To a solution of 5.5 g (31 mmol) of **12** in 150 ml of butanol a hot solution of 5.9 g (78 mmol) of thiourea in 150 ml of butanol was added under stirring. The mixture was heated to 100°C for 10 min. On cooling the precipitation of the product was completed by adding 100 ml of acetone. The white solid was filtered off and washed with acetone to remove any thiourea. Recrystallization from methanol gave 8.3 g (81%) of **22** as colorless crystals, m.p. 226°C (dec.). – ^{1}H NMR ([D$_6$]DMSO): δ = 4.77 (s, 4H, CH_2), 8.77 (s, 2H, 3,6-H), 9.39 (br. s, 4H, NH_2), 9.47 (br. s, 4H, NH_2).

$C_8H_{14}Cl_2N_6S_2$ (329.3)
Calcd. C 29.18 H 4.29 Cl 21.54 N 25.52 S 19.48
Found C 29.39 H 4.45 Cl 21.57 N 25.68 S 19.54

2,6-Bis(isothiouroniomethyl)pyrazine Dichloride (**23**): 6.20 g (35.0 mmol) of **18** in 150 ml of butanol and 6.65 g (87.5 mmol) of thiourea in 150 ml of butanol were treated as described above; from methanol/ethyl acetate 9.70 g (84%) of yellowish needles, m.p. 218–220°C (dec.). – ^{1}H NMR ([D$_6$]DMSO): δ = 4.76 (s, 4H, CH_2), 8.73 (s, 2H, 3,5-H), 9.34 (br. s, 4H, NH_2), 9.45 (br. s, 4H, NH_2).

$C_8H_{14}Cl_2N_6S_2$ (329.3)
Calcd. C 29.18 H 4.29 Cl 21.54 N 25.52 S 19.48
Found C 29.28 H 4.34 Cl 21.46 N 25.48 S 19.69

2,11-Dithia[3.3](2,6)pyrazinophane (**24**): To 1.6 l of boiling methanol/DMF/water (75:4:1) containing 50.40 g (0.3 mol) of cesium hydroxide monohydrate, kept under argon with stirring, a solution of 4.60 g (26.0 mmol) of **18** and 8.56 g (26.0 mmol) of **23** in 500 ml of methanol/water (99:1) was added dropwise over a period of 6 h (addition rate ca. 1.4 ml/min). Heating at reflux was continued for 2 h. After cooling the solvent was distilled off in vacuo. After addition of 100 ml of water, the residue was extracted with trichloromethane (4 × 50 ml). The combined extracts were dried with $MgSO_4$ and evaporated under reduced pressure. Flash chromatography [silica gel, trichloromethane/acetone (3:1)] afforded 3.00 g (42%) of **24** (R_f = 0.37); from trichloromethane/acetone colorless crystals, m.p. 246–247°C (dec.). – UV (Ethanol): λ_{max} (lg ε) = 205 nm (4.11), 222 sh (3.71), 264 (3.88), 291 (3.92), 306 sh (3.79); (5 N H_2SO_4): λ_{max} (lg ε) = 203 nm (4.17), 271 (4.04), 349 (3.55). – ^{1}H NMR ($CDCl_3$): δ = 4.02 (s, 8H, CH_2), 8.24 (s, 4H, CH). – MS: *m/z* (%) = 278 (7), 277 (10), 276 (100) [M$^+$], 244 (5), 243 (48), 169 (14), 139 (22), 138 (59), 137 (5), 120 (7), 109 (6), 108 (28), 107 (5), 71 (5).

$C_{12}H_{12}N_4S_2$ (276.4) Calcd. C 52.15 H 4.38 N 20.27 S 23.20
Found C 52.34 H 4.30 N 20.50 S 23.47

Pseudo-ortho and Pseudo-geminal 2,11-Dithia[3.3](2,5)pyrazinophanes (**25** and **26**): To 2 l of boiling methanol/water (99:1) containing 230.0 g (0.70 mol) of cesium carbonate, kept under argon with stirring, a solution of 46.4 g (0.14 mol) of **22** and 25.0 g (0.14 mol) of **12** in 1 l of methanol/water (99:1) was added dropwise over a period of 8 h (addition rate ca. 2 ml/min). After cooling, the solvent was distilled off under reduced pressure, and the residue was extracted with hot trichloromethane (5 × 100 ml). The combined extracts were evaporated. Silica gel filtration of the residue, using trichloromethane/acetone (1:1) as eluent, yielded 6.5 g ⟨16.7%: 13.7% of **25**, 2.8% of **26**, and 0.2% of *2,11,20,29-tetrathia[3.3.3.3](2,5)pyrazinophane* (**27**), as determined by ^{1}H NMR⟩ of crude cyclization product, which was used in the next step without separation. Flash chromatography [silica gel, trichloromethane/acetone (1:1)] of a 1-g batch of the product mixture afforded the pure compounds. The tentative assignment of the isomers **25** and **26** is based on m.p.s and relative yields.

26: R_f = 0.6; from DMF colorless powder, m.p. >310°C. – ^{1}H NMR ($CDCl_3$): δ = 4.02 (s, 8H, CH_2), 8.27 (s, 4H, CH); ([D$_6$]-DMSO): δ = 3.83, 4.19 (AB q, ^2J = 15.0 Hz, 8H, CH_2), 8.18 (s, 4H, CH). – MS: *m/z* (%) = 276 (16) [M$^+$], 171 (5), 170 (11), 142 (5), 140 (10), 139 (100), 138 (13), 137 (14), 107 (28), 106 (8), 95 (6), 79 (6).

$C_{12}H_{12}N_4S_2$ (276.4) Calcd. C 52.15 H 4.38 N 20.27 S 23.20
Found C 52.26 H 4.10 N 20.23 S 23.10

25: R_f = 0.5; from DMF colorless needles, m.p. 280–281°C (dec.). – ^{1}H NMR ($CDCl_3$): δ = 3.95, 4.01 (AB q, ^2J = 15.0 Hz, 8H, CH_2), 8.23 (s, 4H, CH); ([D$_6$]DMSO): δ = 3.85, 4.15 (AB q, ^2J = 14.6 Hz, 8H, CH_2), 8.16 (s, 4H, CH). – MS: *m/z* (%) = 276 (11) [M$^+$], 231 (11), 170 (10), 140 (7), 139 (100), 138 (3), 137 (10), 108 (7), 107 (16), 106 (9), 97 (5), 93 (7), 79 (9).

Found C 52.10 H 4.41 N 20.20 S 23.18

2,11,20,29-Tetrathia[3.3.3.3](2,5)pyrazinophane (**27**): R_f = 0.3; from DMF colorless crystals, m.p. 184–185°C (dec.). – ^{1}H NMR ($CDCl_3$): δ = 3.82 (s, 16H, CH_2), 8.30 (s, 8H, CH); ([D$_6$]DMSO): δ = 3.83 (s, 16H, CH_2), 8.30 (s, 8H, CH). – MS: *m/z* (%) = 552 (15) [M$^+$], 520 (6), 275 (7), 243 (12), 211 (7), 170 (9), 139 (90), 138 (50), 107 (100).

$C_{24}H_{24}N_8S_4$ (552.8) Calcd. C 52.15 H 4.38 N 20.27 S 23.20
Found C 52.38 H 4.51 N 20.36 S 23.49

[2.2](2,6)Pyrazinophane (**1**): A suspension of 332 mg (1.2 mmol) of **24** in 250 ml of trimethyl phosphite, kept under argon with stirring, was irridiated (125-W mercury high-pressure lamp, quartz) for 2 h. The solvent was distilled off under reduced pressure, and the residue was treated with 20 ml of cold 2 N hydrochloric acid for 30 min. Then the mixture was extracted with dichloromethane (3 × 20 ml) to remove decomposition products. The water layer was made basic with satd. aqueous sodium carbonate solution and extracted with trichloromethane (6 × 50 ml). The combined extracts were dried with $MgSO_4$ and evaporated in vacuo. Flash chromatography (silica gel, acetone) afforded 40 mg (16%) of **1** (R_f = 0.36), from diethyl ether/hexane colorless crystals, m.p. 231°C. – UV (Ethanol): λ_{max} (lg ε) = 211 nm (4.22), 280 (3.94), 318 (3.32); (5 N H_2SO_4): λ_{max} (lg ε) = 212 nm (4.22), 290 (4.06), 340 sh (2.97). – ^{1}H NMR ($CDCl_3$, 303 K): δ = 2.58 (br. s, 4H, CH_2), 3.40 (br. s, 4H, CH_2), 8.39 (br. s, 4H, CH); ($CDCl_2CDCl_2$, 353 K): δ = 3.04 (br. s, 8H, CH_2, coalescence temperature 327 K), 8.41 (s, 4H, CH); (CD_2Cl_2, 263 K): δ = 2.49–3.45 (AA'BB', 8H, CH_2), 8.38 (s, 4H, CH). – MS: *m/z* (%) = 213 (10), 212 (100) [M$^+$], 211 (16), 197 (8), 185 (23), 184 (20), 171 (6), 158 (20), 157 (15), 145 (6), 144 (10), 143 (6).

$C_{12}H_{12}N_4$ (212.3) Calcd. C 67.90 H 5.70 N 26.40
Found C 68.19 H 5.56 N 26.51

Pseudo-ortho and Pseudo-geminal [2.2](2,5)Pyrazinophanes (**2** and **3**) *by Hofmann 1,6-Elimination:* To a stirred solution of 32.30 g (0.16 mol) of **20** in 200 ml of water, freshly prepared silver(I) oxide [from 55.00 g (0.32 mol) of $AgNO_3$ and 162 ml of 2 N NaOH] was added. After 30 min of stirring, the solid was removed by filtration and washed with water (4 × 50 ml). The combined filtrates (ca. 400 ml) were added dropwise to a stirred solution of 1.5 g of phenothiazine in 1.5 l of boiling toluene, placed in a flask fitted with a water separator, at such a rate that addition and azeotropic water separation was in equilibrium (about 8 h). Then the stirred reaction mixture was heated at reflux for 4 h. The hot solution was filtered, and the removed polymeric material was washed with hot toluene (4 × 100 ml). The combined filtrates were evaporated under reduced pressure. Flash chromatography of the residue on silica gel with ethyl acetate/acetone (1:1) afforded four products.

(E)-1,2-Bis(5-methyl-2-pyrazinyl)ethene (**30**): R_f = 0.62; 0.08 g (0.5%) of yellow platelets from ethyl acetate, m.p. 211°C. – ^{1}H NMR ($CDCl_3$): δ = 2.59 (s, 6H, CH_3), 7.73 (s, 2H, HC=CH), 8.46 (s, 2H, 6-H), 8.55 (s, 2H, 3-H, assignment confirmed by NOE). – MS: *m/z* (%) = 213 (9), 212 (92) [M^+], 211 (55), 197 (5), 145 (11), 144 (100), 77 (8).

$C_{12}H_{12}N_4$ (212.3) Calcd. C 67.90 H 5.70 N 26.40
Found C 67.86 H 5.43 N 26.51

Bis[(5-methyl-2-pyrazinyl)methyl]ether (**29**): R_f = 0.38; 5.20 g (28%) of colorless crystals from ethyl acetate/hexane, m.p. 66–67°C. – ^{1}H NMR ($CDCl_3$): δ = 2.57 (s, 6H, CH_3), 4.78 (s, 4H, CH_2), 8.41 (s, 2H, 3-H), 8.62 (s, 2H, 6-H, assignment confirmed by NOE). – MS: *m/z* (%) = 230 (8) [M^+], 123 (55), 109 (6), 108 (100), 107 (8), 80 (8).

$C_{12}H_{14}N_4O$ (230.3) Calcd. C 62.59 H 6.13 N 24.33
Found C 62.48 H 6.20 N 24.42

Pseudo-geminal [2.2](2,5)Pyrazinophane (**3**): R_f = 0.21; 0.25 g (1.5%) of colorless crystals from ethyl acetate, m.p. 297–298°C. – ^{1}H NMR ($CDCl_3$): δ = 3.32–3.45 (AA'BB', 8H, CH_2), 7.73 (s, 4H, 3,6-H). – ^{13}C NMR ($CDCl_3$): δ = 33.62 (CH_2), 141.31 (3,6-CH), 150.89 (2,5-C). – MS: *m/z* (%) = 213 (9), 212 (100) [M^+], 211 (16), 196 (5), 185 (7), 184 (18), 158 (7), 157 (6), 132 (6), 131 (5), 106 (18), 79 (23), 55 (10), 52 (8), 39 (33).

$C_{12}H_{12}N_4$ (212.3) Calcd. C 67.90 H 5.70 N 26.40
Found C 67.87 H 5.74 N 26.70

Pseudo-ortho [2.2](2,5)Pyrazinophane (**2**): R_f = 0.19; 1.48 g (8.7%) of colorless prisms from ethyl acetate, m.p. 258°C. – ^{1}H NMR ($CDCl_3$): δ = 3.21–3.45 (AA'BB', 8H, CH_2), 7.81 (s, 4H, 3,6-H). – ^{13}C NMR ($CDCl_3$): δ = 33.13 (CH_2), 141.86 (3,6-CH), 150.65 (2,5-C). – MS: *m/z* (%) = 213 (9), 212 (100) [M^+], 211 (15), 196 (5), 185 (6), 184 (15), 158 (6), 157 (5), 132 (5), 131 (4), 106 (16), 79 (20), 55 (10), 52 (8), 39 (57).

Found C 67.75 H 5.98 N 26.51

2 *and* **3** *by Photolysis of* **25** *and* **26**: A stirred suspension of 550 mg (2 mmol) of crude **25** and **26** in 250 ml of trimethyl phosphite, kept under argon, was irridiated (125-W mercury high-pressure lamp, quartz) for 1 h. The solvent was removed by distillation under reduced pressure, and the residue was treated with 10 ml of cold 2 N hydrochloric acid for 30 min. Then the mixture was extracted with dichloromethane (2 × 10 ml) to remove decomposition products. The water layer was made basic with satd. aqueous sodium carbonate solution and extracted with trichloromethane (6 × 30 ml). The combined extracts were dried with $MgSO_4$ and evaporated in vacuo. Flash chromatography [silica gel, trichloromethane/acetone (1:1)] afforded 130 mg of starting material, 80 mg (25%) of **2**, and 20 mg (6%) of **3**.

Pseudo-ortho and Pseudo-geminal 5,8,13,16-Tetramethyl[2.2]-(2,5)pyrazinophanes (**6** and **7**): 23.0 g (0.1 mol) of **21** in 200 ml of water, silver(I) oxide (from 35.7 g of $AgNO_3$ and 105 ml of 2 N NaOH), and 1.5 g of phenothiazine in 1.5 l toluene were treated as described for **2** and **3** (Hofmann 1,6-elimination). Flash chromatography (silica gel, acetone) afforded three main products.

2-Hydroxymethyl-3,5,6-trimethylpyrazine (**31**): R_f = 0.66; 1.9 g (13%) of colorless crystals from petroleum ether (b.p. 60–95°C), m.p. 77°C. – ^{1}H NMR ($CDCl_3$): δ = 2.40 (s, 3H, CH_3), 2.51 (s, 6H, CH_3), 4.32 (t, $^3J \approx 4.0$ Hz, 1H, OH), 4.68 (d, 2H, CH_2). – MS: *m/z* (%) = 153 (23), 152 (100) [M^+], 151 (34), 134 (16), 124 (6), 123 (64), 122 (12), 121 (9), 69 (5).

$C_8H_{12}N_2O$ (152.2) Calcd. C 63.13 H 7.95 N 18.41
Found C 63.25 H 7.78 N 18.29

6: R_f = 0.43; 6.8 g (51%) colorless needles from water, m.p. 114°C. – UV ($CHCl_3$): λ_{max} (lg ε) = 260 nm (3.52), 312 (3.88); (ethanol): λ_{max} (lg ε) = 223 nm (4.03), 256 sh (3.51), 312 (3.88); (5 N H_2SO_4): λ_{max} (lg ε) = 227 nm (4.00), 300 sh (3.77), 324 (3.92). – ^{1}H NMR ($CDCl_3$): δ = 2.32 (s, 12H, CH_3), 3.07–3.39 [AA'BB', 8H, CH_2]. – ^{13}C NMR ($CDCl_3$): δ = 20.2 (CH_3), 31.4 (CH_2), 146.2 (C), 148.0 (C). – MS: *m/z* (%) = 269 (12), 268 (100) [M^+], 267 (5), 253 (10), 226 (4), 212 (4), 200 (5), 147 (4), 135 (6), 134 (10), 93 (8), 53 (19).

$C_{16}H_{20}N_4$ (268.4) Calcd. C 71.61 H 7.51 N 20.88
Found C 71.52 H 7.77 N 21.12

7: R_f = 0.21; 0.25 g (1.9%) of colorless prisms from ethyl acetate, m.p. 258°C. – UV ($CHCl_3$): λ_{max} (lg ε) = 289 nm (4.05); (ethanol): λ_{max} (lg ε) = 222 nm (4.21), 290 (4.05); (5 N H_2SO_4): λ_{max} (lg ε) = 223 nm (4.17), 302 (4.11). – ^{1}H NMR ($CDCl_3$): δ = 2.37 (s, 12H, CH_3), 3.21–3.47 (AA'BB', 8H, CH_2). – ^{13}C NMR ($CDCl_3$): δ = 20.0 (CH_3), 31.3 (CH_2), 143.7 (C), 146.4 (C). – MS: *m/z* (%) = 269 (12), 268 (100) [M^+], 267 (5), 253 (11), 226 (4), 212 (7), 200 (4), 147 (4), 135 (4), 134 (8), 93 (8), 53 (16).

Found C 71.59 H 7.75 N 21.02

Pseudo-ortho and Pseudo-geminal 5,8-Dimethyl[2.2](2,5)pyrazinophanes (**4** and **5**) *by "Crossed" Hofmann 1,6-Elimination:* 6.86 g (34 mmol) of **20** and 7.81 g (34 mmol) of **21** in 200 ml of water, silver(I) oxide (from 23.80 g of $AgNO_3$ and 70 ml of 2 N NaOH), and 1.40 g of phenothiazine in 1.5 l of toluene were treated as described above. Flash chromatography (silica gel, acetone) of the residue afforded **4** and **5** besides the previously obtained products **2** (4.4%), **3** (0.8%), **6** (11%), **29** (13%), and **31** (11%).

5: R_f = 0.31; 0.02 g (0.25%) of colorless crystals from petroleum ether (b.p. 60–95°C), m.p. 159–160°C. – UV ($CHCl_3$): λ_{max} (lg ε) = 283 nm (3.98), 310 sh (3.42). – ^{1}H NMR ($CDCl_3$): δ = 2.35 (s, 6H, CH_3), 3.11–3.50 (m, 8H, CH_2), 7.89 (s, 2H, CH). – ^{13}C NMR ($CDCl_3$): δ = 20.1 (CH_3), 32.6 (CH_2), 37.8 (CH_2), 139.2 (CH), 145.1 (C), 147.9 (C), 150.6 (C). – MS: *m/z* (%) = 241 (10), 240 (100) [M^+], 239 (10), 225 (18), 212 (6), 199 (20), 198 (31), 184 (5), 171 (5), 134 (12), 93 (17).

$C_{14}H_{16}N_4$ (240.3) Calcd. C 69.97 H 6.71 N 23.32
Found C 70.21 H 6.78 N 23.56

4: R_f = 0.30; 0.35 g (4.3%) of colorless crystals from petroleum ether (b.p. 60–95°C), m.p. 103–104°C. – UV ($CHCl_3$): λ_{max} (lg ε) = 313 nm (3.75); (ethanol): λ_{max} (lg ε) = 219 nm (4.02), 314 (3.74); (5 N H_2SO_4): λ_{max} (lg ε) = 216 nm (3.99), 327 (3.77). – ^{1}H NMR ($CDCl_3$): δ = 2.36 (s, 6H, CH_3), 3.13–3.44 (m, 8H, CH_2), 7.73 (s, 2H, CH). – ^{13}C NMR ($CDCl_3$): δ = 20.4 (CH_3), 32.0 (CH_2), 32.5 (CH_2), 141.7 (CH), 145.9 (C), 147.7 (C), 150.8 (C). – MS: *m/z* (%) = 241 (11), 240 (100) [M^+], 239 (6), 226 (4), 225 (7), 212 (4), 198 (6), 134 (12), 94 (4), 93 (12).

Found C 70.11 H 6.53 N 23.55

CAS Registry Numbers

(±)-**1**: 123624-86-2 / (±)-**2**: 119521-86-7 / (±)-**3**: 119616-30-7 / (±)-**4**: 123624-87-3 / (±)-**5**: 123673-26-7 / (±)-**6**: 123624-88-4 / (±)-**7**: 123673-27-8 / **8**: 123-32-0 / **9**: 1124-11-4 / **10**: 108-50-9 / **10** ($R^3 = R^5 = CH_2Cl$): 123625-00-3 / **11**: 81831-68-7 / **12**: 58549-95-4 / **13**: 123624-89-5 / **13**: ($R^3 = R^6 = Me$): 123625-02-5 / **14**: 123624-90-8 / **15**: 123624-91-9 / **16**: 123624-92-0 / **17**: 81831-69-8 / **17** ($R^3 = CH_2Cl$, $R^5 = Me$): 123625-01-4 / **18**: 86045-21-8 / **19**: 94127-03-4 / **20**: 119521-85-6 / **21**: 123624-93-1 / **22**: 123624-94-2 / **23**: 123624-95-3 / (±)-**24**: 123624-96-4 / **25**: 123624-97-5 / **26**: 123673-28-9 / **27**: 123624-98-6 / **29**: 119521-88-9 / (*E*)-**30**: 123624-99-7 / **31**: 75907-74-3

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