Synthesis of Optically Active Organoantimony Compounds Having an (*S*)-α-Methylbenzyldimethylamine Group and Its Evaluation for Asymmetric Reaction

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Received May 31, 2002; accepted August 8, 2002

Novel, enantiomerically pure organoantimony compounds having a C-chiral amine moiety, (*S*)-(α-methyl-2-di-*p*-tolylstibanobenzyl)dimethylamine [AMSb] (2) and its (η^6-arene)chromium complex [AMSb–Cr(CO)$_3$] (4), were prepared from common (*S*)-(α-methylbenzyl)dimethylamine (1) *via* its *ortho*-lithiated intermediates in short steps. The catalytic activity and enantioselectivity of the ligands 2 and 4 for asymmetric reaction are evaluated, and the optically active (η^6-arene)chromium complex 4 has been shown to be an effective ligand for rhodium-catalyzed asymmetric hydrosilylation of ketones.

Key words optically active antimony; asymmetric hydrosilylation; (η^6-arene)chromium complex; rhodium catalysis; ketone

The chemistry of asymmetric catalysts is an interesting research field in asymmetric reactions and has recently been the focus of attention.[1)] A number of chiral ligands containing nitrogen,[2)] phosphorus[3—9)] and arsenic[10—13)] have been widely studied and are well documented. With respect to enantiomerically pure phosphine ligands bearing a chiral benzylamine moiety, (*R*/*S*)-[α-methyl-2-(diphenylphosphino)-benzyl]dimethylamine (AMPhos)[14—17)] and its (η^6-arene)-chromium complex[18,19)] have been reported to be effective chiral ligands for enantioselective reductions, cross-coupling reactions, and allylic alkylations. It is also known that a variety of optically active phosphine derivatives bearing a ferrocene skeleton can be used in a wide range of asymmetric reactions.[7)] However, the synthesis of optically active organoantimony compounds and its applications to asymmetric reactions have not been reported so far. In this context, we are interested in the synthesis and utilization of optically active organoantimony compounds for asymmetric synthesis and have recently reported an efficient and stereoselective resolution of racemic Sb-chiral stibindoles[20)] and 2,2′-bis[di(*p*-tolyl)stibano]-1,1′-binaphthyls (BINASb).[21)] Here we report the syntheses of new, optically active antimony compounds having a C-chiral benzylamine moiety, (*S*)-(α-methyl-2-di-*p*-tolylstibanobenzyl)dimethylamine [AMSb] (**2**) and AMSb–Cr(CO)$_3$ complex (**4**), and their use for transition metal-catalyzed enantioselective hydrosilylation of ketones.

The syntheses of the optically pure organoantimony compounds **2** and **4** used in this study are shown in Chart 1. (*S*)-(α-Methylbenzyl)dimethylamine (**1**) was *ortho*-lithiated with *n*-butyllithium (*n*-BuLi) in ether according to the literature method,[17)] followed by trapping with bromodi(*p*-tolyl)stibane [(*p*-Tol)$_2$SbBr] to give AMSb (**2**) in 45% yield; $[\alpha]_D$ +12.6° (*c*=2, $CHCl_3$). On the other hand, (η^6-arene)chromium complexes have some significant properties owing to the strong electron-withdrawing ability and steric bulkiness of the coordinated transition metal, and their applications to organic synthesis have been developed.[22)] It is also known that the arylic hydrogens on the chromium complexes are easily lithiated to functionalize at an appropriate position. The key common starting (*S*)-tricarbony[η^6-(α-methylbenzyl)dimethylamine]chromium (**3**) was obtained by the reaction of **1** with hexacarbonylchromium in 73% yield as yellow crystals.[23)] The novel chiral antimony compound **4** was readily prepared by way of diastereoselective lithiation of **3**. According to the procedure reported by Gibson and co-workers,[24)] the chromium complex **3** was lithiated by treatment with *tert*-butyllithium (*t*-BuLi) in anhydrous diethyl ether at −80 °C under an argon atmosphere. Subsequent treatment of the mixture with (*p*-Tol)$_2$SbBr at the same temperature gave rise to the expected (+)-(1*R*,2*R*)-tricarbonyl[η^6-(*S*)-(α-methyl-2-di-*p*-tolylstibanobenzyl)dimethylamine]chromium [AMSb–Cr(CO)$_3$] (**4**) in 59% yield, $[\alpha]_D$ +441° (*c*=2, $CHCl_3$) as the sole product. The planar chirality of the (η^6-arene)chromium moiety is deduced to be *R* from diastereoselective *ortho*-lithiation of **3** as reported in the literature.[23—26)] Although most of the phosphorus(III) compounds are known to be susceptible to air oxidation, the stibanes **2** and **4** are isolated as relatively stable crystals in air. The structures of **2** and **4** were elucidated mainly by their MS, ^{1}H-NMR, and elemental analyses.

We next examined the catalytic asymmetric hydrosilylation of acetophenone (**5a**) with diphenylsilane using the stibane ligands and several metal catalysts {[RhCl(COD)]$_2$, [RuCl$_2$(C$_6$H$_6$)]$_2$, or [RuCl$_2$(*p*-Cym)]$_2$} to evaluate their abilities as a catalyst and a chiral inducer.[27—33)] The results including the reaction conditions such as ligands, metal catalysts, ratio of metal catalysts to ligands, additive, solvents, and reaction temperatures are summarized in Table 1. These results showed that AMSb–Cr(CO)$_3$ (**4**) is more effective than AMSb (**2**) in both points of catalytic activity and enantioselectivity (Entry 1—3). The ratio of [RhCl(COD)]$_2$ to the ligand **4** affects both catalytic activity and enantioselectivity, and excess ligand resulted in low selectivity (Entry 3—5). The reaction in the presence of AgOTf as additive gave the alcohol **6a** which is inverse configuration, and improved selectivity was not attained even when the reaction was carried out at lower temperature. Also apparent was that no catalytic activity and stereoselectivity were observed when ruthenium catalysts were used instead of a rhodium catalyst. Consequently, the best result was obtained when the reaction was carried out in the presence of [RhCl(COD)]$_2$ and the ligand **4** (1 : 1) in THF at 0 °C, although the enantioselectivity was relatively low (18% ee) (Entry 3). The enantioselectivity of the reaction demonstrated here is comparable with those observed for the same reactions in the presence of phosphine

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Table 1. Catalytic Asymmetric Hydrosilylation of Acetophenone[a)]

Entry	Ligand	Ligand/Cat.[b)]	Catalyst	Additive	Solvent	Temp./°C	Time	Yield/% ( )[c)]	Ee/%[d)]
1	**2**	1	$[RhCl(COD)]_2$	—	THF	0	2 h	22 (27)	0
2	**2**	1	$[RhCl(COD)]_2$	AgOTf	THF	0	2 h	30 (32)	4 (*R*)
3	**4**	1	$[RhCl(COD)]_2$	—	THF	0	2 h	57 (71)	18 (*R*)
4	**4**	2	$[RhCl(COD)]_2$	—	THF	0	2 h	35 (68)	3 (*R*)
5	**4**	4	$[RhCl(COD)]_2$	—	THF	0	2 h	34 (71)	7 (*R*)
6	**4**	1	$[RhCl(COD)]_2$	AgOTf	THF	0	2 h	59 (65)	13 (*S*)
7	**4**	1	$[RhCl(COD)]_2$	—	Et_2O	0	2 h	10 (31)	3 (*R*)
8	**4**	1	$[RhCl(COD)]_2$	—	Toluene	0	2 h	20 (33)	0
9	**4**	1	$[RhCl(COD)]_2$	—	THF	−20	24 h	36 (73)	16 (*R*)
10	**4**	1	$[RhCl(COD)]_2$	—	THF	−40	24 h	12 (81)	13 (*R*)
11	**4**	1	$[RuCl_2(C_6H_6)]_2$	—	THF	0	6 h	—[e)]	—
12	**4**	1	$[RuCl_2(p\text{-cym})]_2$	—	THF	0	6 h	—[e)]	—

a) Conditions: acetophenone (2.5 mmol), Ph_2SiH_2 (3 mmol), transition metal-catalyst (0.0125 mmol). *b*) Calculated based on the consideration that these dimeric transition metal-catalysts react with 2 eq of ligands. *c*) Isolated yields (calculated from **5a** consumed). *d*) The enantiomeric excess (ee) of **6a** was calculated by HPLC analysis with Chiralpak OB. The absolute configuration of the product was assigned by comparison of the retention time on an HPLC chiral column with the commercially available compound. *e*) No reaction.

Table 2. Catalytic Asymmetric Hydrosilylation of Ketones **5a**—**d**[a)]

Ketone	Yield/%[b)]	Ee/%[c)]
5b	35 (83)	7 (*R*)
5c	21 (86)	3 (*R*)
5d	16 (79)	7 (*R*)

a) Conditions: ketone (2.5 mmol), Ph_2SiH_2 (3 mmol), $[RhCl(COD)]_2$ (0.0125 mmol), AMSb–$Cr(CO)_3$ (**4**) (0.025 mmol). *b*) Isolated yields (calculated from **5b**—**d** consumed). *c*) The enantiomeric excess (ee) of **6b**—**d** was calculated by HPLC analysis with Chiralpak OB. The absolute configuration of the product was assigned by comparison of the retention time on an HPLC chiral column with the commercially available compound.

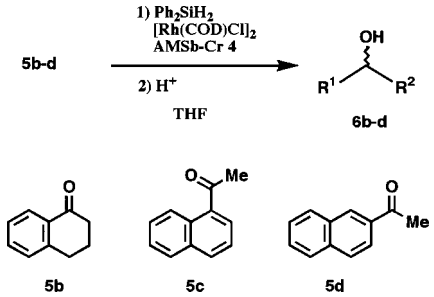

Chart 3

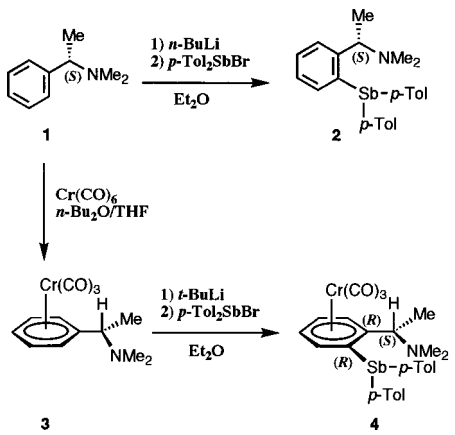

Chart 1

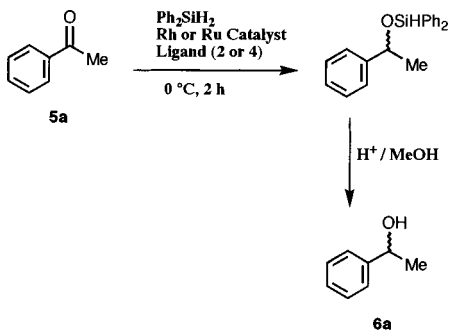

Chart 2

ligand AMPhos (27—51% ee)[14—17] or its arsenic congener AMArs (0% ee).[17]

In order to clarify the ability of the ligand **4** for enantioselective hydrosilylation, we attempted the reaction of the other ketones **5b**—**d**. The ketones were subjected to the standard conditions, shown for entry 3 in Table 1: ketone (2.5 mmol), Ph_2SiH_2 (3 mmol), **4** (0.025 mmol), $[RhCl(COD)]_2$ (0.0125 mmol), 0 °C, 2 h, in THF. The results showed that the chemical yields of the alcohols **6b**—**d** calculated from the consumed ketones **5a**—**d** were relatively higher than those for **5a**, although the reaction rates and enantioslectivities were lower.

In conclusion, novel, enantiomerically pure organoantimony compounds, AMSb (**2**) and AMSb–$Cr(CO)_3$ (**4**), were synthesized by the diastereoselective *ortho*-lithiation of a common (*S*)-(α-methylbenzyl)dimethylamine (**1**), followed by reaction with $(p\text{-Tol})_2SbBr$. The ligands **2** and **4** were tested as a chiral inducer, and AMSb–$Cr(CO)_3$ (**4**) was proved to be an effective ligand in the rhodium-catalyzed asymmetric reduction of ketones. The results imply that these new, optically active stibane ligands will be useful as chiral auxiliary for asymmetric reactions.

Experimental

Melting points were measured on a Yanagimoto micro melting point hot-stage apparatus and are uncorrected. The IR spectra were recorded on a Horiba FT-720 instrument. Mass spectra were recorded on a JEOL JMP-DX300 instrument. ^1H- and ^{13}C-NMR spectra were recorded on a JEOL ECP-500 (500 MHz for ^1H-NMR and 125 MHz for ^{13}C-NMR) spectrometer in $CDCl_3$ using tetramethylsilane as an internal standard. Elementary combustion analyses were performed by a Yanaco CHN CORDER MT-5. Column chromatography was carried out on silica gel (60N, Kanto Chemical).

(*S*)-(α-Methylbenzyl)dimethylamine (**1**)[17] and bromodi(*p*-tolyl)stibane[34] were prepared according to the reported procedures. Chiral HPLC analysis was carried out on a Shimadzu HPLC 10A with a UV–VIS detector using a Chiralcel OB (0.46 cm×25 cm) made by Daicel Chemical Industries Ltd.

AMSb (2) To a solution of **1** (1.49 g, 10 mmol) in ether (15 ml) was added *n*-BuLi (7.2 ml, 11 mmol, 1.52 mol/l in hexane) at 0 °C under an argon atmosphere, and the solution was stirred for 24 h at room temperature. To this was added a solution of bromodi(*p*-tolyl)stibane [prepared from redistribution reaction by heating tri(*p*-tolyl)stibane (3.58 g, 9.1 mmol) and tribromostibane (1.86 g, 4.5 mmol, 90%) for 1 h at 90 °C] in ether (10 ml) over 30 min at 0 °C, and the mixture was stirred for 1.5 h at the same temperature. After the reaction mixture was quenched with water (15 ml) and diluted with ether (50 ml), the organic layer was separated and the aqueous layer was extracted with ether (30 ml). The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated *in vacuo*. The residue was purified by silica gel chromatography with CH_2Cl_2 to give 2.30 g (45%) of **2**; colorless prisms (from EtOH), mp 64—66 °C. $[\alpha]_D^{25}$ +12.6° (*c*=2, benzene). ^{1}H-NMR δ: 1.33 (3H, d, *J*=6.9 Hz, Me), 1.79 (6H, s, NMe_2), 2.31 (6H, s, Tol-Me), 3.76 (1H, q, *J*=6.9 Hz, CH), 7.07 (4H, d, *J*=7.3 Hz, Ar-H), 7.11 (1H, dt, *J*=7.3, 1.4 Hz, Ar-H), 7.22 (1H, dd, *J*=6.9, 1.4 Hz, Ar-H), 7.26 (1H, dt, *J*=7.3, 1.4 Hz, Ar-H), 7.28 (2H, d, *J*=7.8 Hz, Ar-H), 7.32 (2H, d, *J*=7.8 Hz, Ar-H), 7.33 (1H, dd, *J*=7.3, 1.4 Hz, Ar-H). ^{13}C-NMR δ: 11.5 (q), 21.4 (q), 39.7 (q), 63.2 (d), 126.0 (d), 127.2 (d), 128.0 (d), 129.1 (d), 129.2 (d), 136.1 (d), 136.2 (d), 137.1 (s), 137.2 (s), 137.3 (d), 138.5 (s), 138.7 (s), 140.5 (s), 149.3 (s). MS *m*/*z*: 451 (M^+). *Anal.* Calcd for $C_{24}H_{28}NSb$: C, 63.74; H, 6.24; N, 3.10. Found: C, 63.81; H, 6.23; N, 3.13.

(−)-(*S*)-Tricarbonyl[η^6-(α-methylbenzyl)dimethylamine]chromium(0) (3) This compound was prepared by known procedure.[23] Yellow needles (from CH_2Cl_2–hexane), 73% yield, mp 41—42 °C (lit.[24] mp 43—44 °C), $[\alpha]_D^{25}$ −14.6° (*c*=1, $CHCl_3$).

(−)-(*S*)-Tricarbonyl[η^6-(α-methyl-2-di-*p*-tolylstibanobenzyl)dimethylamine]chromium(0) [AMSb–Cr(CO)$_3$] (4) To a solution of **3** (5 g, 17.7 mmol) in ether (40 ml) was added *t*-BuLi (21.8 ml, 35.5 mmol, 1.62 mol/l in pentane) at −80 °C under an argon atmosphere, and the solution was stirred for 0.5 h at the same temperature. A solution of bromodi(*p*-tolyl)stibane [prepared from tri(*p*-tolyl)stibane (9.20 g, 23.3 mmol) and tribromostibane (4.25 g, 11.8 mmol, 90%)] in ether (35 ml) was added dropwise with stirring to the above reaction mixture over 10 min period at −80 °C. The mixture was stirred for 0.5 h at the same temperature and then 3 h at 0 °C. The reaction mixture was quenched with water (150 ml) and diluted with benzene (250 ml). The organic layer was separated and the aqueous layer was extracted with benzene (150 ml). The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated *in vacuo*. The residue was purified by silica gel column chromatography with ether–*n*-hexane (1 : 9) to give 6.17 g (59%) of **4**; yellow needles (from EtOH), mp 155—156.5 °C. $[\alpha]_D^{27}$ +441° (*c*=2, $CHCl_3$). ^{1}H-NMR δ: 1.10 (3H, d, *J*=6.9 Hz, Me), 1.77 (6H, s, NMe_2), 2.32 (3H, s, Tol-Me), 2.35 (3H, s, Tol-Me), 4.02 (1H, q, *J*=6.9 Hz, CH), 5.13 (1H, br t, *J*=6.4 Hz, Ar-H), 5.13 (1H, br d, *J*=6.4 Hz, Ar-H), 5.20 (1H, br d, *J*=6.4 Hz, Ar-H), 5.43 (1H, br t, *J*=6.4 Hz, Ar-H), 7.13 (2H, d, *J*=8.3 Hz, Ar-H), 7.14 (2H, d, *J*=8.3 Hz, Ar-H), 7.30 (2H, d, *J*=7.3 Hz, Ar-H), 7.36 (2H, d, *J*=7.3 Hz, Ar-H). ^{13}C-NMR δ: 5.8 (q), 21.35 (q), 21.39 (q), 38.2 (q), 61.0 (d), 89.9 (d), 92.7 (d), 93.3 (d), 102.0 (d), 104.4 (s), 118.1 (s), 129.3 (d), 129.5 (d), 135.2 (d), 135.4 (s), 136.3 (d), 137.9 (s), 138.0 (s), 138.3 (s), 233.2 (s). IR (KBr) cm^{-1}: 1963, 1913, 1870 (C=O). MS *m*/*z*: 587 (M^+). *Anal.* Calcd for $C_{27}H_{28}CrNO_3Sb$: C, 55.13; H, 4.80; N, 2.38. Found: C, 54.91; H, 4.85; N, 2.43.

General Procedure for Hydrosilylarion with the Rhodium Complexes and Diphenylsilane A solution of $[Rh(COD)Cl]_2$ (6.2 mg, 0.0125 mmol) and **4** (14.7 mg, 0.025 mmol) in THF (1 ml) was stirred for 1 h at room temperature under an argon atmosphere. To the above stirred solution was added a solution of ketones (**5a**—**d**) (2.5 mmol) in THF (0.5 ml) and diphenylsilane (552 mg, 3.0 mmol) in THF (0.5 ml) cooling in an ice-bath. After the mixture was stirred for 2 h at 0 °C, methanol (10 ml) and 10% hydrochloric acid (14 ml) were added to the reaction mixture. The mixture was stirred for 1 h at 0 °C. The resulted reaction mixture was extracted with ether (80 ml, 30 ml), and the combined extract was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography with ether–hexane (1 : 9) to give **6a**—**d**. The optical purity of the alcohol products **6a**—**d** was determined by HPLC [Daicel Chiralcel OB column; eluent, *n*-hexane : *i*-PrOH=9 : 1; flow rate 0.5 ml/min; detection, UV 254 nm; retention times, **6a** (t_S=10.4 min, t_R=13.4 min), **6b** (t_S=9.4 min, t_R=12.9 min), **6c** (t_S=15.4 min, t_R=17.2 min), **6d** (t_S=14.2 min, t_R=17.8 min)].

Acknowledgments Partial financial support for this work was provided by a Grant-in-Aid for Scientific Research from the Ministry of Education, Sciences, Sports, Culture, and Technology, Japan, and by the Specific Research Found of Hokuriku University.

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