JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

Radical Migration−Addition of *N-tert*-Butanesulfinyl Imines with Organozinc Reagents

Wei Huang,[†,∥] Jian-Liang Ye,[‡,∥] Wei Zheng,[†,∥] Han-Qing Dong,[§] and Bang-Guo Wei*[,†]

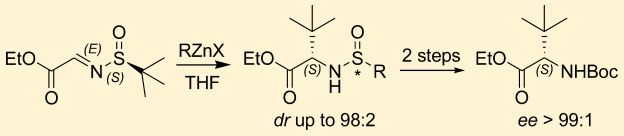
[†]Department of Chemistry and Institutes of Biomedical Sciences, Fudan University, 220 Handan Road, Shanghai 200433, China

[‡]College of Chemistry and Chemical Engineering and the Key Laboratory for Chemical Biology of Fujian Province, Xiamen University, Xiamen 361005, China

[§]OSI Pharmaceuticals, 1 Bioscience Park Drive, Farmingdale, New York 11735, United States

Supporting Information

ABSTRACT: A novel migration−addition sequence was discovered for the reaction of enantioenriched *N-tert*-butanesulfinyl iminoacetate **1a** with functionalized benzylzinc bromide reagents, producing *tert*-leucine derivatives in excellent diastereoselectivity (dr 98:2). The absolute configurations of two new chiral centers were unambiguously assigned by chemical transformations and X-ray crystallography. In addition, the regio- and diastereoselectivities of this novel reaction were both explained through the key *N*-sulfinamine intermediate **M6** generated by the *tert*-butyl radical attack on the imine. Computational analysis of this reaction process, which was performed at the B3LYP/6-311++G(3df,2p)//B3LYP/6-31G*-LANL2DZ level, also supported our proposed two-stage mechanism.



INTRODUCTION

The discovery and development of new asymmetric methods for efficient carbon−carbon bond formation is one of the most challenging tasks in modern organic synthesis.[1] In this context, the enantioselective addition reaction of organozinc reagents with imines[2] serves as a very powerful tool to prepare chiral amines[3] and unnatural amino acids and their derivatives,[4] which are extensively used as key intermediates for agrochemicals, pharmaceuticals, and chiral ligands.[5] For example, enantiopure *tert*-leucine and its derivatives are not only applied as chiral auxiliaries or ligands, but also extensively employed as potentially therapeutic pseudopeptides.[6] Over the past two decades, the asymmetric synthesis of D- or L-leucine and its derivatives has attracted much attention. Among the many highly enantioselective approaches reported so far,[7] the Strecker reaction is still one of the most important strategies in industry,[8] despite the use of highly toxic hydrogen cyanide or acetyl cyanide.

Chiral *N-tert*-butanesulfinyl imines, one class of the most efficient auxiliaries pioneered by Davis and Ellman, have shown versatile applications in the synthesis of various chiral amines.[9] During our continuous interest in the application of *N-tert*-butanesulfinyl imine as a synthetic tool for the total synthesis of natural products,[10] we observed an unusual migration−addition in the reaction of alkylzinc halide with racemic glyoxylate *N-tert*-butanesulfinyl imines.[11] As a result, the *tert*-butyl group migrated from sulfur to the imine carbon atom, while the alkyl group added to the sulfur. The driving force of this novel transformation and the stereochemistry in both the migration and addition steps intrigued us to undertake further studies. Herein we report our investigation of this novel asymmetric migration−addition starting from enantioenriched *N-tert*-butanesulfinyl iminoacetate **1a** (Scheme 1).

RESULTS AND DISCUSSION

In the presence of $Ni(acac)_2$, enantioenriched *N-tert*-butanesulfinyl iminoacetate **1a** reacted with *n*-butylzinc iodide (**2a**) at −78 °C, giving separable isomers **3a** in high yield (89%), albeit with low diastereoselectivity (61:39) (Table 1, entry 1). Other catalysts were screened to improve the diastereoselectivities, but turned out to be unhelpful (Table 1, entries 2−5). In the absence of catalyst, **3a** was obtained with similar diastereoselectivity but in lower yield (Table 1, entry 6). All these results indicated that $Ni(acac)_2$ was important for the yield but had no obvious effect on the diastereoselectivity. The reactions with different alkyzinc iodides in the presence of $Ni(acac)_2$ exhibited similar diastereoselectivities and good yields, as shown in Table 1 (entries 7−10).

Next we turned our attention to examine the reaction between (*S*)-*N-tert*-butanesulfinyl iminoacetate **1a** and benzylzinc bromide (**4a**). To our surprise, high diastereoselectivity was obtained, though the yield was low (Table 2, entry 1). According to our previous experience,[11] we screened various catalysts (Table 2, entries 1−5), attempting to improve the yield. Unfortunately, neither the yield of **5a** nor the diastereoselectivity was significantly improved by the tested catalysts. In addition, a side product from the addition of benzylzinc reagent to the C═N bond was formed in 9−17% yields (Table 2, entries 1−5). Gratifyingly, in the absence of catalyst, the product **5a** not only became predominant in the reaction mixture, but also showed excellent stereoselectivity (dr 98:2), although there was still inseparable side product **6a** (Table 2, entry 6). When DCM was selected as the solvent,[12]

Received: July 28, 2013
Published: October 8, 2013

Scheme 1. Proposed Asymmetric Migration−Addition

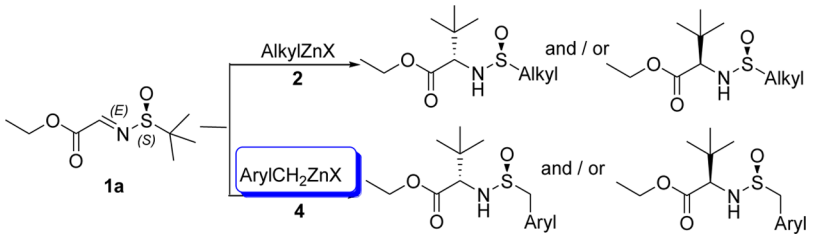
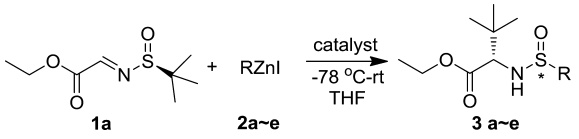


Table 1. Diastereoselective Migration−Addition with Alkylzinc Iodides



entry[a]	R	catalyst	3	yield[b] (%)	dr[c]
1	n-$C_3H_7CH_2$−	$Ni(acac)_2$	**3a**	89	68:32
2	n-$C_3H_7CH_2$−	H_2O	**3a**	45	58:42
3	n-$C_3H_7CH_2$−	$Cu(OTf)_2$	**3a**	23	60:40
4	n-$C_3H_7CH_2$−	$In(OTf)_3$	**3a**	18	65:35
5	n-$C_3H_7CH_2$−	$ZnBr_2$	**3a**	26	59:41
6	n-$C_3H_7CH_2$−	none	**3a**	61	55:45
7	CH_3CH_2−	$Ni(acac)_2$	**3b**	92	61:39
8	cyclohexyl	$Ni(acac)_2$	**3c**	90	60:40
9	$BnOOC(CH_2)_3$−	$Ni(acac)_2$	**3d**	73	62:38
10	n-$C_9H_{19}CH_2$−	$Ni(acac)_2$	**3e**	66	65:35

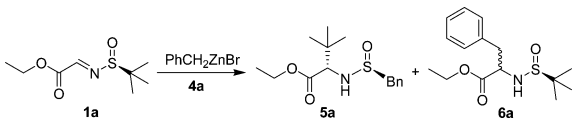
[a]The reactions were performed with *N*-*tert*-butanesulfinyl iminoacetate **1a** (1.0 mmol), catalyst (0.1 mmol), and alkylzinc iodides **2** (2.5 mmol) in dry THF (5 mL) for 12 h, unless otherwise noted. [b]Isolated yield. [c]Diastereoselectivity was determined by GC−MS.

5a could not be determined (Table 2, entry 7). Other solvents such as 1,4-dioxane and Et_2O remarkably decreased the yield (Table 2, entries 8 and 9). The reaction was tried at lower temperature. Obviously, the migration−addition sequence did not take place below −30 °C (Table 2, entry 10), while other options provided no improvement in terms of the yield of **5a** (Table 2, entries 11 and 12). It is noteworthy that the reported byproduct 1-[(*tert*-butylsulfinyl)methyl]benzene (*t*-BuSOBn)[12] in the reaction of imine with organozinc reagents was not observed in all our cases.

To investigate the scope and limitations of this migration−addition, various substituted benzylzinc bromide reagents **4a−o** and several imines **1a−c** were examined under the optimal conditions (Table 2, entry 6). As summarized in Table 3, the migration−addition proceeded smoothly with excellent diastereoselectivities in most cases, although the yields were moderate (entries 1−15). When imines **1b** and **1c** were used, no desired product could be determined. In all cases, the major diastereoisomers **5a−o** could be isolated by chromatography on silica gel while the minor diastereoisomers were inseparable from adducts of the C═N bond.

Two new chiral centers were generated in this migration−addition sequence. To determine the absolute configuration at the α-position of the carboxylate, the isolated product **5a** from the above reaction was converted to the known leucine derivatives **7** and **8** (Scheme 2). Removal of the *N*-sulfinyl group of **5a** and subsequent protection with Boc_2O gave compound **7** in 86% yield {$[\alpha]_D^{20}$ +9.68 (c 1.01, $CHCl_3$)}. Hydrolysis of compound **7** with LiOH according to the literature procedure[13] gave *N*-Boc-protected acid **8** {$[\alpha]_D^{20}$ +5.81 (c 1.62, EtOAc); lit.[14] $[\alpha]_D^{20}$ 5.80 (c 0.6, EtOAc)} in 95% yield. In addition, an authentic sample of compound **7** was

Table 2. Examination of Benzylzinc Bromide

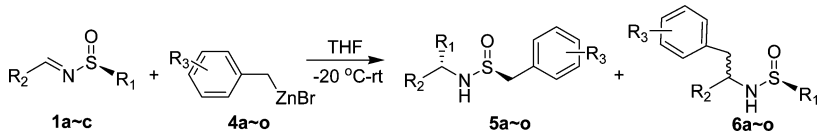


entry[a]	solvent	catalyst	T (°C)	yield of **5a**[b] (%)	dr[c]	yield of **6a** (%)
1	THF	$Ni(acac)_2$	−20 to rt	47	82:18	11[d]
2	THF	$In(OTf)_3$	−20 to rt	19	86:14	9[d]
3	THF	$Cu(OTf)_2$	−20 to rt	27	83:17	nd
4	THF	$Pd(PPh_3)_2Cl_2$	−20 to rt	29	89:11	17[d]
5	THF	$BF_3{\cdot}Et_2O$	−20 to rt	nd		nd
6	THF	none	−20 to rt	75	98:2	8[e]
7	DCM	none	−20 to rt	nd		10
8	dioxane	none	−20 to rt	6	98:2	13
9	Et_2O	none	−20 to rt	<5		11
10	THF	none	−78 to −30	trace		trace
11	THF	none	−30 to +20	25	98:2	trace
12	THF	none	−20 to 0	38	98:2	<5[e]

[a]The reactions were performed with *N*-*tert*-butanesulfinyl iminoacetate **1a** (1.0 mmol), catalyst (0.1 mmol), and benzylzinc bromide (**4a**) (2.5 mmol) in dry solvent (5 mL) for 12 h, unless otherwise noted. [b]Isolated yield of product **5a**. [c]Diastereoselectivity was determined by HPLC of the crude product. [d]Isolated yields of inseparable addition products. [e]The yields of the adducts were determined by LC−MS of the crude reaction mixture.

dx.doi.org/10.1021/jo401640c | J. Org. Chem. 2013, 78, 11229−11237

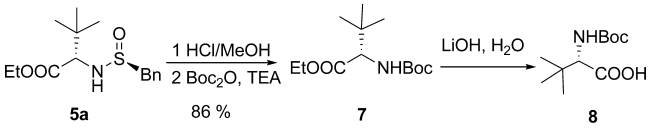
Table 3. Highly Diastereoselective Migration−Addition of Substituted Benzylzinc Bromides



entry[a]	R_1	R_2	R_3	5	yield[b] (%)	dr[c]	yield of adduct[d] (%)
1	*t*-Bu	EtOOC	H	**5a**	75	98:2	8
2	*t*-Bu	EtOOC	2-F	**5b**	46	96:4	<5
3	*t*-Bu	EtOOC	3-F	**5c**	51	95:5	<2
4	*t*-Bu	EtOOC	4-F	**5d**	68	98:2	<2
5	*t*-Bu	EtOOC	2-Cl	**5e**	55	96:4	<2
6	*t*-Bu	EtOOC	3-Cl	**5f**	53	95:5	7
7	*t*-Bu	EtOOC	4-Cl	**5g**	64	96:4	6
8	*t*-Bu	EtOOC	4-Br	**5h**	67	98:2	5
9	*t*-Bu	EtOOC	3-CN	**5i**	41	89:11	6
10	*t*-Bu	EtOOC	4-CN	**5j**	51	97:3	8
11	*t*-Bu	EtOOC	2-CH_3	**5k**	67	98:2	<5
12	*t*-Bu	EtOOC	4-CH_3	**5l**	73	98:2	6
13	*t*-Bu	EtOOC	3-CF_3	**5m**	48	98:2	<3
14	*t*-Bu	EtOOC	4-CF_3	**5n**	66	98:2	<3
15	*t*-Bu	EtOOC	4-COOEt	**5o**	58	94:6	5
16	Ph	EtOOC	H	**5p**	nd		nd
17	*t*-Bu	Ph	H	**5q**	nd		nd

[a]The reactions were performed with iminoacetate **1** (1.0 mml) and substituted benzylzinc bromides **4** (2.5 mmol) in dry solvent (5 mL) for 12 h, unless otherwise noted. [b]Isolated yield. [c]Diastereoselectivity was determined by LC−MS of the crude mixture. [d]The yields of **6** were determined by LC−MS and HPLC of the crude mixtures.

Scheme 2. Configuration Determination of Compound 5a

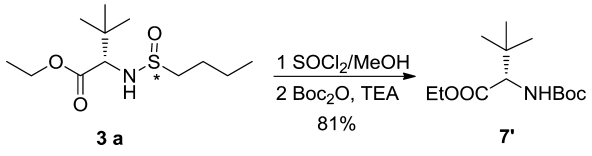


prepared from the commercial L-*tert*-leucine, giving identical ^1H and ^{13}C NMR spectra along with optical rotation $[\alpha]_D^{20}$ = +8.98 (*c* 1.03, $CHCl_3$). The results from these multiple chemical transformations clearly demonstrate the *S* configuration for the *α*-carbon of the carboxylate.

Next the absolute configuration of the chiral sulfoxide was unambiguously determined as the *S* stereocenter by X-ray crystallography analysis of compound **5h**.

To understand the different diasteroselectivities observed for the alkylzinc reagent, the diastereomeric mixture of **3a**, obtained in Table 1, entry 1, was broken down to check the stereochemistry for the process of *tert*-butyl group migration. As such, crude **3a** was treated with $SOCl_2$ in MeOH, and the resulting free amine was protected with Boc_2O in the presence of triethylamine to afford compound **7′** in 84% overall yield (Scheme 3). Interestingly, the optical rotation value of **7′** {$[\alpha]_D^{20}$ +9.57 (*c* 1.00, $CHCl_3$)} was almost identical to that of **7** {$[\alpha]_D^{20}$ +9.68 (*c* 1.01, $CHCl_3$)}, which was prepared from compound **5a**. These data suggested that the *tert*-butyl group added to the

Scheme 3. Configuration Determination of Compound 3a



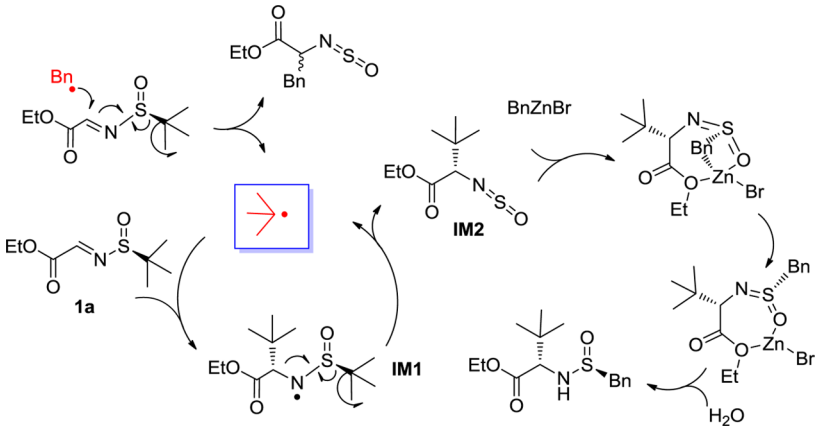
C═N bond in a stereospecific manner for both cases, with either alkylzinc or benzylzinc reagent, generating the new chiral center in the *S* configuration. The observed diastereoisomers should come from the subsequent reaction at the sulfur center.

To explain how this novel migration−addition proceeded, the intramolecular transition state was initially proposed, but the results of density functional theory (DFT) calculations with the B3LYP functional and the 6-31G* basis set with the Gaussian03 quantum chemistry package[15] indicated that the high-energy pathway was not consistent with the observed stereochemical outcome (see the Supporting Information for details). Therefore, a stepwise mechanism involving two different stages was proposed (Scheme 4). At the first stage, a small amount of alkyl or benzyl radical, which was generated from the organozinc reagents in the presence of zinc powder,[16] attacked the carbon atom of the C═N bond and the single electron on the nitrogen atom further formed a new N═S double bond, releasing a more stable *tert*-butyl radical.[17] The resulting *tert*-butyl radical then added to the C═N bond in **1a**, generating the first chiral center in **IM1**. Meanwhile, a new *tert*-butyl radical was released. The resulting *tert*-butyl radical initiated a reaction cycle, producing a key intermediate, **IM2**, for the second step. The attack of the *tert*-butyl group on the imine was stereospecifically controlled by the chiral *tert*-butyl sulfoxide moiety of the substrate **1a**. At the second stage, the zinc reagent reacted with the −N═S═O functionality in **IM2**, creating a new sulfur chiral center. In the second process, the bulkier benzyl group of benzylzinc bromide could attack the sulfur atom of the N═S═O bond from the favorable face, while the alkyl group could not. Thus, different diastereoslectivities were observed between alkyl- and benzylzinc reagents in the migration−addition.

To further demonstrate our proposed radical mechanism, the commercial Et_2Zn was applied as a zinc reagent. It was

dx.doi.org/10.1021/jo401640c | J. Org. Chem. 2013, 78, 11229−11237

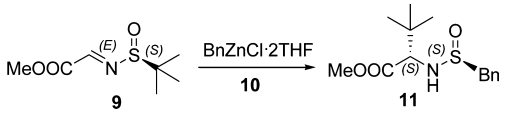
Scheme 4. Proposed Mechanism of the Migration−Addition Process



observed that the migration−addition did not occur in the absence of $Ni(acac)_2$. Interestingly, the addition of 0.1 equiv of zinc powder could promote this reaction to give product **3b** in 25% yield, albeit with low diastereoselectivity (58:42). In the reaction of benzylzinc bromide with **1a**, the migration−addition did not occur when the solvent was replaced with HMPA. Instead, the benzyl group selectively added to imine, giving the side product **6a** in 25% yield. This could be explained by the strong coordinating effect of HMPA,[18] which could minimize the initial generation of benzyl radical. In addition, the coordination with Lewis acids also affected the migration−addition, thus affording **5a** in low yields (Table 2, entries 1−5).

To better understand this migration−addition process at the molecular level, we conducted DFT calculations with the B3LYP functional and the 6-31G* basis set (LANL2DZ for Zn) with the Gaussian03 quantum chemistry package.[15] To reduce the time for calculation in the computational process, a simple model[19] with compounds **9**, **10** (solvated monoorganozinc species readily formed in a THF solution of organozinc reagent),[20] and **11** replacing **1a**, **4a**, and **5a** was chosen to maintain the fundamental characters of the real reaction (Scheme 5).

Scheme 5. Model of Quantum Mechanical Calculation



First, the results showed the energy for benzyl radical to attack the carbon atom of the C═N bond (Figure 1, **TS3** and **TS4**) was lower than that to attack the sulfur atom of the S═O bond (Figure 1, **TS1** and **TS2**) by 9.33−19.77 kcal/mol. Therefore, benzyl radical preferentially added to the C═N bond with high chemoselectivity, generating intermediates **M3** and **M4** and *tert*-butyl radical (Figure 1).

Next *tert*-butyl radical attacked the carbon atom of the C═N bond in the starting material instantly. However, approaching from the *Si* face (Figure 2, **TS8**) was 4.48 kcal/mol lower in energy than that from the *Re* face (Figure 2, **TS7**). Therefore, key intermediate **M6** was generated stereospecifically along with a new *tert*-butyl radical for the cycle. Then organozinc reagent coordinated with carbonyl oxygen atoms in the ester group and N═S═O bond and attacked S═O from the favorable *Si* face. The corresponding transition state **TS11** was 3.25 kcal/mol lower than **TS10** (from the *Re* face). Products **P1** and **P2** were provided exothermically by 3.68 and 11.24 kcal/mol, respectively. As a consequence, (*S*,*S*)-product **P1** was generated with high stereoselectivity. In the EtZnCl case, the transition state **TS13** of EtZnCl addition to S═O from the *Si* face was 1.77 kcal/mol lower than **TS12** (from the *Re* face). The energy difference is in poor agreement with the experimental result. In the *n*-BuZnI and BnZnBr addition cases (Table 1, entry 6, and Table 2, entry 6), assuming a Boltzmann's distribution of the transition states leading to the two diastereomers,[21] the experimental energy differences of the two transition states were 0.08 and 1.96 kcal/mol, respectively, calculated by the dr value. Thus, the computed barrier energy difference (1.48 kcal/mol) in the EtZnCl and BnZnCl addition cases is basically in line with the experimental result (1.88 kcal/mol). In this regard, these results further support our proposed mechanism for this novel migration−addition of *N*-*tert*-butanesulfinyl iminoacetate **1a** with substituted benzylzinc bromide reagents **4a**−**o**.

■ CONCLUSION

In conclusion, this is the first time that a new type of asymmetric addition−migration involving *N*-*tert*-butanesulfinyl iminoacetate **1a** with substituted benzylzinc bromide reagents **4a**−**o** with excellent diastereoselectivities has been demonstrated. This discovery of a new asymmetric method for formation of a C−C bond by rearrangement provides a new approach for asymmetric synthesis of chiral leucine and its derivatives. In addition, the mechanism and regio- and diasteroselectivities of this novel reaction have been investigated by the hybrid density functional B3LYP/6-311++G(3df, 2p)//B3LYP/6-31G*-LANL2DZ level of theory. The theoretical predictions are in line with the experimental results. All these results pose challenging work for imine chemistry. Further exploration and application in organic synthesis for other active imines are now in progress in our laboratory.

■ EXPERIMENTAL SECTION

General Procedures. THF was distilled from sodium/benzophenone. Zinc dust was activated by being stirred for 5 min with HCl (1 N), followed by washing successively with water, acetone, and ether. Reactions were monitored by thin-layer chromatography (TLC) on glass plates coated with silica gel with a fluorescent indicator. Flash chromatography was performed on silica gel with petroleum ether (PE)/EtOAc as the eluent. Melting points were uncorrected. Optical rotations were measured with a sodium lamp. HRMS (MALDI/TOF)

dx.doi.org/10.1021/jo401640c | J. Org. Chem. 2013, 78, 11229−11237

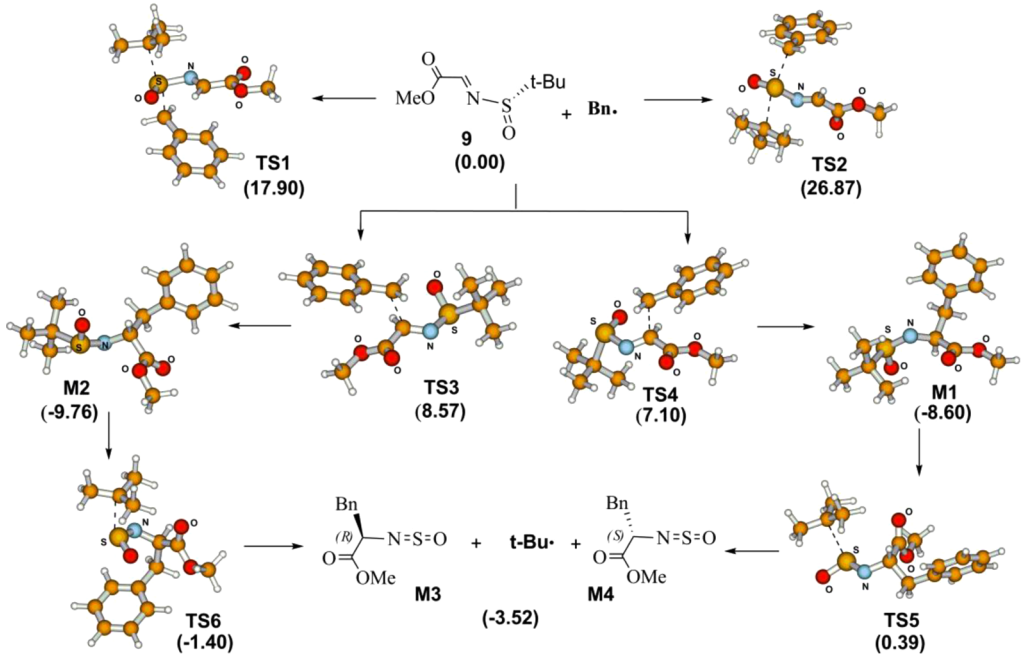


Figure 1. B3LYP/6-31G*-optimized geometries and total energies (kcal/mol, in parentheses) relative to isolated model reactant **9** and the Bn radical at the B3LYP/6-311++G(3df,2p) level of the transition states and intermediates for Bn radical addition to the S═O bond (**TS1**, **TS2**) and to the C═N bond (**TS3**, **TS4**, **M1**, **M2**) and the transition states in generating the *t*-Bu radcial (**TS5**, **TS6**) and corresponding intermediates (**M3**, **M4**).

was performed on an LC/MS-IT-TOF apparatus. IR spectra were recorded using KBr disks or a film. NMR spectra were recorded at 300 or 400 MHz, and chemical shifts are reported in δ (ppm) referenced to an internal TMS standard for ^{1}H NMR and $CDCl_3$ (77.0 ppm) for ^{13}C NMR.

(*R*,*E*)-Ethyl 2-[(*tert*-Butylsulfinyl)imino]acetate (1a). Ethyl glyoxylate (5.00 g, 24.5 mmol, 50% solution in toluene) was depolymerized at 50 °C for 5 min under an argon atmosphere and cooled to room temperature. Molecular sieves (4 Å, 15 g) were added in one portion, and then a solution of (*S*)-2-methylpropane-2-sulfinamide (3.80 g, 24.5 mmol) in CH_2Cl_2 (75 mL) was added dropwise. After being stirred for 72 h, the reaction mixture was filtered through Celite, and the residue was washed with EtOAc (50 mL × 2). The combined organic layers were concentrated under reduced pressure. The residue was purified by chromatography on silica gel (EtOAc/PE) to give **1a** (4.77 g, 95% yield) as a colorless oil: $[\alpha]_D^{25}$ +295.9 (*c* 0.85 in $CHCl_3$); IR (KBr) 2982, 2930, 2871, 1748, 1727, 1609, 1458, 1368, 1333, 1282, 1207, 1097, 1030, 964, 858 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.99 (s, 1H), 4.36 (q, *J* = 7.0 Hz, 2H), 1.36 (t, *J* = 6.5 Hz, 3H), 1.25 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.1, 155.6, 62.4, 58.9, 22.7, 14.0 ppm.

Preparation of Alkylzinc Iodides. Zinc powder (780 mg, 12 mmol) was suspended in anhydrous THF (5 mL) under N_2, and then 1,2-dibromoethane (43 μL, 0.5 mmol) was added. The mixture was heated at 65 °C for 5 min. After the mixture was cooled to rt, (TMS)Cl (63 μL, 0.5 mmol) was added, and the mixture was stirred for another 15 min before the solution of iodide (10 mmol) in anhydrous THF (5 mL) was added dropwise. The resulting mixture was stirred for 10 h at 40 °C to give the alkylzinc iodide as a 1 M solution in THF.

Preparation of Benzylzinc Bromide. Zinc powder (780 mg, 12 mmol) was suspended in anhydrous THF (5 mL) under N_2, and then 1,2-dibromoethane (43 μL, 0.5 mmol) was added. The mixture was heated at 65 °C for 5 min. After the mixture was cooled to 0 °C, a solution of bromide (10 mmol) in anhydrous THF (5 mL) was added dropwise. The resulting mixture was stirred for 10 h at 0 °C to give the benzylzinc bromide as a 1 M solution in THF.

General Procedure for the 1,3-Migration−Addition of Alkylzinc Reagents with 1a. To a solution of **1a** (205 mg, 1 mmol) in anhydrous THF (5 mL) was added dropwise freshly prepared alkylzinc iodide reagents **2** (2.5 mL, 1 M in THF) at −78 °C under an argon atmosphere, and then the mixture was stirred for 12 h while being warmed to room temperature. The reaction was quenched with saturated NH_4Cl aqueous solution (10 mL) and diluted with EtOAc (30 mL). The organic layer was separated, and the aqueous phase was extracted with EtOAc three times. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel to give the title compound.

Data for (*S*)-ethyl 2-[(*S*)-butanesulfinamido]-3,3-dimethylbutanoate [(2*S*,*sS*)-3a]: colorless oil (159 mg, 61%); $[\alpha]_D^{25}$ −52.3 (*c* 0.92 in $CHCl_3$); IR (KBr) 3244, 2960, 2932, 2866, 1732, 1463, 1364, 1315, 1216, 1151 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.69 (d, *J* = 10.5 Hz, 1H), 4.27−4.17 (m, 2H), 3.65 (d, *J* = 11.1 Hz, 1H), 2.75−2.67 (m, 2H), 1.68−1.58 (m, 2H), 1.51−1.41 (m, 2H), 1.29 (t, *J* = 6.6 Hz, 3H), 1.01(s, 9H), 0.94 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.0, 61.2, 60.9, 54.3, 34.0, 26.7, 25.2, 21.9, 14.1, 13.7 ppm; MS (ESI) *m*/*z* 286 (M + Na$^+$); HRMS (MALDI/TOF) *m*/*z* calcd for [$C_{12}H_{25}NO_3S$ + Na$^+$] 286.1455, found 286.1448.

Data for (*S*)-ethyl 2-[(*R*)-butanesulfinamido]-3,3-dimethylbutanoate [(2*S*,*sR*)-3a]: colorless oil (74 mg, 28%); $[\alpha]_D^{25}$ +48.1 (*c* 0.80 in $CHCl_3$); IR (KBr) 3245, 2963, 2935, 1731, 1465, 1362, 1321, 1217 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.45 (d, *J* = 9.3 Hz, 1H), 4.26−4.19 (m, 2H), 3.53 (d, *J* = 9.6 Hz, 1H), 2.85−2.76 (m, 2H), 1.73−1.65 (m, 2H), 1.50−1.42 (m, 2H), 1.30 (t, *J* = 7.2 Hz, 3H), 1.01−0.93 (m, 12H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.6, 66.5, 61.3, 56.2, 34.9, 26.3, 25.1, 21.9, 14.1, 13.7 ppm; MS (ESI) *m*/*z* 286 (M + Na$^+$); HRMS (MALDI/TOF) *m*/*z* calcd for [$C_{12}H_{25}NO_3S$ + Na$^+$] 286.1455, found 286.1446.

Data for (*S*)-ethyl 2-[(*S*)-cyclohexanesulfinamido]-3,3-dimethylbutanoate [(2*S*,*sS*)-3c]: colorless oil (156 mg, 54%); $[\alpha]_D^{25}$ −70.3 (*c* 1.0 in $CHCl_3$); IR (KBr) 3278, 2928, 2854, 1732, 1450, 1368, 1304, 1262, 1215, 1157, 1069 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.48 (d, *J* = 10.8 Hz, 1H), 4.27−4.17 (m, 2H), 3.60 (d, *J* = 10.5 Hz, 1H), 2.58−2.53 (m, 1H), 2.09−2.06 (m, 1H), 1.96−1.82 (m, 3H), 1.41−1.21 (m, 9H), 1.02 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.9, 62.4, 61.1, 60.9, 34.1, 26.7, 26.4, 26.2, 25.5, 25.2, 25.1, 14.1 ppm; MS (ESI) *m*/*z* 312 (M + Na$^+$); HRESIMS *m*/*z* calcd for ($C_{14}H_{27}NO_3S$ + H$^+$) 290.1790, found 290.1781.

Data for (*S*)-ethyl 2-[(*R*)-cyclohexanesulfinamido]-3,3-dimethylbutanoate [(2*S*,*sR*)-3c]: colorless oil (104 mg, 36%); $[\alpha]_D^{25}$ +59.6

dx.doi.org/10.1021/jo401640c | *J. Org. Chem.* 2013, 78, 11229−11237

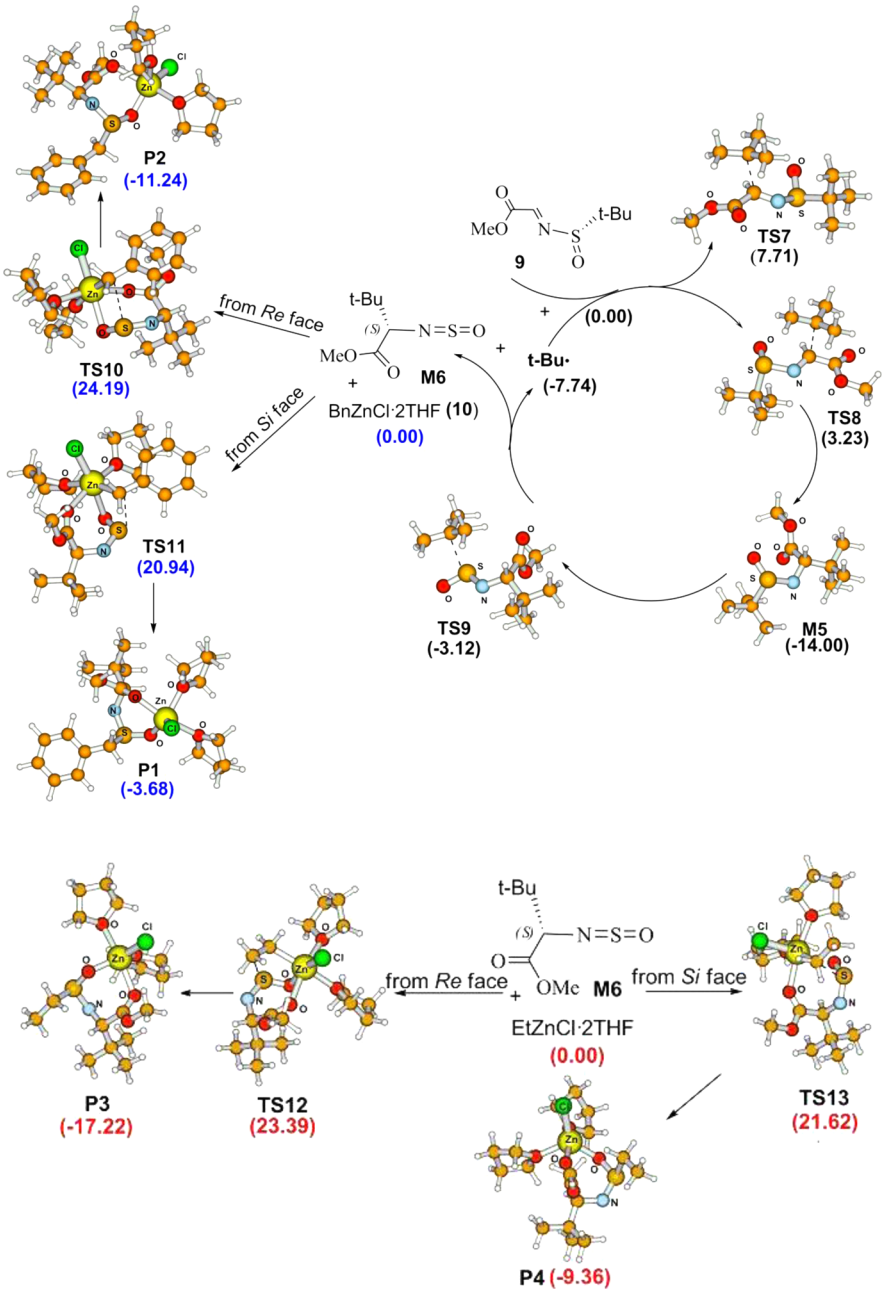


Figure 2. B3LYP/6-31G*(LANL2DZ for Zn)-optimized geometries and total energies (kcal/mol, in parentheses) at the B3LYP/6-311++G(3df,2p) level relative to isolated model reactant **9** and *t*-Bu radical. The transition states involved *t*-Bu radical attack of C═N from the *Re* face (**TS7**) and from the *Si* face (**TS8**) and corresponding intermediate **M5**. The transition state **TS9** involved homolysis of *t*-BuSO in **M5** and generation of intermdiate **M6**. B3LYP/6-31G*(LANL2DZ for Zn)-optimized geometries and total energies (kcal/mol, in parentheses) at the B3LYP/6-311++G(3df,2p) level relative to intermdiate **M6** and BnZnCl·2THF (blue) and EtZnCl·2THF (red). The transition states involved addition to S═O from the *Re* face (**TS10**, **TS12**) to give corresponding products **P2** and **P3** and from the *Si* face (**TS11**, **TS13**) to give corresponding products **P1** and **P4**.

(*c* 0.69 in $CHCl_3$); IR (KBr) 3281, 2927, 2858, 1733, 1446, 1365, 1305, 1266, 1210 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.32 (d, J = 9.3 Hz, 1H), 4.25−4.18 (m, 2H), 3.53 (d, J = 9.3 Hz, 1H), 2.62−2.54 (m, 1H), 2.10−2.01 (m, 2H), 1.92−1.85 (m, 2H), 1.47−1.22 (m, 9H), 1.02 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.9, 66.5, 63.3, 61.3, 35.1, 26.4, 25.9, 25.5, 25.3, 25.1, 14.1 ppm; MS (ESI) m/z 312 (M + Na^+); HRMS (MALDI/TOF) m/z calcd for [$C_{14}H_{27}NO_3S$ + H^+] 290.1790, found 290.1788.

Data for (*S*)-ethyl 2-[(*S*)-4-(benzyloxy)butanesulfinamido]-3,3-dimethylbutanoate [(2*S*,*sS*)-3d]: colorless oil (167 mg, 45%); $[\alpha]_D^{25}$ −49.4 (*c* 0.82 in $CHCl_3$); IR (KBr) 3266, 3167, 2960, 1732, 1478, 1454, 1367, 1312, 1215, 1158, 1100, 1027 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.34−7.28 (m, 5H), 4.78 (br s, 1H), 4.49 (s, 2H), 4.22−4.19 (m, 2H), 3.62 (d, J = 10.5 Hz, 1H), 3.52−3.47 (m, 2H), 2.80−2.65 (m, 2H), 1.79−1.70 (m, 4H), 1.29 (t, J = 7.0 Hz, 3H), 0.99 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.0, 138.3, 128.4, 127.6, 72.9, 69.5, 61.2, 60.8, 53.9, 34.0, 28.7, 26.6, 20.3, 14.1 ppm; MS (ESI) m/z 370 (M + H^+); HRMS (MALDI/TOF) m/z calcd for [$C_{19}H_{31}NO_4S$ + H^+] 370.2052, found 370.2059.

Data for (*S*)-ethyl 2-[(*R*)-4-(benzyloxy)butanesulfinamido]-3,3-dimethylbutanoate [(2*S*,*sR*)-3d]: colorless oil (102 mg, 28%); $[\alpha]_D^{25}$ −47.9 (*c* 1.0 in $CHCl_3$); IR (KBr) 3269, 3168, 2965, 1731, 1476, 1453, 1369, 1217, 1161 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.34−7.28 (m, 5H), 4.50−4.47 (m, 3H), 4.24−4.19 (m, 2H), 3.54−3.48 (m,

dx.doi.org/10.1021/jo401640c | *J. Org. Chem.* 2013, 78, 11229−11237

3H), 2.86−2.78 (m, 2H), 1.85−1.73 (m, 4H), 1.29 (t, J = 7.0 Hz, 3H), 0.96 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.6, 138.3, 128.4, 127.6, 72.9, 69.4, 66.5, 61.3, 56.2, 34.9, 28.7, 26.3, 20.2, 14.1 ppm; MS (ESI) m/z 370 (M + H$^+$); HRMS (MALDI/TOF) m/z calcd for [$C_{19}H_{31}NO_4S$ + H$^+$] 370.2052, found 370.2061.

Data for (*S*)-ethyl 2-[(*S*)-decanesulfinamido]-3,3-dimethylbutanoate [(2*S*,s*S*)-3e]: colorless oil (149 mg, 43%); $[\alpha]_D^{25}$ −54.9 (c 0.84 in $CHCl_3$); IR (KBr) 3211, 2958, 2925, 2855, 1735, 1466, 1369, 1318, 1214, 1156, 1095, 1069, 1024 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.66 (d, J = 10.8 Hz, 1H), 4.27−4.17 (m, 2H), 3.63 (d, J = 10.8 Hz, 1H), 2.75−2.64 (m, 2H), 1.68−1.59 (m, 2H), 1.43−1.26 (m, 17H), 1.01 (s, 9H), 0.88 (t, J = 6.6 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.0, 61.2, 60.8, 54.5, 34.0, 31.8, 29.4, 29.3, 29.2, 28.7, 26.7, 23.2, 22.6, 14.1 ppm; MS (ESI) m/z 370 (M + Na$^+$); HRMS (MALDI/TOF) m/z calcd for [$C_{18}H_{37}NO_3S$ + H$^+$] 348.2572, found 348.2561.

Data for (*S*)-ethyl 2-[(*R*)-decanesulfinamido]-3,3-dimethylbutanoate [(2*S*,s*R*)-3e]: colorless oil (80 mg, 23%); $[\alpha]_D^{25}$ +41.3 (c 1.19 in $CHCl_3$); IR (KBr) 3213, 2959, 2927, 1737, 1465, 1366, 1214, 1162, 1092 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.42 (d, J = 9.3 Hz, 1H), 4.26−4.19 (m, 2H), 3.53 (d, J = 9.3 Hz, 1H), 2.85−2.75 (m, 2H), 1.76−1.66 (m, 2H), 1.43−1.26 (m, 17H), 0.97 (s, 9H), 0.88 (t, J = 6.6 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.6, 66.5, 61.3, 56.5, 34.9, 31.8, 29.4, 29.3, 29.2, 29.2, 28.6, 26.7, 26.3, 23.1, 22.6, 14.1 ppm; MS (ESI) m/z 370 (M + Na$^+$); HRMS (MALDI/TOF) m/z calcd for [$C_{18}H_{37}NO_3S$ + H$^+$] 348.2572, found 348.2569.

General Procedure for the 1,3-Migration−Addition of Benzylzinc Reagent with (*R*,*E*)-Ethyl 2-[(*tert*-butylsulfinyl)imino]acetate (1a). To a solution of **1a** (205 mg, 1 mmol) in anhydrous THF (5 mL) was added dropwise freshly prepared substituted benzylzinc bromide reagents **4** (2.5 mL, 1 M in THF) at −20 °C under an argon atmosphere, and then the mixture was stirred for 12 h while being warmed to room temperature. The reaction was quenched with saturated NH_4Cl aqueous solution (10 mL) and diluted with EtOAc (30 mL). The organic layer was separated, and the aqueous phase was extracted with EtOAc three times. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel to give the title compound.

Data for (*S*)-ethyl 3,3-dimethyl-2-[(*S*)-phenylmethanesulfinamido]butanoate (5a): white solid (223 mg, 75%); mp 148−150 °C; $[\alpha]_D^{25}$ +132.2 (c 0.60 in $CHCl_3$); IR (KBr) 3166, 2959, 1733, 1454, 1366, 1325, 1216, 1160, 1104, 1073, 1052, 1029, 776, 703 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.42−7.32 (m, 5H), 4.33 (d, J = 9.3 Hz, 1H), 4.20−4.12 (m, 2H), 4.03 (s, 2H), 3.48 (d, J = 9.3 Hz, 1H), 1.24 (t, J = 7.2 Hz, 3H), 0.83 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.2, 130.5, 129.3, 128.7, 128.3, 66.4, 62.1, 61.2, 35.0, 26.2, 14.1 ppm; MS (ESI) m/z 298 (M + H$^+$); HRMS (MALDI/TOF) m/z calcd for [$C_{15}H_{23}NO_3S$ + H$^+$] 298.1477, found 298.1469.

Data for (*S*)-ethyl 2-[(*S*)-(2-fluorophenyl)methanesulfinamido]-3,3-dimethylbutanoate (5b): white solid (145 mg, 46%); mp 153−154 °C; $[\alpha]_D^{25}$ +183.4 (c 0.80, $CHCl_3$); IR (KBr) 3171, 2958, 1732, 1491, 1325, 1158, 1084, 1068, 762 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.34−7.30 (m, 2H), 7.16−7.08 (m, 2H), 4.49 (d, J = 9.4 Hz, 1H), 4.21−4.15 (m, 2H), 4.16−4.06 (m, 2H), 3.43 (d, J = 9.4 Hz, 1H), 1.26 (t, J = 7.0 Hz, 3H), 0.77 (s, 9H) ppm; ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −116.77 to −116.88 (m) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.2, 161.2 (d, J = 246.1 Hz), 132.2 (d, J = 3.0 Hz), 130.1 (d, J = 7.6 Hz), 124.4 (d, J = 3.8 Hz), 117.7 (d, J = 15.3 Hz), 115.6 (d, J = 21.3 Hz), 66.7, 61.3, 55.7, 35.0, 26.0, 14.1 ppm; MS (ESI) m/z 316 (M + H$^+$), 338 (M + Na$^+$); HRMS (MALDI/TOF) m/z calcd for ($C_{15}H_{22}FNO_3S$ + H$^+$) 316.1383, found 316.1381.

Data for (*S*)-ethyl 2-[(*S*)-(3-fluorophenyl)methanesulfinamido]-3,3-dimethylbutanoate (5c): white solid (161 mg, 51%); mp 157−159 °C; $[\alpha]_D^{25}$ +118.5 (c 0.74 in $CHCl_3$); IR (KBr) 3172, 2959, 1735, 1614, 1591, 1487, 1450, 1326, 1159, 1104, 1068, 1050, 948, 793 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.38−7.32 (m, 1H), 7.12−7.05 (m, 3H), 4.38 (d, J = 9.3 Hz, 1H), 4.21−4.15 (m, 2H), 4.07−3.98 (m, 2H), 3.49 (d, J = 9.3 Hz, 1H), 1.25 (t, J = 6.6 Hz, 3H), 0.85 (s, 9H) ppm; ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −112.80 to −112.91 (m) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.2, 162.8 (d, J = 245.7 Hz), 131.7 (d, J = 7.9 Hz), 130.3 (d, J = 8.3 Hz), 126.1 (d, J = 2.9 Hz), 117.4 (d, J = 21.7 Hz), 115.3 (d, J = 20.9 Hz), 66.5, 61.6, 61.3, 35.0, 26.2, 14.1 ppm; MS (ESI) m/z 316 (M + H$^+$), 338 (M + Na$^+$); HRMS (MALDI/TOF) m/z calcd for [$C_{15}H_{22}FNO_3S$ + H$^+$] 316.1383, found 316.1375.

Data for (*S*)-ethyl 2-[(*S*)-(4-fluorophenyl)methanesulfinamido]-3,3-dimethylbutanoate (5d): white solid (214 mg, 68%); mp 146−147 °C; $[\alpha]_D^{25}$ +123.6 (c 0.82 in $CHCl_3$); IR (KBr) 3161, 2966, 1736, 1602, 1510, 1368, 1325, 1220, 1160, 1067, 1052, 843 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.33−7.28 (m, 2H), 7.11−7.05 (m, 2H), 4.30 (d, J = 9.6 Hz, 1H), 4.21−4.13 (m, 2H), 4.05 (d, J = 13.1 Hz, 1H), 3.96 (d, J = 13.1 Hz, 1H), 3.49 (d, J = 9.3 Hz, 1H), 1.25 (t, J = 6.9 Hz, 3H), 0.85 (s, 9H) ppm; ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −113.82 to −113.92 (m) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.2, 162.8 (d, J = 247.5 Hz), 132.2 (d, J = 8.2 Hz), 125.3 (d, J = 2.7 Hz), 115.8 (d, J = 21.7 Hz), 66.5, 61.3, 61.1, 35.0, 26.2, 14.1 ppm; MS (ESI) m/z 316 (M + H$^+$), 338 (M + Na$^+$); HRMS (MALDI/TOF) m/z calcd for [$C_{15}H_{22}FNO_3S$ + H$^+$] 316.1383, found 316.1373.

Data for (*S*)-ethyl 2-[(*S*)-(2-chlorophenyl)methanesulfinamido]-3,3-dimethylbutanoate (5e): white solid (183 mg, 55%); mp 118−120 °C; $[\alpha]_D^{25}$ +157.1 (c 0.92 in $CHCl_3$); IR (KBr) 3178, 2956, 1732, 1474, 1366, 1323, 1216, 1158, 1067, 1049, 922, 770 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.43−7.37 (m, 2H), 7.29−7.24 (m, 2H), 4.53 (d, J = 9.4 Hz, 1H), 4.30−4.23 (m, 2H), 4.21−4.16 (m, 2H), 3.43 (d, J = 9.4 Hz, 1H), 1.26 (t, J = 7.0 Hz, 3H), 0.76 (s, 9H); ppm ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.2, 134.6, 132.4, 129.7, 129.6, 128.7, 127.1, 66.8, 61.3, 60.0, 35.0, 26.0, 14.1 ppm; MS (ESI) m/z 354 (M + Na$^+$); HRMS (MALDI/TOF) m/z calcd for [$C_{15}H_{22}ClNO_3S$ + H$^+$] 332.1087, found 332.1079.

Data for (*S*)-ethyl 2-[(*S*)-(3-chlorophenyl)methanesulfinamido]-3,3-dimethylbutanoate (5f): white solid (176 mg, 53%); mp 116−117 °C; $[\alpha]_D^{25}$ +71.6 (c 0.90 in $CHCl_3$); IR (KBr) 3170, 2960, 1732, 1594, 1477, 1366, 1323, 1215, 1157, 1065, 1048, 921, 789 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.32−7.28 (m, 2H), 7.22−7.19 (m, 2H), 4.37 (d, J = 9.5 Hz, 1H), 4.21−4.14 (m, 2H), 4.03−3.96 (m, 2H), 3.48 (d, J = 9.5 Hz, 1H), 1.25 (t, J = 7.0 Hz, 3H), 0.84 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.2, 134.6, 131.5, 130.5, 130.0, 128.6, 128.5, 66.5, 61.6, 61.3, 35.0, 26.2, 14.1 ppm; MS (ESI) m/z 354 (M + Na$^+$); HRMS (MALDI/TOF) m/z calcd for [$C_{15}H_{22}ClNO_3S$ + H$^+$] 332.1087, found 332.1075.

Data for (*S*)-ethyl 2-[(*S*)-(4-chlorophenyl)methanesulfinamido]-3,3-dimethylbutanoate (5g): white solid (212 mg, 64%); mp 139−140 °C; $[\alpha]_D^{25}$ +110.4 (c 0.90 in $CHCl_3$); IR (KBr) 3169, 2957, 1736, 1492, 1368, 1326, 1215, 1154, 1065, 1050, 841 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.37 (d, J = 8.4 Hz, 2H), 7.26 (d, J = 8.1 Hz, 2H), 4.29 (d, J = 9.3 Hz, 1H), 4.23−4.12 (m, 2H), 4.04−3.94 (m, 2H), 3.49 (d, J = 9.3 Hz, 1H), 1.25 (t, J = 6.9 Hz, 3H), 0.86 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.2, 134.4, 131.7, 128.9, 127.8, 66.5, 61.3, 61.2, 35.0, 26.2, 14.1 ppm; MS (ESI) m/z 354 (M + Na$^+$); HRMS (MALDI/TOF) m/z calcd for [$C_{15}H_{22}ClNO_3S$ + H$^+$] 332.1087, found 332.1101.

Data for (*S*)-ethyl 2-[(*S*)-(4-bromophenyl)methanesulfinamido]-3,3-dimethylbutanoate (5h): white solid (252 mg, 67%); mp 147−149 °C; $[\alpha]_D^{25}$ +102.2 (c 0.94 in $CHCl_3$); IR (KBr) 3173, 2955, 1732, 1488, 1368, 1326, 1214, 1155, 1065, 838 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.52 (d, J = 8.1 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H), 4.32 (d, J = 9.0 Hz, 1H), 4.23−4.12 (m, 2H), 4.03−3.93 (m, 2H), 3.49 (d, J = 9.3 Hz, 1H), 1.25 (t, J = 6.9 Hz, 3H), 0.86 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.1, 132.0, 131.9, 128.3, 122.6, 66.4, 61.3, 35.0, 26.2, 14.1 ppm; MS (ESI) m/z 398 (M + Na$^+$); 400 (M + 2 + Na$^+$); HRMS (MALDI/TOF) m/z calcd for [$C_{15}H_{22}BrNO_3S$ + H$^+$] 376.0582, found 376.0573. Single crystals of **5h** suitable for X-ray diffraction were obtained from ethyl acetate. See the Supporting Information for full crystallographic data.

Data for (*S*)-ethyl 2-[(*S*)-(3-cyanophenyl)methanesulfinamido]-3,3-dimethylbutanoate (5i): white solid (132 mg, 41%); mp 99−101 °C; $[\alpha]_D^{25}$ +103.4 (c 1.0 in $CHCl_3$); IR (KBr) 3230, 3058, 2958, 2242, 1738, 1369, 1322, 1212, 1155, 1070, 941, 808 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.67−7.63 (m, 2H), 7.60−7.58 (m,

dx.doi.org/10.1021/jo401640c | J. Org. Chem. 2013, 78, 11229−11237

1H), 7.52−7.49 (m, 1H); 4.36 (d, J = 9.4 Hz, 1H), 4.22−4.10 (m, 2H), 4.10−4.01 (m, 2H), 3.49 (d, J = 9.4 Hz, 1H), 1.26 (t, J = 7.1 Hz, 3H), 0.85 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.1, 134.8, 133.8, 131.9, 131.2, 129.6, 118.2, 113.0, 66.5, 61.4, 61.1, 35.0, 26.2, 14.1 ppm; MS (ESI) m/z 345 (M + Na^+); HRMS (MALDI/TOF) m/z calcd for [$C_{16}H_{22}N_2O_3S$ + Na^+] 345.1251, found 345.1247.

Data for (*S*)-ethyl 2-[(*S*)-(4-cyanophenyl)methanesulfinamido]-3,3-dimethylbutanoate (5j): white solid (164 mg, 51%); mp 128−130 °C; $[\alpha]_D^{25}$ +109.7 (c 0.70 in $CHCl_3$); IR (KBr) 3159, 2959, 2230, 1732, 1319, 1219, 1164, 1064, 1049, 858 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.69 (d, J = 7.8 Hz, 2H), 7.45 (d, J = 8.1 Hz, 2H), 4.42 (m, 1H), 4.22−4.15 (m, 2H), 4.14−4.04 (m, 2H), 3.48 (d, J = 9.6 Hz, 1H), 1.26 (t, J = 7.2 Hz, 3H), 0.85 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.1, 134.9, 132.4, 131.1, 118.4, 112.2, 66.5, 61.7, 61.4, 35.1, 26.2, 22.3, 14.1 ppm; MS (ESI) m/z 345 (M + Na^+); HRMS (MALDI/TOF) m/z calcd for [$C_{16}H_{22}N_2O_3S$ + H^+] 323.1429, found 323.1442.

Data for (*S*)-ethyl 3,3-dimethyl-2-[(*S*)-*o*-tolylmethanesulfinamido]butanoate (5k): white solid (208 mg, 67%); mp 88−89 °C; $[\alpha]_D^{25}$ +153.8 (c 0.72 in $CHCl_3$); IR (KBr) 3176, 2956, 1733, 1366, 1324, 1216, 1156, 1066, 1049, 921, 773 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.25−7.21 (m, 4H), 4.40 (m, 1H), 4.21−4.16 (m, 2H), 4.15−4.06 (m, 2H), 3.46 (d, J = 9.2 Hz, 1H), 2.41 (s, 3H), 1.25 (t, J = 7.3 Hz, 3H), 0.79 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.3, 137.3, 131.5, 130.6, 128.5, 128.4, 126.3, 66.6, 61.3, 60.5, 35.0, 26.1, 19.9, 14.1 ppm; MS (ESI) m/z 312 (M + H^+); HRMS (MALDI/TOF) m/z calcd for [$C_{16}H_{25}NO_3S$ + H^+] 312.1633, found 312.1647.

Data for (*S*)-ethyl 3,3-dimethyl-2-[(*S*)-*p*-tolylmethanesulfinamido]butanoate (5l): white solid (227 mg, 73%); mp 118−119 °C; $[\alpha]_D^{25}$ +131.5 (c 0.68 in $CHCl_3$); IR (KBr) 3157, 2957, 1733, 1367, 1323, 1215, 1158, 1068, 1051, 893, 822 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.22−7.17 (m, 4H), 4.28 (d, J = 9.2 Hz, 1H), 4.19−4.12 (m, 2H), 4.02−3.93 (m, 2H), 3.48 (d, J = 9.2 Hz, 1H), 2.34 (s, 3H), 1.23 (t, J = 7.3 Hz, 3H), 0.85 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.1, 138.1, 130.4, 129.5, 125.9, 66.4, 61.7, 61.2, 35.0, 26.2, 21.2, 14.1 ppm; MS (ESI) m/z 312 (M + H^+); HRESIMS m/z calcd for [$C_{16}H_{25}NO_3S$ + H^+] 312.1633, found 312.1631.

Data for (*S*)-ethyl 3,3-dimethyl-2-[(*S*)-(3-(trifluoromethyl)-phenyl)methanesulfinamido]butanoate (5m): white solid (175 mg, 48%); mp 157−159 °C; $[\alpha]_D^{25}$ +98.7 (c 0.88 in $CHCl_3$); IR (KBr) 3159, 2964, 1735, 1479, 1450, 1369, 1334, 1219, 1160, 1076, 893, 805, 704 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.54−7.51 (m, 2H), 7.62−7.58 (m, 2H), 4.38 (d, J = 9.4 Hz, 1H), 4.21−4.14 (m, 2H), 4.13−4.06 (m, 2H), 3.47 (d, J = 9.4 Hz, 1H), 1.24 (t, J = 7.1 Hz, 3H), 0.82 (s, 9H) ppm; ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −63.1 ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.2, 133.8, 131.2 (q, J = 32 Hz), 130.9, 129.3, 127.2 (q, J = 3.4 Hz), 125.0 (q, J = 3.4 Hz), 123.8 (q, J = 270.7 Hz), 66.7, 61.8, 61.3, 35.0, 26.1, 14.1 ppm; MS (ESI) m/z 388 (M + Na^+); HRMS (MALDI/TOF) m/z calcd for [$C_{16}H_{22}F_3NO_3S$ + Na^+] 388.1170, found 388.1177.

Data for (*S*)-ethyl 3,3-dimethyl-2-[(*S*)-(4-(trifluoromethyl)-phenyl)methanesulfinamido]butanoate (5n): white solid (241 mg, 66%); mp 132−133 °C; $[\alpha]_D^{25}$ +83.0 (c 0.86 in $CHCl_3$); IR (KBr) 3165, 2959, 1730, 1616, 1419, 1369, 1326, 1217, 1162, 1068, 921, 855 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.64 (d, J = 8.2 Hz, 2H), 7.45 (d, J = 8.2 Hz, 2H), 4.39 (d, J = 9.0 Hz, 1H), 4.19−4.15 (m, 2H), 4.13−4.04 (m, 2H), 3.48 (d, J = 9.8 Hz, 1H), 1.24 (t, J = 7.4 Hz, 3H), 0.84 (s, 9H) ppm; ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −63.1 ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.1, 133.6, 130.8, 125.7, 125.6, 66.5, 61.6, 61.3, 35.0, 26.2, 14.0, 14.1 ppm; MS (ESI) m/z 388 (M + Na^+); HRMS (MALDI/TOF) m/z calcd for [$C_{16}H_{22}F_3NO_3S$ + H^+] 366.1351, found 366.1343.

Data for ethyl 4-({(*S*)-*N*-[(*S*)-1-ethoxy-3,3-dimethyl-1-oxobutan-2-yl]sulfinamoyl}methyl)benzoate (5o): white solid (214 mg, 58%); mp 145−147 °C; $[\alpha]_D^{25}$ +101.3 (c 0.60 in $CHCl_3$); IR (KBr) 3165, 2959, 1732, 1708, 1594, 1457, 1408, 1366, 1322, 1279, 1217, 1156, 1065, 1047, 925, 783, 718 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.06 (d, J = 8.0 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H), 4.40−4.32 (m, 3H), 4.20−4.04 (m, 4H), 3.47 (d, J = 9.2 Hz, 1H), 1.39 (t, J = 7.3 Hz, 3H), 1.24 (t, J = 7.3 Hz, 3H), 0.83 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.1, 166.2, 134.3, 130.4, 130.3, 129.9, 66.5, 61.9, 61.3, 61.1, 35.1, 26.2, 14.3, 14.1 ppm; MS (ESI) m/z 370 (M + H^+); HRMS (MALDI/TOF) m/z calcd for [$C_{18}H_{27}NO_5S$ + H^+] 370.1688, found 370.1676.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra, details for computational calculations, and X-ray structural data (CIF) for compound **5h**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: bgwei1974@fudan.edu.cn.

Author Contributions

‖W.H., J.-L.Y., and W.Z. contributed equally to this work.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the National Natural Science Foundation of China (Grants 21272041, 21072034, and 20832005), the Key Laboratory for Chemical Biology of Fujian Province, and the Natural Science Foundation of Fujian Province of China (Grant 2011J01056) for financial support. We also thank Dr. Xin-Sheng Lei and Prof. X. Sun for helpful suggestions. This paper is dedicated to Prof. Guoqiang Lin on the occasion of his 70th birthday.

■ REFERENCES

(1) (a) Tsuji, J. *Transition Metal Reagents and Catalysts: Innovations in Organic Synthesis*; Wiley: Chichester, U.K., 2000. (b) Ojima, I. *Catalytic Asymmetric Synthesis*; Wiley-VCH: Weinheim, Germany, 2000.

(2) For some recent examples, see: (a) Alvaro, G.; Pacioni, P.; Savoia, D. *Chem.—Eur. J.* **1997**, *3*, 726. (b) Fujihara, H.; Nagai, K.; Tomioka, K. *J. Am. Chem. Soc.* **2000**, *122*, 12055. (c) Hermanns, N.; Dahmen, S.; Bolm, C.; Bräse, S. *Angew. Chem., Int. Ed.* **2002**, *41*, 3692. (d) Esquivias, J.; Arrayás, R. G.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2007**, *46*, 9257. (e) Lauzon, C.; Charette, A. B. *Org. lett.* **2006**, *8*, 2743. (f) Almansa, R.; Guijarro, D.; Yus, M. *Tetrahedron: Asymmetry* **2008**, *19*, 603. (g) Almansa, R.; Guijarro, D.; Yus, M. *Tetrahedron Lett.* **2009**, *50*, 4188. (h) Almansa, R.; Collados, J. F.; Guijarro, D.; Yus, M. *Tetrahedron: Asymmetry* **2010**, *21*, 1421.

(3) For general reviews, see: (a) Enders, D.; Reinhold, U. *Tetrahedron: Asymmetry* **1997**, *8*, 1895. (b) Bloch, R. *Chem. Rev.* **1998**, *98*, 1407. (c) For a review on *N*-phosphinoyl imines, see: Weinreb, S. M.; Orr, R. K. *Synthesis* **2005**, 1205. (d) For a review on *N*-acyl imines, see: Petrini, M.; Torregiani, E. *Synthesis* **2007**, 159.

(4) For reviews, see: (a) Greger, H. *Chem. Rev.* **2003**, *103*, 2795. (b) Yet, L. *Angew. Chem., Int. Ed.* **2001**, *40*, 875. (c) Spino, C. *Angew. Chem., Int. Ed.* **2004**, *43*, 1764.

(5) (a) Barrett, G. C. *Chemistry and Biochemistry of the Amino Acids*; Chapman and Hall: London, 1985. (b) Jones, J. H. *Amino Acids and Peptides*; The Royal Society of Chemistry: London, 1992. (c) Seyden-Penne, J. *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*; Wiley: New York, 1995. (d) Blaser, H.-U. *Chem. Rev.* **1992**, *92*, 935.

(6) Fauchere, J.-L.; Petermaan, C. *Helv. Chim. Acta* **1980**, *63*, 824.

(7) For some recent examples, see: (a) Williams, R. M. *Synthesis of Optically Active R-Amino Acids*; Pergamon: Oxford, U.K., 1989. (b) Cativiela, C.; Díaz-de-Villegas, M. D. *Tetrahedron: Asymmetry* **1998**, *9*, 3517. (c) Calmes, M.; Daunis, J. *Amino Acids* **1999**, *16*, 215. (d) Corey, E. J.; Grogan, M. *Org. Lett.* **1999**, *1*, 157. (e) Sigman, M. S.; Vachal, P.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2000**, *39*, 1279.

(f) Ishitani, H.; Komiyama, S.; Hasegawa, Y.; Kobayashi, S. *J. Am. Chem. Soc.* **2000**, *122*, 762. (g) Porter, J. R.; Wirschun, W. G.; Kuntz, K. W.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 2657. (h) Vachal, P.; Jacobsen, E. N. *Org. Lett.* **2000**, *2*, 867. (i) Boesten, W. H. J.; Seerden, J.-P. G.; de Lange, B.; Dielemans, H. J. A.; Elsenberg, H. L. M.; Kaptein, B.; Moody, H. M.; Kellogg, R. M.; Broxterman, Q. B. *Org. Lett.* **2001**, *3*, 1121. (j) Li,, T.; Kootstra, A. B.; Fotheringham, I. G. *Org. Process Res. Dev.* **2002**, *6*, 533.

(8) Strecker, A. *Ann. Chem. Pharm.* **1850**, *75*, 27.

(9) For reviews on the chemistry of *N*-*tert*-butanesulfinyl imines, see: (a) Davis, F. A.; Zhou, P.; Chen, B. C. *Chem. Soc. Rev.* **1998**, *37*, 13. (b) Ellman, J. A.; Owens, T. D.; Tang, T. P. *Acc. Chem. Res.* **2002**, *35*, 984. (c) Ellman, J. A. *Pure Appl. Chem.* **2003**, *75*, 39. (d) Senanayake, C. H.; Krishnamurthy, D.; Lu, Z.-H.; Han, Z.; Gallon, E. *Aldrichimica Acta* **2005**, *38*, 93. (e) Mortan, D.; Stockman, R. A. *Tetrahedron* **2006**, *62*, 8869. (f) Lin, G.-Q.; Xu, M.-H.; Zhong, Y.-W.; Sun, X.-W. *Acc. Chem. Res.* **2008**, *41*, 831. (g) Ferreira, F.; Botuha, C.; Chemla, F.; Pérez-Luna, A. *Chem. Soc. Rev.* **2009**, *38*, 1162. (h) Robak, M. T.; Herbage, M. A.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 3600.

(10) Liu, R.-C.; Wei, J.-H.; Wei, B.-G.; Lin, G.-Q. *Tetrahedron: Asymmetry* **2008**, *19*, 2731.

(11) (a) Sun, X.; Zheng, W.; Wei, B.-G. *Tetrahedron, Lett.* **2008**, *49*, 6195. (b) Wei, B.-G.; Zheng, W.; Jia, X.-Y.; Sun, X.; Lin, G.-Q. Faming Zhuanli Shenqing CN 101875615 A, 2010.

(12) Davis, F. A.; McCoull, W. *J. Org. Chem.* **1999**, *64*, 3396.

(13) Agotsta, E.; Caligiuri, A.; D'Arrigo, P.; Servi, S.; Tessaro, D.; Canevotti, R. *Tetrahedron: Asymmetry* **2006**, *17*, 1995.

(14) Jenssen, K.; Sewald, K.; Sewald, N. *Bioconjugate Chem.* **2004**, *15*, 594.

(15) All calculations were carried out with the Gaussian03 package.[22] This method has been widely used in the theoretical investigations of chemical processes involving organometallic reagents.[23] Geometry optimizations were performed with the hybrid B3LYP[24,25] density functional by using the LanL2DZ[26] basis set + ECP for Zn and the 6-31G* basis set for the rest. Geometry optimizations and vibrational analyses were performed without any constraint. All transition structures are characterized by one imaginary frequency. Total final energy calculations were done on all geometries at the B3LYP/6-311++G(3df,2p) level.

(16) For a recent review, see: (a) Akindele, T.; Yamada, K.-I.; Tomioka, K. *Acc. Chem. Res.* **2009**, *42*, 345. For other papers, see: (b) Vaupel, A.; Knochel, P. *J. Org. Chem.* **1996**, *61*, 5743. (c) Bertrand, M. P.; Feray, L.; Nouguier, R.; Perfetti, P. *J. Org. Chem.* **1999**, *64*, 9189. (d) Van der Deen, H.; Kellog, R. M.; Feringa, B. L. *Org. Lett.* **2000**, *2*, 1593. (e) Bazin, S.; Feray, L.; Siri, D.; Naubron, J.-V.; Bertrand, M. P. *Chem. Commun.* **2002**, 2506. (f) Miyabe, H.; Asada, R.; Yoshida, K.; Takemoto, Y. *Synlett* **2004**, 540. (g) Miyabe, H.; Asada, R.; Takemoto, Y. *Tetrahedron* **2005**, *61*, 385. (h) Bazin, S.; Feray, L.; Vanthuyne, N.; Bertrand, M. P. *Tetrahedron* **2005**, *61*, 4261. (i) Denes, F.; Cutri, S.; Pere-Luna, R.; Chemla, F. *Chem.—Eur. J.* **2006**, *12*, 6506. (j) Cougnon, F.; Feray, L.; Bazin, S.; Bertrand, M. P. *Tetrahedron* **2007**, *63*, 11959. (k) Phapale, V. B.; Buñuel, E.; García-Iglesias, M.; Cárdenas, D. J. *Angew. Chem., Int. Ed.* **2007**, *46*, 8790. (l) Bazin, S.; Feray, L.; Vanthuyne, N.; Siri, D.; Bertrand, M. P. *Tetrahedron* **2007**, *63*, 77. (m) Giboulot, S.; Pérez-Luna, A.; Botuha, C.; Ferreira, F.; Chemla, F. *Tetrahedron Lett.* **2008**, *49*, 3963.

(17) (a) Choi, J.-H.; Nam, M.-J.; Youn, S.-E. *ChemPhysChem* **2006**, *7*, 2526. (b) Pryor, W. A.; Tang, F. Y.; Tang, R. H.; Church, D. F. *J. Am. Chem. Soc.* **1982**, *104*, 2885.

(18) (a) Yamamoto, Y.; Komatsu, T.; Maruyama, K. *J. Am. Chem. Soc.* **1984**, *106*, 5031. (b) Davis, F. A.; Portonovo, P. S.; Reddy, R. E.; Chiu, Y.-H. *J. Org. Chem.* **1996**, *61*, 440. (c) Davis, F. A.; Fanelli, D. L. *J. Org. Chem.* **1998**, *63*, 1981. (d) Sun, X.-W.; Xu, M.-H.; Lin, G.-Q. *Org. Lett.* **2006**, *8*, 4979. (e) Liu, M.; Sun, X.-W.; Xu, M.-H.; Lin, G.-Q. *Chem.—Eur. J.* **2009**, *15*, 10217.

(19) Ye, J.-L.; Huang, P.-Q.; Lu, X. *J. Org. Chem.* **2007**, *72*, 35.

(20) (a) Denmark, S. E.; Edwards, J. P.; Wilson, S. R. *J. Am. Chem. Soc.* **1992**, *114*, 2592. (b) Fleckenstein, J. E.; Koszinowski, K. *Chem.—Eur. J.* **2009**, *15*, 12745.

(21) Frenking, G.; Köhler, K. F.; Reetz, M. T. *Tetrahedron* **1991**, *47*, 9005.

(22) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, revision D.01; Gaussian, Inc.: Wallingford, CT, 2004.

(23) (a) Bare, W. D.; Andrews, L. *J. Am. Chem. Soc.* **1998**, *120*, 7293. (b) Jasien, P. G.; Abbondondola, J. A. *J. Mol. Struct.: THEOCHEM* **2004**, *671*, 111. (c) O'Hair, R. A. J.; Vrkic, A. K.; James, P. F. *J. Am. Chem. Soc.* **2004**, *126*, 12173. (d) Tammiku, J.; Burk, P.; Tuulmets, A. *J. Phys. Chem. A* **2001**, *105*, 8554. (e) Tammiku-Taul, J.; Burk, P.; Tuulmets, A. *J. Phys. Chem. A* **2004**, *108*, 133. (f) Tuulmets, A.; Pallin, V.; Tammiku- Taul, J.; Burk, P.; Raie, K. *J. Phys. Org. Chem.* **2002**, *15*, 701.

(24) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.

(25) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.

(26) (a) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 270. (b) Wadt, W. R.; Hay, P. J. *J. Chem. Phys.* **1985**, *82*, 284. (c) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 299.