Hz), 7.32 (d, J = 8.6 Hz), and 7.57 (d, J = 1.8 Hz), along with the occurrence of three protonated and five nonprotonated sp^2 carbons in the ^{13}C NMR spectra, indicated the existence of a 2,3,5- or 2,3,6-trisubstituted indole ring. Two ^{13}C NMR signals at 126.7 (s) and 135.5 (s) were typical of C-3a and C-7a, respectively, of the indoles.[3,8,9] Further ^1H and ^{13}C NMR assignments for the indole ring, based on consideration of coupling information from COLOC,[10] HETCOR,[11] and HETCOSY[12] experiments (Table I), enabled us to conclude that 1 contained the 2,5-dibromoindol-3-yl moiety.

The remaining subunit as required by the molecular formula was $C_3H_6N_3$. The presence of a guanidine functionality was suggested from the positive Sakaguchi test[13] and a ^{13}C NMR signal at δ 159.8 (s).[14] Two other carbons including a methylene at δ 48.5 (t) and a methine at 51.2 (d), observed in the ^{13}C NMR and DEPT spectra, were nitrogen-bearing from chemical shift arguments. ^1H NMR and COSY spectra illustrated that the corresponding methylene protons (H-5′) at δ 3.99 (dd, J = 10.1, 10.1 Hz) and δ 3.53 (dd, J = 10.1, 7.1 Hz) were geminally coupled, and both protons were coupled to the methine proton (H-4′) at δ 5.23 (dd, J = 10.1, 7.1 Hz). Further 2D NMR experiments (Table I) showed that the guanidino carbon (C-2′) was long-range coupled with H-5′ and H-4′. These data established the presence of the 2-amino-2-imidazolin-4-yl structure feature in 1. Furthermore, long-range correlations were observed from C-2 to H-4′, from C-3 to H-5′, and from C-3a to H-4′, thereby connecting the C-4′ to C-3 to yield the structure 3-(2-amino-2-imidazolin-4-yl)-2,5-dibromoindole[15] for 1. The stereochemistry of the chiral center at C-4′ was not assigned. It may be of chemotaxonomic interest that discodermindole is structurally unrelated to the discodermins[16] and the calyculins,[17] reported previously from sponges of the genus *Discodermia*.

Experimental Section

Isolation of Discodermindole (1). A taxonomic voucher specimen of the sponge *D. polydiscus* was deposited at Harbor Branch Oceanographic Museum (catalog no. 003:00058). The sponge (88 g wet weight) was stored frozen and extracted with MeOH (250 mL × 3). The extract was concentrated to dryness under reduced pressure and then partitioned between EtOAc (100 mL) and H_2O (100 mL). The aqueous layer was lyophilized and triturated with $CHCl_3$–MeOH (1:1, 50 mL × 2). After evaporation of the organic solvent, the oily residue (810 mg) was fractionated by using centrifugal countercurrent chromatography ($CHCl_3$–MeOH-H_2O, 5:10:6, lower phase stationary) to give 30 fractions. Active fractions 18 and 19 were pooled and chromatographed on a Sephadex LH-20 column with MeOH, followed by HPLC on an NH_2 column with $CHCl_3$–MeOH (3:1), to yield 1 (15 mg, 0.017% of wet sponge) as a colorless viscous oil: $[\alpha]^{20}_D$ = −27° (c 1.0, MeOH); HRFABMS MH$^+$ 358.9336 (calcd for $C_{11}H_{11}{}^{79}Br^{81}BrN_4$, Δ −0.6 mmu); HREIMS M$^+$ − $C_3H_5N_3$ 272.8779 (calcd for $C_8H_5{}^{79}Br_2N$, Δ 0 mmu); LREIMS 277/275/273 (rel intensity 49/100/49), 196/194 (41/46), 115 (80), 83 (77), and 57 (59); IR (KBr) ν_{max} 3300 (br), 1670, 1570, 1410, 1330, 1090, 910, and 795 cm^{-1}; ^1H and ^{13}C NMR, Table I.

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Registry No. 1, 133523-28-1.

Supplementary Material Available: ^1H and ^{13}C NMR spectra for compound 1 (2 pages). Ordering information is given on any current masthead page.

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Evidence for Equatorial Bridging in 2,2′-Bis(hexahydropyrimidines), Perhydro-4,5,8a,9a-tetraazafluorenes, and Perhydro-3a,4a,7a,8a-tetraazacyclopentanofluorenes through One-Bond C–H Coupling

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Introduction

2,2′-Bis(hexahydropyrimidines) are molecules that in principle can reside in either of two minimum energy conformations, A or B (Chart II). A study of one tetranitro derivative, 1,1′,3,3′-tetranitro-2,2′-bis(hexahydropyrimidine) (1; Chart I), by X-ray crystallography has shown it to exist entirely in conformation B.[1] In contrast, the molecular structures of free amines 4 and 5, as determined by X-ray crystallography, are consistent with conformation A.[2] However there has been no report of the preferred arrangement of derivatives in solution.[3] This aspect was of interest to us in connection with a study of novel heterocyclic systems derived from bis(hexahydropyrimidines)[1] and was relevant when predictions were to be made of the relative configuration of the substituted heterocycles. The present paper concerns an NMR spectroscopic study of the stereochemistry of 2,2′-bis(hexahydropyrimidines) and related cyclopentano-fused tri- and tetracyclic compounds (Chart I), as their free amines, in solution.

Results and Discussion

The synthesis of compounds **2** and **3** has been described.[1] They are readily converted into tri- and tetracyclic derivatives **6–10** and **12–15**, respectively, through condensation with aldehydes and, in the case of **10**, with acetone.[1]

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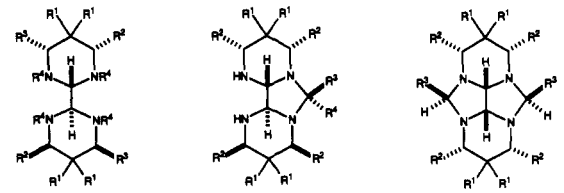
0022-3263/91/1956-4308$02.50/0

Chart I



	R^1	R^2	R^3	R^4
1	H	H	H	NO_2
2	H	H	H	H
3	CH_3	H	H	H
4	H	CH_3	CH_3	H
5	H	CH_3	H	H

	R^1	R^2	R^3	R^4
6	H	H	H	H
7	CH_3	H	H	H
8	H	H	CH_3	H
9	CH_3	H	CH_3	H
10	CH_3	H	CH_3	CH_3
11	H	CH_3	H	H

	R^1	R^2	R^3
12	H	H	H
13	H	H	CH_3
14	CH_3	H	H
15	CH_3	H	CH_3
16	H	CH_3	H

Of the tricyclic compounds, only the trans isomers could be isolated by crystallization. Substituted bis(hexahydropyrimidines) **4** and **5** have been prepared more recently[2] following the method for **2** and **3**, and compound **4** has been converted into its tricyclic and tetracyclic derivatives **11** and **16**, respectively.[4]

At the outset, the relative stabilities of conformations A and B were uncertain. Hexahydropyrimidines are known to prefer a chair conformation with the maximum number of substituents equatorial,[5] but the competing influence of substituents on positions 4–6 is unknown. The ^1H NMR spectra of compounds **2–5** in $CDCl_3$ do show distinct axial and equatorial CH proton signals at room temperature[1] consistent with fixed chair conformations. However, the isolated nature of the C2-protons in these molecules prevents their configurational assignment. Variable-temperature studies show only small, uniform changes in chemical shift in the ^1H NMR spectrum of compound **3** in toluene-d_8 at temperatures from −10 to 100 °C. At lower temperatures, more significant changes take place that are optimal at −33 °C (Figure 1). Additional spin couplings of 6.1 and 7.5 Hz in the signals for the aminal protons (δ 3.26, t) and axial protons adjacent to nitrogen (δ 2.45, dd), respectively, and slight broadening of the signals for the equatorial protons adjacent to nitrogen at this low temperature show that vicinal coupling to the NH protons was now evident. This fact is supported by concomitant sharpening of the NH signal to a partially resolved triplet; above room temperature, the NH signal was extremely broad and barely visible. The changes probably correspond to loss of NH exchange, an event known to occur in hexahydropyrimidines and 1,3-oxazines in the range −30 to −80 °C.[6] There was no evidence of other line broadening or the appearance of new signals that might suggest the "freezing out" of conformational isomers at lower temperatures (as low as −53 °C in toluene-d_8 and −83 °C in $CFCl_3$). Hence, the barrier to ring inversion and therefore interconversion between conformations A and B, at least in the case of **3**, was extremely low, which is unlikely, or the equilibrium was strongly one-sided. Ring inversion in hexahydropyrimidines requires a moderate amount of energy, $\Delta G^{\ddagger}$ 45 kJ mol^{-1};[5] therefore, the latter situation is more likely.

The possibility of inversion at nitrogen is not ruled out by these considerations. However, others[6] have observed that at low temperature, and perhaps even at room temperature,[6-8] the N–H bond in hexahydropyrimidines and

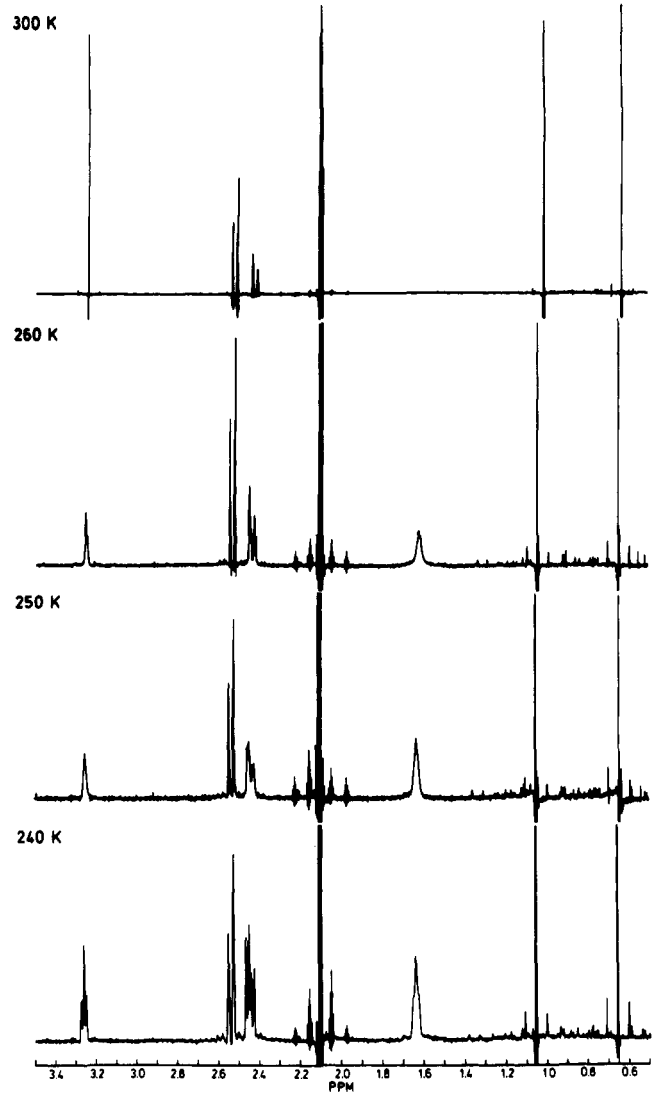
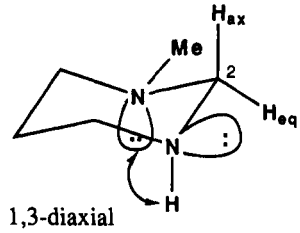


Figure 1. ^1H NMR spectra of compound **3** in perdeuterotoluene at different temperatures.



1,3-diaxial interaction

Figure 2.

1,3-oxazines is predominantly in an axial orientation. For example, 1-methylhexahydropyrimidine has a spin coupling between the NH proton and the axial proton at position 2 of 13 Hz, measured at −70 °C, and a coupling with the equatorial proton at position 2 of less than 3 Hz. The magnitudes of the couplings, along with those between similar protons in 1,3-oxazines, imply that the compounds exist virtually entirely in one conformation with the N–H bond axially oriented. The preference for this orientation has been attributed to electrostatic attraction between the N–H bond and the 1,3-syn-axial lone pair electrons on the adjacent heteroatom (Figure 2). Such an arrangement in **3** would direct the second N–H bond in the same ring into

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Table I. Selected ^{13}C NMR Data from Compounds 2–16

	C2		other relevant signals	
compd	δ	J_{C-H} (Hz)	δ	(multiplicity, J_{C-H} (Hz))
2	74.3	141.1	45.6	(t, 134.1)
3	73.6	142.3	57.3	(t, 133.9)
4	74.1	141.2	50.9	(d, 131.0)
5	74.3	142.1	51.1	(d, 131.8)
			45.4	(t, 134.0)
6	78.3	149.2	68.3	(t, 146.6)
			46.9	(t, 136.1)
			44.3	(t, 135.5)
7	78.3	143.1	71.0	(t, 145.9)
			60.5	(t, 132.7)
			57.3	(t, 135.1)
8	81.5	139.1	75.1	(d, 140.5)
	75.6	151.0	47.8	(t, 133.4)
			45.4	(t, 137.2)
			43.2	(t, 135.5)
			43.0	(t, 138.3)
9	81.9	138.0	75.0	(d, 141.7)
	75.0	141.7	59.9	(t, 131.5)
			57.9	(t, 131.2)
			56.3	(t, 134.6)
			55.7	(t, 134.8)
10	77.2	139.3	74.1	(s)
			57.5	(t, 133.0)
			56.0	(t, 133.5)
11	78.6	141.8	65.4	(t, 146.8)
			54.6	(d, 129.4)
			51.2	(d, 133.4)
12	76.7	165.2	70.3	(t, 143.6)
			43.8	(t, 137.8)
13	75.3	165.0	71.2	(d, 130.7)
			40.1	(t, 137.9)
14	75.9	164.7	75.2	(t, 144.5)
			55.8	(t, 136.6)
15	73.8	164.4	77.9	(d, 134.2)
			54.7	(t, 134.5)
16	77.9	164.7	61.0	(dd, 153.2, 133.2)
			50.0	(d, 133.5)

an equatorial orientation, thereby making the rings unsymmetrical.

The X-ray crystal structures of 4 and 5 support this prediction;[2] however, in solution, the hexahydropyrimidine rings of 3 are symmetrical, even at −83 °C where NH exchange is very slow. Rapid nitrogen inversion must therefore take place between −33 and −83 °C. As a consequence, the magnitudes of the spin coupling between the NH protons and adjacent, axial protons are expected to be much less than the value of 13 Hz reported for $J_{NH,2ax}$ in the spectrum of 1-methylhexahydropyrimidine where only one orientation is possible. This also explains the medium strength of the couplings between the NH proton and H4ax and H6ax. Interestingly, the similarity of this moderate coupling and the coupling to H2 suggests that H2 might also be in an axial position in 3. The spectrum therefore indicates that compound 3 occurs predominantly in conformation A.

Attention was next focused on a more convenient means of assigning the major conformation of bis(hexahydropyrimidine) derivatives at room temperature through measurement of one-bond C–H coupling constants.[9,10]

In Table I are set out the chemical shifts and one-bond C–H coupling constants of carbons at the linkage between the two six-membered rings of a range of related 2,2′-bis(hexahydropyrimidines) 2–5, perhydrotetraazafluorenes 6–11, and perhydrotetraazacyclopentanofluorenes 12–16. Also listed are the values for other aminal carbons where they are present in these examples and the carbons adjacent to single nitrogens.

The magnitude of one-bond ^{13}C–^{1}H coupling constants, for bonds adjacent to heteroatoms such as nitrogen, is known to depend upon substituent electronegativity and upon orientation of the C–H bond relative to the nonbonded electrons on the heteroatom.[9] Since the electronegativity of the nitrogen substituent groups in all three types of molecule considered here is probably very similar, the difference in coupling almost certainly arises from variation in alignment of the C–H bonds with the nonbonded electrons on nitrogen. In six-membered rings this normally means that, for a given heterocycle, ^{1}J for an axial C–H bond is smaller than ^{1}J for an equatorial C–H bond: $^{1}J_{C-Hax} < {}^{1}J_{C-Heq}$.[9,10] The observation is rationalized in terms of an interaction between a pair of nonbonded electrons on the heteroatom and the antibonding orbital $\sigma_{C,H}^*$ of the axial C–H bond on an adjacent carbon, an effect that gives a negative contribution to $^{1}J_{C,H}$ through a decrease in the s character of the bond.[9]

The compounds mentioned in Table I can be divided into two groups according to the magnitude of $^{1}J_{(C2,\ H2)}$: 2–11 J = 138.0–151.0 Hz and 12–16 J = 164.4–165.2 Hz. Those with the larger coupling were noted to have the cyclopentanofluorene skeleton.

The tetracyclic tetraamines 12–16 are all known, from symmetry considerations and observations of multiplicity of ^{1}H and ^{13}C NMR signals, to have cis-bonded hydrogens at the bridgehead between the two six-membered rings.[1] Tetracycle 16 has been shown by X-ray crystallography[4] to have molecular structure C in the solid state, and models suggest that this is a comparatively rigid structure. In this arrangement, the six-membered rings are flattened but the peripheral methylene bridges are in pseudoaxial positions, with the nitrogen lone pairs cis to the hydrogens at the central bridge. In this orientation, the nonbonded orbitals on nitrogen are almost exactly aligned with the neighboring bridgehead C–H bonds. Since a positive contribution to coupling is expected in this orientation, the larger observed C–H coupling constants for tetracycles 12–16 over those of earlier derivatives 2–11, recorded over a narrow range, point very definitely to the molecules also having structures similar to C in solution.

Closer inspection of the spin coupling constants of compounds 2–11 reveals that the values for all the bis(hexahydropyrimidines), i.e., compounds 2–5, also fall within a narrow range ($^{1}J_{(C2,\ H2)}$ = 141.1–142.3 Hz) while those for the tricycles are more variable. As mentioned previously, compounds 4 and 5 have both been shown to exist in conformation A in the solid state.[2] The variable temperature experiments on compound 3 indicated that while an axial arrangement of the N–H bonds is preferred, only one of the two N–H bonds from each ring is likely to reside in this position. A considerable proportion of the equatorial configuration must therefore exist, especially at room temperature. Under these circumstances, the orientation of the nonbonded electrons on nitrogen is very different in conformations A and B (Chart II). In A, the aminal C–H bond resides in an axial position and is aligned antiperiplanar with respect to at least one neighboring nitrogen lone pair, and in B, the aminal hydrogen occupies an equatorial position and the C–H bond is held skew to both pairs of nonbonded electrons. If the assumption of the orientation of the nitrogen lone pairs is correct, the relatively small values of $^{1}J_{C-H}$ observed for compounds 2–5 support solution structures related to A.

What then of the situation in the tetraazafluorenes 6–11?

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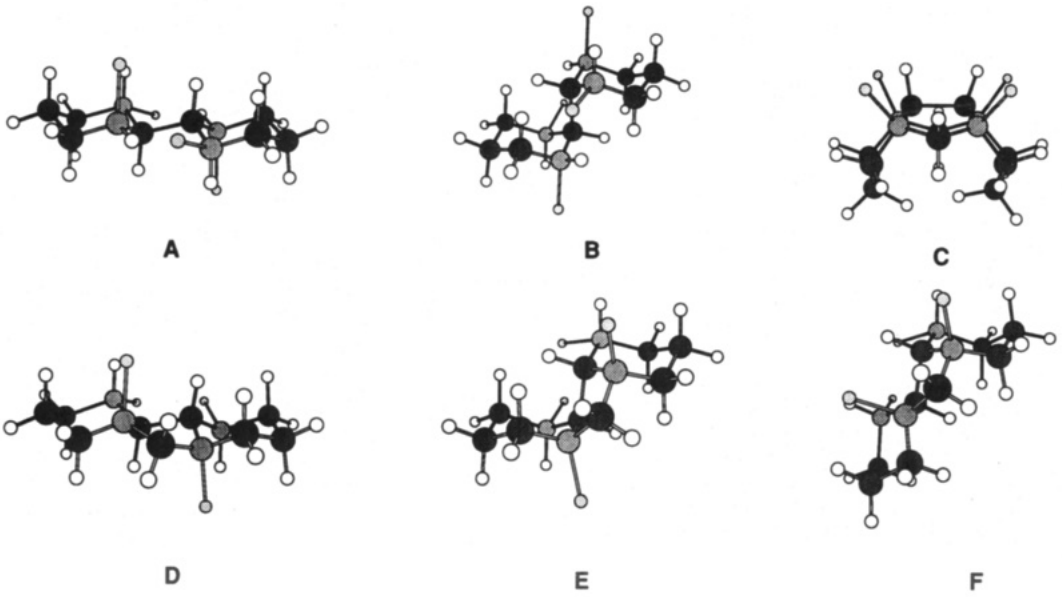
Chart II. Chem 3D Stereochemical Representations of the Major Structural Types, A–F, Considered in This Study



The one-bond C–H coupling constants of compounds **6–11** were more variable than those for the bis(hexahydropyrimidines) **2–5**. However, those for compound **9**, an unsymmetrical derivative, and compounds **7**, **10**, and **11**, symmetrical derivatives, were very similar and of the same magnitude as the values for compounds **2–5**. It is therefore likely that the structures of compounds **7** and **9–11** are like those of bis(hexahydropyrimidines) **2–5**, namely D, where the nonbonded electrons on nitrogen have a similar orientation to the neighboring bridgehead C–H bond. Inversion at the tertiary nitrogen of these molecules is geometrically possible, but fusion of the third ring probably slows this process, thereby giving more bond fixation than in **2–5**. In contrast, compound **6** has a large one-bond coupling, while **8**, another unsymmetrical molecule, shows one large and one small coupling. The conclusion drawn from these observations is that, in solution, compound **6** must have a molecular structure similar to B, i.e., E, where nonbonding electrons on nitrogen are closely aligned with the adjacent aminal C–H bond. Furthermore, compound **8** must have features of both A and B; therefore, structure F is proposed. The difference between the large couplings from **6** and **8** and those from **12–16** is explained by the presence of only one fixed pair of nonbonded electrons in each ring in **6** and **8** compared with two in **12–16**.

The $^1J_{C-H}$ values for the peripheral aminal carbons in **12** and **14** (δ 70.3, J = 143.6 Hz and δ 75.2, J = 144.5 Hz, respectively; see Table I), compounds that have no substituents on the peripheral bridges, are comparable with though somewhat lower than those for compounds **6**, **7**, and **11** (J = 145.9–146.6 Hz). Such an observation is at first surprising, since the corresponding protons in **6**, **7**, and **11** are equivalent and oriented equally toward and away from the nitrogen lone pairs, while in the tetracycles, **12** and **14**, they are nonequivalent. However, the couplings observed for **12** and **14** are probably the mean of large and small couplings. In support of this argument, separate splittings are observed for **16** (^1J = 153.2 and 133.2 Hz). In contrast, the couplings in **13** and **15** (J = 130.7 and 134.2 Hz, respectively) are smaller than those for **12** and **14**. Substitution on the peripheral bridge does not account for this difference because the couplings for compounds **8** and **9** (J = 140.5 and 141.7 Hz, respectively) are only marginally lower than those for **6**, **7**, and **11**. The differences must lie in the relative configuration of the hydrogens with respect to the nitrogen lone pairs. This information can be most useful when assigning stereochemistry to substituents. The relative configuration of substituents on the peripheral one-carbon bridges with respect to the central hydrogen atoms in tetracycles such as **12–16** could not previously be assigned unambiguously without resort to X-ray analysis. However, since structures based on C are inferred for compounds **13** and **15**, one must conclude that their methyl groups reside in such a way as to allow the remaining hydrogen atoms on the peripheral bridges to give the small observed $^1J_{C-H}$ values. This in turn implies that the hydrogen atoms are held away from the nonbonded electrons on nitrogen leaving the methyl groups cis to the bridgehead hydrogens. Such an arrangement is entirely likely since steric interactions involving the methyl groups are minimized.

A very tenuous relationship between C–H coupling at the remaining carbon atoms attached to a single nitrogen atom and the configuration of the bridging bond was also noted. Those bis(hexahydropyrimidines) and tricyclic compounds that have ring systems related to conformation A, i.e., compounds **2–5**, **7**, and **9–11**, all have slightly smaller one-bond couplings for these carbons (^1J = 129.4–135.1 Hz) than the couplings (^1J = 135.5 and 136.1 Hz) observed for the tricycle **6**, which has a configuration like B. As expected, tricycle **8**, which has features of structure A and B, has a set of small (J = 133.4 and 135.5 Hz) and a set of large (J = 137.2 and 138.3 Hz) couplings. While interesting, the origin of this relationship is uncertain.

Thus, it seems from one bond C–H coupling evidence that the bond that bridges the six-membered rings of bis(hexahydropyrimidines) and their tri- and tetracyclic derivatives obtained through condensation with aldehydes is equatorial in most cases, but exceptions can occur. The magnitude of $^1J_{C-H}$ values obtained from carbons that are part of the aminal groups can be used to determine the configuration of this bridging bond in solution. In the future, this information will be useful in determining the configuration of substituents in more complex examples of these novel ring systems.

Experimental Section

Heterocycles **2–10** and **12–15** were available from previous studies.[1,2] Compound **11**, (1*S**,3*R**,4a*R**,4b*R**,6*R**,8*S**)-1,3,6,8-

tetramethylperhydro-4,5,8a,9a-tetraazafluorene [found m/z 237.20895, $C_{13}H_{28}N_4$ requires 237.20792; ^1H NMR δ ($CDCl_3$) 0.89, (dt, J = 13.2, 11.0 Hz, $H_{ax}2$ and $H_{ax}7$), 1.00 (d, J = 6.3 Hz, 1-Me and 8-Me or 3-Me and 6-Me), 1.07 (d, J = 6.4 Hz, 3-Me and 6-Me or 1-Me and 8-Me), 1.58 (dt, J = 13.1, 3.1 Hz, $H_{eq}2$ and $H_{eq}7$), 2.60 (ddq, J = 10.6, 3.3, 6.4 Hz, H1 and H8 or H3 and H6), 2.72 (ddq, J = 11.4, 3.2, 6.4 Hz, H3 and H6 or H1 and H8), 3.27 (s, H4a and H4b), 3.78 (s, H9)], was prepared in diethyl ether by a solvent modification of the method used to prepare compounds **6**-**10**.[1] The substance was obtained in ~90% purity as a sticky white solid, mp 50-65 °C, which was not hygroscopic but could not be completely separated from impurities. Compound **16**, (1*R**,3*S**,5*R**,7*S**,8b*S**,8c*S**)-1,3,5,7-tetramethylperhydro-3a,4a,7a,8a-tetraazacyclopentano[*def*]fluorene [mp 128-130 °C; found C, 67.5, H, 10.2, N, 22.6; $C_{14}H_{26}N_4$ requires C, 67.2, H, 10.5, N, 22.4; ^1H NMR δ ($CDCl_3$) 0.96 (dt, J = 13.2, 2.7 Hz, $H_{eq}2$ and $H_{eq}6$), 1.17 (d, J = 6.9 Hz, 1-Me, 3-Me, 5-Me, and 7-Me), 1.40 (dt, J = 13.2, 11.7 Hz, $H_{ax}2$ and $H_{ax}6$), 3.25 (ddq, J = 11.7, 2.7, 7.0 Hz, H1, H3, H5, and H7), 3.61 (d, J = 2.2 Hz, H_a4 and H_a8), 3.70 (d, J = 2.2 Hz, H_b4 and H_b8), 4.76 (s, H8b and H8c)], is new and was prepared in similar fashion to **12**-**15**.[1]

Single-bond spin coupling measurements were carried out on ~0.01 M solutions in deuteriochloroform at 300 K using a Bruker AM500 instrument operating at 125.8 MHz. Couplings were determined for a spectral width of 12 500 Hz and 32 808 data points. The spectra were printed with zero fill at 24K memory, thereby giving a digital resolution of 0.4 Hz/point. Assignment of the two methine (CH) carbon signals in compounds **8**, **9**, and **13** (compounds **9**, **10**, and **19**, respectively, in ref 1) was confirmed from two dimensional CH correlation data. As expected, the signal for the bridgehead carbon in **13** was considerably sharper than that for the second methine carbon. By analogy, the sharper yet higher field methine signal from **15** was assigned to the bridgehead carbon.

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Synthesis of 4,5-Dimethyl-, 4,5,9-Trimethyl-, and 4,5,9,10-Tetramethylpyrene

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Introduction

Electrophilic reagents attack pyrene at carbons 1, 3, 6, and 8, but not at the other positions (2, 4, 5, 7, 9, and 10).[4,5] Therefore, pyrenes substituted at the latter positions must be prepared in ways other than by direct electrophilic substitution of pyrene itself.[6-8]

We previously reported the preparation of 4-alkylpyrenes such as 4-methyl-, 4-ethyl-, and 4-*n*-propylpyrene from pyrene by using the *tert*-butyl group as a positional protective group.[9,10] Here, we report the application of this method to the preparation of the titled methylpyrenes.

Results and Discussion

When 2,7-di-*tert*-butyl-4-methylpyrene (**1**), prepared from pyrene in three steps,[9] was treated with Cl_2CHOCH_3 in the presence of $TiCl_4$ as a catalyst, it gave a mixture of isomers **2a**-**c** in 87% yield. The isomer distribution of **2a**-**c** was **2a**:**2b** + **2c** = 86:14 according to GLC analysis. Isomer **2a** was isolated from this mixture in 49% yield by fractional recrystallization. In the ^1H NMR spectrum of **2a**, the methyl signal is shifted 0.28 ppm downfield to 3.17 ppm, owing to the influence of the neighboring formyl group, compared to the methyl group (2.89 ppm) of **1**, and ortho coupling (9.1 Hz) between the 9- and 10-positions is observed. Therefore, the formyl group was introduced at the 5-position. The isolation of **2b** and **2c** from this mixture was unsuccessful (Scheme I). However, the structures of the inseparable **2b** and **2c** were determined by reducing the crude mixture **2a**-**c** to a mixture of dimethylpyrenes that on further formylation and reduction gave a single trimethylpyrene **5**.

The preparation of 2,7-di-*tert*-butyl-4,5-dimethylpyrene (**3a**), 2,7-di-*tert*-butyl-4,5,9-trimethylpyrene (**5**), and 2,7-di-*tert*-butyl-4,5,9,10-tetramethylpyrene (**7**) from **2a** are shown in Scheme II.

Dimethyl derivative **3a** was obtained by reduction of **2a** with $LiAlH_4$-$AlCl_3$ in ether. Formylation of **3a** with Cl_2CHOCH_3 gave **4**, which was reduced to afford the trimethyl derivative **5** in good yield. Tetramethyl derivative **7** was obtained by formylation and reduction of **5**.

Also, the 4,5-dimethyl derivative **3a** was prepared from **2a** via the hydroxymethyl and chloromethyl derivatives **3b** and **3c** in 90 and 87% yield, respectively. Compound **3c** was easily converted to **3a** in 97% yield by reduction with $LiAlH_4$.

It was reported[11,12] that when *tert*-butylbenzene derivatives were treated with Nafion-H (DuPont) in boiling toluene, trans-*tert*-butylated benzenes and *tert*-butyltoluene were formed in excellent yields. Thus, trans-*tert*-butylation of **3a**, **5**, and **7** in the presence of Nafion-H was carried out in boiling toluene to obtain desired methylpyrenes **8a**-**c**. The results are summarized in Scheme III.

Experimental Section

Melting points are uncorrected. IR spectra were recorded as KBr pellets. ^1H NMR spectra were taken at 270 MHz in $CDCl_3$ solution. Mass spectra were recorded at 75 eV using a direct-inlet system. GLC was done on a OV-1 column (2 m). Wako C-300 silica gel was used for column chromatography.

2,7-Di-*tert*-butyl-4-methylpyrene-5-carboxaldehyde (2a). To a solution of 3.5 g (10.7 mmol) of **1** and 1.25 g (11 mmol) of

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