Stereochemistry of 1,2,3,4,5,6,7,8-Octakis(dichloromethyl)anthracene

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1,2,3,4,5,6,7,8-Octakis(dichloromethyl)anthracene (1) has been obtained by photochlorination of 1,2,3,4,5,6,7,8-octamethylanthracene. Signals in the ^{1}H NMR spectrum of 1 have been assigned by isotopic labeling and 2D NMR exchange spectroscopy. The relative steric energies of 20 selected conformations of 1 have been estimated by empirical force field calculations. The same calculations indicate that the spatial separation of the two sets of four dichloromethyl groups on the terminal rings of the anthracene skeleton renders the sets moderately independent. Homo- and heterodirectional relationships between subcycles of the molecular model are discussed. An analysis of the proton signal count and of the NOE involving the aromatic and peri dichloromethyl methine protons indicates that the ground-state structure of 1 has an all-geared homodirectional conformation. A topomerization barrier of 22.2 kcal mol^{-1} has been determined for 1 by the spin saturation transfer method.

Elsewhere we have described the stereochemistry of decakis(dichloromethyl)biphenyl, a molecule in which two sets of five gear-meshed dichloromethyl groups are attached to two essentially perpendicular frames and which exists in two enantiomeric all-geared conformations.[2] In this paper we discuss the stereochemistry of 1,2,3,4,5,6,7,8-octakis(dichloromethyl)anthracene, in which two sets of four such groups are attached to two essentially coplanar frames and which exists in two diastereomeric all-geared conformations.[3]

Conformational Analysis of 1,2,3,4,5,6,7,8-Octakis(dichloromethyl)anthracene

In 1,2,3,4,5,6,7,8-octakis(dichloromethyl)anthracene (1), whose synthesis and NMR properties will be described in the next section, two sets of four dichloromethyl groups on the terminal rings of the anthracene skeleton are separated by the pair of hydrogens in the middle ring. How many conformations are there, what are their relative energies, and does the spatial separation between the two sets render them sterically independent? In attempting to answer these questions we shall restrict our analysis to conformations in which all dichloromethyl groups are bisected, as previously observed in the analogous benzene systems.[3d,e]

Enumeration of Structures. Each of the eight dichloromethyl groups in 1 can be oriented in two directions, and the number of arrangements of these groups in 1 is therefore 2^8. This number obviously does not correspond to the number of distinct conformations since many of the arrangements are equivalent.[4]

Let us assume idealized conformations in which the carbon atoms are all located on a molecular symmetry plane (xy), with C(9) and C(10) located on the y axis. Under this constraint each conformation must belong to one of the following point groups: D_{2h}, C_{2v}, C_{2h}, and C_s. We can describe each of the conformations by a one-dimensional configurational matrix[5] that contains eight binary digits (0 or 1) and that can be used as a descriptor of the conformation. The set of eight binaries in each matrix denotes the orientation of the eight corresponding dichloromethyl groups according to an arbitrary convention (Figure 1). The matrices are generally not unique, i.e., a particular conformation can be represented by one or more matrices depending on its symmetry.[6] Thus any given conformation of 1 with C_s symmetry (symmetry number $\sigma = 1$) is represented by four equivalent matrices under the chosen convention, as illustrated in Figure 2. Structures with C_{2v} or C_{2h} symmetry ($\sigma = 2$) are represented by two equivalent matrices; for example, (0100 1101) and (1101 0100) are equivalent matrices for a particular structure with C_{2v} symmetry and (0100 0100) and (1101 1101) for a particular structure with C_{2h} symmetry. Only structures with D_{2h} symmetry ($\sigma = 4$) have matrices that are unique, for example (0011 0011).

It is seen by inspection that the abstract representations of the configurational matrices are invariant under the rotational operations of the four point groups. Let $X = A, B, C, ...$ represent binary digits, and let $\bar{X} = \{0 \text{ if } X = 1; 1 \text{ if } X = 0\}$. Then $(AB\bar{B}\bar{A}\ AB\bar{B}\bar{A})$ is invariant under $C_2(x)$, $C_2(y)$, and $C_2(z)$ in D_{2h}, $(AB\bar{B}\bar{A}\ CD\bar{D}\bar{C})$ under $C_2(x)$ and $(ABCD\ \bar{D}\bar{C}\bar{B}\bar{A})$ under $C_2(y)$ in C_{2v}, $(ABCD\ ABCD)$ under $C_2(z)$ in C_{2h}, and $(ABCD\ EFGH)$ under C_1 in C_s. The number N of matrices that belong to a particular symmetry class is given by $N = 2^n - R$, where $n = 8/\sigma$, the number of independent digits (i.e., different letters in the abstract representation), and R is the number of matrices that conform to the abstract representation in this class but correspond to structures with higher symmetry. Thus for D_{2h}, $n = 2$ and $R = 0$, so that $N = 4$. For C_{2v} or C_{2h}, $n = 4$ and $R = 4$ (corresponding to the four D_{2h} matrices), so that $N = 12$ for each of the three classes. For C_s, $n = 8$ and $R = 40$ (corresponding to the four D_{2h} matrices plus the 36 matrices in the C_{2v} and C_{2h} classes), so that $N = 216$. But, as we saw, some structures may be represented by more than one matrix. This redundancy must be corrected for, and the number of nonequivalent conformations is therefore given by $N\sigma/4$, i.e., by $4(D_{2h})$, $6(C_{2v}(x))$, $6(C_{2v}(y))$, $6(C_{2h})$, and $54(C_s)$, for a grand total of 76. The symmetries and configurational matrices (descriptors) of these conformations were generated by a simple computer program and are listed in Table I.

Relative Steric Energies. The unsubstituted central benzene ring of 1 splits the eight dichloromethyl groups into two sets of four. It is fair to assume that there are

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[2] Biali, S. E.; Kahr, B.; Okamoto, Y.; Aburatani, R.; Mislow, K. *J. Am. Chem. Soc.*, in press.

[3] For related work from our laboratory, see: (a) Weissensteiner, W.; Gutiérrez, A.; Radcliffe, M. D.; Siegel, J.; Singh, M. D.; Tuohey, P. J.; Mislow, K. *J. Org. Chem.* **1985**, *50*, 5822. (b) Siegel, J.; Gutiérrez, A.; Schweizer, W. B.; Ermer, O.; Mislow, K. *J. Am. Chem. Soc.* **1986**, *108*, 1569. (c) Singh, M. D.; Siegel, J.; Biali, S. E.; Mislow, K. *Ibid.* **1987**, *109*, 3397. (d) Kahr, B.; Biali, S. E.; Schaefer, W.; Buda, A. B.; Mislow, K. *J. Org. Chem.* **1987**, *52*, 3713 and references therein. (e) Biali, S. E.; Buda, A. B. *Ibid.* **1988**, *53*, 135.

[4] For example, in hexaisopropylbenzene the 2^6 different arrangements of bisected isopropyl groups reduce to the nine distinct conformations depicted in Figure 5 of ref 3b.

[5] Willem, R.; Pepermans, H.; Hoogzand, C.; Hallenga, K.; Gielen, M. *J. Am. Chem. Soc.* **1981**, *103*, 2297.

[6] The number of configurational matrices describing a particular structure is in the inverse order to the symmetry number. See: Brocas, J.; Gielen, M.; Willem, R. *The Permutational Approach to Dynamic Stereochemistry*; McGraw-Hill: New York, 1983; Chapter 8.

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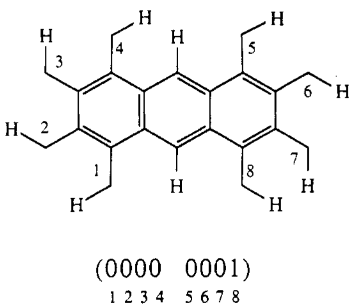

Figure 1. Exemplification of the convention chosen to describe the conformations of **1**. The structure of the molecule is schematically represented by a figure with lines in the plane of the anthracene skeleton projecting from the methine carbons in the direction of the methine hydrogens. Chlorine atoms are suppressed for clarity. The eight binary digits in the matrix denote the orientation of the eight dichloromethyl groups, starting from position 1 and proceeding in a clockwise fashion around the skeleton. The two sets of four binaries that correspond to the two sets of dichloromethyl groups on the terminal rings are separated by a space.

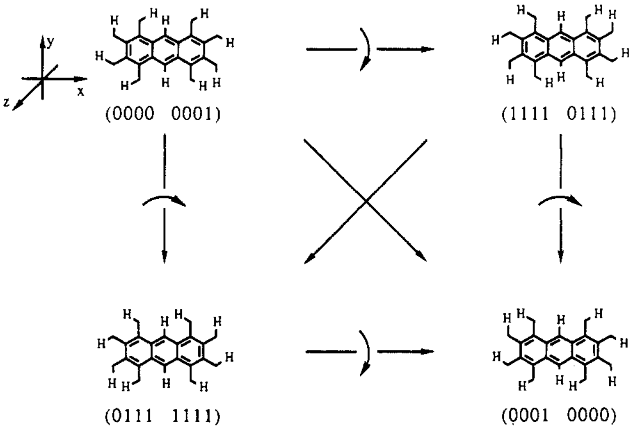

Figure 2. Four equivalent matrices for the conformation shown in Figure 1 (C_s symmetry). Horizontal, vertical, and diagonal arrows represent rotations by π about the x, y, and z axes, respectively.

strong interactions between neighboring groups within each of the two sets but only weak interactions between groups belonging to different sets across the "gap" around the 9- and 10-positions of anthracene. If this assumption holds, the steric effects due to particular orientations of dichloromethyl groups in one set are, to a first approximation, independent of those in the other, and the contributions of the two sets to the molecular steric energy are therefore roughly additive. Under this assumption the steric energy of (*ABCD EFGH*) is the sum of the steric energies of (*ABCD IJKL*) and (*IJKL EFGH*), all relative to (*IJKL IJKL*). Accordingly, the relative steric energy (RSE) of each of the 76 conformations can be estimated from the RSEs of the 16 conformations in which the four dichloromethyl groups in one set are kept in the same position (*IJKL*) while the four groups in the other are oriented in 2^4 ways.

The steric energies of the 16 conformations described by the configurational matrices (0000 *ABCD*), where *A*, *B*, *C*, *D* $\in \{0,1\}$, were calculated by the empirical force field (EFF) method using the MM2(85) force field.[7] Steric energies relative to (0000 0000) are listed in Table I. The 16 conformations can be partitioned into three classes according to the number of $HCCl_2\cdots Cl_2CH$ interactions, in which two pairs of chlorine atoms on vicinal dichloromethyl groups face each other in a gear-clashing conformation. In class I (conformations 5, 17, 23, 25, 29) there are no gear-clashing interactions, in class II (conformations 24, 26–28, 30, 31, 33–36) there is one, and in class III (conformation 32) there are two. Since such gear-clashing interactions lead to substantial increases in strain energy,[3d,e] it is not surprising to find that the corresponding RSEs are also grouped according to class: 0.0–2.6, 7.5–13.5, and 16.6 kcal mol^{-1} for classes I, II, and III, respectively. A similar partitioning of conformer structures and energies has previously been described for hexaethylbenzene,[8] hexaisopropylbenzene,[3b] hexakis(dimethylsilyl)benzene,[9]

Table I. The 76 Bisected Conformations of Octakis(dichloromethyl)anthracene (1) with Achiral Point Group Symmetries[a,b] and Selected Relative Steric Energies[c]

point group		relative steric energy	
D_{2h}	(1) (0011 0011)	3.0	(3) (1010 1010)
	(2) (0101 0101)		(4) (1100 1100)
C_{2v}	(5) (0000 1111)	2.6	(11) (0011 0101)
	(6) (0001 0111)	1.6	(12) (0011 1010)
	(7) (0010 1011)		(13) (0101 0110)
	(8) (0011 1100)		(14) (0101 1010)
	(9) (0100 1101)		(15) (0101 1100)
	(10) (1000 1110)		(16) (1010 1100)
C_{2h}	(17) (0000 0000)	0.0	(20) (0100 0100)
	(18) (0001 0001)	1.2	(21) (0110 0110)
	(19) (0010 0010)		(22) (1000 1000)
C_s	(23) (0000 0001)	0.3	(50) (0010 0100)
	(24) (0000 0010)	7.3	(51) (0010 0101)
	(25) (0000 0011)	1.6	(52) (0010 0110)
	(26) (0000 0100)	11.6	(53) (0010 1000)
	(27) (0000 0101)	8.4	(54) (0010 1001)
	(28) (0000 0110)	8.9	(55) (0010 1010)
	(29) (0000 0111)	0.9	(56) (0010 1100)
	(30) (0000 1000)	11.9	(57) (0010 1101)
	(31) (0000 1001)	13.5	(58) (0010 1110)
	(32) (0000 1010)	16.6	(59) (0011 0100)
	(33) (0000 1011)	9.3	(60) (0011 0110)
	(34) (0000 1100)	12.7	(61) (0011 1000)
	(35) (0000 1101)	10.5	(62) (0100 0101)
	(36) (0000 1110)	12.6	(63) (0100 0110)
	(37) (0001 0010)		(64) (0100 1000)
	(38) (0001 0011)	1.9	(65) (0100 1001)
	(39) (0001 0100)		(66) (0100 1010)
	(40) (0001 0101)		(67) (0100 1100)
	(41) (0001 0110)		(68) (0100 1110)
	(42) (0001 1000)		(69) (0101 1000)
	(43) (0001 1001)		(70) (0110 1000)
	(44) (0001 1010)		(71) (0110 1001)
	(45) (0001 1011)		(72) (0110 1010)
	(46) (0001 1100)		(73) (0110 1100)
	(47) (0001 1101)		(74) (0110 1110)
	(48) (0001 1110)		(75) (1000 1010)
	(49) (0010 0011)		(76) (1000 1100)

[a] Conformations are numbered 1–76 and are identified by one-dimensional configurational matrices. From the set of equivalent matrices for a given structure, the matrix listed is the one with the lowest binary number. [b] Symmetries refer to idealized structures with a (xy) symmetry plane. All EFF-optimized structures deviate from ideality and display lower symmetries. [c] Calculated (EFF), in kcal mol^{-1}. The listed energies refer to the conformations in the left column of the Table.

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(7) Allinger, N. L. *QCPE* MM2(85), 1986. See: Sprague, J. T.; Tai, J. C.; Yuh, Y.; Allinger, N. L. *J. Comput. Chem.* **1987**, *8*, 581. Input geometries (of C_s symmetry) were based on standard bond lengths and angles. All calculations were done assuming a nonplanar π system (option NPLANE = 1). The modified torsional parameters for conjugated systems (Liljefors, T.; Tai, J. C.; Li, S.; Allinger, N. L. *J. Comput. Chem.* **1987**, *8*, 1051) were used as implemented in MM2(85).

(8) Hunter, G.; Blount, J. F.; Damewood, J. R., Jr.; Iverson, D. J.; Mislow, K. *Organometallics* **1982**, *1*, 448.

(9) Schuster, I. I.; Weissensteiner, W.; Mislow, K. *J. Am. Chem. Soc.* **1986**, *108*, 6661.

and chloropentakis(dichloromethyl)benzene.[3e]

With the calculation of the 16 RSEs for the set of (0000 *ABCD*) conformers, it should in principle be possible to estimate the RSEs of the remaining 60 conformers under the additivity assumption. To the limited extent that we have tested this assumption, the agreement is moderately satisfactory. For example, the RSE calculated (EFF) for (0001 0011), 1.9 kcal mol^{-1}, is the sum of the RSEs for (0000 0001) and (0000 0011), 0.3 and 1.6 kcal mol^{-1}, respectively. The RSE calculated for (0011 0011), 3.0 kcal mol^{-1}, is almost exactly twice the value for (0000 0011), and the RSE calculated for (0001 0001), 1.2 kcal mol^{-1}, is comparable to twice the value for (0000 0001). Good additivity is also found for the set of molecules in which all four dichloromethyl groups in the peri positions point their chlorines toward the gap around the 9- and 10-positions. In these conformations the hydrogens attached to the 9- and 10-positions are tucked into the clefts formed by the four pairs of chlorine atoms. Thus the steric energy of (0011 0011) relative to (0001 0001), 1.8 kcal mol^{-1}, is close to twice the steric energy of (0001 0011) relative to (0001 0001), 0.7 kcal mol^{-1}, and the steric energy of (0101 0101) relative to (0001 0001), 14.2 kcal mol^{-1}, is twice the steric energy of (0001 0101) relative to (0001 0001), 7.1 kcal mol^{-1}. On the other hand, when both groups in the 1,8- or 4,5-positions point their methine hydrogens at the aromatic hydrogen in the 9- or 10-positions, respectively, the additivity of the steric energies becomes less satisfactory. For example, a RSE of 2.6 kcal mol^{-1} is calculated for (0000 1111), whereas, under the additivity assumption, the RSE should be the same as that for (0000 0000), i.e., 0.0 kcal mol^{-1}.

That this generally satisfactory agreement is crucially dependent on the size of the "gap" that separates the two sets of groups may be shown by the counterexample of tetraisopropylethylene (2).[10] In this molecule the four isopropyl groups are gear-meshed much in the same fashion as the dichloromethyl groups in 1, and the ground state (M_1) has C_{2h} symmetry. However, because the "gap" in 2 consists only of a double bond, it can no longer be assumed that interactions between groups belonging to different sets are weak. It is therefore not surprising to find that the contributions of the two sets to the molecular steric energy are not even approximately additive. For example, using Ermer's conformational descriptors,[10] the RSEs of M_4 and M_5 are 6.77 and 9.39 kcal mol^{-1}, respectively, instead of 0.0 (the RSE of M_1).

Ground-State Structure. According to the EFF calculations, (0000 0000) is the lowest energy conformation of 1 among the 16 in the set (0000 *ABCD*). Among the remaining 60 conformations, only four (conformations 1, 6, 18, 38) need additionally to be considered because they are the only ones outside the five in class I that lack gear-clashing interactions between chlorines of vicinal dichloromethyl groups. The RSEs of the four were calculated and found to range from 1.2 to 3.0 kcal mol^{-1} (see Table I). The calculated ground-state conformation of 1 is therefore (0000 0000).

The calculated structure and structural parameters are shown in Figure 3. The dihedral angles of the anthracene skeleton show small but significant distortions from planarity, with an average deviation of 6°. The molecule is bent into a shallow boat conformation, and the calculated structure displays approximate C_2 symmetry. Structural parameters for the anthracene skeleton of 1 are quite similar to those calculated (MM2(85)) for anthracene itself:[11] the average differences in C–C bond lengths and C–C–C bond angles are 0.013 Å and 1.9°, respectively.

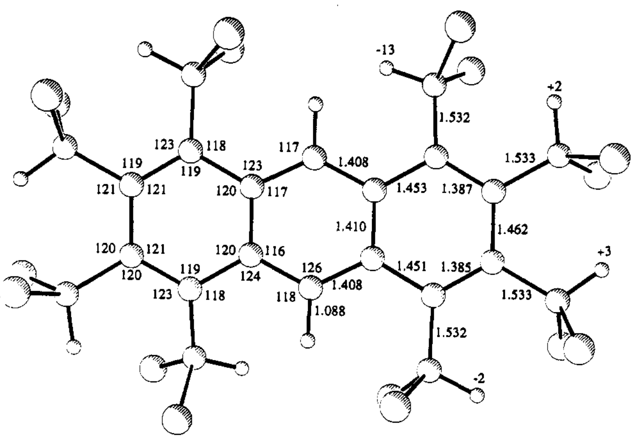

Figure 3. Projection of the calculated (MM2(85)) lowest energy conformation (0000 0000) of 1 along the approximate C_2 axis and selected average (over C_2 symmetry) structural parameters. Bond lengths and angles are in Å and degrees, respectively. Torsional angles for C_{ar}–C_{ar}–C_t–H are depicted near the methine hydrogens.

Cyclic Directionality. A feature of special interest is the cyclic directionality[13] that is associated with the dichloromethyl groups in 1. Let a cycle be defined by the points corresponding to the C_t's and H's of all eight dichloromethyl groups in 1:[15] then of the 76 idealized conformations in Table I, those with C_{2h} and C_s symmetry have directed cycles whereas those with D_{2h} and C_{2v} symmetry have undirected ones. Consider next the bisection of these cycles along the x or y axis into two subcycles, each of which involves four dichloromethyl groups.[16] For conformations with D_{2h} symmetry such bisection affords two undirected subcycles, whereas for all other conformations the subcycles are directed. In C_{2h} and C_{2v} conformations the two subcycles are related by symmetry, whereas no symmetry operation relates the subcycles in C_s conformations.

The mode of bisection that is most relevant to the chemical features of 1 is the one along the y axis which separates the two sets of dichloromethyl groups in the terminal rings. The sense of directionality of the subcycles is given by a spectator point[14] located above or below the mean plane of the cycle. Viewed from such a spectator point the two subcycles are homodirectional in (0000 0000) whereas in (0000 1111) they are heterodirectional (Figure 4).[17] In this and all similar cases, reversal of the sense of directionality of one subcycle, e.g., by rotation of four dichloromethyl groups through π, results in interconversion

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(10) Ermer, O. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 998.

(11) The bonding parameters in the X-ray structure of anthracene[12] are satisfactorily reproduced in these calculations. The largest discrepancy is for the C(4a)–C(9a) bond (calculated, 1.419 Å; observed,[12] 1.433 Å).

(12) Mason, R. *Acta Crystallog.* **1964**, *17*, 547.

(13) A cycle is defined by three or more noncollinear points in the molecular model. A cycle is undirected if it is bisected by a molecular C_{2n} axis in, or by a molecular σ plane perpendicular to, the mean plane of the cycle. Otherwise it is directed.[3c,14]

(14) Mislow, K. *Chimia* **1986**, *40*, 395.

(15) In principle an infinite number of different cycles can be defined in a given model, and the choice of one particular set of points is therefore merely a matter of convenience.

(16) The bisection of directed and undirected cycles and the symmetry relationships of the resulting halves parallels the corresponding bisection of chiral and achiral objects in two-dimensional space. See: Anet, F. A. L.; Miura, S. S.; Siegel, J.; Mislow, K. *J. Am. Chem. Soc.* **1983**, *105*, 1419.

(17) Since the homodirectional/heterodirectional pairing is based on symmetry, the relation is independent of any convention used for defining the sense of directionality of the subcycles. In contrast, the subcycles in C_s conformations of 1 are symmetry-nonequivalent and the homodirectional/heterodirectional relationship between the subcycles is therefore dependent on such a convention.

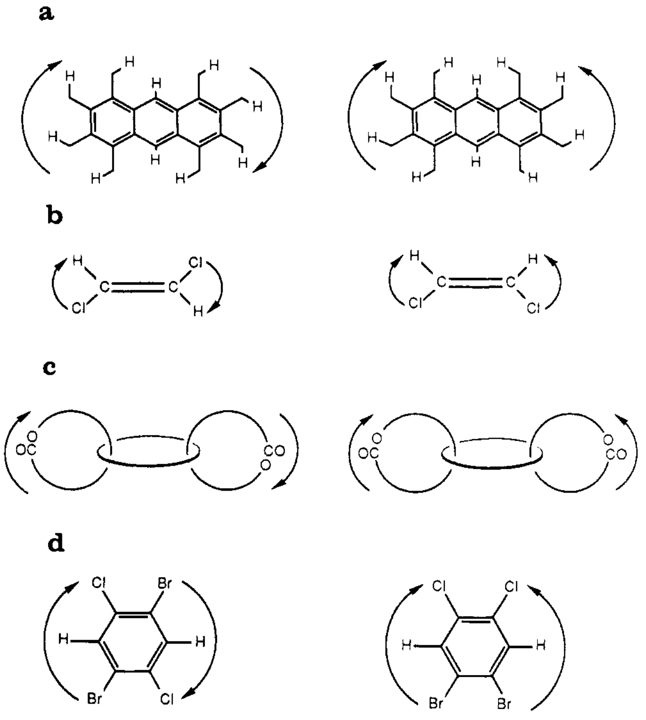

Figure 4. Isomeric pairs that bear the homodirectional/heterodirectional relationship and have C_{2h} and C_{2v} symmetries, respectively. The curved arrows symbolize the sense of cyclic directionality according to an arbitrary convention. From the top: (a) Two all-geared conformations of 1. Left: (0000 0000), right: (0000 1111). (b) (*E*)- and (*Z*)-1,2-dichloroethenes. (c) Two hypothetical [3]catenanes. The internal, undirected ring is a cycloalkane of formula type $(CH_2)_n$, whereas the outer, directed rings contain an additional lactone functionality. (d) 1,4-Dibromo-2,5-dichlorobenzene and 1,2-dibromo-4,5-dichlorobenzene.

of the diastereomeric C_{2h}/C_{2v} pair, whereas reversal of both subcycles results in homomerization.

Isomeric pairs that bear the homodirectional/heterodirectional relationship and share the symmetries of the previously described pair are ubiquitous in chemistry. One of the simplest examples is H_2O_2 in its eclipsed and anti conformations. Other examples are (*E*)- and (*Z*)-1,2-dichloroethenes, M_1 and idealized M_4 and M_5 conformations of **2**,[10] *cis*- and *trans*-dichlorodiaminoplatinates, and the pair of "topological diastereomers"[18] shown in Figure 4. Note that these mappings are not restricted to diastereomers: for example, the constitutionally isomeric pair 1,4-dibromo-2,5-dichlorobenzene/1,2-dibromo-4,5-dichlorobenzene also fits this classification. This illustrates our thesis that any analysis of molecular models that gives primacy to symmetry rather than constitution is blind to distinctions between diastereomers and constitutional isomers.[19]

Synthesis and NMR Properties of 1,2,3,4,5,6,7,8-Octakis(dichloromethyl)anthracene

The procedure for the synthesis of 1 was patterned after the synthesis of hexakis(dichloromethyl)benzene by Imhof[20] and by Mark and Pattison.[21] Exhaustive photochemical chlorination of the known 1,2,3,4,5,6,7,8-octamethylanthracene afforded 1. The compound crystallized from 1,1,2,2-tetrachloroethane as fine needles. Upon filtration the crystals immediately turned opaque, probably due to loss of solvent of crystallization.

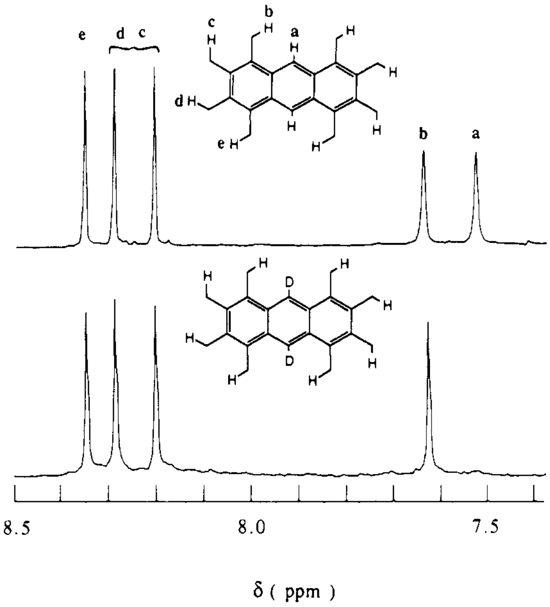

Figure 5. Top: 250.13 MHz ^1H NMR spectrum of 1 in $CDCl_2CDCl_2$ at room temperature. Bottom: Corresponding spectrum of [9,10-$^2H_2$]-1.

The 250-MHz ^1H NMR spectrum of 1 in $CDCl_2CDCl_2$ (Figure 5, top) features five signals, two in the upfield (δ 7.5–7.7) region and three at lower field (δ 8.21–8.33). While the signals in the low-field set appear sharp, the two high-field signals show some broadening, presumably due to mutual unresolved long-range coupling. The signal count (five) is consistent with the (0000 0000) conformation depicted in Figure 5. The low-field signals arise from the three symmetry-nonequivalent dichloromethyl methine protons that are tucked into the clefts of the chlorines on neighboring dichloromethyl groups and are therefore deshielded. The two upfield signals are assigned to the aromatic proton and to the dichloromethyl group in the peri position whose methine proton points toward the aromatic hydrogen. Replacement of the aromatic hydrogens by deuteriums resulted in a ^1H NMR spectrum differing from that of 1 by the absence of the most upfield signal (a) and a sharpening of the next most upfield signal (b) (Figure 5, bottom).[22] Accordingly, a is assigned to the aromatic proton and b to the methine proton of the proximal dichloromethyl group in the peri position. Additional assignments were made on the basis of the NMR behavior of 1 at elevated temperatures.

NMR Spectra at Elevated Temperatures. On the time scale of rapid internal rotation, topomerization of (0000 0000) to (1111 1111) equivalences b and e signals and also c and d signals, and thus allows further signal assignments. However, a sample of 1 in $CDCl_2CDCl_2$ did not exhibit any appreciable line broadening of the ^1H NMR signals at 250 MHz up to 391 K. We therefore resorted to the saturation spin-transfer (SST) method which measures rates that are comparable to $1/T_1$ and can therefore be conveniently carried out at relatively lower

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[18] Walba, D. M. *Tetrahedron* **1985**, *41*, 3161.

[19] Mislow, K. *Bull. Soc. Chim. Belg.* **1977**, *86*, 595. Mislow, K.; Siegel, J. *J. Am. Chem. Soc.* **1984**, *106*, 3319.

[20] Imhof, W., Dissertation ETH, Zürich, 1964 (prom. no. 3507), pp 22–24, 48–49. See also: Hopff, H. *Chimia* **1964**, *18*, 140.

[21] Mark, V.; Pattison, V. A. *J. Chem. Soc., Chem. Commun.* **1971**, 553. Mark, V., private communication.

[22] H–D couplings are ca. 6.5 times smaller than the corresponding H–H couplings,[23] and the diminution of the long-range coupling between a and b causes the sharpening of b.

[23] Sandström, J. *Dynamic NMR Spectroscopy*; Academic: New York, 1982; p 124.

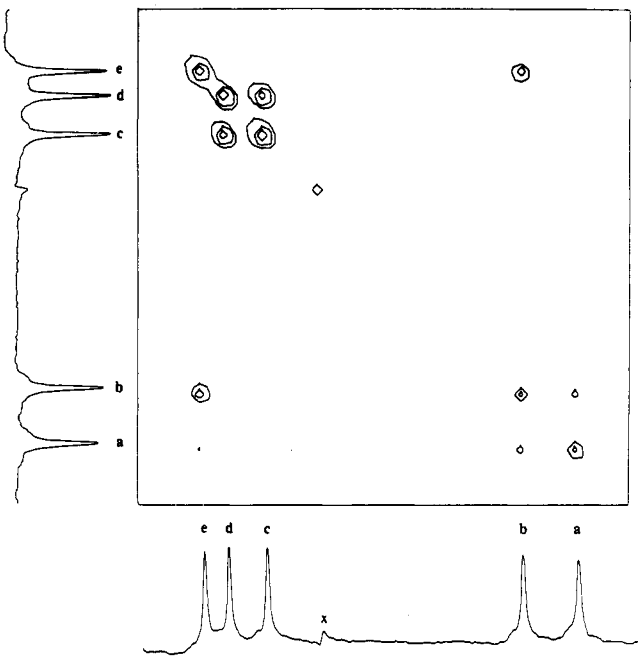


Figure 6. 250.13 MHz ^{1}H 2D exchange NMR spectrum of 1 in $CDCl_2CDCl_2$ at 390 K. The signal marked x is due to an impurity.

temperatures. The experiment was carried out in $CDCl_2CDCl_2$ at 391 K by delivering a selective 180° pulse on signal b, followed by a nonselective 90° pulse after increasingly longer delay times. The only one of the four other signals to show a diminution of intensity as a consequence of transfer of saturation from the irradiated signal was the one located at lowest field, e. Accordingly, this signal can be assigned to the methine proton on the dichloromethyl group para to b (Figure 5). Treatment of the change of intensities of the b and e signals as a function of time according to the literature procedure[24] afforded a topomerization rate constant of 2.65 s^{-1}. From the Eyring equation and assuming a transmission coefficient equal to unity, a topomerization barrier of 22.2 kcal mol^{-1} was calculated.

The ^{1}H 2D exchange NMR spectrum[25] of 1 in $CDCl_2CDCl_2$ at 390 K is depicted in Figure 6. In this kind of spectrum the contours along the diagonal represent cross sections of the 1D spectrum at chosen levels. The off-diagonal contours (cross peaks) at coordinates ij and ji indicate mutual magnetization transfer between magnetic sites i and j. This magnetization transfer can be the result of either dynamic exchange (i.e., via rotation of the side chains) or NOEs. Figure 6 shows strong cross peaks at coordinates (b,e), (e,b), (c,d), and (d,c), which indicates that signals b and e as well as c and d are involved in mutual exchange. Cross peaks of lower intensity are observed at coordinates (a,b) and (b,a) due to NOEs between a and b. These NOEs as well as saturation transfer effects were corroborated by 1D NMR spectra. The NOE between a and b indicates that the two corresponding protons are in spatial proximity. We note that there are cross peaks at coordinates (a,e) and (e,a) of very low intensity. It seems plausible that these cross peaks arise due to a combination of NOEs between sites a and b and dynamic exchange between b and e. The 2D exchange spectrum thus fully establishes the relationships among the five nonequivalent hydrogens depicted in Figure 5; the only remaining uncertainty is in the relative position of the signals corresponding to c and d.

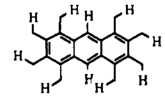
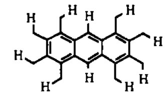
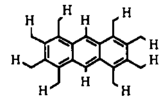
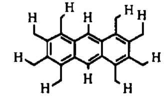
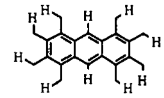
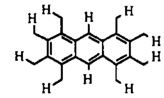
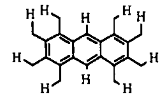
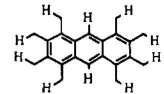
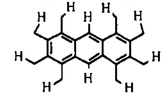
Descriptor		No. of NMR signals	NOE
(0000 0000)		5	yes
(0000 0001)		10	yes
(0000 0011)		10	yes
(0000 0111)		10	yes
(0001 0001)		5	no
(0001 0011)		10	no
(0001 0111)		5	no
(0011 0011)		3	no
(0000 1111)		6	yes

Figure 7. The nine lowest energy conformations of 1, the expected number of ^{1}H NMR signals for each, and the expectation that a NOE will be observed between the aromatic hydrogens and the proximal dichloromethyl hydrogens.

The Preferred Conformation in Solution. According to the EFF calculations there are nine conformations of 1, the calculated ground-state (0000 0000) among them, that range in RSE from 0.0 to 3.0 kcal mol^{-1} and that are characterized by the absence of gear-clashing interactions between chlorines of vicinal dichloromethyl groups. However, the NMR spectrum (Figure 5) is consistent only with a *single* conformation and cannot be reconciled with a conformational mixture in rapid equilibrium because rotation of the dichloromethyl side chains is frozen on the NMR time scale at room temperature. It is possible to exclude all but one of the nine low-energy conformations of 1 by considering, first, the number of ^{1}H NMR signals expected for each conformation (barring accidental isochrony) and, second, the question of whether or not a NOE is expected between the protons corresponding to signals a and b (on the assumption that such an effect will be observed whenever a peri dichloromethyl proton points at an aromatic hydrogen). As shown in Figure 7, only the (0000 0000), (0001 0001), and (0001 0111) conformations are expected to display five signals in the ^{1}H NMR spectrum at the slow-exchange limit, and of these only the (0000 0000) conformation is expected to exhibit a NOE. It can therefore be safely concluded that 1 exists in solution as a single conformer with the calculated ground-state structure. By the same token, the nonobservation of other conformers, particularly of (0000 0001), which has a RSE of only 0.3 kcal mol^{-1}, suggests that other effects not ac-

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[24] Dahlquist, F. W.; Longmuir, K. J.; Du Vernet, R. B. *J. Magn. Reson.* **1975**, *17*, 406.

[25] For a review of 2D NMR techniques, see: Benn, R.; Günther, H. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 350. Willem, R. *Progr. Nucl. Magn. Reson. Spectrosc.* **1987**, *20*, 1.

counted for by the EFF calculations are operative for 1 in solution.

Experimental Section

NMR spectra were recorded on a Bruker WM-250 spectrometer. Temperature measurements were based on the chemical shift separation of an ethylene glycol sample, and utilization of the Van Geet relationship.[26] For the 2D spectra a sequence of three pulses (90°–t_1–90°–t_m–90°)$_n$, where t_m is the mixing time, was used as implemented in Bruker's program NOESY.AU. Thirty-two FIDs (each consisting of 16 scans of 128 data points) were accumulated. The FIDs were zero-filled to $128w$ in the F_1 dimension. The determination and the simulation of the molecular ion cluster was performed on a Kratos MS 50 RFA spectrometer. The high-resolution mass spectrum was obtained by the Midwest Center for Mass Spectrometry.

1,2,3,4,5,6,7,8-Octakis(dichloromethyl)anthracene (1). 1,2,3,4,5,6,7,8-Octamethylanthracene (90 mg, 0.31 mmol), prepared from 1,2,3,4,5,6,7,8-octamethyl-9,10-dihydroanthracene[27] according to the literature procedure,[28] was dissolved in 30 mL of CCl_4. The solution was heated under reflux and irradiated with a 150-W lamp while a slow stream of chlorine gas was introduced. After 16 h the reaction was stopped. The solid that had deposited on the gas inlet tube was collected to give 140 mg (64%) of essentially pure 1 (^{1}H NMR). The compound was recrystallized from 1,1,2,2-tetrachloroethane to afford transparent crystals, which turned immediately opaque upon filtration. The crystals were repeatedly washed with ether and dried by suction to yield a product, mp >300 °C, free of solvent. ^{1}H NMR (room temperature, $CDCl_2CDCl_2$) δ 7.53 (s, 1 H, br); 7.64 (s, 1 H, br); 8.21 (s, 1 H); 8.30 (s, 1 H); 8.33 (s, 1 H). High-resolution mass spectra (only the three most intense signals of the molecular ion cluster are given), *m/z* 839.5703 (839.5707 calcd for $C_{22}H_{10}{}^{35}Cl_{13}{}^{37}Cl_3$), 841.5674 (841.5676 calcd for $C_{22}H_{10}{}^{35}Cl_{12}{}^{37}Cl_4$), 843.5655 (843.5646 calcd for $C_{22}H_{10}{}^{35}Cl_{11}{}^{37}Cl_5$). The experimentally determined and calculated molecular ion clusters are in good agreement.

[9,10-$^2H_2$]-1,2,3,4,5,6,7,8-Octakis(dichloromethyl)anthracene. A solution of 1 (10 mg) and CF_3COOD (1 mL, Aldrich, 99 atom % D) in 4 mL of hexane was stirred and heated under reflux for 20 h. After evaporation of the solvent, the ^{1}H NMR spectrum showed that the 9,10-positions were completely exchanged by deuterium. The deuteriated anthracene was chlorinated according to the procedure described for the unlabeled compound. ^{1}H NMR (room temperature, $CDCl_2CDCl_2$) δ 7.64 (s, 1 H); 8.21 (s, 1 H); 8.30 (s, 1 H); 8.33 (s, 1 H).

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Registry No. 1, 112947-60-1; 1,2,3,4,5,6,7,8-octamethylanthracene, 64094-28-6.

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[26] Van Geet, A. L. *Anal. Chem.* **1968**, *40*, 2227; *Ibid.* **1970**, *42*, 679.

[27] Welch, C. M.; Smith, H. A. *J. Am. Chem. Soc.* **1951**, *73*, 4391.

[28] Backer, H. J.; Strating, J.; Huisman, L. H. H. *Recl. Trav. Chim. Pays-Bas* **1939**, *58*, 761.

A Regiocontrolled Synthesis of N^7- and N^9-Guanine Nucleosides

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The reaction of 2-O-acetylated and 2-O-benzoylated glycosides **3a**,**b**/**4a**,**b** with silylated N^2-acetylguanine **7** selectively gave N^7-guanine nucleosides **8a**,**b**/**9a**,**b** under kinetically controlled conditions ($SnCl_4/CH_3CN$, room temperature), whereas 2-O-benzoylated glycosides **3b**/**4b** selectively gave the isomeric N^9-guanine nucleosides **10b**/**11b** under thermodynamically controlled conditions (TMSOTf/$(CH_2Cl)_2$, reflux). Unambiguous assignment of nucleoside structure was accomplished after hydrolysis (NH_3/MeOH) of the initial products to the known nucleosides **8c**, **9c**, **10c**, and **11c** followed by ^{1}H and ^{13}C NMR spectral analysis. The described procedures provide the best method to date for the selective synthesis of either N^7- or N^9-guanine nucleosides from a common substrate.

As part of a program directed toward the synthesis of the nucleoside antibiotics amipurimycin (1) and miharamycin (2),[1] we required a method for the synthesis of N^9-pyranosyl-2-aminopurines from their corresponding glycosidic precursors. In this context a coupling procedure that involved the use of a readily available silylated guanine derivative in conjunction with a Lewis acid catalyst seemed most appropriate even though the regioselectivity of this reaction (ie. N^7- vs N^9-glycosylation) is not generally high with this base.[2–4] Once the desired N^9-nucleoside is obtained, however, modification of the guanine moiety to give the 2-aminopurine could then follow well established procedures.[5] Herein we report on work which has cul-

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[1] Amipurimycin: Goto, T.; Toya, Y.; Ohgi, T.; Kondo, T. *Tetrahedron Lett.* **1982**, 1271. Miharamycin: Seto, H.; Koyama, M.; Ogino, H.; Tsuruoka, T.; Inouye, S.; Otake, N. *Ibid.* **1983**, 1805.

[2] For a review of developments in the area of nucleoside synthesis, see: Dekker, C. A.; Goodman, L. In *The Carbohydrates*, 2nd Ed.; Pigman, W., Horton, D., Herp, A., Eds.; Academic: New York, 1970. And more recently: Vorbrüggen, H. *NATO Adv. Study Inst. Ser., Ser. A* **1979**, *26*, 35.

[3] (a) Lichtenthaler, F. W.; Voss, P.; Heerd, A. *Tetrahedron Lett.* **1974**, 2141. (b) Vorbrüggen, H.; Krolikiewicz, K.; Bennua, B. *Chem. Ber.* **1981**, *114*, 1234. (c) Morr, M. *Liebigs Ann. Chem.* **1982**, 666. The NMR data reported in this paper seems to indicate that a (2.5:1) mixture of N^9:N^7 regioisomers was obtained rather than the reported anomeric mixture of N^9-nucleosides—see Table I. (d) For a related "transnucleosidation", see: Azuma, T.; Isono, K. *Chem. Pharm. Bull.* **1977**, *25*, 3347.

[4] Previous approaches to nucleosides (and nucleotides) that also employed guanine derivatives directly for the coupling include: (a) Imai, K.; Nohara, A.; Honjo, M. *Chem. Pharm. Bull.* **1966**, *14*, 1377. (b) Nomura, H.; Suhara, I.; Uno, N. *Ibid*, **1967**, *15*, 1258. (c) Furukawa, Y.; Honjo, M. *Ibid.* **1968**, *16*, 1076. (d) Furukawa, Y.; Imai, K.; Honjo, M. *Tetrahedron Lett.* **1968**, 4655. (e) Suzaki, S.; Yamazaki, A.; Kamimura, A.; Mitsugi, K.; Kumashiro, I. *Chem. Pharm. Bull.* **1970**, *18*, 172. (f) Lee, W. W.; Martinez, A. P.; Goodman, L. *J. Org. Chem.* **1971**, *36*, 842. (g) Iwamura, H.; Miyakado, M.; Hashizume, T. *Carbohydr. Res.* **1973**, *27*, 149. (h) Hobbs, J. B.; Eckstein, F. *J. Org. Chem.* **1977**, *42*, 714.

0022-3263/88/1953-1294$01.50/0