Atropisomeric Amides as Chiral Ligands: Using (−)-Sparteine-Directed Enantioselective Silylation to Control the Conformation of a Stereogenic Axis

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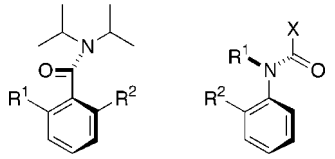
An enantiomerically pure (1-trimethylsilyl)ethyl group, constructed by a (−)-sparteine-directed enantioselective quench of a laterally lithiated tertiary aromatic amide, exerts powerful thermodynamic control over the conformation of the adjacent tertiary amide substituent. Ortholithiation and functionalization of the amide in the 6-position allows the single amide conformer to be trapped as an enantiomerically and diastereoisomerically pure amide atropisomer. Protodesilylation of the amide gives functionalized atropisomeric amides with a stereogenic axis of single absolute configuration, whose barriers to racemization have been determined by polarimetry. Enantiomerically pure amides bearing phosphine substituents are effective ligands in a Pd-catalyzed allylic substitution reaction—the first use of a nonbiaryl atropisomer as a chiral ligand—and give products with 90% ee. The rate of racemization of the phosphine-substituted amide is powerfully influenced by the presence of palladium.

Introduction

Atropisomeric biaryls are well established as one of the most important classes of ligands for asymmetric metal-catalyzed reactions.[1] The angled aromatic rings serve as a useful scaffold for the attachment of metal-coordinating heteroatoms, and biaryl-complexed transition metals provide modern chemistry with some of its most powerful asymmetric catalysts.[2]



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Nonbiaryl atropisomers, on the other hand, have never been used as chiral ligands.[3] A number of types of nonbiaryl atropisomers are known,[4] and most prominent among them recently have been the chiral tertiary amides **1**[5] and the chiral anilides **2**.[6] Both types have a powerful ability to control relative stereochemistry in the racemic series,[7,8] and both have been used as chiral auxiliaries.[9,10] Single enantiomers of compounds related to **1** have been made by kinetic resolution using (−)-sparteine,[11] by atroposelective transformation of an enantiomerically pure arene−chromium tricarbonyl complex,[12] and by a dynamic resolution under thermodynamic control using a proline-derived diamine as the source of asymmetry.[13] Conformational stability sufficient for the existence of atropisomers requires severe steric hindrance, and this leads to the unreactivity that prevents the successful recycling of chiral auxiliaries derived from **1** and **2**. Our aim more recently has therefore been to synthesize single enantiomers of amides **1** for use, not as auxiliaries, but as chiral ligands for metal-catalyzed asymmetric reactions. We set out to make bidentate target ligands containing a second point of coordination (in addition to the amide O or N) which we would introduce using the amides' versatile ortholithiation chemistry.[14]

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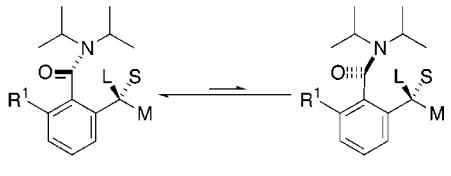
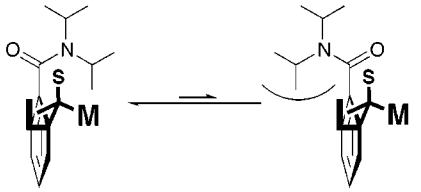
The potential thermal lability of a chiral axis makes thermodynamically controlled equilibration an attractive method for the synthesis of single atropisomeric diastereoisomers. The proline-derived diamine mentioned above[13] exerts its effect by favoring one diastereoisomeric conformer over the other at equilibrium. In general, a stereogenic center bearing sterically well differentiated groups S, M, and L becomes conformationally interlocked with an adjacent tertiary amide, resulting in a strong preference for a single axial conformation.[5] For example, with R^1 = H, conformer **3a** is significantly favored over conformer **3b** when S = H, M = Me, L = R_3Si,[15] or S = H, M = NHMe, L = secondary alkyl.[16] For such 2-substituted benzamides, the diastereoisomeric conformers about the Ar−CO bond interconvert rapidly (on the laboratory, though not the NMR, time scale), with a half-life of <1 s.[17,18] For a 2,6-disubstituted benzamides, on the other hand, with $R^1 \neq$ H, the diastereoisomeric conformers interconvert much more slowly:[19] they become diastereoisomeric *atropisomers*[20] and heat may be required to convert **3b** to **3a**.

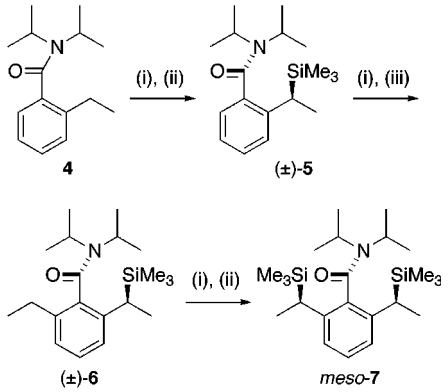




We have exploited the preferences of amides bearing chiral 2-substituents by using rotationally restricted amides to relay stereochemistry from one stereogenic center to another, for example, by the route shown in Scheme 1.[15] Lateral lithiation and silylation gives racemic amide **5**, which adopts predominantly the conformation shown. Ortholithiation and introduction of a 6-substituent then lock this conformation into the structure of a single atropisomeric diastereoisomer (±)-**6**. Finally, diastereoselective lateral lithiation, controlled by the Ar−CO axis, and stereospecific quench with Me_3SiCl, gives *meso*-**7**.

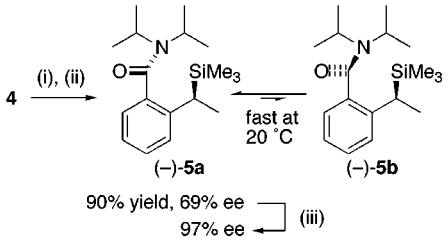
In this paper, we describe the application of (−)-sparteine-mediated silylation of **4**[21,22] to the asymmetric synthesis of **1** via enantiomerically enriched **5**. We also describe the first use of nonbiaryl atropisomers as chiral ligands for metal-catalyzed reactions, showing that phosphine derivatives of **1** function as ligands for asymmetric palladium-catalyzed allylic substitution reactions.

Scheme 1. Relaying Stereochemistry through an Amide Axis[a]



[a] Key: (i) *s*-BuLi, −78 °C, THF; (ii) Me_3SiCl; (iii) EtI.

Scheme 2. Asymmetric Silylation of a 2-Ethylbenzamide[a]



[a] Key: (i) *s*-BuLi, (−)-sparteine, *t*-BuOMe, pentane, −78 °C; (ii) Me_3SiCl; (iii) recrystallize × 2 (petroleum ether).

Results

Asymmetric Synthesis of Atropisomeric Amides. Amide **4** was laterally lithiated and silylated in the presence of freshly distilled and rigorously degassed (−)-sparteine, using the method of Beak and co-workers (Scheme 2).[21] We obtained the product silane (*S*)-**5** in 93% yield and 69% ee. Two recrystallizations from petroleum ether returned material of >97% ee, and this material was used for all subsequent reactions. From the X-ray crystal structure (Figure 1) of (*S*)-**5**, we were able to confirm its absolute stereochemistry, which in earlier work had been deduced by conversion to a compound of known optical rotation.[21]

Figure 1b shows the X-ray crystal structure of **5** viewed along the Ar−CH(Me)$SiMe_3$ bond. It indicates that the conformation of **5** in the crystalline state is in accord with our proposal that compounds of the general structure **3** adopt a conformation **3a**, though it does not prove that this conformation is preferred in solution. We were, however, able to use ^{1}H NMR to deduce that (*S*)-**5** exists in predominantly one conformer about its Ar−CO axis in $CDCl_3$. The Ar−CO rotation of 2-substituted tertiary benzamides, while not leading to separable atropisomers, is typically slow on the NMR time scale.[18] When the interconverting conformers are enantiomeric, this slow rotation manifests itself in the appearance of two pairs of diastereotopic doublets corresponding to the diastereotopic N-*i*-Pr_2 methyl groups. For (−)-**5**, Ar−CO rotation leads to *diastereoisomeric* conformers, which we would expect to see as two complete sets of signals in

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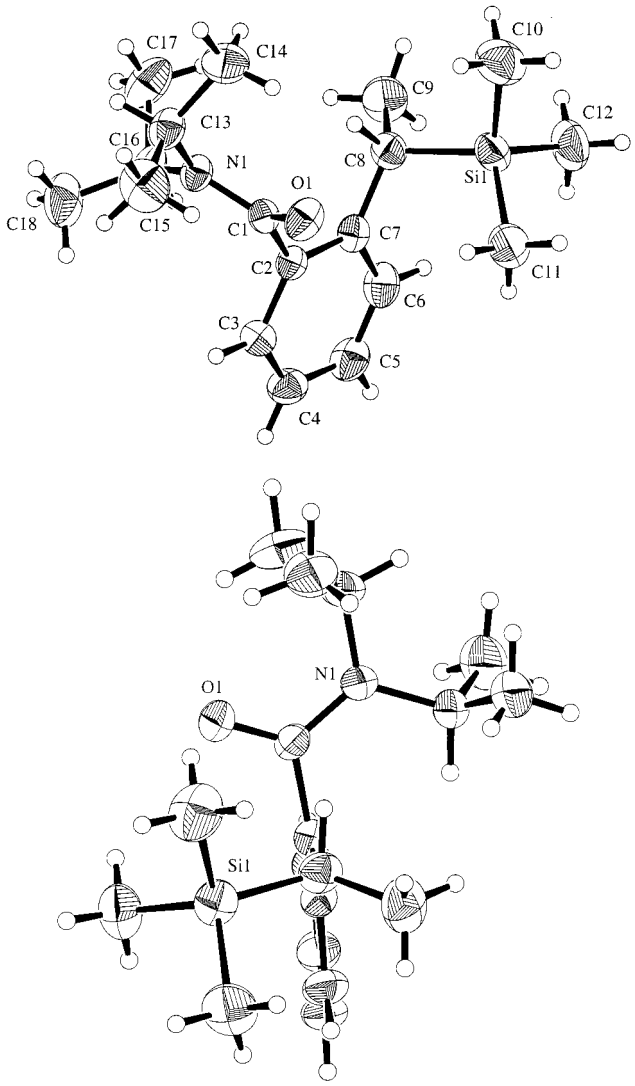


Figure 1. X-ray crystal structure of (*S*)-**5**: (a) viewed from front; (b) viewed along Ar−CH(Me)$SiMe_3$ bond.

Table 1. Enantioselective Synthesis of Atropisomeric Amides

electrophile	R	**8**, yield (%)	**9**, yield (%)	**8**, $[\alpha]^{23}_D$	**9**, $[\alpha]^{23}_D$
acetone	$Me_2C(OH)$−	**8a**, 50	**9a**, 99	+42.5	+32.0
MeI	Me−	**8b**, 98	**9b**, 99	+18.9	+3.2
$Ph_2P(O)Cl$	$Ph_2P(O)$−	**8c**, 81	**9c**, 99	+40.3	+18.0
Ph_2PCl	Ph_2P−	**8d**, 79	**9d**, 86	−44.0	−4.0
PhSSPh	PhS−	**8e**, 87	**9e**, 100	−28.9	−29.2

the ^{1}H NMR spectrum at ambient temperature. The ^{1}H NMR spectrum of (−)-**5** shows these two sets of signals in a ratio of 10:1, indicating that (−)-**5** is 90% one conformer about the Ar−CO axis at ambient temperature.

Trapping the major *conformer* of (−)-**5** as a major *atropisomer* allowed us to cash in the absolute stereochemistry of the silicon-bearing center. To do this, rotation of the amide group was blocked with a second ortho substituent on the benzamide ring. The amide (−)-**5** was treated with *s*-BuLi to ortholithiate it,[14] and the organolithium was quenched with the range of electrophiles shown in Table 1 to give **8a**−**e** (Scheme 3). The NMR spectra of the crude reactions mixtures indicated >10:1 atroposelectivity (in some cases much higher[36]) in these reactions, and all of the products were obtained as

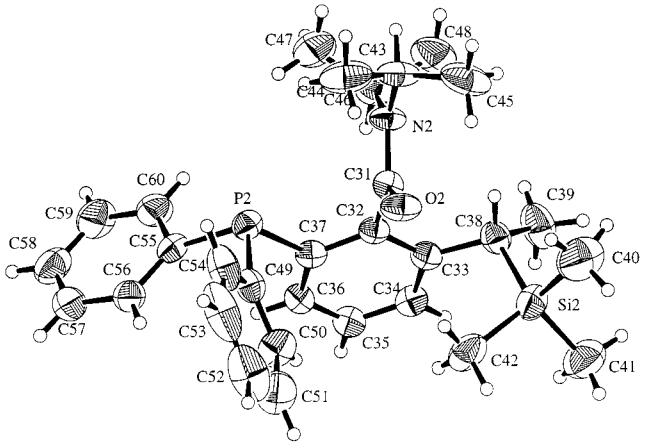
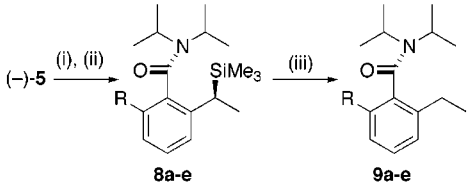


Figure 2. X-ray crystal structure of **8d**.

Scheme 3. Enantioselective Synthesis of Atropisomeric Amides[a]



single diastereoisomeric atropisomers (by ^{1}H NMR) after purification by chromatography. Oxidation of **8d** to **8c** was minimized by using a nonaqueous workup procedure.

The final step in the asymmetric synthesis required removal of the silyl group to leave single *enantiomeric* atropisomers. Protodesilylation was easily achieved for all five compounds **8a**−**e** by treatment with TBAF at 20 °C for 5 min, giving **9a**−**e** (Scheme 3 and Table 1).

The stereochemistry of **8d** was proved by X-ray crystal structure determination (Figure 2), which, although it could not re-confirm the absolute stereochemistry of the compound, did confirm the relative stereochemistry between the stereogenic center and the amide axis, which remains as shown for **5**. Presumably, therefore, the major conformer of **5** in solution, whose lithiation leads to **8**, has the same Ar−CO conformation as that shown by **5** in the crystalline state. Figure 2 also clearly indicates the perpendicular arrangement of the ring and the amide group, and the continued conformational preference of the (trimethylsilyl)ethyl substituent.

The enantiomeric purity of **9b** was confirmed to be >98% ee by ^{1}H NMR in the presence of the chiral solvating agent (+)-TFAE,[22] which clearly split the Ar-Me singlet of racemic **9b** into two enantiomeric signals.

Barriers to Racemization of the Atropisomers. Although compounds **9** are still 2,6-disubstituted benzamides, and are therefore expected to be kinetically stable to racemization,[18] their silylated precursors **8** had, additionally, *thermodynamic* stability relative to their atropisomeric diastereoisomers (see discussion below and Scheme 5). With this thermodynamic resistance to Ar−CO rotation removed, there was a danger that slow racemization of **9** might take place even at room temperature. We assessed the ease of racemization of each of the final products by following the first-order decay in optical rotation with time at a suitable temperature. The Eyring equation[23] was used to derive a value for $\Delta G^{\ddagger}_{rac}$ from the rate constant *k*. For **9d** we repeated the

Table 2. Rate of Racemization of Atropisomeric Amides

entry	amide	R	additive[a]	T/°C[b]	$k/10^{-5}$ s^{-1}	$\Delta G^{\ddagger}_{rac}$/kJ mol^{-1}	$t_{1/2}{}^{25}{}_{rac}$
1	**9a**	$Me_2C(OH)-$		93[c]	1.04 ± 0.03	125.2 ± 0.3	30 years
2	**9b**	Me		50	2.76 ± 0.01	107.5 ± 0.3	10 days
3	**9c**	$Ph_2P(O)-$		50	7.65 ± 0.07	104.8 ± 0.3	3 days
4	**9d**	Ph_2P		55	18.7 ± 0.1	104.0 ± 0.3	2 days
5	**9d**	Ph_2P		45	5.17 ± 0.005	104.2 ± 0.3	2 days
6	**9d**	Ph_2P		35	1.49 ± 0.01	104.0 ± 0.3	2 days
7	**9e**	PhS		40	21.40 ± 0.07	98.8 ± 0.3	6 hours
8	**9b**	Me	$[PdCl(\pi\text{-allyl})]_2$	50	2.27 ± 0.15	108.1 ± 0.5	10 days
9	**9d**	Ph_2P	$[PdCl(\pi\text{-allyl})]_2$	45	2400 ± 50	87.9 ± 0.3	5 min
10	**9d**	Ph_2P	$Ti(OEt)_2$	45	5.30 ± 0.04	104.1 ± 0.3	2 days
11	**9d**	Ph_2P	$AlMe_3$	45	4.83 ± 0.14	104.4 ± 0.5	2 days

[a] 1 equiv in metal. [b] ±0.5 °C. [c] Dioxane as solvent.

experiment at three temperatures and determined that $|\Delta S^{\ddagger}_{rac}| < 30$ J mol^{-1} K^{-1}.[24] On the basis of this assumption, we estimated half-lives for racemization of **9a**−**e** at 25 °C. All of these values are presented in Table 2 (entries 1−7).

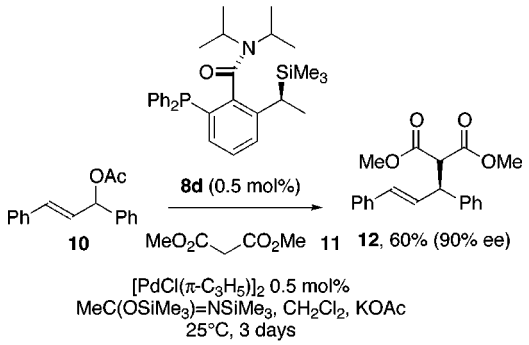
Racemization was slowest with R = alkyl, and **9a** (with a tertiary alkyl substituent) had almost complete conformational stability (entry 1). Even **9b**, with R = Me (entry 2), racemised more slowly than the phosphorus compounds **9c** and **9d** (entries 3 and 4). We have already noted that a trialkylsilyl group provides a poor block to bond rotation,[18] and this feature appears to be general for the second row elements, with sulfide **9e** racemizing still more rapidly (entry 7). Phosphine **9d** was nonetheless conformationally stable enough for us to hope for its successful application as a chiral ligand at room temperature or below and on time-scales shorter than 24 h. There was little difference between the rate of racemization of the phosphine **9d** and the phosphine oxide **9c**.

The First Use of Nonbiaryl Atropisomers as Chiral Ligands. A wide range of heterosubstituted arylphosphines have been used as ligands in palladium-catalyzed asymmetric allylic substitution reactions.[25] Among the most successful of these are Trost's amidophosphines, and many others are P,N or P,O-bidentate ligands. The stereoelectronics of such "soft−hard" ligand−metal complexes has been proposed as a key factor in the stereocontrol exerted by some of these ligands.[26,27]

Our first trial allylic substitutions were carried out with **8d**, whose silyl group eliminates the danger of slow atropisomerization during the reaction by making it *thermodynamically* stable to epimerization. 1,3-Diphenylpropenyl acetate **10** and dimethyl malonate **11** were treated with 1 mol % Pd (as $[PdCl(\pi\text{-allyl})]_2$) in the presence of 0.5 mol % **8d** as a chiral ligand (Scheme 4). The reaction took 3 days at 25 °C to give 60% yield of product (−)-**12**, which was formed with 90% ee (by chiral GC).

We presume the asymmetric induction in this reaction arises from the chirality of the stereogenic axis of **8d**, and that the silicon-bearing stereogenic center has little direct influence on the reaction center. We therefore expected a similar result with the silyl-"deprotected" ligand **9d**. However, when the reaction of **10** and **11** was repeated using this ligand, although the rate was similar (36% yield after 48 h) the product **12** was racemic. Moreover, the ligand **9d** recovered from the reaction turned out to be optically inactive, rather than having the ca. 35−40% ee we would expect after 3 days at 25 °C (see Table 2, entry 4).

Scheme 4. Asymmetric Allylic Substitution Using 8d as a Chiral Ligand



To find out why **9d** had racemized so quickly, its rate of racemization was re-determined in the presence of palladium (Table 2, entry 9). Remarkably, palladium caused the barrier to racemization to drop by 16 kJ mol^{-1}, and the rate of racemization to increase 500-fold, giving an estimated half-life for the racemization of **9d** at 25 °C in the presence of palladium of only 5 min. The lack of enantiomeric enrichment in the allylic substitution product is simply explained by the fact that racemization of the ligand occurs much faster than the substitution reaction.

The increase in rate of racemization appears to be due both to the phosphine substituent and to the presence of palladium, since adding palladium to the methyl-substituted **9b** (entry 8) had almost no effect on the rate of racemization. The hard, oxophilic Lewis acids $Ti(OEt)_4$ and $AlMe_3$ similarly had essentially no effect on the rate of racemization of the phosphine **9d** (entries 10, 11).

Discussion

The novel strategy employed in the asymmetric synthesis of **9** is outlined in Scheme 5. The starting amide **4** is a pair of rapidly interconverting (small $\Delta G^{\ddagger}_{rac}$) enantiomeric (*a*R and *a*S) conformers about the Ar−CO bond. Asymmetric construction of the stereogenic center in **5** perturbs the populations of the conformers, favoring *a*R over *a*S. This thermodynamic perturbation of populations is then fixed kinetically, by introduction of the substituent R into **8**. Now the thermodynamic perturbation—the

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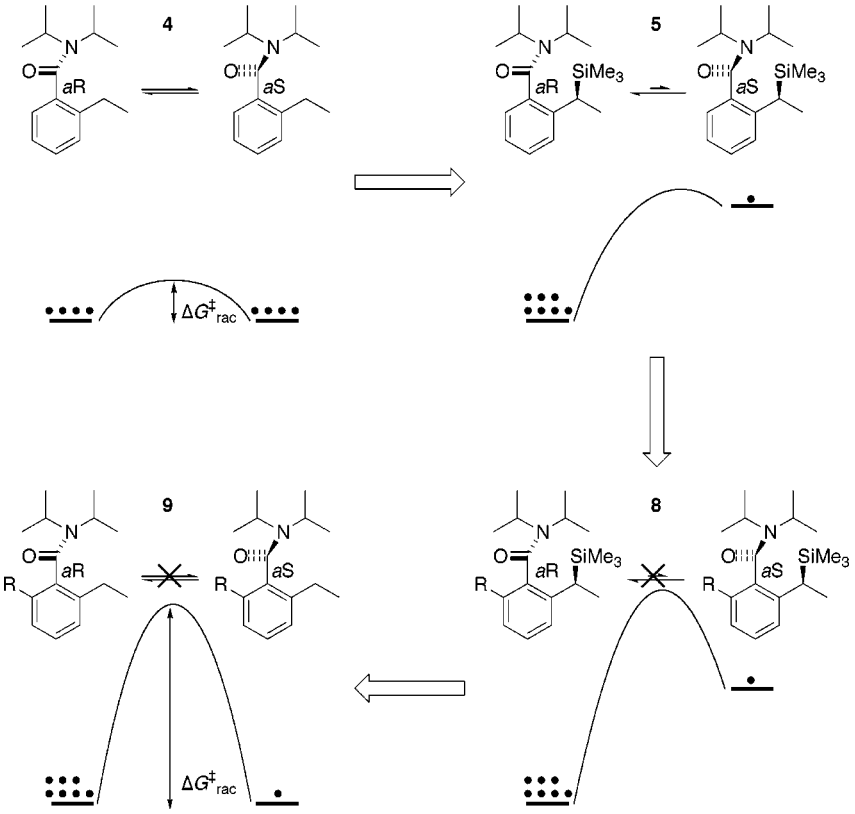
Scheme 5. Strategy in the Asymmetric Synthesis of 9



stereogenic center—can be removed, and the kinetic barrier to reestablishment of equilibrium (large $\Delta G^{\ddagger}_{rac}$) allows enantiomeric excess to be retained in the products **9**.

The Pd-catalyzed substitution reactions presumably involve phosphines **8d** and **9d** as bidentate ligands for Pd. Trost's secondary amido-phosphine ligands[28] are superficially similar in structure, and they too perform better when some degree of conformational restriction is introduced into the amide and C−P bonds, allowing chirality to be transferred from the ligand backbone to the metal. Our ligand has a soft (P) and a hard (probably N, but possibly O) coordination site, each surrounded by considerable steric encumbrance, and with few bonds able to rotate freely. Further investigation will be required before we can propose a detailed transition state for the reaction.

As for the accelerated racemization of **9d** in the presence of palladium − presumably, a P−Pd−N (or maybe a P−Pd−O) chelate stabilizes the transition state for Ar−CO rotation. Metal complexation is known to affect rates of C−N rotation in amides, with hard, oxophilic Lewis acids lowering the rate,[29] and soft, azaphilic metals raising it.[30] We have found, in a similar amide, that C−N rotation and Ar−CO rotation are interlocked, with the two occurring simultaneously through a gearing effect.[31] In other cases, rates of C−N and Ar−CO rotation are closely matched, again pointing to interlocked rotation.[18] Yet if the increased rate of Ar−CO rotation in this case had been a consequence simply of an increased rate of C−N rotation due to N−Pd coordination, a similar effect would be expected for methyl-substituted **9b**. Addition of the same palladium complex to **9b** to resulted in no increase in rotation rate. Similarly, Ti and Al Lewis acids, which would be expected to slow C−N rotation, had no significant effect on Ar−CO rotation in **9d**.

While the racemization of **9d** precludes the use of this, and similar, atropisomeric compounds as ligands for palladium, the use of conformational interlocking (such as that in **8d**) to control the conformation around a ligand's binding site is an important and more generally exploitable concept. The 90% ee obtained in the reaction of **8d** is remarkble because presumably the palladium also lowers the barrier to atropisomerization of **8d**. However, the silyl group makes **8d** thermodynamically stable relative to its diastereoisomer and prevents it epimerising. We now aim to use the versatile lithiation chemistry of tertiary amides to develop a novel range of conformationally constrained ligands for use in this, and other, metal catalyzed reactions.

Experimental Section

General Methods. Pentane was distilled under nitrogen from calcium hydride. *tert*-Butyl methyl ether, diethyl ether (referred to as "ether") and tetrahydrofuran (THF) were distilled under nitrogen from sodium benzophenone ketyl. Dry solvents were transferred to reaction vessels by syringe. "Petrol" refers to redistilled bp 40−60 °C petroleum ether. (−)-Sparteine was distilled at reduced pressure from calcium hydride directly before use. Commercial *sec*-butyllithium (as a solution in hexanes) was titrated using diphenylacetone tosylhydrazone prior to use. Melting points are uncorrected. Column chromatography was performed using the method of Still, Kahn and Mitra[32] with Merck silica gel 60H (230−300

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mesh) as the stationary phase. Thin-layer chromatography was performed using Merck silica 60 F_{254} aluminum-backed plates.

***N,N*-Diisopropyl-2-ethylbenzamide 4.**[21] *sec*-Butyllithium (9.48 mL, 1.3 M solution in cyclohexane, 12.32 mmol) was added dropwise to a solution of *N,N*-diisopropylbenzamide (2.30 g, 11.20 mmol) in THF (120 mL), cooled to −78 °C under an atmosphere of nitrogen. After 1 h at − 78 °C, ethyl iodide (1.79 mL, 22.40 mmol) was added. The solution was allowed to warm to room temperature, water (50 mL) was added, and the THF was removed under reduced pressure. The aqueous phase was extracted with dichloromethane (3 × 30 mL), and the combined extracts were washed with water (30 mL), dried over magnesium sulfate, and filtered. The solvent was evaporated, and the crude product was purified by column chromatography (eluting with 5% ethyl acetate in light petroleum) to give the amide **4** as a white crystalline solid (2.61 g, 100%): mp 90−92 °C (lit.[21] mp 91−93 °C); R_f(petrol/EtOAc 9:1) 0.47; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.34−7.17 (3H, m), 7.11 (1H, d, J = 7.3 Hz), 3.71 (1H, sept, J = 7 Hz), 3.54 (1H, sept, J = 7 Hz), 2.79−2.58 (2H, m), 1.61 (6H, d, J = 7 Hz), 1.29 (3H, t, J = 7.5 Hz), 1.14 (3H, d, J = 7 Hz), 1.11 (3H, d, J = 7 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.5, 139.8, 138.0, 128.5, 128.1, 125.6, 124.6, 50.6, 45.6, 25.6, 20.6, 20.6, 20.5, 20.4, 15.1.

(*S*)-*N,N*-Diisopropyl-2-(1-trimethylsilylethyl)benzamide 5.[21] Freshly distilled (−)-sparteine (644 mg, 3 mmol, 1.2 equiv) was added to 2-ethylbenzamide **4** (582 mg, 2.5 mmol, 1 equiv) in a predried, nitrogen filled flask. Pentane (75 mL) and *tert*-butyl methyl ether (75 mL) were added, and the resulting solution degassed using three freeze−pump−thaw cycles. The solution was cooled to −78 °C, and *sec*-butyllithium (2 mL of a 1.4 M solution, 1.1 equiv) was added, turning the solution deep purple. After a further 1.5 h at −78 °C, trimethylsilyl chloride (0.5 mL, 1.5 equiv) was added. Stirring at −78 °C was continued for a further 7 h, after which the solution was pale red in color. Methanol (1 mL) was added, and the solution was allowed to warm to room temperature. Phosphoric acid (0.5 M aq) was added, and the mixture was extracted into ether. The organic layer was separated and washed again with phosphoric acid (0.5 M aq) and then with water, before being dried (magnesium sulfate) and concentrated under reduced pressure to give the crude product as a viscous clear oil. The crude product was purified by column chromatography (eluting with petrol/EtOAc 19:1), to give the *title compound* **5** (708 mg, 93%), as a colorless, crystalline solid with an enantiomeric excess of 69% (by GC on chiral stationary phase). Successive recrystallization of this compound from petrol afforded material of 98% ee [by chiral GC: 25m × 0.32 mm 0.25u CP-Chirasil-DEX CB, retention times 77:08.1 (99.133%), 77:43.3 (0.867%)]. mp 71−72 °C (Lit.[21] 68−70 °C), R_f(petrol/EtOAc 19:1) 0.15; IR (film/$CHCl_3$) 2962, 1632 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.05−7.29 (5H, m), 3.67 (1H, sept, J = 6.5 Hz), 3.49 (1H, sept, J = 6.5 Hz), 2.17 (1H, q, J = 7.5 Hz), 1.57 (6H, t, J = 6.5 Hz), 1.34 (3H, d, J = 7.5 Hz), 1.13 (3H, d, J = 6.5 Hz), 1.04 (3H, d, J = 6.5 Hz), 0.00 (9H, s) − about 10% of less stable conformer visible at 3.81 (sept, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.6, 142.5, 137.4, 127.9, 126.4, 125.0, 124.4, 50.3, 45.5, 25.4, 20.6, 20.3, 16.3, −2.9; MS (CI) *m/z* (rel intensity) 306 (MH^+, 100); HRMS (EI) calcd for $C_{18}H_{31}NOSi$ (M^+) 305.2175, found 305.2172 (0.9 ppm).

Ortholithiation of Silylated Benzamide 5. *sec*-Butyllithium (1.1 equiv) was added to a solution of benzamide **5** (1 equiv) in THF (0.03M) at −78 °C. The resulting orange solution was then stirred at this temperature for 30 min, followed by addition of the electrophile (1.5 equiv). The reaction was allowed to warm to room temperature, poured into water, and extracted into EtOAc. The combined extracts were dried (magnesium sulfate) and concentrated under reduced pressure to give the crude product, which was purified by column chromatography to give **8a**−**e**.

(*S,R*$_a$)-*N,N*-Diisopropyl-2-(1-trimethylsilylethyl)-6-(1-hydroxy-1-methyl)ethylbenzamide 8a. By this method, benzamide **5** (153 mg) and acetone gave an oil which was purified by column chromatography (eluting with petrol/EtOAc 9:1) to yield the *title compound* **8a** (91 mg, 50%) as a white solid: mp 83−84 °C; R_f(petrol/EtOAc 4:1) 0.37; IR (film/$CHCl_3$) 3540 (br), 2958, 1602 cm^{-1};^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.21 (1H, t, J = 8 Hz), 6.99 (2H, dq, J = 1.5, 8 Hz), 3.66 (1H, sept, J = 6.5 Hz), 3.51 (1H, sept, J = 7 Hz), 3.11 (1H, br s), 2.34 (1H, q, J = 7.5 Hz), 1.58 (6H, s), 1.57 (3H, d, J = 7 Hz), 1.55 (3H, d, J = 7 Hz), 1.37 (3H, d, J = 7.5 Hz), 1.14 (3H, d, J = 6.5 Hz), 1.13 (3H, d, J = 6.5 Hz), −0.05 (9 H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.1, 145.8, 143.2, 132.0, 127.2, 124.0, 123.2, 74.4, 50.5, 45.8, 34.9, 31.2, 24.2, 20.6, 20.3, 19.6, 19.5, 16.5, −2.8; MS (EI) *m/z* (rel intensity) 363 (M^+, 30), 304 (53), 263 (100); HRMS (EI) calcd for $C_{21}H_{37}NO_2Si$ (M^+) 363.2593, found 363.2587 (1.7 ppm); $[\alpha]^{23}_D$ +42.5 ($CHCl_3$, c = 1).

(*S,R*$_a$)-*N,N*-Diisopropyl-2-(1-trimethylsilylethyl)-6-methylbenzamide 8b. In the same way, benzamide **5** (153 mg) and methyl iodide gave an oil that was purified by column chromatography (eluting with petrol/EtOAc 19:1) to yield the *title compound* **8b** (156 mg, 98%) as a white solid: mp 84−85 °C; R_f(petrol/EtOAc 19:1) 0.17; IR (film/$CHCl_3$) 2960, 1628, cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.16 (1H, t, J = 7.5 Hz), 6.96 (1H, d, J = 7.5 Hz), 6.94 (1H, d, J = 7.5 Hz), 3.69 (1H, sept, J = 6.5 Hz), 3.52 (1H, sept, J = 6.5 Hz), 2.30 (3H, s), 2.15 (1H, q, J = 7.5 Hz), 1.62 (3H, d, J = 6.5 Hz), 1.61 (3H, d, J = 6.5 Hz), 1.35 (3H, d, J = 7.5 Hz), 1.14 (3H, d, J = 6.5 Hz), 1.10 (3H, d, J = 6.5 Hz), 0.00 (9H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.0, 142.4, 136.6, 133.4, 127.3, 126.1, 123.4, 50.1, 45.6, 25.3, 21.0, 20.9, 20.3 (×2), 19.3, 16.4, −2.9; MS (CI) *m/z* (rel intensity) 320 (MH^+, 100); HRMS (CI) calcd for $C_{19}H_{33}NOSi$ (MH^+) 319.2331, found 319.2325 (2.0 ppm); $[\alpha]^{23}_D$ +18.9 ($CHCl_3$, c = 3). Anal. Calcd for $C_{19}H_{33}NOSi$: C, 71.41; H, 10.41; N, 4.38. Found: C, 71.73; H, 10.04; N, 4.42.

(*S,S*$_a$)-*N,N*-Diisopropyl-2-(1-trimethylsilylethyl)-6-diphenylphosphonylbenzamide 8c. In the same way, benzamide **5** (153 mg) and diphenylphosphinic chloride gave an oil which was purified by column chromatography (eluting with petrol/EtOAc 1:1) to yield the *title compound* **8** (204 mg, 81%) as a white solid: mp 165−167 °C, R_f(petrol/EtOAc 1:1) 0.23; IR (film/$CHCl_3$) 2956, 2928, 1631, 1204 cm^{-1};^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.29−7.61, (11H, m), 7.18 (1H, dt, J = 3, 7.5 Hz), 6.84 (1H, ddd, J = 1, 7.5, 13.5 Hz), 3.66 (1H, sept, J = 7 Hz), 3.51 (1H, sept, J = 6.5 Hz), 2.44 (1H, q, J = 7.5 Hz), 1.59 (3H, d, J = 7 Hz), 1.49 (3H, d, J = 7 Hz), 1.40 (3H, d, J = 6.5 Hz), 1.39 (3H, d, J = 7.5 Hz), 1.13 (3H, d, J = 6.5 Hz), −0.07 (9H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 167.6 (d, J = 3.5 Hz), 144.8 (d, J = 10.0 Hz), 140.5 (d, J = 8.0 Hz), 134.4 (d, J = 103.0 Hz), 133.4 (d, J = 105.5 Hz), 132.3 (d, J = 9.0 Hz), 131.8 (d, J = 10.5 Hz), 131.4 (d, J = 3.5 Hz), 131.4 (d, J = 3.0 Hz), 129.6 (d, J = 13.0 Hz), 129.5 (d, J = 3.0 Hz), 128.4 (d, J = 100.5 Hz), 128.2 (d, J = 12.0 Hz), 128.0 (d, J = 5.5 Hz), 126.6 (d, J = 13.5 Hz), 50.4, 45.8, 24.5, 21.2, 20.4, 19.7, 19.5, 16.1, −2.9; MS (CI) *m/z* (rel intensity) 506 (MH^+, 100); HRMS (EI) calcd for $C_{30}H_{40}NO_2PSi$ (M^+) 505.2566, found 505.2754 (1.6 ppm); $[\alpha]^{23}_D$ +40.3 ($CHCl_3$, c = 4). Anal. Calcd for $C_{30}H_{40}NO_2PSi$: C, 71.25; H, 7.97; N, 2.77; P, 6.12. Found: C, 71.33; H, 8.09; N, 2.77; P, 6.27.

(*S,S*$_a$)-*N,N*-Diisopropyl-2-(1-trimethylsilylethyl)-6-diphenylphosphinylbenzamide 8d. In the same way, benzamide **5** (153 mg) was lithiated and treated with chlorodiphenylphosphine. In place of the usual aqueous workup, the reaction was allowed to warm to room temperature and was then poured quickly through a pad of Celite. The flask and the Celite were washed with ether, and the filtrate was concentrated under reduced pressure. The resulting sticky oil was purified by column chromatography (eluting with petrol) to give the *title compound* **8d** (193 mg, 79%) as a white foam, which crystallized from petrol as colorless needles: mp 140−142 °C; R_f(petrol/EtOAc 9:1) 0.54; IR (film/$CHCl_3$) 3053, 2956, 2871, 1629 cm^{-1};^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.19−7.36 (12H, m), 6.83−6.87 (1H, m), 3.84 (1H, sept, J = 6.5 Hz), 3.57 (1H, sept, J = 7 Hz), 2.32, (1H, q, J = 7.5 Hz), 1.67 (3H, d, J = 7 Hz), 1.59 (3H, d, J = 7 Hz), 1.42 (3H, d, J = 7.5 Hz), 1.31 (3H, d, J = 6.5 Hz), 1.19 (3H, d, J = 6.5 Hz), 0.00 (9H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.0 (d, J = 5.0 Hz), 143.0 (d, J = 35.5 Hz), 143.0 (d, J = 8.0 Hz), 138.4 (d, J = 12.0 Hz), 137.0 (d, J

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= 11.0 Hz), 133.8 (d, J = 15.5 Hz), 133.3 (d, J = 19.0 Hz), 133.2 (d, J = 19.5 Hz), 130.6 (d, J = 2.0 Hz), 128.3 (d, J = 6.0 Hz), 128.1 (d, J = 4.0 Hz), 128.0 (d, J = 6.5 Hz), 127.7, 126.8, 50.3, 45.8, 25.3, 21.1, 20.8 (d, J = 6.0 Hz), 20.4, 20.0 (d, J = 2.0 Hz), 16.1, −2.8; MS (CI) *m/z* (rel intensity) 490 (MH^+, 100), 306 (35) 187 (70); HRMS (EI) calcd for $C_{30}H_{40}NOPSi$ (M^+) 489.2617, found 489.2622 (1.1 ppm); $[\alpha]^{23}_D$ −44.0 ($CHCl_3$, c = 2.68). Anal. Calcd for $C_{30}H_{40}NOPSi$: C, 73.58; H, 8.23; N, 2.86; P, 6.32. Found: C, 73.46; H, 8.29; N, 2.70; P, 6.32.

(*S,S*$_a$)-*N,N*-Diisopropyl-2-(1-trimethylsilylethyl)-6-phenylsulfanylbenzamide 8e. In the same way, benzamide **5** (76 mg) and diphenyl disulfide (55 mg, 1.5 equiv, as a solution in 2 mL of THF) gave a waxy crude product that was purified by column chromatography (eluting with petrol/EtOAc 19:1) to give the *title compound* **8e** (90 mg, 87%) as a white solid: mp 140−142 °C; R_f(petrol/EtOAc 19:1) 0.27; IR (film/$CHCl_3$) 2960, 1631, cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.10−7.36 (6H, m), 7.00 (1H, dd, J = 1, 8 Hz), 6.95 (1H, dd, J = 1, 8 Hz), 3.72 (1H, sept, J = 6.5 Hz), 3.51 (1H, sept, J = 6.5 Hz), 2.21 (1H, q, J = 7.5 Hz), 1.60 (3H, d, J = 6.5 Hz), 1.57 (3H, d, J = 6.5 Hz), 1.35 (3H, d, J = 7.5 Hz), 1.19 (3H, d, J = 6.5 Hz), 1.13 (3H, d, J = 6.5 Hz), 0.00 (9H, s); ^1H NMR ($CDCl_3$, 75 MHz) δ 168.0, 143.9, 138.4, 136.1, 132.3, 131.0, 128.9, 128.2, 128.1, 126.8, 124.9, 50.4, 45.8, 25.6, 21.0, 20.8, 20.3, 20.1, 16.3, −2.8; MS (CI) *m/z* 414 (MH^+, 100); HRMS (EI) calcd for $C_{24}H_{35}NOSSi$ (M^+) 413.2209, found 413.2223 (3.5 ppm); $[\alpha]^{23}_D$ −28.4 ($CHCl_3$, c = 1). Anal. Calcd for $C_{24}H_{35}NOSSi$: C, 69.68; H, 8.53; N, 3.39; S, 7.75. Found: C, 69.65; H, 8.84; N, 3.43; S, 7.92.

Desilylation of Benzamides 8. TBAF (1 M solution in THF, 10 equiv) was added to a solution of the silylated amide **8** in THF (0.02M) at room temperature. The resulting solution was stirred for 5 min, then poured into cold water and extracted into ether. The combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure at <20 °C to give the crude products, which were purified by column chromatography (fractions kept at ca. 0−5 °C), to give the desilylated products **9**.

(*S*$_a$)-*N,N*-Diisopropyl-2-ethyl-6-(1-hydroxy-1-methyl)-ethylbenzamide 9a. Silylated benzamide **8a** (35 mg) was treated with TBAF according to the general procedure. Purification of the crude product by column chromatography (eluting with petrol/EtOAc 9:1 at ca. 0−5 °C) gave the *title compound* **9a** (28 mg, 99%) as a white solid: mp 96−98 °C; R_f(petrol/EtOAc 4:1) 0.17; IR (film/$CHCl_3$) 3415, 2975, 2932, 2874, 1609 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.22 (1H, t, J = 8 Hz), 7.12 (1H, d, J = 7 Hz), 7.07 (1H, d, J = 8 Hz), 3.61 (1H, sept, J = 7.5 Hz), 3.50 (1H, sept, J = 6.5 Hz), 2.85 (1H, br s), 2.75 (1H, dq, J = 15, 7.5 Hz), 2.58 (1H, dq, J = 15, 7.5 Hz), 1.60 (3H, s), 1.57 (3H, s), 1.57 (3H, d, J = 6.5 Hz), 1.56 (3H, d, J = 6.5 Hz), 1.22 (3H, t, J = 7.5 Hz), 1.16 (3H, d, J = 6.5 Hz), 1.09 (3H, d, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.0, 145.4, 140.1, 133.5, 127.6, 126.4, 124.7, 74.5, 50.9, 45.7, 34.7, 31.2, 25.3, 20.2, 20.1, 19.5, 15.3; MS (CI) *m/z* (rel intensity) 292 (MH^+, 100), 274 (20); HRMS (CI) calcd for $C_{18}H_{30}NO_2$ (MH^+) 292.2276, found 292.2274 (0.6 ppm); $[\alpha]_D^{23}$ +32.0 ($CHCl_3$, c = 1). Anal. Calcd for $C_{18}H_{30}NO_2$: C, 74.18; H, 10.03; N, 4.81. Found: C, 73.83; H, 10.24; N, 4.72.

(*R*$_a$)-*N,N*-Diisopropyl-2-ethyl-6-methylbenzamide 9b. Silylated benzamide **8b** (150 mg) was treated with TBAF according to the general procedure. Purification of the crude product by column chromatography (eluting with petrol/EtOAc 9:1 at ca. 0−5 °C) gave the *title compound* **9b** (115 mg, 99%) as white solid: mp 102−103 °C; R_f(petrol/EtOAc 9:1) 0.49; IR (film/$CHCl_3$) 2629, 2933, 2876, 1621 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.08 (1H, t, J = 7.5 Hz), 6.99 (1H, d, J = 7.5 Hz), 6.93 (1H, d, J = 7.5 Hz), 3.52 (1H, sept, J = 6.5 Hz), 3.43 (1H, sept, J = 6.5 Hz), 2.57 (1H, dq, J = 15, 7.5 Hz), 2.46 (1H, dq, J = 15, 7.5 Hz), 2.21 (3H, s), 1.52 (3H, d, J = 6.5 Hz), 1.16 (3H, t, J = 7.5 Hz), 1.03 (3H, d, J = 6.5 Hz), 1.01 (3H, d, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.0, 139.4, 137.5, 133.1, 127.6, 127.5, 125.3, 50.6, 45.7, 25.7, 21.0, 20.4, 20.4, 19.0, 15.1; MS (EI) *m/z* (rel intensity) 247 (M^+, 10), 232 (15), 218 (15), 204 (10), 147 (100); HRMS (EI) calcd for $C_{16}H_{25}NO$ (M^+) 247.1936, found 247.1929 (2.8 ppm); $[\alpha]^{23}_D$ +3.2 (CHCl3, c = 1). Anal. Calcd for $C_{16}H_{25}NO$: C, 77.68; H, 10.19; N, 5.66. Found: C, 77.76; H, 10.47; N, 5.72.

The ^1H NMR spectrum of this material in the presence of (+)-2,2,2-trifluoro-1-(9-anthryl)ethanol (TFAE)22 showed an Ar-Me signal originating from the minor enantiomer of comparable size to the ^{13}C-coupled side-peaks of the Ar-Me signal of the major enantiomer, from which we deduce an ee of >98%. Addition of (±)-**9b** to the sample of (+)-**9b** proved the identity of this minor peak.

(*S*$_a$)-*N,N*-Diisopropyl-2-ethyl-6-diphenylphosphonyl-benzamide 9c. Silylated benzamide **8c** (170 mg) was treated with TBAF according to the general procedure. Purification of the crude product by column chromatography (eluting with petrol/EtOAc 3:1 at ca. 0−5 °C) gave the *title compound* **9c** (144 mg, 99%), as a white foam: R_f(petrol/EtOAc) 0.40; IR (film/$CHCl_3$) 2975, 2929, 1630 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.59−7.67 (4H, m), 7.38−7.55 (7H, m), 7.23 (1H, dt, J = 3.0, 8.0 Hz), 7.00 (1H, ddd, J = 1.0, 7.5, 13.5 Hz), 3.68 (1H, sept, J = 7.0 Hz), 3.50 (1H, sept, J = 7.0 Hz), 2.80 (1H, dq, J = 15, 7.5 Hz), 2.65 (1H, dq, J = 15, 7.5 Hz), 1.55, (3H, d, J = 7.0 Hz), 1.51 (3H, d, J = 7.0 Hz), 1.36 (3H, d, J = 6.5 Hz), 1.25 (3H, t, J = 7.5 Hz), 1.10 (3H, d, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 167.6 (d, J = 3.5 Hz), 142.1 (d, J = 8.0 Hz), 141.4 (d, J = 10.0 Hz), 134.1 (d, J = 103.0 Hz), 132.9 (d, J = 108.0 Hz), 132.2 (d, J = 9.0 Hz), 131.9 (d, J = 9.0 Hz), 131.8 (d, J = 5.5 Hz), 131.5 (d, J = 3.0 Hz), 131.5 (d, J = 2.0 Hz), 131.0 (d, J = 13.0 Hz), 128.3 (d, J = 12.0 Hz), 128.1 (d, J = 101.5 Hz), 128.1 (d, J = 13.0 Hz), 126.9 (d, J = 13.5 Hz), 51.0, 45.9, 25.1, 20.9, 20.3, 19.9, 19.7, 14.9; MS (EI) *m/z* (rel intensity) 434 (MH^+, 100), 333 (20) 100 (42); HRMS (EI) calcd for $C_{27}H_{32}NO_2P$ (M^+) 433.2171, found 433.2175 (1.0 ppm); $[\alpha]_D^{23}$ +18.0 ($CHCl_3$, c = 1.6). Anal. Calcd for $C_{27}H_{32}NO_2P$: C, 74.80; H, 7.44; N, 3.23; P, 7.14. Found: C, 74.56; H, 7.61; N, 3.05; P, 6.83.

(*S*$_a$)-*N,N*-Diisopropyl-2-ethyl-6-diphenylphosphinyl-benzamide 9d. Silylated benzamide **8d** (112 mg) was treated with TBAF according to the general procedure. Purification of the crude product by column chromatography (eluting with petrol/EtOAc 9:1 at ca. 0−5 °C) gave the *title compound* **9d** (82 mg, 86%) as white solid: mp 129−130 °C; R_f(petrol/EtOAc 4:1) 0.46; IR (film/$CHCl_3$) 2969, 1628 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.22−7.38 (12H, m), 7.05 (1 H, ddd, J = 1, 3.5, 7.5 Hz), 3.80 (1H, sept, J = 6.5 Hz), 3.59 (1H, sept, J = 6.5 Hz), 2.81 (1H, dq, J = 15, 7.5 Hz), 2.67 (1H, dq, J = 15, 7.5 Hz), 1.70 (3H, d, J = 6.5 Hz), 1.63 (3H, d, J = 6.5 Hz), 1.32 (3H, d, J = 7.5 Hz), 1.24 (3H, d, J = 6.5 Hz), 1.18 (3H, d, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.9 (d, J = 5.0 Hz), 144.5 (d, J = 36.5 Hz), 139.6 (d, J = 8.5 Hz), 138.1 (d, J = 11.5 Hz), 137.0 (d, J = 11.5 Hz), 133.6 (d, J = 15.5 Hz), 133.4 (d, J = 19.5 Hz), 133.1 (d, J = 19.0 Hz), 132.1 (d, J = 2.5 Hz), 129.0, 128.3, 128.3 (d, J = 5.5 Hz), 128.2 (d, J = 7.5 Hz), 128.0, 127.8, 21.0, 20.8 (d, J = 6.0 Hz), 20.5, 20.1 (d, J = 2.0 Hz), 14.7; MS (EI) *m/z* (rel intensity) 418 (MH^+, 10 − self-CI), 417 (M^+, 8), 374 (50), 332 (100); HRMS (EI) calcd for $C_{27}H_{32}NOP$ (M^+) 417.2221, found 417.2218 (0.7 ppm); $[\alpha]_D^{23}$ −4.0 ($CHCl_3$, c = 1). Anal. Calcd for $C_{27}H_{32}NOP$: C, 77.67; H, 7.72; N, 3.35; P, 7.42. Found: C, 77.38; H, 8.05; N, 3.31; P, 7.35.

(*S*$_a$)-*N,N*-Diisopropyl-2-ethyl-6-phenylsulfanylbenzamide 9e. Silylated benzamide **8e** (47 mg) was treated with TBAF according to the general procedure. Purification of the crude product by column chromatography (eluting with petrol/EtOAc 9:1 at ca. 0−5 °C) gave the *title compound* **9e** (42 mg, quantitative) as a white solid: mp 94−95 °C; R_f(petrol/EtOAc 4:1) 0.45; IR (film/$CHCl_3$) 2971, 1630 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.51−7.54 (2H, m), 7.37−7.46 (3H, m), 7.27−7.29 (2H, m), 7.14−7.17 (1H, m), 3.83 (1H, sept, J = 6.5 Hz), 3.67 (1H, sept, J = 7 Hz), 2.87 (1H, dq, J = 15, 7.5 Hz), 2.71 (1H, dq, J = 15, 7.5 Hz), 1.75 (6H, t, J = 7 Hz), 1.41 (3H, t, J = 7.5 Hz), 1.36 (3H, d, J = 6.5 Hz), 1.25 (3H, d, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.0 (DEPT: quat), 140.6 (quat), 139.3 (quat), 135.5 (quat), 132.3 (quat), 131.5 (CH), 129.2 (CH), 129.0 (CH), 128.3 (CH), 127.0 (CH), 126.7 (CH), 50.9 (CH), 45.9 (CH), 25.6 (CH_2), 21.0 (CH_3), 20.9 (CH_3), 20.5 (CH_3), 20.1 (CH_3), 14.8 (CH_3); MS (CI) *m/z* (rel intensity) 342 (MH^+, 100); HRMS (EI) calcd for $C_{21}H_{27}NOS$ (M^+) 341.1813, found 341.1816 (0.8

ppm); $[\alpha]_D^{23}$ −29.2 ($CHCl_3$, $c = 1$). Anal. Calcd for $C_{21}H_{27}NOS$: C, 73.86; H, 7.97; N, 4.10. Found: C, 73.66; H, 8.11; N, 4.14.

Rates of Racemization of 9. The barriers to rotation of the amide axis in compounds **9a**−**e** were established by racemization studies at constant temperature. These studies were carried out by monitoring the optical rotations of solutions of the amides (in chloroform or dioxane, using a mercury source at 578 nm) in a jacketed cell. The cell was kept at constant temperature by pumping water from a thermostatically controlled heating bath through the cell jacket. Observation of the optical rotation (α) over regular time intervals gave a smooth first-order decay curve from which the rate constant for racemization (k) was calculated using the curve-fitting application "Ultrafit" for the Macintosh.

Asymmetric Allylic Substitution Reactions.[33,34] Potassium acetate (1 mg), *N*,*O*-bistrimethylsilyl acetamide (BSA, 609 mg, 3 equiv), dimethyl malonate (396 mg, 3 equiv), and acetate **10** (252 mg, 1 equiv) were added to a solution of allylpalladium dichloride dimer (1.8 mg, 1 mol % Pd) and phosphine **8d** (2.5 mg, 0.5 mol %) in dichloromethane (2 mL) under nitrogen. The mixture was stirred at room temperature for 36 h, poured into water, extracted into dichloromethane, dried over magnesium sulfate, and concentrated under reduced pressure to give the crude product oil. The crude product was purified by column chromatography (eluting with petrol/EtOAc 9:1) to give the substitution product (−)-**12** as a crystalline solid, with data matching that described in the literature[35] and enantiomeric excess of 90% (by HPLC on chiral stationary phase: Regis Whelk-O1 column 4.6 × 250 mm, eluting with 20% IPA in hexane, flow rate 1 mL/min, retention times 10.1 and 11.06 min): mp 95−96 °C; IR ($CHCl_3$)/cm^{-1} 3028, 2952, 1757, 1738;^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.14−7.31 (10H, m), 6.45 (1H, d, 15.5 Hz), 6.29 (1H, dd, 8.5, 15.5 Hz), 4.23 (1H, dd, J = 8.5, 11.0 Hz), 3.92 (1H, d, J = 11.0 Hz), 3.67 (3H, s), 3.48 (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.1, 167.7, 140.1, 136.8, 131.8, 129.1, 128.7, 128.4, 127.8, 127.5, 127.1, 126.4, 57.6, 52.5, 52.4, 49.1; $[\alpha]_D^{23}$ −16.9 ($CHCl_3$, $c = 1$).

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of compounds **8a**−**e** and **9a**−**e**. X-ray crystal data for (−)-**5** and **8d**. ^{1}H NMR spectrum of (+)-**9b** in the presence of (+)-TFAE. This material is available free of charge via the Internet at http://pubs.acs.org.

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(36) Higher selectivity may be obtained because the 10:1 ratio of conformers may improve at −78 °C or in THF (though NMR experiments at −30 °C showed conformational ratios similar to those at +25 °C) or because of epimerization of the thermodynamically less stable isomer during the reaction workup. The yield of diastereoisomerically pure **8b** suggests that at least in this case this second mechanism is operating.