Resolution of racemic Sb-chiral stibindoles using an optically active *ortho*-palladated benzylamine derivative, *via* their diastereomeric complexes

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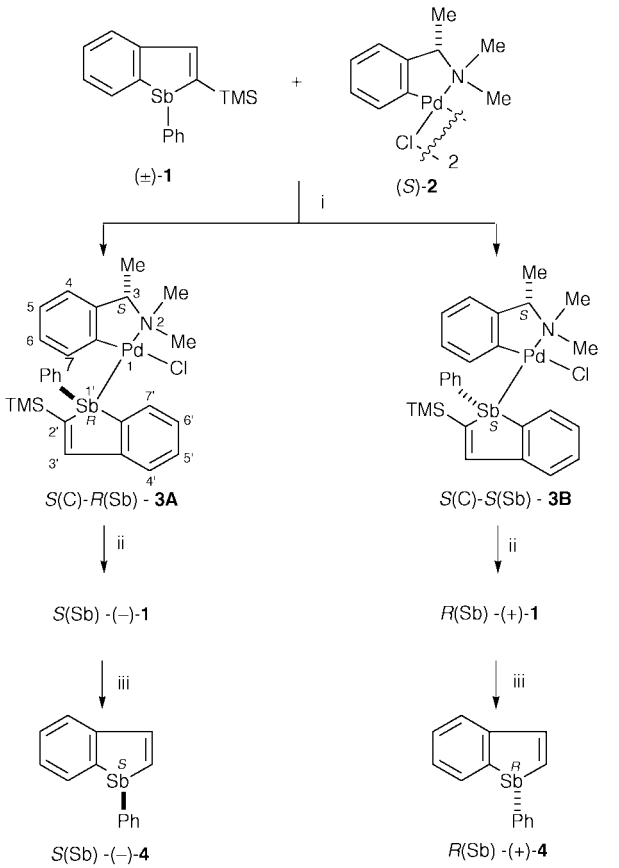
Resolution of racemic Sb-chiral (±)-1-phenyl-2-trimethylsilylstibindole 1 has been achieved by the separation of a mixture of the diastereomeric palladium(II) complexes 3A and 3B derived from the reaction of (±)-1 with di-μ-chlorobis{(*S*)-2-[1-(dimethylamino)ethyl]phenyl-*C*,*N*}dipalladium(II) 2, and optically pure 1-phenylstibindoles (-)-4 and (+)-4 have also been obtained from resolved (−)-1 and (+)-1, respectively.

The asymmetric synthesis and resolution of optically active trivalent phosphines and arsines have been extensively studied because of their use as chiral auxiliaries for a wide range of enantioselective transition-metal-catalyzed processes, such as hydrogenation of olefins, ketones and imines,[1,2] hydrosilylation of ketones, coupling reactions of olefins, and allylic alkylations.[2,3] For the preparation of optically active P-chiral phosphines and As-chiral arsines, a variety of chiral organometallic reagents, *e.g. ortho*-palladated α-arylalkylamines,[4–7] π-pinenyl nickel halides,[8] bisphosphine platinum complexes[9] and iron cationic complexes,[10] have been used as efficient resolving reagents. However, as far as optically active antimony(III) compounds are concerned, only a few limited examples of Sb-chiral stibafluorenes and triarylstibines bearing a hydroxycarbonyl or an amino group have been reported;[11] these functional groups are essential for resolution. Here, we report on an efficient and stereoselective resolution of the racemic Sb-chiral (±)-1-phenyl-2-trimethylsilylstibindole **1**,[12] *via* the separation of the diastereomeric stibindole–palladium complexes **3A** and **3B**, formed by the reaction of (±)-**1** with an optically active *ortho*-palladated benzylamine derivative **2**, and on the molecular structures of the complexes **3A** and **3B**. Optically pure Sb-chiral 1-phenylstibindole (−)-**4** and (+)-**4** are also obtained from resolved (−)-**1** and (+)-**1**, respectively. The present results are the first examples of resolution of neutral Sb-chiral compounds.

Treatment of racemic **1** with 0.5 equiv. of di-μ-chlorobis{(*S*)-2-[1-(dimethylamino)ethyl]phenyl-*C*,*N*}dipalladium(II) **2** (Scheme 1) resulted in coordination of the antimony atom to the palladium atom to give a 1 : 1 mixture of the diastereomeric Pd-complexes **3A** and **3B** quantitatively, which could be separated by silica gel column chromatography; **3A**: mp 158−159 °C, $[\alpha]_D^{23}$ −16.2 (*c* 0.6, acetone) and **3B**: mp 161–162 °C, $[\alpha]_D^{23}$ −79.7 (*c* 0.6, acetone).† Treatment of **3A** and **3B** with triphenylphosphine resulted in decomplexation to afford optically pure (−)-**1** and (+)-**1** {mp 73–75 °C; $[\alpha]_D^{23}$ ±415 (*c* 0.6 MeOH)}, respectively, in quantitative yields. The optically active (−)-**1** and (+)-**1** revert back to **3A** and **3B** on treatment with (*S*)-**2**. The trimethylsilyl group in (−)-**1** and (+)-**1** can be readily removed by treatment with TBAF in water-containing THF to give the corresponding optically pure 1-phenylstibindoles (−)-**4** and (+)-**4** {mp 49–50 °C; $[\alpha]_D^{23}$ ±726 (*c* 0.5 MeOH)}, without any loss of optical purity.‡ The racemic stibindole **4**[12] having no trimethylsilyl group also reacts with (*S*)-**2**, however, the resulting complexes are relatively unstable and attempts at separation were unsuccessful. Unlike stibafluorenes which have been reported to racemize in solution,[11a,b] the optically active stibindoles **1** and **4** possess high optical stability and did not undergo racemization even when heated at 80 °C for 8 h in benzene, although they gradually decomposed at that temperature. Furthermore, the rotations of optically active **1** and **4** were unchanged in either an acidic (10% AcOH–MeOH) or a basic (10% Et_3N–MeOH) solution over 48 h at room temperature.

When the dimeric palladium reagent (*S*)-**2** was treated with 8 equiv. of (±)-**1** and the resulting residue was recrystallized from benzene–hexane, the pure complex **3B** was obtained in 95% yield (calculated from (*S*)-**2**) without chromatographic separation. However, the reaction of (*S*)-**2** with 4 mol equiv. of (±)-**1** gave a 1 : 2.4 mixture of **3A** and **3B** in 94% yield. These results indicate preferential stereoselective formation of **3B** over **3A**. The use of a naphthalene-substituted palladium complex, di-μ-chlorobis{(*R*)-dimethyl-[1-(1-naphthyl)ethyl]-aminato-*C*^{2},*N*}dipalladium(II)[5,7] which has been reported to be a superior



Scheme 1 *Reagents and conditions*: i, dichloromethane, room temp., 5 min, quantitative; ii, PPh_3 (1.05 equiv.), dichloromethane, room temp., 30 min, quantitative; iii, TBAF/5% H_2O–THF, 60–65 °C, 3 h, 92–94%.

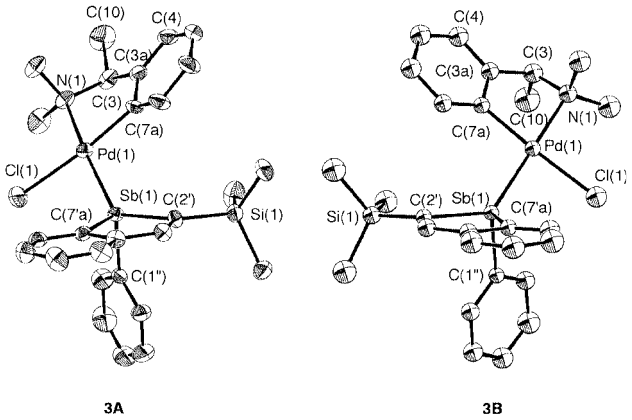


Fig. 1 Molecular structures of **3A** and **3B**. All hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (°). For **3A**: Pd(1)–Sb(1) 2.4926(8), Pd(1)–C(7a) 1.984(8), Pd(1)–N(1) 2.144(7), Pd(1)–Cl(1) 2.407(3), Sb(1)–Pd(1)–N(1) 170.2(2), Cl(1)–Pd(1)–C(7a) 171.0(3), C(10)–C(3)–C(3a)–C(4) 17(1), plane N(1)–Pd(1)–C(7a)–plane Sb(1)–Pd(1)–Cl(1) 14.12. For **3B**: Pd(1)–Sb(1) 2.4942(6), Pd(1)–C(7a) 2.003(6), Pd(1)–N(1) 2.161(6), Pd(1)–Cl(1) 2.408(2), Sb(1)–Pd(1)–N(1) 178.1(2), Cl(1)–Pd(1)–C(7a) 176.2(2), C(10)–C(3)–C(3a)–C(4) 91(1), plane N(1)–Pd(1)–C(7a)–plane Sb(1)–Pd(1)–Cl(1) 4.099.

chiral reagent relative to **2** for the resolution of trivalent phosphines and arsines, was found to give inferior results for the resolution of (±)-**1**.

The solid-state molecular structures of **3A** and **3B**, including absolute configuration were determined by single crystal X-ray analyses (Fig. 1),§ which reveals that in **3A** and **3B**, the coordinated antimony ligand is situated *trans* to the dimethylamine moiety as in the related phosphine[4,5] and arsine[6] complexes. Also apparent is that the antimony atom in **3A** and **3B** has *S*- and *R*-configuration, respectively, and no noticeable difference in the Pd–Sb distance is seen between **3A** (2.493 Å) and **3B** (2.494 Å). One of the most conspicuous differences in molecular structure between **3A** and **3B** is the geometry of their benzylic methyl groups. The methyl groups are located in a pseudo-equatorial orientation for **3A** and are pseudo-axial for **3B**. It is known that both equatorial and axial conformations of the benzylic methyl group are accessible in phosphine–palladium complexes of phenyl ethylamino derivatives.[7b]

Despite a detailed inspection of the X-ray structures of **3A** and **3B**, no significant intracomplex H···H or H···C interactions between the stibindole and the palladacycle moiety were observed. It has recently been suggested that square planarity around the palladium atom is important when considering the conformational stability of bidentate phosphine–palladium complexes, since deviation from square planarity around palladium will occur to prevent hard atomic contacts between the ligands and palladacycles.[7b] In both diastereomers **3A** and **3B**, the four substituents around the palladium atom lead to a distorted square planar geometry and significant differences in the bond angles Sb(1)–Pd(1)–N(1) and Cl(1)–Pd(1)–C(7a) between **3A** (170–171°) and **3B** (176–178°) are observed. These differences give rise to a difference in the dihedral angles between the planes N(1)–Pd(1)–C(7a) and Sb(1)–Pd(1)–Cl(1), *i.e.* 14.1° for **3A** and 4.1° for **3B**. These results indicate that **3A** is more distorted than **3B**. Consequently, the more sterically stable **3B** forms preferentially to the less stable **3A** in the present reaction.

Notes and references

† For a typical procedure; a mixture of (±)-**1** and (*S*)-**2** in dichloromethane was stirred for 5 min at room temperature. After removal of the solvent *in vacuo*, the resulting residue was separated by chromatography on silica gel [dichloromethane–hexane–diethyl ether (10 : 10 : 1)], followed by recrystallization from benzene–hexane (1 : 8) to give **3A** and **3B**. *Selected* ^{1}*H NMR data* (400 MHz, $CDCl_3$, *J*/Hz): **3A**, δ 0.13 (9H, s, TMS), 1.66 (3H, d, *J* 6.6, CHCH_3), 2.75 and 2.99 (3H, s, NCH_3), 4.03 (1H, q, *J* 6.6, C*H*CH$_3$), 6.61 (1H, m, 5-H), 6.85 (1H, br d, *J* 7.3, 7-H), 6.9–7.0 (2H, m, 4- and 6-H), 7.25–7.7 (8H, 4′-, 5′-, 6′- and Ph-H), 7.82 (1H, br d, *J* 7.3, 7′-H), 8.00 (1H, s, 3′-H). **3B**, δ 0.08 (9H, s, TMS), 1.76 (3H, d, *J* 6.6, CHCH_3), 2.84 and 2.89 (3H, s, NCH_3), 3.81 (1H, q, *J* 6.6, C*H*CH$_3$), 6.63 (1H, m, 5-H), 6.86 (1H, br d, *J* 7.3, 7-H), 6.9–7.0 (2H, m, 4- and 6-H), 7.2–7.7 (8H, 4′-, 5′-, 6′- and Ph-H), 7.81 (1H, br d, *J* 7.3, 7′-H), 8.00 (1H, s, 3′-H).

‡ The optical purities of (−)-**4** and (+)-**4** could be determined by comparison of the ^{1}H NMR signals due to the 3′- and 7′-protons of their Pd complexes with those of (*S*)-**2**. *Selected* ^{1}*H NMR data* (400 MHz, $CDCl_3$, *J*/Hz): (−)-**4**+(*S*)-**2**, δ 1.67 (3H, d, *J* 6.6, CHCH_3), 2.79 and 2.98 (3H, s, NCH_3), 3.94 (1H, q, *J* 6.6, C*H*CH$_3$), 6.80 (1H, m, 5-H), 6.95–7.05 (2H, m, 4- and 6-H), 7.16 (1H, br d, *J* 7.7, 7-H), 7.25–7.75 (9H, 2′-, 4′-, 5′-, 6′- and Ph-H), 7.79 (1H, d, *J* 8.8, 3′-H), 8.01 (1H, br d, *J* 7.3, 7′-H). (+)-**4**+(*S*)-**2**, δ 1.72 (3H, d, *J* 6.6, CHCH_3), 2.82 and 3.93 (each 3H, each s, NCH_3), 3.90 (1H, q, *J* 6.6, C*H*CH$_3$), 6.81 (1H, m, 5-H), 6.95–7.05 (2H, m, 4- and 6-H), 7.18 (1H, br d, *J* 7.7, 7-H), 7.25–7.7 (9H, 2′-, 4′-, 5′-, 6′- and Ph-H), 7.82 (1H, d, *J* 8.8, 3′-H), 7.97 (1H, br d, *J* 7.3, 7′-H).

§ *Crystal data* for **3A**{**3B** where different}: $C_{27}H_{33}ClNPdSbSi$, *M* = 663.25, *a* = 11.679(2) {11.738(3)}, *b* = 20.597(3) {20.626(2)}, *c* = 11.631(1) {11.494(2)} Å, *V* = 2797.8(7) {2782.6(7)} Å^3, *T* = 296 {298} K, space group $P2_12_12_1$ (no. 19), *Z* = 4, μ(Mo-Kα) = 17.59 {17.70} cm^{-1}, 3641 {3608} reflections measured (Rigaku AFC5R diffractometer), 3365 {3151} reflections [$I > 3\sigma(I)$] were used in all calculations, *R* = 0.049 {0.028}, R_w = 0.060 {0.046}. The structures of **3A** and **3B** were solved by direct methods and all of the non-hydrogen atoms were refined anisotropically using full-matrix least squares based on F^2. The absolute configurations of the antimony atoms in **3A** and **3B** were determined by comparison with the known configuration (*S*) of the benzylic methine moiety of the palladium reagent (*S*)-**2**, used as a resolving agent. CCDC 182/1510.

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