Optically Active Arsenic Macrocycles. Highly Stereoselective Syntheses of Diastereomers and Enantiomers of 14-Membered Macrocyclic Dimers of (±)-2,3-Dihydro- and (±)-2,3,4,5-Tetrahydro-1-methyl-1,4-benzazarsepine

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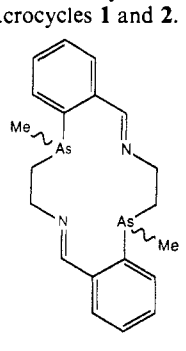
Abstract: The 14-membered *trans*-As_2N_2 macrocycle (9*R**,18*S**)-7,8,9,16,17,18-hexahydro-9,18-dimethyldibenzo[*e*,*l*]-[1,8,4,11]diazadiarsacyclotetradecine [(*R**,*S**)-**1**] is formed with complete stereoselectivity when (±)-1,3-dimethyl-2-[2-[methyl(2-aminoethyl)arsino]phenyl]imidazolidine [(±)-**3**] is heated at 80 °C in vacuo. The achiral macrocycle quantitatively rearranges into seven-membered (±)-2,3-dihydro-1-methyl-4,1-benzazarsepine [(±)-**5**] in the presence of acid, although the monoimine spontaneously and stereoselectively dimerizes into (*R**,*S**)-**1** when heated. Resolution of (±)-2-[methyl(2-aminoethyl)arsino]benzenemethanol [(±)-**4**] on [(*R*)-1-[1-(dimethylamino)ethyl]-2-naphthalenyl-C^2,*N*]palladium(II) [[(*R*)-1-$C_{10}H_6CH(Me)NMe_2$-C^2,*N*]Pd^+] followed by oxidation of the less soluble diastereomer (R_{As},*R*)-**17**·$Me_2CH(OH)$ with $BaMnO_4$, affords yellow distorted square-planar [[(*R*)-$C_{10}H_6CH(Me)NMe_2$-C^2,*N*]Pd{(*S*,*S*)-**1**-*As*,*As*,*N*}]PF_6, [(R_{As},S_{As},*R*)-**20**] or orange trigonal-bipyramidal [(*R*)-$C_{10}H_6CH(Me)NMe_2$-C^2,*N*]Pd{(*S*,*S*)-**1**-*As*,*As*,*N*}]PF_6·0.5Me_2CO [(S_{As},S_{As},*R*)-**20**·0.5Me_2CO], depending upon the solvents used for recrystallization. Resolving agent with (*R**,*S**)-**1** in the presence of trifluoroacetic acid yields the same complexes after treatment of the reaction mixture with ammonium hexafluorophosphate. The yellow form of the complex crystallizes in the orthorhombic space group $P2_12_12_1$ (No. 19) with a = 12.235 (5) Å, b = 15.176 (3) Å, c = 19.379 (3) Å, and Z = 4; the orange form crystallizes in the same space group with a = 18.358 (3) Å, b = 18.392 (3) Å, c = 11.927 (3) Å, and Z = 4. Optically pure macrocycle (*R*,*R*)-**1**, $[\alpha]_D$ −99.8° (CH_2Cl_2), is displaced from either form of the diastereomers by chelating bis(tertiary phosphines). The mixing together of equimolar solutions of the mirror-image enantiomers of the diimine macrocycle in dichloromethane leads to the spontaneous crystallization of (*R**,*S**)-**1** in a second-order asymmetric transformation involving monoimine (±)-**5**. Thus, racemic macrocycle (*R**,*R**)-**1** cannot be isolated. Lithium aluminum hydride reductions of the various forms of **1** produce the corresponding macrocyclic diamines, viz., (*R**,*S**)-**2**, (*R*,*R*)-**2**, and (*S*,*S*)-**2**. The optically active forms of the diamine crystallize from chloroform as *dichloroform solvates*, $[\alpha]_D$ ±190° (CH_2Cl_2). Treatment of the macrocyclic diimines with acid prior to reduction affords the racemic and optically active forms of (±)-2,3,4,5-tetrahydro-1-methyl-4,1-benzazarsepine [(±)-**6**]. The racemic *diamine* macrocycle (*R**,*R**)-**2** was obtained by asymmetric transformation of (*R**,*S**)-**2** on palladium(II). Thus, [Pd{(*R**,*S**)-**2**}]X_2 (X = Cl, PF_6) upon being heated in water or dimethyl sulfoxide is quantitatively transformed into [Pd{(*R**,*R**)-**2**}]X_2, as demonstrated by recovery of pure (*R**,*R**)-**2** from the rearranged complex. Apart from (*R**,*R**)-**2**, which is an oil, all forms of the macrocycles are air-stable crystalline solids. The macrocycles have excellent prospects as ligands for the stereospecific chelation of "soft" metals.

Given the wealth of chemistry, both organic[1] and inorganic,[2] based upon the macrocyclic chelate effect[3] on the one hand and the coordination chemistry of tertiary arsines and phosphines[4] on the other, it is surprising that few fully characterized chelating macrocyclic tertiary arsines and phosphines are known.[5] Macrocycles chiral at arsenic (E_{inv} >40 kcal mol^{-1}) or phosphorus (E_{inv} ca. 30 kcal mol^{-1})[6] will exist as stable enantiomers or diastereomers of potential use as stereospecific chelating agents for "soft" metal ions like palladium(II) and rhodium(I) with rich synthetic chemistries.[7] We recently reported highly stereoselective syntheses of enantiomers and diastereomers of a 14-membered chelating *trans*-As_2S_2 macrocycle by palladium(II) template dimerizations of a chiral 2-mercaptoethyl-substituted tertiary arsine.[8] In this paper, we describe syntheses of the first optically active *trans*-As_2N_2 macrocycles **1** and **2**. The synthetic strategy for diimines **1** involved the Schiff base dimerization of (±)-2-[(2-aminoethyl)methylarsino]benzaldehyde (or its enantiomers) generated from (±)-**3** by hydrolysis or from (±)-**4** by oxidation. Diamines **2** could then be obtained by reductions of the various forms of **1** under appropriate conditions.



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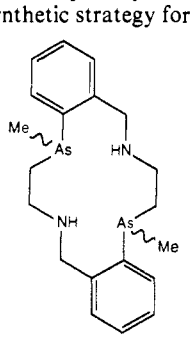

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[†] Australian National University.
[‡] Macquarie University.

(1) See, for example: Cram, D. J.; Cram, J. M. *Acc. Chem. Res.* **1978**, 8-14. Tabushi, I. *Acc. Chem. Res.* **1982**, *15*, 66-72. Kellogg, R. M. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 782-794. Lehn, J.-M. *Science (Washington, D.C.)* **1985**, *227*, 849-856.

(2) Melson, G. A. *Coordination Chemistry of Macrocyclic Compounds*; Plenum: New York, 1979.

(3) Cabbiness, D. K.; Margerum, D. W. *J. Am. Chem. Soc.* **1969**, *91*, 6540-6541.

(4) McAuliffe, C. A.; Levason, W. *Phosphine, Arsine and Stibine Complexes of the Transition Elements*; Elsevier: Amsterdam, 1979.

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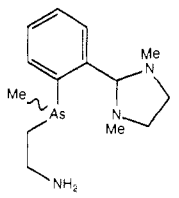
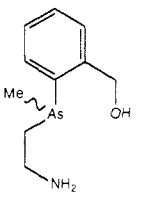


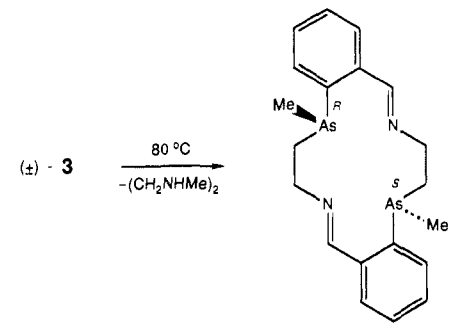
(±)-3



(±)-4

Results and Discussion

Stereoselective Synthesis of Achiral *trans*-As_2N_2 Diimine Macrocycle (*R,*S**)-1.** Precursor (±)-**3** was prepared from 1,3-dimethyl-2-phenylimidazolidine (**7**) in six steps as shown in Scheme I. *N*,*N*′-Dimethyl-1,2-ethanediamine was known to be a direct protecting reagent for the aldehyde group of benzaldehyde under sodium in ammonia conditions.[9] In the present synthesis, the imidazolidine group also facilitated ortho-lithiation of the aromatic ring and the *N*,*N*′-dimethyl-1,2-ethanediamine subsequently acted as the leaving group for the Schiff base condensation leading to the macrocycle. Thus, spectroscopically characterized (±)-**3** (an oil) was quantitatively converted into 14-membered bis(Schiff base) (*R**,*S**)-**1** with complete stereoselectivity when heated for ca. 24 h at 80 °C in vacuo. The achiral (*R**,*S**)

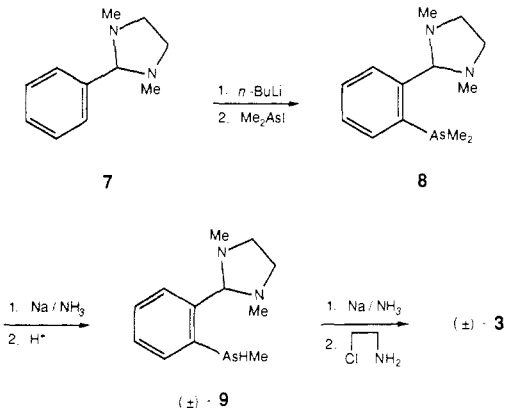


(*R**, *S**)-1

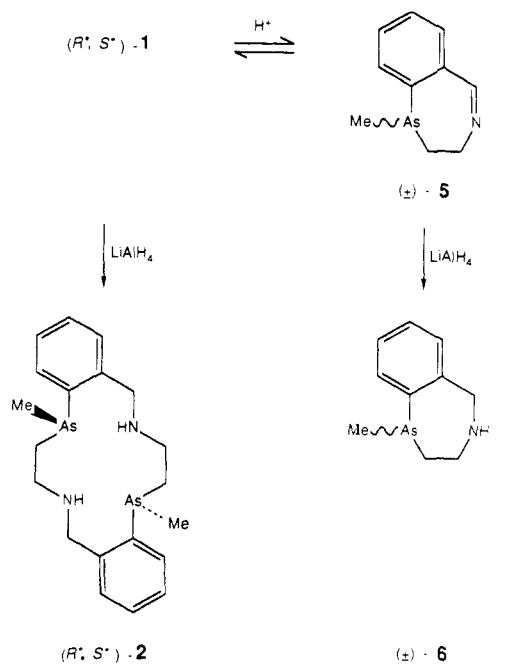
diimine macrocycle crystallizes from dichloromethane–methanol as sparingly soluble air-stable needles, mp 180 °C. It is noteworthy that the 14-membered macrocycle was produced cleanly without the use of either of the ploys usually adopted for the avoidance of competitive linear polymerizations, namely the use of metal ions as templates or the use of high reagent dilutions.[5,8] Reduction of the diimine with lithium aluminum hydride gave the more soluble diamine (*R**,*S**)-**2**. The assignment of the (*R**,*S**) relative configuration to the pairs of asymmetric tertiary arsine As stereocenters in the diimine and the diamine was based upon ^1H NMR spectroscopic comparisons between the optically inactive and optically active forms of the two macrocycles (see below).

The ^1H NMR spectrum of (*R**,*S**)-**1** in $CDCl_3$ after 48 h indicated quantitative conversion into a new compound; the new compound spontaneously reverted into the (*R**,*S**) diimine when heated (after removal of solvent). A molecular weight determination after rearrangement, together with isolation and characterization of reduction product (±)-**6**, established the new compound to be (±)-2,3-dihydro-1-methyl-4,1-benzazarsepine [(±)-**5**; Scheme II]. The rate of formation of (±)-**5** from (*R**,*S**)-**1** is solvent and concentration dependent. For example, (*R**,*S**)-**1** is stable in freshly distilled tetrahydrofuran for 1 week, but if a small quantity of trifluoroacetic acid is added to the solution, rearrangement into seven-membered monoimine occurs within minutes. Analogous macrocycles containing CH_2,[10] O,[11] or S[12] (in place of the AsMe group in **1**) behave similarly with

Scheme I

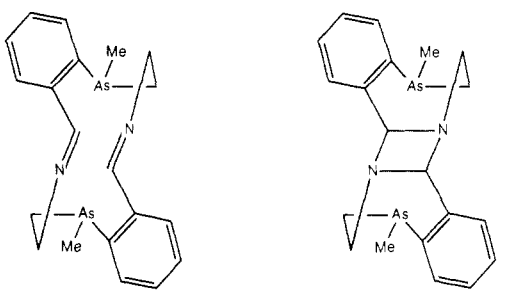


Scheme II



respect to the monomer–dimer rearrangement; only 3,4-dihydro-5*H*-2-benzazepine and 3,4-dihydro-1,4-benzoxazepine, however, are stable enough to be isolated.

Although other pathways may be available, the present data suggest that the interconversions between (*R**,*S**)-**1** and (±)-**5** are acid catalyzed. A simple stepwise scheme, involving a 1,3-diazetidine intermediate, has been proposed for the dimerization of 3,4-dihydro-5*H*-2-benzazepine.[10] We propose a similar mechanism for the interconversion of (*R**,*S**)-**1** and (±)-**5**. In agreement with the earlier work, molecular models suggest that the most stable configuration for (*R**,*S**)-**1** is the trans–trans "chair" structure **10**, and for the intermediate, the cis–anti–cis structure **11**. Although there was no evidence of 1,3-diazetidine



10 **11**

formation in the work, Schiff base dimerizations to 1,3-diazetidines

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(10) Goldman, I. M.; Larson, J. K.; Tretter, J. R.; Andrews, E. G. *J. Am. Chem. Soc.* **1969**, *91*, 4941–4942.
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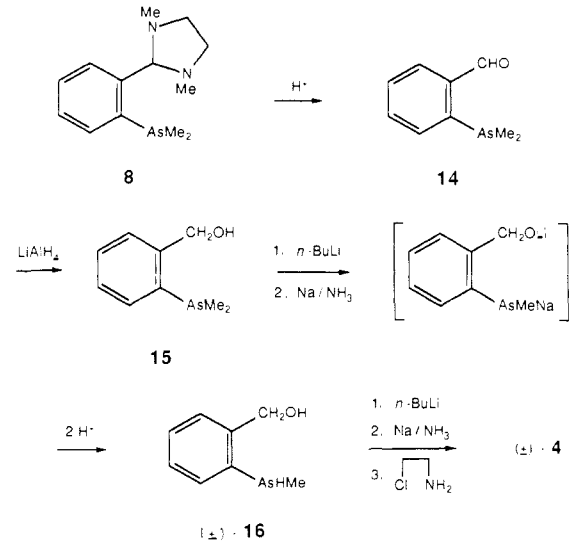
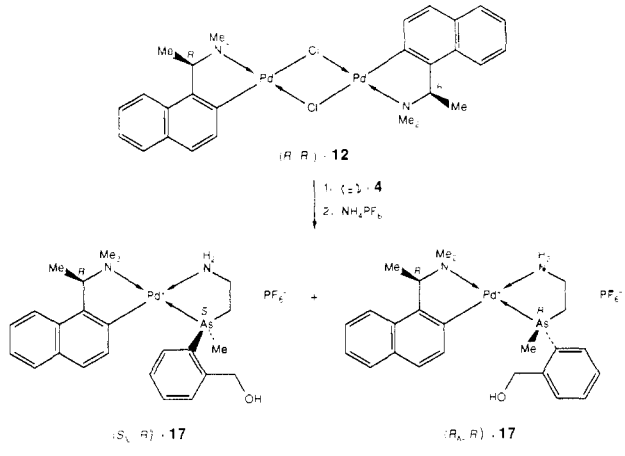
(12) Martin, J. W. L.; Wainwright, K. P.; Weerasuria, K. D. V.; Wild, S. B. *Inorg. Chim. Acta* **1985**, *99*, L5–L7. Martin, J. W. L.; Organ, G. J.; Wainwright, K. P.; Weerasuria, K. D. V.; Willis, A. C.; Wild, S. B. *Inorg. Chem.* **1987**, *26*, 2963–2968.

Scheme III

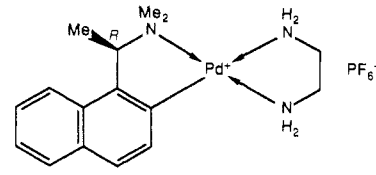


Scheme IV



and Schiff base exchange reactions via diazetidines have been reported.[13] An equatorial disposition of the methyl group on the pyramidally stable asymmetric tertiary arsine As stereocenter fixes the helicity of the asymmetric nonplanar seven-membered ring. Thus, an arsenic stereocenter of (*R*) absolute configuration stabilizes a ring of (*S*) absolute configuration. Moreover, models indicate that the dimerization of seven-membered rings of opposite helicity is strongly favored on steric grounds, thus providing a rationale for the highly stereoselective synthesis of (*R**,*S**)-**1** from (±)-**5**.

Stereoselective Template Synthesis of Optically Active *trans*-As_2N_2 Diimine Macrocycle (*R*,*R*)-1. (a) Synthesis and Resolution of Precursor (±)-4. Asymmetric bidentate (±)-**4** was prepared from 1,3-dimethyl-2-phenylimidazolidine as shown in Scheme III. Lithiation protected the hydroxyl group from reduction in each of the two sodium in ammonia steps. Ligand (±)-**4** reacted quantitatively with resolving agent (*R*,*R*)-**12**·CH_2Cl_2 in methanol to give an equimolar mixture of salts that were converted into (R_{As},*R*)-**17** and (S_{As},*R*)-**17** by treatment with aqueous ammonium hexafluorophosphate (Scheme IV). As for other unsymmetrical and asymmetric bidentates, coordination of (±)-**4** to the asymmetric palladium(II) auxiliary was regioselective, giving two of the four diastereomers possible, the "softer" tertiary arsine As donor presumably taking up a position trans to the NMe_2 group in the ortho-metalated ring.[14,15] The individual diastereomers were obtained by fractional crystallization of the mixture from a dichloromethane–propan-2-ol solvent mixture. Both compounds were isolated in ca. 60% yield as crystalline *monopropan-2-ol solvates*: (R_{As},*R*)-**17**·Me_2CHOH has $[\alpha]_D$ + 87° (Me_2CO); (S_{As},*R*)-**17**·$Me_2CH(OH)$ has $[\alpha]_D$ −134° (Me_2CO).[16] The purity of the diastereomers was confirmed by ^1H NMR spectroscopy. The ^{13}C NMR spectra of the two compounds were also recorded and assigned by comparisons with the spectrum of (±)-**4** itself and with use of the INEPT procedure.[19] The individual enantiomers of (±)-**4** were obtained by displacements from the pure complex diastereomers with ethane-1,2-diamine; byproduct (*R*)-**19**



(*R*)-**19**

precipitated from each of the reaction mixtures and was reconverted into resolving agent (*R*,*R*)-**12** with hydrochloric acid.[15] The optically pure tertiary arsines distill with bp 160 °C (0.08 mmHg); (R_{As},*R*)-**17**·$Me_2CH(OH)$ gave (*S*)-**4** of $[\alpha]_D$ +65° (CH_2Cl_2) and (S_{As},*R*)-**17**·$Me_2CH(OH)$ gave (*R*)-**4** of $[\alpha]_D$ −65° (CH_2Cl_2).[21]

(b) Oxidative Dimerization of Coordinated (±)-4. Diastereomer (S_{As},*R*)-**17**·$Me_2CH(OH)$ reacts with a suspension of $BaMnO_4$ in dichloromethane over 16 h to give an 87% yield of crystalline (S_{As},*R*)-**18**, a coordinatively protected form of (*R*)-2-[(2-aminoethyl)methylarsino]benzaldehyde. The role of the palladium(II) auxiliary in the reaction was twofold: it protected the amino aldehyde from self-condensation, and it protected the tertiary arsine group from oxidation. Enantiomers (R_{As},*R*)-**18**, (S_{As},*S*)-**18**, and (R_{As},*S*)-**18** were prepared in similar reactions.

The strategy now called for protection of the aldehyde group in (S_{As},*R*)-**18** with *N*,*N*′-dimethyl-1,2-ethanediamine prior to the displacement of optically active imidazolidine (*S*)-**3**. When the protecting reagent was added to the colorless solution of (S_{As},*R*)-**18** in the presence of molecular sieves, however, the reaction mixture turned orange. After ca. 10 h, the sieves were removed and the solution was evaporated to dryness. Recrystallization of the orange residue from dichloromethane–methanol afforded bright yellow crystals of (R_{As},S_{As},*R*)-**20** (Scheme V). The yield of the four-coordinate complex based upon (S_{As},*R*)-**18** was 80%. Byproduct (*R*)-**21** was isolated from the mother liquor. Interestingly, re-

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(15) Leung, P.-H.; McLaughlin, G. M.; Martin, J. W. L.; Wild, S. B. *Inorg. Chem.* **1986**, *25*, 3392–3395.

(16) The nomenclature adopted here is based upon recent Chemical Abstracts Service practice[17] with non-carbon stereocenters specified in cases where more than one type of stereocenter is present. Enantiomers have simplified descriptors. Full stereochemical descriptors are given in the Experimental Section. Absolute chiralities are expressed in terms of the Cahn–Ingold–Prelog (CIP) sequence rules.[18]

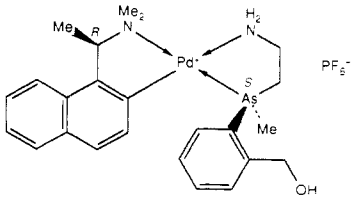
(17) Blackwood, J. E.; Giles, P. M., Jr. *J. Chem. Inf. Comput. Sci.* **1975**, *1*, 67–72. *Chemical Abstracts, Index Guide to Volume 76*; Chemical Abstracts Service: Columbus, OH, 1972. *Chemical Abstracts, Ninth Collective Index, Index Guide to Volume 76–85*: Chemical Abstracts Service: Columbus, OH, 1977; paragraph 203. Also see: Cahn, R. S.; Dermer, O. C. *Introduction to Chemical Nomenclature*, 5th ed.; Butterworths: London, 1979; pp 140–150.

(18) Cahn, R. S.; Ingold, C. K.; Prelog, V. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 385–415.

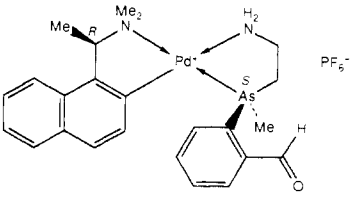
(19) INEPT (Insensitive Nuclei Enhancement by Polarization Transfer).[20]

(20) Morris, G. A.; Freeman, R. *J. Am. Chem. Soc.* **1979**, *101*, 760–762. Dodrell, D. M.; Pegg, D. T. *J. Am. Chem. Soc.* **1980**, *102*, 6388–6390.

(21) Since the replacement of a lone pair by a heavy metal changes the priority of that ligand (or phantom ligand) from 4 to 1, the CIP descriptor[18] must be reversed when the ligand is displaced from the metal and vice versa.

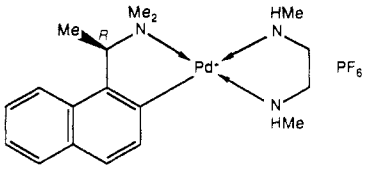


(S_{As},R)-**17**



(S_{As},R)-**18**

crystallization of the yellow complex, or indeed of the original orange residue, from hot acetone gave deep orange (S_{As},S_{As},R)-**20**·0.5Me_2CO, a five-coordinate *linkage isomer* of the yellow compound (Scheme V). Both isomers have the same nonresolved ^1H NMR spectrum in CD_2Cl_2 at 20 °C, although at −20 °C nonequivalent As*Me* and C*H*=N singlets are observed. Treatment of (R_{As},R)-**18**·$Me_2CH(OH)$ with $(CH_2NHMe)_2$ did not give a characterizable product.



(R)-**21**

(c) Template-Controlled Asymmetric Transformation: (*R,*S**)-1 → (*R*,*R*)-1.** Reaction of (*R**,*S**)-**1** with (*R*,*R*)-**12**·CH_2Cl_2 in methanol, in the presence of a trace of trifluoroacetic acid [to induce formation of (±)-**5**], produced an orange solution from which ammonium hexafluorophosphate precipitated an orange product. Recrystallization of this material from dichloromethane–methanol yielded 98% of the theoretical quantity of yellow (R_{As},S_{As},R)-**20**. This is the preferred method of synthesizing (*R*,*R*)-**1**. No other crystalline material could be obtained from the mother liquor. Data are insufficient for other than speculation to be given on the mechanism for the diastereoselective synthesis of the macrocycle on the asymmetric palladium(II) auxiliary, but the following comments may be pertinent. If two molecules of (*R*)-**5** coordinate as unidentates to the palladium auxiliary of (*R*) absolute configuration [models suggest that chelation of (*R*)-**5** is unlikely], one As-bonded trans to the "soft" NMe_2 group, the other N-bonded trans to the relatively "hard" ortho-metalated carbon atom, models suggest that the imine dipoles are closely aligned for formation of coordinated (*R*,*R*)-**1** via diazetidine **11**. Two molecules of (*S*)-**5**, or indeed one each of (*R*)-**5** and (*S*)-**5**, do not produce an intermediate with a favorable geometry for ring expansion.

(d) Crystal and Molecular Structures of (R_{As},S_{As},R)-20 (Yellow) and (R_{As},R_{As},S)-20·0.5Me_2CO (Orange).[22] The molecular structures of the cations in the orange and the yellow isomers of **20** are shown in Figure 1. Crystal data for the two complexes are given in Table I. Table II gives positional parameters for the two compounds, employing the atom-numbering

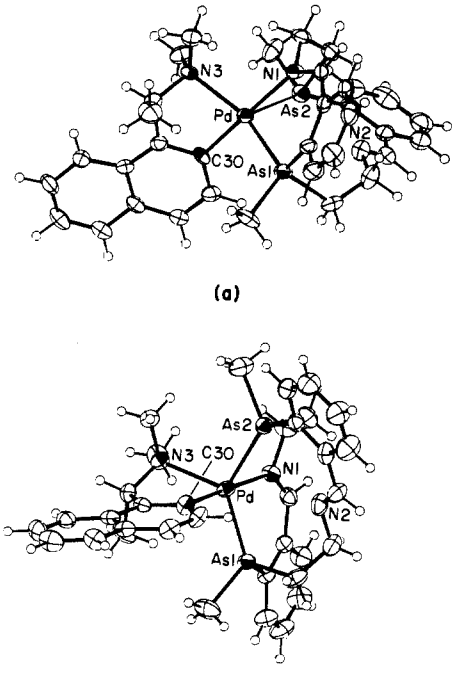
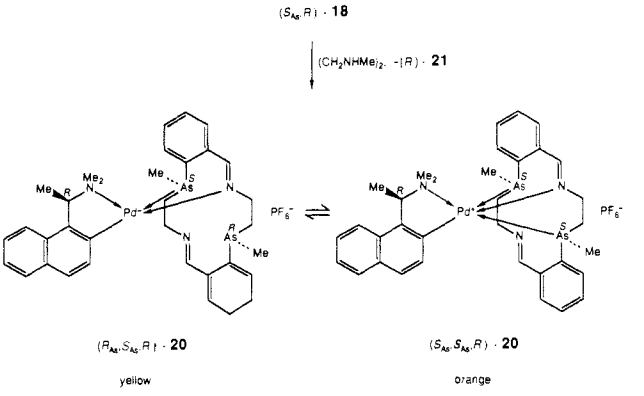


Figure 1. ORTEP drawing of the cation of the yellow isomer (R_{As},S_{As},R)-**20** (a) and of the cation in the orange isomer (R_{As},R_{As},S)-**20**·0.5Me_2CO (b).[21] Thermal ellipsoids enclose 35% probability levels. The complete numbering scheme is available in the supplementary material.

Scheme V



schemes given in Figures 1 and 2 of the supplementary material; Table III lists the most important distances and angles.

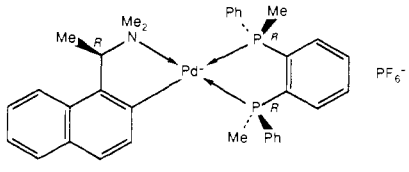
The asymmetric stereocenters in the two compounds have absolute configurations as follows. Orange isomer: As(1) (*R*), As(2) (*R*), C(3) (*S*). Yellow isomer: As(1) (*S*), As(2) (*R*), C(3) (*R*).[21] In both structures corresponding molecular dimensions in the individual chelate rings are similar and typical for the atoms involved. The striking difference between the two structures lies in the coordination environments of the palladium atoms: in orange (R_{As},R_{As},S)-**20**·0.5Me_2CO the palladium atom is trigonal-bipyramidal with the macrocycle acting as an As_2N tridentate; in yellow (R_{As},S_{As},R)-**20** the palladium stereochemistry is distorted square-planar with the macrocycle acting as an AsN bidentate. In both cations the N(1), Pd, and C(30) atoms are almost collinear with an equivalence of the bond lengths in the two compounds (Table III). The Pd–As(1) distance is substantially shorter than the Pd–As(2) distance in both compounds [in (R_{As},S_{As},R)-**20**, Pd···As(2) is not within bonding range]. Molecular models suggest that the molecular arrangement adopted in the yellow isomer is the limit to which the macrocyclic diimine ligand can be twisted without excessive strain in attempting to satisfy the palladium(II) with square-planar coordination. Both Pd–As(1) and Pd–N(3) distances in the distorted square-planar structure are shorter than in the trigonal-bipyramidal structure; this is consistent with the lower coordination number of the palladium(II) stereocenter in

(22) The crystal structure was inadvertently determined on the yellow isomer of the complex containing the palladium(II) auxiliary of (*R*) absolute configuration and on the orange isomer of the complex containing the auxiliary of (*S*) absolute configuration. Apart from any confusion this may engender, the oversight is of no consequence.

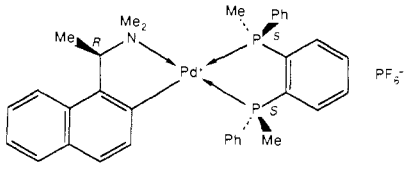
the former. There are also large variations in the bond angles around the arsenic stereocenters in the two structures, and uncoordinated N(2) is further from the palladium in the yellow form than it is in the orange form (see Table III).

The spatial arrangement of the macrocyclic ligand in each structure is similar; the change in the environment about the metal atom in each case appears to arise from an accumulation of a number of relatively small variations in the macrocyclic ligand geometry, accompanied by a rotation of the essentially planar asymmetric palladium(II) auxiliary about the Pd–C(30) bond. As expected, the largest variations in twist involve the flexible 1,2-ethane linkages with torsion angles for C(n7)–N(n)–C(n8)–C(N9) of 62.1 and 112.6° (for n = 1 and 2, respectively) in the orange isomer and 82.6 and 125.1° for the corresponding angles in the yellow isomer. Another difference between the two is found in the packing of the ions in the crystal lattices. The distorted square-planar cation (yellow) is almost spherical, whereas the trigonal-bipyramidal complex (orange) is cylindrical with solvent molecules (0.5 Me_2CO per Pd) occupying holes in a less efficiently packed lattice.

(e) Liberation of Optically Active *trans*-As_2N_2 Diimine Macrocycle (*R*,*R*)-1. Optically active (*R*,*R*)-**1** was displaced from (S_{As},S_{As},*R*)-**20**·0.5Me_2CO [or from (R_{As},S_{As},*R*)-**2**] with (*R**,*R**)-1,2-C_6H_4(PMePh)$_2$[23] in dichloromethane. The sparingly soluble diastereomers of the bis(tertiary phosphine) complex [(R_P,R_P,*R*)-**22**, (S_P,S_P,*R*)-**22**] precipitated from the reaction



(R_P,R_P,*R*) · **22**



(S_P,S_P,*R*) **22**

mixture and were retained as future sources of resolved (*R**,*R**)-1,2-C_6H_4(PMePh)$_2$.[23,24] Optically pure (*R*,*R*)-**1**, mp 173 °C, $[\alpha]_D$ +99.8° (CH_2Cl_2), crystallized from the mother liquor during concentration. Enantiomer (*S*,*S*)-**1**, $[\alpha]_D$ −99.8° (CH_2Cl_2), was similarly obtained from (R_{As},R_{As},*S*)-**20**·0.5Me_2CO [or from (R_{As},S_{As},*S*)-**20**]. The ^1H NMR spectrum of (*R*,*R*)-**1** in $CDCl_3$ contains a doublet at δ 9.00 ($^4J_{HH}$ = 1.5 Hz) for the azomethine protons and a singlet at δ 1.22 for the magnetically equivalent As*Me* groups. The molecular weights of the optically active diimine macrocycles in dichloromethane corresponded to the formula weights, and the mass spectrum of each enantiomer contained peaks at *m*/*e* 442 amu [M^+] and at *m*/*e* 427 amu [M − Me^+] (base peak).

Optically active (*R*,*R*)-**1** slowly rearranges in $CDCl_3$ into (*R*)-**5**, which has a ^1H NMR spectrum identical with that of the rearrangement product of (*R**,*S**)-**1**, viz., (±)-**5** (Scheme VI). Removal of solvent from solutions of the optically active monoimine results in spontaneous reformation of the optically active diimine, although $LiAlH_4$ reduction gives (*R*)-**6**. Moreover, the mixing together of equimolar solutions of (*R*,*R*)-**1** and (*S*,*S*)-**1** in dichloromethane leads to the crystallization of sparingly soluble (*R**,*S**)-**1** [presumably via (±)-**5**]; thus, (±)-(*R**,*R**)-**1** cannot be isolated.

$$(R,R)\text{-}\mathbf{1} + (S,S)\text{-}\mathbf{1} \rightarrow [(\pm)\text{-}\mathbf{5}] \rightarrow (R^*,S^*)\text{-}\mathbf{1}\downarrow$$

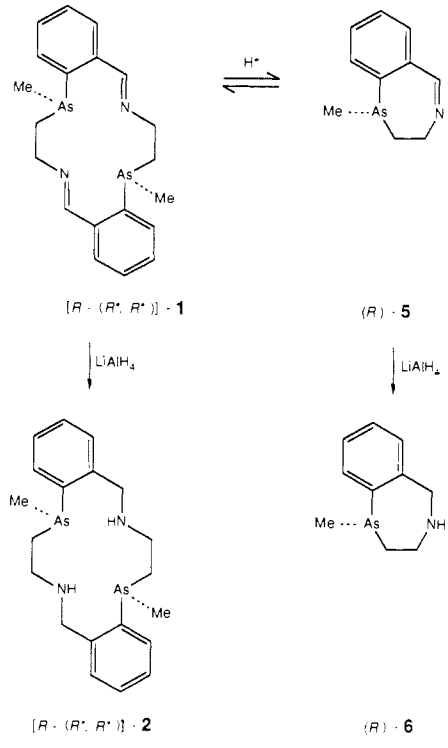
(23) Roberts, N. K.; Wild, S. B. *J. Am. Chem. Soc.* **1979**, *101*, 6254–6260.
(24) Other chelating bis(tertiary phosphines) would undoubtedly displace (*R*,*R*)-**1** from the complex, but it was convenient for us to use (*R**,*R**)-1,2-C_6H_4(PMePh)$_2$.

Table I. Summary of Crystal Parameters and Experimental Data for X-ray Diffraction Measurements on (R_{As},S_{As},*R*)-**20** and (R_{As},R_{As},*S*)-**20**·0.5Me_2CO[a]

parameter	(R_{As},S_{As},*R*)-**20**	(R_{As},R_{As},*S*)-**20**·0.5Me_2CO
formula	$C_{34}H_{40}As_2F_6N_3PPd$	$C_{35.5}H_{43}As_2F_6N_3O_{0.5}PPd$
color	yellow	orange
mol wt	891.93	920.97
cryst size, mm	0.45 × 0.42 × 0.25	0.55 × 0.55 × 0.55
space group	$P2_12_12_1$ (No. 19)	$P2_12_12_1$ (No. 19)
a, Å	12.235 (5)	18.358 (3)
b, Å	15.176 (3)	18.392 (3)
c, Å	19.379 (3)	11.927 (3)
V, Å^3	3598.3	4027.0
Z	4	4
d_{calcd}, g cm^{-3}	1.65	1.52
μ(Mo K_α), cm^{-1}	24.3	21.7
radiation	graphite-monochromated Mo Kα (λ = 0.71069 Å)	
2θ range, deg	3–52	3–55
total no. of data	3971	5126
no. of unique data, $I > 3\sigma(I)$	2664	3127
N (parameters)	425	476
R, R_w[b]	0.042, 0.036	0.042, 0.036
$(\Delta/\sigma)_{max}$	0.1	0.1
Δ map ρ, e Å^{-3}	−0.45 to +0.65	0.45

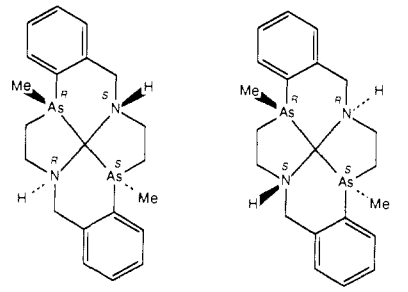
[a] The estimated standard deviation in the least significant digit is shown in parentheses for each entry in this and subsequent tables. [b] $R = \sum||F_o| - |F_c||/\sum|F_o|$; $R_w = [\sum_w(|F_o| - |F_c|)^2/\sum_w|F_o|^2]^{1/2}$.

Scheme VI



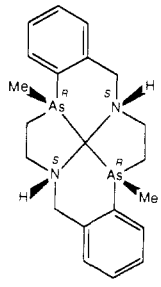
Syntheses of *trans*-As_2N_2 Diamine Macrocycles (*R,*S**)-2, (*R**,*R**)-2, (*R*,*R*)-2, and (*S*,*S*)-2.** The potentially quadridentate diamine macrocycles (*R**,*S**)-**2**, (*R*,*R*)-**2**, and (*S*,*S*)-**2** were prepared from the corresponding forms of the diimine macrocycles in reductions with lithium aluminum hydride. The meso macrocycle (*R**,*S**)-**2** crystallizes from dichloromethane–methanol as air-stable cubes, mp 161–162 °C. Optically active (*R*,*R*)-**2**, $[\alpha]_D$ +190° (CH_2Cl_2), and (*S*,*S*)-**2**, $[\alpha]_D$ −190° (CH_2Cl_2), crystallize from chloroform as *dichloroform solvates*, mp 55 °C. The racemic diamine macrocycle (*R**,*R**)-**2**, however, cannot be prepared directly because of the unavailability of (*R**,*R**)-**1**. Diamine (*R**,*R**)-**2** was prepared by a quantitative asymmetric transformation involving the racemization of the tertiary arsine As stereocenters in the palladium(II) chelate of (*R**,*S**)-**2**. Thus, [Pd{(*R**,*S**)-**2**}]Cl_2 was prepared from (*R**,*S**)-**2** and tetra-

chloropalladate(II) in methanol; the ^{1}H NMR spectrum of the product contains a single sharp As*Me* resonance, which is consistent with the presence of one of the two centrosymmetrical complex diastereomers possible for this form of the ligand, viz., (R^*_{As},S^*_{As},R^*_N,S^*_N)-**23** or (R^*_{As},S^*_{As},S^*_N,R^*_N)-**23** [the other



(R_{As},S_{As},R_N,S_N)-**23**
C_1

(R_{As},S_{As},S_N,R_N)-**23**
C_i



(R_{As},R_{As},S_N,S_N)-**23**
C_2

diastereomer possible is asymmetric (R^*_{As},S^*_{As},S^*_N,S^*_N) with nonequivalent As*Me* groups]. The (R^*,S^*) form of a related *trans*-As_2S_2 macrocycle was shown by X-ray crystallography to produce both of the centrosymmetrical complexes.[8] Upon being heated in water for 1 h at 60 °C, [Pd{(R^*,S^*)-**2**}]Cl_2 is quantitatively converted into [Pd{(R^*,R^*)-**2**}]Cl_2 with complete stereoselectivity, the most stable form of which contains the dissymmetric cation (R^*_{As},R^*_{As},S^*_N,S^*_N)-**23** (asymmetric transformation of the first kind).[8] The corresponding palladium(II) hexafluorophosphate salt of (R^*,S^*)-**2** requires 4 h at 110 °C in water for complete conversion, although the asymmetric transformation is complete within 5 min at 150 °C in dimethyl sulfoxide:

$$[Pd\{(R^*,S^*)\text{-}\mathbf{2}\}]X_2 \rightarrow [Pd\{(R^*,R^*)\text{-}\mathbf{2}\}]X_2$$

The transformations between the diastereomers can be monitored by ^{1}H NMR spectroscopy in D_2O. Anion participation is implied by the milder conditions required for conversion of the chloride salt. Indeed, coordinated inner tertiary arsine As stereocenters in a cobalt(III) chloride complex of a linear tetrakis(tertiary arsine) racemize when the complex is heated in boiling dimethylformamide.[25] We have also observed coordinated tertiary arsine As stereocenter inversions in palladium(II) perchlorate complexes of the *trans*-As_2S_2 analogue of **2**, where detailed studies, including the isolation and characterization by X-ray crystallography of three of the six possible diastereomers of [Pd{*trans*-As_2S_2}]$(ClO_4)_2$, showed that the (R^*_{As},R^*_{As},S^*_S,S^*_S) complex is the most stable of the six possible complex diastereomers for both diastereomers of the ligand.[8] Decomposition of (R^*_{As},R^*_{As},S^*_N,S^*_N)-**23** with cyanide affords (R^*,R^*)-**2**, a highly soluble compound that could not be induced to crystallize.

The synthesis of (R^*,R^*)-**2** by the palladium(II)-assisted asymmetric transformation of (R^*,S^*)-**2** completes the original objective of synthesizing all isolable forms of the 14-membered *trans*-As_2N_2 macrocycles **1** and **2**. As shown by the ready complexation of palladium(II) by the diastereomers **2**, the diamine ligands are potentially powerful sequesterers of soft metal ions, giving soluble complexes with high stereoselectivity. The diimine macrocycles **1** impose other constraints on metals; for example, we have shown that the *trans*-N_2S_2 analogue of **1** produces an air-stable copper(I) derivative of distorted tetrahedral geometry that is a model for the active sites in the blue (type I) copper enzymes.[26]

This work highlights the utility of metal complexation as a means of modifying and controlling organic reactivity. Readily prepared complex auxiliary [(*R*)-1-[1-(dimethylamino)ethyl]-2-naphthalenyl-C^2,*N*]palladium(II) was shown to act as a resolving agent, as a protecting group, and as a template in a contigual sequence of reactions culminating in the highly stereoselective synthesis of an optically active 14-membered *trans*-As_2N_2 macrocycle. Moreover, it was subsequently shown that the palladium(II) ion facilitated a stereospecific transformation between the (R^*,S^*) and (R^*,R^*) forms of the reduced macrocycle, thus emphasizing further the potential of metal complexation as an adjunct to organic synthesis.

Experimental Section

Reactions involving air-sensitive compounds were carried out under a positive pressure of argon. ^{1}H NMR spectra were recorded at 34 °C on JEOL FX 200 and Bruker CXP 200 spectrometers. A JEOL FX 200 spectrometer operating at 50.3 MHz was used to obtain ^{13}C NMR spectra. ^{1}H and ^{13}C NMR chemical shifts are reported (δ) relative to internal Me_4Si. Optical rotations were measured at 20 °C on the specified solutions in a 1-dm cell with a Perkin-Elmer Model 241 polarimeter. Elemental analyses were performed by staff within the Research School of Chemistry.

Optically active primary amines were purchased from Norse Laboratories, Inc., Santa Barbara, CA, and methylated by standard procedures. Bis(μ-chloro)bis[(*R*)-1-[1-(dimethylamino)ethyl]-2-naphthalenyl-C^2,*N*]dipalladium(II) dichloromethane solvate [(*R*,*R*)-**12**·CH_2Cl_2] was prepared from $Li_2[PdCl_4]$ by treatment with 1 equiv each of (*R*)-[1-(dimethylamino)ethyl]naphthalene and triethylamine in methanol (yield 92%).[14] X-ray structure determinations of compounds were performed at Macquarie University (F. S. Stephens) and the Crystalitics Co., Lincoln, NE 68501.

Macrocyclic Diimine (R^*,S^*)-1 and Seven-Membered (±)-5. 1,3-Dimethyl-2-[2-(dimethylarsino)phenyl]imidazolidine (8). A solution of *n*-BuLi in *n*-hexane (500 mL of 1.5 M, 0.75 mol) was added dropwise over 1 h into a stirred and cooled (−78 °C) solution of 1,3-dimethyl-2-phenylimidazolidine[9] (**7**; 140 g, 0.79 mol) in diethyl ether (600 mL). The reaction mixture was stirred for a further 16 h at room temperature, and then it was cooled to 0 °C and treated with a solution of dimethyliodoarsine (165 g, 0.71 mol) in diethyl ether (100 mL). After 1 h, water (75 mL) was added, and the organic layer was separated. The aqueous layer was extracted with diethyl ether (2 × 250 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and distilled. The product was obtained as a viscous yellow oil: bp 94–96 °C (0.05 mmHg); yield 167 g (84%); ^{1}H NMR ($CDCl_3$) δ 1.12 (s, 6 H, As*Me*), 2.16 (s, 6 H, N*Me*), 2.45–2.65 (m, 2 H, CH_2N), 3.30–3.50 (m, 2 H, CH_2N), 4.06 (s, 1 H, NC*H*N), 7.15–7.65 (m, 4 H, Ar*H*); ^{13}C NMR ($CDCl_3$) δ 143.4, 129.6, 129.1, 128.8, 128.4, 128.3 (Ar*C*), 89.6 (NCHN), 53.4 (CH_2), 39.6 (N*Me*), 11.2 (As*Me*). Anal. Calcd for $C_{13}H_{21}AsN_2$: C, 55.7; H, 7.6; N, 10.0. Found: C, 55.8; H, 7.4; N, 10.4.

1,3-Dimethyl-2-[2-(methylarsino)phenyl]imidazolidine [(±)-9]. Small pieces of sodium foil (9.62 g, 0.41 mol) were added to a well-stirred mixture of **8** (58.6 g, 0.20 mol) in liquid ammonia (500 mL). After 2 h, the ammonia was evaporated off, and diethyl ether (300 mL) and water (50 mL) were added. The organic layer was separated, and the aqueous phase was extracted with diethyl ether (2 × 250 mL). The combined extracts were dried ($MgSO_4$), filtered, and evaporated. The yellow oil that remained was purified by distillation. The pure product was thus obtained as a colorless oil: bp 91–93 °C (0.05 mmHg); yield 46.8 g (84%); ^{1}H NMR ($CDCl_3$) δ 1.21 (d, 3 H, ^3J = 6.6 Hz, As*Me*), 2.16 (s, 6 H, N*Me*), 2.40–2.70 (m, 2 H, CH_2N), 3.30–3.60 (m, 2 H, CH_2N), 3.65 (s, 1 H, NC*H*N), 3.71 (q, 1 H, ^3J = 6.6 Hz, As*H*), 7.10–7.70 (m, 4 H, Ar*H*); IR (neat) 2100 cm^{-1} (ν_{AsH}). Anal. Calcd for $C_{12}H_{19}AsN_2$: C, 54.1; H, 7.2; N, 10.5. Found: C, 54.2; H, 7.1; N, 10.7.

1,3-Dimethyl-2-[2-[methyl(2-aminoethyl)arsino]phenyl]imidazolidine [(±)-3]. Method 1. Secondary arsine (±)-**9** (38 g, 0.14 mol) was added dropwise into a solution of sodium (3.25 g, 0.14 mol) in liquid ammonia (750 mL). After 2 h, a solution of 2-chloroethanamine [1.7 equiv, gen-

(25) Bosnich, B.; Jackson, W. G.; Wild, S. B. *J. Am. Chem. Soc.* **1973**, *95*, 8269–8280.

(26) Sheldrick, G. M. *SHELTX User Manual, Revision 3*; Nicolet XRD Corp.: Cupertino, CA, 1981.

Table II. Final Positional Parameters

	(R_{As},S_{As},R)-**20**			(R_{As},R_{As},S)-**20**·0.5Me_2CO		
atom	*x*	*y*	*z*	*x*	*y*	*z*
Pd	1579.5 (6)	4520.3 (6)	5556.9 (4)	4009 (1)	704 (1)	2100 (1)
As(1)	2768.4 (8)	4504.3 (9)	6493.6 (5)	4851 (1)	104 (1)	952 (1)
As(2)	1341.2 (10)	6632.9 (8)	5136.9 (6)	4236 (1)	1801 (1)	3423 (1)
P	3206 (3)	856 (3)	7576 (2)	1615 (1)	-3446 (2)	2626 (2)
F(1)	4050 (5)	211 (5)	7224 (4)	903 (3)	-2989 (4)	2731 (7)
F(2)	3557 (8)	480 (6)	8271 (4)	1985 (4)	-2761 (4)	2098 (7)
F(3)	2364 (7)	1467 (6)	7940 (5)	2325 (3)	-3883 (4)	2503 (8)
F(4)	2304 (7)	135 (7)	7502 (6)	1874 (5)	-3185 (4)	3769 (6)
F(5)	2883 (8)	1194 (8)	6858 (4)	1237 (3)	-4115 (4)	3136 (7)
F(6)	4100 (7)	1578 (6)	7625 (6)	1373 (5)	-3685 (5)	1459 (6)
N(3)	600 (6)	3832 (6)	4779 (4)	2795 (3)	312 (3)	2443 (5)
C(N3a)	355 (9)	4355 (8)	4155 (6)	2494 (4)	636 (5)	3463 (7)
C(N3b)	-417 (8)	3477 (7)	5066 (6)	2296 (5)	452 (5)	1508 (8)
C(3)	1326 (9)	3101 (7)	4560 (5)	2898 (4)	-486 (4)	2659 (6)
C(C3)	1392 (11)	2362 (8)	5090 (7)	2943 (5)	-929 (4)	1602 (7)
C(30)	2742 (8)	4139 (6)	4913 (5)	4160 (4)	-81 (4)	3224 (6)
C(31)	3777 (7)	4562 (7)	4838 (5)	4795 (4)	-172 (5)	3832 (6)
C(32)	4490 (8)	4319 (7)	4329 (5)	4882 (4)	-727 (5)	4567 (6)
C(33)	4203 (8)	3624 (7)	3879 (5)	4312 (4)	-1232 (4)	4743 (6)
C(34)	4969 (9)	3346 (7)	3358 (5)	4390 (5)	-1793 (5)	5550 (6)
C(35)	4704 (11)	2656 (8)	2929 (6)	3839 (6)	-2303 (5)	5686 (7)
C(36)	3742 (10)	2199 (7)	3014 (5)	3209 (6)	-2241 (5)	5053 (7)
C(37)	2997 (9)	2461 (7)	3506 (6)	3122 (5)	-1702 (4)	4297 (6)
C(38)	3175 (7)	3181 (6)	3944 (4)	3658 (5)	-1169 (4)	4133 (7)
C(39)	2463 (7)	3464 (6)	4466 (5)	3593 (4)	-566 (4)	3359 (6)
C(As1)	3885 (9)	3572 (7)	6475 (6)	4973 (6)	-950 (4)	950 (9)
C(11)	1886 (8)	4178 (7)	7290 (5)	4632 (4)	324 (4)	-614 (6)
C(12)	2323 (10)	3692 (8)	7817 (5)	4879 (5)	-151 (5)	-1437 (7)
C(13)	1731 (12)	3490 (8)	8402 (5)	4760 (5)	3 (7)	-2557 (8)
C(14)	702 (11)	3801 (8)	8487 (6)	4431 (5)	642 (5)	-2870 (7)
C(15)	235 (8)	4298 (7)	7962 (5)	4210 (5)	1114 (5)	-2069 (7)
C(16)	799 (8)	4487 (7)	7355 (4)	4296 (4)	969 (4)	-926 (7)
C(17)	165 (8)	5005 (6)	6851 (5)	4014 (5)	1547 (4)	-167 (7)
N(1)	333 (6)	5065 (5)	6203 (4)	3889 (4)	1545 (3)	871 (5)
C(18)	-415 (8)	5676 (7)	5832 (5)	3655 (5)	2249 (4)	1335 (7)
C(19)	94 (8)	6602 (7)	5783 (5)	4197 (5)	2527 (4)	2203 (7)
C(As2)	473 (11)	6821 (8)	4302 (5)	3443 (5)	2224 (6)	4312 (8)
C(21)	1768 (8)	7869 (7)	5307 (5)	5076 (4)	2087 (4)	4340 (7)
C(22)	1514 (10)	8525 (8)	4810 (5)	4939 (5)	2312 (5)	5442 (7)
C(23)	1808 (10)	9389 (9)	4920 (7)	5506 (6)	2531 (5)	6148 (8)
C(24)	2311 (10)	9662 (8)	5529 (7)	6195 (5)	2505 (6)	5792 (9)
C(25)	2570 (9)	9042 (8)	6014 (6)	6360 (5)	2284 (6)	4721 (9)
C(26)	2304 (9)	8136 (8)	5913 (5)	5790 (4)	2051 (4)	3985 (7)
C(27)	2682 (9)	7535 (8)	6455 (6)	6023 (4)	1779 (4)	2866 (7)
N(2)	2458 (8)	6728 (6)	6490 (4)	5621 (4)	1516 (4)	2164 (6)
C(28)	2941 (11)	6283 (7)	7085 (5)	5936 (5)	1235 (5)	1139 (7)
C(29)	3607 (8)	5499 (8)	6866 (5)	5859 (5)	412 (5)	1073 (7)
C(1s)				7406 (13)	835 (9)	6258 (11)
C(2s)				7481 (14)	1296 (13)	7481 (17)
C(3s)				6883 (15)	843 (11)	8017 (22)
C(4s)				7829 (15)	677 (12)	8674 (22)

Table III. Selected Bond Lengths and Angles

	(R_{As},S_{As},R)-**20**	(R_{As},R_{As},S)-**20**·0.5Me_2CO
	Bond Lengths, Å	
Pd-As(1)	2.326 (1)	2.341 (1)
Pd-As(2)	3.320 (1)	2.595 (1)
Pd-N(1)	2.139 (8)	2.141 (6)
Pd-N(3)	2.191 (8)	2.377 (6)
Pd-C(30)	1.979 (8)	2.991 (8)
	Bond Angles, deg	
As(1)-Pd-As(2)	101.9 (1)	128.0 (1)
As(1)-Pd-N(1)	73.0 (2)	82.6 (2)
As(1)-Pd-N(3)	104.1 (2)	106.4 (1)
As(1)-Pd-C(30)	101.0 (3)	97.6 (2)
As(2)-Pd-N(1)	90.5 (2)	89.6 (2)
As(2)-Pd-N(3)	150.9 (2)	125.2 (1)
As(2)-Pd-C(30)	92.3 (3)	87.7 (2)
N(1)-Pd-N(3)	101.3 (3)	103.9 (2)
N(1)-Pd-C(30)	174.0 (3)	177.8 (3)

erated from [$H_3NCH_2CH_2Cl$]Cl and NaOH] in diethyl ether was added to the reaction mixture, which was stirred for 1 h. The ammonia was evaporated off, and the residue was extracted with diethyl ether (2 × 500 mL). The extract was filtered, and then it was evaporated to dryness. The pale yellow oil, according to a ^{1}H NMR spectrum, was the expected product, although a satisfactory elemental analysis could not be obtained due to an ongoing reaction of the monoimine into the macrocyclic diimine (see below): yield 43 g (98%); ^{1}H NMR ($CDCl_3$) δ 1.17 (s, 3 H, As*Me*), 1.34 (s, 2 H, NH_2), 1.83–1.88 (m, 2 H, CH_2As), 2.19 (s, 6 H, N*Me*), 2.57–2.64 (m, 2 H, CH_2N), 2.76–2.85 (m, 2 H, CH_2NH$_2$), 3.38–3.45 (m, 2 H, CH_2N), 4.15 (s, 1 H, NC*H*N), 7.29–7.61 (m, 4 H, Ar*H*).

Method 2. Compound (±)-**3** was also prepared from the reaction between tertiary arsine **8**, sodium, and 2-chloroethanamine in liquid ammonia. (This avoided the isolation of secondary arsine (±)-**9**). In a typical run, the tertiary arsine (45 g, 0.16 mol) was added dropwise into a solution of sodium (7.4 g, 0.32 mol) in liquid ammonia (500 mL) and the resulting mixture was stirred for 5 h. A diethyl ether solution of 2-chloroethanamine (1.7 equiv) was then added to the reaction mixture, whereupon the ammonia was allowed to evaporate off over 18 h. The residue was then worked up (as described in method 1) to give (±)-**3** as a pale yellow oil, yield 40 g (80%).

(9*R,18*S**)-7,8,9,16,17,18-Hexahydro-9,18-dimethyldibenzo[e,*l*]-[1,8,4,11]diazadiarsacyclotetradecine [(*R**,*S**)-1].** Precursor (±)-**3** (45 g, 0.15 mol) was heated at 80 °C in vacuo (0.05 mmHg) for ca. 24 h; liberated *N*,*N*′-dimethyl-1,2-ethanediamine was collected in a liquid ni-

trogen trap. The light yellow solid that remained was washed with methanol (300 mL) until it was colorless. Recrystallization of the crude product from methanol–dichloromethane gave colorless needles of the pure macrocyclic diimine: yield 31 g (95%); mp 180 °C dec; ^{1}H NMR ($CDCl_3$) δ 1.24 (s, 6 H, As*Me*), 1.94 (m, 2 H, CH_2As), 2.48 (m, 2 H, CH_2As), 2.94 (m, 2 H, CH_2N), 4.13 (m, 2 H, CH_2N), 7.31–7.62 (m, 6 H, Ar*H*), 8.19 (dd, 2 H, ^3J = 7.1 Hz, ^4J = 2.0 Hz, ortho *H*), 8.83 (d, 2 H, ^4J = 2.0 Hz, C*H*=N); IR (Nujol) 1640 cm^{-1} ($\nu_{C=N}$); mass spectrum, *m/e* 442 [M]$^+$, 427 [M – Me]$^+$. Anal. Calcd for $C_{20}H_{24}As_2N_2$: C, 54.3; H, 5.5; N, 6.3. Found: C, 54.1; H, 5.5; N, 6.1.

(±)-2,3-Dihydro-1-methyl-4,1-benzazarsepine [(±)-5]. Trifluoroacetic acid (0.5 mL) was added to a suspension of diimine (*R*,S**)-**1** (2 g, 4.5 mmol) in dichloromethane (75 mL), and the resulting mixture was stirred at room temperature for 2 days. The solution was then filtered, and the filtrate was evaporated to dryness, leaving a yellow oil: ^{1}H NMR ($CDCl_3$) δ 1.29 (s, 3 H, As*Me*), 2.05–2.19 and 2.60–2.73 (m, 2 H, CH_2As), 3.72–3.89 (m, 2 H, CH_2N), 7.31–7.62 (m, 4 H, Ar*H*), 8.52 (s, 1 H, C*H*=N); ^{13}C NMR ($CDCl_3$) δ 163.5 (C_5), 142.1, 138.0, 133.3, 129.6, 129.0, 128.2 (Ar*C*), 50.0 (C_3), 32.4 (C_3), 10.1 (As*Me*); IR (neat) 1635 cm^{-1} ($\nu_{C=N}$). Attempted distillation resulted in formation of (*R*,S**)-**1**.

Macrocyclic Diamine (*R*,S)-2 and Seven-Membered (±)-6. (9*R**,18*S**)-5,6,7,8,9,14,15,16,17,18-Decahydro-9,18-dimethyldibenzo[e,*l*][1,8,4,11]diazadiarsacyclotetradecine [(*R*,S**)-2].** Diimine (*R*,S**)-**1** (10 g, 0.02 mol) was added in small portions to a stirred suspension of $LiAlH_4$ (2 g, 0.05 mol) in tetrahydrofuran (500 mL). The mixture was heated under reflux for 3 h, and then it was cooled to 0 °C before excess $LiAlH_4$ was decomposed by the sequential addition of water (2 mL), 4 N NaOH (2 mL), and water (6 mL). After the reaction mixture was stirred for 30 min, the alumina was filtered off and the filtrate was dried ($MgSO_4$), filtered, and evaporated under reduced pressure. The colorless product, after recrystallization from a methanol–dichloromethane mixture, was obtained as white cubes: mp 161–162 °C; yield 9 g (90%); ^{1}H NMR ($CDCl_3$) δ 1.13 (s, 6 H, As*Me*), 1.80–2.13 (m, 4 H, CH_2As), 2.64–2.91 (m, 4 H, CH_2N), 3.65, 4.28 (AB q, 4 H, $^2J_{AB}$ = 11.8 Hz, benzylic CH_2), 7.26–7.52 (m, 8 H, Ar*H*); ^{13}C NMR ($CDCl_3$) δ 144.9, 140.3, 130.9, 129.2, 128.4, 127.4 (Ar*C*), 53.9, 46.7 (C_7, C_{16}), 32.3 (C_8, C_{17}), 8.8 (As*Me*); IR (Nujol) 3280 cm^{-1} (ν_{NH}); mass spectrum, *m/e* 446 [M]$^+$, 431 [M – Me]$^+$; mol wt (osmometry, CH_2Cl_2) 446 (calcd), 439 (found). Anal. Calcd for $C_{20}H_{28}As_2N_2$: C, 53.8; H, 6.3; N, 6.3. Found: C, 53.9; H, 6.5; N, 6.3.

(±)-2,3,4,5-Tetrahydro-1-methyl-4,1-benzazarsepine [(±)-6]. Trifluoroacetic acid (0.5 mL) was added to a suspension of diimine (*R*,S**)-**1** (2 g, 4.5 mmol) in diethyl ether (150 mL), and the resulting mixture was heated under refluxing conditions for 2 days to obtain a solution. This solution was cooled to room temperature and filtered, and the filtrate was added dropwise to a suspension of $LiAlH_4$ (500 mg, excess) in diethyl ether (200 mL). After the mixture was boiled for 2 h, it was cooled and treated with water (0.5 mL), 4 N NaOH (0.5 mL), and water (1.5 mL) to decompose excess $LiAlH_4$. The alumina was filtered off, and the filtrate was dried ($MgSO_4$) and filtered. Removal of the solvent under reduced pressure afforded a yellow oil, which, after distillation, was colorless: bp 115 °C (0.04 mmHg; Kugelrohr); yield 1.5 g (74%); ^{1}H NMR ($CDCl_3$) δ 1.26 (s, 3 H, As*Me*), 1.79–1.85 (m, 2 H, CH_2As), 3.29–3.45 (m, 2 H, CH_2N), 3.98, 4.02 (AB q, 2 H, $^2J_{AB}$ = 15.1 Hz, benzylic CH_2), 7.07–7.41 (m, 4 H, Ar*H*); ^{13}C NMR ($CDCl_3$) δ 144.7, 143.8, 130.3, 128.2, 127.2, 126.7 (Ar*C*), 53.7, 48.8 (C_3, C_5), 29.2 (C_2), 8.3 (As*Me*); IR (neat) 3300 cm^{-1} (ν_{NH}); mass spectrum, *m/e* 223 [M]$^+$, 208 [M – Me]$^+$; mol wt (osmometry, CH_2Cl_2) 223 (calcd), 225 (found). Anal. Calcd for $C_{10}H_{14}AsN$: C, 53.8; H, 6.3; N, 6.3. Found: C, 53.2; H, 6.4; N, 6.3.

Optically Active Macrocyclic Diimines (*R*,*R*)-1 and (*S*,*S*)-1. 2-(Dimethylarsino)benzaldehyde (14). Concentrated HCl (10 M, 150 mL) was added to a solution of **8** (167 g, 0.60 mol) in dichloromethane (500 mL), and the mixture was vigorously stirred at room temperature for 30 min. The organic layer was then separated, and the aqueous layer was extracted with dichloromethane (2 × 150 mL). The combined organic extracts were washed with water (300 mL), dried ($MgSO_4$), filtered, and evaporated. The yellow oil that remained was distilled: bp 82–84 °C (0.04 mmHg); yield 116 g (93%); ^{1}H NMR ($CDCl_3$) δ 1.17 (s, 6 H, As*Me*), 7.25–7.90 (m, 4 H, Ar*H*), 10.24 (s, 1 H, C*H*O); ^{13}C NMR ($CDCl_3$) δ 192.8 (*C*HO), 147.4, 138.4, 133.3, 133.1, 130.8, 127.9 (Ar*C*), 10.6 (As*Me*); IR (neat) 1690 cm^{-1} ($\nu_{C=O}$). Anal. Calcd for $C_9H_{11}AsO$: C, 51.5; H, 5.3. Found: C, 51.7; H, 5.1.

2-(Dimethylarsino)benzenemethanol (15). A solution of **14** (125 g, 0.60 mol) in methanol (900 mL) was reacted with sodium borohydride (49 g, 1.3 mol) at room temperature for 3 h. After evaporation of the solvent, the residue was treated with deoxygenated HCl (1 M, 2 L) and the mixture was extracted with dichloromethane (500 mL). The organic layer was dried ($MgSO_4$), filtered, and evaporated. Distillation of the residue gave the colorless product as an oil: bp 76–78 °C (0.01 mmHg); yield 122 g (97%); ^{1}H NMR ($CDCl_3$) δ 1.05 (s, 6 H, As*Me*), 2.70 (O*H*), 4.70 (s, 2 H, CH_2OH), 7.05–7.45 (m, 4 H, Ar*H*); IR (neat) 3320 cm^{-1} (ν_{OH}). Anal. Calcd for $C_9H_{13}AsO$: C, 51.0; H, 6.2; As, 35.3. Found: C, 51.2; H, 6.2; As, 35.7.

(±)-2-(Methylarsino)benzenemethanol (16). A solution of *n*-BuLi in *n*-hexane (142 mL of 1.5 M, 0.21 mol) was added to a solution of **15** (45 g, 0.21 mol) in tetrahydrofuran (300 mL) at 0 °C. After 1 h, the clear solution was slowly added to a well-stirred solution of sodium (9.8 g, 0.43 mol) in liquid ammonia (500 mL). The mixture was stirred for 1 h prior to allowing the ammonia to evaporate. Diethyl ether (500 mL) and water (50 mL) (dropwise) were added to the residue, and the layers were separated. The aqueous layer was extracted with diethyl ether (2 × 200 mL), and the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated. Distillation of the residual yellow oil gave the product as a pale yellow liquid: bp 92–94 °C (0.08 mmHg); yield 39 g (93%); ^{1}H NMR ($CDCl_3$) δ 1.21 (d, 3 H, ^3J = 6.8 Hz, As*Me*), 3.00 (O*H*), 3.54 (q, 1 H, ^3J = 6.8 Hz, As*H*), 4.62 (s, 2 H, CH_2OH), 6.95–7.70 (m, 4 H, Ar*H*); IR (neat) 3450 (ν_{OH}), 2110 cm^{-1} (ν_{AsH}). Anal. Calcd for $C_8H_{11}AsO$: C, 48.5; H, 5.6. Found: C, 48.5; H, 5.5.

(±)-2-[Methyl(2-aminoethyl)arsino]benzenemethanol [(±)-4]. Method 1. A solution of *n*-BuLi in *n*-hexane (114 mL of 1.6 M, 0.18 mol) was added to a stirred and cooled solution (0 °C) of **16** (33.7 g, 0.17 mol) in tetrahydrofuran (250 mL). After 15 min, the mixture was added dropwise to a solution of sodium (4.2 g, 0.18 mol) in liquid ammonia (500 mL). The reaction mixture was vigorously stirred for 1.5 h, and then a diethyl ether solution of 2-chloroethanamine (1.7 equiv) was added. Stirring was continued for a further 30 min, and then the reaction mixture was evaporated to dryness and the residue was treated with water (100 mL) and dichloromethane (500 mL). The organic layer was separated, dried ($MgSO_4$), filtered, and evaporated. The residual viscous oil upon distillation gave the product as an almost colorless oil: bp 146–148 °C (0.05 mmHg); 32.5 g (79%); ^{1}H NMR ($CDCl_3$) δ 1.21 (s, 3 H, As*Me*), 1.86 (m, 2 H, CH_2As), 2.63 (s, 3 H, NH_2, O*H*), 2.19, 2.73 (m, 2 H, CH_2N), 4.51, 5.19 (AB q, 2 H, $^2J_{AB}$ = 11.6 Hz, benzylic CH_2), 7.26–7.50 (m, 4 H, Ar*H*); ^{13}C NMR ($CDCl_3$) δ 146.5, 142.8, 131.2, 129.5, 128.9, 128.3 (Ar*C*), 65.57 (*C*H$_2$OH), 40.0 (*C*H$_2$N), 33.0 (*C*H$_2$As), 8.43 (As*Me*); IR (neat) 3500–3200 cm^{-1} (ν_{OH}, ν_{NH_2}). Anal. Calcd for $C_{10}H_{16}AsNO$: C, 49.8; H, 6.7; As, 31.1. Found: C, 49.8; H, 6.8; As, 30.9.

Method 2. In a typical run, *n*-BuLi in *n*-hexane (114 mL of 1.6 M, 0.18 mol) was added dropwise to a solution of **16** (38 g, 0.18 mol) in tetrahydrofuran (250 mL). After 15 min, the mixture was added slowly to a solution of sodium (8.3 g, 0.36 mol) in liquid ammonia (500 mL). After the mixture was stirred for 5 h, a diethyl ether solution of 2-chloroethanamine (1.7 equiv) was added and the resultant mixture was stirred for a further 30 min. The reaction mixture was worked up (as in method 1) to give (±)-**4** in 60% yield (26 g).

Resolution of (±)-3. Formation and Separation of Internal Diastereomers: [*SP*-4-2-(*R*),(*R*)]- and [*SP*-4-2-1(*S*),2(*R*)]-[1-[1-(Dimethylamino)ethyl]-2-naphthalenyl-*C*^{2},*N*][2-[methyl(2-aminoethyl)arsino]benzenemethanol-*As*,*N*]palladium(II) Hexafluorophosphate Propan-2-ol Solvate [(R_{As},*R*)-17·Me$_2$CH(OH), (S_{As},*R*)-17·Me$_2$CH(OH)]. A solution of (±)-**4** (15 g, 0.06 mol) in methanol (50 mL) was added to a suspension of (*R*)-bis(μ-chloro)bis[1-[1-(dimethylamino)ethyl]-2-naphthalenyl-*C*^{2},*N*]dipalladium(II) dichloromethane solvate [(*R*,*R*)-**12**·CH_2Cl_2; 21.2 g, 0.03 mol] in the same solvent (200 mL), and the mixture was stirred until complete dissolution of the resolving agent had occurred (ca. 1 h at 25 °C). An excess of NH_4PF_6 (20 g) in water (250 mL) was then added. After 30 min, the granular white precipitate of the mixture of (R_{As},*R*)-**17** and (S_{As},*R*)-**17** was filtered off and washed successively with water, methanol–diethyl ether (1:10), and diethyl ether. The dried product (42.3 g) had $[\alpha]_D$ –30.4° (*c* 1.3, Me_2CO). The mixture was dissolved in the minimum quantity of hot dichloromethane (150 mL) and cooled, and propan-2-ol (25 mL) was added. The solution, after standing at 20 °C for 2 days, deposited crystals enriched in (R_{As},*R*)-17·Me$_2$CH(OH) (10 g), $[\alpha]_D$ +71° (*c* 0.5, Me_2CO). The mother liquor was evaporated to dryness under reduced pressure, the residue was dissolved in hot dichloromethane (100 mL), and the resultant solution was diluted with propan-2-ol (20 mL). Upon standing at 20 °C, the solution gave crystals enriched in (S_{As},*R*)-17·Me$_2$CH(OH) [12 g, $[\alpha]_D$ –120° (*c* 0.5, Me_2CO)]. This process was repeated to give additional crystalline material. The fractions enriched in each diastereomer were combined, and then each was given a final recrystallization from dichloromethane–propan-2-ol. Crystalline (R_{As},*R*)-17·Me$_2$CH(OH) was thus obtained in 56% yield (13 g): mp 148–150 °C; $[\alpha]_D$ +87° (*c* 0.5, Me_2CO); ^{1}H NMR (CD_2Cl_2) δ 1.15 (d, 6 H, ^2J = 6.1 Hz, *Me*$_2$CH), 1.84 (d, 3 H, ^3J = 6.3 Hz, NCH*Me*), 1.85 (s, 3 H, As*Me*), 1.50, 1.75, 3.15 (br s, 4 H, NH_2, O*H*), 2.21–2.50 (m, 2 H, CH_2As), 2.90 (s, 3 H, N*Me*), 2.92 (s, 3 H, N*Me*), 3.20–3.55 (m, 2 H, CH_2N), 3.76 (m, 1 H, ^3J = 6.1 Hz, C*H*OH), 4.41 (q, 1 H, ^3J = 6.3 Hz, NC*H*Me), 4.87, 5.81 (AB q, 2 H, $^2J_{AB}$ = 12.0

Hz, benzylic CH_2), 6.68 (d, 1 H, ^3J = 8.3 Hz, Ar*H*), 7.13 (d, 1 H, ^3J = 8.3 Hz, Ar*H*), 7.11–7.78 (m, 8 H, Ar*H*); ^{13}C NMR (CD_2Cl_2) δ 150.3–123.6 (Ar*C*), 73.5 (N*C*HMe), 64.6 (*C*H_2OH), 52.7 (N*Me*), 47.9 (N*Me*), 42.0 (*C*H_2N), 32.4 (*C*H_2As), 25.4 (NCH*Me*), 7.9 (As*Me*). Anal. Calcd for $C_{27}H_{40}AsF_6N_2O_2PPd$: C, 43.2; H, 5.4; N, 3.7. Found: C, 42.7; H, 5.3; N, 3.9.

Diastereomer (S_{As},*R*)-**17**·$Me_2CH(OH)$ was obtained in 66% yield (15.4 g): mp 155–158 °C; $[\alpha]_D$ −134° (*c* 0.5, Me_2CO); ^{1}H NMR (CD_2Cl_2) δ 1.15 (d, 6 H, ^3J = 6.2 Hz, *Me*$_2$CH), 1.86 (d, 3 H, ^3J = 6.6 Hz, NCH*Me*), 2.07 (s, 3 H, As*Me*), 2.21–2.55 (m, 2 H, CH_2As), 1.45–2.75 (br s, 4 H, NH_2, 2 O*H*), 2.87 (s, 3 H, N*Me*), 2.88 (s, 3 H, N*Me*), 2.96–3.45 (m, 2 H, CH_2N), 3.76 (m, 1 H, ^3J = 6.2 Hz, C*H*OH), 4.40 (q, 1 H, ^3J = 6.6 Hz, NC*H*Me), 4.65, 5.35 (AB q, 2 H, $^2J_{AB}$ = 12.0 Hz, benzylic CH_2), 6.85 (d, 1 H, ^3J = 8.3 Hz, Ar*H*), 7.17 (d, 1 H, ^3J = 8.3 Hz, Ar*H*), 7.14–7.74 (m, 8 H, Ar*H*); ^{13}C NMR (CD_2Cl_2) δ 150.2–123.6 (Ar*C*), 73.7 (N*C*HMe), 64.4 (*C*H_2OH), 53.1 (N*Me*), 48.0 (N*Me*), 41.8 (*C*H_2N), 33.0 (*C*H_2As), 23.8 (NCH*Me*), 7.3 (As*Me*). Anal. Calcd for $C_{27}H_{40}AsF_6N_2O_2PPd$: C, 43.2; H, 5.4; N, 3.7. Found: C, 42.9; H, 5.3; N, 3.8.

[*SP*-4-2-(*S*),(*S*)]- and [*SP*-4-2-1(*R*),2(*S*)]-[1-[1-(Dimethylamino)ethyl]-2-naphthalenyl-*C*^{2},*N*][2-[methyl(2-aminoethyl)arsino]benzenemethanol-*As*,*N*]palladium(II) Hexafluorophosphate Propan-2-ol Solvate [(S_{As},*S*)-17·$Me_2CH(OH)$ and (R_{As},*S*)-17·$Me_2CH(OH)$]. Diastereomers (S_{As},*S*)-**17**·$Me_2CH(OH)$, $[\alpha]_D$ −87° (*c* 0.5, Me_2CO), and (R_{As},*S*)-**17**·$Me_2CH(OH)$, $[\alpha]_D$ +134° (*c* 0.5, Me_2CO), were prepared similarly from (±)-**4** and (*S*,*S*)-**12**·CH_2Cl_2. The ^{1}H NMR spectra of the compounds were identical with those of the corresponding enantiomorphs.

(*R*)-2-[Methyl(2-aminoethyl)arsino]benzenemethanol [(*R*)-4]. A solution of (S_{As},*R*)-**17**·$Me_2CH(OH)$ (4.3 g, 5.7 mmol) in dichloromethane (100 mL) was treated with 1,2-ethanediamine (2 mL, excess) at room temperature. After ca. 30 min, diethyl ether (200 mL) was added to the reaction mixture, and the 1,2-ethanediamine complex (*R*)-**19** was filtered off and washed with diethyl ether. The residue obtained after evaporation of the solvent from the filtrate gave, after distillation, pure (*R*)-**4** as a viscous colorless oil: bp 160 °C (0.08 mmHg; Kugelrohr); yield 1.35 g (90%); $[\alpha]_D$ −65° (*c* 4.0, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) and ^{13}C NMR ($CDCl_3$) spectra of the optically active arsine were identical with the spectra of the corresponding racemic arsine.

(*S*)-2-[Methyl(2-aminoethyl)arsino]benzenemethanol [(*S*)-4]. Enantiomer (*S*)-**4** was obtained from the diastereomer (R_{As},*R*)-**17**·$Me_2CH(OH)$ by the method described above. The pure product was obtained as a viscous colorless oil after distillation: bp 160 °C (0.08 mmHg; Kugelrohr); yield 0.2 g (88%); $[\alpha]_D$ +65° (*c* 4.0, CH_2Cl_2). The spectral data were identical with those of its enantiomorph.

[*SP*-4-2-1(*S*),2(*R*)][1-[1-(Dimethylamino)ethyl]-2-naphthalenyl-*C*^{2},*N*][2-[methyl(2-aminoethyl)arsino]benzaldehyde-*As*,*N*]palladium(II) Hexafluorophosphate [(S_{As},*R*)-18]. A solution of (S_{As},*R*)-**17**·$Me_2CH(OH)$ (10 g, 13.3 mmol) in dichloromethane (500 mL) was stirred over $BaMnO_4$ (70 g, excess) for 16 h at room temperature. The solid was then filtered off, and the filtrate was dried ($MgSO_4$), filtered, and evaporated to dryness. The pale yellow glass that remained crystallized from dichloromethane–methanol as pale yellow microcrystals: mp 153–155 °C dec; yield 8 g (87%); $[\alpha]_D$ −106° (*c* 0.5, Me_2CO); ^{1}H NMR (CD_2Cl_2) δ 1.80 (d, 3 H, ^3J = 6.2 Hz, NCH*Me*), 2.11 (s, 3 H, As*Me*), 1.92–2.51 (m, 2 H, CH_2As), 2.86 (s, 3 H, N*Me*), 2.94 (s, 3 H, N*Me*), 3.00–3.57 (m, 2 H, CH_2N), 3.15 (br s, 2 H, NH_2), 4.38 (q, 1 H, ^3J = 6.2 Hz, NC*H*Me), 6.85–8.01 (m, 10 H, Ar*H*), 9.98 (s, 1 H, C*H*O); ^{13}C NMR (CD_2Cl_2) δ 193.1 (*C*H=O), 150.0–123.4 (Ar*C*), 73.5 (N*C*HMe), 52.7 (N*Me*), 47.9 (N*Me*), 42.1 (*C*H_2N), 31.0 (*C*H_2As), 23.7 (NCH*Me*), 7.7 (As*Me*); IR (Nujol) 1690 cm^{-1} ($\nu_{C=O}$). Anal. Calcd for $C_{24}H_{30}AsF_6N_2OPPd$: C, 41.9; H, 4.4; N, 4.1. Found: C, 41.6; H, 4.5; N, 3.9.

[*SP*-4-2-(*R*),(*R*)][1-[1-(Dimethylamino)ethyl]-2-naphthalenyl-*C*^{2},*N*][2-[methyl(2-aminoethyl)arsino]benzaldehyde-*As*,*N*]palladium(II) Hexafluorophosphate [(R_{As},*R*)-18]. Compound (R_{As},*R*)-**18** was obtained by oxidation of (R_{As},*R*)-**17**·$Me_2CH(OH)$ (2 g, 2.7 mmol) with $BaMnO_4$ as described above: mp 168–170 °C; yield 1.7 g (93%); $[\alpha]_D$ +31° (*c* 0.5, Me_2CO); ^{1}H NMR (CD_2Cl_2) δ 1.84 (d, 3 H, ^3J = 6.2 Hz, NCH*Me*), 1.89 (s, 3 H, As*Me*), 2.00–2.51 (m, 2 H, CH_2As), 2.86 (s, 3 H, N*Me*), 2.93 (s, 3 H, N*Me*), 3.20 (br s, 2 H, NH_2), 2.90–3.50 (m, 2 H, CH_2N), 4.40 (q, 1 H, ^3J = 6.2 Hz, NC*H*Me), 6.54–8.13 (m, 10 H, Ar*H*), 10.15 (s, 1 H, C*H*O); ^{13}C NMR (CD_2Cl_2) δ 193.2 (*C*H=O), 150.0–123.6 (Ar*C*), 73.6 (N*C*HMe), 52.8 (N*Me*), 48.2 (N*Me*), 42.3 (*C*H_2N), 30.9 (*C*H_2As), 24.2 (NH*Me*), 9.1 (As*Me*); IR (Nujol) 1690 cm^{-1} ($\nu_{C=O}$). Anal. Calcd for $C_{24}H_{30}AsF_6N_2OPPd$: C, 41.9; H, 4.4; N, 4.1. Found: C, 42.0; H, 4.5; N, 4.0.

[*SP*-4-2-(*S*),(*S*)]- and [*SP*-4-2-1(*R*),2(*S*)][1-[1-(Dimethylamino)ethyl]-2-naphthalenyl-*C*^{2},*N*][2-[methyl(2-aminoethyl)arsino]benzaldehyde-*As*,*N*]palladium(II) Hexafluorophosphate [(S_{As},*S*)-18 and (R_{As},*S*)-18, Respectively]. Diastereomers (S_{As},*S*)-**18**, $[\alpha]_D$ −31° (*c* 0.5, Me_2CO), and (R_{As},*S*)-**18**, $[\alpha]_D$ +106° (*c* 0.5, Me_2CO), were obtained by oxidation of (S_{As},*S*)-**17**·$Me_2CH(OH)$ or (R_{As},*S*)-17·$Me_2CH(OH)$ with $BaMnO_4$, respectively. The NMR spectra were identical with those of their enantiomorphs.

[*SP*-4-4-1[*S*-(*R,*S**)],3(*R*)][1-[1-(Dimethylamino)ethyl]-2-naphthalenyl-*C*^{2},*N*][7,8,9,16,17,18-hexahydro-9,18-dimethyldibenzo[e,-*l*][1,8,4,11]diazadiarsacyclotetradecine-*As*^{9},*N*^{6}]palladium(II) Hexafluorophosphate [(R_{As},S_{As},*R*)-20]. Method 1.** *N*,*N*′-Dimethyl-1,2-ethanediamine (1.5 g, 18 mmol) was added to a solution of (S_{As},*R*)-**18** (12.5 g, 18 mmol) in dichloromethane (250 mL) (over molecular sieves, 3 h), and the mixture was stirred at room temperature for 10 h. The solution was then filtered, the filtrate evaporated to dryness, and the yellow residue dried in vacuo. Recrystallization of the solid from methanol–dichloromethane gave bright yellow crystals of the pure diastereomer (5.62 g). The mother liquor upon concentration yielded additional product (0.87 g): total yield 6.5 g (80%); mp 230–234 °C dec; $[\alpha]_D$ −142.8° (*c* 0.5, CH_2Cl_2); ^{1}H NMR (CD_2Cl_2, −20 °C) δ 1.29 (s, 3 H, As*Me*), 1.49 (s, 3 H, As*Me*), 1.51 (d, 3 H, ^3J = 6.3 Hz, NCH*Me*), 1.85–2.33 (m, 4 H, CH_2As), 2.56 (br s, 3 H, N*Me*), 2.69 (br s, 3 H, N*Me*), 4.20 (q, 1 H, ^3J = 6.3 Hz, NC*H*Me), 3.68–3.98 and 4.21–4.38 (m, 4 H, CH_2N), 7.06–7.77 (m, 14 H, Ar*H*), 8.45 (s, 1 H, C*H*=N), 8.65 (s, 1 H, C*H*=N); ^{1}H NMR (CD_2Cl_2) (25 °C) δ 1.43 (br s, 6 H, As*Me*), 1.54 (d, 3 H, ^3J = 6.4 Hz, NCH*Me*), 1.86–2.39 (m, 4 H, CH_2As), 2.65 (s, 6 H, N*Me*$_2$), 4.20 (q, 1 H, ^3J = 6.4 Hz, NC*H*Me), 3.66–4.93 (m, 4 H, CH_2N), 7.08–7.73 (m, 14 H, Ar*H*), 8.59 (br s, 2 H, C*H*=N); IR (Nujol) 1640, 1635 cm^{-1} ($\nu_{C=N}$). Anal. Calcd for $C_{34}H_{40}As_2F_6N_3PPd$: C, 45.8; H, 4.5; N, 4.7. Found: C, 46.1; H, 4.6; N, 4.7.

Alternative Method of Preparing (R_{As},S_{As},*R*)-20. Method 2. Trifluoroacetic acid (1 mL) was added to a suspension of (*R*,*R*)-**12**·CH_2Cl_2 (20 g, 0.03 mol) and (*R**,*S**)-**1** (26 g, 0.06 mol) in methanol (500 mL). The mixture was stirred at room temperature until the solids had dissolved (2 days). The bright orange solution was then filtered, and a solution of NH_4PF_6 (15 g, excess) in water (40 mL) was added slowly with stirring. After 1 h, water (500 mL) was added; the bright yellow precipitate of diastereomers was filtered off and washed with water, methanol–diethyl ether (1:10), and diethyl ether: yield 51 g (98%). Fractional crystallization of the mixture from methanol–dichloromethane gave pure (R_{As},S_{As},*R*)-**20** as yellow prisms (21 g, 40%). Spectral and other data for the compound were identical with those of the material prepared from (S_{As},*R*)-**18**.

The yellow ill-defined material remaining after the evaporation of the mother liquor from the isolation of crystalline (R_{As},S_{As},*R*)-**20** was triturated in a small quantity of methanol–diethyl ether. The resulting yellow powder, $[\alpha]_D$ −91° (*c* 0.4, CH_2Cl_2), was identical with the compound obtained from the reaction between (*R*,*R*)-**12**·CH_2Cl_2 and (*S*,*S*)-**1** in methanol after treatment with aqueous NH_4PF_6. The highly soluble compound could not be induced to crystallize under any of the conditions tried: ^{1}H NMR (CD_2Cl_2) δ 1.29 (s, 3 H, As*Me*), 1.45 (s, 3 H, As*Me*), 1.78 (d, 3 H, ^3J = 6.3 Hz, NCH*Me*), 1.89–2.10 (m, 4 H, CH_2As), 2.30 (s, 6 H, N*Me*), 3.85–4.25 (m, 4 H, CH_2N), 4.35 (q, 1 H, ^3J = 6.3 Hz, NC*H*Me), 6.55–7.70 (m, 14 H, Ar*H*), 8.63 (s, 1 H, C*H*=N), 8.70 (s, 1 H, C*H*=N). Anal. Calcd for $C_{34}H_{40}As_2F_6N_3PPd$: C, 45.8; H, 4.5; N, 4.7. Found: C, 46.3; H, 4.8; N, 4.4.

[*SP*-4-2-(*R*)][1-[1-(Dimethylamino)ethyl]-2-naphthalenyl-*C*^{2},*N*][*N*,-*N*′-dimethyl-1,2-ethanediamine-*N*,*N*′-]palladium(II) Hexafluorophosphate [(*R*)-21]. Silver nitrate (220 mg, 1.3 mmol) in acetonitrile (5 mL) was added to a stirred solution of (*R*,*R*)-**12**·CH_2Cl_2 (500 mg, 0.7 mmol) in dichloromethane (25 mL). The mixture was stirred in the dark for 15 min, the AgCl precipitate was then filtered off, and a solution of *N*,-*N*′-dimethyl-1,2-ethanediamine (130 mg, 1.48 mmol) in acetonitrile (5 mL) was slowly added to the stirred filtrate. After the addition was complete, the solvent mixture was removed under reduced pressure, and the residue was dissolved in hot methanol (50 mL), the solution filtered, and the filtrate treated with aqueous NH_4PF_6 (2 g, in 5 mL of H_2O). The pale yellow precipitate was filtered off, dried, and recrystallized from dichloromethane–diethyl ether. The pure compound was thus obtained as a pale yellow microcrystalline solid: mp 201–202 °C dec; yield 88%; $[\alpha]_D$ −58° (*c* 0.5, CH_2Cl_2); ^{1}H NMR (CD_2Cl_2) δ 1.86 (d, 3 H, ^3J = 6.5 Hz, NCH*Me*, methylene protons obscured by NMe protons), 2.50–2.80 (m, 12 H, N*Me*), 2.90 (br s, 2 H, N*H*), 4.20 (q, 1 H, ^3J = 6.5 Hz, NC*H*Me), 7.12–7.55 (m, 6 H, Ar*H*). Anal. Calcd for $C_{18}H_{28}F_6N_3PPd$: C, 40.2; H, 5.3; N, 7.8. Found: C, 40.3; H, 5.1; N, 7.7.

This material was isolated in 65% yield (by product) from the mother liquor remaining after the isolation of (R_{As},S_{As},*R*)-**20**.

[*TB*-5-34-1[*S*-(*R,*R**)],3(*R*)][1-[1-(Dimethylamino)ethyl]-2-naphthalenyl-*C*^{2},*N*][7,8,9,16,17,18-hexahydro-9,18-dimethyldibenzo[e,-*l*][1,8,4,11]diazadiarsacyclotetradecine-*As*^{9},*As*^{18},*N*^{6}]palladium(II) Hexafluorophosphate Hemiacetone Solvate [(S_{As},S_{As},*R*)-20)·0.5Me_2CO].** Compound (R_{As},S_{As},*R*)-**20** (20 g, 0.02 mol) was recrystallized from hot acetone (500 mL) giving deep orange (S_{As},S_{As},*R*)-**20**·0.5Me_2CO (19.8

g, 97%): mp 180–182 °C; $[\alpha]_D$ −133° (*c* 0.5, CH_2Cl_2); ^1H NMR (CD_2Cl_2) data for the orange form are identical with those of the yellow form (except for the acetone peak); IR (Nujol) 1650, 1630 ($\nu_{C=N}$), 1720 cm^{-1} ($\nu_{C=O}$). Anal. Calcd for $C_{35.5}H_{43}As_2F_6N_3O_{0.5}PPd$: C, 46.3; H, 4.7; N, 4.6. Found: C, 46.6; H, 4.8; N, 4.3.

[*SP*-4-4-1[*R*-(*R,*S**)],3(*S*)][1-[1-(Dimethylamino)ethyl]-2-naphthalenyl-C^2,*N*][7,8,9,16,17,18-hexahydro-9,18-dimethyldibenzo[e,*l*][1,8,4,11]diazadiarsacyclotetradecine-As^9,N^6]palladium(II) Hexafluorophosphate [(R_{As},S_{As},*S*)-20].** Compound (R_{As},S_{As},*S*)-**20** was prepared similarly from (R_{As},*S*)-**18** by $BaMnO_4$ oxidation (method 1) or from (*R**,*S**)-**1** and (*S*,*S*)-**12**·CH_2Cl_2 in the presence of acid (method 2). The pure enantiomer has mp 230–234 °C and $[\alpha]_D$ +142° (*c* 0.5, CH_2Cl_2). The spectral data are identical with those of enantiomorph (R_{As},S_{As},*R*)-**20**.

[*TB*-5-34-1[*R*-(*R,*R**)],3(*S*)][1-[1-(Dimethylamino)ethyl]-2-naphthalenyl-C^2,*N*][7,8,9,16,17,18-hexahydro-9,18-dimethyldibenzo[e,*l*][1,8,4,11]diazadiarsacyclotetradecine-As^9,As^{18},N^6]palladium(II) Hexafluorophosphate Hemiacetone Solvate [(R_{As},R_{As},*S*)-20·0.5Me_2CO].** This compound was obtained by recrystallization of (R_{As},S_{As},*S*)-**20** from boiling acetone as deep orange prisms: mp 180–182 °C; $[\alpha]_D$ +133° (*c* 0.5, CH_2Cl_2).

[*R*-(9*R,18*R**)]-(−)-7,8,9,16,17,18-Hexahydro-9,18-dimethyldibenzo[e,*l*][1,8,4,11]diazadiarsacyclotetradecine [(*R*,*R*)-1].** A solution of (*R**,*R**)-(±)-1,2-phenylenebis(methylphenylphosphine)[23] (1.78 g, 5.5 mmol) in dichloromethane was added slowly to a solution of [(R_{As},S_{As},*R*)]-**20** (4.95 g, 5.5 mmol) in the same solvent (100 mL). After 30 min, diethyl ether (150 mL) was added, and the resulting precipitate of (R_P,R_P,*R*)- and (S_P,S_P,*R*)-**20** was filtered off and washed with diethyl ether. Concentration of the combined filtrate and washings gave the product as colorless prisms: mp 173 °C; yield 2 g (90%); $[\alpha]_D$ −99.8° (*c* 0.5, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 1.22 (s, 6 H, As*Me*), 1.95 (m, 2 H, CH_2As), 2.39 (m, 2 H, CH_2As), 3.69 (m, 2 H, CH_2N), 4.30 (m, 2 H, CH_2N), 7.00–7.56 (m, 8 H, Ar*H*), 9.00 (d, 2 H, ^4J = 1.5 Hz, C*H*=N); ^{13}C NMR ($CDCl_3$) δ 160.9 (C_5, C_{14}), 143.1, 139.1, 131.1, 130.2, 127.6, 126.8 (Ar*C*), 60.2 (C_7, C_{16}), 32.0 (C_8, C_{17}), 8.6 (As*Me*); IR (Nujol) 1635 cm^{-1} ($\nu_{C=N}$); mass spectrum, *m/e* 442 $[M]^+$, 427 $[M - Me]^+$; mol wt (osmometry, CH_2Cl_2) 442 (calcd), 434 (found). Anal. Calcd for $C_{20}H_{24}As_2N_2$: C, 54.3; H, 5.5; N, 6.3. Found: C, 54.7; H, 5.4; N, 6.5.

[*S*-(9*R,18*R**)]-(+)-7,8,9,16,17,18-Hexahydro-9,18-dimethyldibenzo[e,*l*][1,8,4,11]diazadiarsacyclotetradecine [(*S*,*S*)-1].** This compound was obtained from (R_{As},S_{As},*S*)-**20** by the method described above in 90% yield: mp 173 °C; $[\alpha]_D$ +99.8° (*c* 0.5, CH_2Cl_2). Anal. Calcd for $C_{20}H_{24}As_2N_2$: C, 54.3; H, 5.5; N, 6.3. Found: C, 54.4; H, 5.6; N, 6.3.

Similar yields of the optically pure diimines were obtained from the orange isomers of the palladium(II) complexes.

[*R*-(9*R,18*R**)]-(−)-5,6,7,8,9,14,15,16,17,18-Decahydro-9,18-dimethyldibenzo[e,*l*][1,8,4,11]diazadiarsacyclotetradecine [(*R*,*R*)-2].** Diimine (*R*,*R*)-**1** (4 g, 9 mmol) was added in small portions with stirring to a suspension of $LiAlH_4$ (700 mg, 18.4 mmol) in tetrahydrofuran (200 mL) at 0 °C. The mixture was heated under reflux for 1 h, and then it was cooled to 0 °C. Excess $LiAlH_4$ was decomposed by the addition of water (0.7 mL), 4 N NaOH (0.7 mL), and water (2.1 mL). Anhydrous $MgSO_4$ (20 g) was then added to the mixture, which, after 20 min, was filtered to remove solid material. The latter was washed with tetrahydrofuran (2 × 50 mL), and the combined washings and the filtrate were evaporated to dryness. The viscous oil that remained was purified by flash chromatography on basic alumina (activity 90) with methanol–dichloromethane (1:99) as eluent: yield 4 g (99%); $[\alpha]_D$ −298° (*c* 0.5, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 1.16 (s, 6 H, As*Me*), 1.84–2.17 (m, 4 H, CH_2As), 2.59–2.92 (m, 4 H, CH_2N), 3.42, 4.40 (AB q, 4 H, $^2J_{AB}$ = 11.5 Hz, benzylic CH_2), 7.07–7.48 (m, 8 H, Ar*H*); ^{13}C NMR ($CDCl_3$) δ 144.0, 141.5, 132.9, 130.0, 128.5, 127.5 (Ar*C*), 54.5 (C_5, C_{14}), 46.8 (C_7, C_{16}), 30.5 (C_8, C_{17}), 9.5 (As*Me*); mass spectrum, *m/e* 446 $[M]^+$, 431 $[M - Me]^+$. Anal. Calcd for $C_{20}H_{28}As_2N_2$: C, 53.8; H, 6.3. Found: C, 53.8; H, 6.5.

The product crystallized from chloroform as the disolvate (*R*,*R*)-**2**·$2CHCl_3$: mp 55 °C; $[\alpha]D$ −190° (*c* 0.5, CH_2Cl_2); mol wt (osmometry, CH_2Cl_2) 685 (calcd), 668 (found). The ^1H NMR ($CDCl_3$) spectrum of the solvate was identical with that of the solvent-free material. Anal. Calcd for $C_{20}H_{28}As_2N_2(2CHCl_3)$: C, 38.6; H, 4.4; N, 4.1. Found: C, 36.9; H, 4.4; N, 3.8.

[*S*-(9*R,18*R**)]-(+)-5,6,7,8,9,14,15,16,17,18-Decahydro-9,18-dimethyldibenzo[e,*l*][1,8,4,11]diazadiarsacyclotetradecine [(*S*,*S*)-2].** This enantiomer was prepared in the same way as its enantiomorph: $[\alpha]_D$ +298° (*c* 0.5, CH_2Cl_2); mp 55 °C; $[\alpha]_D$ + 190° (*c* 0.5, CH_2Cl_2).

(*R*)-2,3-Dihydro-1-methyl-4,1-benzazarsepine [(*R*)-5]. A solution of diimine (*R*,*R*)-**1** (200 mg, 0.45 mmol) in dichloromethane was treated with trifluoroacetic acid (0.01 mL). After 1 day the solvent was removed. A yellow liquid remained, which rearranged into dimer (*R*,*R*)-**1** upon attempted distillation. The spectral data for the optically active monomer were identical with those for (±)-**5**.

(*S*)-2,3-Dihydro-1-methyl-4,1-benzazarsepine [(*S*)-5]. This compound was prepared from (*S*,*S*)-**1** as described above.

(*R*)-(−)-2,3,4,5-Tetrahydro-1-methyl-4,1-benzazarsepine [(*R*)-6]. A solution of (*R*,*R*)-**1** (200 mg, 0.45 mmol) in diethyl ether (50 mL) was heated under reflux for 1 day in the presence of trifluoroacetic acid (0.01 mL). This solution was then added to a suspension of $LiAlH_4$ (100 mg, excess) in diethyl ether (100 mL). The resulting mixture was boiled for 1 h, and excess $LiAlH_4$ was decomposed by addition of water (0.1 mL), 4 N NaOH (0.1 mL), and water (0.3 mL). The solid was filtered off and was washed with diethyl ether (2 × 50 mL). The filtrate, upon evaporation, left a viscous oil, which upon distillation gave the pure product as a colorless liquid: bp 115 °C (0.04 mmHg; Kugelrohr); yield 150 mg (75%); $[\alpha]_D$ −104° (*c* 1.3, CH_2Cl_2). The spectral data were identical with those of (±)-**6**.

(*S*)-(+)-2,3,4,5-Tetrahydro-1-methyl-4,1-benzazarsepine [(*S*)-6]. This compound was obtained from (*S*,*S*)-**1** by the method described above: bp 115 °C (0.04 mmHg; Kugelrohr); $[\alpha]_D$ +104° (*c* 1.2, CH_2Cl_2).

Preparation of (*R,*R**)-2: Asymmetric Transformation [Pd{(*R**,*S**)-2}]X_2 → [Pd{(*R**,*R**)-2}]X_2 (Where X = Cl of PF_6), [*SP*-4-1-(*R**,*S**)][5,6,7,8,9,14,15,16,17,18-Decahydro-9,18-dimethyldibenzo[e,*l*][1,8,4,11]diazadiarsacyclotetradecine-As^9,As^{18},N^6,N^{15}]palladium(II) Chloride [[Pd{(*R**,*S**)-2}]Cl_2].** A solution of $Li_2[PdCl_4]$ was prepared from $[PdCl_2]_n$ (235 mg, 1.33 mmol) and excess LiCl (1 g) in methanol (25 mL). The chloropalladate(II) solution was added to a solution of (*R**,*S**)-**2** (589 mg, 1.32 mmol) in the same solvent (100 mL). After 1 h, the colorless product was filtered off and was washed with methanol and diethyl ether. This solid, after recrystallization from aqueous acetone, formed colorless microcrystals: mp 234–236 °C; yield 535 mg (65%). Anal. Calcd for $C_{20}H_{28}As_2Cl2N_2Pd$: C, 38.5; H, 4.5; N, 4.5. Found: C, 38.7; H, 5.0; N, 4.3.

[*SP*-4-1-(*R,*S**)][5,6,7,8,9,14,15,16,17,18-Decahydro-9,18-dimethyldibenzo[e,*l*][1,8,4,11]diazadiarsacyclotetradecine-As^9,As^{18},N^6,N^{15}]palladium(II) Hexafluorophosphate [[Pd{(*R**,*S**)-2}]-(PF_6)$_2$].** A solution of NH_4PF_6 (1 g) in water (20 mL) was added to a solution of [Pd{(*R**,*S**)-2}]Cl_2 (250 mg, 0.4 mmol) in hot (50 °C) water (20 mL). The white precipitate was filtered off and was washed with water, aqueous methanol, and diethyl ether. This material was recrystallized from dichloromethane–acetone to afford the pure complex: mp 248–249 °C; yield 260 mg (79%); ^1H NMR (DMSO-d_6) δ 1.97 (s, 6 H, As*Me*), 2.30–2.52 (m, 4 H, CH_2As), 3.20–3.70 (m, 4 H, CH_2N), 4.18–4.40 (m, 4 H, benzylic CH_2), 6.60 (br s, 2 H, N*H*), 7.53–8.02 (m, 8 H, Ar*H*). Anal. Calcd for $C_{20}H_{28}As_2F_6N_2P_2Pd$: C, 28.5; H, 3.4; N, 3.3. Found: C, 28.7; H, 3.5; N, 3.3.

(9*R,18*R**)-(±)-5,6,7,8,9,14,15,16,17,18-Decahydro-9,18-dimethyldibenzo[e,*l*][1,8,4,11]diazadiarsacyclotetradecine [(*R**,*R**)-2]. Method 1.** A solution of [Pd{(*R**,*S**)-2}]Cl_2 (5 g, 8 mmol) in water (40 mL) was heated on a steam bath for 1 h. The resulting solution was filtered to remove a trace of solid, and the filtrate was cooled to room temperature. Dichloromethane (100 mL) and KCN (2 g, excess) were then added, and the reaction mixture was stirred for 1 h. The layers were separated, and the organic phase was dried ($MgSO_4$), filtered, and evaporated to dryness. The pale yellow oil that remained was purified by flash chromatography on basic alumina (activity 90) with dichloromethane–methanol (99:1) as eluent, whereupon it was isolated as a viscous oil: yield 3.3 g (93%); ^1H NMR ($CDCl_3$) identical with that of optically active material.

Method 2. A solution of [Pd{(*R**,*S**)-2}](PF_6)$_2$ (5 g, 5.9 mmol) in DMSO (50 mL) was heated at 110 °C for 4 h. The reaction mixture was then cooled to room temperature, and the solvent was removed under reduced pressure. The residue was dissolved in dichloromethane (200 mL) and added to a solution of KCN (3 g, excess) in water (50 mL). After 1 h, the dichloromethane layer was then separated, washed with water, dried ($MgSO_4$), filtered, and concentrated. The viscous oil was purified by flash chromatography on basic alumina as described for the previous preparation; yield 2.1 g (80%).

Optically Active Complexes of (*R,*R**)-2: [*SP*-4-1-[*R*-(*R**,*R**)]]-[5,6,7,8,9,14,15,16,17,18-Decahydro-9,18-dimethyldibenzo[e,*l*]-[1,8,4,11]diazadiarsacyclotetradecine-As^9,As^{18},N^6,N^{15}]palladium(II) Hexafluorophosphate [(−)-[Pd{(*S*,*S*)-2}](PF_6)$_2$·0.25$MeCOCH_2CH_3$].** The diamine (*S*,*S*)-**2** (600 mg, 1.35 mmol) was suspended in methanol (350 mL), and a solution of $Li_2[PdCl_4]$ [from 238 mg $[PdCl_2]_n$ (1.35 mmol) and excess LiCl (1 g)] in the same solvent (75 mL) was added. The solution was stirred at room temperature for 30 min, and then it was filtered and the filtrate was treated with an excess of NH_4PF_6 (4 g) in water (20 mL). The solvent was then evaporated, and the residue was extracted with water (2 × 100 mL). The solid, after recrystallization from diethyl ethyl–butan-2-one, was isolated as fine needles: mp 233–234 °C dec; yield 583 mg (51%); $[\alpha]_D$ −171° (*c* 0.3, Me_2CO); ^1H NMR (DMSO-d_6) δ 2.04 (s, 6 H, As*Me*), 2.10–2.40 (m, 4 H, CH_2As),

2.95-3.25 (m, 4 H, CH_2N), 4.12-4.34 (m, 4 H, benzylic CH_2), 7.40-7.82 (m, 8 H, ArH). Anal. Calcd for $C_{21}H_{30}As_2F_{12}N_2O_{0.25}P_2Pd$: C, 29.3; H, 3.5; N, 3.3. Found: C, 29.1; H, 3.4; N, 3.1.

[*SP*-4-1-[*S*-(*R,*R**)]][5,6,7,8,9,14,15,16,17,18-Decahydro-9,18-dimethyldibenzo[e,*l*][1,8,4,11]diazadiarsacyclotetradecine-*As*^{9},*As*^{18},*N*^{6},*N*^{15}]palladium(II) Hexafluorophosphate [(+)-[Pd{(*R*,*R*)-2}](PF$_6$)$_2$·0.25MeCOCH$_2$CH$_3$].** This compound was prepared from (*R*,*R*)-**2** and chloropalladate(II) as described above: mp 233-234 °C dec; $[\alpha]_D$ +172° (*c* 0.5, Me_2CO). Anal. Calcd for $C_{21}H_{30}As_2F_{12}N_2O_{0.25}P_2Pd$: C, 29.3; H, 3.5; N, 3.3. Found: C, 29.1; H, 3.6; N, 3.0.

Structural Analyses. Crystal data for both compounds are summarized in Table I. The yellow complex (R_{As},S_{As},*R*)-**20** crystallized from dichloromethane-methanol as elongated (010) plates lying on (001) with pinacoids {101} and {10$\bar{1}$}; orange (R_{As},R_{As},*S*)-**20**·0.5Me_2CO was isolated from acetone solution as almost perfect cubes. A Nicolet XRD P3 four-circle diffractometer[26] was used for the experimental work on the yellow isomer, and a Nicolet four-circle autodiffractometer[27] was used for the orange isomer. The data were corrected for Lorentz and polarization effects. Analytical absorption corrections were applied with transmission factors ranging between 0.473 and 0.647 for (R_{As},S_{As},*R*)-**20**; empirical absorption corrections within the relative range 0.808-1.000 were applied for (R_{As},R_{As},*S*)-**20**·0.5Me_2CO. Atomic scattering factors and anomalous dispersion corrections were taken from ref 28. The structures were solved by the heavy-atom method and refined by least-squares techniques with $\sum w\Delta^2$ minimized; weightings for each reflection were obtained from counter statistics.

Selected molecular dimensions for the two isomers are listed in Table III according to the atom-labeling scheme shown in Figure 1. Final atomic coordinates for the non-hydrogen atoms in the two complexes are given in Table II.

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Supplementary Material Available: Labeling scheme, ORTEP drawings, and tables of bond lengths and bond angles, and atomic and thermal parameters for (R_{As},S_{As},*R*)-**20** and (R_{As},R_{As},*S*)-**20**·0.5Me_2CO (13 pages); tables of observed and calculated structure factors (31 pages). Ordering information is given on any current masthead page.

(27) *Nicolet (Syntex) E-XTL or SHELX Interactive Crystallographic Software Package*; modified by Crystalytics Company, Lincoln, NE.

(28) *International Tables of Crystallography*; Kynoch: Birmingham, England, 1974; Vol. 4.

Total Synthesis of Linear Polyprenoids. 3.[1] Syntheses of Ubiquinones via Palladium-Catalyzed Oligomerization of Monoterpene Monomers

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Abstract: A general methodology for highly regio- and stereoselective Pd(0)-catalyzed, stepwise allylic coupling of bifunctional monomers was developed, representing a practical approach for total synthesis of naturally occurring polyprenoids. As an example, the total synthesis of the cardiovascular agent ubiquinone 10 (coenzyme Q_{10}), as well as shorter ubiquinones, was carried out via selective coupling of monomers easily derived from geraniol that contain either one or two reacting functional end groups. One of these functionalities is a latent allylic electrophile activated by the Pd(0) catalyst and the other is a latent nucleophile activated by an appropriate base. After the desired decaprenyl carbon skeleton of Q_{10} was achieved, the synthesis was completed by removal of the activating groups: Methyl ester was deleted via a highly efficient demethoxycarbonylation procedure involving 4-aminothiophenol and catalytic amounts of cesium carbonate, and the allylic sulfones were deleted by Pd(0)-catalyzed allylic reduction. Finally, oxidation of the aromatic ring to quinone affords ubiquinone 10.

Quinones and hydroquinones with polyprenyl side chains, such as ubiquinones, plastoquinones, phylloquinone (vitamin K_1), and menaquinones (vitamin K_2), are widely distributed in animal and plant tissues.[2] In addition to important biological roles in promoting electron transfer in respiratory chains and photosynthesis, these compounds exhibit various pharmacological activities. Of special interest is ubiquinone 10 (coenzyme Q_{10}, **1**),[3] which is used clinically as a cardiovascular agent and has attracted significant synthetic activity within the past two decades.[4-6] However, because construction of linear polyprenoid chains is still a major synthetic challenge, a practical total synthesis of ubiquinone 10 has not yet been achieved. Available industrial processes for Q_{10} involve either biotechnological[7] or semisynthetic methods, the latter employing solanesol, a nonaprenol extracted from tobacco leaves.[8]

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