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[2.2](2,5)Pyrimidinophanes: Synthesis and Molecular Structure

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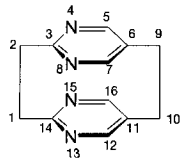
The title compounds **1** and **2** are synthesized by photolytic sulfur extrusion from the 2,11-dithia[3.3](2,5)pyrimidinophane **17**. The molecular structures of **1** and **2** are determined by X-ray structure analysis and are discussed with regard to the steric strain in these molecules. Thermolysis of [(5-methyl-2-pyrimidinyl)methyl]- or [(2-methyl-5-pyrimidinyl)methyl]-trimethylammonium hydroxide (**10** or **11**) does not generate **1** and **2**. α-Chlorination of 2,5-dimethylpyrimidine (**3**) with *N*-chlorosuccinimide provides the required precursors **4**–**6**.

Cyclophanes are valuable models for studying how intramolecular interactions of two π systems depend on their distance, orientation, and mutual fixation. Previous studies[1–7] of transannular interactions in N-heterocyclic [2.2]-cyclophanes with π-electron-deficient rings have directed out interest to [2.2]pyrimidinophanes. This paper describes the syntheses of the isomeric [2.2](2,5)pyrimidinophanes **1** (pseudo-geminal) and **2** (pseudo-*para*) and their molecular structures as determined by X-ray crystallography.



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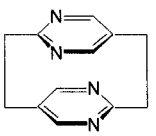

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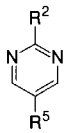
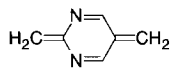


	R^2	R^5
3[8]	CH_3	CH_3
4	CH_2Cl	CH_3
5	CH_3	CH_2Cl
6	CH_2Cl	CH_2Cl
7	$CH_2N(CH_3)_3]Cl$	CH_3
8	CH_3	$CH_2N(CH_3)_3]Cl$
9	$CH_2SC(NH_2)_2]Cl$	$CH_2SC(NH_2)_2]Cl$
10	$CH_2N(CH_3)_3]OH$	CH_3
11	CH_3	$CH_2N(CH_3)_3]OH$
12	CH_3	CH_2OH

A direct synthetic approach leading to **1** and **2** was based upon the dimerization of the intermediate 2,5-dihydro-2,5-dimethylenepyrimidine (**13**) which could be generated by a Hofmann 1,6-elimination of either [(5-methyl-2-pyrimidinyl)methyl]- or [(2-methyl-5-pyrimidinyl)methyl]trimethylammonium hydroxide (**10** or **11**). The required precursors 2-(chloromethyl)-5-methylpyrimidine (**4**) and 5-(chloromethyl)-2-methylpyrimidine (**5**) are obtained by side-chain chlorination of 2,5-dimethylpyrimidine (**3**) with *N*-chlorosuccinimide. The reaction of the starting compounds in a molar ratio of 1:1.05 yields, besides **4** (14%) and **5** (35%), 2,5-bis(chloromethyl)pyrimidine (**6**; 9%). Treatment of **3** with two equivalents of *N*-chlorosuccinimide affords **6** in higher yield (38%), and **4** (8%) and **5** (21%) as by-products. The reaction of **4** and **5** with trimethylamine provides the trimethylammonium chlorides **7** and **8**, respectively, which are converted into the corresponding hydroxides **10** and **11**. However, thermolysis of these free bases does not lead to the target molecules, the pyrimidinophanes **1** and **2**, but rather to 5-(hydroxymethyl)-2-methylpyrimidine[9] (**12**), bis-[(2-methyl-5-pyrimidinyl)methyl]ether (**14**), and (*E*)-1-(5-methyl-2-pyrimidinyl)-2-(2-methyl-5-pyrimidinyl)ethene (**15**).



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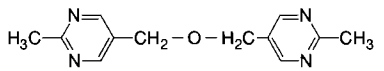

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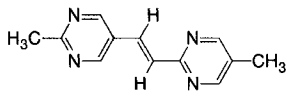

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Another synthetic approach to **1** and **2** was based on the photochemical sulfur extrusion from 2,11-dithia[3.3](2,5)-pyrimidinophanes. Treatment of 2,5-bis(chloromethyl)pyrimidine (**6**) with thiourea readily affords the bis(isothiouronium) salt **9**. This salt is used without further purification in the subsequent cyclization reaction which is accomplished by slow addition of a 1:1 solution of **6** and **9** in methanol/water (19:1) over 8 h to boiling methanol/dimethylformamide (13:1) in the presence of excess cesium hydroxide. This cyclization yields the two anticipated isomeric 2,11-dithia[3.3](2,5)pyrimidinophanes, separable by flash chromatography [**16**: m.p. ≥ 320°C (pseudo-geminal, 3%); **17**: m.p. 300–301°C (pseudo-*para*, 8%); tentative assignment of the isomers based on the ratio of yields]. Photolytic sulfur extrusion of **17** in trimethyl phosphite results in the formation of both [2.2](2,5)pyrimidinophanes [**1**: m.p.

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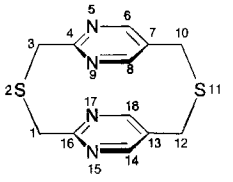
271–272°C (pseudo-geminal, 4%); **2**: m.p. 244–246°C (pseudo-*para*, 28%)], the structures of which have unambiguously been established by X-ray crystallography. The electronic spectra of **1** and **2** and of 2,5-dimethylpyrimidine (**3**) are very similar showing no characteristic features which would have allowed an isomer assignment. Only a slight bathochromic shift of the pyrimidinophane bands is observed [($CHCl_3$): **3**: λ_{max} (lg ε) = 265 nm (3.44), 293 (2.66); **1**: λ_{max} (lg ε) = 267 (3.58), 305 sh (2.86); **2**: λ_{max} (lg ε) = 265 (3.60), 297 sh (2.96)].



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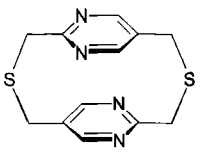

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Besides allowing the assignment of the isomers, the X-ray structure determinations of **1** and **2** give evidence of the strain in these molecules and the deviation of the pyrimidine rings from planarity. The crystallographic data and parameters of structure refinement are given in Table 1[10]. In Figure 1 the structures of **1** and **2** are shown with bond lengths in top-views perpendicular to the least-squares planes through the four non-bridgehead atoms of the pyrimidine moieties [the bond lengths C(1)–C(2) and C(9)–C(10) of **1** and C(1)–C(2) of **2** are shown in Figure 2]. Bond angles are listed in Table 2. The numbering of atoms (Figure 1) follows the "phane" rules. The bond lengths and angles in the pyrimidine moieties are very similar to those of pyrimidine itself[11] and to mean pyrimidine data[12]: C–C 138.7(18), N(1)–C(2) 133.3(13), and N(1)–C(8) 133.8(15) pm.

Both [2.2](2,5)pyrimidinophanes avoid eclipsing of the pyrimidine moieties by a slight shift parallel to the mean ring planes (Figure 1). In **2** the ring components are shifted ca. 25 pm in the C(1i)···C(2) direction (*para* axis) of the molecule, whereas in **1** the pyrimidine moieties are displaced by ca. 20 pm perpendicular to the *para* axis. The side-views of **1** and **2** in Figure 2 show the twist boat-type deformation of the pyrimidine rings which are more bent than the aromatic rings of [2.2]paracyclophane (interplanar angle α = 12.6°)[13]. For **1** and **2**, respectively, the interplanar angles are found to be different. The angles between the N(4), C(5), C(7), N(8) and the C(3), N(4), N(8) planes (**1**: 15.8°; **2**: 15.4°) are larger than those between the N(4), C(5), C(7), N(8) and the C(5), C(6), C(7) planes (**1**: 14.6°; **2**: 13.7°). An increase of the interplanar angle α effects a decrease of the interplanar angle β. Therefore, the exocyclic bonds at the bridgehead carbon atoms of the pyrimidine rings are bent less (range of β: 9.0–5.9°) than in [2.2]paracyclophane (β = 11.2°)[13]. The transannular distances (also the mean distance defined as the vertical distance between the centers of the pyrimidine rings: **1**: 308; **2**: 304 pm) in the pseudo-*para* isomer **2** are a little smaller than those of the pseudo-geminal compound **1**. This reduction is apparently a consequence of the more pronounced lateral shift of the ring components in **2**. The results obtained clearly indicate that the inherent strain of the [2.2](2,5)pyrimidinophanes is mainly accommodated by the "softer" pyrimidine rings and, particularly, by their more bendable N–C–N segments. Related phanes, [2.2](2,5)-

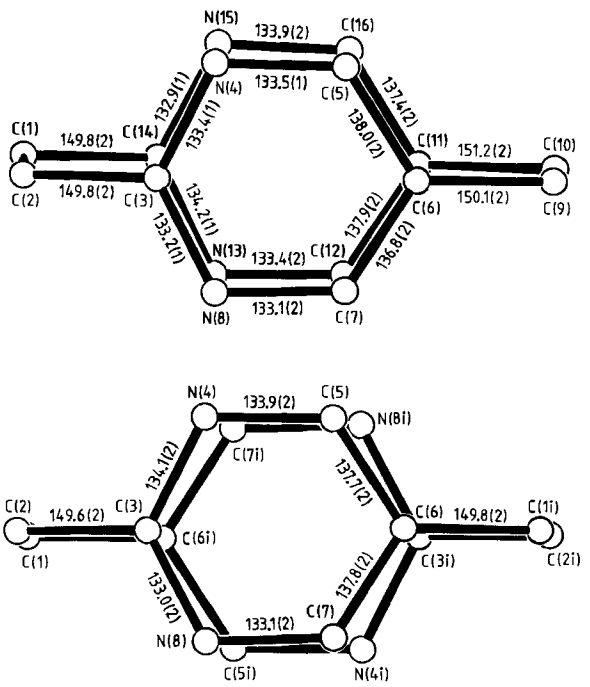

Figure 1. Molecular structures of **1** (top) and **2** (bottom) in top-views perpendicular to the least-squares planes through the four non-bridged atoms of the pyrimidine rings with bond lengths [pm]

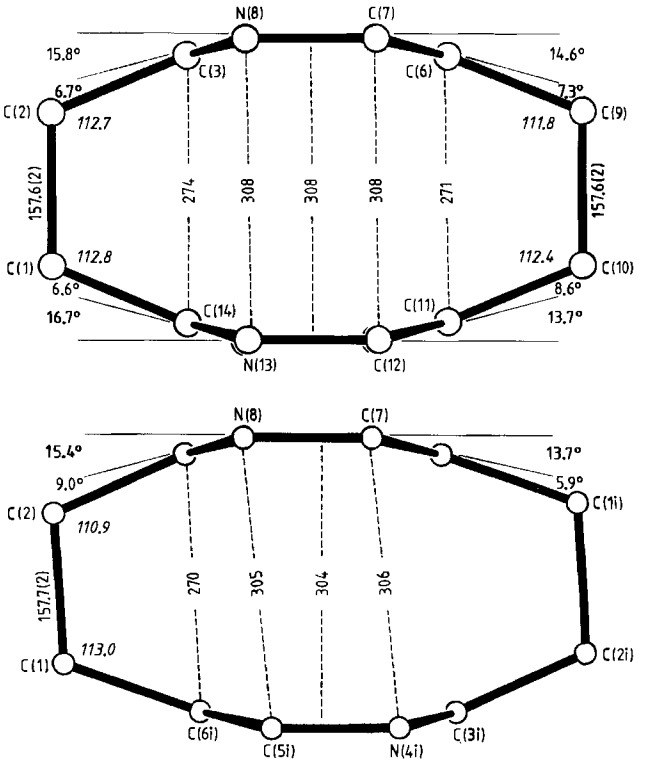

Figure 2. Molecular structures of **1** (top) and **2** (bottom) in side-views along the pyrimidine rings with transannular distances [pm] and bending angles [°] of the pyrimidine rings

pyridinophanes[3] and [2.2](2,5)pyrazinophanes[6,7], also display increased flexibility in their ring components relative to the all-carbon parent system[13]. Apparently, the aza ring components in [2.2]paracyclophanes contribute to a greater "softness" with regard to deviation from planarity.

Experimental

Melting points were determined with a Büchi apparatus and are uncorrected. – UV: Cary 2300 spectrophotometer. – ^1H and ^{13}C NMR: Bruker HX-360 or AM-500 spectrometer at 303 K, unless otherwise stated (with TMS as internal standard). – MS: Dupont CEC 21-492 (70 eV) or Finnigan MAT 212 (70 eV) spectrometer. – TLC was carried out on silica gel (Macherey-Nagel G/UV$_{254}$ plates); flash chromatography was performed on Amicon matrex silica Si (particle size 35–70 μm).

X-ray Structure Analyses of **1** *and* **2**: Intensity data were measured with an Enraf-Nonius CAD-4 four-circle diffractometer, using graphite-monochromated Mo-K_α radiation (λ = 71.069 pm, $\Theta/2\Theta$ scanning technique). The structures 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 atoms[14]. Atomic scattering factors and anomalous dispersion corrections were taken from "International Tables for X-ray Crystallography"[15]. The crystallographic data and the parameters of structure refinement are given in Table 1[10]. Bond lengths are shown in Figure 1, bond angles are listed in Table 2, and the final fractional atomic coordinates and equivalent isotropic thermal parameters [pm^2] for non-hydrogen atoms are given in Table 3.

Table 1. Crystallographic data and refinement parameters of **1** and **2**

	1	**2**
Formula	$C_{12}H_{12}N_4$	$C_{12}H_{12}N_4$
Molecular mass	212.3	212.3
Crystallized from	ethyl acetate	ethyl acetate
Crystal size [mm]	0.2 × 0.2 × 0.15	0.1 × 0.1 × 0.2
Crystal system	monoclinic	monoclinic
Space group	$P2_1/n$	$P2_1/n$
a [pm]	614.5(2)	615.3(1)
b [pm]	1455.5(3)	705.3(1)
c [pm]	1173.0(2)	1138.2(2)
β [°]	103.07(2)	94.12(1)
Z	4	2
Symmetry of molecule in crystal	C_1	C_i
F(000) [e]	448	224
D_X [g cm^{-3}]	1.380	1.431
μ [cm^{-1}] (Mo K_α)	0.818	0.848
Measured reflections	2580	1260
max. $\sin\Theta/\lambda$ [nm^{-1}]	6.82	6.82
Observed reflections [$I \geq 3\sigma(I)$]	1740	922
Refinement *R*	0.047	0.044
max. $\Delta\varrho$/e [nm^{-3}]	200	90

UV Data of **3** *for Comparison:* ($CHCl_3$): λ_{max} (lg ε) = 252 nm sh (3.47), 257 (3.54), 265 (3.44), 293 (2.66).

α-Chlorination of 2,5-Dimethylpyrimidine[8] (**3**): a) To a stirred suspension of 21.6 g (0.2 mol) of **3** and 28.0 g (0.21 mol) of finely divided *N*-chlorosuccinimide (NCS) in 500 ml of boiling anhydrous tetrachloromethane was added 0.80 g of dibenzoyl peroxide. 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 concentrated under reduced pressure. Flash chromatography of the oily residue [silica gel; dichloromethane/ethyl acetate (10:1)] yielded, besides the starting compound **3** [R_f = 0.22 (ethyl acetate)], three products.

Table 2. Bond angles [°] of **1** and **2** with standard deviations in parentheses

Molecule **1**		Molecule **2**	
C(6)-C(9)-C(10)	111.8(1)	C(2)-C(1)-C(6i)	113.0(1)
C(9)-C(10)-C(11)	112.4(1)		
C(1)-C(2)-C(3)	112.7(1)	C(1)-C(2)-C(3)	110.9(1)
C(2)-C(1)-C(14)	112.8(1)		
C(2)-C(3)-N(4)	116.7(1)	C(2)-C(3)-N(4)	117.5(1)
C(1)-C(14)-N(15)	118.1(1)		
C(2)-C(3)-N(8)	118.9(1)	C(2)-C(3)-N(8)	117.5(1)
C(1)-C(14)-N(13)	117.5(1)		
N(4)-C(3)-N(8)	123.9(1)	N(4)-C(3)-N(8)	124.2(1)
N(13)-C(14)-N(15)	124.1(1)		
C(3)-N(4)-C(5)	115.5(1)	C(3)-N(4)-C(5)	115.7(1)
C(14)-N(15)-C(16)	115.4(1)		
C(3)-N(8)-C(7)	115.8(1)	C(3)-N(8)-C(7)	115.4(1)
C(12)-N(13)-C(14)	115.3(1)		
N(4)-C(5)-C(6)	123.2(1)	N(4)-C(5)-C(6)	123.1(1)
C(11)-C(16)-N(15)	123.8(1)		
C(6)-C(7)-N(8)	123.4(1)	C(6)-C(7)-N(8)	124.0(1)
C(11)-C(12)-N(13)	123.6(1)		
C(5)-C(6)-C(7)	113.4(1)	C(5)-C(6)-C(7)	113.3(1)
C(12)-C(11)-C(16)	113.1(1)		
C(5)-C(6)-C(9)	122.9(1)	C(1i)-C(6)-C(5)	124.1(1)
C(10)-C(11)-C(16)	123.4(1)		
C(7)-C(6)-C(9)	123.1(1)	C(1i)-C(6)-C(7)	122.2(1)
C(10)-C(11)-C(12)	122.7(1)		

2,5-Bis(chloromethyl)pyrimidine (**6**): R_f = 0.67 (ethyl acetate): 3.1 g (9%), colorless, slowly decomposing oil. – ^1H NMR ($CDCl_3$): δ = 4.59 (s, 2H, 5-CH_2), 4.76 (s, 2H, 2-CH_2), 8.79 (s, 2H, 4-, 6-H). – MS: *m/z* (%) = 180 (11), 178 (65), 176 (100) [M$^+$], 143 (33), 141 (96) [M$^+$ – Cl], 114 (52).

2-(Chloromethyl)-5-methylpyrimidine (**4**): R_f = 0.53 (ethyl acetate); 4.0 g (14%), colorless crystals, m.p. 41–43°C. – ^1H NMR ($CDCl_3$): δ = 2.34 (s, 3H, 5-CH_3), 4.72 (s, 2H, 2-CH_2), 8.59 (s, 2H, 4-, 6-H); irradiation of 5-CH_3 (δ = 2.34) yielded an NOE response for 4-, 6-H (δ = 8.59). – MS: *m/z* (%) = 144 (33), 143 (12), 142 (100) [M$^+$], 141 (7), 107 (32) [M$^+$ – Cl], 80 (20), 78 (9), 76 (20).

$C_6H_7ClN_2$ (142.6) Calcd. C 50.54 H 4.95 Cl 24.87 N 19.65
Found C 49.91 H 4.80 Cl 25.12 N 19.24

5-(Chloromethyl)-2-methylpyrimidine (**5**): R_f = 0.38 (ethyl acetate); 10.0 g (35%), colorless, slowly decomposing oil. – ^1H NMR ($CDCl_3$): δ = 2.75 (s, 3H, 2-CH_3), 4.54 (s, 2H, 5-CH_2), 8.66 (s, 2H, 4-, 6-H); irradiation of 5-CH_2 (δ = 4.54) yielded an NOE response for 4-, 6-H (δ = 8.66). – MS: *m/z* (%) = 144 (9), 142 (40) [M$^+$], 108 (5), 107 (100) [M$^+$ – Cl], 80 (97).

Table 3. Fractional atomic coordinates and equivalent isotropic thermal parameters [pm²] for non-hydrogen atoms of **1** and **2** with e.s.d.'s of the least significant figure in parentheses; $U_{eq} = 1/3\ \Sigma_i\ \Sigma_j\ U_{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j$

	x	y	z	U_{eq}
Molecule 1				
C(1)	0.3367(3)	0.0731(1)	0.0768(1)	439(6)
C(2)	0.2889(3)	-0.0223(1)	0.1299(1)	460(6)
C(3)	0.1911(3)	-0.0123(1)	0.2353(1)	370(5)
N(4)	0.3329(2)	0.0077(1)	0.3362(1)	427(5)
C(5)	0.2438(3)	0.0508(1)	0.4153(1)	427(6)
C(6)	0.0214(3)	0.0750(1)	0.3951(1)	356(5)
C(7)	-0.1103(3)	0.0294(1)	0.3028(2)	441(6)
N(8)	-0.0301(2)	-0.0137(1)	0.2210(1)	439(5)
C(9)	-0.0613(3)	0.1535(1)	0.4568(2)	513(6)
C(10)	-0.0244(3)	0.2489(1)	0.4003(2)	468(6)
C(11)	0.0757(3)	0.2386(1)	0.2945(1)	374(5)
C(12)	-0.0496(3)	0.2147(1)	0.1856(2)	451(6)
N(13)	0.0343(2)	0.1719(1)	0.1045(1)	450(5)
C(14)	0.2534(3)	0.1528(1)	0.1356(1)	372(5)
N(15)	0.3953(2)	0.1938(1)	0.2232(1)	441(5)
C(16)	0.3017(3)	0.2368(1)	0.3011(2)	440(6)
Molecule 2				
C(1)	0.2233(3)	0.2904(3)	-0.0885(2)	423(6)
C(2)	0.2637(3)	0.3390(3)	0.0465(2)	386(6)
C(3)	0.4122(3)	0.1966(3)	0.1078(1)	321(5)
N(4)	0.3214(2)	0.0399(2)	0.1496(1)	361(5)
C(5)	0.4488(3)	-0.1141(3)	0.1571(2)	354(6)
C(6)	0.6592(3)	-0.1153(3)	0.1233(1)	311(5)
C(7)	0.7449(3)	0.0636(3)	0.1112(2)	369(6)
N(8)	0.6255(3)	0.2210(2)	0.1020(1)	362(5)

b) 16.2 g (0.15 mol) of **3**, 40.0 g (0.3 mol) *N*-chlorosuccinimide, and 1.0 g of dibenzoyl peroxide in 600 ml of anhydrous tetrachloromethane were treated as described above: 10.2 g (38%) of **6**, 1.8 g (8%) of **4**, and 4.5 g (21%) of **5**.

Trimethyl[(5-methyl-2-pyrimidinyl)methyl]ammonium Chloride (**7**): 10.0 g (0.17 mol) of trimethylamine was added to 80 ml of dimethylformamide (DMF), cooled to 0°C. Then a solution of 4.0 g (28 mmol) of **4** in 25 ml of ethyl acetate was added, and the reaction mixture was stirred at room temp. for 12 h. After addition of 40 ml of ethyl acetate, the product was filtered and recrystallized from acetonitrile/ethyl acetate to yield 4.4 g (78%) of colorless needles, m.p. 228°C (dec.). – ^{1}H NMR (CD_3CN): δ = 2.35 (s, 3H, CH_3), 3.27 [s, 9H, $N(CH_3)_3$], 4.70 (s, 2H, CH_2), 8.71 (s, 2H, 4-, 6-H); irradiation of 5-CH_3 (δ = 2.35) yielded an NOE response for 4-, 6-H (δ = 8.82). – MS: *m/z* (%) = 151 (61), 144 (16), 142 (48), 108 (100), 80 (60), 76 (5).

$C_9H_{16}ClN_3$ (201.7) Calcd. C 53.59 H 8.00 Cl 17.58 N 20.83
Found C 53.44 H 8.01 Cl 17.85 N 20.84

Trimethyl[(2-methyl-5-pyrimidinyl)methyl]ammonium Chloride (**8**): 15.0 g (0.25 mol) of trimethylamine in 100 ml of DMF and 10.0 g (70 mmol) of **5** (crude product) in 30 ml of DMF were treated as describe above. The precipitation of the product was completed by adding 50 ml of diethyl ether. The collected product was recrystallized from acetonitrile/ethyl acetate to yield 8.6 g (61%) of colorless crystals, m.p. 224–225°C. – ^{1}H NMR ([D_6]DMSO): δ = 2.69 (s, 3H, CH_3), 3.12 [s, 9H, $N(CH_3)_3$], 4.74 (s, 2H, CH_2), 8.90 (s, 2H, 4-, 6-H); irradiation of 5-CH_2 (δ = 4.74) yielded an NOE response for 4-, 6-H (δ = 8.90). – MS: *m/z* (%) = 151 (34), 150 (26), 144 (12), 142 (40), 107 (100), 80 (53).

$C_9H_{16}ClN_3$ (201.7) Calcd. C 53.59 H 8.00 Cl 17.58 N 20.83
Found C 53.60 H 8.08 Cl 17.70 N 20.86

2,5-Bis(isothiouroniomethyl)pyrimidine Dichloride (**9**): To a solution of 3.0 g (17 mmol) of **6** in 50 ml of butanol a hot solution of 3.0 g (39 mmol) of thiourea in 150 ml of butanol was added with stirring. The mixture was then heated to the boiling point. 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 yield 4.5 g (80%) of pure **9** as colorless needles, m.p. 217°C (dec.). – ^{1}H NMR ([D_6]DMSO): δ = 4.66 (s, 2H, CH_2), 4.76 (s, 2H, CH_2), 8.93 (s, 2H, 4-, 6-H), 9.33 (br. s, NH_2), 9.51 (br. s, 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 29.26 H 4.22 Cl 21.76 N 25.22 S 19.57

Thermolysis of Trimethyl[(5-methyl-2-pyrimidinyl)methyl]ammonium Hydroxide (**10**): To a stirred solution of 12.1 g (60 mmol) of **7** in 150 ml of water, freshly prepared silver(I) oxide [from 22.1 g (0.13 mol) of $AgNO_3$ and 65 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 were added dropwise to a stirred solution of 1.2 g 10*H*-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 were 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 × 50 ml). The combined filtrates were concentrated in vacuo. Flash chromatography of the residue on silica gel with acetone afforded two products.

(E)-1-(5-Methyl-2-pyrimidinyl)-2-(2-methyl-5-pyrimidinyl)ethene (**15**): R_f = 0.50 (acetone); 60 mg (1%), colorless crystals from ethyl acetate/cyclohexane, m.p. 239–240°C. – ^{1}H NMR ($CDCl_3$): δ = 2.34 (s, 3H, 5-CH_3, ring 1), 2.77 (s, 3H, 2-CH_3, ring 2), 7.31, 7.82 (AB q, ^3J = 16 Hz, 2H, HC=CH), 8.58 (s, 2H, 4-, 6-H, ring 1), 8.84 (s, 2H, 4-, 6-H, ring 2); irradiation of 4-, 6-H (δ = 8.58) yielded an NOE response for 5-CH_3 (δ = 2.34), irradiation of 4-, 6-H (δ = 8.84) yielded an NOE response for CH (δ = 7.31, strong) and for CH (δ = 7.82, weak). – ^{13}C NMR ($CDCl_3$): δ = 15.64 (5-CH_3), 25.78 (2-CH_3), 126.87 (C-5, ring 1), 128.83 (C-5, ring 2), 129.82 (CH), 129.98 (CH), 155.26 (2 C, CH, ring 1), 157.31 (2 C, CH, ring 2), 161.37 (C-2, ring 2), 167.75 (C-2, ring 1). – MS: *m/z* (%) = 212 (60) [M^+], 211 (100), 171 (9), 170 (14), 144 (28), 77 (7).

$C_{12}H_{12}N_4$ (212.3) Calcd. C 67.90 H 5.70 N 26.40
Found C 67.67 H 5.71 N 26.12

Bis[(2-methyl-5-pyrimidinyl)methyl]ether (**14**): R_f = 0.30 (acetone); 1.80 g (26%), colorless crystals from hexane, m.p. 98–99°C. – ^{1}H NMR ($CDCl_3$): δ = 2.75 (s, 6H, CH_3), 4.57 (s, 4H, CH_2), 8.63 (s, 4H, CH). – MS: *m/z* (%) = 230 (100) [M^+], 123 (13), 107 (48), 106 (6), 95 (10), 80 (21).

$C_{12}H_{14}N_4O$ (230.3) Calcd. C 62.59 H 6.13 N 24.33
Found C 62.64 H 6.03 N 24.12

Thermolysis of Trimethyl[(2-methyl-5-pyrimidinyl)methyl]ammonium Hydroxide (**11**): 20.1 g (0.1 mol) of **8** in 150 ml of water, silver(I) oxide [from 34.0 g (0.2 mol) of $AgNO_3$ and 100 ml of 2 N NaOH], and 1.2 g of 10*H*-phenothiazine in 1.5 l of toluene were treated as described for **10**. Flash chromatography [silica gel; ethyl acetate/acetone (1:1)] afforded two products.

5-(Hydroxymethyl)-2-methylpyrimidine (**12**): R_f = 0.32 [ethyl acetate/acetone (1:1)]; 0.50 g (4%), colorless needles from petroleum

ether (b.p. 60–95°C), m.p. 102–103°C (ref.[9] 105°C). – ^{1}H NMR ($CDCl_3$): δ = 2.72 (s, 3H, CH_3), 2.95 (br. s, 1H, OH), 4.71 (s, 2H, CH_2), 8.62 (s, 2H, 4-, 6-H).

$C_6H_8N_2O$ (124.1) Calcd. C 58.05 H 6.50 N 22.57
Found C 57.79 H 6.54 N 22.31

Bis[(2-methyl-5-pyrimidinyl)methyl]ether (**14**): R_f = 0.16 [ethyl acetate/acetone (1:1)]; 1.50 g (13%), m.p. 98–99°C.

Pseudo-geminal and Pseudo-para 2,11-Dithia[3.3](2,5)pyrimidinophanes **16** *and* **17**: To 1 l boiling methanol/DMF (13:1), containing 84 g (0.5 mol) of cesium hydroxide monohydrate and kept under argon with stirring, a solution of 5.0 g (28.2 mmol) of **6** and 9.3 g (28.2 mmol) of **9** in 500 ml of methanol/water (19:1) was added dropwise over a period of 8 h (addition rate ca 1 ml/min). Heating at reflux was continued for 2 h. After cooling, the mixture was concentrated to 50 ml under reduced pressure. The residue was then diluted with 100 ml of water and extracted with trichloromethane (8 × 50 ml). The combined extracts were dried with $MgSO_4$ and concentrated to give a residue, which was subjected to flash chromatography [silica gel; trichloromethane/acetone (1:1)].

16: R_f = 0.23; 220 mg (3%), colorless crystals from trichloromethane/acetone, m.p. > 320°C. – UV ($CDCl_3$): λ_{max} (lg ε) = 246 nm (3.75), 262 sh (3.65), 300 sh (3.14). – ^{1}H NMR ($CDCl_3$): δ = 3.82 (s, 4H, probably 10-, 12-H_2, see **14**), 4.11 (s, 4H, 1-, 3-H_2), 8.35 (s, 4H, CH). – MS: *m/z* (%) = 276 (100) [M^+], 243 (20), 170 (33), 140 (15), 139 (20), 138 (19), 107 (83).

$C_{12}H_{12}N_4S_2$ (276.4) Calcd. C 52.15 H 4.38 N 20.27 S 23.20
Found C 52.25 H 4.50 N 20.39 S 23.22

17: R_f = 0.22; 640 mg (8%), colorless needles from trichloromethane/acetone, m.p. 300–301°C (dec.). – UV ($CDCl_3$): λ_{max} (lg ε) = 246 nm (3.72), 268 (3.69), 300 sh (3.09). – ^{1}H NMR ($CDCl_3$): δ = 3.78 (s, 4H, 1-, 10-H_2), 4.06 (s, 4H, 3-, 12-H_2), 8.41 (s, 4H, CH); irradiation of 1-, 10-H_2 (δ = 3.78) yielded an NOE response for CH (δ = 8.41). – MS: *m/z* (%) = 276 (90) [M^+], 170 (11), 141 (16), 140 (13), 139 (100), 138 (26), 107 (64), 105 (19), 101 (20), 98 (12), 91 (18), 85 (12), 83 (40).

$C_{12}H_{12}N_4S_2$ (276.4) Calcd. C 52.15 H 4.38 N 20.27 S 23.20
Found C 52.36 H 4.22 N 20.49 S 23.30

Pseudo-geminal and Pseudo-para [2.2](2,5)Pyrimidinophanes **1** *and* **2**: A solution of 276 mg (1 mmol) of **17** in 250 ml of trimethyl phosphite, kept under argon with stirring, was irradiated (125-W mercury high-pressure lamp, quartz) for 2.5 h. The solvent was evaporated in vacuo, and the residue was treated with 20 ml of cold 2 N hydrochloric acid for 30 min. The mixture was then extracted with 30 ml of dichloromethane to remove decomposition products. The aqueous layer was made basic with ca. 30 ml of 2 N NaOH and extracted with trichloromethane (6 × 50 ml). The combined extracts were dried with $MgSO_4$ and concentrated to give a residue which was subjected to flash chromatography (silica gel). Elution with trichloromethane/acetone (1:1) separated some starting material. Further elution with acetone afforded **1** and **2**.

1: R_f = 0.14 (acetone); 8 mg (4%), colorless crystals from ethyl acetate, m.p. 271–272°C (sealed capillary). – UV ($CDCl_3$): λ_{max} (lg ε) = 267 nm (3.58), 305 sh (2.86). – ^{1}H NMR ($CDCl_3$): δ = 3.13 (s, 4H, 9-, 10-H_2), 3.52 (s, 4H, 1-, 2-H_2), 7.89 (s, 4H, CH). – ^{13}C NMR ($CDCl_3$): δ = 29.77 (C^9-, C^{10}-H_2), 36.98 (C^1-, C^2-H_2), 128.82 (C-6, -11), 155.60 (C^5-, C^7-, C^{12}-, C^{16}-H), 169.41 (C-3, -14). – MS: *m/z* (%) = 213 (9), 212 (100) [M^+], 211 (16), 185 (8), 184 (19), 157 (6), 131 (5), 106 (6), 79 (8).

$C_{12}H_{12}N_4$ (212.3) Calcd. C 67.90 H 5.70 N 26.40
Found C 67.96 H 5.84 N 26.58

2: R_f = 0.12 (acetone); 60 mg (28%), colorless crystals from ethyl acetate, m.p. 244–246°C. – UV ($CDCl_3$): λ_{max} (lg ε) = 265 nm (3.60), 297 sh (2.96). – ^{1}H NMR ($CDCl_3$): δ = 3.07–3.11 (m, 4H, 1-, 9-H_2), 3.39–3.44 (m, 4H, 2-, 10-H_2), 8.07 (s, 4H, CH); irradiation of 1-, 9-H_2 (δ = 3.09) yielded an NOE response for CH (δ = 8.07). – ^{13}C NMR ($CDCl_3$): δ = 28.34 (C^1-, C^9-H_2), 37.51 (C^2-, C^{10}-H_2), 127.06 (C-6, -14), 157.76 (C^5-, C^7-, C^{13}-, C^{15}-H), 169.53 (C-3, -11). – MS: *m/z* (%) = 212 (100) [M^+], 211 (10), 184 (16), 172 (7), 106 (29), 79 (15).

$C_{12}H_{12}N_4$ (212.3) Calcd. C 67.90 H 5.70 N 26.40
Found C 67.70 H 5.92 N 26.53

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[1] H. A. Staab, W. K. Appel, *Liebigs Ann. Chem.* **1981**, 1065.
[2] B. Lintner, D. Schweitzer, R. Benn, A. Rufinska, M. W. Haenel, *Chem. Ber.* **118** (1985) 4907.
[3] H. A. Staab, H.-J. Hasselbach, C. Krieger, *Liebigs Ann. Chem.* **1986**, 751.
[4] H.-J. Hasselbach, C. Krieger, M. Decker, H. A. Staab, *Liebigs Ann. Chem.* **1986**, 765.
[5] F. A. Neugebauer, H. Fischer, *Tetrahedron Lett.* **27** (1986) 5367.
[6] U. Eiermann, C. Krieger, F. A. Neugebauer, H. A. Staab, *Tetrahedron Lett.* **29** (1988) 3655.
[7] U. Eiermann, C. Krieger, F. A. Neugebauer, H. A. Staab, *Chem. Ber.* **123** (1990) 523.
[8] R. Kruse, E. Breitmaier, *Chem.-Ztg.* **101** (1977) 305, and references therein.
[9] A. Schellenberger, W. Rödel, *Angew. Chem.* **76** (1964) 226; *Angew. Chem. Int. Ed. Engl.* **3** (1964) 227.
[10] Further details of the crystal structure investigations of **1** and **2** (including the tables of atomic coordinates, thermal parameters, bond lengths as well as bond and torsional angles) are available on request from the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-7514 Eggenstein-Leopoldshafen 2, on quoting the depository number CSD-54643, the names of the authors, and the journal citation.
[11] P. J. Wheatley, *Acta Crystallogr.* **13** (1960) 80.
[12] F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen, R. Taylor, *J. Chem. Soc., Perkin Trans. 2*, **1987**, S1.
[13] H. Hope, J. Bernstein, K. N. Trueblood, *Acta Crystallogr., Sect. B*, **28** (1972) 1733.
[14] B. A. Frenz and Associates Inc., *Structure Determination Package*, 4th revised edition, College Station, Texas 77840, USA, and Enraf-Nonius, Delft, The Netherlands, 1982; P. Main, S. J. Fiske, S. E. Hull, L. Lessinger, G. Germain, J.-P. Declercq, M. M. Woolfson, *MULTAN 80*, Univ. of York, England, and Louvain, Belgium, 1980.
[15] *International Tables for X-ray Crystallography*, vol. IV, Kynoch Press, Birmingham, 1974.

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