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Resolutions of tertiary phosphines and arsines with orthometallated palladium(II)–amine complexes

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Contents

Abstract

The use of the homochiral forms of chloro-bridged palladium(II) complexes containing orthometallated *N,N*-dimethyl(α-methylbenzyl)amines and related naphthylamines for the resolution of trivalent phosphines and arsines chiral at phosphorus and arsenic is reviewed. Work with a wide variety of ligands is discussed and references to applications of the ligands as probes of inorganic stereochemistry and as auxiliaries for asymmetric synthesis are given. Most examples have been taken from work carried out in the author's laboratories. © 1997 Elsevier Science S.A.

Keywords: Resolutions with metal complexes; Phosphines; Arsines

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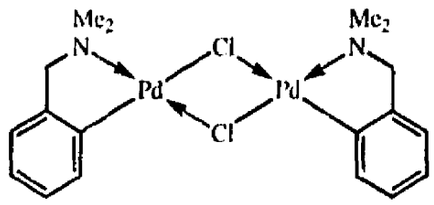
1. Introduction

Simple non-cyclic tertiary phosphines and arsines of the type (±)-$ER^1R^2R^3$ in homochiral form are valuable auxiliaries for asymmetric synthesis and as probes of stereochemistry and rearrangement in coordination compounds [1,2]. Early attempts at obtaining such compounds were thwarted by manipulative difficulties, especially those associated with the fractional crystallization of diastereomeric quaternary arsonium salts [3], and the recovery of the optically active tertiary phosphines and arsines from the configurationally homogeneous salts. In a series of papers beginning in 1959, however, the resolutions were reported of some simple salts of the type (±)-$[PR^1R^2R^3R^4]X$ containing one aryl and three alkyl groups with the use of the resolving agent sodium *D*-(−)-dibenzoylhydrogentartrate [4], as well as various transformations that enabled a connection to be made between the absolute configurations of the resolved phosphonium ions, phosphine oxides and tertiary phosphines [5]. In 1962, the enantiomers of (±)-ethylmethylphenylarsine were obtained by the electrochemical reduction of the corresponding optically active benzylarsonium perchlorates, which in turn had been recovered from the corresponding *D*-(−)-dibenzoylhydrogentartrate salts [6]. Interconversions between various optically active arsonium salts and tertiary arsines revealed that both cathodic cleavage of a benzyl group from an arsonium ion and quaternization of a tertiary arsine with a benzyl halide proceeded with retention of configuration at arsenic [7]. It was subsequently shown that the benzylidene group could be quantitatively transferred from an arsonium ion to benzaldehyde with retention of configuration at arsenic [8].

Following the resolution of certain *trans*-(±)-*cyclo*-alkenes [9] and (±)-ethyl-*p*-tolyl sulfoxide [10] via the separation of neutral diastereomeric dichloroplatinum(II) complexes containing (*R*)-(+)- or (*S*)-(−)-α-methylbenzylamine, the resolution of (±)-*t*-butylmethylphenylphosphine was achieved in a similar manner with use of (+)-deoxyephedrine as the resolving ligand, although the free optically active phosphine was not isolated [11]. In 1970, (±)-ethylmethylphenylarsine was resolved in a chloroplatinum(II) salt containing (*R,R*)-(+)-stilbene diamine and the individual enantiomers of the arsine characterized [12].

A significant development in the field occurred in 1970 when, following the earlier preparation of the achiral complex **1** from lithium tetrachloropalladate(II) and 2 equiv. of *N,N*-dimethylbenzylamine [13], the optically active compound (*S,S*)-**2** was isolated from a similar reaction involving (*S*)-(−)-*N,N*-dimethyl-α-methylbenzylamine and employed for the partial kinetic resolution of a variety of tertiary phosphines of the type (±)-$PR^1R^2R^3$ by bridge-splitting reactions [14]. In a subsequent paper, the 3-naphthalenyl complex (*R,R*)-**3** was employed successfully for the kinetic resolution of certain chiral dialkylarylphosphines and (±)-1-phenyl-3-methyl-2-phospholene, although it was not effective for the resolution of triarylphosphines [15]. For the triarylphosphines, *cis*-dichlorobis[(*S*)-*sec*-butyl isocyanide]-palladium(II) was employed, which gave with 2 equiv. of the particular phosphine in benzene, a precipitate of the diastereomerically enriched *trans* phosphine–isocyanide complex and optically active phosphine in the mother liquor. It was noted

however, that the efficiency of the isocyanide complex for the resolution of the triarylphosphines investigated varied drastically with the type of phosphine.



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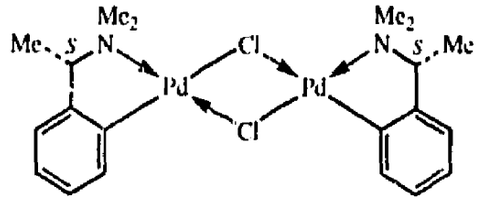
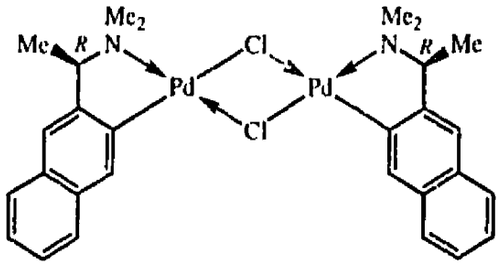
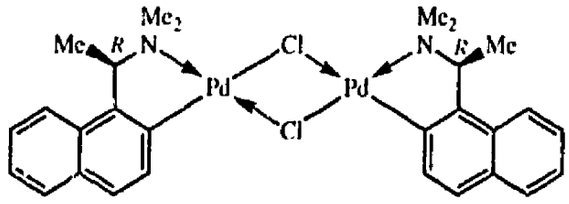


(*S,S*)-2



(*R,R*)-3



(*R,R*)-4

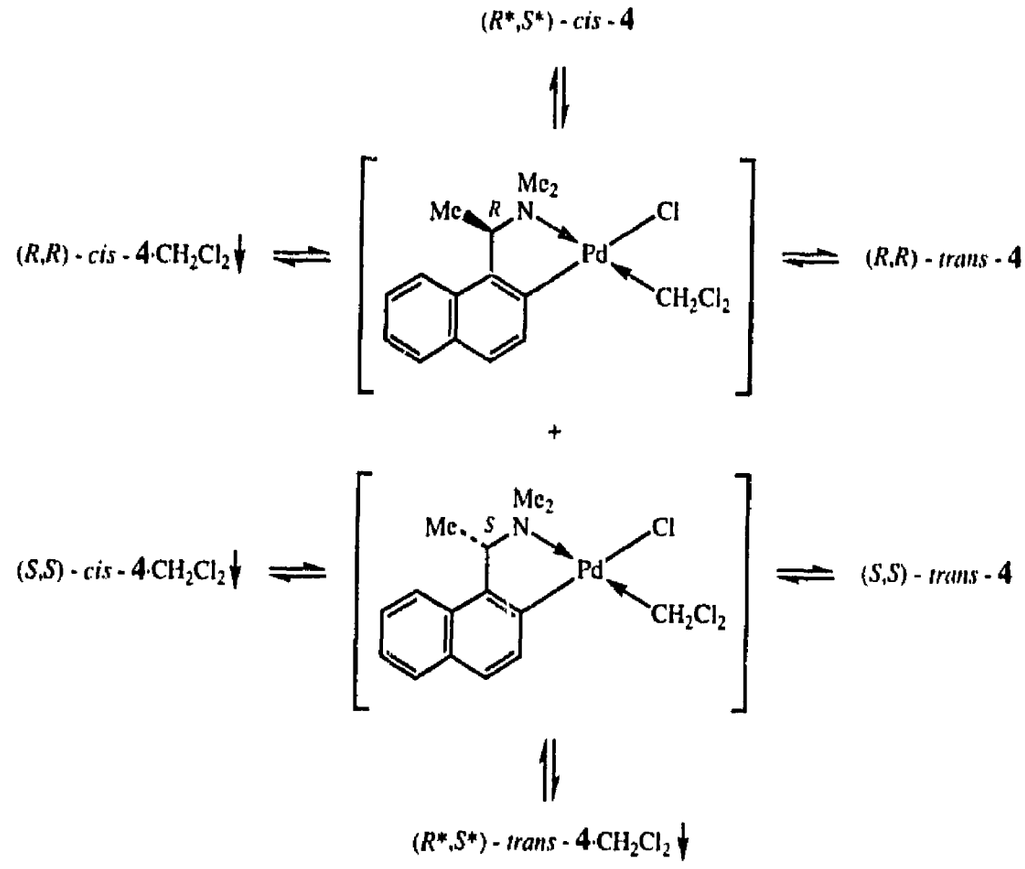
We have found that (*R,R*)-**2** and (*R,R*)-**4** and their enantiomers are especially suited to the resolution of chiral tertiary phosphines and arsines and the development of this field is the subject of this review. The reader should consult Ref. [1] for a comprehensive account of methods of resolution of tertiary arsines.

2. Cyclometallated palladium(II)–amine resolving agents

The crystal and molecular structures of (*S,S*)-**4**·CH_2Cl_2 have been determined. The complex undergoes a facile rearrangement into an unequal mixture of *cis* and *trans* diastereomers in chloroform or dichloromethane, although concentration of the solution in each case affords in high yield the pure *cis* diastereomer of the complex as the corresponding mono-solvate in a typical second-order asymmetric transformation [16]. The rearrangement is believed to occur via a highly reactive mononuclear palladium intermediate (undetected) that rapidly dimerizes with

$$(S,S)\text{-}cis\text{-}\mathbf{4}\cdot CH_2Cl_2 \overset{CH_2Cl_2}{\rightleftharpoons} (S,S)\text{-}trans\text{-}\mathbf{4} \qquad (1)$$

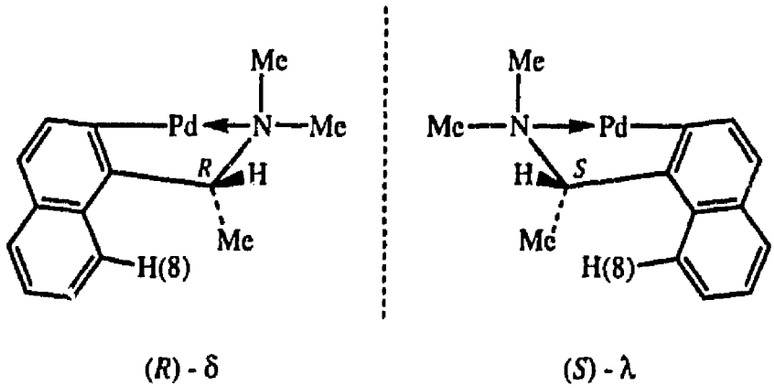
cis:*trans* ca. 4:3 diastereoselectivity (Eq. (1)) . When equimolar solutions of (*R,R*)-*cis*-**4**·CH_2Cl_2 and (*S,S*)-*cis*-**4**·CH_2Cl_2 in chloroform-d_1 were mixed together at 25 °C, the ^1H NMR spectrum of the solution exhibited four pairs of N*Me* resonances corresponding to an unequal mixture of the *cis* and *trans* isomers of (*R**,*R**)-(±)- and (*R**,*S**)-**4** in equilibrium (Scheme 1) [1]. A similar solution in dichloromethane afforded sparingly soluble crystals of (*R**,*S**)-*trans*-**4**·CH_2Cl_2 upon concentration by second-order asymmetric transformation.



Scheme 1.

The chloro-bridged dimer (*S,S*)-**2** undergoes a similar *cis–trans* rearrangement in chloroform or dichloromethane into an almost equal mixture of *cis* and *trans* diastereomers that can be detected by ^{1}H NMR spectroscopy at 300 MHz [18]. Crystal structure determinations on the formally achiral 1-, 2-, and 3-methoxybenzyldimethylamine analogues of **2** revealed *trans* geometries for the complexes [19].

The facile *cis–trans* rearrangements between the chloro-bridged dipalladium resolving complexes provide an explanation for the ease with which the dimers undergo bridge-splitting reactions with phosphines and arsines (and other ligands) to give mononuclear palladium–phosphine and –arsine complexes. There are, however, three factors that are crucial to the successful use of the cyclometallated complexes for the resolution of ligands capable of carrying out the bridge-splitting reaction – these are the following: (a) the dipalladium complex must be enantiomerically pure; (b) the coordination of the incoming bridge-splitting ligand to the palladium must be completely regioselective in order that a single pair of mononuclear palladium–phosphine or –arsine diastereomers is generated; and (c) the diastereomers of the mononuclear palladium–phosphine or –arsine complexes must be capable of separation in stereochemically homogeneous form. These factors are addressed in detail in Ref. [16] in connection with an investigation of interconversions between the diastereomers of (*R,R*)-**4** and its enantiomer and mixtures thereof. The five-membered organometallic ring in (*S,S*)-**4** · CH_2Cl_2 has the locked asymmetric envelope conformation due to an unfavourable interaction between the carbon–methyl group of the organometallic ring and H(8) of the naphthalenyl ring. This



(*R*) - δ (*S*) - λ

Fig. 1. Enantiomorphic (*R*)-δ and (*S*)-λ envelope conformations of five-membered organometallic rings of (*R**,*R**)-(±)-**4**.

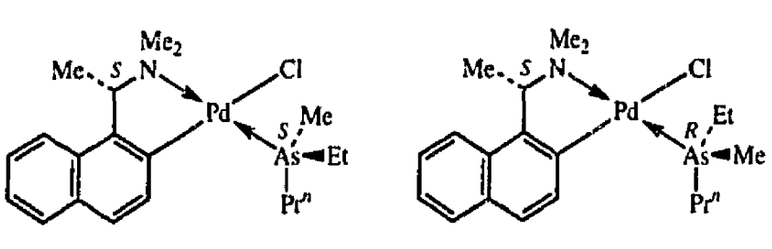
steric interaction causes the carbon–methyl group to adopt an axial disposition in a ring of δ conformation when the chiratopic atom to which it is attached has the *R* configuration (Fig. 1). The locked-organometallic ring conformation persists in solution in certain mononuclear palladium derivatives of (*S,S*)-**4** · CH_2Cl_2, according to detailed ^1H NMR investigations [20]. Because of this structural feature and because (*S,S*)-**4** · CH_2Cl_2 admirably fulfils criteria (a)–(c), the naphthalenyl complex is frequently superior to (*S,S*)-**2** (or its enantiomer) as a resolving agent, although the latter is less expensive and is used whenever possible.

Tertiary phosphines and arsines chiral at phosphorus and arsenic are attractive targets for resolution because of their high barriers to unimolecular inversion, viz. E_{inv} = ca. 30 kcal mol^{-1} for (±)-$PR^1R^2R^3$ and E_{inv} > 40 kcal mol^{-1} for (±)-$AsR^1R^2R^3$ [21]. Applications of the resolving agents (*S,S*)-**2** and (*S,S*)-**4** · CH_2Cl_2 to the resolutions of a variety of chiral phosphines and arsines are presented in the sections that follow. Very little work on the resolution of chiral arsines has been carried out in other laboratories: the reason for this is difficult to fathom – apart from the lack of an NMR detectable spin-half nucleus (which can be compensated for to a large extent by the attachment of a methyl group to the arsenic), tertiary arsines have reduced air-sensitivity compared to analogous phosphines, as well as increased configurational stability and are easier to recover from arsonium salts and metal complexes.

3. Resolutions of phosphines and arsines

3.1. Resolutions of C_1-unidentates

The resolution of (±)-ethylmethyl-*n*-propylarsine with (*S,S*)-**4** · CH_2Cl_2 afforded,



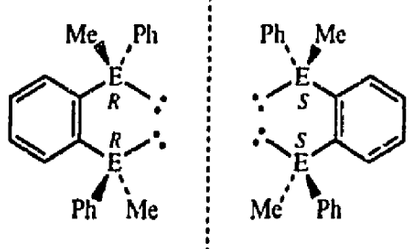
5a **5b**

after nine recrystallizations of the initial mixture of diastereomers **5a** and **5b** from benzene–*n*-pentane, pale yellow crystals of **5b** as determined by an X-ray crystal structure determination [22]. It had been long known that ethyl-*n*-propylarsinic acid

$$AsO(OH)EtPr^n \xrightarrow{S.\ brevicaulis} (\pm)\text{-}AsEtMePr^n \qquad (2)$$

was converted into (±)-ethylmethyl-*n*-propylarsine (Eq. (2)) by the mould *Scopulariopsis brevicaulis* when growing on bread [23], although it was not known at that time that simple non-cyclic tertiary arsines chiral at arsenic were configurationally stable and amenable to resolution [6,7]. We showed that the microorganism produced the *R*-arsine with an enantiomeric excess (e.e.) of 60% by trapping the volatile arsine produced with (*S,S*)-*4* · CH_2Cl_2 in toluene and recording the ^1H NMR spectrum of the diastereomers **5a/5b**. It is important in this type of work, and for determinations of optical purities of tertiary phosphines and arsines in general, that (*S,S*)-**4** · CH_2Cl_2 of high enantiomeric purity be employed. An NMR method for determining the enantiomeric purity of (*S,S*)-**4** · CH_2Cl_2 and related compounds with use of (1*R*,2*S*,5*R*)-menthyldiphenylphosphine or (1*S*,2*S*,5*R*)-neomenthyldiphenylphosphine is given in Ref. [16].

The energy barrier for the pyramidal inversion of phosphines of the type (±)-PXR^{1}R^2 increases with increasing electronegativity of substituents [24]. Thus, the barrier to unimolecular inversion for (±)-PHPh*i*Pr was estimated to be $>97.5 \pm 0.5$ kJ mol^{-1} [25]. Nevertheless, because of the sensitivity of secondary phosphines to intermolecular proton exchange in the presence of traces of acids or cationic secondary phosphine–platinum(II) complexes, it was not possible to displace optically active (±)-methylphenylphosphine from a configurationally homogeneous diastereomer of a secondary phosphine–platinum(II) complex [25]. It was subsequently shown that the secondary phosphine-*P* stereocentre in (±)-menthylmesitylphosphine of high configurational purity could be obtained by performing fractional crystallizations on the mixture of epimers in acetonitrile containing sodium acetylacetate as proton scavenger, or by deboranation of the secondary phosphine–borane adduct of 97% diastereomeric purity [26]. It had earlier been shown that (±)-PHMePh [27] and (±)-AsHMePh [28] could be resolved and stereoselectively alkylated at low temperatures in cyclopentadienyliron(II) complexes containing a homochiral form of (*R**,*R**)-(±)-**8** (E = P).



(*R**,*R**) - (±) - **8** (E = P or As)

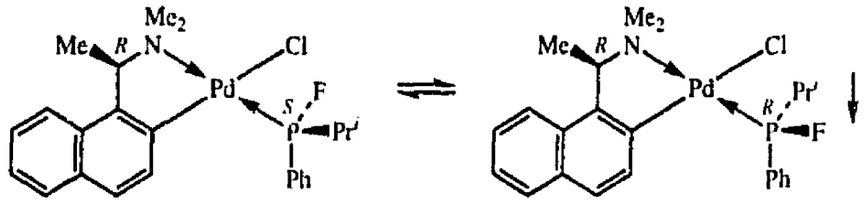
Compounds of the type (±)-PFR^{1}R^2 have high configurational stabilities, but low thermodynamic stabilities because of their propensity for redox-disproportiona-

tion [29]. We showed that (±)-fluorophenylisopropylphosphine of 86% purity could be isolated at low temperatures, but that it decomposed over 16 h at 25 °C by

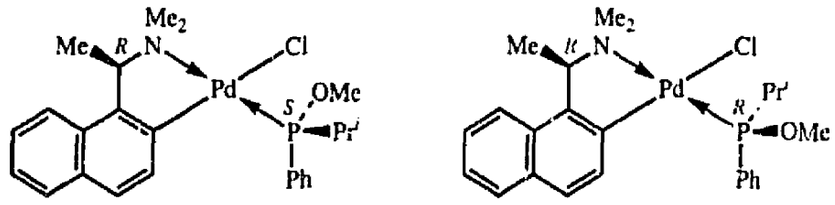
$$3\ PFPhPr^i \rightleftharpoons PF_3PhPr^i + PhPr^iPPPhPr^i \quad (3)$$

$$(R^*,R^*)\text{-}(\pm) / (R^*,S^*)$$

equilibrium redox disproportion (Eq. (3)) [30] . In benzene, however, solutions of the fluorophosphine displayed considerable stability and could be used for the preparation of the diastereomers **6a** and **6b** by reaction with (R,R)-**4**·CH_2Cl_2. The diastereomers of **6** were produced in almost equal amounts in the reaction, but equilibrated over 18 h in dichloromethane into a **6a**:**6b** = 3:1 mixture from which a 64% yield of **6a** was obtained by second-order asymmetric transformation and characterized by X-ray crystallography. Enantiomeric pure (*S*)-(−)-fluorophenylisopropylphosphine was liberated from **6a** by displacement with (R^*,S^*)-**8** (E = P). The free phosphine racemized over 6 h in benzene without discernible redox disproportionation. The phosphinous ester (±)-methoxyphenylisopropylphosphine was also resolved with use of (R,R)-**4**·CH_2Cl_2 via the diastereomers **7a** and **7b** and the individual enantiomers liberated with high e.e's. The barrier to unimolecular inversion in the phosphinous ester was determined to be $>82.9 \pm 0.5$ kJ mol^{-1} by variable temperature ^{1}H NMR spectroscopy. Substitution of fluoride in **6a** was shown to proceed with predominant inversion of configuration at phosphorus.



6a **6b**

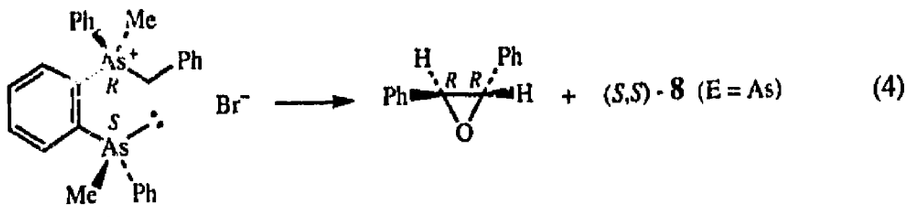


7a **7b**

3.2. Resolutions of C_2-bidentates

Complexes (±)-**2** and (±)-**4**·CH_2Cl_2 in homochiral form are particularly effective resolving agents for chiral bidentates. For C_2 bidentates, the regioselectivity of coordination of the bidentate to the palladium is immaterial because a single pair of diastereomeric complexes is formed in the bridge-splitting reaction. For C_1 bidentates (chiral AB bidentates), however, two pairs of diastereomeric complexes will result from a non-regioselective bridge-splitting reaction. For all C_1 bidentates inves-

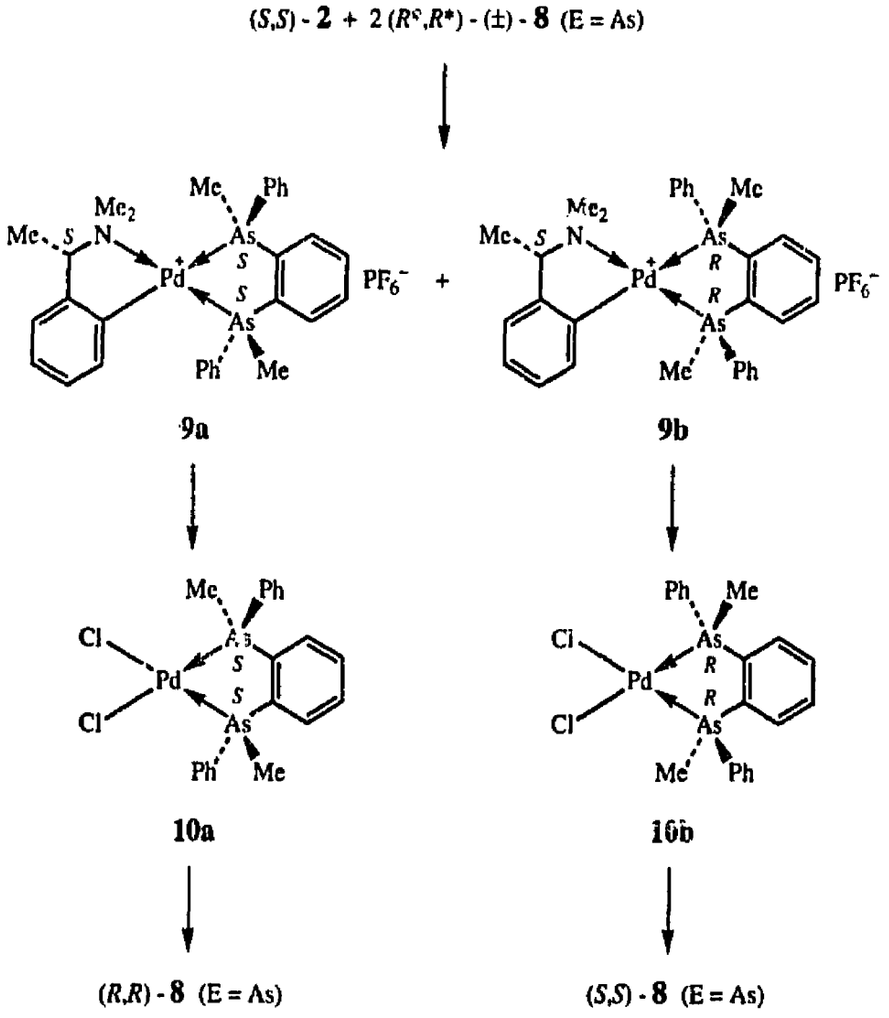
tigated in our laboratories, complex (*R,R*)-**4**·CH_2Cl_2 has yielded a single pair of diastereomers in the bridge-splitting step. For the C_2 bidentates (*R*,R**)-(±)-**8** (E=As) and the phosphorus congener, (*R*,R**)-(±)-**8** (E=P), the cheaper resolving complex **2** in homochiral form was employed, but **4** in similar form was used for most C_1 bidentates. Thus, for (*R*,R**)-(±)-**8** (E=As) the reaction with (*S,S*)-**2** afforded in high yield the diastereomers **9a** and **9b** after exchange of chloride for hexafluorophosphate (Scheme 2) [31]. The configurational homogeneities of **9a** and **9b** were confirmed by ^{1}H NMR spectroscopy. Decomposition of less-soluble **9a** with hydrochloric acid gave **10a** with recovery of the hydrochloride of the optically amine and cyanide treatment of **10a** liberated the (*R,R*) enantiomer of the arsine in high yield [32]. It was found subsequently that 1,2-ethanediamine displaced the arsine from **9a** with formation of the corresponding palladium–diamine complex from which (*S,S*)-**2** was regenerated by treatment with hydrochloric acid [33]. The configurational purity of the liberated arsine was readily confirmed by repreparation of **9a** from (*S,S*)-**2** and recording its ^{1}H NMR spectrum. The diastereomers and enantiomers of both ligands are air-stable crystalline solids that were employed as probes of stereochemistry and rearrangement in bis(bidentate) complexes of nickel(II) [34], palladium(II) and platinum(II) [35], ruthenium(II) [36], gold(I) [37], and copper(I) and silver(I) [38]. The optically active C_2 tertiary arsines and phosphines (*R*,R**)-(±)-**8** (E=P or As) have been employed also as chiral auxiliaries for a number of stereoselective organic reactions. Thus, quaternization of (*S,S*)-**8** (E=As) with benzyl bromide afforded the optically active benzylarsonium salt **11** (retention of configuration at arsenic), which upon deprotonation with lithium ethoxide gave the semi-stabilized ylide **11**; the ylide reacted with benzaldehyde to give (*R,R*)-*trans*-2,3-diphenyloxirane in 96% chemical yield and 23% e.e., and regen-



11 (4)

eration of the pure (*S,S*) diarsine (Eq. (4)) [39]. Indeed, benzylidene transfer from a resolved benzylarsonium salt is perhaps the simplest and cleanest method of recovering optically active arsines from arsonium salts [8]. Both (*S,S*)-**8** (E=As) and the phosphorus isostere are effective auxiliaries as their rhodium(I) chelates for the asymmetric hydrogenation of prochiral enamides [40]. The enantioselectivity of the reduction, however, is remarkably dependent upon the nature of the β-substituent on the enamide–olefin bond. The catalyst containing the bis(tertiary arsine) outperformed the phosphorus isostere in several cases. For example, the hydrogenation of α-benzamido-β,β-dimethylacrylic acid gave *N*-benzoyl-(*S*)-valine of 89% e.e. with the (*S,S*) arsine, but a product of 37% e.e. with the isosteric phosphine. Indeed, the e.e. of the valine with the arsine–rhodium catalyst was significantly higher than that obtained with most phosphine–rhodium catalysts. The homochiral forms of certain rhodium(I) complexes of the C_2 bis(tertiary phosphines and arsines) are also highly

efficient catalysts for the asymmetric hydrosilylation of prochiral ketones [41]. The rates of the reaction observed for both ligands were amongst the fastest reported. For $C_6H_5COCH_3$ and $CH_3COC(CH_3)_3$ e.e's varied between 18–41%, depending upon catalyst and substrate.

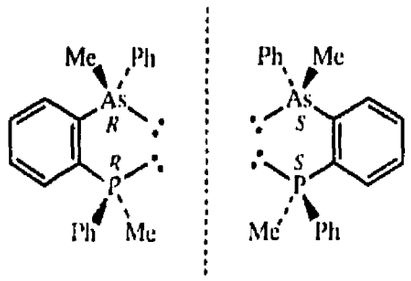


Scheme 2.

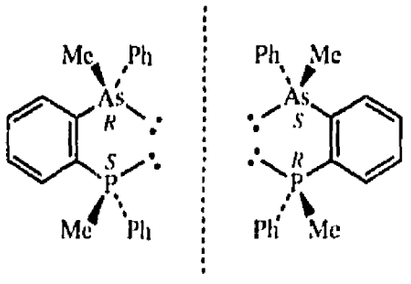
3.3. Resolutions of C_1-bidentates

The resolution of the (*R**,*R**)-(±)-**12** was achieved by the fractional crystallization of the pair of diastereomers (P *trans* to N) generated by the bridge-splitting of (*R*,*R*)-**2** with the ligand and exchange of chloride for hexafluorophosphate in the resulting salts [42]. The resolution of the (*R**,*S**)-(±) form of the ligand required the use of (*R*,*R*)-**4**·CH_2Cl_2. All four enantiomers of the air-stable ligand were obtained in enantiomerically pure form. It was possible to thermally epimerize the phosphorus stereocenters in the various forms of **12** without affecting the integrity of the arsenic centres and configuratively pure protonated phosphonium salts were isolated that were stable to heating in the presence of hydrogen bromide. The stereochemistry and dynamic properties of square-planar and square-pyramidal complexes containing the various forms of the ligand in conjunction with nickel(II), palladium(II) and platinum(II) were investigated [43].

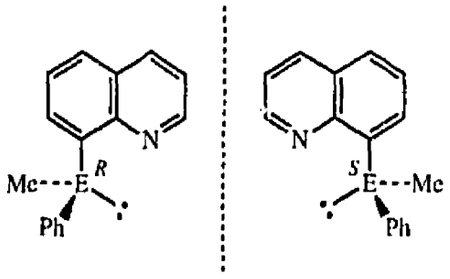
The 8-quinolyl-substituted phosphine and arsine (±)-**13** (E=P or As) were



(R^*,R^*)-(±)-**12**



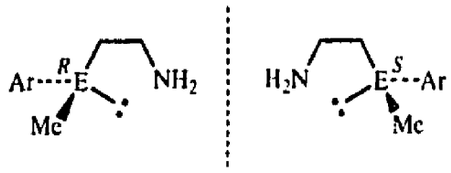
(R^*,S^*)-(±)-**12**



(±)-**13** (E = P or As)

resolved with use of (*R,R*)-**4**·CH_2Cl_2 [44]. The absolute configuration of the *R* enantiomer of the phosphine was established by determining the crystal and molecular structures of the palladium(II) complex containing the phosphine and the orthometallated *R*-naphthylamine. The ligands coordinate to the palladium in a regiospecific manner with the arsenic or phosphorus *trans* to nitrogen. The resolved arsines were displaced from the configurationally homogeneous diastereomers of the complex with 1,2-ethanediamine and the by-product palladium(II)-diamine complex was converted into (*R,R*)-**4** by treatment with hydrochloric acid. Liberation of the phosphine required conditions similar to those employed for the recovery of the enantiomers of (R^*,R^*)-(±)-**8** (E=P) from the corresponding palladium complexes (Scheme 1). The crystal structure determination on the less soluble diastereomer in the resolution of (±)-**13** (E=P) was the first to be reported on a homochiral [1-[1-(dimethylamino)ethyl]-2-naphthalenyl-*C,N*]palladium(II) complex and revealed the conformational locking mechanism of the five-membered organometallic ring – that is, the unfavourable interaction between the carbon–methyl of the organometallic ring and H(8) of the naphthalenyl ring, which stabilizes the δ conformation of the ring when the chiratopic carbon atom has the *R* configuration.

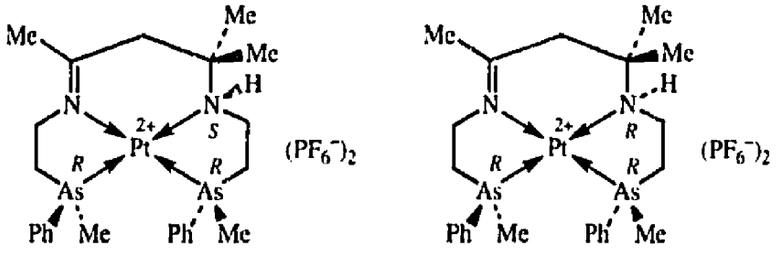
Square-planar and square-pyramidal complexes of both ligands with palladium(II) and platinum(II) were prepared and their behaviour in solution was investigated by variable temperature ^{1}H NMR spectroscopy [45].



(±) - **14** (E = P or As, Ar = Ph)

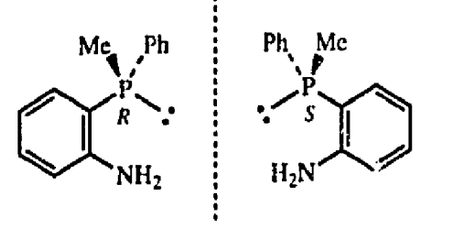
(±) - **15** (E = As, Ar = 2-$C_6H_4CH_2OH$)

The C_1 bidentates (±)-**14** (E=P or As: Ar=Ph) and (±)-**15** (E=As; R=2-$C_6H_4CH_2OH$) were resolved with use of (*R,R*)-**4**·CH_2Cl_2 as resolving agent [46]. The absolute configurations of the individual enantiomers of the two ligands were deduced from the ^{1}H NMR spectra of the diastereomeric palladium(II) resolving complexes, where a pronounced upfield shift of the γ-naphthalene proton was evident in the complexes containing phosphorus and arsenic stereocentres of *S* configuration. The enantiomers of the tertiary arsine were displaced from the individual palladium(II) diastereomers with 1,2-ethanediamine; the phosphine complexes required use of (*R**,*R**)-(±)-**8** (E=P) to effect the displacements. The complex (+)-*cis*-[Pt((*R*)-**14**)$_2$]$(PF_6)_2$, when stirred for 16 h in acetone at 25 °C in the presence



16a **16b**

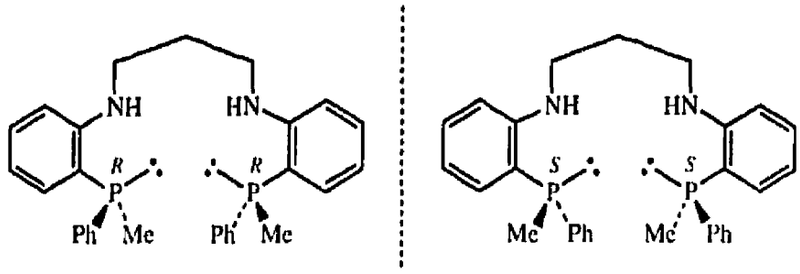
of a trace of (+)-**14**, produced a mixture of the epimers **16a** and **16b** in high yield . The highly functionalized arsine (±)-**15** was resolved similarly: oxidation of the (R,S_{As}) diastereomer with $BaMnO_4$ afforded the corresponding aldehyde complex that was stereoselectively converted into a complex of an optically active 14-membered *trans*-As_2N_2 macrocycle (see below).



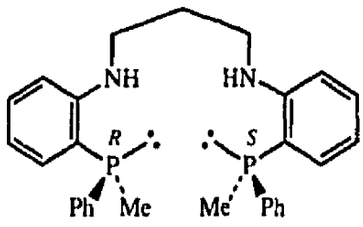
(±) - **17**

The 2-amino-substituted phosphine (±)-**17** was resolved with use of (*S,S*)-**4**·CH_2Cl_2 and the coordination chemistry of the various forms of the ligand with nickel(II), palladium(II) and platinum(II) was investigated [47]. The reaction of (±)-**17** with *n*-butyllithium and *N,N,N',N'*-tetramethyl-1,2-ethanediamine followed

by 1,3-bis(*p*-tolylsulphonyloxy)propane gave (*R**,*R**)-(±)- and (*R**,*S**)-**18**, which were separated on nickel(II).

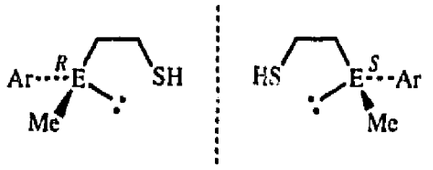


(*R**,*R**) - (±) - **18**



(*R**,*S**) - **18**

The 2-mercaptoethylarsine (±)-**19** (E=As; Ar=Ph) formed the unusual pair of μ-thiolato diastereomers **21a** (E=As) and **21b** (E=As) when reacted with

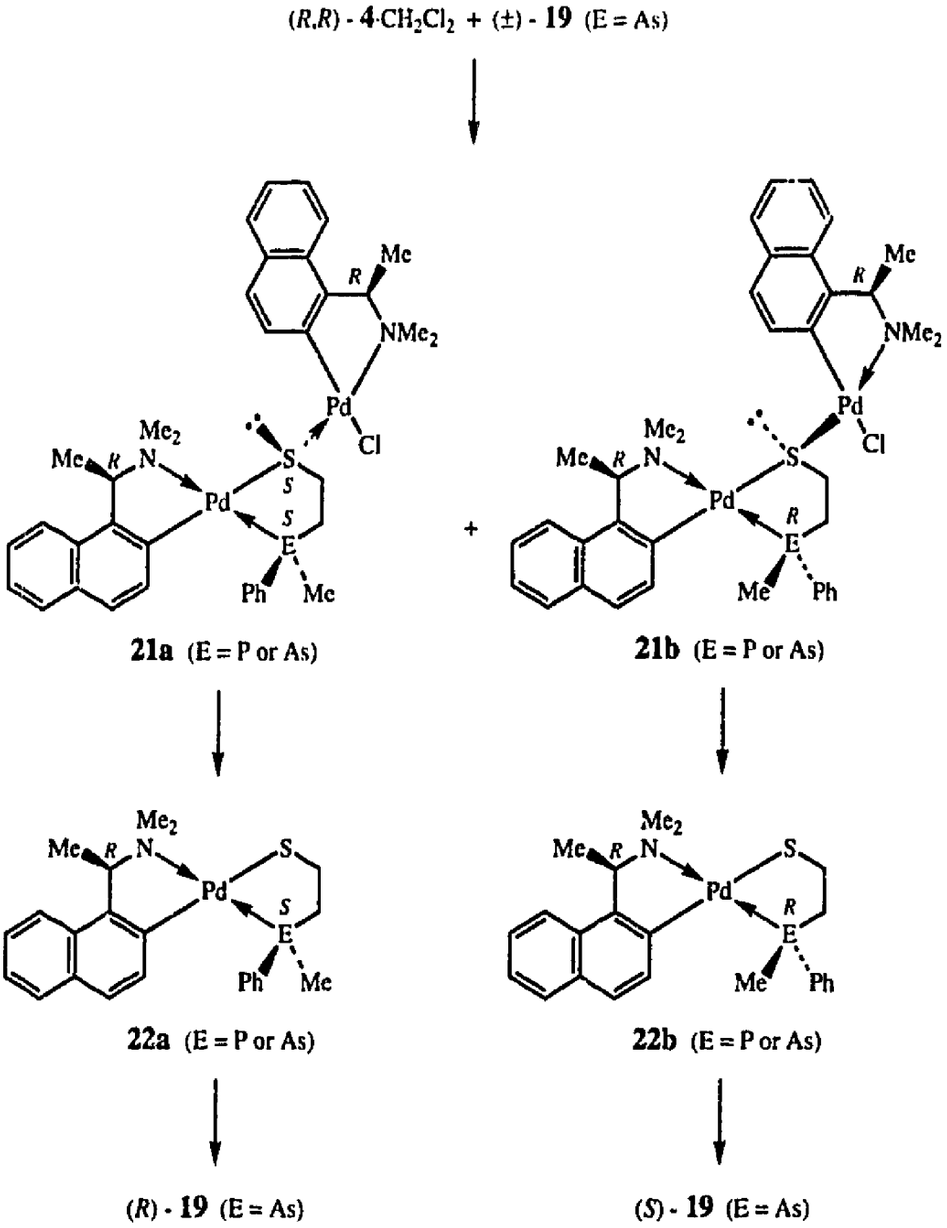


(±) - **19** (E = P or As, Ar = Ph)

(±) - **20** (E = P or As, Ar = 2-$C_6H_4CH_2OMe$)

(*R*,*R*)-**4** · CH_2Cl_2 (Scheme 3) [48] . The crystal and molecular structures of the less-soluble dipalladium(II) complex **21a** (E=As) were determined. Treatment of **21a** (E=As) with 1,2-ethanediamine removed the terminal resolving unit, giving **22a** (E=As) from which optically pure (*R*)-**19** (E=As; Ar=Ph) was liberated with cyanide. A similar reaction between (±)-**19** (E=P; Ar=Ph) gave the pair of isostructural dipalladium(II) diastereomers **21a** (E=P) and **21b** (E=P) from which removal of the terminal resolving units afforded **22a** (E=P) and **22b** (E=P), respectively [49]. The phosphine was removed from **22a** (E=P) by reaction with benzyl bromide and displacing the benzyl thioether (*R*)-**24** from **23** with (*R**,*R**)-(±)-**8** (E=P) (Scheme 4). The thioether **24** was cleaved by sodium in ammonia into a separable mixture of enantiomerically pure (*R*)-**19** (E=P; Ar=Ph) and (*R*)-ethylmethylphenylphosphine. The phosphine (*R*)-**19** rearranges in light by an intermolecular radical chain mechanism into enantiomerically pure (*S*)-ethylmethylphenylphosphine sul-

phide [49,50]. Diastereomerism in square-planar complexes of nickel(II), palladium(II) and platinum(II) containing the enantiomers of (±)-**19** (E = P or As) was investigated [51]. The resolution of (±)-**20** (E = As; Ar = 2-$C_6H_4CH_2OMe$) was subsequently achieved with use of (*R,R*)-**4**·CH_2Cl_2 via a similar pair of μ-thiolato dipalladium(II) diastereomers and the pure enantiomers of the arsine were employed for palladium(II) template syntheses of optically active 14-membered *trans*-As_2S_2 macrocycles (see below).

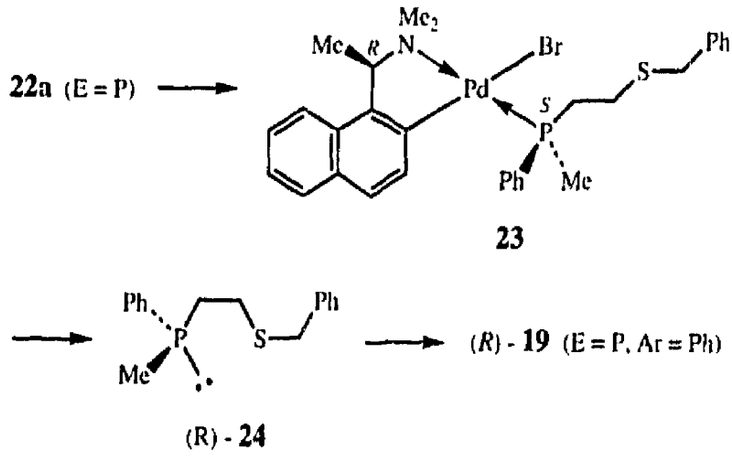


Scheme 3.

3.4. *Resolutions of C_2-quadridentates*

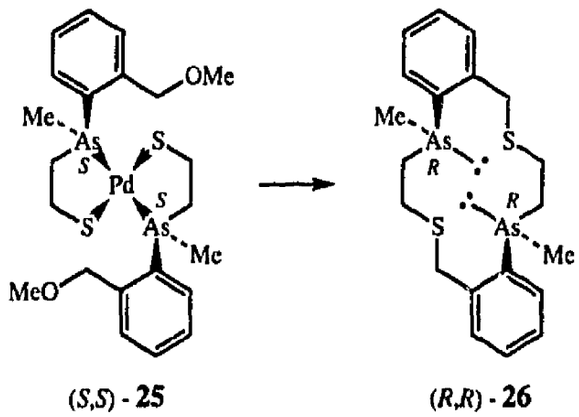
3.4.1. *Trans-As_2S_2 and trans-As_2N_2 macrocycles*

The first optically active macrocycles containing arsenic were synthesized by template dimerizations of the enantiomers of deprotonated (±)-**20** (E = As; Ar = 2-$C_6H_4CH_2OMe$) on palladium(II) with boron tribromide [52]. The enantiomerically pure enantiomers of the precursor bidentate were obtained by fractional



Scheme 4.

crystallization of μ-thiolato-bridged dipalladium(II) diastereomers analogous to those indicated in Scheme 3. The enantiomeric purity of each enantiomer of the bidentate was confirmed by recording the ^{1}H NMR spectrum of the kinetically labile bis(bidentate)nickel(II) complex of the deprotonated ligand in chloroform, where there was no evidence of the thermodynamically stable (*R**,*S**) diastereomer of the complex in either case. The cyclization of (*S*,*S*)-**25** with boron tribromide gave, after displacement from the metal with cyanide, a 66% yield of air-stable (*R*,*R*)-**26** along

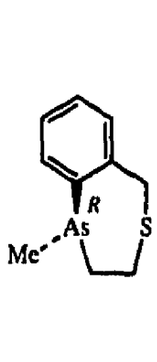


(5)

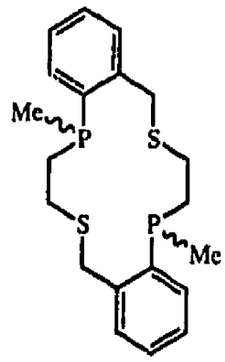
with a 13% yield of the seven-membered heterocycle (*R*)-**27** (Eq. (5)). Use of (±)-**25** in the cyclization gave a 50% yield of (*R**,*R**)-(±)-**26** and 38% yield of (±)-**27**. Treatment of (*R**,*R**)-(±)-**26** in chloroform with a trace of hydrochloric acid afforded a quantitative yield of sparingly soluble (*R**,*S**)-**26** in a typical second-order asymmetric transformation. When coordinated to palladium(II), however, (*R**,*S**)-**26** was transformed quantitatively into the complex of (*R**,*R**)-(±)-**26** by heating briefly in dimethyl sulphoxide at 150 °C.

The dimerization of deprotonated (±)-**20** (E=P; Ar=2-$C_6H_4CH_2OMe$) on platinum(II) with boron tribromide afforded low yields of the (*R**,*R**)-(±) and (*R**,*S**) forms of **28** after liberation from the metal [53]. The crystal and molecular structures of the nickel(II) perchlorate derivative of (*R**,*R**)-(±)-**28** were determined.

The pinnacle of our work on syntheses of optically active arsenic macrocycles was the asymmetric synthesis of an enantiomer of (*R**,*R**)-(±)-**29** [54]. Interestingly, the racemate of (*R**,*R**)-(±)-**29** could not be isolated because of spontaneous rearrangement and crystallization of sparingly soluble (*R**,*S**)-**29** via (±)-**30** (Scheme 5). It



(*R*)-27



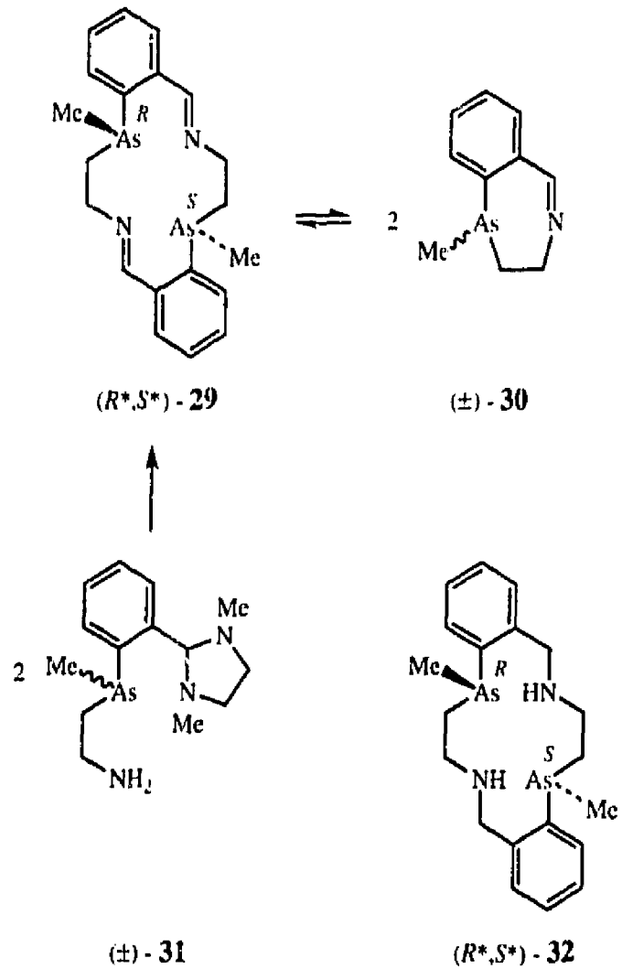
28

was also significant that (*R**,*S**)-**29** alone was formed quantitatively when the protected benzaldehyde (±)-**31** was heated at 80 °C in vacuo (with elimination of *N*,*N*′-dimethyl-1,2-ethanediamine). In solution in the presence of a trace of acid (*R**,*S**)-**29** rearranges quantitatively into (±)-**30** – removal of solvent, however, results in the recovery of (*R**,*S**)-**29**. Under acid-free conditions, (*R**,*S**)-**29** was reduced by lithium aluminium hydride into (*R**,*S**)-**32**. The asymmetric synthesis of (*R*,*R*)-**29** was achieved by the reaction of (±)-**30** (generated from (*R**,*S**)-**29** by treatment with a trace of trifluroacetic acid in methanol) with (*R*,*R*)-**4**·CH_2Cl_2 in methanol (Scheme 6). When the chiral auxiliary (*R*,*R*)-*4*·CH_2Cl_2 had dissolved, the reaction mixture was treated with aqueous ammonium hexafluorophosphate, which gave an almost quantitative yield of the diastereomers **33a** and **33b**. Recrystallization of the product from methanol–dichloromethane gave pure yellow **33a**, which contained tetrahedral palladium(II), whereas recrystallization from hot acetone afforded deep orange crystals of **33b**·0.5Me_2CO, a five-coordinate linkage isomer of **33a**. Both isomers of the complex displayed the same ^1H NMR spectrum in dichloromethane-d_2. The liberation of (*R*,*R*)-**29** from **33a** or **33b** was effected with use of (*R**,*R**)-(±)-**8** (E=P). The enantiomer (*R*,*R*)-**29** was isolated as a crystalline solid and from which (*R*,*R*)-**32** was obtained by reduction with lithium aluminium hydride. The coordination chemistry of the various forms of **32** with palladium(II) was investigated.

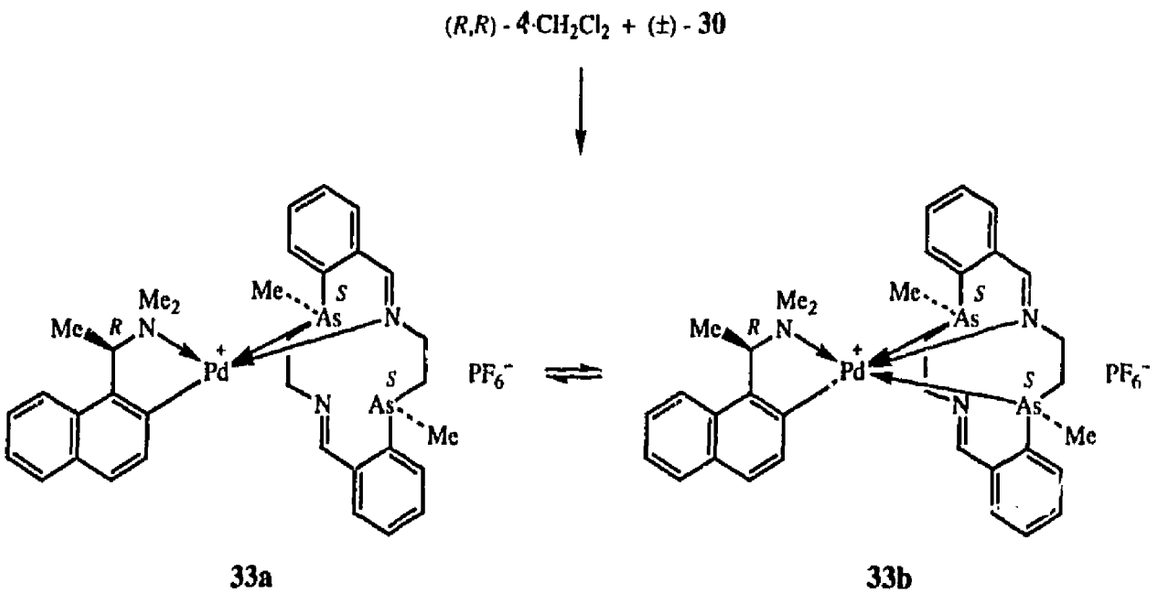
3.4.2. C_2-As_4 and C_2-P_4 linear quadridentates

The linear tetra(tertiary arsine) **34** was separated into the component (*R**,*R**)-(±) and (*R**,*S**) diastereomers by the fractional crystallization of the corresponding dichlorocobalt(III) complexes: the (*R**,*R**)-(±) form of the ligand formed a deep blue *cis*-α complex and the (*R**,*S**) form a green *trans* complex [55]. Decomposition of the individual diastereomers of the complex with cyanide afforded pure (*R**,*R**)-(±)- and (*R**,*S**)-**34**. The enantiomers of (*R**,*R**)-(±)-**34** were obtained by similar decompositions of the enantiomers of the (*R**,*R**)-(±)-*cis*-α cobalt(III) complex. Detailed investigations of the stereochemistry and interconversions of the five possible diastereomers of the octahedral cobalt(III) complexes of the various forms of **34** were undertaken [56].

The linear tetra(tertiary phosphine) **35** was separated into diastereomers and the (*R**,*R**)-(±) form was resolved with use of (*R**,*R**)-**2** as the resolving agent (Scheme 7) [57]. This is the first tetra(tertiary phosphine) to be resolved.

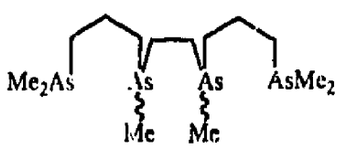


Scheme 5.

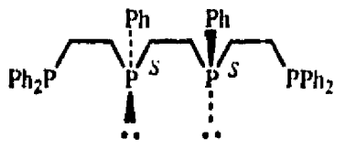


Scheme 6.

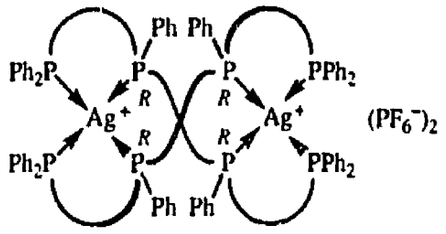
Enantiomerically pure (*S,S*)-**35** spontaneously self-assembled into left-handed double-stranded D_2-double helix (**36a**) and C_2-side-by-side helix (**36b**) conformers of the disilver(I) cation when reacted with silver(I) perchlorate; the crystal and molecular structures of the corresponding hexafluorophosphate salt were determined [58]. The analogous gold(I) complex has the side-by-side structure in the solid state,



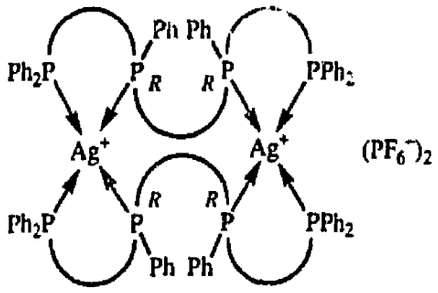
(R*,R*)- (±)/(R*,S*) - 34



(S,S) - 35

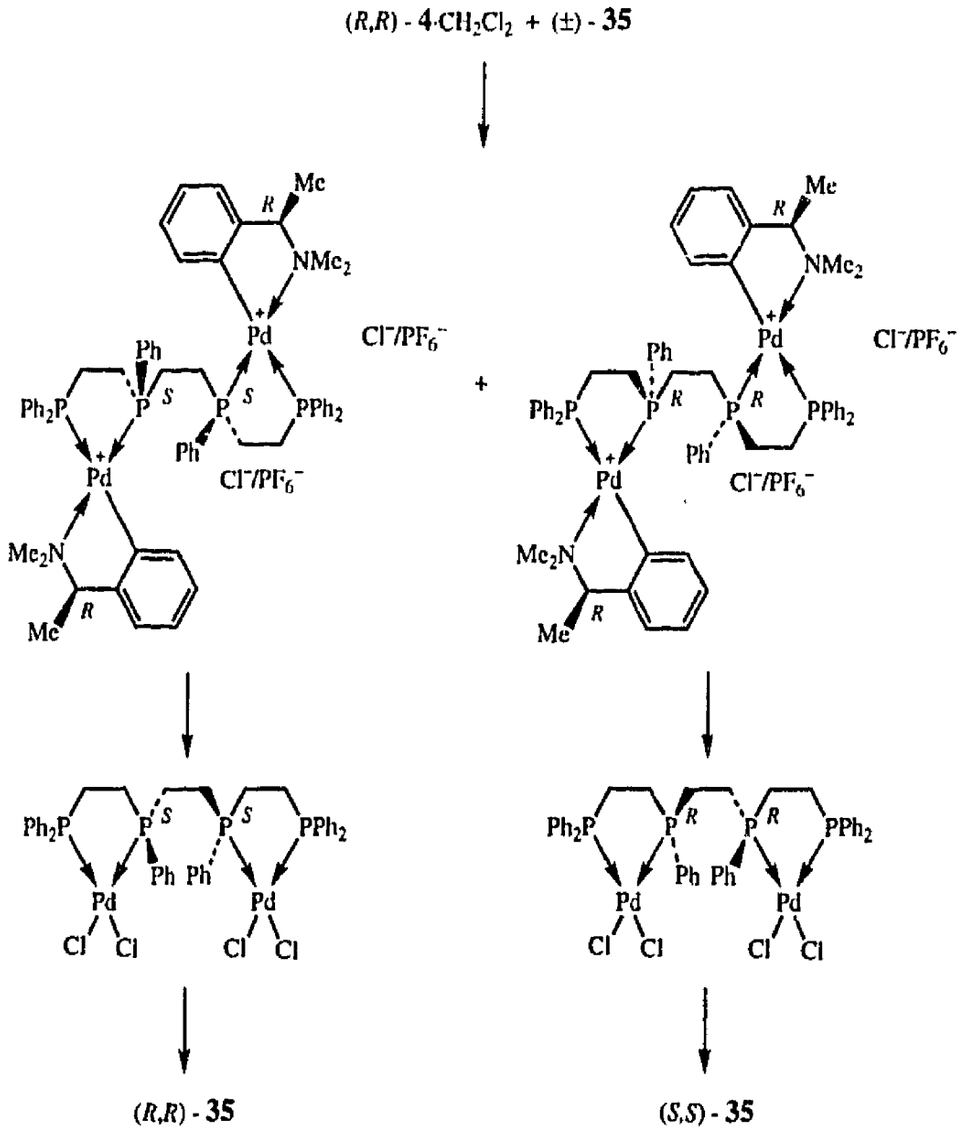


36a



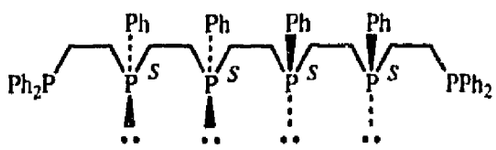
36b

and copper(I) forms a mononuclear metal complex [59]. The structure determinations on the silver and gold complexes were the first to be reported on enantiomerically pure dimetal helicates. The essential difference between the two conformers of the disilver complex lies in the relationship between the helicities of the central ten-membered rings, which have the twist-boat–chair–boat (TBCB) conformation rather than the BCB conformation of cyclodecane and its derivatives, and the configurations of the inner phosphorus stereocentres: when the ten-membered ring has the λ conformation, the phenyl groups attached to the inner phosphorus stereocentres of (*R*) configuration adopt equatorial dispositions and the axial terminal diphenylphosphinoethyl groups are in position to generate the D_2-double helix conformation of the complex; when the central ring has the δ conformation, the terminal diphenylphosphinoethyl groups have equatorial dispositions, which results in the tighter turns of the side-by-side helix conformation of the complex. In the double helix conformer **36a**, each molecule of the homochiral tetra(tertiary phosphine) completes one half-turn of a left-handed or λ helix (as does the overall helix); in the side-by-side conformer **36b**, each of the ligands completes one and one-half turns of a λ helix. Molecular mechanics calculations with use of the program SPARTAN 3.0 indicated that the homochiral hexa(tertiary phosphine) **37a** would stereoselectively generate double-stranded trinuclear metal helicates with univalent Group 11 ions and **37b** would generate stereoselectively side-by-side trinuclear metal helicates with these

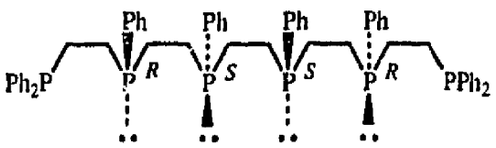


Scheme 7.

ions. Work on the synthesis and isolation of configurationally homogeneous forms of optically active hexa- and octa-tertiary phosphines derived from (*S*,*S*)-**35** is in progress [60].



37a



37b

4. Concluding remarks

Homochiral chloro-bridged palladium complexes containing the enantiomers of *N,N*-dimethyl(α-methylbenzyl)amine and related naphthylamines are extremely effective resolving agents for chiral phosphines and arsines. The diastereomers generated by bridge-splitting of the chloro-bridged dipalladium dimers can usually be separated in high yield by fractional crystallization. The procedures are suited to large-scale resolutions because of the ready availability and stability of the resulting diastereomers and the ease with which configurational purities can be determined by NMR spectroscopy. Moreover, the availability of the variety of *enantiomerically pure* phosphines and arsines afforded by this method permits detailed investigations of stereochemistries and rearrangements in coordination complexes, as well as the use of certain of the homochiral ligands for the construction of more complicated molecules in stereochemically homogeneous form. The enantiomerically pure ligands have also important applications as chiral auxiliaries for asymmetric synthesis.

Acknowledgements

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