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Highly Enantioselective (−)-Sparteine-Mediated Lateral Metalation-Functionalization of Remote Silyl Protected *ortho*-Ethyl *N,N*-Dialkyl Aryl *O*-Carbamates[§]

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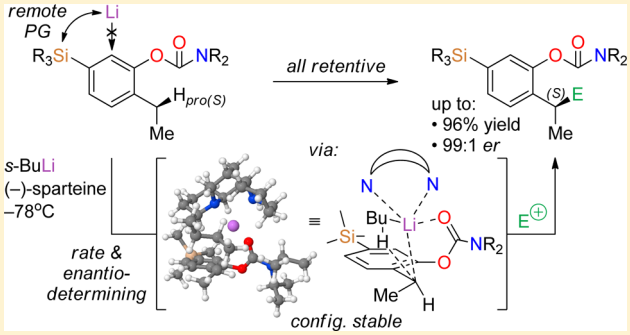
Supporting Information

ABSTRACT: We report the enantioselective, lateral deprotonation of *ortho*-protected or functionalized tertiary *N,N*-dialkyl aryl *O*-carbamates **5**−**7** (Scheme 2) and *meta*-protected carbamates **14**, **15**, and **20** (Schemes 5 and 7) by *s*-BuLi/(−)-sparteine and subsequent quench with a variety of electrophiles to give products **11**−**13** and **16**, **17**, and **21** in yields up to 96% and enantiomeric ratios up to 99:1. The influence of organolithium reagents, ratio of organolithium/(−)-sparteine pair versus *N,N*-dialkyl aryl *O*-carbamate starting materials, temperature, solvents, electrophiles, substituents located *ortho* or *meta* to the *O*-carbamate moiety, and *O*-carbamate *N*-substituents was investigated. The identical absolute configuration of the stereogenic center of the major enantiomers of the products, as established by single-crystal X-ray analysis for substrates (*S*)-**11c**, (*S*)-**19**, and (*S*)-**21a**, provides evidence for a consistent stereochemical course in the enantioselective deprotonation. Mechanistic investigations, including an estimate of the configurational stability of the benzyllithium species **9** (starting from **12e**; Scheme 8) and **23** (starting from **17e**; Scheme 9), both derived by tin−lithium exchange, and **24** (starting from **20**; Scheme 9) are reported. The experimental results, together with semiempirical molecular orbital calculations (PM3/SMD), are consistent with a process in which enantioinduction occurs in the deprotonation step (Scheme 11).



INTRODUCTION

Since the original work of Nozaki[1] and Guetté[2] 4 decades ago and the pioneering contributions of the groups of Hoppe[3a−f] and, subsequently, Beak,[4] the application of the enantiopure lupine alkaloid (−)-sparteine as an additive in "carbanionic"[5] enantioselective synthesis has gained considerable prominence. Thus, the broad scope of (−)-sparteine-mediated carbanionic transformations[3,4,6] has been demonstrated, *inter alia*, in the preparation of enantioenriched natural and unnatural amino acids,[7] asymmetric inter-[8] and intramolecular[9] carbolithiations, an enantioselective Li-ene-reaction,[10] the enantioselective preparation of functionalized 1,5-cyclononadienes[11] and *anti* homoaldol products,[12] enantioselective functionalization of small[13] and medium-sized[14] rings, the generation of P-stereogenic centers,[15] and the enantioselective lithiation of unsaturated carbamates.[16]

Subsequent to the initial observations of Nozaki[1] and the seminal studies of Hoppe[3] and Beak,[4] (−)-sparteine-mediated benzylic metalation has been investigated on several types of derivatives, **1**−**4** (Scheme 1), which take advantage of an α-heteroatom **1a**−**f**,[17] an *ortho*-heteroatom **2**,[18] an allyl amino moiety **3**,[19] a β-heteroatom **4**[20] and their coordination effects.[21]

Stimulated by these findings, we previously investigated the (−)-sparteine-induced, highly enantioselective preparation of planar chiral ferrocenes and their application in an asymmetric alkylation and Pd(0)-catalyzed allylic substitution.[22] The original studies of Clark[23] and the results of Beak[4b] especially motivated our work in establishing a (−)-sparteine-mediated enantioselective synthesis of tetrahydroisoquinolin-1-ones.[24] Involvement in studies of the *O*-carbamate as the most

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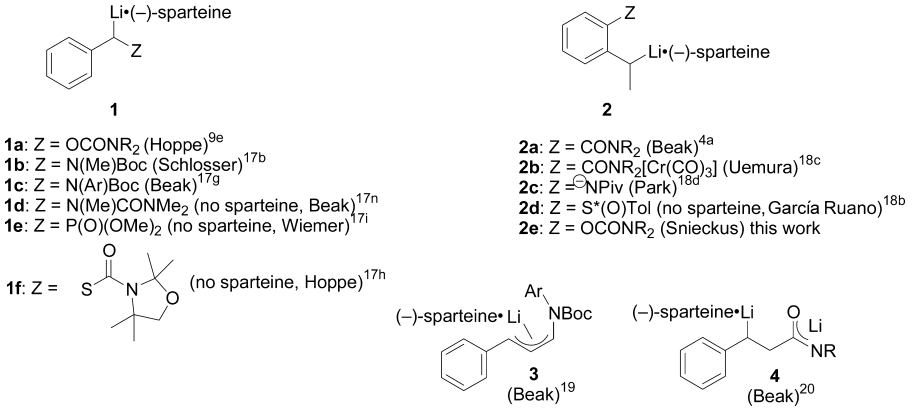
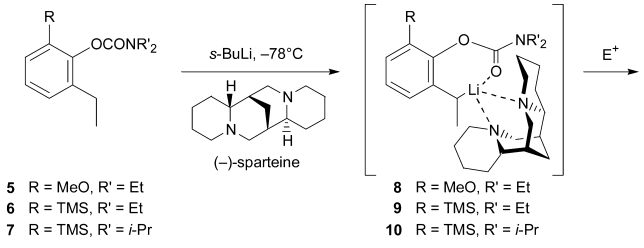
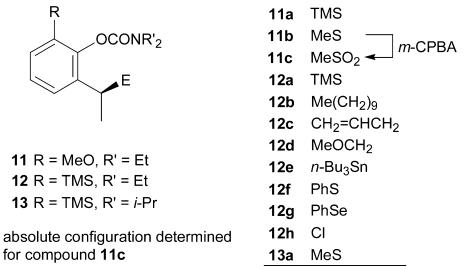
Scheme 1. Previous Work on Enantioselective Benzylic Metalation



powerful directed metalation group (DMG)[25] provided the impetus to undertake the investigation of the (−)-sparteine-mediated lateral metalation of tertiary *ortho*-ethyl *N*,*N*-dialkyl aryl *O*-carbamates. We now detail results on studies concerning *O*-carbamates **5**−**7** (Scheme 2), **14**, **15** (Scheme 5), and **20** (Scheme 7) with respect to variation of conditions, electrophiles, and ratio of organolithium/(−)-sparteine complex to starting *N*,*N*-dialkyl aryl *O*-carbamate as well as, perhaps of particular interest, the effect of *ortho* and *meta* substitution on the enantioselectivity of the reaction. We thereby offer a contribution that may serve in the further rational improvement of new methodologies for asymmetric synthesis.

Scheme 2. Lateral Metalation of 2-Ethyl Aryl *O*-Carbamates: Evading the Anionic *Ortho* Fries Rearrangement



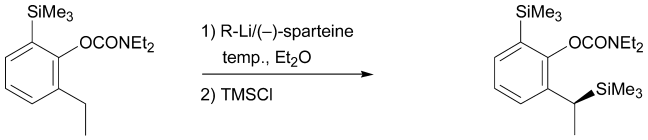


E	
11a	TMS
11b	MeS
11c	$MeSO_2$ ← *m*-CPBA
12a	TMS
12b	$Me(CH_2)_9$
12c	$CH_2{=}CHCH_2$
12d	$MeOCH_2$
12e	*n*-Bu_3Sn
12f	PhS
12g	PhSe
12h	Cl
13a	MeS

RESULTS AND DISCUSSION

Effect of Base and Solvent on the (−)-Sparteine-Mediated Lateral Metalation of *N*,*N*-Dialkyl Aryl *O*-Carbamates. 6-MeO- and 6-TMS-2-ethyl phenyl diethyl O-carbamates **5** and **6**[26] were chosen for the initial studies in order to preclude competitive anionic *ortho*-Fries rearrangement[25a] along with considerations of synthetic potential in desilylation,[27] hydrolysis,[28] and cross-coupling[29] reactions. (−)-Sparteine-mediated lateral metalation conditions were tested on carbamate **6** using alkyllithiums and LDA and TMSCl as the electrophile quench (Scheme 3). A temperature effect was noted with the *n*-BuLi/(−)-sparteine combination. Thus, from

Scheme 3. (−)-Sparteine-Mediated Lateral Metalation of Compound 6: Optimization of Enantioinduction as a Function of the Base



R-Li	temp.	yield	er
n-BuLi	−78°C	16%	92:8
n-BuLi	−40°C	64%	82:18
s-BuLi	−78°C	60%	83:17
t-BuLi	−78°C	84%	racemic
LDA	−78°C	no reaction	–
LDA	−30°C	82%	racemic

absolute configuration assigned by analogy with compound **11c**

the reaction at −78 °C, in addition to recovery of unreacted **6**, compound **12a** was obtained in 16% yield and 92:8 er, whereas at −40 °C, **12a** was isolated in 64% yield and 82:18 er. Application of *t*-BuLi/(−)-sparteine at −78 °C afforded **12a** in high yield (84%), but as a racemic mixture, a result consistent with the observation by Beak in using these base/(−)-sparteine conditions for the metalation of *N*-Boc-pyrrolidine.[30] While use of LDA/(−)-sparteine at −78 °C gave no product, at −30 °C, **12a** was obtained in 82% yield, but as a racemate. Metalation using *s*-BuLi/(−)-sparteine (2.2 equiv/2−3 h optimum conditions) at −78 °C furnished **12a** in 60% yield and 83:17 er. These conditions were adopted in all subsequent studies as a reasonable compromise in terms of yield and enantioselectivity at the lower temperature.

To determine the influence of solvent, the *N*,*N*-dialkyl aryl *O*-carbamates **5** and **6** were metalated under the optimized conditions in single and mixed solvent systems, and the resulting benzyllithium species were quenched with TMSCl or dimethyl disulfide (MeSSMe) to afford compounds **11a** and **11b** and **12a** and **13a**, respectively (Table 1).

As gleaned from Table 1, no enantioenrichment was observed when the metalation of 6-MeO-substituted *N*,*N*-dialkyl aryl *O*-carbamate **5** was carried out in THF (entry 1). The absence of enantioinduction suggests that the coordination effect of THF is competitively stronger than that of (−)-sparteine. Unlike Et_2O, THF saturates the coordination sphere of the lithium cation and thereby excludes complexation

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Table 1. Effect of Solvent on the (−)-Sparteine-Mediated Lateral Metalation of *N*,*N*-Dialkyl Aryl *O*-Carbamates 5−7

entry	starting material	solvent	product	yield, %[a]	er[b]
1	**5**	THF	**11a**	93	50:50
2	**5**	Et_2O	**11a**	34	96:4
3[c]	**5**	Et_2O	**11b**	46	94:6
4	**5**	*t*-BuOMe	**11a**	48	89:11
5	**5**	$(i\text{-Pr})_2O$	**11a**	50	96:4
6	**5**	hexanes	**11a**	<5	>99:1
7	**6**	Et_2O	**12a**	60	83:17
8	**6**	*t*-BuOMe	**12a**	75	76:24
9	**6**	$(i\text{-Pr})_2O$	**12a**	58	85:15
10	**6**	hexanes	**12a**	46	88:12
11	**6**	toluene	**12a**	9	88:12
12	**6**	*t*-BuOMe/toluene 1:3	**12a**	78	86:14
13[c]	**7**	Et_2O	**13a**	84	69:31

[a]Yields of isolated products. [b]Determined by CSP-HPLC (see Experimental Section). [c]MeSSMe used as electrophile.

with a bidentate ligand such as (−)-sparteine.[31] Although numerous low and absent enantioinductions in (−)-sparteine-mediated transformations of organolithium reagents in THF have been reported,[32] several instances of moderate-to-high enantioselectivities in reactions in this solvent should be noted.[33]

In the case of acyclic ethereal solvents, moderate-to-high enantiomeric ratios but only moderate yields of **11a** and **11b** (34−50%) were observed (entries 2−5). Attempted optimization by increasing the reaction time resulted in side reactions.[34] Although high er's were observed in hexanes (entry 6), limited solubility of **5** precluded attainment of acceptable yields. In comparison, the more soluble 6-TMS carbamate **6** showed reasonable enantioinduction and yields in ethereal (entries 7−9) as well as hydrocarbon (entry 10) and aromatic (entry 11) solvents. The best result was obtained when the optimal solvents regarding yield (entry 8) and enantioinduction (entry 11) were combined (entry 12). The results depicted in Table 2 show consistent enantioenrichments for a variety of products resulting from carbon (**12b−d**) and heteroatom (**12e−h**) electrophile introduction under these conditions.

The absolute configuration of the major enantiomer of **11b** was established by single-crystal X-ray crystallographic analysis of the corresponding sulfone **11c** obtained by oxidation using *m*-CPBA (Scheme 4; see Experimental Section).

Comparative Study of Diethyl- vs Diisopropyl Aryl *O*-Carbamates and *Ortho*-Methoxy vs *Ortho*-Trimethylsilyl Substituents.

A comparison of the effect of two substituents with different electronic and steric properties (6-MeO vs 6-TMS) and the steric influence of *N*-substituents (diethyl vs diisopropyl) is demonstrated by the results shown in Table 1. Thus, 6-MeO *N*,*N*-diethyl *O*-carbamate **5** afforded **11a** (entry 2) in 34% yield and 96:4 er and **11b** (entry 3) in 46% yield and 94:6 er. Under identical conditions (2.2 equiv *s*-BuLi/(−)-sparteine/Et_2O/−78 °C/2 h), the 6-TMS-substituted diethyl *O*-carbamate **6** gave **12a** (entry 7) in 60% yield and 83:17 er. When *ortho*-TMS-substituted *N*,*N*-diisopropyl aryl *O*-carbamate **7** was subjected to the conditions used for *N*,*N*-diethyl aryl *O*-carbamates **5** and **6**, product **13a** was isolated in 84% yield (entry 13), which is variably comparable to the yields obtained for **12a−h** (Tables 1 and 2), but with a substantially decreased er (69:31). These findings suggest that bulky substituents located *ortho* to the *O*-carbamate moiety together with sterically demanding *N*-carbamate substituent lead to a considerable loss of enantioselectivity.[35]

Table 2. Lateral Metalation−Electrophile Quench Reactions of 6 Using *s*-BuLi/(−)-Sparteine in *t*-BuOMe/Toluene 1:3

E^+	E	product	yield, %[a]	er
$Me(CH_2)_9Br$	$Me(CH_2)_9$	**12b**	54	83:17
$H_2C{=}CHCH_2Br$	$H_2C{=}CHCH_2$	**12c**	75	87:13
$MeOCH_2Cl$	$MeOCH_2$	**12d**	39	84:16
n-Bu_3SnCl	*n*-Bu_3Sn	**12e**	63	86:14
PhSSPh	PhS	**12f**	71	85:15
PhSeSePh	PhSe	**12g**	69	84:16
Cl_3CCCl_3	Cl	**12h**	64	90:10

[a]Yields of isolated products.

Introduction of Remote TBS Protection.

Guided by these results and based on the assumption that a bulky silyl substituent located *meta* to the carbamate would prevent the onset of the well-known *ortho*-deprotonation and anionic Fries rearrangement,[25a] the lateral metalation of 5-TBS derivatives **14** and **15** was investigated (Scheme 5).[36]

Gratifyingly, when compound **14**[37] was subjected to the optimized metalation conditions developed for **12a** (Table 1, entry 12) followed by TMSCl quench, product **16a** was obtained in 97:3 er (Scheme 5). However, as observed with other solvent systems,[38] the high enantioenrichment was compromised by low yields due to decarbamoylation (with C-to-O TMS migration). This problem was circumvented by the use of the corresponding *N*,*N*-diisopropyl aryl *O*-carbamate **15**,[37] whose solubility allowed deprotonation (2.2 equiv *s*-BuLi/(−)-sparteine, −78 °C, 2 h)[39] to be carried out in hexanes. Under these conditions and after TMSCl quench, product **17a** was obtained in both high yield and enantioselectivity (Table 3). As in the deprotonation studies of **5**−**7** (Scheme 2), use of less base was detrimental to the reaction. For example, the use of 1.2 equiv of *s*-BuLi/(−)-sparteine in the MeSSMe quench experiment afforded **17g** in 36% yield and 76:24 er. In previous studies, with few exceptions (in which up to 2[30b] or ≥2[10,11,30b] equiv of alkyllithium/(−)-sparteine were used), a range of 1.1−1.6 equiv of alkyllithium/(−)-sparteine had been applied.[18] As shown in Scheme 5, a sequential lateral metalation reaction consisting of deprotonation of **15** with 1.05 equiv *s*-BuLi/(−)-sparteine and quench with 1.05 equiv MeSSMe followed by 1 equiv *s*-BuLi/(−)-sparteine resulted in the formation of **17g** in 16% yield and 86:14 er. This suggests that, for this particular system, the total amount of *s*-BuLi/(−)-sparteine required to achieve synthetically useful yields must be added at the beginning of the reaction. Using the 5-TBS *N*,*N*-dialkyl aryl *O*-carbamate **15**, a broad scope of electrophiles was introduced to give products **17b−i** in good yields and enantioselectivities, with one exception (**17i**) that was not investigated further.

The absolute configuration of the major (*S*)-enantiomer of **17g** was determined by single-crystal X-ray crystallographic analysis of the (−)-camphanoate derivative **19** prepared by reductive cleavage of the carbamoyl group followed by esterification using enantiomerically pure (−)-camphanic acid chloride (Scheme 6; see Experimental Section).

Introduction of Remote TMS Protection.

Interestingly, and in contrast to previous metalation studies in the absence of

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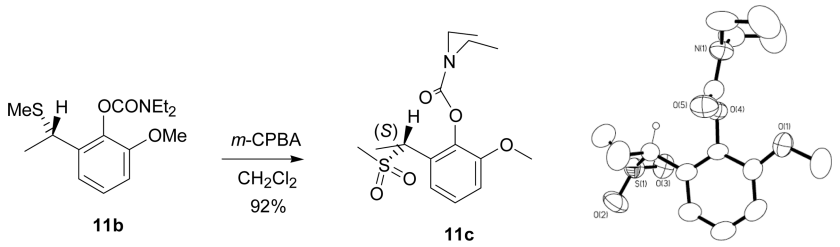
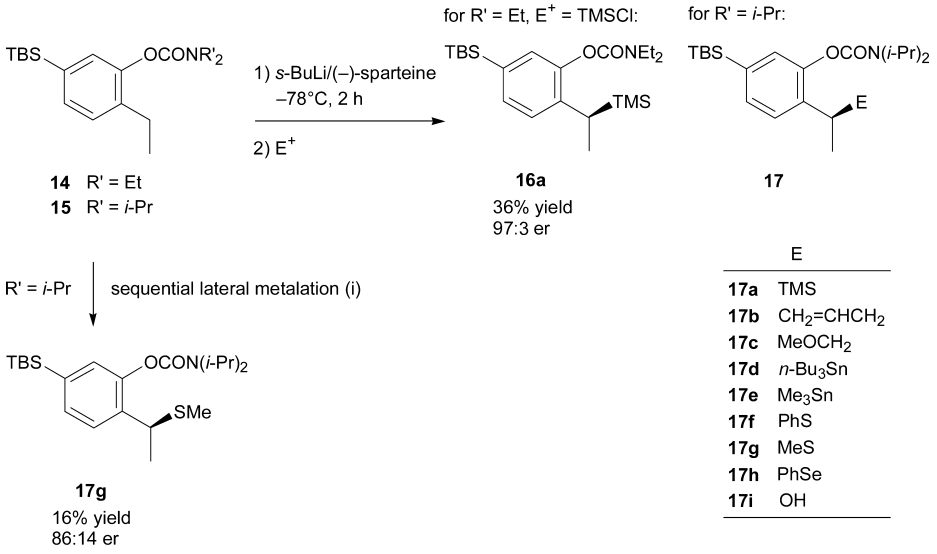
Scheme 4. Synthesis and ORTEP Plot of 11c[a]



[a]C-atoms are not labeled; H-atoms are omitted for clarity.

Scheme 5. Lateral Metalation of 2-Ethyl Aryl *O*-Carbamates: The Effect of Remote Protection



	E
17a	TMS
17b	CH_2=$CHCH_2$
17c	$MeOCH_2$
17d	*n*-Bu_3Sn
17e	Me_3Sn
17f	PhS
17g	MeS
17h	PhSe
17i	OH

i: 1.05 equiv *s*-BuLi/(–)-sparteine, Et_2O, –78°C, 2 h, then 1.05 equiv MeSSMe, –78°C, 1 h, then 1 equiv *s*-BuLi/(–)-sparteine, –78°C, 1 h.

Table 3. Lateral Metalation–Electrophile Quench Reactions of 15 Using *s*-BuLi/(–)-Sparteine in Hexanes

E^+	E	product	yield, %[a]	er
TMSCl	TMS	**17a**[b]	80	98:2
H_2C=$CHCH_2Br$	H_2C=$CHCH_2$	**17b**	85	—[c]
$MeOCH_2Cl$	$MeOCH_2$	**17c**	87	98:2
n-Bu_3SnCl	*n*-Bu_3Sn	**17d**	71	98:2
Me_3SnCl	Me_3Sn	**17e**[d]	91	96:4
PhSSPh	PhS	**17f**	91	99:1
MeSSMe	MeS	**17g**[d,e]	89	97:3
PhSeSePh	PhSe	**17h**	90	94:6
$Me_3SiOOSiMe_3$	OH	**17i**[d]	27	92:8

[a]Yields of isolated products. [b]Use of *n*-BuLi and *s*-BuLi in Et_2O led to a 77% yield and 98:2 er and 96% yield and 94:6 er, respectively. [c]Determination of er's using CSP-HPLC was unsuccessful. [d]Performed in Et_2O. [e]*s*-BuLi/(–)-sparteine (1.2 equiv) in Et_2O led to **17g** (36% yield, 76:24 er) and recovered starting material (41%).

(–)-sparteine which showed that *ortho*-deprotonation-anionic Fries rearrangement and lateral deprotonation are competitive,[28b] treatment of **20** under the standard *s*-BuLi/(–)-sparteine conditions followed by electrophile quench led to **21a** (E = MeS) and **21b** (E = Me_3Sn) in good yields and enantioselectivities with only a moderate solvent effect (Scheme 7), and no products resulting from *ortho* lithiation were observed.[40] The absolute configuration of the stereogenic center of the major (*S*)-enantiomer of **21a** was determined by single-crystal X-ray crystallographic analysis (Scheme 7; see Supporting Information).

Mechanistic Aspects. In the lithiation-substitution pathway, asymmetry is introduced by free energy differences in either the formation or reaction of the diastereomeric lithiated species.[4c] In order to distinguish between asymmetric deprotonation and asymmetric substitution, the protocol established by Beak was followed.[4a,b] Thus, compound **6** was subjected to metalation using *s*-BuLi in Et_2O for 2 h, and the resulting racemic lithio species **rac-9** was treated with (–)-sparteine followed by TMSCl (Scheme 8).

The isolated product **12a** (E = TMS), obtained in 70% yield, showed <51:49 er. A control experiment was conducted demonstrating the formation of **rac-9** in the absence of (–)-sparteine. Thus, quenching **rac-9** with TMSCl afforded **rac-12a** in 60% yield. In order to establish the enantiodetermining step, entantioenriched **12e** (86:14 er, prepared from **6** using 2.2 equiv of *s*-BuLi/(–)-sparteine, *t*-BuOMe/toluene 1:3, –78 °C, 2 h) was subjected to tin–lithium exchange (MeLi/TMEDA/Et_2O/–78 °C) followed by quench with TMSCl to afford **12a** with retention of (*S*)-configuration in 88% yield and with 76:24 er. We attribute the erosion in er from **12e** to **12a** to be possibly due to the conditions of the tin–lithium exchange reaction (conversion was unsuccessful in the absence of TMEDA), as has been previously observed.[41] These observations demonstrate that racemic lithiated species **rac-9** does not

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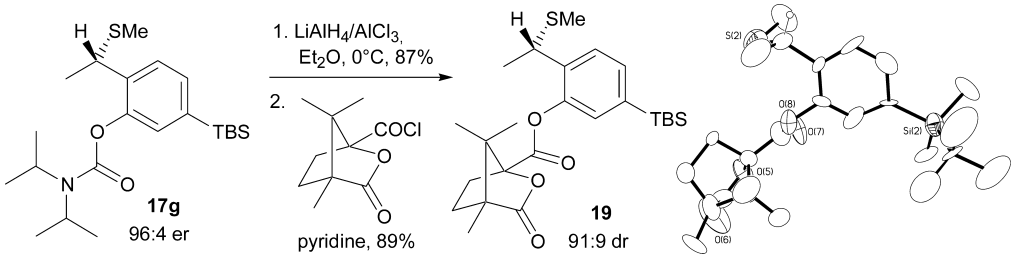
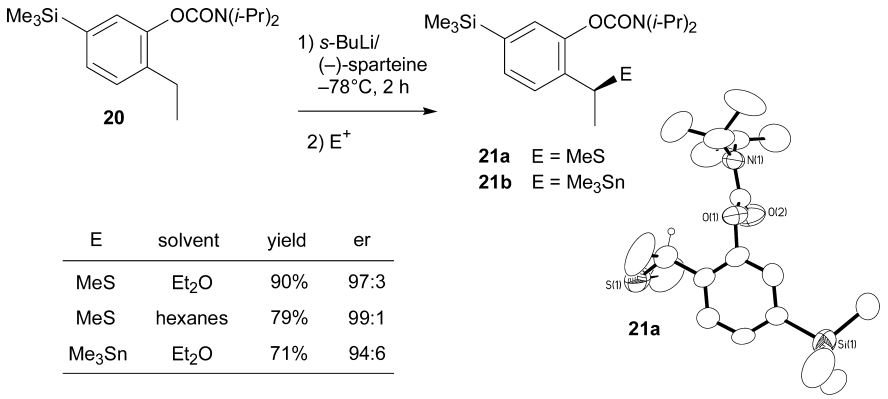
Scheme 6. Synthesis and ORTEP Plot of 19[a]



[a]H-atoms omitted for clarity.

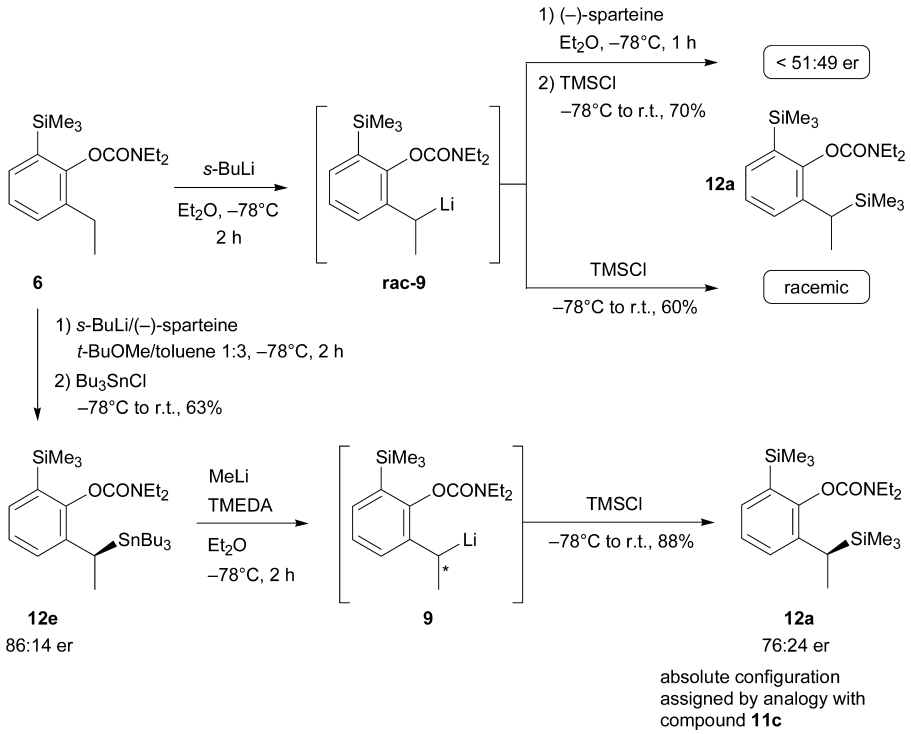
Scheme 7. TMS as a Remote Protecting Group and ORTEP Plot of 21a[a]



E	solvent	yield	er
MeS	Et_2O	90%	97:3
MeS	hexanes	79%	99:1
Me_3Sn	Et_2O	71%	94:6

[a]H-atoms omitted for clarity.

Scheme 8. Lateral Metalation of 6: Origin of the Observed Stereochemistry



lead to enantioinduction upon treatment with (−)-sparteine and subsequent reaction with TMSCl and that the enantioenriched lithiated **9** maintains, in large part, its configurational stability under the reaction conditions.[42] Therefore, the enantiodiscriminating step in the formation of compounds of type **12** and, by inference, other carbamates **11**, **16**, **17**, and **21**, occurs in the deprotonation and not in the substitution step. These results are in contrast to the studies of Beak, which reported leaving group-differentiated enantioselective alkylations in the (−)-sparteine-mediated lateral

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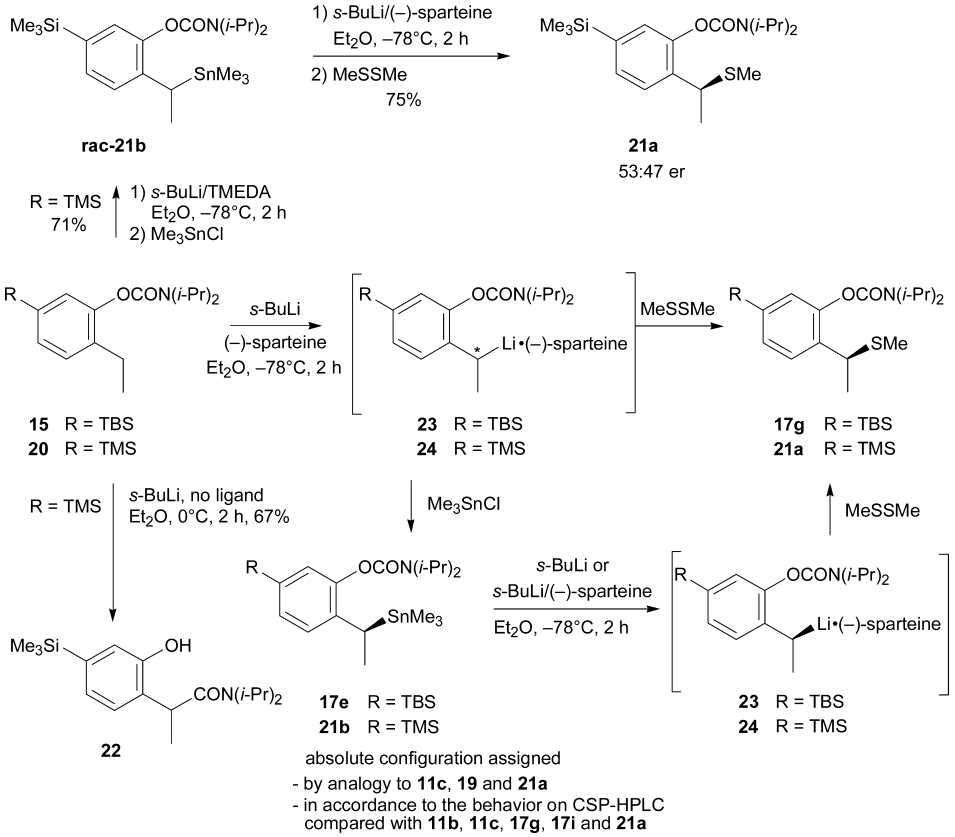
Scheme 9. Evidence for the Stereochemical Course of the (−)-Sparteine-Mediated Lateral Deprotonation Reaction



lithiation of *ortho*-ethyl *N*,*N*-diisopropyl benzamides.[4a,b] For the amide series, it was demonstrated that transfer of stereochemical information occurs in the postdeprotonation step via dynamic kinetic resolution. Addressing the enantiodiscriminating step, our results also contrast with those of Beak concerning the enantioselective lateral metalation of *N*-(2-ethylphenyl) pivalamides.[4b] In this series, enantioinduction was found to be independent of the electrophile and the configurational stability of the benzylic organolithium species was found to be strongly dependent on coordination with the diamine ligand. Transfer of stereochemical information was also found to occur postdeprotonation, but via dynamic thermodynamic resolution.[4a,b]

In order to obtain additional information on the stereodifferentiating step, a parallel study was performed on the *N*,*N*-dialkyl aryl *O*-carbamate **20** (Scheme 9). Attempts to prepare racemic **21a** by *s*-BuLi metalation in the absence of a ligand and MeSSMe quench afforded only the lateral carbamoyl migration product **22**, as precedented.[28b] To overcome this difficulty, **rac-21b** was prepared, subjected to tin−lithium exchange (2.2 equiv *s*-BuLi/(−)-sparteine, Et_2O, −78 °C, 2 h), and subsequently quenched with MeSSMe. Product **21a** was obtained in 75% yield and essentially racemic form (53:47 er). In addition to confirming that the extent of organolithium intermediate formation from tin−lithium exchange and from direct deprotonation are essentially identical,[30b] these results suggest that the asymmetric substitution reaction does not appear to be the enantiodetermining step for the described reactions of *ortho*-ethyl *N*,*N*-dialkyl aryl *O*-carbamates.

In a study aimed to obtain confirmation of the results observed on the enantioenriched stannylated diethyl *O*-carbamate **12e** (Scheme 8), the corresponding tin derivatives **17e** and **21b** (prepared by metalation-stannylation of **15** and **20**, respectively) were investigated (Scheme 9). Unfortunately, neither **17e** nor **21b** were amenable to single-crystal X-ray crystallographic analysis. However, the assignment of (*S*)-**17e** and (*S*)-**21b** configurations may be deduced on the basis of their elution behavior on CSP-HPLC (CHIRALCEL OD column) by comparison with that of **11c** (Scheme 4), **19** (Scheme 6), and **21a** (Scheme 7), whose absolute configurations were established by X-ray analysis. Thus, all major enantiomers of **11c**, **17e**, **19**, **21a**, and **21b** (as well as similar compounds **11b**, **17g**, and **17i**) had lower retention times and eluted first. On the basis of this assumption, the transformation of (*S*)-**17e** to (*S*)-**17g** was investigated in order to ascertain the configurational stability of species **23** on the time scale of the reaction (Scheme 9 and Table 4). In this pursuit,

Table 4. Configurational Stability of 23: Transformations of 17e to 17g[a]

er (**17e**)	*s*-BuLi, equiv	(−)-sparteine, equiv	yield, %[b]	er (**17g**)
82:18	1.2	1.2	49	77:23
82:18	2.1	2.1	67	78:22
82:18	2.1	—	49	74:26

[a]Metalation conditions: −78 °C/Et_2O/2 h. [b]Yields of isolated products.

enantioenriched (*S*)-**17e** (82:18 er) was subjected to tin−lithium exchange with 1.2 and 2.1 equiv of *s*-BuLi/(−)-sparteine and with 2.1 equiv of *s*-BuLi in the absence of the (−)-sparteine ligand followed by quench with 3.0 equiv of MeSSMe. Under the generally accepted assumption that tin−lithium exchange proceeds with retention of configuration,[43] (*S*)-**23** is the formed reactive intermediate. The degree of

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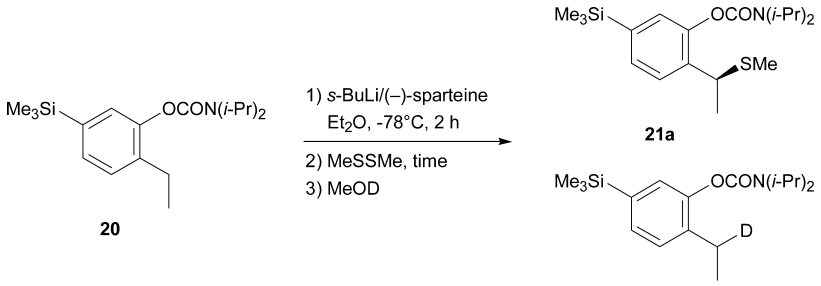
Scheme 10. Poor Man's Hoffmann Test



s-BuLi/(–)-sparteine	MeSSMe	time	yield (**21a**) %	er (**21a**)	yield (**d-20**) %
2.25 equiv	3 equiv	1 h	54	95:5	–
2.27 equiv	0.2 equiv	2 min	7	68:32	59

enrichment of isolated **17g**, whose configuration was identical to (*S*)-**17g** prepared by the *s*-BuLi/(−)-sparteine/MeSSMe route, varied from 74:26 er (*s*-BuLi without (−)-sparteine) to 78:22 er (2.1 equiv *s*-BuLi/(−)-sparteine), indicating that species **23** (and possibly **24**) is largely configurationally stable in the presence as well as in the absence of (−)-sparteine with respect to the rate of its reaction with MeSSMe under these conditions.[44]

Surprisingly, in contrast to observations by Beak[4b,17g,32b] and Hoppe,[10] attempts to obtain the (*R*)-enantiomer of **17g** by tin−lithium exchange in order to offer the desired confirmatory evidence for these observations were not successful. The aforementioned experiments offer indirect evidence for the substitution step in the conversion of **17e** into **17g** proceeding by retention of configuration. In the analogous lithiated species of *ortho*-ethyl benzamides, Beak has conclusively demonstrated that the retention and inversion pathways are a function of the nature and reactivity of the electrophile.[4b]

On the basis of the elegant studies of Hoffmann[45] concerning the configurational stability of diastereomeric lithiated species relative to the time scale of reaction with an electrophile (the Hoffmann test), Beak developed a modification that avoids the need for enantiomerically enriched reagents (poor man's Hoffmann test).[4b,17g,19,20,46] In one variation of this test, the product stereoselectivities for two reactions are compared: one with an excess and the other with a deficiency of electrophile. If these two reactions lead to products with different enantioselectivities, then nonequilibrating diastereomeric complexes undergoing reaction at different rates are involved. In adapting this test, two separate experiments were performed in parallel by subjecting **20** to identical lithiation conditions (Scheme 10). The resulting lithiated species were trapped with MeSSMe under the same conditions, except that one was treated with an excess and the other with a substoichiometric amount of the electrophile.

Use of 3.0 equiv of MeSSMe led to the isolation of **21a** with 95:5 er. If the benzyllithium species (**24**) is configurationally stable on the time scale of the electrophilic quench reaction, then this er reflects the relative population of diastereomeric complexes in solution; on the other hand, if **24** is configurationally unstable on this time scale, then the er reflects the difference in reaction rates of the two diastereomeric complexes. When 0.2 equiv of MeSSMe was used, **21a** was obtained with 68:32 er. The er obtained from quench with this deficient amount of electrophile reflects the relative rates of reaction of the two diastereomeric complexes. Since the er's resulting from these two experiments are significantly different, this suggests that **24** is configurationally stable on the time scale of the electrophilic trapping experiment, a prerequisite if, as outlined above, asymmetric deprotonation is the enantiodetermining step for the reaction.[32c,41b] As a further confirmatory experiment, in order to rule out the possibility of further lithiation of **21a**, especially when 0.2 equiv of MeSSMe is used, the reactions were quenched with MeOD, and the products were analyzed by ^{2}H NMR and MS analyses. Aside from the expected formation of **d-20** isolated in 59% yield (0.2 equiv of MeSSMe), no indication of further lithiation of **21a** (3.0 equiv of MeSSMe) was detected, as evidenced by a lack of deuterium incorporation.

The observed configurational stability of the laterally lithiated *ortho*-ethyl *N*,*N*-dialkyl aryl *O*-carbamates is in contrast to the observations of Beak for both the *ortho*-ethyl *N*,*N*-diisopropyl benzamides and *N*-(2-ethylphenyl) pivalamides,[4a,b] where the diastereomeric lithium complexes were found to be configurationally labile and enantioinduction occurs postdeprotonation via dynamic resolution processes. Furthermore, our mechanistic studies suggest that configurational stability in this series is independent of the steric environment surrounding the DMG and the lithiated center. The lithiated species are configurationally stable regardless of *ortho* (**9**) or *meta* (**23**, **24**) silyl substituion. This is in contrast with the results of Clayden,[47] which demonstrate that lithiated *ortho*-ethyl-*N*,*N*-diisopropyl benzamides are less configurationally stable than their more hindered lithiated 2-ethyl *N*,*N*-diisopropyl-1-naphthylamide analogues.[4a,b]

Molecular Modeling. In order to glean further information regarding the stereochemical course of the reaction, a series of semiempirical molecular orbital calculations (PM3) was carried out using a gas phase as well as a solvated (SMD) model.[48] Results for the reaction path of all substrates examined (**5**, **6**, **20**) are similar; thus, only one (**20**) is discussed in detail using the solvated model. A conformational search revealed three possible low-energy geometries (**A**, **B**, **C**) of the substrate which differ by rotation about the Ph−Et bond. Introduction of the *s*-BuLi/(−)-sparteine complex results in coordination of lithium to the carbamoyl carbonyl group in each case. Subsequent prochiral hydrogen deprotonation may occur for the adducts of conformations **A** and **B** (Scheme 11) but not for

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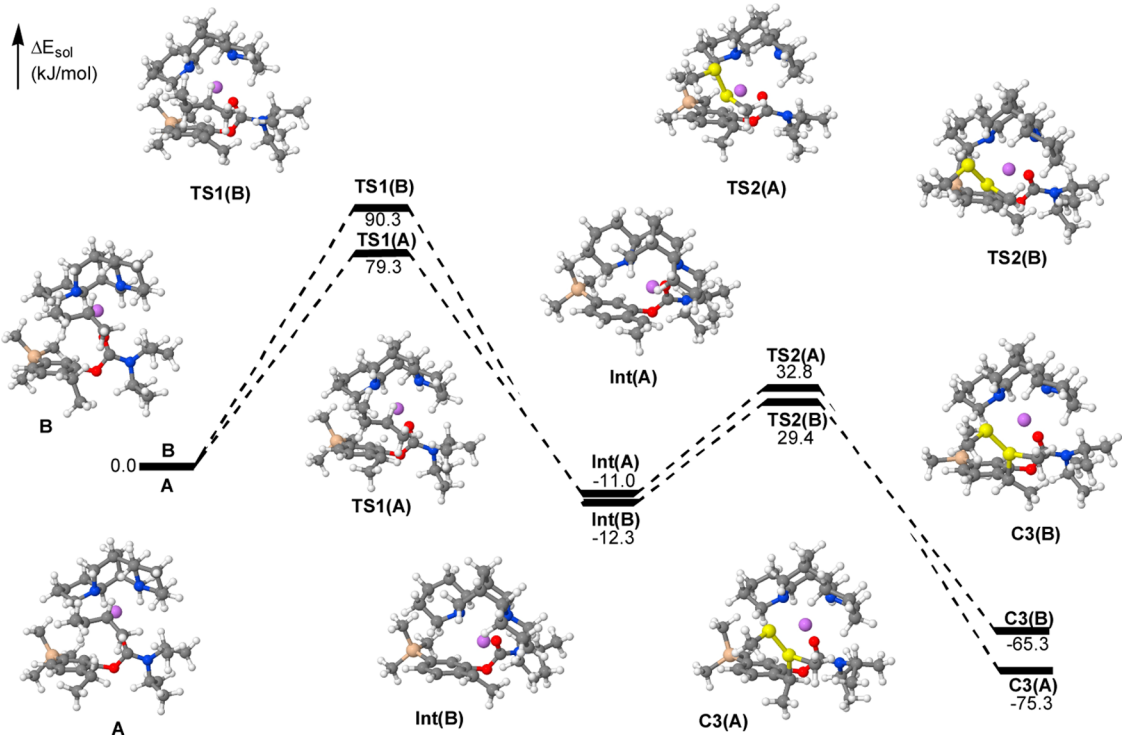
Scheme 11. Solvated Model Reaction Pathway for the Conversion of 20 to 21a[a]



[a]Atom colors: Li − purple, S − yellow, Si − pink.

conformation **C** (not depicted in Scheme 11) because the hydrogens are oriented away from the coordinated alkyllithium. Thus, only the pathways for **A** and **B** are considered further.

For conformation **A**, the calculations show that abstraction of the *pro*-(*S*) hydrogen occurs, whereas for **B**, the *pro*-(*R*) hydrogen is abstracted. This enantioselective deprotonation was found experimentally by tin−lithium exchange studies to be responsible for the observed enantioselectivity for *ortho*-TMS substrate **6** (Scheme 8) and for *meta*-TMS substrate **20** (Scheme 9). Comparison of the transition state models reveals that **TS1(A)** is more stable than **TS1(B)** by 11.0 kJ/mol in the solvated state (Scheme 11), which is in qualitative agreement with the experimentally determined er.[49] Complete transfer of the proton results in the formation of intermediates **Int(A)** and **Int(B)**.

Introduction of MeSSMe as an electrophile results in reaction with the lithiated intermediates. On the basis of electrostatic potentials and the location of the highest density LUMO of the lithiated intermediates **Int(A)** and **Int(B)**, the electrophile is found to approach from the top face for both **TS2(A)** and **TS2(B)**, leading to insertion into the C−Li bond. The outcome is retention of configuration in the formation of complexes **C3(A)** and **C3(B)**. The results of the calculated kinetically favored formation of intermediate **Int(A)** over **Int(B)** and the energetically favorable insertion of the electrophile with retention of stereochemistry are qualitatively in agreement with our experimental results for the stereochemical outcome in the conversion of **20** to **21a**.

Limitations in the precision of these calculations prevent us from making quantitative comparisons between the enantioselectivities observed for different substrates, i.e., *ortho*- vs *meta*-TMS and *N*,*N*-diethyl- vs *N*,*N*-diisopropyl aryl *O*-carbamates. However, calculations are qualitatively in agreement with the observed er's for other substrates.[48]

Subsequent Functionalizations: *N*,*N*-Dialkyl Aryl *O*-Carbamate Hydrolysis and Desilylation. In order to convert *N*,*N*-dialkyl aryl *O*-carbamates into synthetically useful phenols following benzylic functionalization, several methods were tested. Diisopropyl *O*-carbamates show considerable stability toward hydrolysis.[25a] After some judicious experimentation, we were pleased to observe that reductive cleavage of **17g** using $LiAlH_4$ (1.2 equiv)/$AlCl_3$ (1.6 equiv) in Et_2O (0 °C → rt, 2−3 h) was successful and afforded the corresponding phenol (Scheme 6). The configuration of **17g** was preserved to a large extent during its conversion into the camphanoate derivative **19**. In contrast, when compound **21a**, differing in silyl protecting group compared to **17g** was subjected to these conditions, partial racemization was observed.[50]

Selected examples of desilylation are shown in Scheme 12. The TMS-substituted **12b** was desilylated to **25** using TBAF (6 equiv) in 62% yield without erosion of optical activity, and the TBS-substituted **17f** (99:1 er) was converted into **26** (98:2 er) in neat TFA at room temperature in 78% yield.

■ CONCLUSIONS

A general synthesis of enantioenriched, laterally substituted *ortho*-ethyl *N*,*N*-dialkyl aryl *O*-carbamates using a (−)-sparteine-mediated, directed lateral metalation strategy was demonstrated by applying a reliable, preparatively simple protocol. Thus, optically active products **11**−**13**, **16**, **17**, and **21** were obtained in high yields and enantioselectivities from the corresponding *ortho*-silyl or functionalized **5**−**7** and *meta*-silyl **14**, **15**, and **20** *O*-carbamates. *N*,*N*-Diisopropyl aryl *O*-carbamates proved to be superior to *N*,*N*-diethyl aryl *O*-carbamates in terms of minimizing side reactions, and *s*-BuLi was found to be the optimal reagent for deprotonation. For preparative reactions, 2.2 equiv of *s*-BuLi/(−)-sparteine

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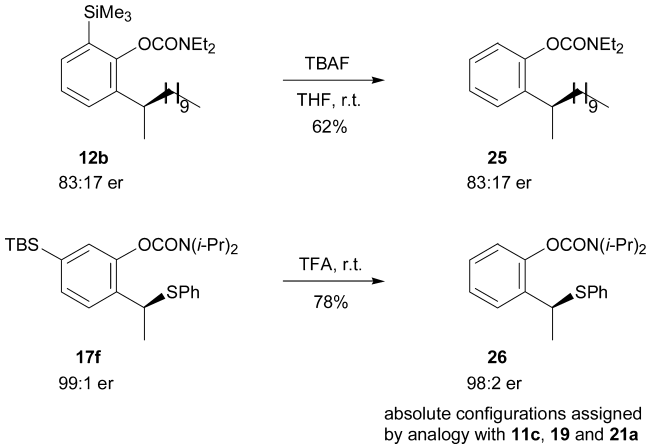
Scheme 12. Subsequent Reactions: Deprotection



complex and up to 3 equiv of the electrophile in a variety of solvents (Et_2O, *t*-BuOMe, $(i\text{-Pr})_2O$, hexanes, toluene, or *t*-BuOMe/toluene 1:3 at −78 °C) gave satisfactory results. Sterically demanding *ortho*-substituted *N*,*N*-dialkyl aryl *O*-carbamates **5**−**7** gave products **11**−**13** with low-to-moderate enantioinduction. *Meta*-substituted silyl derivative **15** afforded product **17g** with higher enantioinduction than in the conversion of the corresponding *ortho* derivative **7** to **13a**, suggesting a concept of remote silicon protection, which may be of more general synthetic value. The identical absolute configuration of the major enantiomers at the newly formed benzylic stereogenic center, demonstrating a consistent stereochemical course for the reaction, was determined for three sulfur-containing substrates **11c**, **19**, and **21a**. A mechanistic investigation of the reaction starting from **6** and **15** revealed that the enantioinduction occurs in the deprotonation step rather than in the substitution step to give products **20a** and **17g** with retention of configuration with respect to their lithiated intermediates. Benzyllithium species **9** and **23**, generated from the corresponding tin derivatives, were observed to be largely configurationally stable on the time scale of the reaction in the presence or absence of (−)-sparteine. The configurational stability of the benzyllithium species **24** prepared by direct lithiation was confirmed by a modified Hoffmann test. The results of semiempirical molecular orbital calculations (PM3/SMD) support the experimental observations concerning the retentive stereochemical course of the reaction in which enantioinduction occurs in the deprotonation step. Desilylation of **12b** and **17f** was performed using TBAF or TFA to give products **25** and **26**, and the decarbamoylation of **17g** using $LiAlH_4/AlCl_3$ followed by treatment with (−)-camphenic acid chloride was achieved to afford the corresponding ester **19**. The overall results are expected to be valuable in constructing chiral benzyl derivatives which, by further manipulation, may be adaptable to application in biomolecule and natural product synthesis.[51]

EXPERIMENTAL SECTION

General Methods. Solvents and reagents were used without further purification unless otherwise indicated. Diethyl ether (Et_2O), *tert*-butyl methyl ether (*t*-BuOMe), toluene, and tetrahydrofuran (THF) were distilled from sodium/benzophenone under an Ar atmosphere. Hexanes was distilled from CaH_2 under an Ar atmosphere. TMEDA and (−)-sparteine were distilled from CaH_2 under an Ar atmosphere. Solutions of *n*-BuLi in hexanes, *s*-BuLi in cyclohexane, and *t*-BuLi in pentane were titrated periodically according to the method of Watson and Eastham.[52] A −78 °C bath refers to a mixture of dry ice in acetone; a 0 °C bath refers to an ice/water slush. ^1H NMR spectra were recorded on 200, 250, 300, or 400 spectrometers using tetramethylsilane (TMS) as internal standard. Chemical shifts are reported in ppm relative to TMS. For peak multiplicities, the following abbreviations are used: s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of a doublet; m, multiplet; br, broad. ^{13}C NMR spectra were proton-decoupled and recorded on 200, 250, and 300 spectrometers at 50, 62.5, or 75 MHz using the respective solvent as internal standard. IR spectra were recorded on an infrared spectrophotometer as KBr disc or thin film (NaCl plates). Electron impact mass spectra (EI MS) were recorded (4 kV, 35 eV, 220 °C) on triple quadrupole mass spectrometer instruments. Melting points are not corrected. Chiral HPLC analyses using chiral columns were performed at room temperature at 254 nm. Enantiomeric purity assays using chiral HPLC columns were completed with both racemic and enantioenriched materials and repeated at least once in order to ensure accuracy of the method used. Flash chromatography (FC) was performed with silica gel (230−400 mesh, 60 Å). Analytical thin-layer chromatography was performed on silica gel UV_{254} plates. If microanalyses are not reported, then the purities of the compounds were determined to be >90% by ^1H NMR and ^{13}C NMR spectra, and the molecular ion was confirmed by high-resolution mass spectrometry (HR MS). All reported yields are isolated yields unless specified otherwise.

*Preparation of 2-Ethyl-6-methoxyphenyl Diethylcarbamate (**5**). 2-Methoxyphenyl Diethylcarbamate.* A mixture of 2-methoxyphenol (10.0 g, 80.55 mmol), diethylcarbamoyl chloride (11.23 mL, 88.63 mmol), and K_2CO_3 (12.25 g, 88.64 mmol) in CH_3CN (250 mL) was heated at reflux for 14 h. Remaining K_2CO_3 was removed by filtration. The organic phase was concentrated in vacuo, and the residue was dissolved in Et_2O (200 mL) and washed with 10% aq. KOH and H_2O. The organic layer was dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. FC (hexanes/Et_2O 2:1) provided 17.95 g (99%) of 2-methoxyphenyl diethylcarbamate as a colorless oil: bp 110−115 °C (0.05 mmHg). ^1H NMR (250 MHz, $CDCl_3$): δ 7.17−6.90 (m, 4H), 3.82 (s, 3H), 3.42 (q, J = 7.4 Hz, 4H), 1.23 (t, J = 7.6 Hz, 6H). ^{13}C NMR ($CDCl_3$): δ 154.1, 151.7, 140.6, 126.0, 123.3, 120.6, 112.3, 55.8, 42.2, 41.9, 13.9, 13.3. IR υ_{max} (film): 2974, 1722, 1606, 1503, 1419, 1260, 1203, 1155, 1113 cm^{-1}. EI MS *m*/*z*: 223 ($[M]^+$, 3), 109 (16), 100 (100). Anal. Calcd for $C_{12}H_{17}NO_3$: C, 64.55; H, 7.67; N, 6.27. Found: C, 64.46; H, 7.78; N, 6.16.

*2-Ethyl-6-methoxyphenyl Diethylcarbamate (**5**).* A solution of *s*-BuLi (41.0 mL, 53.7 mmol, 1.31 M solution in cyclohexane) and TMEDA (8.1 mL, 53.7 mmol) in THF (300 mL) was kept at −78 °C for 5 min; then, a solution of 2-methoxyphenyl diethylcarbamate (10.0 g, 44.79 mmol) in THF (50 mL) was added dropwise via cannula at −78 °C, and the resulting yellow solution was stirred at −78 °C for 1 h. Iodoethane (10.8 mL, 134.4 mmol) was added dropwise, and the resulting solution was allowed to warm to room temperature overnight. The mixture was quenched with saturated aq. NH_4Cl solution and extracted with Et_2O. The organic extracts were washed with H_2O and brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. FC (hexanes/Et_2O 1:1) afforded 8.96 g (80%) of **5** as a pale orange viscous liquid. ^1H NMR (300 MHz, $CDCl_3$): δ 7.11−7.06, 6.83−6.77 (2 t-like m, 3H), 3.81 (s, 3H), 3.49−3.39 (m, 4H), 2.58 (q, J = 7.6 Hz, 2H), 1.3−1.2 (m, 6H), 1.19 (t, J = 7.6 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 153.7, 151.7, 138.6, 137.6, 125.5, 120.6, 109.7, 55.7, 42.0, 41.8, 23.1, 14.2, 13.9, 13.3. IR υ_{max} (film): 2971, 1721, 1475, 1419, 1276, 1195, 1156, 1087 cm^{-1}. EI MS *m*/*z*: 251 ($[M]^+$, 15), 152 (20), 137 (71), 135 (22). HR MS (EI) calcd. for $C_{14}H_{21}NO_3$, 251.1521; found, 251.1510.

General Procedure A for Lithiation/Electrophile Quench of 2-Ethyl-6-methoxyphenyl Diethylcarbamate (5). To a stirred solution of (−)-sparteine in anhydrous solvent at −78 °C was added *s*-BuLi, and stirring was continued at −78 °C for 15 min. A solution of **5** in anhydrous solvent was added dropwise, and the resulting yellow solution (suspension) was stirred at −78 °C. The electrophile was added, and the resulting colorless suspension was stirred at −78 °C for 1 h and then allowed to warm to room temperature. The mixture was

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quenched with a saturated aq. NH_4Cl solution and extracted with Et_2O, and the combined organic extract was washed with H_2O and brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. Purification by FC followed. The molar ratios of reagents and quantities of solvents are specified for TMSCl quench in the following procedure. For the different solvents that have been used, yields and enantiomeric ratios are specified in Table 1.

2-Methoxy-6-[(1*S*)-1-(trimethylsilyl)ethyl]phenyl diethylcarbamate (11a). According to General Procedure A: A solution of **5** (293 mg, 1.16 mmol) in *i*-Pr_2O (5 mL) was added to a mixture of *s*-BuLi (2.14 mL, 2.57 mmol, 1.20 M solution in cyclohexane) and (−)-sparteine (0.59 mL, 2.57 mmol) in *i*-Pr_2O (10 mL) at −78 °C. After addition of trimethylsilyl chloride (0.44 mL, 3.47 mmol) at −78 °C, the mixture was worked up and purified by FC (hexanes/Et_2O 1:1) to give 191 mg (50%) of **11a** as colorless oil: $[\alpha]_D^{25}$= +26.3 (EtOAc, *c* = 1.60). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.05 (t, *J* = 8.0 Hz, 1H), 6.68 (m, 2H), 3.77 (s, 3H), 3.39 (b, 4H), 2.38 (q, *J* = 7.5 Hz, 1H), 1.30 (d, *J* = 7.6 Hz, 3H), 1.24 (b, 6H), −0.06 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 153.5, 151.5, 139.6, 137.6, 124.9, 118.9, 108.0, 55.6, 41.9, 41.7, 21.6, 14.7, 13.9, 13.1, −10.2. IR υ_{max} (film): 2957, 1722, 1469, 1419, 1270, 1159, 844 cm^{-1}. EI MS *m*/*z*: 323 ([M]$^+$, 12), 308 (14), 251 (19), 223 (49), 174 (11), 135 (4), 100 (100), 72 (90). HR MS (EI) calcd. for $C_{17}H_{30}NO_3Si$, 324.19949; found, 324.19961.

The enantiomeric ratio was determined to be 96:4 ((*S*,*S*)-WHELK-01 column, 1% 2-propanol in hexanes, 1.0 mL/min).

2-Methoxy-6-[(1*S*)-1-(methylsulfanyl)ethyl]phenyl Diethylcarbamate (11b). According to General Procedure A: A solution of **5** (364.9 mg, 1.45 mmol) in Et_2O (5 mL) was added to a mixture of *s*-BuLi (2.54 mL, 3.63 mmol, 1.43 M solution in cyclohexane) and (−)-sparteine (851 mg, 3.63 mmol) in Et_2O (15 mL) at −78 °C. After addition of a solution of dimethyl disulfide (479 mg, 5.1 mmol) in Et_2O (3 mL) at −78 °C, the mixture was worked up and purified by FC (hexanes/EtOAc 6:1) to give 198 mg (46%) of **11b** as yellowish oil: $[\alpha]_D^{25}$ = −0.19 (EtOAc, *c* = 0.5). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.19−7.11 (m, 2H), 6.82−6.79 (m, 1H), 4.15 (q, *J* = 7.1 Hz, 1H), 3.81 (s, 3H), 3.49−3.37 (m, 4H), 1.92 (s, 3H), 1.52 (d, *J* = 7.1 Hz, 3H), 1.31−1.18 (m, 6H). ^{13}C NMR ($CDCl_3$): δ 153.5, 151.4, 138.4, 137.3, 125.8, 118.9, 110.2, 55.8, 42.1, 41.9, 38.4, 21.5, 14.4, 14.1, 13.2. IR υ_{max} (film): 2972, 1723, 1587, 1475, 1419, 1274, 1155, 1094, 1049, 958, 781 cm^{-1}. EI MS *m*/*z*: 297 ([M]$^+$, 8), 250 (100), 150 (27). HR MS (EI) calcd. for $C_{15}H_{23}NO_3S$, 297.1399; found, 297.1380.

The enantiomeric ratio was determined to be 94:6 (CHIRALCEL OD column, hexanes/EtOAc/2-propanol 92:7:1, 1.0 mL/min).

2-Methoxy-6-[(1*S*)-1-(methylsulfonyl)ethyl]phenyl Diethylcarbamate (11c). To a solution of **11b** (104 mg, 0.35 mmol, 93:7 enantiomeric ratio) in CH_2Cl_2 (2 mL) was added a solution of *m*-CPBA (ca. 55%, 990 mg, 3.16 mmol) in CH_2Cl_2 (5 mL) at room temperature. After 6 h, the mixture was diluted with Et_2O and washed with a saturated aq. $Na_2S_2O_8$ solution, $NaHCO_3$ solution, and brine. The organic layer was dried over anhydrous $MgSO_4$ and concentrated in vacuo. FC (hexanes/EtOAc 1:1) afforded 105.9 mg (92%) of **11c** as a colorless solid: mp 106−107 °C (from oil). $[\alpha]_D^{25}$ = +0.02 (EtOAc, *c* = 0.5). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30−7.20 (m, 2H), 6.97−6.93, (m, 1H), 4.54 (q, *J* = 7.1 Hz, 1H), 3.83 (s, 3H), 3.49 (q, *J* = 7.1 Hz, 2H), 3.38 (q, *J* = 7.1 Hz, 2H), 2.69 (s, 3H), 1.72 (d, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 153.3, 151.6, 139.0, 129.3, 126.4, 119.4, 112.2, 56.6, 55.8, 42.4, 42.1, 38.8, 14.0, 13.1, 13.0. IR υ_{max} (KBr): 2978, 2931, 1728, 1422, 1297, 1279, 1179, 1142, 1042, 958, 790 cm^{-1}. CI MS (isobutane) *m*/*z*: 330 ([M + H]$^+$, 23), 250 (43), 150 (100), 137 (15), 110 (30). HR MS (EI) calcd. for $C_{15}H_{23}NO_5S$, 329.1297; found, 329.1282.

The enantiomeric ratio was determined to be 93:7 (CHIRALCEL OD column, hexanes/2-propanol 90:10, 0.9 mL/min).

*Preparation of 2-Ethyl-6-(trimethylsilyl)phenyl Diethylcarbamate (**6**). 2-Ethylphenyl Diethylcarbamate.* A mixture of 2-ethylphenol (10.0 g, 81.85 mmol), diethylcarbamoyl chloride (10.40 mL, 82.07 mmol), and K_2CO_3 (15.0 g, 108.53 mmol) in CH_3CN (250 mL) was heated at reflux for 24 h. Remaining K_2CO_3 was removed by subjecting to filtration. The organic phase was concentrated in vacuo, and the residue was dissolved in $CHCl_3$ (200 mL) and washed with 10% aq. KOH and H_2O. The organic layer was dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. FC (hexanes/EtOAc 9:1) provided 14.50 g (80%) of 2-ethylphenyl diethylcarbamate as a colorless oil: bp 136−140 °C (0.4 mmHg, bulb-to-bulb distillation). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.23−7.00 (m, 4H), 3.60−3.30 (m, 4H), 2.59 (q, *J* = 7.6 Hz, 2H), 1.29−1.17 (m, 9H). ^{13}C NMR ($CDCl_3$): δ 153.9, 149.3, 135.9, 129.0, 126.4, 125.2, 122.3, 42.0, 41.6, 23.1, 14.1, 13.2. IR υ_{max} (film): 2972, 2935, 1719, 1465, 1418, 1274, 1220, 1178, 1156 cm^{-1}. EI MS *m*/*z*: 221 ([M]$^+$, 23), 100 (100), 77 (16), 72 (44). Anal. Calcd for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65; N, 6.33. Found: C, 70.66; H, 8.56; N, 6.38.

*2-Ethyl-6-(trimethylsilyl)phenyl Diethylcarbamate (**6**).* A solution of 2-ethylphenyl diethylcarbamate (5.09 g, 23.03 mmol) in THF (40 mL) was added to a stirred solution of *s*-BuLi (19.0 mL, 25.27 mmol, 1.33 M solution in cyclohexane) and TMEDA (3.82 mL, 25.31 mmol) in THF (110 mL) at −78 °C. After 30 min, trimethylsilyl chloride (8.75 mL, 68.94 mmol) was added, and the mixture was stirred at −78 °C for 1 h and then was allowed to warm to room temperature overnight. The mixture was quenched with a saturated aq. NH_4Cl solution and extracted with CH_2Cl_2. The organic extracts were washed with H_2O and brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. FC (hexanes/EtOAc 9:1) provided 5.98 g (88%) of **6** as colorless oil: bp 140 °C (0.01 mmHg, bulb-to-bulb distillation). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.32−7.10 (m, 3H), 3.80−3.15 (m, 4H), 2.50 (q, *J* = 7.5 Hz, 2H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.21 (t, *J* = 7.5 Hz, 3H), 1.19 (t, *J* = 7.0 Hz, 3H), 0.26 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 154.2, 153.9, 136.0, 132.5, 132.3, 130.4, 125.5, 41.7, 41.4, 22.9, 14.2, 13.9, 13.2, −0.7. IR υ_{max} (film): 2962, 1718, 1408, 1266, 1205, 1154, 961, 841, 754 cm^{-1}. EI MS *m*/*z*: 293 (M$^+$, 1), 278 (16), 221 (9), 163 (12), 100 (100), 72 (29). Anal. Calcd for $C_{16}H_{27}NO_2Si$: C, 65.48; H, 9.27; N, 4.77. Found: C, 65.33; H, 9.01; N, 4.71.

*Preparation of 2-Ethyl-6-(trimethylsilyl)phenyl Diisopropylcarbamate (**7**). 2-Ethylphenyl Diisopropyl Carbamate.* To a 0 °C cold suspension of NaH (1.76 g, 40 mmol, 60% dispersion in mineral oil) in THF (35 mL) was added 2-ethylphenol (2.47 g, 20.22 mmol) dropwise. The ice bath was removed for 15 min, and after recooling to 0 °C, a solution of diisopropylcarbamoyl chloride (3.64 g, 22.24 mmol) in THF (10 mL) was added. The mixture was stirred at room temperature for 22 h and then quenched with a saturated aq. NH_4Cl solution and extracted with Et_2O. The organic extracts were washed with brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. FC (hexanes/Et_2O 10:1) afforded 4.86 g (96%) of 2-ethylphenyl diisopropylcarbamate as slightly yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.22 (m, 3H), 7.14 (d, *J* = 8.1 Hz, 1H), 4.07 (m, 2H), 2.61 (q, *J* = 7.1 Hz, 2H), 1.35 (br s, 12H), 1.24 (t, *J* = 7.1 Hz, 3H).

*2-Ethyl-6-(trimethylsilyl)phenyl Diisopropylcarbamate (**7**).* *s*-BuLi (4.47 mL, 6.3 mmol, 1.41 M solution in cyclohexane) was added to a stirred solution of TMEDA (733 mg, 6.31 mmol) in Et_2O (25 mL) at −78 °C, and stirring was continued at −78 °C for 15 min. A solution of 2-ethylphenyl diisopropyl carbamate (699 mg, 2.8 mmol) in Et_2O (10 mL) was added slowly, and the resulting yellowish mixture was stirred at −78 °C for 1 h. A solution of trimethylsilyl chloride (914 mg, 8.41 mmol) in Et_2O (5 mL) was slowly added at −78 °C, and the mixture was allowed to warm to 0 °C over a period of 2 h; then, the cooling bath was removed, and the mixture was stirred at room temperature for 2.5 h. A saturated aq. NH_4Cl solution was added followed by extraction with Et_2O. The combined organic extract was washed with brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. FC (hexanes/EtOAc 35:1) afforded 850 mg (85%) of **7** as a colorless solid: mp 91−92 °C (from oil). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.37−7.28, 7.22−7.17 (2 m, 3H), 4.67 (hept, *J* = 6.8 Hz, 1H), 3.59 (hept, *J* = 6.8 Hz, 1H), 2.60−2.51 (m, 2H), 1.44 (t-like m, 6H), 1.33 (d-like m, 6H), 1.27 (t, *J* = 7.6 Hz, 3H), 0.33 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 154.0, 152.1, 136.0, 132.5, 132.4, 130.5, 125.3, 47.7, 45.1, 23.0, 21.1, 20.6, 20.3, 13.9, −0.7. IR υ_{max} (KBr): 2966, 1709, 1417, 1316, 1166, 1149, 1042, 987, 839, 750 cm^{-1}.

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CI MS (isobutane) m/z: 322 ([M + H]$^+$, 29), 128 (100). HR MS (EI) calcd. for $C_{18}H_{31}NO_2Si$, 321.2124; found, 321.21039.

General Procedure B for Lithiation/Electrophile Quench of 2-Ethyl-6-(trimethylsilyl)phenyl Diethylcarbamate (6) and 2-Ethyl-6-(trimethylsilyl)phenyl Diisopropylcarbamate (7). To a stirred solution of (−)-sparteine in anhydrous solvent at −78 °C was added *s*-BuLi, and stirring was continued for 15 min at −78 °C. A solution of **6** or **7** in anhydrous solvent was added dropwise via cannula, and the resulting orange solution was stirred at −78 °C for 2 h. The electrophile (neat or as a solution in the corresponding solvent) was added, and the resulting mixture was stirred at −78 °C for 3 h (1 h for **7**) and then allowed to warm to room temperature. The mixture was quenched with a saturated aq. NH_4Cl solution and extracted with CH_2Cl_2 (Et_2O for **7**), and the combined organic extract was washed with H_2O and brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. Purification by FC followed. For the different solvents that have been used, and for the quench with TMSCl (or MeSSMe), yields and enantiomeric ratios are specified in Table 1 (**12a** and **13a**) and in Table 2 (**12b**−**h**). The molar ratios of reagents, quantities of solvents, yields, and enatiomeric ratios are specified for each of the following procedures.

2-(Trimethylsilyl)-6-[(1*S*)-1-(trimethylsilyl)ethyl]phenyl Diethylcarbamate (12a). According to General Procedure B: A solution of **6** (250 mg, 0.85 mmol) in toluene/*t*-BuOMe 3:1 (12 mL) was added to a mixture of *s*-BuLi (1.66 mL, 1.99 mmol, 1.20 M solution in cyclohexane) and (−)-sparteine (0.46 mL, 2.00 mmol) in toluene/*t*-BuOMe 3:1 (20 mL) at −78 °C. After addition of trimethylsilyl chloride (0.33 mL, 2.60 mmol), the mixture was worked up and purified by FC (hexanes/EtOAc 9:1) to give 250 mg (78%) of **12a** as a colorless wax: $[\alpha]_D^{25}$ = +23.6 (EtOAc, c = 1.37). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.26−7.13 (m, 3H), 3.70−3.23 (m, 4H), 2.09 (q, J = 7.5 Hz, 1H), 1.32 (d, J = 7.5 Hz, 3H), 1.28 (d, J = 7.2 Hz, 3H), 1.18 (t, J = 7.1 Hz, 3H), 0.25 (s, 9H), −0.08 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 154.0, 153.0, 138.2, 131.9, 130.7, 128.5, 125.2, 41.5, 41.0, 22.0, 14.3, 13.0, −0.8, −3.4. IR υ_{max} (film): 2950, 1715, 1405, 1268, 1248, 1154, 1136, 840, 753 cm^{-1}. EI MS m/z: 365 ([M]$^+$, 3), 350 (14), 293 (88), 177 (17), 100 (100), 73 (49). Anal. Calcd for $C_{19}H_{35}NO_2Si_2$: C, 62.41; H, 9.65; N, 3.83. Found: C, 62.19; H, 9.62; N, 3.81.

The enantiomeric ratio was determined to be 86:14 ((*S*,*S*)-WHELK-01 column, 1% 2-propanol in hexanes, 1.0 mL/min).

2-[(1*R*)-1-Methylundecyl]-6-(trimethylsilyl)phenyl Diethylcarbamate (12b). According to General Procedure B: A solution of **6** (250 mg, 0.85 mmol) in toluene/*t*-BuOMe 3:1 (12 mL) was added to a mixture of *s*-BuLi (1.38 mL, 1.87 mmol, 1.35 M solution in cyclohexane) and (−)-sparteine (0.43 mL, 1.87 mmol) in toluene/*t*-BuOMe 3:1 (20 mL) at −78 °C. After addition of 1-bromodecane (0.53 mL, 2.55 mmol), the mixture was worked up and purified by FC (hexanes/EtOAc 9:1) to give 200 mg (54%) of **12b** as a colorless oil: $[\alpha]_D^{25}$ = +16.0 (EtOAc, c = 1.54). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.30−7.15 (m, 3H), 3.62−3.31 (m, 4H), 2.68 (m, 1H), 1.55−1.15 (m, 27H), 0.87 (t, J = 6.6 Hz, 3H), 0.26 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 154.2, 153.6, 140.0, 139.9, 132.23, 132.20, 128.2, 125.5, 41.7, 41.4, 38.6, 32.2, 31.9, 29.6, 29.3, 27.7, 22.0, 20.6, 14.2, 14.0, 13.1, −0.7. IR υ_{max} (film): 2910, 1718, 1409, 1263, 1153, 960, 846, 786, 756 cm^{-1}. EI MS m/z: 433 (M$^+$, 1), 418 (32), 361 (33), 177 (18), 100 (100). Anal. Calcd for $C_{26}H_{47}NO_2Si$: C, 72.05; H, 10.85; N, 3.23. Found: C, 71.78; H, 10.69; N, 3.26.

The enantiomeric ratio was determined to be 83:17 (CHIRALCEL OD column, 0.5% 2-propanol in hexanes, 0.7 mL/min).

2-[(1*R*)-1-Methylbut-3-en-1-yl]-6-(trimethylsilyl)phenyl Diethylcarbamate (12c). According to General Procedure B: A solution of **6** (265 mg, 0.90 mmol) in toluene/*t*-BuOMe 3:1 (12 mL) was added to a mixture of *s*-BuLi (1.40 mL, 1.98 mmol, 1.35 M solution in cyclohexane) and (−)-sparteine (0.50 mL, 1.98 mmol) in toluene/*t*-BuOMe 3:1 (20 mL) at −78 °C. After addition of allyl bromide (0.25 mL, 2.70 mmol), the mixture was worked up and purified by FC (hexanes/EtOAc 9:1) to give 225 mg (75%) of **12c** as a colorless oil: $[\alpha]_D^{25}$ = +22.0 (EtOAc, c = 1.44). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.36−7.22 (m, 3H), 5.72 (m, 1H), 5.3−5.03 (m, 2H), 3.7−3.37 (m, 4H), 2.85 (m, 1H), 2.6−2.2 (m, 2H), 1.32 (t, J = 7.2 Hz, 3H), 1.27 (d, J = 9.1 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H), 0.3 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 154.2, 153.5, 137.4, 136.9, 134.6, 128.3, 125.6, 115.8, 41.9, 41.5, 32.2, 14.3, 13.2, −0.7. IR υ_{max} (film): 2940, 1719, 1409, 1260, 1154, 960, 846, 753 cm^{-1}. EI MS m/z: 333 ([M]$^+$, 1), 318 (45), 261 (40), 100 (100). Anal. Calcd for $C_{19}H_{31}NO_2Si$: C, 68.47; H, 9.31; N, 4.20. Found: C, 68.42; H, 9.37; N, 4.23.

The enantiomeric ratio was determined to be 87:13 (CHIRALCEL OD column, 0.5% 2-propanol in hexanes, 0.7 mL/min).

2-[(1*S*)-2-Methoxy-1-methylethyl]-6-(trimethylsilyl)phenyl Diethylcarbamate (12d). According to General Procedure B: A solution of **6** (250 mg, 0.85 mmol) in toluene/*t*-BuOMe 3:1 (12 mL) was added to a mixture of *s*-BuLi (1.38 mL, 1.87 mmol, 1.35 M solution in cyclohexane) and (−)-sparteine (0.43 mL, 1.87 mmol) in toluene/*t*-BuOMe 3:1 (20 mL) at −78 °C. After addition of chloromethyl methyl ether (0.19 mL, 2.55 mmol), the mixture was worked up and purified by FC (hexanes/EtOAc 9:1) to give 113 mg (39%) of **12d** as a colorless oil: $[\alpha]_D^{25}$ = +34.0 (EtOAc, c = 1.23). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.35−7.16 (m, 3H), 3.63−3.31 (m, 6H), 3.31 (br s, 3H), 3.05 (m, 1H), 1.29 (t, J = 7.2 Hz, 3H), 1.27 (d, J = 5.0 Hz, 3H), 1.19 (t, J = 7.2 Hz, 3H), 0.26 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 153.8, 135.9, 132.6, 132.3, 128.3, 125.2, 78.0, 41.6, 41.3, 32.1, 13.8, 12.8, −1.0. IR υ_{max} (film): 2965, 1716, 1399, 1263, 1126, 961, 847, 789, 755 cm^{-1}. EI MS m/z: 337 ([M]$^+$, 1), 322 (19), 290 (7), 100 (100), 72 (41). Anal. Calcd for $C_{18}H_{31}NO_3Si$: C, 64.10; H, 9.20; N, 4.15. Found: C, 63.91; H, 9.12; N, 4.08.

The enantiomeric ratio was determined to be 84:16 (CHIRALCEL OD column, 1% 2-propanol in hexanes, 0.7 mL/min).

2-[(1*S*)-1-(Tributylstannyl)ethyl]-6-(trimethylsilyl)phenyl Diethylcarbamate (12e). According to General Procedure B: A solution of **6** (580 mg, 1.98 mmol) in toluene/*t*-BuOMe 3:1 (12 mL) was added to a mixture of *s*-BuLi (3.28 mL, 4.33 mmol, 1.32 M solution in cyclohexane) and (−)-sparteine (0.99 mL, 4.31 mmol) in toluene/*t*-BuOMe 3:1 (35 mL) at −78 °C. After addition of *n*-Bu_3SnCl (0.70 mL, 2.58 mmol), the mixture was worked up and purified by FC (hexanes/EtOAC 9:1) to give 0.72 g (63%) of **12e** as a colorless oil: $[\alpha]_D^{25}$ = +60.3 (EtOAc, c = 1.08). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.24−7.08 (m, 3H), 3.62−3.20 (m, 4H), 2.51 (q, J = 7.5 Hz, 1H), 1.54 (d, J = 7.5 Hz, 3H), 1.48−1.10 (m, 18H), 0.92−0.70 (m, 15H), 0.25 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 154.1, 151.9, 141.1, 131.7, 129.8, 127.8, 125.5, 41.5, 41.2, 29.0, 27.5, 19.8, 14.3, 13.6, 13.1, 8.9, −0.7. IR υ_{max} (film): 2957, 2926, 1718, 1406, 1270, 1151, 867 cm^{-1}. EI MS m/z: [M]$^+$ not detected, 526 (5), 292 (6), 277 (31), 235 (4), 208 (6), 177 (29), 100 (100), 72 (40). Anal. Calcd for $C_{28}H_{53}NO_2SiSn$: C, 57.73; H, 9.17; N, 2.40. Found: C, 57.85; H, 9.05; N, 2.42.

The enantiomeric ratio was determined to be 86:14 (CHIRALCEL OD column, 8% (0.5% Et_2NH in Et_2O) in hexanes, 1.0 mL/min).

2-[(1*S*)-1-(Phenylsulfanyl)ethyl]-6-(trimethylsilyl)phenyl Diethylcarbamate (12f). According to General Procedure B: A solution of **6** (250 mg, 0.85 mmol) in toluene/*t*-BuOMe 3:1 (12 mL) was added to a mixture of *s*-BuLi (1.38 mL, 1.87 mmol, 1.35 M solution in cyclohexane) and (−)-sparteine (0.43 mL, 1.87 mmol) in toluene/*t*-BuOMe 3:1 (20 mL) at −78 °C. After addition of phenyl disulfide (557 mg, 2.55 mmol) in toluene/*t*-BuOMe 3:1 (10 mL), the mixture was worked up and purified by FC (hexanes/EtOAc 9:1) to give 240 mg (71%) of **12f** as a colorless oil: $[\alpha]_D^{25}$ = +31.1 (EtOAc, c = 1.08). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.57−7.16 (m, 8H), 4.30 (m, 1H), 3.6−3.3 (m, 4H), 1.62 (d, J = 6.5 Hz, 3H), 1.3−1.1 (m, 6H), 0.22 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 153.8, 152.9, 135.9, 135.0, 133.5, 132.4, 132.0, 129.3, 128.3, 126.8, 125.7, 125.3, 41.6, 41.3, 41.0, 14.1, 13.0, −1.0. IR υ_{max} (film): 2950, 1716, 1420, 1264, 959, 867, 747 cm^{-1}. EI MS m/z: 401 ([M]$^+$, 1), 386 (1), 292 (27), 177 (3), 159 (2), 100 (100), 72 (13). Anal. Calcd for $C_{22}H_{31}NO_2SSi$: C, 65.83; H, 7.73; N, 3.49. Found: C, 66.00; H, 7.78; N, 3.58.

The enantiomeric ratio was determined to be 85:15 (CHIRALCEL OD column, 1% 2-propanol in hexanes, 0.5 mL/min).

2-[(1*S*)-1-(Phenylselanyl)ethyl]-6-(trimethylsilyl)phenyl Diethylcarbamate (12g). According to General Procedure B: A solution of **6** (250 mg, 0.85 mmol) in toluene/*t*-BuOMe 3:1 (12 mL)

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was added to a mixture of *s*-BuLi (1.38 mL, 1.87 mmol, 1.35 M solution in cyclohexane) and (−)-sparteine (0.43 mL, 1.87 mmol) in toluene/*t*-BuOMe 3:1 (20 mL) at −78 °C. After addition of diphenyl diselenide (795 mg, 2.55 mmol) in toluene/*t*-BuOMe 3:1 (10 mL), the mixture was worked up and purified by FC (hexanes/EtOAc 9:1) to give 261 mg (69%) of **12g** as a colorless oil: $[\alpha]_D^{25}$ = +25.9 (EtOAc, *c* = 1.86). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.5−7.13 (m, 8H), 4.4 (q, *J* = 7.0 Hz, 1H), 3.5−3.3 (m, 4H), 1.72 (d, *J* = 7.0 Hz, 3H), 1.3−1.1 (m, 6H), 0.21 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 153.8, 152.5, 136.2, 135.9, 135.0, 133.3, 132.4, 132.1, 130.2, 129.5, 128.4, 127.5, 125.6, 41.6, 41.2, 35.2, 14.1, 12.9, −0.9. IR υ_{max} (film): 2946, 1716, 1423, 1168, 1085, 960, 848, 748 cm^{-1}. EI MS *m*/*z*: 449 ([M]$^+$, 1), 434 (3), 292 (49), 277 (15), 177 (61), 100 (100). Anal. Calcd for $C_{22}H_{31}NO_2SeSi$: C, 58.93; H, 6.92; N, 3.13. Found: C, 60.59; H, 7.13; N, 3.52.

The enantiomeric ratio was determined to be 84:16 (CHIRALCEL OD column, 1% 2-propanol in hexanes, 0.5 mL/min).

2-[(1*S*)-1-Chloroethyl]-6-(trimethylsilyl)phenyl Diethylcarbamate (12h). According to General Procedure B: A solution of **6** (586 mg, 2.0 mmol) in toluene/*t*-BuOMe 3:1 (20 mL) was added to a mixture of *s*-BuLi (3.19 mL, 4.4 mmol, 1.38 M solution in cyclohexane) and (−)-sparteine (0.97 mL, 4.4 mmol) in toluene/*t*-BuOMe 3:1 (40 mL) at −78 °C. After addition of hexachloroethane (1.4 g, 6.0 mmol) in toluene/*t*-BuOMe 3:1 (15 mL), the mixture was worked up and purified by FC (hexanes/EtOAc 9:1) to give 420 mg (64%) of **12h** as a colorless solid: mp 66−69 °C (from oil). $[\alpha]_D^{25}$ = −18.0 (EtOAc, *c* = 0.98). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.63 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.42 (dd, *J* = 7.3, 1.8 Hz, 1H), 7.26 (dd, *J* = 7.5, 7.3 Hz, 1H), 5.83 (q, *J* = 6.8 Hz, 1H), 3.4−3.3 (m, 4H), 1.84 (d, *J* = 6.4 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 6H), 0.27 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 153.8, 152.1, 135.2, 135.0, 132.9, 128.7, 125.9, 52.3, 41.9, 41.7, 25.3, 14.1, 13.0, −0.2. IR υ_{max} (KBr): 2940, 1714, 1409, 1263, 1151, 840 cm^{-1}. EI MS *m*/*z*: [M]$^+$ not detected, 292 (1), 277 (36), 100 (100). Anal. Calcd for $C_{16}H_{26}ClNO_2Si$: C, 58.63; H, 7.94; N, 4.27. Found: C, 58.35; H, 7.85; N, 4.30.

The enantiomeric ratio was determined to be 90:10 (CHIRALCEL OD column, 0.5% 2-propanol in hexanes, 0.5 mL/min).

2-[(1*S*)-1-(Methylsulfanyl)ethyl]-6-(trimethylsilyl)phenyl Diisopropylcarbamate (13a). According to General Procedure B: A solution of **7** (440 mg, 1.36 mmol) in Et_2O (7 mL) was added along the wall of the flask over a period of 12 min to a mixture of *s*-BuLi (2.18 mL, 3.1 mmol, 1.41 M solution in cyclohexane) and (−)-sparteine (722 mg, 3.08 mmol) in Et_2O (15 mL) at −78 °C. After addition of a solution of dimethyl disulfide (258 mg, 2.74 mmol) in Et_2O (4 mL) over a period of 6 min, the mixture was worked up and purified by FC (hexanes/EtOAc 50:1) to give 424 mg (84%) of **13a** as a colorless solid: mp 80−82 °C (from oil). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83−7.81, 7.58−7.54 (2 m, together 1H), 7.39−7.30 (m, 1H), 7.30−7.23 (m, 1H), 4.70−4.59 (m, 1H), 4.04−3.88 (m, 1H), 3.57−3.50 (m, 1H), 1.96 (s, 1H), 1.90 (s, 2H), 1.58 (d, *J* = 6.9 Hz, 3H), 1.43−1.28 (m, 12H), 0.30 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 152.2, 135.9, 133.6, 133.5, 132.2, 129.2, 129.0, 125.8, 47.8, 45.2, 45.1, 38.5, 29.6, 21.2, 20.8, 20.7, 20.52, 20.46, 20.3, 14.8, 14.4, −0.7, −0.8. IR υ_{max} (KBr): 2966, 2924, 1709, 1416, 1300, 1203, 1137, 1040, 981, 840, 794 cm^{-1}. CI MS (isobutane) *m*/*z*: 368 ([M + H]$^+$, 100), 321 (15), 320 (57), 248 (21), 128 (48). HR MS (EI) calcd. for $C_{19}H_{33}NO_2SSi$, 367.2001; found, 367.20247.

The enantiomeric ratio was determined to be 69:31 (CHIRALCEL OD column, 5% MTBE in hexanes, 1.0 mL/min).

*5-[tert-Butyl(dimethyl)silyl]-2-ethylphenyl Diethylcarbamate (**14**). 3-[tert-Butyl(dimethyl)silyl]phenol.* *t*-BuLi (59.7 mL, 100 mmol, 1.71 M solution in pentane) was added to a stirred solution of 3-bromophenol (5.52 g, 31.91 mmol) in THF (50 mL) at −78 °C, and stirring was continued at −78 °C for 30 min. A solution of *t*-butyldimethylsilyl chloride (5.65 g, 37.49 mmol) in THF (10 mL) was added dropwise, and the resulting solution was allowed to warm to −60 °C over a period of 3 h; then, the cooling bath was removed, and it was stirred at room temperature for 2.5 h. Quench with a saturated aq. NH_4Cl solution followed, and the pH of the mixture was adjusted to ca. 8 with a diluted aq. HCl solution and extracted with Et_2O. The combined organic extract was washed with brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. FC (hexanes/EtOAc 10:1) provided 4.41 g (66%) of 3-[*tert*-butyl(dimethyl)silyl]phenol as a colorless solid: mp 65−67 °C (from oil). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.23 (m, 1H), 7.05 (m, 1H), 6.97 (m, 1H), 6.80 (dq, *J* = 8.0, 1.5, 1.0 Hz, 1H), 4.60 (br s, 1H), 0.87 (s, 9H), 0.25 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 154.6, 139.9, 128.8, 127.0, 121.0, 115.7, 26.5, 16.8, −6.2. IR υ_{max} (KBr): 3281 (br), 2926, 1575, 1428, 1327, 1231, 776 cm^{-1}. EI MS *m*/*z*: 208 ([M]$^+$, 14), 151 (100), 91 (3). Anal. Calcd for $C_{12}H_{20}SiO$: C, 69.17; H, 9.67. Found: C, 68.98; H, 9.49.

3-[tert-Butyl(dimethyl)silyl]phenyl Diethylcarbamate. A mixture of 3-[*tert*-butyl(dimethyl)silyl]phenol (1.18 g, 5.66 mmol), diethylcarbamoyl chloride (0.80 mL, 6.31 mmol), and K_2CO_3 (1.17 g, 8.46 mmol) in CH_3CN (75 mL) was refluxed for 15 h. Remaining K_2CO_3 was removed by filtration. The organic phase was evaporated to dryness in vacuo, and the residue was dissolved in EtOAc (ca. 100 mL) and washed with a 10% aq. KOH solution and H_2O. The organic layer was dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. FC (hexanes/EtOAc 98:2) provided 1.59 g (92%) of 3-[*tert*-butyl(dimethyl)silyl]phenyl diethylcarbamate as a colorless oil: bp 110−115 °C (0.2 mmHg, bulb-to-bulb distillation). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.37−7.28 (m, 2H), 7.20 (m, 1H), 7.20−7.05 (m, 1H), 3.45−3.40 (m, 4H), 1.30−1.20 (m, 6H), 0.88 (s, 9H), 0.27 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 154.2, 150.9, 139.4, 131.0, 128.2, 127.1, 122.2, 42.1, 41.8, 26.4, 16.8, 14.2, 13.4, −6.2. IR υ_{max} (film): 2947, 2856, 1721, 1469, 1410, 1267, 1206, 1158, 833, 770 cm^{-1}. EI MS *m*/*z*: 307 ([M]$^+$, 2), 292 (2), 250 (100), 135 (7), 100 (39), 72 (24). HR MS (EI) calcd. for $C_{17}H_{29}NO_2Si$, 307.19674; found, 307.19582.

*5-[tert-Butyl(dimethyl)silyl]-2-ethylphenyl Diethylcarbamate (**14**).* To a −78 °C cold solution of 3-[*tert*-butyl(dimethyl)silyl]phenyl diethylcarbamate (1.16 g, 3.77 mmol) and TMEDA (1.25 mL, 8.28 mmol) in THF (75 mL) was added *t*-BuLi (4.98 mL, 8.27 mmol, 1.66 M solution in pentane) dropwise at −78 °C. After 1 h, iodoethane (0.90 mL, 11.25 mmol) was added, and the mixture was allowed to warm to room temperature overnight. The mixture was treated with a saturated aq. NH_4Cl solution and extracted with Et_2O. The organic extracts were washed with H_2O and brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. FC (hexanes/EtOAc 95:5) provided 0.88 g (70%) of **14** as a colorless oil: bp 155−160 °C (0.3 mmHg, bulb-to-bulb distillation). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.27 (dd, *J* = 7.5, 0.8 Hz, 1H), 7.20 (d, *J* = 7.5 Hz, 1H), 7.15 (d, *J* = 0.8 Hz, 1H), 3.50−3.35 (m, 4H), 2.57 (q, *J* = 7.6 Hz, 2H), 1.30−1.18 (m, 6H), 1.21 (t, *J* = 7.6 Hz, 3H), 0.87 (s, 9H), 0.25 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 154.0, 148.5, 136.6, 136.3, 131.6, 128.3, 128.2, 42.1, 41.8, 26.5, 23.3, 16.9, 14.3, 14.1, 13.4, −6.1. IR υ_{max} (film): 2961, 2930, 2850, 1721, 1418, 1270, 1215, 1189, 1156 cm^{-1}. EI MS *m*/*z*: 335 ([M]$^+$, 3), 278 (100), 178 (5), 135 (3), 100 (30), 72 (20). Anal. Calcd for $C_{19}H_{33}NO_2Si$: C, 68.01; H, 9.91; N, 4.17. Found: C, 68.32; H, 9.73; N, 4.21.

*5-[tert-Butyl(dimethyl)silyl]-2-ethylphenyl Diisopropylcarbamate (**15**). 3-[tert-Butyl(dimethyl)silyl]phenyl Diisopropylcarbamate.* To an ice-cold suspension of NaH (600 mg, 15 mmol, 60% dispersion in mineral oil) in THF (25 mL) was slowly added a solution of 3-[*tert*-butyl(dimethyl)silyl]phenol (1.56 g, 7.51 mmol) in THF (7 mL). The ice bath was removed for 15 min, and after recooling to 0 °C, a solution of diisopropylcarbamoyl chloride (1.35 g, 8.27 mmol) in THF (5 mL) was added. The mixture was stirred at room temperature for 22 h, quenched with a saturated aq. NH_4Cl solution, and extracted with Et_2O. The organic extracts were washed with brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. FC (gradient hexanes/EtOAc 25:1 to 20:1) afforded 2.29 g (90%) of 3-[*tert*-butyl(dimethyl)silyl]phenyl diisopropylcarbamate as a colorless solid: mp 61−63 °C (from oil). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.34−7.28 (m, 2H), 7.18 (m, 1H), 7.14−7.10 (m, 1H), 4.05 (br s, 2H), 1.32 (br s, 12H), 0.88 (s, 9H), 0.27 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 153.9, 150.8, 139.4, 131.0, 128.2, 127.2, 122.3, 46.9, 45.9, 26.5, 21.8, 20.7, 16.9, −6.2. IR υ_{max} (film): 2959, 2931, 2856, 1715, 1314, 1292, 1207, 1153, 832, 769 cm^{-1}. EI MS *m*/*z*: 335 ([M]$^+$, 2), 320 (3), 278

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(33), 151 (47), 128 (100), 86 (71). Anal. Calcd for $C_{19}H_{33}NO_2Si$: C, 68.01; H, 9.91; N, 4.17. Found: C, 68.05; H, 9.80; N, 4.22.

*5-[tert-Butyl(dimethyl)silyl]-2-ethylphenyl Diisopropylcarbamate (**15**).* To a solution of 3-[*tert*-butyl(dimethyl)silyl]phenyl diisopropylcarbamate (2.29 g, 6.82 mmol) and TMEDA (1.74 g, 15 mmol) in THF (25 mL) at −78 °C was added *t*-BuLi (9 mL, 15 mmol, 1.66 M solution in pentane) dropwise via syringe. The solution was stirred at −78 °C for 1 h; then, iodoethane (3.19 g, 20.5 mmol) was added dropwise at −78 °C, and the mixture was allowed to warm to −25 °C over a period of 2.5 h. The mixture was kept at room temperature overnight; then, it was quenched with a saturated aq. NH_4Cl solution and extracted with Et_2O. The organic extracts were washed with brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. FC (hexanes/EtOAc 25:1) afforded 2.46 g (95%) of **15** as a colorless solid, mp 38−39 °C (from oil). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.28 (dd, J = 7.4, 1.1 Hz, 1H), 7.20 (d, J = 7.4 Hz, 1H), 7.09 (d, J unresolved, 1H), 4.06 (m, 2H), 2.56 (q, J = 7.6 Hz, 2H), 1.32 (br s, 12H), 1.20 (t, J = 7.6 Hz, 3H), 0.87 (s, 9H), 0.25 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 153.5, 148.9, 136.8, 136.1, 131.5, 128.3, 128.2, 46.2, 26.4, 23.2, 21.4, 20.5, 16.8, 14.0, −6.2. IR υ_{max} (KBr): 2963, 2931, 2856, 1714, 1314, 1190, 1134, 825 cm^{-1}. EI MS m/z: 363 ([M]$^+$, 3), 348 (2), 306 (22), 221 (7), 179 (31), 128 (100), 86 (98). Anal. Calcd for $C_{21}H_{37}NO_2Si$: C, 69.37; H, 10.26; N, 3.85. Found: C, 69.55; H, 10.07; N, 3.92.

5-[*tert*-Butyl(dimethyl)silyl]-2-[(1*S*)-1-(trimethylsilyl)ethyl]-phenyl Diethylcarbamate (16a). A solution of **14** (160 mg, 0.48 mmol) in toluene/*t*-BuOMe 3:1 (5 mL) was added to a mixture of *s*-BuLi (0.77 mL, 1.04 mmol, 1.35 M solution in cyclohexane) and (−)-sparteine (0.25 mL, 1.09 mmol) in toluene/*t*-BuOMe 3:1 (10 mL) at −78 °C under argon. After 45 min, trimethylsilyl chloride (0.18 mL, 1.42 mmol) was added dropwise, and the mixture was stirred at −78 °C for 3 h. The reaction mixture was treated with a saturated aq. NH_4Cl solution and concentrated. The resulting aqueous solution was extracted with Et_2O (3 × 25 mL), and the combined organic extracts were washed with H_2O (2 × 50 mL), dried over $MgSO_4$, subjected to filtration, and concentrated in vacuo to afford a pale yellow oil. FC (hexanes/EtOAc 9:1) afforded 68 mg (35%) of **16a** as a colorless solid: mp 55−57 °C (from oil). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.20 (d, J = 7.6 Hz, 1H), 7.10 (d, J = 1.0 Hz, 1H), 7.05 (d, J = 7.6 Hz, 1H), 3.50−3.35 (m, 4H), 2.36 (q, J = 7.4 Hz, 1H), 1.30 (d, J = 7.4 Hz, 3H), 1.30−1.17 (m, 6H), 0.84 (s, 9H), 0.22 (s, 6H), −0.07 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 154.0, 147.8, 138.6, 133.7, 131.1, 128.1, 126.3, 42.0, 41.6, 26.5, 21.7, 16.9, 14.7, 14.4, 13.4, −3.2, −6.2. IR υ_{max} (KBr): 2956, 2923, 1711, 1470, 1423, 1382, 1252, 1215, 1152, 833, 799, 753 cm^{-1}. EI MS m/z: 407 ([M]$^+$, 7), 392 (11), 350 (67), 335 (30), 307 (100), 277 (8), 100 (63), 73 (46). Anal. Calcd for $C_{22}H_{41}NO_2Si_2$: C, 64.81; H, 10.14; N, 3.44. Found: C, 64.69; H, 9.99; N,3.42.

The enantiomeric ratio was determined to be 97:3 ((*S*,*S*)-WHELK-01 column, 1% Et_2O in hexanes, 0.5 mL/min).

*2-Ethyl-5-(trimethylsilyl)phenyl Diisopropylcarbamate (**20**). 3-(Trimethylsilyl)phenol.* *t*-BuLi (80.4 mL, 92 mmol, 1.15 M solution in pentane) was added to a stirred solution of 3-bromophenol (5.04 g, 29.1 mmol) in THF (50 mL) at −78 °C, and stirring was continued at −78 °C for 30 min. Trimethylsilyl chloride (9.28 g, 85.4 mmol) was added at −78 °C, and the mixture was allowed to warm to 0 °C over a period of 3 h. The cooling bath was removed, and the mixture was kept at room temperature for 3 h. A saturated aq. NH_4Cl solution was added followed by extraction with Et_2O. The organic phase was washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The residue was dissolved in MeOH (50 mL); then, K_2CO_3 (ca. 300 mg) was added at room temperature. After 2.5 h at room temperature, the mixture was concentrated in vacuo, and H_2O was added, followed by extraction with Et_2O. The organic phase was washed with brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. FC (hexanes/EtOAc 12:1) afforded 3.72 g (77%) of 3-(trimethylsilyl)phenol as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30−7.25 (m, 1H), 7.13−7.09 (m, 1H), 7.01−7.00 (m, 1H), 6.86−6.82 (m, 1H), 4.73 (br s, 1H), 0.28 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 154.9, 142.5, 129.1, 125.5, 119.9, 115.8, −1.3. IR υ_{max} (film): 3400 (br), 2956, 1575, 1426, 1248, 1112, 896, 837, 754 cm^{-1}. EI MS m/z: 165 ([M]$^+$, 5), 151 (33), 69 (100).

3-(Trimethylsilyl)phenyl Diisopropylcarbamate. A solution of 3-(trimethylsilyl)phenol (488 mg, 2.93 mmol) in THF (4 mL) was slowly added to a suspension of NaH (235 mg, ca. 5.9 mmol, 60% dispersion in mineral oil) in THF (20 mL) at 0 °C. The cooling bath was removed for 15 min; then, after recooling to 0 °C, a solution of diisopropylcarbamoyl chloride (576 mg, 3.52 mmol) in THF (4 mL) was added. The cooling bath was removed, and the mixture was stirred at room temperature overnight. A saturated aq. NH_4Cl solution was added followed by extraction with Et_2O. The organic phase was washed with brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. FC (hexanes/EtOAc 20:1) afforded 812 mg (94%) of 3-(trimethylsilyl)phenyl diisopropylcarbamate as a yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40−7.32 (m, 2H), 7.24−7.23 (m, 1H), 7.14−7.10 (m, 1H), 4.14, 3.97 (2 br s, 2H), 1.34 (br s, 12H), 0.29 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 153.9, 150.9, 142.1, 129.8, 128.6, 126.0, 122.4, 46.8, 45.7, 21.7, 20.4, −1.2. IR υ_{max} (film): 2965, 1715, 1434, 1314, 1296, 1204, 1153, 1042, 838, 754 cm^{-1}. CI MS (isobutane) m/z: 294 ([M + H]$^+$, 24), 128 (100). HR MS (EI) calcd. for $C_{16}H_{27}NO_2Si$, 293.1811; found, 293.1813.

*2-Ethyl-5-(trimethylsilyl)phenyl Diisopropylcarbamate (**20**).* *t*-BuLi (19.5 mL, 18.7 mmol, 0.96 M solution in pentane) was slowly added to a stirred solution of 3-(trimethylsilyl)phenyl diisopropylcarbamate (2.51 g, 8.56 mmol) and TMEDA (2.18 g, 18.74 mmol) in THF (40 mL) at −78 °C. The bright yellow solution was kept at −78 °C for 1 h; then, iodoethane (3.99 g, 25.6 mmol) was added dropwise at −78 °C. The mixture was allowed to warm to −20 °C over a period of 2.5 h; then, the cooling bath was removed, and the mixture was stirred overnight at room temperature. A saturated aq. NH_4Cl solution was added followed by extraction with Et_2O. The organic phase was washed with brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. FC (hexanes/EtOAc 25:1) afforded 2.71 g (98%) of **20** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33−7.24 (m, 2H), 7.14 (d, J = 0.9 Hz, 1H), 4.10−4.05 (quint-like m, 2H), 2.60 (q, J = 7.6 Hz, 2H), 1.37−1.34 (d-like m, 12H), 1.23 (t, J = 7.6 Hz, 3H), 0.27 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 153.7, 149.1, 139.0, 136.9, 130.5, 128.8, 127.0, 46.6, 46.1, 23.2, 21.5, 20.5, 14.1, −1.1. IR υ_{max} (film): 2966, 1715, 1433, 1314, 1192, 1136, 1043, 838 cm^{-1}. CI MS (isobutane) m/z: 322 ([M + H]$^+$, 27), 128 (100). HR MS (EI) calcd. for $C_{18}H_{31}NO_2Si$, 321.2124; found, 321.2108.

General Procedure C for Lithiation/Electrophile Quench of 5-[*tert*-Butyl(dimethyl)silyl]-2-ethylphenyl Diisopropylcarbamate (15) and 2-Ethyl-5-(trimethylsilyl)phenyl Diisopropylcarbamate (20). *s*-BuLi was added to a stirred solution of (−)-sparteine in hexanes or Et_2O at −78 °C, and stirring was continued at −78 °C for 15 min. A solution of **15** or **20** in hexanes or Et_2O was added dropwise via cannula, and the resulting pale orange or yellow solution was stirred at −78 °C for 2 h. The electrophile (neat or as a solution in hexanes or Et_2O) was added, and the mixture (remaining in the cooling bath) was allowed to warm to room temperature. The mixture was quenched with a saturated aq. NH_4Cl solution and extracted with Et_2O. The combined organic extract was washed with H_2O and brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. Purification followed by FC. The molar ratios of reagents, quantities of solvents, and yields are specified for each of the following procedures.

5-[*tert*-Butyl(dimethyl)silyl]-2-[(1*S*)-1-(trimethylsilyl)ethyl]-phenyl Diisopropylcarbamate (17a). According to General Procedure C: A solution of **15** (360 mg, 1.0 mmol) in hexanes (10 mL) was added to a mixture of *s*-BuLi (1.59 mL, 2.30 mmol, 1.45 M solution in cyclohexane) and (−)-sparteine (0.53 mL, 2.30 mmol) in hexanes (20 mL). Addition of trimethylsilyl chloride (0.38 mL, 3.0 mmol) and FC (hexanes/EtOAc 98:2) afforded 350 mg (80%) of **17a** as a colorless solid: mp 96−98 °C (from oil). $[\alpha]_D^{25}$ = −2.6 (EtOAc, c = 1.29). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.21 (dd, J = 7.6, 1.2 Hz, 1H), 7.08 (d, J = 7.6 Hz, 1H), 7.05 (d, J = 1.2 Hz, 1H), 4.18 (br s, 1H), 3.90 (br s, 1H), 2.32 (q, J = 7.5 Hz, 1H), 1.31 (br s, 15H), 0.86 (s, 9H), 0.24 (s, 6H), −0.05 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 153.2, 147.9, 139.0,

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133.8, 131.1, 128.1, 126.5, 46.3, 26.6, 21.8, 21.7, 20.6, 16.9, 15.0, −3.0, −6.1. IR υ_{max} (KBr): 2957, 2856, 1715, 1312, 1252, 1215, 835 cm^{-1}. EI MS *m*/*z*: 435 ([M]$^+$, 4), 420 (4), 378 (7), 335 (14), 307 (23), 203 (10), 177 (7), 128 (67), 86 (100), 73 (42). Anal. Calcd for $C_{24}H_{45}NO_2Si_2$: C, 66.15; H, 10.41; N, 3.21. Found: C, 66.02; H, 10.27; N, 3.31.

The enantiomeric ratio was determined to be 98:2 ((*S*,*S*)-WHELK-01 column, 1% Et_2O in hexanes, 0.5 mL/min).

5-[*tert*-Butyl(dimethyl)silyl]-2-[(1*R*)-1-methylbut-3-en-1-yl]-phenyl Diisopropylcarbamate (17b). According to General Procedure C: A solution of **15** (210 mg, 0.58 mmol) in hexanes (10 mL) was added to a mixture of *s*-BuLi (0.95 mL, 1.28 mmol, 1.35 M solution in cyclohexane) and (−)-sparteine (0.29 mL, 1.26 mmol) in hexanes (10 mL). Addition of allyl bromide (0.15 mL, 1.73 mmol) and FC (hexanes/EtOAc 95:5) afforded 200 mg (85%) of **17b** as a colorless oil: $[\alpha]_D^{25}$ = −13.8 (EtOAc, *c* = 1.18). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.30 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.26 (d, *J* unresolved, 1H), 7.07 (d, *J* = 1.0 Hz, 1H), 5.83−5.60 (m, 1H), 5.06−4.90 (m, 2H), 4.05 (br s, 2H), 3.01−2.91 (m, 1H), 2.48−2.27 (m, 1H), 2.24−2.12 (m, 1H), 1.31 (br s, 12H), 1.20 (d, *J* = 6.9 Hz, 3H), 0.87 (s, 9H), 0.25 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 153.5, 148.3, 139.7, 137.1, 136.0, 131.5, 128.4, 125.9, 115.8, 46.3, 41.6, 32.3, 26.5, 21.5, 20.5, 20.0, 16.9, −6.2. IR υ_{max} (film): 2961, 2931, 2857, 1714, 1309, 1214, 824 cm^{-1}. EI MS *m*/*z*: 403 ([M]$^+$, 6), 388 (2), 346 (31), 261 (5), 219 (13), 178 (12), 128 (100), 86 (56). Anal. Calcd for $C_{24}H_{41}NO_2Si$: C, 71.41; H, 10.24; N, 3.47. Found: C, 71.22; H, 10.04; N, 3.55.

The determination of the enantiomeric ratio of **17b** was unsuccessful with both CHIRALCEL OD and (*S*,*S*)-WHELK-01 columns.

5-[*tert*-Butyl(dimethyl)silyl]-2-[(1*S*)-2-methoxy-1-methylethyl]phenyl Diisopropylcarbamate (17c). According to General Procedure C: A solution of **15** (290 mg, 0.80 mmol) in hexanes (10 mL) was added to a mixture of *s*-BuLi (1.32 mL, 1.78 mmol, 1.35 M solution in cyclohexane) and (−)-sparteine (0.41 mL, 1.78 mmol) in hexanes (20 mL). Addition of chloromethyl methyl ether (0.19 mL, 2.50 mmol) and FC (hexanes/EtOAc 9:1) afforded 290 mg (87%) of **17c** as a colorless oil: $[\alpha]_D^{25}$ = +20.2 (EtOAc, *c* = 0.90). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.31−7.20 (m, 2H), 7.08 (d, *J* = 1.05 Hz, 1H), 4.04 (br s, 2H), 3.53 (dd, *J* = 9.0, 5.0 Hz, 1H), 3.37 (d, *J* = 9.0 Hz, 1H), 3.32 (s, 3H), 3.25−3.16 (m, 1H), 1.33 (br s, 12H), 1.27 (d, *J* = 6.8 Hz, 3H), 0.87 (s, 9H), 0.24 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 154.0, 149.5, 137.8, 137.1, 131.9, 129.1, 126.9, 77.8, 58.8, 53.8, 46.9, 33.4, 26.8, 20.7, 17.9, 17.3, −5.9. IR υ_{max} (film): 2923, 1715, 1447, 1314, 1205, 1142, 826 cm^{-1}. EI MS *m*/*z*: 407 ([M]$^+$, <1), 375 (11), 350 (29), 265 (10), 223 (29), 128 (100), 86 (74). Anal. Calcd for $C_{23}H_{41}NO_3Si$: C, 67.76; H, 10.14; N, 3.43. Found: C, 67.90; H, 9.96; N, 3.47.

The enantiomeric ratio was determined to be 98:2 (CHIRALCEL OD column, 1.5% Et_2O in hexanes, 0.8 mL/min).

5-[*tert*-Butyl(dimethyl)silyl]-2-[(1*S*)-1-(tributylstannyl)ethyl]-phenyl Diisopropylcarbamate (17d). According to General Procedure C: A solution of **15** (290 mg, 0.80 mmol) in hexanes (10 mL) was added to a mixture of *s*-BuLi (1.27 mL, 1.84 mmol, 1.45 M solution in cyclohexane) and (−)-sparteine (0.42 mL, 1.83 mmol) in hexanes (15 mL). Addition of tributyltin chloride (0.54 mL, 1.99 mmol) and FC (hexanes/EtOAc 98:2) afforded 370 mg (71%) of **17d** as a colorless oil: $[\alpha]_D^{25}$ = +21.7 (EtOAc, *c* = 1.33). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.13 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.06 (d, *J* = 7.7 Hz, 1H), 6.92 (d, *J* = 1.1 Hz, 1H), 3.98 (br s, 2H), 2.68 (q, *J* = 7.1 Hz, 1H), 1.48 (d, *J* = 7.1 Hz, 3H), 1.38−1.02 (m, 23H), 0.92−0.60 (m, 16H), 0.79 (s, 9H), 0.16 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 153.5, 146.9, 142.1, 132.6, 131.4, 127.7, 125.8, 46.3, 28.9, 27.4, 26.5, 21.6, 20.5, 19.9, 17.5, 16.9, 13.6, 9.1, −6.2. IR υ_{max} (film): 2957, 2928, 2856, 1715, 1450, 1311, 1217, 821 cm^{-1}. EI MS *m*/*z*: [M]$^+$ not detected, 596 (5), 409 (1), 362 (2), 305 (4), 235 (6), 177 (18), 128 (87), 86 (100). Anal. Calcd for $C_{33}H_{63}NO_2SiSn$: C, 60.73; H, 9.73; N, 2.15. Found: C, 61.00; H, 9.63; N, 2.10.

The enantiomeric ratio was determined to be 98:2 ((*S*,*S*)-WHELK-01 column, 1% Et_2O in hexanes, 0.5 mL/min).

5-[*tert*-Butyl(dimethyl)silyl]-2-[(1*S*)-1-(trimethylstannyl)-ethyl]phenyl Diisopropylcarbamate (17e). According to General Procedure C: A solution of **15** (79 mg, 0.22 mmol) in Et_2O (1.0 mL) was added to a mixture of *s*-BuLi (0.38 mL, 0.49 mmol, 1.31 M solution in cyclohexane) and (−)-sparteine (0.11 mL, 0.49 mmol) in Et_2O (3.5 mL). After addition of a solution of trimethyltin chloride (73 mg, 0.37 mmol) in Et_2O (1.0 mL), the mixture was worked up and purified by FC (hexanes/EtOAc 30:1) to give 103 mg (91%) of **17e** as a colorless solid: $[\alpha]_D^{25}$ = +17.8 (CH_2Cl_2, *c* = 0.035). mp 54−55 °C (aq. EtOH). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22 (d, *J* = 7.3 Hz, 1H), 7.08 (d, *J* = 7.3 Hz, 1H), 7.01 (s, 1H), 4.03 (m, 2H), 2.63 (q, *J* = 7.3 Hz, 1H), 1.52 (d, *J* = 7.3 Hz, 3H), 1.31 (br s, 12H), 0.85 (s, 9H), 0.23 (s, 6H), −0.03 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.8, 147.3, 141.9, 133.1, 131.8, 128.2, 125.4, 46.8, 46.5, 26.9, 23.6, 22.0, 21.0, 20.5, 17.1, −5.8, −9.9. IR υ_{max} (KBr): 1716, 1425, 1368, 1314, 1249, 1191, 1133, 1038 cm^{-1}. EI MS *m*/*z*: 525 ([M]$^+$, <1), 510 (4), 306 (23), 165 (72), 128 (100). HR MS (EI) calcd. for $C_{24}H_{45}NO_2SiSn$, 525.2242; found, 525.2247.

The enantiomeric ratio was determined to be 96:4 (CHIRALCEL OD column, 3% MTBE in hexanes, 0.8 mL/min).

5-[*tert*-Butyl(dimethyl)silyl]-2-[(1*S*)-1-(phenylsulfanyl)ethyl]-phenyl Diisopropylcarbamate (17f). According to General Procedure C: A solution of **15** (260 mg, 0.71 mmol) in hexanes (10 mL) was added to a mixture of *s*-BuLi (1.18 mL, 1.59 mmol, 1.35 M solution in cyclohexane) and (−)-sparteine (0.37 mL, 1.61 mmol) in hexanes (15 mL). Addition of phenyl disulfide (0.40 g, 1.83 mmol) and FC (hexanes/EtOAc 98:2) afforded 310 mg (91%) of **17f** as a colorless oil: $[\alpha]_D^{25}$ = −34.7 (EtOAc, *c* = 1.98). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.40−7.15 (m, 7H), 7.05 (d, *J* = 1.0 Hz, 1H), 4.50 (q, *J* = 7.0 Hz, 1H), 4.1−3.9 (m, 2H), 1.60 (d, *J* = 7.0 Hz, 3H), 1.30 (d, *J* = 6.8 Hz, 12H), 0.87 (s, 9H), 0.24 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 153.2, 147.9, 137.8, 135.9, 135.0, 132.8, 132.1, 131.6, 128.5, 128.2, 126.86, 126.83, 46.4, 41.0, 26.5, 21.6, 20.5, 16.9, −6.3. IR υ_{max} (film): 2960, 2931, 2857, 1716, 1312, 1215, 1042, 826 cm^{-1}. EI MS *m*/*z*: 471 ([M]$^+$, 2), 362 (88), 235 (13), 177 (37), 128 (100). Anal. Calcd for $C_{27}H_{41}NO_2SSi$: C, 68.74; H, 8.76; N, 2.97. Found: C, 68.84; H, 8.68; N, 3.07.

The enantiomeric ratio was determined to be 99:1 (CHIRALCEL OD column with 3% (0.5% Et_2NH in Et_2O) in hexanes, 0.8 mL/min).

5-[*tert*-Butyl(dimethyl)silyl]-2-[(1*S*)-1-(methylsulfanyl)ethyl]-phenyl Diisopropylcarbamate (17g). According to General Procedure C: A solution of **15** (216.2 mg, 0.60 mmol) in Et_2O (5 mL) was added along the wall of the flask over a period of 8 min to a mixture of *s*-BuLi (0.96 mL, 1.34 mmol, 1.4 M solution in cyclohexane) and (−)-sparteine (314 mg, 1.34 mmol) in Et_2O (7 mL). Addition of a solution of dimethyl disulfide (112 mg, 1.19 mmol) in Et_2O (2 mL) over a period of 3 min and FC (hexanes/EtOAc 25:1) afforded 216 mg (89%) of **17g** as a colorless solid: mp 69.5−70 °C (from oil). $[\alpha]_D^{25}$ = −0.23 (EtOAc, *c* = 0.5). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.54 (d, *J* = 7.7 Hz, 1H), 7.35 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.10 (d, *J* = 1.0 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 1H), 4.02 (br s, 2H), 1.92 (s, 3H), 1.56 (d, *J* = 7.1 Hz, 3H), 1.36−1.34 (d-like m, 12H), 0.90 (s, 9H), 0.28 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 153.3, 148.3, 137.5, 136.4, 131.7, 128.2, 126.7, 46.4, 38.6, 26.4, 21.4, 20.4, 16.9, 14.4, −6.2. IR υ_{max} (KBr): 2960, 2931, 1714, 1430, 1376, 1316, 1258, 1219, 1047, 996, 828, 804, 769 cm^{-1}. EI MS *m*/*z*: 409 ([M]$^+$, 6), 362 (89), 354 (10), 353 (24), 352 (100), 346 (12), 305 (10), 281 (33). HR MS (EI) calcd. for $C_{22}H_{39}NO_2SSi$, 409.2471; found, 409.2475.

The enantiomeric ratio was determined to be 97:3 (CHIRALCEL OD column, 5% MTBE in hexanes, 0.8 mL/min).

5-[*tert*-Butyl(dimethyl)silyl]-2-[(1*S*)-1-(phenylselanyl)ethyl]-phenyl Diisopropylcarbamate (17h). According to General Procedure C: A solution of **15** (230 mg, 0.63 mmol) in hexanes (8 mL) was added to a mixture of *s*-BuLi (1.06 mL, 1.43 mmol, 1.35 M solution in cyclohexane) and (−)-sparteine (0.33 mL, 1.44 mmol) in hexanes (12 mL). After addition of diphenyl diselenide (0.51 g, 1.63 mmol), the mixture was worked up and purified by FC (hexanes/EtOAc 97:3) to give 300 mg (90%) of **17h** as a colorless oil: $[\alpha]_D^{25}$ = −12.6 (EtOAc, *c* = 0.92). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.38−7.03 (m, 8H), 4.56 (q, *J* = 7.1 Hz, 1H), 4.02 (br s, 2H), 1.73 (d, *J* = 7.1 Hz,

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3H), 1.30 (d, J = 6.7 Hz, 12H), 0.88 (s, 9H), 0.24 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 153.1, 147.6, 137.5, 136.3, 135.4, 131.3, 129.4, 128.5, 128.2, 127.6, 126.8, 46.4, 35.1, 26.4, 21.7, 21.5, 20.5, 16.8, −6.3. IR υ_{max} (film): 2950, 2857, 1715, 1312, 1257, 1221, 821, 803 cm^{-1}. EI MS m/z: [M]$^+$ not detected, 391 (1), 362 (59), 305 (3), 235 (8), 177 (48), 128 (91), 86 (100). Anal. Calcd for $C_{27}H_{41}NO_2SeSi$: C, 62.52; H, 7.97; N, 2.70. Found: C, 62.70; H, 7.86; N, 2.79.

The enantiomeric ratio was determined to be 94:6 (CHIRALCEL OD column, 2.5% Et_2O in hexanes, 1.0 mL/min).

5-[*tert*-Butyl(dimethyl)silyl]-2-[(1*S*)-1-hydroxyethyl]phenyl Diisopropylcarbamate (17i). According to General Procedure C: To a −78 °C cold solution of (−)-sparteine (111 mg, 0.48 mmol) in Et_2O (3 mL) was added *s*-BuLi (0.37 mL of a 1.3 M solution in cyclohexane, 0.48 mmol). The mixture was stirred at −78 °C for 15 min; then, a solution of **15** (76.7 mg, 0.21 mmol) in Et_2O (3 mL) was added along the wall of the flask at −78 °C over a period of 4 min. A solution of $Me_3SiO-OSiMe_3$[53] (0.09 mL, ca. 75 mg, ca. 0.42 mmol) in Et_2O (2 mL) was added along the wall of the flask at −78 °C over a period of 3 min. The mixture was stirred at −78 °C for 1.5 h; then, it was allowed to warm to 0 °C over a period of 2.5 h. The cooling bath was removed, and the mixture was stirred at room temperature for 30 min. A saturated aq. NH_4Cl solution was added, and the mixture was extracted with Et_2O. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The residue was dissolved in AcOH/H_2O/THF 3:1:1 (2.5 mL) and stirred at room temperature for 5 h. The solvents were removed in vacuo, and purication with FC (hexanes/EtOAc 5:1) afforded 21.8 mg (27%) of **17i** as a slightly yellowish oil: $[\alpha]_D^{25}$ = −0.11 (EtOAc, c = 0.52). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.53 (d, J = 7.6 Hz, 1H), 7.38 (d, J = 7.6 Hz, 1H), 7.08 (s, 1H), 4.96 (q, J = 6.5 Hz, 1H), 4.16−3.98 (m, 2H), 2.98 (s, 1H), 1.50 (d, J = 6.5 Hz, 3H), 1.41−1.27 (m, 12H), 0.88 (s, 9H), 0.26 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 154.4, 147.7, 138.7, 138.2, 132.2, 127.9, 125.6, 63.8, 46.8, 46.4, 26.4, 22.1, 21.5, 20.4, 16.9, −6.2. IR υ_{max} (film): 3440 (br), 2965, 2932, 2859, 1712, 1466, 1436, 1376, 1316, 1256, 1213, 1191, 1137, 1075, 1044, 827 cm^{-1}. EI MS m/z: 379 ([M]$^+$, 2), 322 (20), 237 (37), 235 (63), 195 (76), 179 (37), 178 (34), 177 (100), 161 (18). HR MS (EI) calcd. for $C_{21}H_{37}NO_3Si$, 379.2543; found, 379.2513.

The enantiomeric ratio was determined to be 92:8 (CHIRALCEL OD column, hexanes/2-propanol 98:2, 0.4 mL/min).

5-[*tert*-Butyl(dimethyl)silyl]-2-[(1*S*)-1-(methylsulfanyl)ethyl]-phenol (18). To an ice-cold solution of anhydrous $AlCl_3$ (116.9 mg, 0.88 mmol) and $LiAlH_4$ (25.6 mg, 0.67 mmol) in Et_2O (8 mL) was added a solution of **17g** (207.4 mg, 0.51 mmol, 96:4 enantiomeric ratio) in Et_2O (4 mL). The ice bath was removed, and the mixture was stirred at room temperature for 3.5 h. The mixture was cooled with an ice bath, a saturated aq. NH_4Cl solution was added, and the mixture was extracted with Et_2O/CH_2Cl_2. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. FC (hexanes/EtOAc 25:1) afforded 123.9 mg (87%) of **18** as colorless solid: mp 71−72 °C (from oil). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.14 (s, 1H), 7.08−6.99 (m, 3H), 4.06 (q, J = 7.1 Hz, 1H), 1.94 (s, 3H), 1.64 (d, J = 7.1 Hz, 3H), 0.88 (s, 9H), 0.25 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 154.1, 138.8, 127.8, 127.1, 126.6, 123.4, 43.0, 26.5, 20.0, 16.9, 13.9, −6.2. IR υ_{max} (KBr): 3243 (br), 2951, 1567, 1397, 1248, 833, 815, 801, 774 cm^{-1}. EI MS m/z: 282 ([M]$^+$, 7), 235 (98), 225 (100), 177 (95). HR MS (EI) calcd. for $C_{15}H_{26}OSSi$, 282.1474; found, 282.1456.

The diastereomeric ratio was determined upon esterification with (−)-camphanic acid chloride; see the preparation of compound **19**.

5-[*tert*-Butyl(dimethyl)silyl]-2-[(1*S*)-1-(methylsulfanyl)ethyl]-phenyl (1*S*,4*R*)-4,7,7-Trimethyl-3-oxo-2-oxabicyclo[2.2.1]-heptane-1-carboxylate (19). To a mixture of **18** (123.9 mg, 0.44 mmol) and (−)-camphanic acid chloride (125.8 mg, 0.58 mmol) was added pyridine (2.5 mL) at room temperature. The mixture was stirred at room temperature for 5 h; then, it was concentrated in vacuo. FC (hexanes/EtOAc 10:1) afforded 180.4 mg (89%) of **19** as colorless solid: mp 102.5−104 °C (from oil). $[\alpha]_D^{25}$ = −0.17 (EtOAc, c = 0.5). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51 (d, J = 7.5 Hz, 1H), 7.39 (d, J = 7.5 Hz, 1H), 7.09 (s, 1H), 4.06 (q, J = 7.0 Hz, 1H), 2.63−2.53 (m, 1H), 2.28−2.19 (m, 1H), 2.04−1.95 (m, 1H), 1.88 (s, 3H), 1.81−1.72 (m, 1H), 1.54 (d, J = 7.0 Hz, 3H), 1.17 (s, 6H), 1.13 (s, 3H), 0.87 (s, 9H), 0.26 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 177.7, 166.1, 147.2, 138.4, 135.5, 132.7, 127.6, 127.2, 90.9, 54.9, 54.4, 38.4, 31.1, 29.0, 26.4, 21.0, 16.9, 16.86, 16.84, 14.1, 9.7, −6.29, −6.30. IR υ_{max} (KBr): 2953, 2928, 2856, 1800, 1771, 1469, 1386, 1306, 1256, 1217, 1166, 1101, 1048, 1016, 957, 932, 899, 836, 821, 806, 777 cm^{-1}. CI MS (NH_3) m/z: 480 ([M+NH_4]$^+$, <1), 463 ([M + H]$^+$, <1), 432 (29), 415 (100), 235 (10). HR MS (EI) calcd. for $C_{25}H_{38}O_4SSi$, 462.2260; found, 462.2241.

The diastereomeric ratio was determined to be 91:9 (two serially connected CHIRALCEL OD columns, hexanes/MTBE/2-propanol 93:5:2, 0.5 mL/min).

2-[(1*S*)-1-(Methylsulfanyl)ethyl]-5-(trimethylsilyl)phenyl Diisopropylcarbamate (21a). According to General Procedure C: A solution of **20** (104.7 mg, 0.33 mmol) in hexanes (5 mL) was added over a period of 30 min (syringe pump) to a mixture of *s*-BuLi (0.53 mL, 0.73 mmol, 1.37 M solution in cyclohexane) and (−)-sparteine (172 mg, 0.73 mmol) in hexanes (7 mL). After addition of a solution of dimethyl disulfide (92 mg, 0.98 mmol) in hexanes (4 mL) over a period of 20 min (syringe pump), the mixture was kept at −78 °C for 2 h, worked up (addition of a saturated aq. NH_4Cl solution at −78 °C), and purified by FC (hexanes/EtOAc 30:1) to give 94.7 mg (79%) of **21a** as a colorless solid: mp 84−85 °C (from oil). $[\alpha]_D^{25}$ = −0.25 (EtOAc, c = 0.5). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.54 (d, J = 7.6 Hz, 1H), 7.37 (dd, J = 7.6, 1.0 Hz, 1H), 7.10 (d, J = 1.0 Hz, 1H), 4.07 (q, J = 7.0 Hz, 1H, further 2H underneath), 1.91 (s, 3H), 1.53 (d, J = 7.0 Hz, 3H), 1.35−1.30 (m, 12H), 0.26 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 153.2, 148.4, 140.1, 136.5, 130.6, 127.01, 126.99, 46.4, 46.3, 38.6, 21.4, 20.3, 14.3, −1.3. IR υ_{max} (KBr): 2967, 1714, 1428, 1313, 1257, 1222, 1043, 995, 838 cm^{-1}. EI MS m/z: 367 ([M]$^+$, 1), 320 (14), 193 (79), 177 (96), 159 (10), 147 (11), 128 (100). HR MS (EI) calcd. for $C_{19}H_{33}NO_2SSi$, 367.2001; found, 367.1987.

The enantiomeric ratio was determined to be 99:1 (CHIRALCEL OD column, hexanes/MTBE 95:5, 0.8 mL/min).

If the reaction was performed in Et_2O (90% yield), then the enantiomeric ratio was determined to be 97:3.

5-(Trimethylsilyl)-2-[(1*S*)-1-(trimethylstannyl)ethyl]phenyl Diisopropylcarbamate (21b). According to General Procedure C: A solution of **20** (57 mg, 0.18 mmol) in Et_2O (1.0 mL) was added over a period of 30 min (syringe pump) to a mixture of *s*-BuLi (0.31 mL, 0.40 mmol, 1.27 M solution in cyclohexane) and (−)-sparteine (0.09 mL, 0.40 mmol) in Et_2O (3.0 mL). After addition of a solution of trimethyltin chloride (90 mg, 0.45 mmol) in Et_2O (1.0 mL) over a period of 20 min (syringe pump), the mixture was kept at −78 °C for 2 h, worked up (addition of a saturated aq. NH_4Cl solution at −78 °C), and purified by FC (hexanes/EtOAc 30:1) to give 61 mg (71%) of **21b** as colorless solid: $[\alpha]_D^{25}$ = +24.3 (CH_2Cl_2, c = 0.27). mp 71−72 °C (aq. EtOH). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (d, J = 7.8 Hz, 1H), 7.09 (d, J = 7.8 Hz, 1H), 7.04 (s, 1H), 4.03 (m, 2H), 2.68 (q, J = 7.6 Hz, 1H), 1.52 (d, J = 7.6 Hz, 3H), 1.31 (br s, 12H), 0.23 (s, 9H), −0.01 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 147.4, 141.9, 135.9, 130.7, 127.0, 125.9, 46.8, 46.5, 22.0, 20.9, 20.4, 17.2, −0.7, −9.9. IR υ_{max} (KBr): 1715, 1431, 1377, 1253, 1208, 1139, 822, 772 cm^{-1}. EI MS m/z: 485 ([M]$^+$, <1), 470 (13), 355 (13), 165 (74), 128 (100). HR MS (EI) calcd. for $C_{21}H_{39}NO_2SiSn$, 485.1772; found, 485.1780.

The enantiomeric ratio was determined to be 94:6 (CHIRALCEL OD column, 3% MTBE in hexanes, 0.8 mL/min).

2-[(1*R*)-1-Methylundecyl]phenyl Diethylcarbamate (25). To a solution of **12b** (30 mg, 0.069 mmol, 83:17 enantiomeric ratio enantiomeric excess) in THF (5 mL) was added TBAF (0.4 mL, 0.4 mmol, 1 M solution in THF) at room temperature. The mixture was stirred at room temperature for 20 h; then, a saturated aq. NH_4Cl solution was added, and extraction with Et_2O followed. The combined organic extract was washed with H_2O and brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. FC (hexanes/EtOAc 19:1) afforded 14 mg (62%) of **25** as a colorless oil. $[\alpha]_D^{25}$ = +6.9 (EtOAc, c = 0.23). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.23−7.00 (m, 4H), 3.46−3.36 (m, 4H), 2.90 (m, 1H), 1.52 (br s, 2H), 1.20 (m, 25H), 0.85 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 154.2, 149.2, 139.6, 126.8, 126.3, 125.4, 122.6, 42.1, 41.9, 37.4, 32.6, 31.9, 29.8, 29.7, 29.6, 29.3, 27.7, 22.7, 21.1, 14.3,

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14.1, 14.0. IR υ_{max} (film): 2933, 1722, 1417, 1271, 1213, 1156 cm^{-1}. EI MS m/z: 361 ($[M]^+$, <1), 177 (2), 121 (5), 100 (100), 72 (16). Anal. Calcd for $C_{23}H_{39}NO_2$: C, 76.40; H, 10.87; N, 3.87. Found: C, 76.48; H, 10.68; N, 4.05.

The enantiomeric ratio was determined to be 83:17 (CHIRALCEL OD column, 15% (0.5% Et_2NH in Et_2O) in hexanes, 0.8 mL/min).

2-[(1*S*)-1-(Phenylsulfanyl)ethyl]phenyl Diisopropylcarbamate (26). A mixture of **17f** (130 mg, 0.276 mmol, 99:1 enantiomeric ratio enantiomeric excess) and trifluoracetic acid (0.8 mL, 10.4 mmol) was stirred at room temperature for 24 h; then, a saturated aq. NH_4Cl solution was added, and extraction with Et_2O followed. The combined organic extract was washed with H_2O and brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. FC (hexanes/EtOAc 19:1) afforded 74 mg (78%) of **26** as colorless oil: $[\alpha]_D^{25}$ = +0.5 (EtOAc, c = 0.80). ^1H NMR (250 MHz, $CDCl_3$): δ 7.44 (dd, J = 7.5, 1.8 Hz, 1H), 7.27−7.10 (m, 7H), 7.02 (dd, J = 7.8, 1.5 Hz, 1H), 4.54 (q, J = 7.1 Hz, 1H), 4.20−3.85 (br s, 2H), 1.60 (d, J = 7.1 Hz, 3H), 1.35−1.30 (d-like m, 12H). ^{13}C NMR ($CDCl_3$): δ 153.2, 148.6, 135.5, 135.2, 131.8, 128.6, 127.8, 126.8, 125.4, 122.7, 46.6, 40.9, 21.8, 21.5, 20.4. IR υ_{max} (film): 2971, 1714, 1310, 1214, 1042, 748 cm^{-1}. EI MS m/z: 357 ($[M]^+$, 1), 248 (76), 128 (89), 6 (100). HR MS (EI) calcd. for $C_{21}H_{27}NO_2S$, 357.1779; found, 357.1757. Anal. Calcd for $C_{21}H_{27}NO_2S$: C, 70.55; H, 7.61; N, 3.92. Found: C, 70.65; H, 7.49; N, 4.07.

The enantiomeric ratio was determined to be 98:2 (CHIRALCEL OD column, 7% (0.5% Et_2NH in Et_2O) in hexanes, 0.8 mL/min).

Enantioselective Deprotonation vs Asymmetric Substitution. A solution of **6** (50 mg, 0.17 mmol) in Et_2O (1 mL) was dropwise added to a solution of *s*-BuLi (0.32 mL, 0.38 mmol, 1.20 M solution in cyclohexane) in Et_2O (2.5 mL) at −78 °C. The mixture was stirred for 2 h; then, a solution of (−)-sparteine (89 mg, 0.38 mmol) in Et_2O (1 mL) was added dropwise at −78 °C followed by a solution of trimethylsilyl chloride (0.065 mL, 0.51 mmol) in Et_2O (1 mL). The mixture was stirred at −78 °C for 1 h and then allowed to warm to room temperature, quenched with a saturated aq. NH_4Cl solution, and extracted with Et_2O. The combined organic extract was washed with brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. Purification by FC (hexanes/EtOAc 9:1) afforded 43.5 mg (70%) of **12a**.

The enantiomeric ratio was determined to be <51:49 ((*S*,*S*)-WHELK-01 column, 1% 2-propanol in hexanes, 1.0 mL/min).

Proof of Formation of rac-9. A solution of **6** (50 mg, 0.17 mmol) in Et_2O (1 mL) was dropwise added to a solution of *s*-BuLi (0.32 mL, 0.38 mmol, 1.20 M solution in cyclohexane) in Et_2O (2.5 mL) at −78 °C. The mixture was stirred for 2 h; then, a solution of trimethylsilyl chloride (0.065 mL, 0.51 mmol) in Et_2O (1 mL) was added dropwise at −78 °C. The mixture was stirred at −78 °C for 1 h, allowed to warm to room temperature, worked up, and purified to afford 37.3 mg (60%) of **rac-12a**.

Rearrangement Reaction from Attempted Generation of Benzyllithium Species in the Absence of a Ligand Starting from 20. A solution of **20** (31 mg, 0.10 mmol) in Et_2O (1.0 mL) was dropwise added to a solution of *s*-BuLi (0.17 mL, 0.22 mmol, 1.25 M solution in cyclohexane) in Et_2O (2.0 mL) at 0 °C. The mixture was stirred at 0 °C for 2 h and then cooled to −78 °C, and a solution of dimethyl disulfide (0.03 mL, 0.29 mmol) in Et_2O (1.0 mL) was added dropwise at −78 °C. The mixture was stirred at −78 °C for 1 h, quenched with a saturated aq. NH_4Cl solution at −78 °C, and, after the mixture warmed to room temperature, extracted with Et_2O. The combined organic extract was washed with brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. Purification by FC (hexanes/EtOAc 9:1) afforded 21 mg (67%) of 2-[4-(trimethylsilyl)-2-hydroxyphenyl]-*N*,*N*-diisopropylpropanamide (**22**) as a colorless solid: mp (sublimes) 150−152 °C (CH_2Cl_2/hexanes). ^1H NMR (400 MHz, $CDCl_3$): δ 7.12 (s, 1H), 6.99 (d, J = 7.8 Hz, 1H), 6.93 (d, J = 7.8 Hz, 1H), 4.21 (m, 2H), 3.96 (q, J = 7.3 Hz, 1H), 1.56 (d, J = 7.3 Hz, 3H), 1.35 (m, 12H), 0.26 (s, 9H), signal for 1H not visible. ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.2, 156.5, 141.6, 130.1, 126.6, 124.8, 124.0, 47.0, 20.8, 20.7, 18.2, −0.8. IR υ_{max} (KBr): 3277, 1619, 1594, 1403, 1346, 1270, 1060, 1037 cm^{-1}. EI MS m/z: 321 ($[M]^+$, 29), 306 (6), 205 (25), 128 (42), 86 (100). HR MS (EI) calcd. for $C_{18}H_{31}NO_2Si$, 321.2124; found, 321.2121.

Generation of a Benzyllithium Species in the Presence of (−)-Sparteine via Tin−Lithium Exchange from Racemic Starting Material and Subsequent Reaction with Dimethyl disulfide. A solution of **rac-21b** (52 mg, 0.11 mmol) in Et_2O (1.0 mL) was dropwise added to a solution of *s*-BuLi (0.19 mL, 0.24 mmol, 1.28 M solution in cyclohexane) and (−)-sparteine (57 mg, 0.24 mmol) in Et_2O (2.5 mL) at −78 °C. The mixture was stirred at −78 °C for 2 h; then, a solution of dimethyl disulfide (31 mg, 0.32 mmol) in Et_2O (1.0 mL) was added dropwise at −78 °C. The mixture was stirred at −78 °C for 2 h, quenched with a saturated aq. NH_4Cl solution at −78 °C, and, after the mixture warmed to room temperature, extracted with Et_2O. The combined organic extract was washed with brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. Purification by FC (hexanes/EtOAc 30:1) afforded 30 mg (75%) of **21a**.

The enantiomeric ratio was determined to be 53:47 (CHIRALCEL OD column, hexanes/MTBE 95:5, 0.8 mL/min).

Configurational Stability of Enantiomerically Enriched Benzyllithium Species. *In the Presence of TMEDA.* To a solution of **12e** (75 mg, 0.13 mmol, 86:14 enantiomeric ratio) and TMEDA (0.023 mL, 0.15 mmol) in Et_2O (4 mL) was added MeLi (0.1 mL, 0.16 mmol, 1.6 M solution in Et_2O) at −78 °C. The mixture was stirred at −78 °C for 2 h; then, a solution of trimethylsilyl chloride (0.05 mL, 0.40 mmol) in Et_2O (1 mL) was added dropwise at −78 °C. The mixture was stirred at −78 °C for 1 h, quenched with a saturated aq. NH_4Cl solution at −78 °C, and, after the mixture warmed to room temperature, extracted with Et_2O. The combined organic extract was washed with brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. Purification by FC (hexanes/EtOAc 9:1) afforded 41.4 mg (88%) of **12a**.

The enantiomeric ratio was determined to be 76:24 ((*S*,*S*)-WHELK-01 column, 1% 2-propanol in hexanes, 1.0 mL/min).

In the Presence of (−)-Sparteine. To a solution of **17e** (50 mg, 0.10 mmol, 82:18 enantiomeric ratio) in Et_2O (2.5 mL) were added *s*-BuLi (0.17 mL, 0.21 mmol, 1.25 M solution in cyclohexane) and (−)-sparteine (50 mg, 0.21 mmol) at −78 °C. The mixture was stirred at −78 °C for 2 h; then, a solution of dimethyl disulfide (27 mg, 0.29 mmol) in Et_2O (1.0 mL) was added dropwise at −78 °C. The mixture was stirred at −78 °C for 1 h, quenched with a saturated aq. NH_4Cl solution at −78 °C, and, after the mixture warmed to room temperature, extracted with Et_2O. The combined organic extract was washed with brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. Purification by FC (hexanes/EtOAc 30:1) afforded 26 mg (67%) of **17g**.

The enantiomeric ratio for **17g** was determined to be 78:22 (CHIRALCEL OD column, 5% MTBE in hexanes, 0.8 mL/min).

Starting from **17e** (82:18 enantiomeric ratio), the identical reaction using 1.2 equiv *s*-BuLi/(−)-sparteine afforded 49% of **17g** with an enantiomeric ratio of 77:23.

In the Absence of a Ligand. To a solution of **17e** (50 mg, 0.10 mmol, 82:18 enantiomeric ratio) in Et_2O (2.5 mL) was added *s*-BuLi (0.21 mL, 0.21 mmol, 1.00 M solution in cyclohexane) at −78 °C. The mixture was stirred at −78 °C for 2 h; then, a solution of dimethyl disulfide (27 mg, 0.29 mmol) in Et_2O (1.0 mL) was added dropwise at −78 °C. The mixture was stirred at −78 °C for 1 h, quenched with a saturated aq. NH_4Cl solution at −78 °C, and, after the mixture warmed to room temperature, extracted with Et_2O. The combined organic extract was washed with brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. Purification by FC (hexanes/EtOAc 30:1) afforded 19 mg (49%) of **17g**; 13 mg (26%) of **17e** were recovered.

The enantiomeric ratio for **17g** was determined to be 74:26 (CHIRALCEL OD column, 5% MTBE in hexanes, 0.8 mL/min).

The enantiomeric ratio of recovered **17e** was determined to be 82:18 (CHIRALCEL OD column, hexanes/MTBE 95:5, 0.8 mL/min).

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Poor Man's Hoffmann Test.[4b,17g,19,20,46] In order to achieve, as far as possible, identical reaction conditions, the following two reactions were performed in parallel in the same cooling bath.

Reaction Using an Excess of the Electrophile (3 Equiv). To a −78 °C cold solution of (−)-sparteine (82 mg, 0.35 mmol) in Et_2O (2.5 mL) was added *s*-BuLi (0.35 mL, 0.35 mmol, 1.0 M solution in cyclohexane). The mixture was kept 15 min at −78 °C; then, a solution of **20** (50 mg, 0.156 mmol) in Et_2O (1.0 mL) was added along the wall of the flask over a period of 10 min. The yellow solution was stirred at −78 °C for 2 h; then, a solution of dimethyl disulfide (44 mg, 0.47 mmol, 3 equiv) in Et_2O (1.0 mL) was added along the wall of the flask over a period of about 10 min. The mixture was stirred at −78 °C for 1 h; then, it was quenched with MeOD (2.0 mL) at −78 °C and stirred for additional 15 min at −78 °C. A saturated aq. NH_4Cl solution was added at −78 °C, and extraction with Et_2O followed after warming to room temperature. The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. FC (hexanes/EtOAc 30:1) afforded 31 mg (54%) of **21a**.

The enantiomeric ratio was determined to be 95:5 (CHIRALCEL OD HPLC column, hexanes/MTBE 95:5, 0.8 mL/min).

The possibility of a further lithiation of **21a** resulting in deuterated **d-21a** was ruled out by applying ^2H NMR and mass analyses. No indication of deuterium content >5% was found.

Reaction Using Substoichiometric Amount of the Electrophile (0.2 Equiv). To a −78 °C cold solution of (−)-sparteine (84 mg, 0.36 mmol) in Et_2O (2.5 mL) was added *s*-BuLi (0.36 mL, 0.36 mmol, 1.0 M solution in cyclohexane). The mixture was kept 15 min at −78 °C; then, a solution of **20** (51 mg, 0.159 mmol) in Et_2O (1.0 mL) was slowly added along the wall of the flask over a period of about 10 min. The yellow solution was kept at −78 °C for 2 h; then, a solution of dimethyl disulfide (1.1 mL of a 0.030 M stock solution in Et_2O, 0.032 mmol, 0.2 equiv) was added along the wall of the flask over a period of about 10 min. The mixture was kept at −78 °C for 2 min, quenched with MeOD (2.0 mL) at −78 °C, and stirred for an additional 15 min at −78 °C. A saturated aq. NH_4Cl solution was added at −78 °C, and extraction with Et_2O followed after warming to room temperature. The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. FC (hexanes/EtOAc 30:1) afforded 4 mg (7%) of **21a** and 30 mg (59%) of monodeuterated **d-20**.

The enantiomeric ratio of **21a** was determined to be 68:32 (CHIRALCEL OD HPLC column, hexanes/MTBE 95:5, 0.8 mL/min).

Data for **d-20:** ^1H NMR (400 MHz, CD_2Cl_2): δ 7.47 (m, 2H), 7.30 (d, J = 1.0 Hz, 1H), 4.22 (m, 2H), 2.73 (q, J = 7.6 Hz, 1H), 1.54 (m, 12H), 1.37 (d, J = 7.6 Hz, 3H), 0.47 (s, 9H). ^2H NMR (400 MHz, CH_2Cl_2): δ 2.73 (br s). EI MS m/z: 322 ($[M]^+$, 10), 180 (36), 128 (100). HR MS (EI) calcd. for $C_{18}H_{30}DNO_2Si$, 322.2186; found, 322.2178.

Deprotonation of 15 with 1 Equiv *s*-BuLi/(−)-Sparteine, Reaction with 1.05 Equiv Dimethyl Disulfide Followed by 1 Equiv *s*-BuLi/(−)-Sparteine. A solution of **15** (55 mg, 0.15 mmol) in Et_2O (1 mL) was added along the wall of the flask to a mixture of *s*-BuLi (0.12 mL, 0.15 mmol, 1.28 M solution in cyclohexane) and (−)-sparteine (36 mg, 0.15 mmol) in Et_2O (2.5 mL). The yellow solution was stirred at −78 °C for 2 h; then, a solution of dimethyl disulfide (15 mg, 0.16 mmol) in Et_2O (1 mL) was added over a period of 3 min. The solution was allowed to stir at −78 °C for 1 h, followed by addition of (−)-sparteine (36 mg, 0.15 mmol) in Et_2O (1 mL) and *s*-BuLi (0.12 mL, 0.15 mmol, 1.28 M solution in cyclohexane). The mixture was stirred at −78 °C for 1 h, quenched with a saturated aq. NH_4Cl solution at −78 °C, and, after the mixture warmed to room temperature, extracted with Et_2O. The combined organic extract was washed with brine, dried over anhydrous $MgSO_4$, subjected to filtration, and concentrated in vacuo. Purification by FC (hexanes/EtOAc 30:1) afforded 10 mg (16%) of **17g** as a colorless solid.

The enantiomeric ratio was determined to be 86:14 (CHIRALCEL OD column, 5% MTBE in hexanes, 0.8 mL/min).

■ ASSOCIATED CONTENT

Supporting Information

Computational details as well as ^1H and ^{13}C spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ DEDICATION

§Dedicated to Professor Bob Gawley: in Memoriam.

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(34) When Et_2O was used as the solvent, major attack at the *O*-carbamate carbonyl by the RLi reagent was observed, starting material was consumed, and the desired product **11a** was formed in only moderate yield.
(35) For observations concerning decreased enantioselectivty in the presence of bulky subtituents in reactions using (−)-sparteine, see refs 21a and 24c.
(36) Substituents located *meta* to a *N*,*N*-dialkyl phenyl-*O*-carbamate DMG have been demonstrated to favor lateral metalation (non-enantioselective) over D*o*M at the mutual *ortho* position in other systems. For an example, see: Marcos, I. S.; Beneitez, A.; Moro, R. F.; Basabe, P.; Díez, D.; Urones, J. G. *Tetrahedron* **2010**, *66*, 7773.
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(38) For example, Et_2O (37% yield, 95:5 er) and *t*-BuOMe (59% yield, 93:7 er).
(39) Treatment of **14** and **15** using 2.2 equiv of *s*-BuLi/TMEDA/−78 °C/2 h followed by TMSCl quench afforded racemic compounds **16a** (84%) and **17a** (94%), respectively. See Experimental Section.
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