min at room temperature, the reaction mixture was washed with $NaHCO_3$ solution and extracted with CH_2Cl_2. Evaporation of the CH_2Cl_2 gave a crude product that was purified by chromatography (silica gel, hexane–ethyl acetate), providing **11** as orange-red, irregular prisms. **11a** (69%): mp 121.5 °C; ^1H NMR ($CDCl_3$) δ 9.85 (s, 1 H, aromatic), 8.82 (s, 1 H, aromatic), 8.27 (d, 1 H, aromatic, J = 8.1 Hz), 7.90 (m, 3 H, aromatic), 7.52 (m, 3 H, aromatic), 7.42 (dd, 1 H, aromatic, J = 1.9 Hz, J = 5.5 Hz); UV (CH_3CN) nm (log ϵ) 422 (3.96), 320 (3.94), 293 (4.01); high-resolution mass spectra, experimental m/z 298.0223 (calcd m/z 298.0234). **11b** (40%): mp 164 °C; ^1H NMR ($CDCl_3$) δ 9.76 (s, 1 H, aromatic), 8.85 (br s, 1 H, aromatic), 8.26 (br s, 1 H, aromatic), 7.91 (d, 2 H, aromatic, J = 8.7 Hz), 7.88 (m, 1 H, aromatic), 7.41 (br s, 1 H, aromatic), 7.01 (d, 2 H, aromatic, J = 8.7 Hz), 3.90 (s, 3 H, ArOCH_3); UV (CH_3CN) nm (log ϵ) 429 (4.29), 352 (4.07), 239 (4.55); high-resolution mass spectra, experimental m/z 328.0342 (calcd m/z 328.0340). **11c** (70%): mp 182–184 °C; ^1H NMR ($CDCl_3$) δ 10.15 (s, 1 H, aromatic), 8.86 (d, 1 H, aromatic, $J_{6,5}$ = 4.4 Hz), 8.78 (dd, 1 H, aromatic, $J_{6,4}$ = 1.3 Hz, $J_{6,5}$ = 4.8 Hz), 8.25 (d, 1 H, aromatic, J = 8.05 Hz), 8.05 (d, 1 H, aromatic, J = 7.4 Hz), 7.88 (m, 2 H, aromatic), 7.42 (m, 2 H, aromatic); UV (CH_3CN) nm (log ϵ) 428 (3.56), 318 (3.62), 265 (3.64); high-resolution mass spectra, experimental m/z 299.0194 (calcd m/z 299.0187).

Dimer 14 of Compound 3f. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (42 mg, 0.185 mmol) was added to a solution of **3f** (50 mg, 0.185 mmol) in acetonitrile (2 mL). The solution was concentrated to half volume, and upon cooling, a dark solid was collected by filtration and then dried in vacuo. The crude product was purified by column chromatography (silica gel, hexane–ethyl acetate) to provide a red solid: 55 mg; field desorption mass spectrum, m/z 538.

Oxidation of Compound 3e with TCNQ. A hot solution of tetracyanoquinodimethane (5.3 mg, 0.026 mmol) in acetonitrile (1.5 mL) was added to a hot solution of **3e** (7.7 mg, 0.026 mmol) in acetonitrile (1.5 mL). The dark reaction mixture was concentrated to half volume, and after cooling, no precipitate had formed. Evaporation to dryness yielded a residue that on analysis by field desorption mass spectrometry was shown to be a mixture of products other than starting materials. Purification by column chromatography (silica-C_{18}, water–acetonitrile) of this residue provided several fractions. First fraction: **TCNQ-radical anion**[17] **19**; 5.1 mg; UV (CH_3CN) nm 840, 721; in acid 395 nm (TCNQ). Second fraction: **1:1 adduct 20**; 1.6 mg (13%); UV (CH_3CN) nm 550, 318; high-resolution mass spectra, experimental m/z 476.0765 (calcd m/z 476.0766). Third fraction: **3e**; 4.5 mg (58% recovery of starting material); UV (CH_3CN) nm 442, 308. Fourth fraction: **dimer 23**; 1.4 mg (18%); UV (CH_3CN) nm 460, 312; EI mass spectrum 596 (M^+), 532 [M^+ – 2S], 531, 431.

Acknowledgment. We express our appreciation to Dr. R. Kullnig for the determination of the single-crystal X-ray structures.

Registry No. **3a**, 141511-37-7; **3b**, 141511-38-8; **3c**, 141526-51-4; **3d**, 141511-39-9; **3e**, 141511-40-2; **3f**, 141511-41-3; **4a**, 141511-35-5; **4b**, 141511-36-6; **4c**, 117635-47-9; **4d**, 117635-48-0; **4e**, 22779-13-1; **4f**, 29768-12-5; **5a**, 1445-78-9; **5b**, 141511-42-4; **6a**, 886-66-8; **6b**, 91508-53-1; **10**, 141511-43-5; **11a**, 141511-44-6; **11b**, 141511-45-7; **11c**, 141511-46-8; **14**, 141511-47-9; **19**, 34507-61-4; **20**, 141511-49-1; **23**, 141511-48-0.

Supplementary Material Available: Tables of atomic coordinates, bond distances and bond angles, and anisotropic thermal parameters for (pyridinylmethylidene)dithiole **3a** and also for **10**, the bromination product of **3f**, Z-matrices of optimized structures, a table of calculated frequencies for ***Z*-1′**, ***Z*-1″**, and NMR spectral data for compounds **3b**, **3d**, and **10** (22 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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Synthesis and Stereochemical Assignment of Heterocycles Derived from (2*S**,2′*S**,4*R**,4′*R**,6*S**,6′*S**)-4,4′,6,6′-Tetramethylperhydro-2,2′-bipyrimidine

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(2*S**,2′*S**,4*R**,4′*R**,6*S**,6′*S**)-4,4′,6,6′-Tetramethylperhydro-2,2′-bipyrimidine (**1**) reacts with excess formaldehyde in MeOH to give predominantly the tetracycle (1*R**,3*S**,5*R**,7*S**,8b*S**,8c*S**)-1,3,5,7-tetramethylperhydro-3a,4a,7a,8a-tetraazacyclopentano[*def*]fluorene (**2**) and in Et_2O to give exclusively tetracycle (1*R**,3*S**,5*S**,7*R**,8b*S**,8c*S**)-1,3,5,7-tetramethylperhydro-3a,4a,7a,8a-tetraazacyclopentano[*def*]fluorene (**3**). With less formaldehyde, compound **1** yields an unusual 1:5 mixture of trans and cis tricycles, (1*R**,3S*,4a*S**,4b*S**,6*S**,8*R**)-1,3,6,8-tetramethylperhydro-4,5,8a,9a-tetraazafluorene (**5**) and (1*R**,3*S**,4a*S**,4b*S**,6*R**,8*S**)-1,3,6,8-tetramethylperhydro-4,5,8a,9a-tetraazafluorene (**6**), respectively, in MeOH solvent but gives almost exclusively the trans tricycle **5** in Et_2O. The structure of tetracycle **2** is supported by X-ray crystallographic data. Compounds **3** and **6** represent new structural types, and they appear to be conformationally stable. A mechanistic scheme for the formation of the tricycles and tetracycles which is consistent with the observed stereochemical changes is proposed.

Introduction

The condensation of 1,3-alkanediamines with glyoxal was rediscovered recently as a convenient route to perhydro-2,2′-bipyrimidines [2,2′-bis(hexahydropyrimidines)].[1] X-ray crystallographic analysis has since provided the first unambiguous proof of the molecular structure of perhydrobipyrimidines as their free amines,[2] and ^{13}C NMR data have been used to support the presence of similar structures in solution.[3] Subsequent conversion of perhydrobipyrimidines into perhydro-4,5,8a,9a-tetraazafluorenes and perhydro-3a,4a,7a,8a-tetraazacyclopentano[*def*]fluorenes has also been demonstrated in relatively simple cases.[1] The latter

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0022-3263/92/1957-3901$03.00/0

transformations are important because they allow rapid entry into a series of new, comparatively rigid nitrogen heterocycles. Unlike their cis perhydro-3a,5a,8a,10a-tetraazapyrene counterparts[4] and certain related heterocycles,[5-7] including the 1,4,5,8-tetraazadecalins,[6,7] the former polycyclic heterocycles do not show dynamic NMR behavior in solution. Instead, the cis and trans tricyclic and cis tetracyclic compounds retain their structural integrity, except for ring tautomerism which occurs primarily in protic solvents and to a degree depending upon substituents. Such rigidity should impart advantages to these compounds in applications wherein the amines serve as ligands or take part in coordination or hydrogen bonding. Similar highly ordered systems are a key feature of many enzyme mimics, including those developed by Rebek,[8] Nolte,[9] and Mock.[10]

In continuation of our studies of highly ordered polycyclic systems derived from perhydro-2,2'-bipyrimidines, we have examined a series of compounds derived from *meso*-2,4-pentanediamine. Structural variants of the tetracyclic and tricyclic nucleus have been identified, and the mechanistic implications of their formation are discussed.

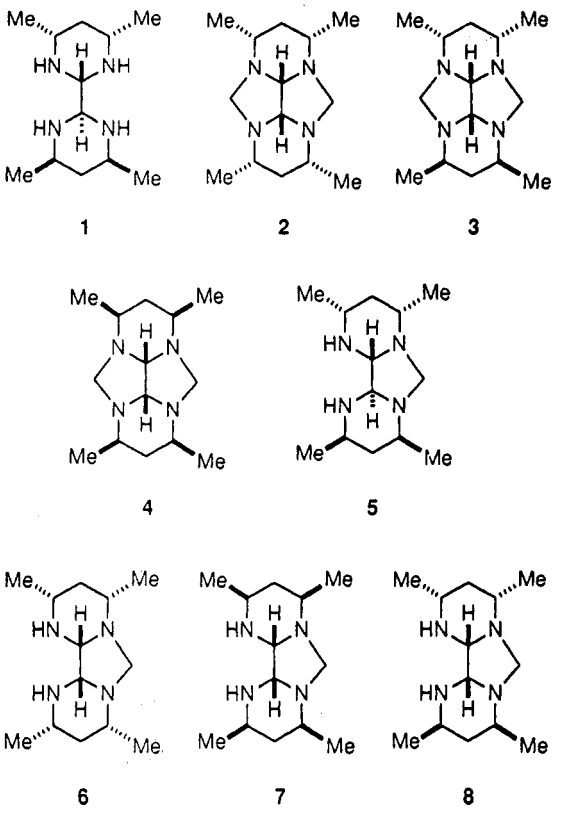
Results and Discussion

The molecular structure of perhydrobipyrimidine **1** has been determined in the solid state by X-ray crystallography.[2] Unlike previous precursors to the polycyclic compounds, and crucial to the findings here, this molecule allows changes in configuration at the aminal carbons to be monitored.

When perhydrobipyrimidine **1** was treated in refluxing MeOH with 2–4 mol equiv of formaldehyde, reaction for 1.5 h in the case of 4 equiv and overnight in the case of 2 equiv gave a 3:1 mixture of isomeric tetracycles **2** and **3**. The major isomer was separated in 30% yield by fractional crystallization from Et_2O. Its symmetrical nature was evident from the relatively few proton and carbon signals in its ^1H and ^{13}C NMR spectra (seven proton signals, ratio 1:6:1:2:1:1:1, and five carbon signals, 1 × CH_3, 2 × CH_2, and 2 × CH). The methyl groups were determined to be in equatorial positions from the magnitudes of the vicinal proton spin coupling constants of the associated methine protons ($^3J_{H-H}$ 11.7, 2.7 Hz) as measured from the methylene proton signals at C2 and C6.

There are two configurations that the symmetrically substituted tetracycle might have adopted, **2** or **4**. Single-crystal X-ray crystallographic analysis (see supplementary material) indicated that the molecule resembled the former in which the bridgehead hydrogens and methyl groups were in a trans relationship **2a** (Scheme I). The molecular structure also revealed that the nitrogens were pyramidalized through somewhat flattened (e.g., the combined C–N–C angles about N(1), N(2), N(3), and N(4) range from 336.3° to 341.9°) so that the bridging methylene group was directed in a pseudoaxial position with respect to each hexahydropyrimidine ring. As a consequence, the nonbonded electrons on the nitrogen atoms were directed into equatorial positions and aligned with the bridgehead C–H bonds. The latter finding was used earlier to rationalize the large one-bond C–H spin couplings observed for this and all former cyclopentanotetraazafluorene tetracycles;[3] novel arrangements of the trans tricycles were also identified by an extension of this technique.[3]

Chart I



Previously it had been found that the condensation of perhydrobipyrimidines with aldehydes also proceeded in ether solvents. In practice, treatment of **1** with 4 molar equiv of formaldehyde (as formalin) in Et_2O at reflux gave the second, previously minor tetracycle, **3**, as virtually the sole product in 68% yield. The compound could not be crystallized and was characterized as an oil. Its ^1H and ^{13}C NMR features indicated that the substance had nonequivalent hexahydropyrimidine rings. However, the molecule retained a plane of symmetry that bisected it and passed along the central C–C bridging bond. Again, all four methyl substituents appeared to reside in equatorial positions, as deduced from the magnitudes of vicinal spin coupling constants ($^3J_{H-H}$ 11.7, 2.7 Hz for protons at C2 and $^3J_{H-H}$ 12.1, 3.9 Hz for protons at C6). Structure **3** is consistent with these findings if the two hexahydropyrimidine rings adopt different configurations. One possible consequence is for the two rings to have different chair conformations, **3a** (Scheme I), while another is for one ring to reside in a chair conformation while the other rests in a boat or twist-boat conformation **3b**. These two arrangements are related as conformers and are therefore indistinguishable at ambient temperature. The former structure involves placement of the bridging methylene groups in pseudoequatorial positions rather than the pseudoaxial positions found in **2a**, but with this comes major concomitant interring interactions with no obvious energy advantages. Three-dimensional structures **2a** and **3b** were therefore deduced for the "symmetrical" and "unsymmetrical" tetracycles.

Treatment of perhydrobipyrimidine **1** with 1 mol equiv of formaldehyde in MeOH at room temperature, normal

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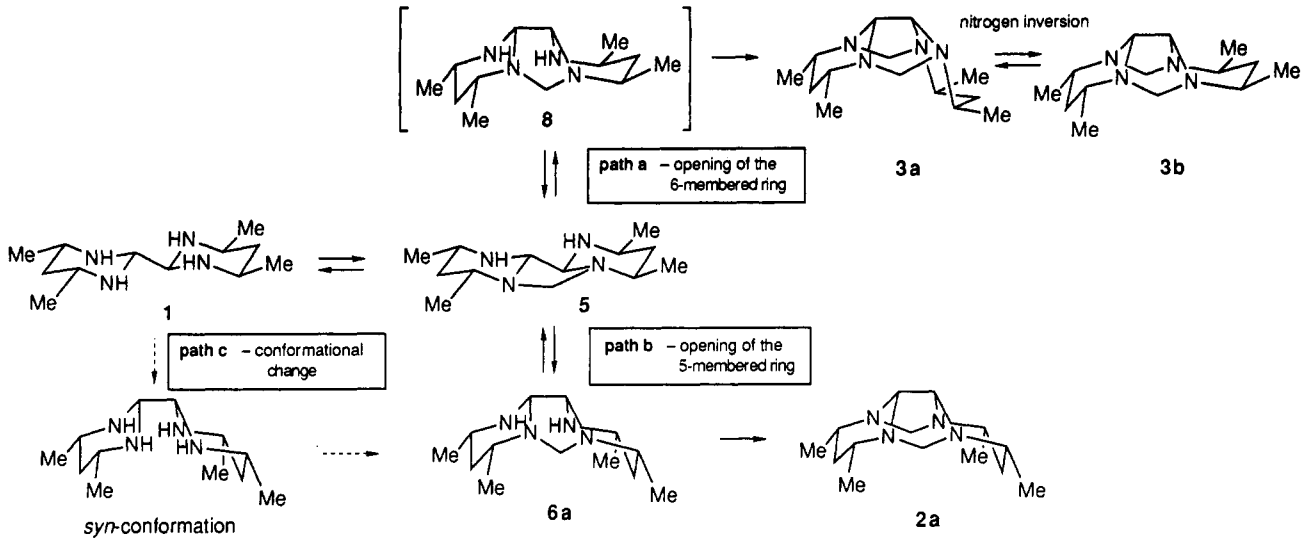
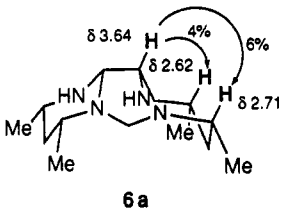
Scheme I. Mechanistic Pathways Available during the Condensation of Perhydrobipyrimidine 1 with Formaldehyde





6a

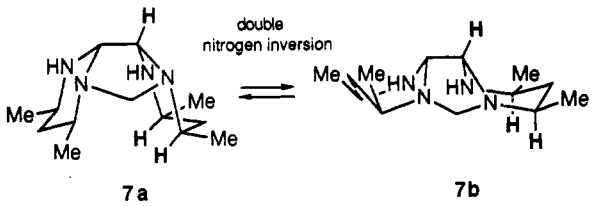


Figure 1. Possible arrangements of the cis tricycles 6 and 7 and results of NOE experiments.

conditions for formation of tricyclic tetraazafluorene products, gave no noticeable reaction. Warming the solution in MeOH to reflux gave a mixture of tricycles after 1 h. In all previous examples the trans-fused tricycles predominated in such product mixtures, sometimes to the exclusion of the cis-fused tricycles. However, 1 afforded a 1:5 mixture of trans and cis tricycles **5** and **6**, respectively, from which the cis tricycle **6** was isolated pure in 29% yield.

Curiously, treatment of 1 with an equimolar amount of formaldehyde in Et_2O at reflux gave only the trans-tricycle **5**, admixed with an equal quantity of unchanged perhydrobipyrimidine 1, after 1 h. Similar treatment of perhydrobipyrimidine 1 with 2 mol equiv of formaldehyde in Et_2O for 1 h consumed all the starting material but again yielded only the trans tricycle **5** which was isolated in 62% yield.

The trans and cis configurational assignments of **5** and **6** were based mainly upon the number and multiplicity of proton signals in the ^1H NMR spectra and were supported by ^{13}C NMR data. In both cases the methyl groups were also found to reside in equatorial configurations. The magnitudes of the one-bond C–H spin coupling constants from the equivalent methine bridgehead carbons from each isomer, $^1J_{C-H}$ 141.8 Hz and $^1J_{C-H}$ 149.8 Hz, respectively, demonstrated that the orientation of the C–H bonds relative to the nonbonded electrons on nitrogen were different.[3] The C–H bonds of the trans isomer must have resided in axial configurations, as found in earlier examples of the trans tricycles, and its structure, **5**, then appears to be settled and its formation is not exceptional.

In contrast, the nonbonded electrons on nitrogen in the cis isomer **6** appears to have been more closely aligned with the bridgehead C–H bonds. This is the first example in which such a cis tricycle has been obtained in the pure state.[11] Comparison of the one-bond C–H coupling data (e.g., $^1J_{C-H}$ 149.8 Hz for the bridgehead aminal carbon) with those for tetracycle **2** ($^1J_{C-H}$ 164.7 Hz),[3] prompted us to consider an analogous structure to **2**, represented by **6a** (Figure 2), for the cis tricycle. The smaller observed coupling for **6** than that observed for the tetracycle could be attributed to the occurrence of secondary nitrogens in the tricycle and therefore the possibility of a significant contribution from nitrogen inversion at these centers. Inversion of this type would lead to reduced interaction between the nonbonded electrons on nitrogen and the central C–H bond.

Another cis tricyclic structure, **7**, with *cis*-methyl substituents and bridgehead hydrogens was also considered. For this isomer to have equatorial methyl groups, the hexahydropyrimidine rings must have resided in alternative chair **7a** or, more likely, boat **7b** arrangements of the rings (Figure 1). NOE experiments provided a clear distinction between structures **6a** and **7a** or **7b**. Most notably, irradiation of the bridgehead proton signal (δ 3.64) gave 4% and 6% enhancements of the methine proton signals at δ 2.62 and 2.71, respectively, a result consistent only with structure **6a**. Irradiation of the methine signals gave reciprocal enhancements which supported the structural assignment and others which were useful in fully assigning the remaining proton and carbon NMR signals.

Mechanistic Comments. The reactions using perhydrobipyrimidine 1 were much slower than those previously experienced with other perhydrobipyrimidines. These observations were made using identical batches of formalin thus ruling out the effect of acid impurities. One explanation for the differences in rates is the greater steric demand of the 4,6-dimethyl-substituted hexahydropyrimidine rings. This may have a bearing on the success of condensation reactions when groups larger than methyl radicals are present in the 4- and 6-positions and when

(11) Examples which were admixed with the corresponding trans isomers were reported in ref 1.

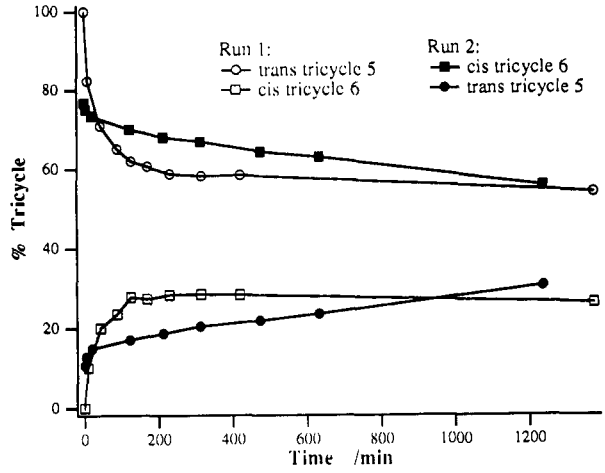


Figure 2. Variation of tricycle concentrations in deuteriomethanol at 60 °C with time.

larger aldehydes are used in the condensation.

The marked change in selectivity of the reactions in going from MeOH to ether solvents is also noteworthy. Others have noted the decrease in the rate of formation of aminal bonds in nonpolar solvents such as toluene and nitrobenzene.[7] Presumably, nonpolar solvents like Et_2O would slow the first step of any condensation reactions because the reactions involve the generation of very polar, if not ionic intermediates; these species would be extremely reactive. Methanol could stabilize such intermediates due to its strong dipole moment. However, as an hydroxylic solvent, MeOH might also react with intermediate immonium ions ($R^1R^2N^+{=}CH_2$) to generate long-lived, neutral amino ether species (e.g., $R^1R^2N{-}CH_2{-}OMe$). Reactions carried out in Et_2O should therefore give primary products while those carried out in MeOH might lead to secondary products or products obtained under equilibrating conditions. The preference with which **1** gives the trans tricycle **5** in Et_2O is therefore easily understood. This reaction simply involves bridging of two nitrogens from **1** in its preferred configuration and conformation. Ring opening of one of the hexahydropyrimidine rings of **5** and reclosure to generate a cis ring fusion (path a, Scheme I) would then lead to a direct precursor of the less symmetrical tetracycle **3**. Interestingly, the intermediate cis tricycle **8** could not be detected in our studies, but pure samples of tetracycles **2** and **3** were found not to isomerize or revert to tricycles upon warming their solutions in MeOH. One can also speculate that the tetracycle **2** is derived from the trans tricycle **5**. Conversion to the symmetrical tetracycle **2** must involve the following sequence: opening of the imidazolidine ring, rotation about the central C–C bridging bond, and reclosure to give the intermediate cis tricycle **6** (path b, Scheme I). Generation of the cis-fused tricycle **6** might have proceeded directly from the syn conformation of the perhydrobipyrimidine **1** (path c, Scheme I) but is more likely to have occurred through isomerization of the trans tricycle **5**. Indeed, warming a solution of the pure trans tricycle **5** in CD_3OD at 60 °C in the probe of the NMR spectrometer afforded a gradual decrease in the concentration of **5** with a concomitant increase in the concentration of the cis isomer **6** until an optimum ratio of trans/cis isomers of 67:33 was reached after 4.0 h (see Figure 2). In this experiment there was also detected minor amounts of the parent perhydrobipyrimidine **1** and the two tetracycles **2** and **3**. Formation of **1** and **2** supported a mechanism involving opening of the five-membered ring of tricycle **5**. However, the presence of both tetracycles indicated that a mechanism involving opening of the six-membered ring operated to at least some extent.

A sample containing primarily the cis tricycle **6** was also found to isomerize to the trans tricycle **5** in CD_3OD, but the process in this direction occurred much more slowly (Figure 2) and had not reached equilibrium even after 21 h. Equilibration between the tricycles is therefore possible, and the trans tricycle **5** is the more stable partner, but the barrier to isomerization is greater from the cis tricycle **6**.

From these simple experiments a reaction scheme for the formation of tricycles and tetracycles has been deduced and is expressed in Scheme I. The driving force for the latter transformation must be the greater stability of the cis tricycle **6** over the trans isomer **5**. However, the reason for this preference is not at all clear.

In conclusion, it is noteworthy that all the heterocycles identified in this study are derivatives of one or other of the eight major configurations of the perhydrobipyrimidine skeleton.[1] Compounds **3** and **6** represent new structural types, and it is significant that they are conformationally stable. In addition, this work has provided strong evidence that trans tricycles are precursors of the cis tricycles and that they are formed more readily than the latter; two mechanisms can operate in the conversion of trans to cis tricycles.

Experimental Section

Condensation of (2*S,2′*S**,4*R**,4′*R**,6*S**,6′*S**)-4,4′,6,6′-Tetramethylperhydro-2,2′-bipyrimidine (1) with Formaldehyde. (a) With 4 equiv of Formaldehyde in MeOH.** Formalin (0.7 mL of 40%, 10.0 mmol) was added to a solution of (2*S**,2′*S**,4*R**,4′*R**,6*S**,6′*S**)-4,4′,6,6′-tetramethylperhydro-2,2′-bipyrimidine (1)[1] (0.6 g, 2.7 mmol) in MeOH (12 mL), and the mixture was heated at reflux for 1.5 h. The mixture was allowed to cool and the MeOH removed by rotary evaporation to give a crystalline residue (0.9 g) which consisted of a symmetrical and an unsymmetrical tetracycle in a ratio of 3:1. Recrystallization from Et_2O gave **(1*R**,3*S**,5*R**,7*S**,8b*S**,8c-*S**)-1,3,5,7-tetramethylperhydro-3a,4a,7a,8a-tetraazacyclopentano[*def*]fluorene** (**2**) as white prisms (0.2 g, 30%), mp 128–130 °C, suitable for X-ray analysis: IR (Nujol) 3350, 3244, 2784, 2702, 1690, 1382, 1360, 1321, 1284, 1222, 1203, 1173, 1126, 1099, 1022, 919, 891, 868, 752, 675, 583, 484, 428, 333 cm^{-1}; ^1H NMR see ref 3; ^{13}C NMR δ 20.51 (q, J = 121.0 Hz, 1-CH_3, 3-CH_3, 5-CH_3 and 7-CH_3), 29.30 (t, J = 119.5 Hz, C2 and C6), 51.04 (d, J = 133.5 Hz, C1, C3, C5 and C7), 61.05, (dd, J = 153.2, 133.2 Hz, C4 and C8), 77.91 (d, J = 164.7 Hz, C8b and C8c); mass spectrum m/z 251 (M + 1, 7), 250 (M, 51), 249 (100), 235 (38), 206 (21), 192 (20), 179 (75), 164 (34), 152 (24), 138 (20), 109 (24), 98 (60), 69 (25), 56 (67), 41 (38). The same results were obtained when 2 equiv of formalin were used and the mixture was allowed to reflux overnight.

(b) With 4 equiv of Formaldehyde in Et_2O. Formalin (2.9 mL of 40%, 30.9 mmol) was added to a solution of the 4,4′,6,6′-tetramethyl-2,2′-bipyrimidine (1) (2.0 g, 8.8 mmol) in Et_2O (40 mL), and the mixture was heated at reflux for 1.5 h. The mixture was cooled and the solvent removed to give an oily residue (1.9 g). The residue consisted of mainly one compound which was purified by Kugelrohr distillation twice, 120 °C (0.05 mmHg), 120 °C (0.07 mmHg), to give the unsymmetrical tetracycle **(1*R**,3*S**,5*S**,7*R**,8b*S**,8c*S**)-1,3,5,7-tetramethylperhydro-3a,4a,7a,8a-tetraazacyclopentano[*def*]fluorene** (**3**) as a colorless oil (1.5 g, 68%), bp 120 °C (0.07 mmHg): IR (film) 3393, 3235, 2965, 2924, 2879, 2740, 2701, 2674, 1656, 1454, 1390, 1368, 1292, 1248, 1223, 1204, 1192, 1173, 1087, 1071, 1030, 1016, 970, 917, 872, 660 cm^{-1}; ^1H NMR δ 0.92 (dt, J = 13.2, 2.7 Hz, $H_{eq}2$), 1.12 (d, J = 6.2 Hz, 5-CH_3 and 7-CH_3), 1.14 (d, J = 6.8 Hz, 1-CH_3 and 3-CH_3), 1.34 (dt, J = 13.9, 12.1 Hz, $H_{ax}6$), 1.40 (dt, J = 13.1, 11.7 Hz, $H_{ax}2$) 1.60 (dt, J = 14.0, 3.9 Hz, $H_{eq}6$) 2.77 (ddq, J = 12.2, 3.9, 6.2 Hz, H5 and H7), 3.20 (ddq, J = 11.7, 2.7, 6.9 Hz, H1 and H3), 3.44 (d, J = 2.2 Hz, H_a4 and H_a8) 4.00 (d, J = 2.2 Hz, H_b4 and H_b8), 4.65 (d, J 4.9 Hz, H8c), 4.80 (d, J = 4.9 Hz, H8b); ^{13}C NMR δ 20.10 (q, J = 124.8 Hz, 1-CH_3 and 3-CH_3), 23.03 (q, J =

125.3 Hz, 5-CH_3 and 7-CH_3), 28.98 (t, J = 125.2 Hz, C2), 36.90 (t, J = 125.2 Hz, C6), 50.49 (d, J = 134.0 Hz, C1 and C3), 52.14 (d, J = 129.6 Hz, C5 and C7), 70.17 (t, J = 134.4 Hz, C4 and C8), 73.33 (d, J = 169.1 Hz, C8c), 77.98 (d, J = 164.3 Hz, C8b); mass spectrum m/z 251 (M + 1, 6), 250 (M, 34), 249 (85), 235 (39), 176 (66), 98 (56); calcd for $C_{14}H_{25}N_4$ m/z 249.2079, found m/z 249.2069.

(c) With 1 equiv of Formaldehyde in MeOH. Formalin (0.4 mL of 40%, 5.6 mmol) was added to a solution of the 4,4′,6,6′-tetramethyl-2,2′-bipyrimidine (1) (1.3 g, 5.6 mmol) in MeOH (10 mL). The mixture was heated at reflux for 1 h. Removal of the solvent gave an oily residue (1.6 g) which was shown from ^1H NMR examination to be trans and cis tricycles **5** and **6** in a 1:5 ratio. Distillation twice by Kugelrohr gave **(1*R**,3*S**,4a*S**,4b*S**,6*R**,8*S**)-1,3,6,8-tetramethylperhydro-4,5,8a,9a-tetraazafluorene (6)** in about 95% purity as a colorless oil (0.4 g, 29%), bp 150 °C (1.0 mmHg): IR (film) 3390 br, 3290 br, 2967, 2930, 1657, 1458, 1438, 1380, 1352, 1338, 1319, 1302, 1221, 1203, 1164, 1117, 1089, 1035, 1018, 936, 880, 856, 799, 707, 623 cm^{-1}; ^1H NMR δ 0.79 (dt, J = 13.1, 11.1 Hz, $H_{ax}2$ and $H_{ax}7$), 0.93 (d, J = 6.6 Hz, 1-CH_3 and 8-CH_3) 0.99, (d, J = 6.5 Hz, 3-CH_3 and 6-CH_3), 1.32 (dt, J = 13.1, 2.8 Hz, $H_{eq}2$ and $H_{eq}7$), 2.62 (m, H3 and H6), 2.71 (ddq, J = 11.1, 2.8, 6.7 Hz, H1 and H8), 3.32 (d, J = 4.2 Hz, H_a9), 3.64 (brs, H4a and H4b), 3.85 (d, J = 4.2 Hz, H_b9); ^{13}C NMR δ 20.23 (q, J = 123.5 Hz, 1-CH_3 and 8-CH_3),[12] 22.42 (q, J = 122.7 Hz, 3-CH_3 and 6-CH_3),[12] 39.81 (t, J = 119.5 Hz, C2 and C7), 50.51 (d, J = 132.9 Hz, C1 and C8),[12] 53.39 (d, J = 129.6 Hz, C3 and C6),[12] 62.17 (t, J = 146.5 Hz, C9), 75.90 (d, J = 149.8 Hz, C4a and C4b); mass spectrum m/z 238 (M, 2), 237 (7), 126 (66), 113 (100); calcd for $C_{13}H_{26}N_4$ m/z 238.2157, found m/z 238.2129.

(d) With 2 equiv of Formaldehyde in Et_2O. Formalin (1.7 g of 36%, 17.6 mmol) was added to a solution of the 4,4′,6,6′-tetramethyl-2,2′-bipyrimidine (1) (2.0 g, 8.8 mmol) in Et_2O (40 mL), and the mixture was heated at reflux for 1 h. Removal of the solvent gave an oil (2.2 g) which consisted of one trans tricyclic compound. Kugelrohr distillation 140 °C (0.1 mmHg) and crystallization and recrystallization from EtOAc/light petroleum gave **(1*R**,3*S**,4a*S**,4b*S**,6*S**,8*R**)-1,3,6,8-tetramethylperhydro-4,5,8a,9a-tetraazafluorene (5)** as a sticky white solid (1.3 g, 62%), mp 50–65 °C: IR (Nujol) 3502, 3475, 3274, 3218, 1686, 1464, 1381, 1337, 1300, 1276, 1246, 1213, 1185, 1131, 1108, 1084, 1065, 1041, 984, 965, 928, 907, 887, 836, 796, 700, 660, 551 cm^{-1}; ^1H NMR δ 0.89 (dt, J = 13.2, 11.0 Hz, $H_{ax}2$ and $H_{ax}7$), 1.00 (d, J = 6.3 Hz, 1-CH_3 and 8-CH_3 or 3-CH_3 and 6-CH_3), 1.07 (d, J = 6.4 Hz, 1-CH_3 and 8-CH_3 or 3-CH_3 and 6-CH_3), 1.58 (dt, J = 13.1, 3.1 Hz, $H_{eq}2$ and $H_{eq}7$), 2.60 (ddq, J = 10.6, 3.0, 6.4 Hz, H1 and H8), 2.72 (ddq, J = 11.4, 3.2, 6.4 Hz, H3 and H6), 3.27 (s, H4a and H4b),[13] 3.78 (s, H9);[13] ^{13}C NMR δ 20.49 (q, J = 125.1 Hz, 1-CH_3 and 8-CH_3 or 3-CH_3 and 6-CH_3), 22.01 (q, J = 125.5 Hz, 1-CH_3 and 8-CH_3 or 3-CH_3 and 6-CH_3), 42.79 (t, J = 125.4 Hz, C2 and C7), 51.15 (d, J = 133.4 Hz, C3 and C6), 54.57 (d, J = 129.4 Hz, C1 and C8), 65.40 (t, J = 146.8 Hz, C9), 78.56 (d, J = 141.8 Hz, C4a and C4b); mass spectrum m/z 238 (M, 5), 126 (69), 113 (100), 87 (18), 69 (20), 59 (17), 56 (15), 44 (31); calcd for $C_{13}H_{25}N_4$ m/z 237.2079, found m/z 237.2089.

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Supplementary Material Available: Crystal structure determination for tetracycle 2, including all positional and thermal parameters, tables of bond lengths, angles, and torsional angles, and an ORTEP representation of the structure (9 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(12) Signal assignments may be interchanged with those of the same type.

(13) Assignments confirmed by C–H correlation experiments.