Inorg. Chem. **2007**, *46*, 9278–9284

Inorganic Chemistry Article

Diastereoselectivity in the Self-Assembly of $As_2L_2Cl_2$ Macrocycles is Directed by the As–π Interaction

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Received June 29, 2007

The As–π interaction, in conjunction with reversible As–thiolate bond formation, is used to direct the self-assembly of dinuclear $As_2L_2Cl_2$ (L = a dithiolate) macrocycles that exist as equilibrium mixtures of both syn and anti diastereomers. The diastereomeric excess of these self-assembly reactions is controlled in a predictable manner by prudent choice of different achiral, isomeric ligands. A general method for the preparation of $As_2L_2Cl_2$ macrocycles is established, and strategies to control the diastereoselective self-assembly of regioisomeric macrocycles in solution and the crystalline state are described. A mechanism for the interconversion between diastereomers (a slow process on the NMR time scale) is suggested, and variable-temperature NMR spectroscopic data show that the diastereomeric excess (de) decreases with increasing temperature. *anti*-$As_2(\mathbf{L}^{2,6})_2Cl_2$ crystallizes in monoclinic space group $P2_1/n$ with $a = 6.3949(13)$, $b = 19.675(4)$, $c = 10.967(2)$ Å, $\beta = 106.817(3)°$, and $Z = 2$. *anti*-$As_2(\mathbf{L}^{1,5})_2Cl_2$ crystallizes in monoclinic space group $P2_1/c$ with $a = 6.813(4)$, $b = 19.085(12)$, $c = 10.277(6)$ Å, $\beta = 107.788(10)°$, and $Z = 4$. *syn*-$As_2(\mathbf{L}^{1,4})_2Cl_2{\cdot}CHCl_3$ crystallizes in triclinic space group $P\bar{1}$ with $a = 19.313(4)$, $b = 19.923(4)$, $c = 24.508(5)$ Å, $\alpha = 78.110(4)°$, $\beta = 78.860(5)°$, $\gamma = 89.183(5)°$, and $Z = 12$. $As_2(\mathbf{L}^{1,4})_2Cl_2{\cdot}C_6H_6$ crystallizes in monoclinic space group $P2_1/n$ with $a = 10.3332(7)$, $b = 34.375(2)$, $c = 17.8593(12)$ Å, $\beta = 98.9650(10)°$, and $Z = 8$.

Introduction

The use of main-group ions as directing elements in metal–ligand self-assembly reactions is rare, and few predictive design strategies for forming self-assembled supramolecular main-group compounds exist.[1–3] We have recently developed a strategy to synthesize self-assembled dinuclear arsenic-containing structures[4,5] that are stabilized by arsenic–π interactions.[6,7] $As_2\mathbf{L}_2Cl_2$ ($H_2\mathbf{L}$ = *p*-bis(mercaptomethyl)benzene) macrocyclic structures synthesized by this strategy exist in equilibrium as a statistical mixture of syn and anti diastereomers (Scheme 1), in which the arsenic–π interaction directs the arsenic atoms into the macrocyclic cavity formed by the arene rings of the ligands.

Metal–ligand self-assembly reactions that can lead to two or more possible diastereomers typically proceed diastereoselectively.[8,9] To the best of our knowledge, only a few examples exist of metal–ligand self-assembly reactions that provide a mixture of diastereomers: 1) in rare instances, multiple diastereomeric M_4L_6 tetrahedra (T, C_3, or S_4) exist in equilibrium,[10] and 2) diastereomeric excess (de) values have been reported in the formation of host–guest *complexes*

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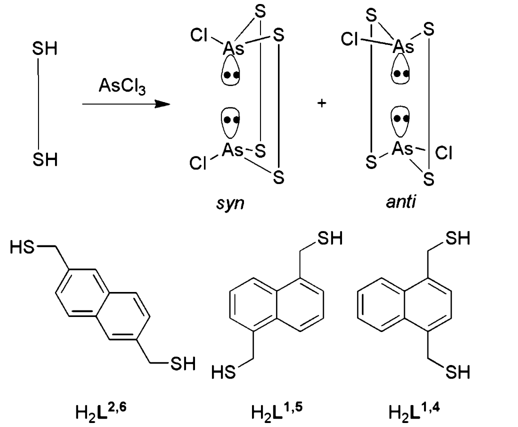
(1) Healey, E. R.; Vickaryous, W. J.; Berryman, O. B.; Johnson, D. W. In *Bottom-up Nanofabrication: Supramolecules, Self-Assemblies, and Organized Films*; Nalwa, H. S., Ed.; American Scientific Publishers, 2007.
(2) Pitt, M. A.; Johnson, D. W. *Chem. Soc. Rev.* **2007**, *36*, 1441–1453.
(3) Cook, V. C.; Willis, A. C.; Zank, J.; Wild, S. B. *Inorg. Chem.* **2002**, *41*, 1897–1906.
(4) Vickaryous, W. J.; Herges, R.; Johnson, D. W. *Angew. Chem., Int. Ed.* **2004**, *43*, 5831–5833.
(5) Vickaryous, W. J.; Healey, E. R.; Berryman, O. B.; Johnson, D. W. *Inorg. Chem.* **2005**, *44*, 9247–9252.
(6) The arsenic–π interaction is an attraction between a π base and a Lewis acidic arsenic center. For a more detailed discussion of the nature of these interactions in a supramolecular context, see: Carter, T. G., Vickaryous, W. J.; Cangelosi, V. M.; Johnson, D. W. *Comm. Inorg. Chem.* 2007, in press.
(7) Schmidbaur, H.; Bublak, W.; Huber, B.; Muller, G. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 234–236. Schmidbaur, H.; Nowak, R.; Steigelmann, O.; Muller, G. *Chem. Ber.* **1990**, *123*, 1221–1226.
(8) Hamilton, T. D.; MacGillivray, L. R. *Cryst. Growth Des.* **2004**, *4*, 419–430.
(9) Seeber, G. T., Bryan E. F.; Raymond, Kenneth N. In *Top. Curr. Chem.*; Springer Berlin: Heidelberg, Germany, 2006; Vol. 265, pp 147–183.

10.1021/ic701290h CCC: $37.00
Published on Web 09/20/2007

Scheme 1. Self-Assembly of $As_2L_2Cl_2$ Macrocycles[a]



[a] In the syn macrocycle, both chlorine atoms are on the same side of the arsenic atoms. In the anti macrocycle, the chlorine atoms are on opposite sides of the macrocyclic cavity.

in which two enantiomers of a chiral guest have different binding affinities within two enantiomers of a chiral host molecule.[11]

We now show that the de of self-assembled arsenic-containing macrocycles can be controlled by the appropriate choice of achiral, isomeric dithiol ligands (Scheme 1). This demonstrates the generality of our design strategy for forming $As_2L_2Cl_2$ macrocycles and shows an unusual example of multiple supramolecular interactions (reversible As−S bond formation and As−π interactions) acting in tandem to dictate the stereochemical outcome of a self-assembly reaction.

Experimental Section

General Procedures. ^{1}H NMR spectra were measured using a Varian INOVA-500 spectrometer operating at 500.11 MHz ($As_2(\mathbf{L}^{2,6})_2Cl_2$ and $As_2(\mathbf{L}^{1,4})_2Cl_2$) and a Varian INOVA-600 spectrometer operating at 599.98 MHz ($As_2(\mathbf{L}^{1,5})_2Cl_2$). All of the variable-temperature experiments were carried out on the Varian INOVA-500 spectrometer on compounds dissolved in 1,1,2,2-tetrachloroethane-d_2. Spectra were referenced using either TMS or the residual solvent resonances as internal standards. Single-crystal X-ray diffraction studies were performed on a Bruker SMART APEX diffractometer. Commercially available reagents were used as received. All of the ligands were prepared following a modified literature procedure. (See Supporting Information for details on changes to the literature procedure).[12]

^{1}H NMR spectroscopy revealed complete transformation (>99% yield) of the ligand and $AsCl_3$ to macrocycles $As_2(\mathbf{L}^{2,6})_2Cl_2$ and $As_2(\mathbf{L}^{1,4})_2Cl_2$. (This was not measurable for $As_2(\mathbf{L}^{1,5})_2Cl_2$ because of poor product solubility). The reported yields below are for isolated single crystals. *Caution: Arsenic compounds are hazardous and should be handled with care!* (This accounts for the small scale of the reactions reported herein.)

$As_2(L^{2,6})_2Cl_2$. $AsCl_3$ (6.37 μL, 0.0746 mmol) was added slowly to a solution of $H_2\mathbf{L}^{2,6}$ (16.5 mg, 0.0746 mmol) in $CDCl_3$ (5 mL) to yield a solution containing only a mixture of syn and anti diastereomers in a ratio of 1.7:1 after 3 days. Single crystals were grown by slow vapor diffusion of pentane into a $CHCl_3$ solution of $As_2(\mathbf{L}^{2,6})_2Cl_2$ yielding colorless crystals after 3 days (4.7 mg, 0.0072 mmol, 19%).

syn-$As_2(\mathbf{L}^{2,6})_2Cl_2$: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, 2H, C*H*, J = 8.8 Hz), 7.56 (s, 2H, C*H*), 7.35 (m, 2H, C*H*), 4.26 (ABq, CH_2, 4H,, J = 12.9 Hz).

anti-$As_2(\mathbf{L}^{2,6})_2Cl_2$: ^{1}H NMR ($CDCl_3$) δ 7.63 (d, 2H, C*H*, J = 8.5 Hz), 7.51 (s, 2H, C*H*), 7.38 (m, 2H, C*H*), 4.25 (ABq, CH_2, 4H, J = 12.9 Hz).

$As_2(L^{1,5})_2Cl_2$. $AsCl_3$ (5.13 μL, 0.0601 mmol) was added slowly to a solution of $H_2\mathbf{L}^{1,5}$ (13.3 mg, 0.0601 mmol) in $CHCl_3$ (5 mL) and mixed well, causing white crystals to crash out of solution that were suitable for single-crystal X-ray structure determination (52.0 mg, 0.079 mmol, 35%). Sparingly soluble crystals were dissolved in CD_2Cl_2, and the ^{1}H NMR spectrum was collected over 10 h: ^{1}H NMR (600 MHz, CD_2Cl_2) δ 7.98 (d, C*H*, J = 8.2 Hz), 7.37 (m, C*H*), 7.33 (m, C*H*), 7.24 (m, C*H*), 7.18 (m, C*H*), 4.51 (ABq, CH_2, J = 12 Hz), 4.39, (ABq, CH_2, J = 4 Hz).

$As_2(L^{1,4})_2Cl_2$. $AsCl_3$ (17.4 μL, 0.203 mmol) was added slowly to a solution of $H_2\mathbf{L}^{1,4}$ (45.0 mg, 0.203 mmol) in $CHCl_3$ (15 mL) and mixed well to yield a solution of syn and anti diastereomers in a ratio of 20:1. Slow diffusion of pentane into a chloroform solution of the complex yielded clear, colorless crystals that were suitable for structure determination using single-crystal X-ray diffraction methods (6.9 mg, 0.010 mmol, 10%). Single crystals were also obtained by slow diffusion of pentane into a benzene solution of the complex. Single crystals were dissolved in $CDCl_3$:

syn-$As_2(\mathbf{L}^{1,4})_2Cl_2$: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (m, 4H, C*H*), 7.53 (m, 4H, C*H*), 7.32 (s, 4H, C*H*), 4.58 (ABq, 16H, CH_2, J = 13.2 Hz).

anti-$As_2(\mathbf{L}^{1,4})_2Cl_2$: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (m, 4H, C*H*), 7.47 (m, 4H, C*H*), 7.28 (s, 4H, C*H*), 4.57 (s, 16H, CH_2).

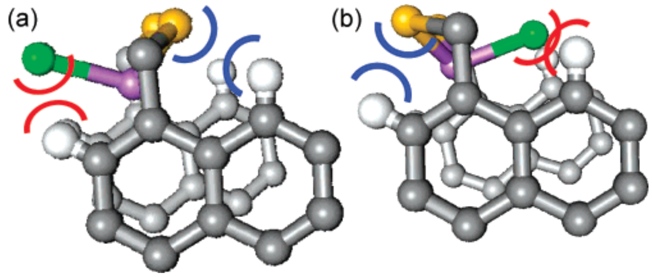


Figure 1. Partial ball-and-stick models showing two conformations for this molecule with the chlorine atom pointing (a) away from and (b) toward the hydrocarbon backbone. Possible points for steric repulsion are marked in red (with chlorine) and blue (with sulfur).

Results and Discussion

Scheme 1 illustrates a series of isomeric bis(mercaptomethyl)naphthalene ligands that form equilibrium mixtures of diastereomeric macrocycles when combined with $AsCl_3$ in solution. Depending on the choice of ligand, either no de is observed ($H_2\mathbf{L}^{2,6}$), the syn isomer is favored ($H_2\mathbf{L}^{1,4}$), or the anti isomer ($H_2\mathbf{L}^{1,5}$) is favored. The naphthalene rings of these ligands provide added steric bulk to the macrocyclic cavity (compared to $H_2\mathbf{L}$), which forces either the chlorine or sulfur atoms into close proximity with these aromatic backbones (Figure 1). The repulsive interaction between the electron-rich chlorine atoms coordinated to arsenic and the aromatic rings of the ligand causes the diastereomer that

(10) Beissel, T.; Powers, R. E.; Parac, T. N.; Raymond, K. N. *J. Am. Chem. Soc.* **1999**, *121*, 4200−4206.
(11) Fiedler, D.; Leung, D. H.; Bergman, R. G.; Raymond, K. N. *Acc. Chem. Res.* **2005**, *38*, 349−358.
(12) (a) Givens, R. S.; Venkatramanan, M. K.; Figard, J. *Tetrahedron Lett.* **1984**, *25*, 2187−2190. (b) Givens, R. S.; Olsen, R. J.; Wylie, P. L. *J. Org. Chem.* **1979**, *44*, 1608−1613. (c) Haenel, M. W. *Chem. Ber.* **1982**, *115*, 1425−1436.

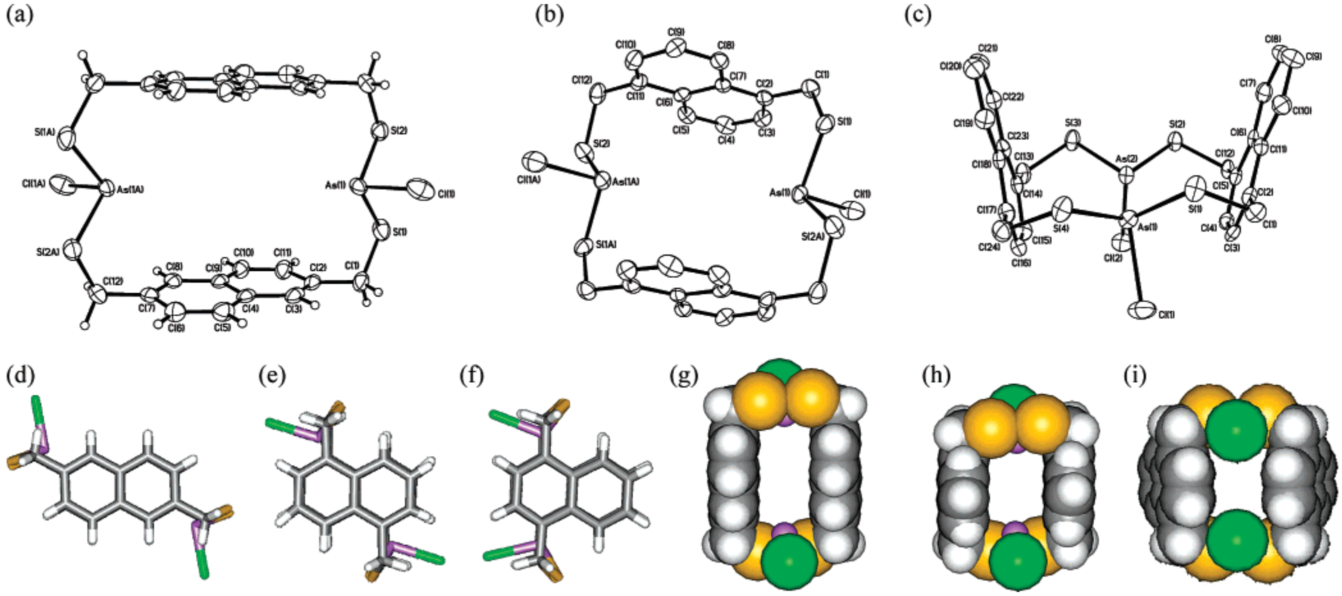


Figure 2. ORTEP (30% probability ellipsoids), wireframe, and space-filling representations of single-crystal X-ray structures for *anti*-$As_2(\mathbf{L}^{2,6})_2Cl_2$ (a,d,g), *anti*-$As_2(\mathbf{L}^{1,5})_2Cl_2$ (b,e,h), and *syn*-$As_2(\mathbf{L}^{1,4})_2Cl_2 \cdot CHCl_3$ macrocycles (c,f,i). Carbon is shown in black, hydrogen in white, sulfur in yellow, chlorine in green, and arsenic in purple. The ligands are planar within 0.02 Å. The angle between the average planes of the ligands is 28° in $As_2(\mathbf{L}^{1,4})_2Cl_2 \cdot CHCl_3$ and 0° in $As_2(\mathbf{L}^{2,6})_2Cl_2$ and $As_2(\mathbf{L}^{1,5})_2Cl_2$. Hydrogens (a,b,c) and cocrystallized $CHCl_3$ (c,f,i) are omitted for clarity, and only one of the six $As_2(\mathbf{L}^{1,4})_2Cl_2$ macrocycles contained in the asymmetric unit is shown for brevity (c,f,i).

Table 1. Crystallographic Data and Refinement Parameters for $As_2(\mathbf{L}^{2,6})_2Cl_2$, $As_2(\mathbf{L}^{1,5})_2Cl_2$, $As_2(\mathbf{L}^{1,4})_2Cl_2 \cdot CHCl_3$, and $As_2(\mathbf{L}^{1,4})_2Cl_2 \cdot C_6H_6$

	$As_2(\mathbf{L}^{2,6})_2Cl_2$	$As_2(\mathbf{L}^{1,5})_2Cl_2$	$As_2(\mathbf{L}^{1,4})_2Cl_2 \cdot CHCl_3$	$As_2(\mathbf{L}^{1,4})_2Cl_2 \cdot C_6H_6$
empirical formula	$C_{24}H_{20}As_2Cl_2S_4$	$C_{24}H_{20}As_2Cl_2S_4$	$C_{25}H_{21}As_2Cl_5S_4$	$C_{30}H_{26}As_2Cl_2S_4$
fw	657.38	657.38	776.75	735.49
temperature (K)	153(2)	173(2)	173(2)	173(2)
wavelength (Å)	0.71073	0.71073	0.71073	0.71073
space group	$P2_1/n$	$P2_1/c$	$P\bar{1}$	$P2_1/n$
a (Å)	6.395(1)	6.813(4)	19.313(4)	10.3332(7)
b (Å)	19.675(4)	19.08(1)	19.923(4)	34.375(2)
c (Å)	10.967(2)	10.277(6)	24.508(5)	17.859(1)
α (deg)	90	90	78.110(4)	90
β (deg)	106.817(3)	107.79(1)	78.860(5)	98.965(1)
γ (deg)	90	90	89.183(5)	90
V (Å^3)	1320.8(5)	1272.5(14)	9050(3)	6266.3(7)
Z, Z'	2, 0.5	4, 1	12, 6	8, 2
D_{calcd} (mg/m^3)	1.653	1.716	1.710	1.559
μ (cm^{-1})	0.3061	0.3177	0.2951	0.2590
N measured	10 816	6949	102 535	53 433
N ind [R_{int}]	2322 [0.0264]	2750 [0.0816]	39 214 [0.0953]	11 027 [0.0315]
N obs [$I > 2\sigma(I)$]	1904	1632	19 406	9741
no. of params	145	145	1937	708
GOF on F^2	1.053	1.037	0.981	1.260
R1/wR2 [$I > 2\sigma(I)$]	0.0486/0.1226	0.0816/0.1779	0.0687/0.1278	0.0577/0.1155
R1/wR2 (all data)	0.0603/0.1314	0.1482/0.2138	0.1577/0.1646	0.0657/0.1185

positions the chlorine atoms farthest away from the arene rings to form in excess. The result is a predictable strategy that controls the syn-to-anti ratio of the self-assembly reaction on the basis of the shape of the ligand.

To test the stereocontrol of these self-assembly reactions, three regioisomers of bis(mercaptomethyl)naphthalene were prepared with mercaptomethyl substituents in the 2,6-, 1,5-, and 1,4-positions. It was predicted that $H_2\mathbf{L}^{1,5}$ would give mostly anti product, $H_2\mathbf{L}^{1,4}$ would give mostly syn product, and $H_2\mathbf{L}^{2,6}$ would show no preference. These predictions result from the minimization of unfavorable steric repulsions (part b of Figure 1) exhibited in both *anti*-$As_2(\mathbf{L}^{1,5})_2Cl_2$ and *syn*-$As_2(\mathbf{L}^{1,4})_2Cl_2$, in which the chlorine atoms are directed away from the sterically congested macrocyclic cavity (Figure 2). Conversely, $As_2(\mathbf{L}^{2,6})_2Cl_2$ should show no such preference: the chlorine atom is directed away from the macrocycle in both diastereomers. When $AsCl_3$ is added to a chloroform solution of each ligand, $As_2L_2Cl_2$ macrocycles self-assemble in each case, showing that our design strategy[4,5] for forming these macrocycles is general, despite the differences in geometry of these ligands.

Single-crystal X-ray diffraction studies confirm that each macrocycle consists of two arsenic atoms spanned by two bridging ligands that create a cavity that is roughly 6 Å across (Figure 2, Tables 1 and 2). Each arsenic atom also remains coordinated by a lone chlorine atom that is not displaced when the reactions are performed in the absence of base.[4,5] Each structure reveals that As$-\pi$ interactions are influencing the stereochemistry of the assemblies by directing arsenic, and thus its coordination sphere, into the macrocyclic cavities

Table 2. Selected Bond Lengths (Angstroms) and Angles (Degrees)

$As_2(\mathbf{L}^{2,6})_2Cl_2$		$As_2(\mathbf{L}^{1,5})_2Cl_2$		$As_2(\mathbf{L}^{1,4})_2Cl_2\cdot CHCl_3$[a]	
As(1)−S(1)	2.1987(16)	As(1)−S(2A)	2.210(3)	As(1)−S(4)	2.216(2)
As(1)−S(2)	2.2078(15)	As(1)−S(1)	2.215(3)	As(1)−S(1)	2.227(2)
As(1)−Cl(1)	2.2494(18)	As(1)−Cl(1)	2.237(3)	As(1)−Cl(1)	2.246(2)
S(1)−As(1)−S(2)	89.33(6)	S(1)−C(1)	1.839(9)	As(2)−S(3)	2.224(2)
S(1)−As(1)−Cl(1)	100.42(7)	S(2A)−As(1)−S(1)	85.81(10)	As(2)−S(2)	2.227(2)
S(2)−As(1)−Cl(1)	98.74(6)	S(2A)−As(1)−Cl(1)	100.99(12)	As(2)−Cl(2)	2.240(2)
C(1)−S(1)−As(1)	99.4(2)	S(1)−As(1)−Cl(1)	102.16(11)	S(4)−As(1)−S(1)	89.53(8)
C(12)−S(2)−As(1A)	98.89(19)	C(1)−S(1)−As(1)	102.1(3)	S(4)−As(1)−Cl(1)	100.39(9)
		C(12)−S(2)−As(1A)	102.1(3)	S(1)−As(1)−Cl(1)	100.78(10)
				S(3)−As(2)−S(2)	88.77(8)
				S(3)−As(2)−Cl(2)	100.43(9)
				S(2)−As(2)−Cl(2)	101.88(9)
				C(1)−S(1)−As(1)	99.9(3)
				C(12)−S(2)−As(2)	99.2(3)
				C(13)−S(3)−As(2)	99.0(3)
				C(24)−S(4)−As(1)	100.2(3)
syn(1)−$As2(\mathbf{L}^{1,4})_2Cl_2\cdot C_6H_6$ and *anti*(1)−$As_2(\mathbf{L}^{1,4})_2Cl_2\cdot C_6H_6$[b]		*syn*(2)−$As2(\mathbf{L}^{1,4})_2Cl_2\cdot C_6H_6$ and *anti*(2)−$As_2(\mathbf{L}^{1,4})_2Cl_2\cdot C_6H_6$[b]			
As(1A)−S(4A)	2.208(2)	As(1)−S(1)	2.2021(15)		
As(1A)−S(1A)	2.2109(17)	As(1)−S(4)	2.2077(16)		
As(1A)−Cl(1A)	2.255(2)	As(1)−Cl(1)	2.223(2)		
As(2A)−S(2A)	2.2112(19)	As(2)−S(2)	2.2158(15)		
As(2A)−S(2B)	*2.055(15)*				
As(2A)−S(3A)	2.2027(17)	As(2)−S(3)	2.2198(16)		
As(2A)−S(3B)	*2.167(12)*				
As(2A)−Cl(2A)	2.2757(19)	As(2)−Cl(2)	2.261(3)		
As(2A)−Cl(2B)	*2.295(14)*	*As(2)−Cl(2′)*	*2.286(4)*		
S(4A)−As(1A)−S(1A)	87.07(7)	S(1)−As(1)−S(4)	89.68(6)		
S(4A)−As(1A)−Cl(1A)	101.01(10)	S(1)−As(1)−Cl(1)	100.71(9)		
S(1A)−As(1A)−Cl(1A)	102.42(9)	S(4)−As(1)−Cl(1)	99.84(9)		
S(2A)−As(2A)−S(3A)	89.31(7)	S(2)−As(2)−S(3)	88.06(6)		
S(2B)−As(2A)−S(3B)	*100.6(6)*				
S(2A)−As(2A)-Cll(2A)	96.91(8)	S(2)−As(2)-Cl(2)	101.75(8)		
S(2B)-As(2A)−Cl(2B)	*100.4(7)*	*S(2)−As(2)−Cl(2′)*	*103.85(10)*		
S(3A)−As(2A)−Cl(2A)	100.14(8)	S(3)−As(2)−Cl(2)	97.00(11)		
S(3B)−As(2A)−Cl(2B)	*99.7(6)*	*S(3)−As(2)−Cl(2′)*	*97.93(11)*		
C(1A)−S(1A)−As(1A)	101.5(2)	C(1)−S(1)−As(1)	100.0(2)		
C(12A)−S(2A)−As(2A)	98.4(2)	C(12)−S(2)−As(2)	101.33(19)		
C(12A)−S(2B)−As(2A)	*97.6(2)*				
C(13A)−S(3A)−As(2A)	101.3(2)	C(13)−S(3)−As(2)	99.3(2)		
C(13A)−S(3B)−As(2A)	*107.3(2)*				
C(24A)−S(4A)−As(1A)	100.3(2)	C(24)−S(4)−As(1)	98.1(2)		

[a] Data from only one of six conformers is shown for brevity. See the Supporting Information for data from the other six conformers. [b] This structure contains two macrocycles in the asymmetric unit, both of which are disordered over syn and anti conformations (denoted *syn*(1), *anti*(1), *syn*(2), and *anti*(2)). *anti*(1) and *anti*(2) refer to the two conformers of the anti macrocycle present in the disordered structure (Figure 6). The structure *anti*(2) results from disorder of the chlorine atom that is bonded to As(2) over two sites: Cl(2) and Cl(2′). The structure *anti*(1) results from disorder of the chlorine and sulfur atoms bonded to As(2a) in the other macrocycle. The bond distances and angles for the anti isomers are italicized in the table.

of the complexes. Only one of the two possible diastereomers of each macrocycle crystallizes out of chloroform: *anti*-$As_2(\mathbf{L}^{2,6})_2Cl_2$ (parts a and d of Figure 2, Table 1), *anti*-$As_2(\mathbf{L}^{1,5})_2Cl_2$ (parts b and e of Figure 2), and *syn*-$As_2(\mathbf{L}^{1,4})_2Cl_2\cdot CHCl_3$[13] (parts c and f of Figure 2, Table 1). Although the As⋯As distances in these structures vary widely (7.45, 5.64, and 4.66 Å, respectively), the As⋯C distances between the arsenic atom and the nearest carbon atom in the naphthalene rings (3.30, 3.22, and 3.14 Å, respectively) consistently indicate the presence of As−π interactions (Table 2).[7,14]

Each macrocycle exists as a mixture of diastereomers in differing amounts, in solution. A nearly equal mixture of *syn*- and *anti*-$As_2(\mathbf{L}^{2,6})_2Cl_2$ macrocycles is observed in solution (de = 9%) by ^{1}H NMR spectroscopy (part a of Figure 3). The ^{1}H NMR spectrum of this mixture reveals that the methylene protons of each diastereomer appear as an AB quartet.

In the ^{1}H NMR spectrum obtained by dissolving single crystals of *anti*-$As_2(\mathbf{L}^{1,5})_2Cl_2$, it is clear that there is a large excess of one diastereomer, presumably the anti isomer (part b of Figure 3).[15] The de was calculated to be 85%, although the low solubility of the complex, as shown by the noisy NMR spectrum (obtained from an overnight scan of a saturated solution on a 600 MHz spectrometer), leads to a high error in this value.

(13) *syn*-$As_2(\mathbf{L}^{1,4})_2Cl_2$ crystallizes exclusively out of chloroform with six macrocycles present in the asymmetric unit. The six syn macrocycles vary slightly in their conformations. A full description of the structural details and refinement and a listing of bond lengths and angles are included in the Supporting Information. A roughly 3:1 mixture of *syn*-to-*anti*-$As_2(\mathbf{L}^{1,4})_2Cl_2\cdot C_6H_6$ crystallizes out of benzene. Full details of the modeling of the disorder are contained in the Supporting Information.

(14) Schmidbaur, H.; Bublak, W.; Huber, B.; Muller, G. *Angew. Chem., Int. Ed. Engl.* **1987**, *99*, 248.

(15) *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 234−235.

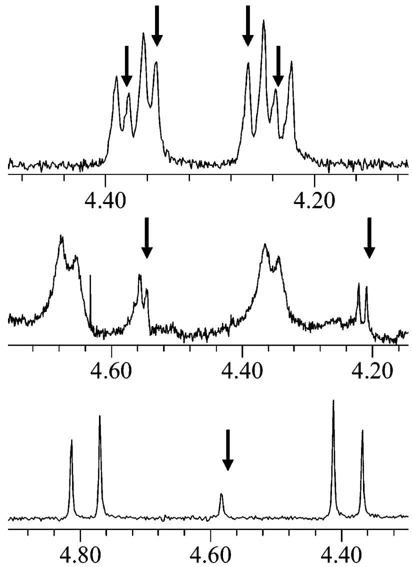


Figure 3. Methylene region of the ^{1}H NMR spectra (in ppm) of As_2L_2-Cl_2 macrocycles with arrows marking the least thermodynamically stable isomers. The equilibrium mixtures of *syn*- and *anti*- (a) $As_2(\mathbf{L^{2,6}})_2Cl_2$, (b) $As_2(\mathbf{L^{1,5}})_2Cl_2$, and (c) $As_2(\mathbf{L^{1,4}})_2Cl_2$ at 25 °C are shown.

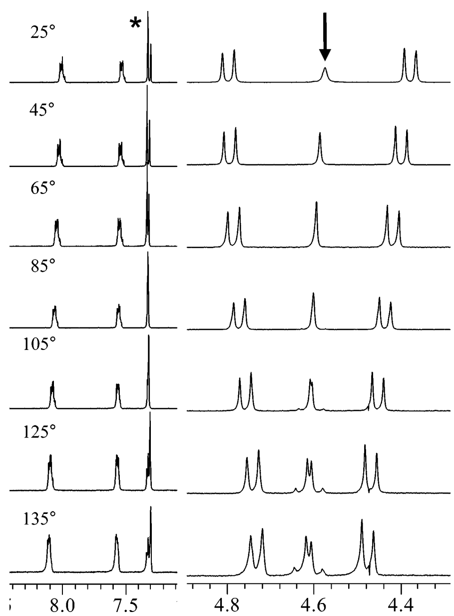


Figure 4. Variable-temperature ^{1}H NMR spectra (in ppm) for $As_2(\mathbf{L^{1,4}})_2$-Cl_2 macrocycles with the arrow marking the resonances for the methylene protons of the anti diastereomer. The resonance with the * corresponds to $CHCl_3$.

A large excess of syn isomer is observed in solution for the $As_2(\mathbf{L^{1,4}})_2Cl_2$ macrocycles (de = 90%) (part c of Figure 3). In this case, the anti macrocycle appears as a singlet in the center of the syn AB quartet. Variable-temperature NMR spectroscopy revealed that, at high temperatures, this singlet splits into the AB quartet expected for the geminal methylene protons (Figure 4). At room temperature, the methylene resonances are coincidental, and, as a result, do not split each other. As the temperature is raised, these resonances shift slightly, are no longer coincidental, and split into the characteristic AB quartet. Interestingly, as the temperature is raised, the de decreases, reminiscent of organic reactions in which de's are typically optimized by performing reactions at lower temperatures.[16] This indicates that the syn macrocycle is entropically favored over the anti isomer. In a related supramolecular example, Stang and co-workers have reported that a mixture of self-assembled macrocyclic dimers and trimers exists in a temperature-dependent equilibrium favoring the entropically preferred dimer at higher temperatures.[17]

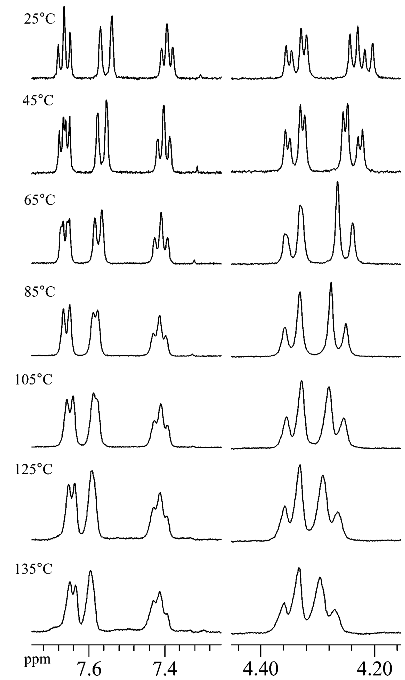


Figure 5. Variable-temperature ^{1}H NMR spectra (in ppm) for $As_2(\mathbf{L^{2,6}})_2$-Cl_2 macrocycles.

Variable-temperature ^{1}H NMR spectroscopic experiments were also carried out on the $As_2(\mathbf{L^{2,6}})_2Cl_2$ macrocycles and revealed incomplete coalescence at temperatures of up to 135 °C, suggesting that the interconversion between syn and anti isomers is slow on the NMR time scale (Figure 5). As the sample is heated, the syn and anti resonances shift to a point where they overlap, making a quantitative measurement of the de at temperatures above 45 °C impossible. EXSY experiments confirmed that conversion between diastereomers is slow on the NMR time scale for both $As_2(\mathbf{L^{2,6}})_2Cl_2$ and $As_2(\mathbf{L^{1,4}})_2Cl_2$ at room temperature on a 400 MHz spectrometer.

Mechanism of Interconversion. We previously showed that the interconversion of syn-to-anti macrocycles is not occurring by (1) pyramidal inversion of one As(III) center, (2) complete ligand dissociation, or (3) HCl-catalyzed inversion for the following reasons.[5] First, the barrier to arsine inversion is too high to occur at room temperature, making pyramidal inversion followed by bond rotation an unlikely route for interconversion.[18] Second, complete ligand exchange was not observed for a related mixture of $As_2\mathbf{L}_2$-Cl_2 macrocycles ($H_2\mathbf{L}$ = bis(mercaptomethyl)benzene).[5] Finally, hydrochloric acid, a side-product of macrocycle

(16) This is similar to the established case of organic addition reactions, which can exhibit temperature dependent de's when the enthalpically and entropically favored products are not the same: Cainelli, G.; Giacomini, D.; Galletti, P. *Eur. J. Org. Chem.* **1999**, 61−65.

(17) Yamamoto, T.; Arif, A. M.; Stang, P. J. *J. Am. Chem. Soc.* **2003**, *125*, 12309−12317.

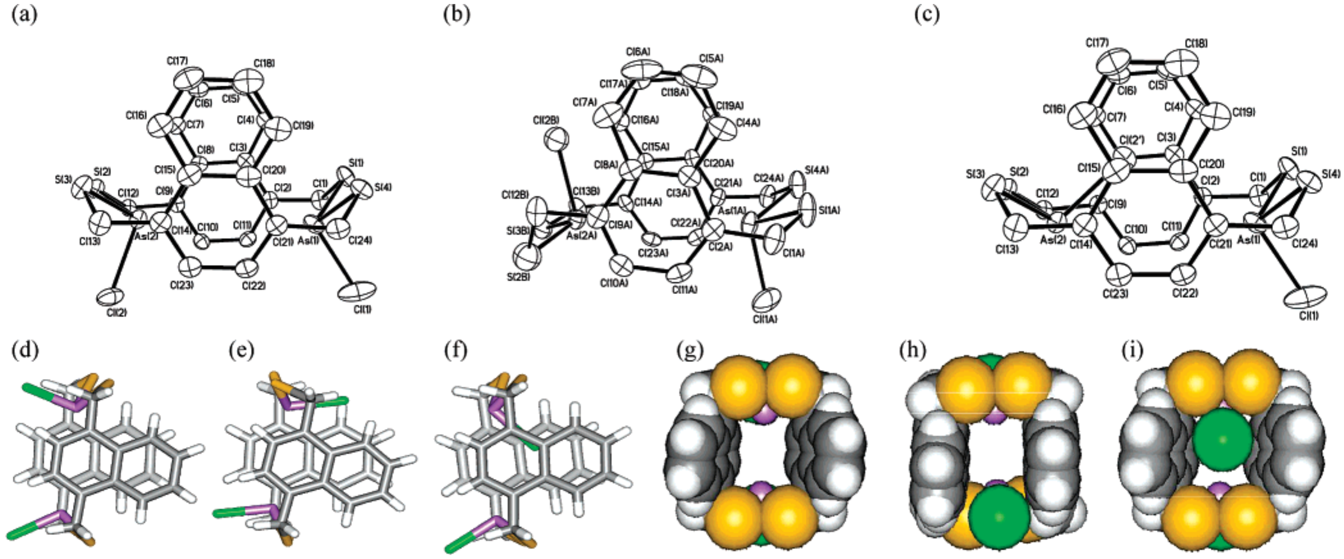
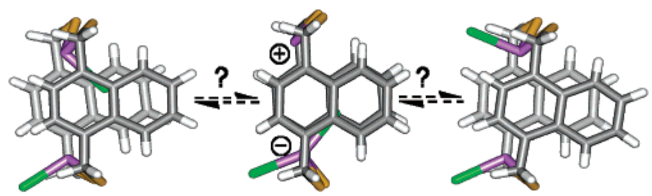


Figure 6. ORTEP (30% probability ellipsoids), wireframe, and space-filling representations of three conformers found in the crystal structure of $As_2(\mathbf{L^{1,4}})_2Cl_2{\cdot}C_6H_6$: *syn*(1)-$As_2(\mathbf{L^{1,4}})_2Cl_2{\cdot}C_6H_6$ (a,d,g), *anti*(1)-$As_2(\mathbf{L^{1,4}})_2Cl_2{\cdot}C_6H_6$ (b,e,h), and *anti*(2)-$As_2(\mathbf{L^{1,4}})_2Cl_2{\cdot}C_6H_6$ (c,f,i) macrocycles. The ligands are planar within 0.03 Å. The dihedral angle between the average planes of the ligands in the isomers are different: 7.4° in *anti*(1)-$As_2(\mathbf{L^{1,4}})_2Cl_2{\cdot}C_6H_6$ (b,e,h) and 36.0° in both *syn*-$As_2(\mathbf{L^{1,4}})_2Cl_2{\cdot}C_6H_6$ (a,d,g) and *anti*(2)-$As_2(\mathbf{L^{1,4}})_2Cl_2{\cdot}C_6H_6$ (c,f,i). Cocrystallized C_6H_6 (a−i) and hydrogens (a,b,c) are omitted for clarity.

formation, is known to cause racemization of chiral arsines[19,20] and was initially thought to be involved in the interconversion of syn-to-anti macrocycles. However, when crystals of exclusively one diastereomer are dissolved in chloroform that has been neutralized with basic alumina to remove any traces of HCl, interconversion still occurs rapidly to give an equilibrium mixture of diastereomers.[5] Having shown that arsine inversion, complete ligand dissociation, and HCl-catalyzed racemization are unlikely to be involved in the interconversion of syn-to-anti macrocycles, a new mechanism based on the disproportionation of two arsenic centers is proposed.

X-ray crystal data reveal that when crystals of $As_2(\mathbf{L^{1,4}})_2Cl_2$ are grown by slow diffusion of pentane into benzene, they contain two conformers of both the syn macrocycle and the anti macrocycle (Figure 6). In the anti(2) conformer shown in part c of Figure 6, one chlorine atom is pointing into the cavity with an As−Cl distance of 2.286(4) and a short As−Cl contact to the other arsenic center of 3.54 Å. This nonbonding distance is shorter than the sum of the van der Waals radii for arsenic and chlorine (3.80 Å). On the basis of this structure and the observation that $AsCl_3$ can disproportionate into $AsCl_2^+$ and $AsCl_4^-$,[21−23] it is reasonable that the interconversion of syn-to-anti macrocycles could occur by disproportionation of two arsenic centers. This

Scheme 2. Proposed Mechanism for the Intramolecular Disproportionation Leading to Interconversion between syn and anti macrocycles



interconversion could occur intramolecularly through a zwitterionic intermediate (Scheme 2), or intermolecularly. We are currently studying this interconversion mechanism to determine (1) if the halide ligand is involved in the interconversion, (2) how the halide ligand affects the rate of interconversion, and (3) if the rate depends on halide concentration. Furthermore, it is possible that partial ligand dissociation (breakage of only one As−S bond) could result in interconversion. The results of these studies will be reported in due course.

In summary, this study represents an unusual example of a self-assembly reaction in which the de is controlled in a predictable manner through the use of achiral, isomeric ligands. The As−π interaction acts as the directing force for the self-assembly of $As_2L_2Cl_2$ macrocycles that exist as an equilibrium mixture of both syn and anti diastereomers in solution. By controlling the syn-to-anti ratio of our $As_2L_2Cl_2$ macrocycles in solution, we gain some understanding

(18) The barrier to pyramidal inversion was found to be 39 kcal/mol for AsH_3, 45 kcal/mol for AsF_3, (Nagase, S. *The Chemistry of Organic Arsenic, Antimony, and Bismuth Compounds*; Wiley: Chichester, U.K., 1994.) and at least 42 kcal/mol for chiral arsines (Cross, W. I.; Godfrey, S. M.; McAuliffe, C. A.; Mackie, A. G.; Pritchard, R. B. In *Chemistry of Arsenic, Antimony, and Bismuth*; Norman, N. C., Ed.; Blackie Academic & Professional: London, 1998.).

(19) Doak, G. O.; Freedman, L. D. *Organometallic Compounds of Arsenic, Antimony, and Bismuth*; Wiley Intersciences: New York, 1970.

(20) Westheimer, F. H. *Acc. Chem. Res.* **1968**, *1*, 70−78.

(21) Godfrey, S. M.; McAuliffe, C. A.; Mackie, A. G.; Pritchard, R. G. In *Chemistry of Arsenic, Antimony, and Bismuth*; Norman, N. C., Ed.; Blackie Academic & Professional: London, 1998, p 94.

(22) Gutmann, V. *Quart. Revs.* **1956**, *10*, 451−462.

(23) $AsCl_3$ is known to disproportionate into $AsCl_2^+$ and $AsCl_4^-$.[21,22] It seems plausible that AsL_2Cl complexes (where L = thiolate) could also disproportionate into AsL_2^+ and $AsL_2Cl_2^-$ ions. Upon the reformation of AsL_2Cl, inversion at the arsenic center can occur. In the anionic form, either chloride ligand could leave with equal likelihood, scrambling the stereochemistry at arsenic. Conversely, in the planar cation, the incoming chloride could either attack above or below the plane of the complex, leading to two different configurations at arsenic. This mechanism of interconversion could occur *intra- or intermolecularly* in $As_2L_2Cl_2$ macrocycles.

of how these macrocycles could act as synthons for larger assemblies. We are currently pursuing this goal, as well as designing macrocycles with improved diastereocontrol and studying the mechanism of syn-to-anti interconversion.

Acknowledgment. We gratefully acknowledge the National Science Foundation for a CAREER award (CHE-0545206) and the University of Oregon for generous financial support. D.W.J. is a Cottrell Scholar of Research Corporation. O.B.B. acknowledges the NSF for an Integrative Graduate Education and Research Traineeship. The purchase of the X-ray diffractometer was made possible by a grant from the NSF (CHE-0234965) to the University of Oregon. We thank Rodger Kohnert for expert assistance in performing the EXSY experiments.

Supporting Information Available: X-ray data in CIF format, details of X-ray diffraction studies, discussion of the disorder modeling in $As_2\mathbf{L}^{1,4}Cl_2{\bullet}C_6H_6$, and experimental details for the ligands synthesized from a modified literature procedure. This material is available free of charge via the Internet at http://pubs.acs.org.

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