Pergamon

Tetrahedron Vol. 50, No. 8, pp. 2497-2506, 1994

0040-4020/94 $6.00+0.00

0040-4020(93)E0177-H

Synthesis and Stereochemical Assignment of 2,5-*trans*-2',5'-*trans*-5,5'-Dimethylperhydro-2,2'-bipyrimidine and Heterocycles Derived from Its Condensation with Formaldehyde

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Abstract. 2-Methylpropane-1,3-diamine reacts with glyoxal to give 2,5-*trans*-2',5'-*trans*-5,5'-dimethylperhydro-2,2'-bipyrimidine **5**. Subsequent treatment of **5** (i) with one equiv of HCHO gives a tricyclic product mixture from which (2*R**,4a*R**,4b*R**,5*R**)-2,7-dimethylperhydro-4,5,8a,9a-tetraazafluorene **6a** is obtained crystalline, and (ii) with two equiv of HCHO gives a 1.5 : 1.0 mixture of (2*R**,6*S**,8b*R**,8c*R**)-dimethylperhydro-3a,4a,7a,8a-tetraazacyclopentano-[*def*]fluorene **11** and (2*R**,6*R**,8b*R**,8c*R**)-dimethylperhydro-3a,4a,7a,8a-tetraazacyclopentano[*def*]fluorene **12** from which **11** is obtained pure. The configurational assignment of **6a** is made on the basis of molecular mechanics calculations and these lead to a revision of a previous conformational assignment of the parent tricycle 4a,4b-*trans*-perhydro-4a,5,8a,9a-tetraazafluorene **7** and of its 9-methyl derivative **9**.

Assignment of the relative configuration of substituents in heterocycles derived through aldehyde condensation reactions with perhydro-2,2'-bipyrimidines **1** remains a non-trivial exercise.[1] Configurationally different structural types of the three main heterocyclic skeletons, **1** – **3**, have been identified recently by using techniques such as X-ray crystallography[2,3] and ^1H and ^{13}C NMR spectroscopic analysis.[3-5] The types of structures that are generated appear to depend upon the substituents attached to the skeleton and upon the reaction conditions. For example, in an earlier paper,[5] condensation of the *meso*-tetramethyl derivative **4** with excess formaldehyde gave a 3 : 1 mixture of tetracycles with different heterocyclic configurations when carried out in MeOH. In contrast, only the minor component was produced when Et_2O was used as the solvent. There is a need to extend these studies to allow the discovery of other structural types and to better understand the control factors responsible for their selective formation.

In this paper a closely related series of compounds, the unknown perhydro-2,2'-bipyrimidine derived from 2-methylpropane-1,3-diamine and glyoxal, and the products from its reactions with HCHO will be described. A revision of some earlier conclusions concerning structural assignments of tricycles **2** will be shown to be warranted and will be discussed.

RESULTS AND DISCUSSION

Condensation of 2-methylpropane-1,3-diamine with glyoxal afforded perhydro-2,2'-bipyrimidine **5** with the now familiar arrangement of puckered, equatorially bridged hexahydropyrimidine rings ($^1J_{C2-H2}$ = 142.0

Hz) (Fig. 1).[4,6] As expected, the methyl substituents also resided in equatorial positions ($^3J_{H5\text{-}Ha4\ (Ha6)}$ = 11.3 Hz and $^3J_{H5\text{-}He4\ (He6)}$= 4.2 Hz) and thus were in a *trans* relationship with respect to the second ring system.

Treatment of the perhydrobipyrimidine **5** with an equimolar amount of HCHO in MeOH readily gave tricycle, **6**, in 52% yield, after distillation. The ^1H and ^{13}C NMR spectra showed clearly the presence of a two-fold axis of rotation, and therefore the *trans* nature of the tricycle, through equivalence of the signals for the carbons and protons at positions 4a and 4b while at the same time showing equivalence of the protons on the bridging methylene group at position 9. In addition it was noted that the methyl substituents were equivalent and located in equatorial positions. However it was not possible to distinguish stereoisomers **6a** or **6b** from the foregoing data. Surprisingly, one-bond C–H coupling data ($^1J_{C4a\text{–}H4a} = {}^1J_{C4b\text{–}H4b}$ = 152.5 Hz) indicated that the bonds to the protons at the bridgehead positions, 4a and 4b, were closely aligned with the lone pairs on adjacent nitrogens in the two six-membered rings.[4] This is the third occasion upon which such large one-bond couplings have been detected in *trans*-tricyclic molecules of type **2**; the other examples are the parent tricycle **7** ($^1J_{C4a\text{–}H4a} = {}^1J_{C4b\text{–}H4b}$ = 149.2 Hz), for which a structure with an axial central bridging bond between the two six-membered rings was suggested, and **9** ($^1J_{C4a\text{–}H4a}$ = 151.0 Hz; $^1J_{C4b\text{–}H4b}$ = 139.1 Hz), for which the C4a-C4b bond was proposed to be axial with respect to one six-membered ring and equatorial with respect to the other.[4]

Changing the NMR solvent from $CDCl_3$ to C_6D_6 did not influence greatly the $^1J_{C\text{-}H}$ values for **7** ($^1J_{C4a\text{-}H4a} = {}^1J_{C4b\text{-}H4b}$ = 151.4 Hz) and for its perhydrobipyrimidine precursor ($^1J_{C2\text{-}H2}$ = 140.9 Hz). Hence equilibrium factors that might have been affected by solvent appeared to be of little importance.

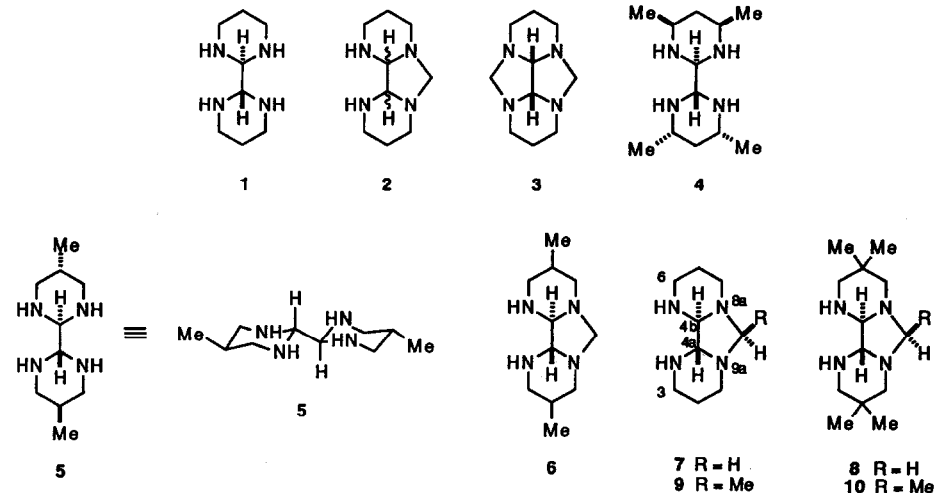


Figure 1

Difficulty in assigning configuration to compound **6** and concern over the likely instability of these unusual structures turned our attention to validating earlier predictions of structure based upon one-bond

couplings.[4] Force-field energy minimisation studies using the MacroModel BatchMin version 3.5a molecular mechanics computer program[7] with its MM2 basis set were carried out on C_2 symmetric configurations (**A** and **B**, Table 1) of compounds **6a**, **6b** and **7**, and all possible configurational isomers (**A** - **D**) of compound **9**. Global minimisation of 250 - 1000 conformations was carried out in each case and the total steric energies of the minimum energy conformations were recorded (Table 1). Similar minimisations were carried out on the isomers of compounds **8** (**A** and **B**) and **10** (**A** - **D**), substances for which smaller one-bond coupling constants (**8**, $^1J_{C4a-H4a} = {}^1J_{C4b-H4b} = 143.1$ Hz; **10**, $^1J_{C4a-H4a} = 141.7$ Hz, $^1J_{C4b-H4b} = 138.0$ Hz),[4] representative of those of the majority of other *trans* tricycles of this type, were observed.

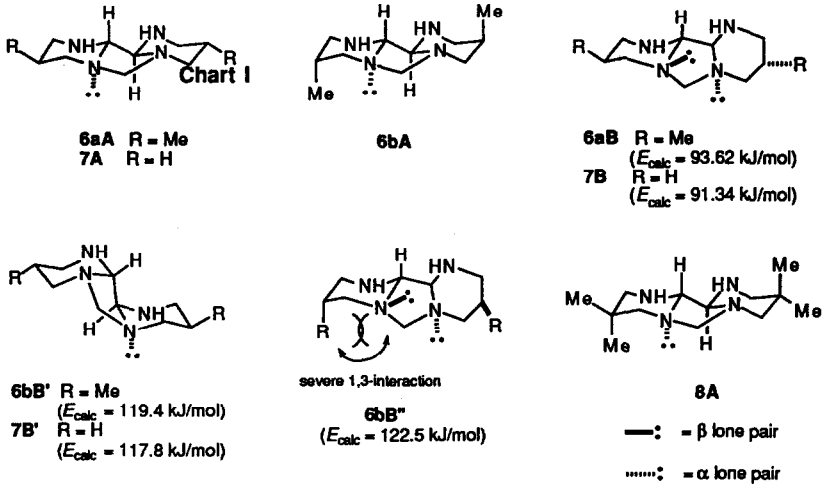


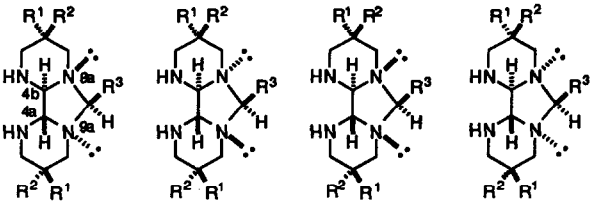
Figure 2

The results for **6a**, **6b**, **7** and **8** (Table 1) reveal consistently lower energies for tricycles with equatorially bound rings compared with tricycles with axial bridging bonds. For example, for compound **7**, the parent C_2 symmetric substance for which an unusually large one bond coupling constant was observed, there was a conformation with 8a,4b-*cis*-4b,4a-*anti*-4a,9a-*cis* configuration (**7B'**, Fig. 2 and 3) that had axially bound rings. It was calculated to have a total energy of 117.8 kJ/mol but this was considerably higher than the energy of the global minimum of the same configuration (**7B**, 91.34 kJ/mol, Table 1) with equatorially bound rings.

Of the tricycles with 8a,4b-*trans*-4b,4a-*anti*-4a,9a-*trans* configuration, those with conformations that had a linear arrangement of coplanar hexahydropyrimidine rings, similar to that predicted earlier for compound **8**, were of lowest energy. In contrast, the lowest energy conformations of most 8a,4b-*cis*-4b,4a-*anti*-4a,9a-*cis* tricycles adopted a linear but twisted arrangement of the rings. The only exception was in the case of compound **6b** (Table 1, entry 2**B**) in which the two global minimum conformers (**6bB**, Fig. 3) were of equal energy (116.7 kJ/mol) and were unsymmetrical. Each bore one ring in a boat conformation and the other in a chair conformation. Rapid equilibration between these two conformers cannot be ruled out as the mechanism by which the two rings become equivalent in the NMR spectrum, but the next highest energy conformer (**6bB'**,

119.4 kJ/mol) (Table 1, entry **2B**) was symmetrical and, interestingly, contained rings in chair conformations joined by a bond which was axial to both rings (see Fig. 2 and 3). The mean planes of the two rings in this second lowest energy conformation were not twisted, nor coplanar, but were parallel. The preference for axial bridging of the two rings in this case must be a device to accommodate the methyl substituents in the equatorial positions on the rings. The alternative conformation of the *cis.anti.cis*-isomer, that with axial methyl substituents and an equatorial bridging bond, **6bB''** (Fig. 3), suffers severe 1,3-diaxial interaction between the methyl substituent and the peripheral methylene group and has somewhat higher energy (122.5 kJ/mol). However, **6aB**, the lowest energy conformation of the same tricycle with 8a,4b-*trans*-4b,4a-*anti*-4a,9a-*trans* configuration (Table 1, entry 2A) contains axial methyl substituents while retaining the equatorial bridging of the rings (Fig. 3).

Table 1. Selected Configurational Isomers of Tricycles **6a, 6b,** and **7 - 10,** and the Calculated Steric Energies of Their Minimum Energy Conformations.



Entry	Compound number	R^1	R^2	R^3	A	B	C	D
					Total steric energy (kJ/mol) of global minimum conformations§			
1	**6a**	Me	H	H	94.66	93.62	—	—
2	**6b**	H	Me	H	107.5	116.7 (119.4)*	—	—
3	**7**	H	H	H	92.63	91.34	—	—
4	**8**	Me	Me	H	110.4	129.0	—	—
5	**9**	H	H	Me	105.8	115.0	115.5	124.4
6	**10**	Me	Me	Me	122.7	141.0	130.7	140.1

§ Calculated using MacroModel BatchMin version 3.5a.[7] * Value in parentheses refers to second lowest energy conformation.

Comparison of the energies of the global minimum conformations of the *trans.anti.trans*-tricycles (**A**) and the *cis.anti.cis*-tricycles (**B**) was revealing. Compound **8A** was significantly lower in energy than its isomer **8B** while the energy of the compounds **6aA** and **7A** were marginally higher than those of their *cis.anti.cis* isomers **6aB** and **7B**. Particularly important in the assignment of structure to compound **6**, tricycle **6a** was of markedly

lower energy than tricycle **6b** in both **A** and **B** configurations at nitrogen and there was a slight preference for the *cis.anti.cis* isomer of **6a, 6aB**, as in the case of compound **7**.

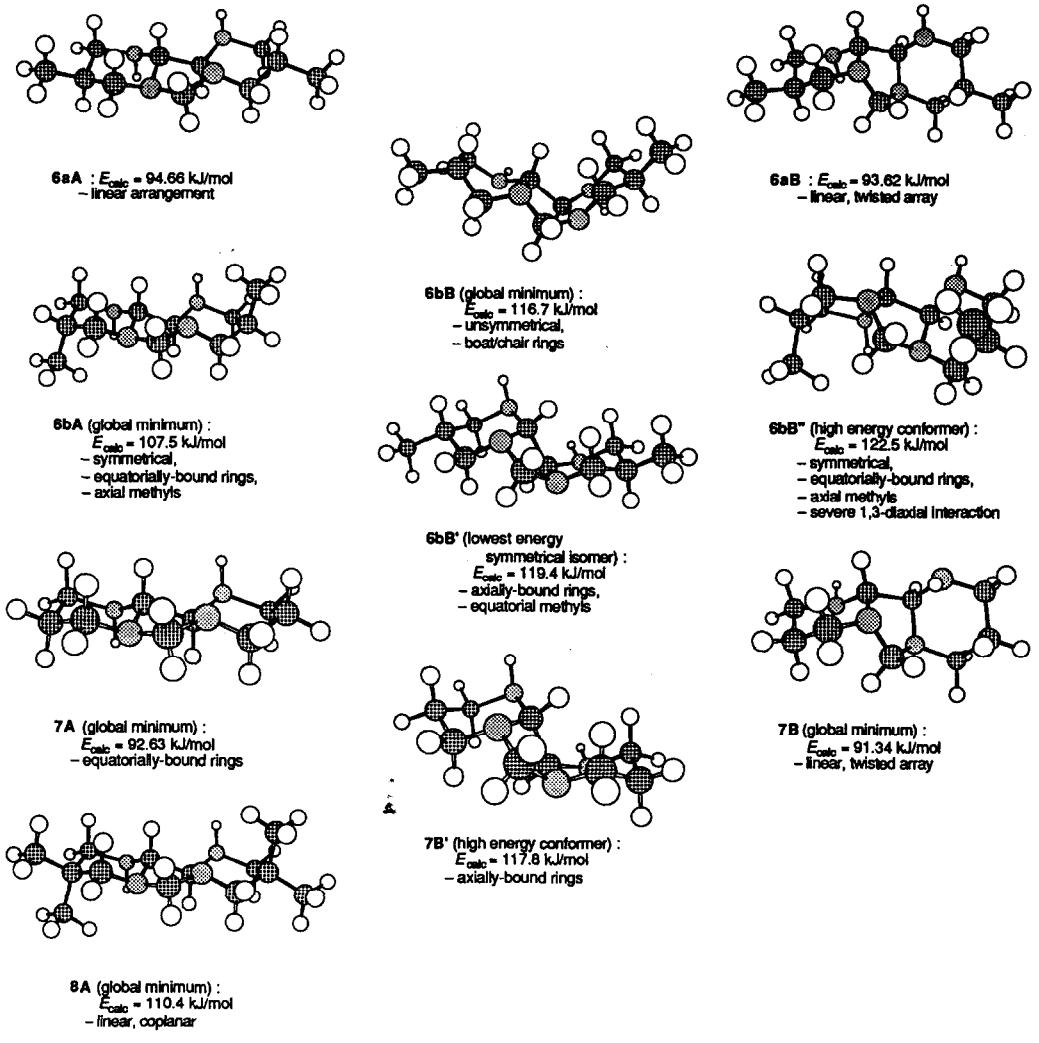


Figure 3

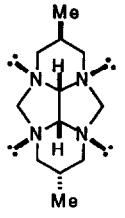
There is consistency in the magnitudes of the bridgehead C–H one bond couplings if one accepts as correct these supposedly preferred stereochemical structures of compounds **6**, **7** and **8**. Thus the preferred conformer of **8** (**8A**) has the antiperiplanar arrangement of C–H and neighbouring tertiary nitrogen non-bonded electrons which leads to small spin coupling constants. Meanwhile the similarly energetic isomeric partners of **6a** and **7** will contribute significantly to an equilibrium mixture. The NMR spin couplings associated with compounds **6a**

and **7** probably reflect this average. Since the minimum energy conformers of the *cis.anti.cis* isomers of **6a** and **7** have the non-bonded electron pairs on their tertiary nitrogens aligned gauche to the bridgehead C–H bonds (Fig. 3), there is no negative contribution to the spin coupling from the n–σ^* interaction and therefore the magnitude of the coupling should be high.

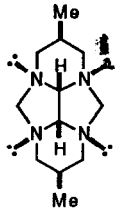
It appears from the data that the structure of **7** should be revised to that of a rapidly equilibrating mixture of **7A** and **7B** in which **7B** is preferred, whilst the structure of compound **8** is as was predicted.[4] It is also evident that the dimethyl-substituted derivative **6** should be assigned structure **6a**, with the methyl groups *cis* to the bridgehead hydrogens, but that **6a** is probably an equilibrating mixture of isomers **6aA** and **6aB**, with **6aB** preferred. This again is consistent with the observed single large one bond C–H coupling.

Analysis of the structures of compounds **9** and **10** was made complex by the unsymmetrical nature of the molecules. Molecular mechanics calculations of the energies of the 4b,4a-*anti* isomers (Table 1) gave results that were consistent with the molecules having structures **9A** and **10A** in which linear, coplanar arrangements of their rings were preferred. This is contrary to the earlier conclusion[4] in which compound **9** was supposed to have axial and equatorially bound hexahydropyrimidine rings. Indeed, the global minimum conformations of configurations **9C**, **9D**, **10C**, and **10D** were of this axial-equatorial type, but the high energies of these isomers precluded them from consideration as likely structures. Notably, compound **9B** was calculated to have the twisted conformation that was observed for compound **7B**, while **10B** was calculated to adopt a boat-chair conformation of its rings in its most stable conformation. A more detailed analysis of these and other 9-substituted derivatives will be discussed in a forthcoming paper.

Returning to the reactions of perhydrobipyrimidine **5**, treatment of the compound with 2 equiv of HCHO in refluxing MeOH gave two tetracyclic compounds in the ratio 1.5 : 1 in nearly quantitative yield. Repeated fractional crystallization eventually gave a pure sample of the major component which was found to have structure **11**.



11

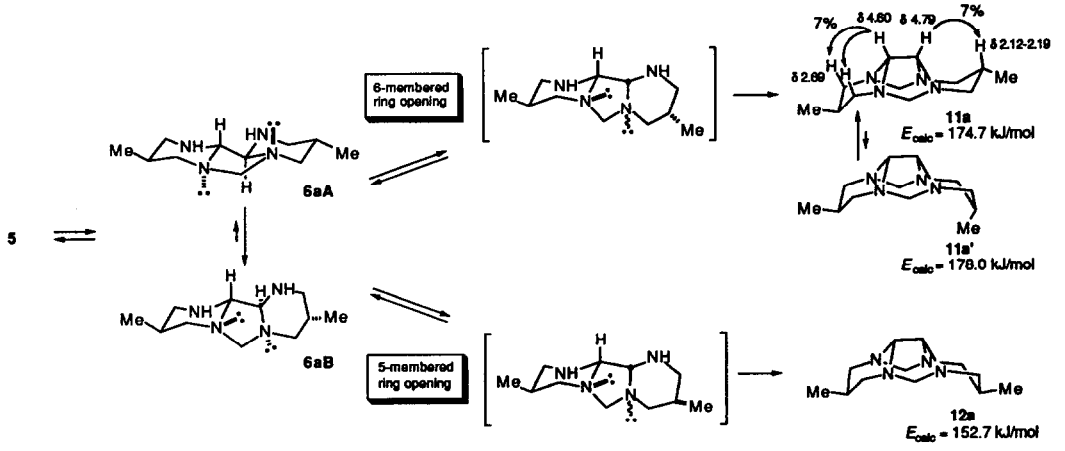


12

—: = β lone pair

The gross structure of **11** was evident from analysis of elemental composition and routine spectroscopic data but assignment of its configuration was possible only after detailed examination of its NMR spectra. The molecule is constrained to have *cis* geometry about its central C–C bond and as expected the protons on the bridging methylene carbon were non-equivalent. More interestingly, the NMR data also indicated that the two hexahydropyrimidines rings were different. In particular there appeared two 3-proton doublet resonances at δ 0.72 and 0.93 from the two methyl substituents and two 1-proton doublet resonances (δ 4.60 and 4.79, $J = 4.8$ Hz) due to the protons attached to the central bridge. There appeared nine signals in the ^{13}C NMR spectrum

instead of the five expected for a symmetrical molecule. This number best fits a structure with a plane of symmetry bisecting the hexahydropyrimidine rings and passing along the length of the central bridgehead bond. The magnitudes of the vicinal spin couplings between the adjacent ring methylene and methine protons (J = 10.8, 4.1 and 11.7, 4.0 Hz respectively) indicated that the methine protons were largely in axial positions. As a corollary, the methyl groups must have been in equatorial positions. This finding, with the fact that the hexahydropyrimidine rings were different but symmetrical, indicated that the *cis* tetracycle must have had one ring in the boat configuration and the other in the normal chair configuration. An alternative in which one ring was in an alternative chair configuration with the central bridging bond axial to the ring was considered less likely on the basis of NOE difference experiments. Irradiation of the signals for the central bridgehead protons (δ 4.60 and 4.79) gave 7% enhancements of the neighbouring axial methylene (δ 2.69) and "axial" methine (δ 2.12-2.19) proton signals, respectively (Scheme 1).



Scheme 1

These conclusions about different ring configurations were supported by molecular mechanics calculations (MacroModel v3.5a) which revealed that the chair-boat conformation (**11a**, E_{calc} = 174.7 kJ/mol) with both methyl groups equatorial was marginally more stable than the alternative chair-chair conformation with one methyl group in an axial configuration and the other equatorial (**11a'**, E_{calc} = 178.0 kJ/mol). The only chair-chair arrangement detected by the conformer search that had rings bound by axial and equatorial bonds also had one methyl group axial and the other equatorial, and was predicted to have much higher energy (E_{calc} = 207.8 kJ/mol) than the previous isomers. As a result of these considerations the compound was deduced to have structure **11** with the stereochemical relationships as shown in **11a** and **11a'**.

Subtraction of the signals due to **11** from those in the ^{1}H NMR spectrum of the crude material enabled the minor product of the above reaction to be identified as **12**. The spectrum gave two 2-proton doublet signals at δ 3.40 and 4.07 (J = 2.0 Hz), due to the peripheral methylene protons, and one 2-proton singlet (δ 4.67) which

could be assigned to the central bridgehead protons. Coincidence of the latter proton resonances and the presence of only one doublet signal (δ 0.72) for the two methyl substituents, confirmed that the compound had identical hexahydropyrimidine rings. Calculations showed that the "so-called" "normal" tetracycle **12a** was of much lower energy (E_{calc} = 152.7 kJ/mol) than either of its configurational isomers **11a** and **11a'**.

Efforts were made to influence the ratio of **11** and **12** by changing solvent. However, when the reaction with two equivalents of HCHO was repeated using Et_2O as solvent, no distinguishable condensation products were evident in the complex mixture obtained after normal workup.

Consideration of these findings enables a mechanism (Scheme 1) to be formulated in which the twisted or coplanar *trans* tricycle **6a** can undergo isomerism through opening of its 5-membered or 6-membered rings to give the highly symmetrical tetracycle **12** and less symmetrical tetracycle **11**, respectively. The preference for formation of **11** despite the lower steric energy of **12** is remarkable. It indicates that opening of the 6-membered ring is a lower energy process than the alternative pathway. The reason for this is not clear and requires further study, but the observation is consistent with the earlier findings[5] concerning transformations of perhydrobipyrimidine **4**.

ACKNOWLEDGMENTS

One of us (RWR) wishes to thank Professor Scott E. Denmark for helpful discussions and for hospitality at the University of Illinois, Urbana-Champaign, during the preparation of this paper. We thank Mark E. Schnute for technical assistance with the MacroModel program, and gratefully acknowledge financial assistance from the Australian Research Council.

EXPERIMENTAL SECTION

General Methods. The general methods used in this paper were essentially the same as described previously.[5]

Preparation of 5,5'-Dimethylperhydro-2,2'-bipyrimidine 5

Aqueous glyoxal (0.4 g of 40%, 2.8 mmol) was added dropwise to a solution of 2-methylpropane-1,3-diamine (1.0 g, 11.4 mmol) in EtOH (10 mL) precooled to 0°. The mixture was warmed at 70-75° on a water bath for 3.5 h, then refrigerated overnight. The precipitate of partially hydrated *5,5'-dimethylperhydro-2,2'-bipyrimidine 5* was obtained as white plates (0.3 g, 40%) mp 118-120°: IR (Nujol) 3305, 3284, 3242, 3212, 3113, 1515, 1457, 1435, 1379, 1330, 1289, 1212, 1164, 1124, 1084, 987, 963, 927, 902, 878, 842, 810, 794, 683, 669 cm^{-1}; ^1H NMR (500 MHz) δ 0.71, d, J = 6.6 Hz, 5-CH_3; 1.53, m, H5; 2.33, dd, J = 13.0, 11.3 Hz, $H_{ax}4$ and $H_{ax}6$; 3.07, dd, J = 13.0, 4.2 Hz, $H_{eq}4$ and $H_{eq}6$; 3.30 s, H2; ^{13}C NMR δ 16.41, q, J = 122.2 Hz, 5-CH_3; 32.35, d, J = 126.5 Hz, C5; 53.23, t, J = 130.2 Hz, C4 and C6; 73.74, d, J = 142.0 Hz, C2; mass spectrum: *m/z* 198 (M, absent), 99(100%). Anal. Calcd for $C_{10}H_{24}N_4 \cdot \frac{1}{4}H_2O$: C, 59.2; H, 11.2; N, 27.6. Found: C, 59.4; H, 11.5; N 27.7.

Condensation of 5,5'-Dimethylperhydro-2,2'-bipyrimidine 5 with HCHO

(i) with one equiv of HCHO in MeOH. Formalin (0.8 g of 36%, 10.1 mmol) was added dropwise to a solution of 5,5'-dimethylperhydro-2,2'-bipyrimidine **5** (2.0 g, 10.1 mmol) in MeOH (20 mL) precooled to 0°. The mixture was allowed to stir at rt for 1 h and the solvent removed under vacuum at room temperature to give an oil (2.2 g). Kugelrohr distillation gave *(2R*,4aR*,4bR*,5R*)-2,7-dimethylperhydro-4,5,8a,9a-tetraazafluorene* ***6a*** as a sticky white solid (1.1 g, 52%) bp 120°/0.05 mmHg. Recrystallization from Et_2O gave the *tricycle* as clear prisms mp 103-105°: IR 3246, 1462, 1377, 1316, 1301, 1283, 1251, 1226, 1179, 1110, 1082, 1052, 1025, 946, 937, 895, 842, 796, 723, 680, 642, 533, 504, 454 cm^{-1}; ^1H NMR (300 MHz) δ 0.71, d, J = 6.6 Hz, 2-CH_3 and 7-CH_3; 1.71, m, H2 and H7; 2.28, dd, J = 13.4, 11.2 Hz, $H_{ax}3$ and $H_{ax}6$; 2.44, dd, J = 13.3, 11.2 Hz, $H_{ax}1$ and $H_{ax}8$; 2.91, ddd, J = 13.3, 4.2, 2.1 Hz, $H_{eq}1$ and $H_{eq}8$; 3.03, ddd, J = 13.3, 4.1, 2.1 Hz, $H_{eq}3$ and $H_{eq}6$; 3.59, s, H4a and H4b; 3.83, s, $(H9)_2$; ^{13}C NMR δ 16.26, q, J = 125.2 Hz, 2-CH_3 and 7-CH_3; 26.52, d, J = 125.7 Hz, C2 and C7; 51.80, t, J = 133.0 Hz, C3 and C6; 53.96, t, J = 134.2 Hz, C1 and C8; 68.10, t, J = 145.9 Hz, C9; 77.38, d, J = 152.5 Hz, C4a and C4b; mass spectrum: *m/z* 211(M+1, 1%), 210(M, 1), 209(4), 180(2), 138(4), 112(86), 99(100), 89(12), 70(28). Anal. Calcd for $C_{11}H_{22}N_4$: C, 62.8; H, 10.5; N, 26.6. Found: C, 62,7; H, 10.7; N, 26.6.

(ii) with two equiv of HCHO in MeOH. Formalin (1.7 g of 36%, 0.02 mol) was added to a solution of 5,5'-dimethylperhydro-2,2'-bipyrimidine **5** (2.0 g, 0.01 mol) in MeOH (20 mL) and the mixture was heated at reflux for 1.5 h. The mixture was allowed to cool and the solvent removed by rotary evaporation to leave a gum (2.5 g) which consisted of two tetracyclic compounds in a ratio of 1.5 : 1. The gum was taken up in light petroleum and the solution allowed to stand at rt overnight. The crystals that separated were collected (0.4 g, 18%) and recrystallized from Et_2O to give an enriched sample (87 : 13) of the major tetracycle. Crystallization from a dilute Et_2O solution gave a small amount of *(2*R**,6*S**,8*b*R**,8*c*R*)-2,6-dimethylperhydro-3a,4a,7a,8a-tetraazacyclopentano*[def]*fluorene* ***11*** as clear rods mp 125-127°: IR (dissolved in $CHCl_3$ and oven dried as a cast film on KBr plate) 2947, 2919, 2898, 2865, 2820, 2764, 2709, 2674, 1687, 1631, 1511, 1471, 1453, 1375, 1323, 1267, 1217, 1199, 1182, 1133, 1115, 1075, 943, 897, 865, 851, 752, 581 cm^{-1}; ^1H NMR (500 MHz) δ 0.72, d, J = 6.5 Hz, 2-CH_3; 0.93, d, J = 6.6 Hz, 6-CH_3; 2.01-2.10, m, H2; 2.12-2.19, m, H6; 2.31, dd, J = 12.2, 10.8 Hz, $H_{ax}5$ and $H_{ax}7$; 2.69, dd, J = 14.9, 11.7 Hz, $H_{ax}1$ and $H_{ax}3$; 3.07, dd, J = 14.9, 4.0 Hz, $H_{eq}1$ and $H_{eq}3$; 3.42, dd, J = 10.8, 4.1 Hz, $H_{eq}5$ and $H_{eq}7$; 3.74, d, J = 2.1 Hz, H_a4 and H_a8; 3.93, d, J = 2.1 Hz, H_b4 and H_b8; 4.60, d, J = 4.8 Hz, H8b; 4.79, d, J = 4.9 Hz, H8c; ^{13}C NMR δ 16.31, q, J = 124.9 Hz, 2-CH_3; 17.22, d, J = 113.8 Hz, C2; 18.00, q, J = 125.5 Hz, 6-CH_3; 27.75, d, J = 124.3 Hz, C6; 51.62,* t, J = 134.9 Hz, C1 and C3; 53.54,* t, J = 134.3 Hz, C5 and C7; 74.82, d, J = 169.0 Hz, C8c; 75.41, d, J = 165.0 Hz, C8b; 76.64, t, J = 143.4 Hz, C4 and C8; mass spectrum: *m/z* 222(M, 35%), 221 (62), 193 (18), 178 (17), 151(85), 138 (34), 111(55), 109(29), 84(100), 69(22), 55(32), 42(74). (* These carbon signals may be interchanged.) Anal. Calcd for $C_{12}H_{22}N_4$ requires C, 64.8; H, 9.7; N, 25.2. Found: C, 65.1; H, 10.0; N, 25.5. The following signals were used to identify the minor isomer (2*R**,6*R**,8b*R**,8c*R**)-2,6-dimethylperhydro-3a,4a,7a,8a-tetraazacyclopentano[*def*]fluorene **12**: ^1H NMR (500MHz) δ 0.72, d, J = 6.5Hz, 2-CH_3 and 6-CH_3; 2.01-2.10, m, H2 and H6; 2.69, obscured multiplet, $H_{ax}1$, $H_{ax}3$, $H_{ax}5$ and $H_{ax}7$; 3.07, obscured multiplet, $H_{eq}1$, $H_{eq}3$, $H_{eq}5$ and $H_{eq}7$; 3.70, d, J = 2.0Hz, H_a4 and H_a8; 4.07, d, J = 2.0 Hz, H_b4 and H_b8; 4.67, s H8b and H8c.

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(*Received in UK* 11 *November* 1993; *accepted* 26 *November* 1993)