

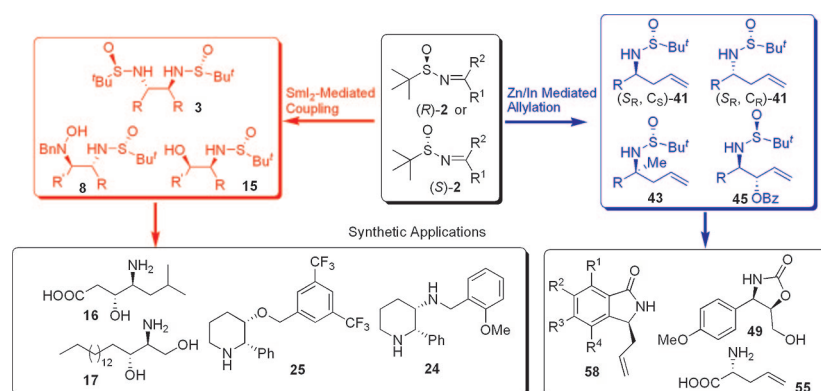
An Advance on Exploring *N*-*tert*-Butanesulfinyl Imines in Asymmetric Synthesis of Chiral Amines

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CON SPECTUS



Although catalytic asymmetric synthesis has undergone tremendous growth in the last 30 years, chiral auxiliary-aided asymmetric synthesis continues to attract considerable attention. Chiral *N*-*tert*-butanesulfinamide, as pioneered by Ellman and co-workers, is undoubtedly one of the most efficient auxiliaries developed to date; it allows the preparation, through simple conversion, of a diverse range of enantiopure amines, which are ubiquitous in natural products and biologically active molecules. Following on from our studies of the Sml_2 -mediated asymmetric syntheses of α,γ -substituted γ -butyrolactones, we found that simple homocoupling of chiral *N*-*tert*-butanesulfinyl imines in the presence of Sml_2 produced enantiopure vicinal C_2 -symmetric diamines in high yield. In addition, C_2 -unsymmetric chiral diamines are readily prepared through Sml_2 -mediated cross-couplings of *N*-*tert*-butanesulfinyl imines and nitrones; these transformations represented the first successful examples of asymmetric cross-coupling between two different imine species. Subsequently, we discovered another useful reaction induced by Sml_2 , the efficient cross-coupling of *N*-*tert*-butanesulfinyl imines and aldehydes, which provides ready access to enantiopure *anti*-1,2-amino alcohols. The synthetic applicability of this reaction was demonstrated through its use in the facile total syntheses of (3*R*,4*S*)-statine, *D*-*erythro*-sphinganine, (+)-CP-99,994, and (+)-L-733,060.

The Zn/In-mediated allylation of chiral *N*-*tert*-butanesulfinyl imines yields homoallylic amines. After pondering the reaction mechanism, we developed optimal reaction conditions for reversing the stereogenic outcome, thereby allowing the preparation of enantiopure homoallylic amines of either handedness from single enantiomers of the (*R*)- or (*S*)-sulfinyl imine. When a benzoyl-substituted allyl bromide is used for allylation, the reaction proceeds smoothly to give 2-vinyl-substituted *anti*-1,2-amino alcohols in high yields and diastereoselectivities, another simple method for preparing enantiopure amino alcohols. We employed these reactions in the syntheses of enantiopure allylglycine, 3-allyl-isoinidolones, and (–)-cytozoxane. Further studies led to the discovery that the allylations of *N*-*tert*-butanesulfinyl aldimines can be performed in water.

The reactions described in this Account are among the simplest and most efficient synthetic methods available for preparing enantio-enriched diamines, amino alcohols, homoallylic amines, and other amine derivatives. These reactions are additionally attractive because of the ready availability of the starting materials, the simplicity of the reaction conditions, and the high degree of stereochemical control. Their applications in the total syntheses of several biologically interesting molecules illustrate the versatility of these transformations; we hope that they will stimulate the development of new synthetic methods.

Introduction

The great demand in life science for enantiopure compounds has led to an extreme significance of asymmetric synthesis. The organometallic complex-based and metal-free organic catalysis as well as biotransformation provide most of the enantiopure compounds. However, the development of practical and efficient synthetic methods for the synthesis of these compounds using chiral auxiliaries still attracts wide interest. Since its introduction, *N*-*tert*-butanesulfinamide,¹ (*R/S*)-**1** (Figure 1), has drawn great attention in the auxiliary-aided asymmetric synthesis of a broad range of chiral amines, which are present in numerous pharmaceutical agents, natural products, and synthetic materials (for example, ligands). *N*-*tert*-Butanesulfinyl imines, (*R/S*)-**2**, which can be prepared from readily available (*R/S*)-**1** and aldehydes or ketones,² exhibit unique reactivity and stereoselectivity in various reactions and have been proven to be extremely versatile chiral reagents. Up to now, the *N*-*tert*-butanesulfinamide-related reactions mainly included the nucleophilic addition to imine **2**, metalloenamine additions to electrophiles,³ transition-metal catalyzed additions of organoboronic acids to imines,⁴ and other types of reactions.⁵ To further expand the use of *N*-*tert*-butanesulfinamide for the synthesis of enantiopure amines, new synthetic strategies are still desirable in terms of efficiency, practicability, and diversity.

Our investigations in the synthesis of enantio-enriched amines using *N*-*tert*-butanesulfinyl imines were rooted in the SmI₂-mediated asymmetric synthesis of α,γ -substituted γ -butyrolactones.⁶ Single-electron reduction of ketone by 1 equiv of SmI₂ gives a radical intermediate, which adds to an α,β -unsaturated ester, followed by second electron transfer by another equiv of SmI₂ and the subsequent intramolecular lactonization to finish the synthesis of γ -butyrolactone. Considering the substrate scope of this reaction, we envisioned that a similar reaction between imine **2** and an α,β -unsaturated ester could possibly give an enantiopure γ -butyrolactam, since imine **2** was activated by a chiral sulfinyl group and the samarium atom tended to bind tightly to nitrogen and oxygen atoms.⁷ To our disappointment, this reaction only produced intractable mixtures after several attempts. However, we later found that imine **2** was very efficient in the SmI₂-mediated pinacol-type coupling reactions, such as homocoupling or

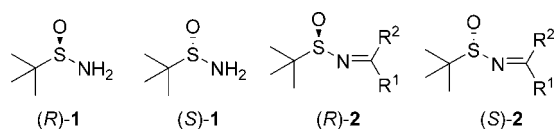


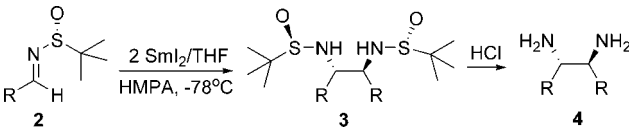
FIGURE 1. *N*-*tert*-Butanesulfinamides, **1**, and *N*-*tert*-butanesulfinyl imines, **2**.

cross-coupling with nitrones and aldehydes to provide enantiopure vicinal C₂-symmetrical and unsymmetrical diamines and β -amino alcohols. Following that, the efficient synthesis of enantiopure homoallylic amines by using *N*-*tert*-butanesulfinamide as chiral auxiliary was also achieved, in which attention was paid to the reversal of the stereochemical outcome under different reaction conditions or by using different reagents. The applications of these synthetic methods have been demonstrated in total syntheses of some biologically interesting molecules.

SmI₂-Mediated Synthesis of Enantiopure 1,2-Diamines and 1,2-Amino Alcohols

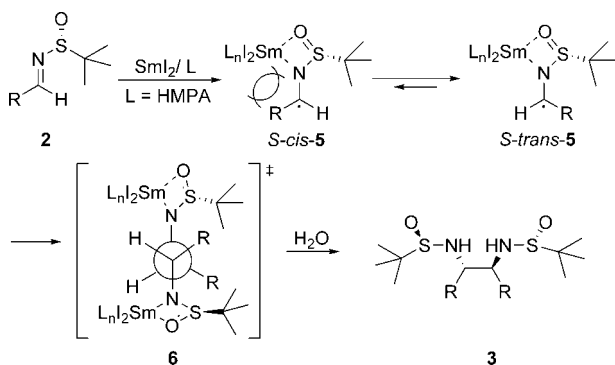
Enantiopure 1,2-diamines and 1,2-amino alcohols are prevalent in drug and natural products and serve as important precursors to many chiral ligands or organocatalysts for asymmetric catalysis.⁸ The most straightforward method for forming vicinal diamines is perhaps the direct reductive coupling between two imine species.⁹ A number of reaction systems have been developed for the homocoupling of two imines but very often with low stereoselectivity.¹⁰ Cross-coupling of two different imines is rather difficult because of the competition of the homocoupling of each imine substrate. Only one example of synthesis of racemic 1,2-diamines through direct intermolecular cross-coupling of two different imine species was reported.¹¹ Recently, we reported a reductive homocoupling of *N*-*tert*-butanesulfinyl imine to chiral C₂-symmetrical vicinal diamine.¹² Upon treatment with 2 equiv of SmI₂ and 2 equiv of hexamethylphosphoramide (HMPA) as additive, the homocoupling of aldimine **2** successfully proceeded at -78 °C in tetrahydrofuran (THF) to give **3** as a single diastereomer (Table 1). Imines **2** containing either electron-withdrawing or electron-donating substituents were all coupled to afford the corresponding 1,2-diamines in modest to high yields. In the case of substrates bearing electron-donating groups (entries 5, 6, and 10), better yields were achieved in the presence of 6 equiv of HMPA. After removal of the chiral auxiliary under acidic condition, free diamines **4** were obtained with excellent ee's.

A proposed reaction mechanism is shown in Scheme 1. Substrate **2** could undergo one-electron reduction to give a radical intermediate (*S*)-*cis*-**5**, which because of the bulkiness of the Sm complex coordinating with HMPA could be rapidly transformed into structurally more stable intermediate (*S*)-*trans*-**5**. Directed by the chiral *N*-*tert*-butanesulfinyl group, both Re-face approaches of two (*S*)-*trans*-**5** radicals could occur to provide the homocoupling product with excellent diastereoselectivity. This kind of diamine bearing a *para*-halogen, an

TABLE 1. SmI₂-Mediated Reductive Homocoupling of Chiral *N*-*tert*-Butanesulfinyl Imines^a


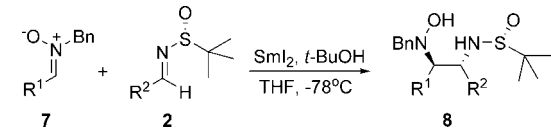
entry	R	yield of 3 (%)
1	4-ClC ₆ H ₄	99
2	4-BrC ₆ H ₄	93
3	4-FC ₆ H ₄	83
4	4-AcOC ₆ H ₄	61
5	4-MeC ₆ H ₄	71 (72) ^b
6	4-MeOC ₆ H ₄	58 (80) ^b
7	C ₆ H ₅	25
8	3,4-Cl ₂ C ₆ H ₃	81
9	3,4-F ₂ C ₆ H ₃	69
10	3,4-(MeO) ₂ C ₆ H ₃	52 (85) ^b

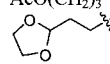
^a Reactions were carried out with 0.5 mmol of imine **2**, 1.0 mmol of SmI₂, and 1.0 mmol of HMPA in 12 mL of THF at -78 °C. ^b Performed with 6 equiv of HMPA.

SCHEME 1. Proposed Reaction Mechanism of SmI₂-Mediated Homocoupling of **2**

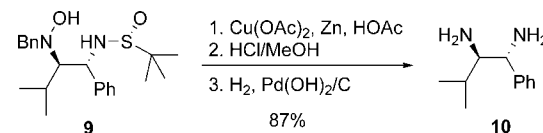
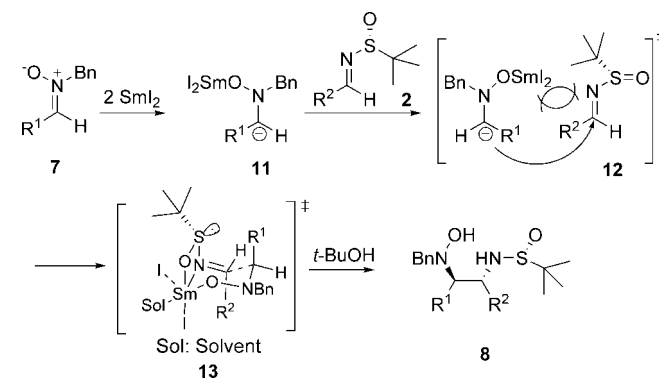
acetoxyl, or a methoxy substituent on the phenyl ring (entries 1–4 and 6 in Table 1), in addition to being useful chiral ligands in asymmetric synthesis with different electronic properties, would be a useful functionality for further attachment onto solid support material such as via O-alkylation or Suzuki coupling reaction.

A further extension but more challenging subject is the cross-coupling of *N*-*tert*-butanesulfinyl imines with nitrones or aldehydes to afford enantiopure unsymmetrical vicinal diamines¹³ or *anti*-β-amino alcohols¹⁴ in a broad substrate scope. In the presence of SmI₂, a reductive cross-coupling between various nitrones **7** and chiral aromatic *N*-*tert*-butanesulfinyl imines afforded the expected unsymmetrical vicinal diamines **8** with high diastereoselectivities (Table 2). This is the first successful example of asymmetric cross-coupling between two different imine species. Conversion of the cross-coupling product to the corresponding free diamine was then accomplished in a three-step reaction sequence. For example, as shown in Scheme 2, deoxygenation of the hydroxy-

TABLE 2. SmI₂-Induced Reductive Cross-coupling of Nitrones with *N*-*tert*-Butanesulfinyl Imines^a


entry	R ¹	R ²	time (h)	yield(%) (dr)
1	^t Pr	Ph	3	75
2	C ₆ H ₁₁	Ph	3	65
3	CH ₃ (CH ₂) ₅	Ph	4	85 (15:1)
4	^t PrCH ₂	Ph	2.5	67 (10:1)
5	PhCH ₂ CH ₂	Ph	2.5	54 (>10:1)
6	^t Bu	Ph	5	22
7	^t Pr	4-CH ₃ C ₆ H ₄	7	71
8	^t Pr	4-CH ₃ OC ₆ H ₄	8	65
9	^t Pr	4-ClC ₆ H ₄	1.5	52
10	^t Pr	4-BrC ₆ H ₄	1	51
11	^t Pr	4-AcOC ₆ H ₄	4	69
12	BnO(CH ₂) ₃	Ph	4	55 (10:1)
13	AcO(CH ₂) ₃	Ph	4	68 (7:1)
14		Ph	4	71 (>10:1)

^a Reactions were carried out with 0.5 mmol of imine **2**, 0.7 mmol of nitron **7**, 1.0 mmol of SmI₂, and 1.0 mmol of *t*-BuOH in 11 mL of THF at -78 °C.

SCHEME 2. Synthesis of Diamine **10****SCHEME 3.** Proposed Reaction Mechanism of the Cross-Coupling Reaction between Nitron and Imine Induced by SmI₂

amine moiety of the coupling product **9** by Zn/Cu(OAc)₂, followed by removal of the sulfinyl and benzyl groups, furnished the optically pure (*R,R*)-3-methyl-1-phenylbutane-1,2-diamine (**10**) as HCl salt in 87% overall yield.

The proposed mechanism of this cross-coupling reaction is shown in Scheme 3. The nitron **7** could be reduced by two electrons transferred from 2 equiv of SmI₂ to give an α-azanyl anion **11**, which could add intermolecularly to C=N bond of the imine **2** to form intermediate **12**. Herein, chiral sulfinylimine **2** could act as an electrophile. The steric bulkiness of R¹ in the nitron anion and R² in *N*-*tert*-butane-

TABLE 3. Sml₂-Induced Reductive Cross-Coupling of Aldehydes with **2**^a

entry	R ¹	R ²	yield (%)	dr	ee
1	4-CH ₃ C ₆ H ₄	ⁱ Pr	92	>99:1	98
2	4-CH ₃ C ₆ H ₄	C ₆ H ₁₁	90	99:1	>99
3	4-CH ₃ C ₆ H ₄	(Et) ₂ CH	73	>99:1	99
4	4-CH ₃ C ₆ H ₄	<i>n</i> -C ₅ H ₁₁	90	91:9	95
5	4-CH ₃ C ₆ H ₄	PhC ₂ H ₄	95	88:12	95
6	C ₆ H ₅	ⁱ Pr	86	99:1	97
7	4-FC ₆ H ₄	ⁱ Pr	89	98:2	>99
8	4-ClC ₆ H ₄	ⁱ Pr	71	99:1	98
9	4-BrC ₆ H ₄	ⁱ Pr	70	>99:1	>99
10	4-AcOC ₆ H ₄	ⁱ Pr	82	>99:1	>99
11	4-CH ₃ OC ₆ H ₄	ⁱ Pr	84	>99:1	>99
12	3,4-(MeO) ₂ C ₆ H ₃	ⁱ Pr	90	>99:1	>99
13	2,4-(MeO) ₂ C ₆ H ₃	ⁱ Pr	73	>99:1	>99
14	ⁱ Pr	ⁱ Pr	88	>99:1	98
15	PhCH ₂ CH ₂	ⁱ Pr	87	96:4	>99
16	CH ₃ (CH ₂) ₄	ⁱ Pr	95	98:2	97
17	BnOCH ₂	ⁱ Pr	82	>99:1	97

^a Reactions were carried out with 0.5 mmol of imine **2**, 0.7 mmol of aldehyde **14**, 1.0 mmol of Sml₂, and 1.0 mmol of *t*-BuOH in 11 mL of THF at -78 °C.

sulfinyl imine group within the transition state **13** could result in the preferable attack of the anion to the *Si*-face of the C=N bond in imine. The lone electron pair on the sulfur atom in **13** was possibly responsible for the limitation of R¹ to be only an aliphatic group in order to avoid the *n*- π electron repulsion.

The above cross-coupling allows us to extend to the pinacol-type reaction between carbonyls and imines to furnish vicinal amino alcohols. In principle, the pinacol-type cross-coupling between carbonyls and imines is the most straightforward route to β -amino alcohols. However, only a few examples of employing this strategy have been reported because of the difficulty of achieving satisfactory stereoselectivity.¹⁵ Our results are shown in Table 3. A series of *N*-*tert*-butanesulfinyl imines **2** react with various aldehydes **14** smoothly in the presence of Sml₂ and *t*-BuOH to give products **15** in good to excellent yields and with extremely high diastereomeric ratios. The use of a little excess of aldehyde substrate and *t*-BuOH was found to be helpful for the achievement of high yields. Cleavage of the sulfinyl group under acidic conditions subsequently afforded β -amino alcohols in >95% yields in all cases. This method is effective for the preparation of a broad range of chiral β -amino alcohols. When R¹ substituents are an aryl or aliphatic group, even bulky, all coupling reactions proceeded smoothly, demonstrating the great capacity and efficiency of this method. It provides a good solution to a long-standing difficulty in the construction of enan-

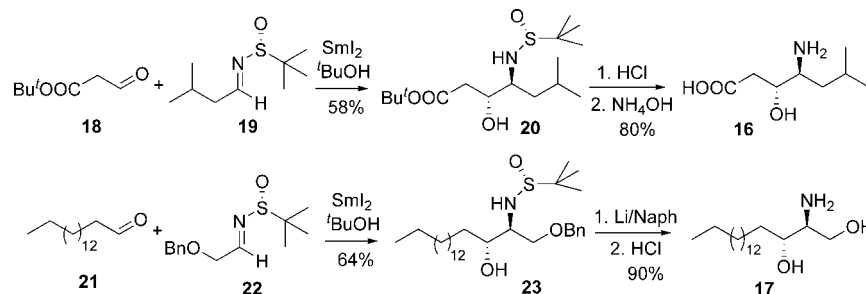
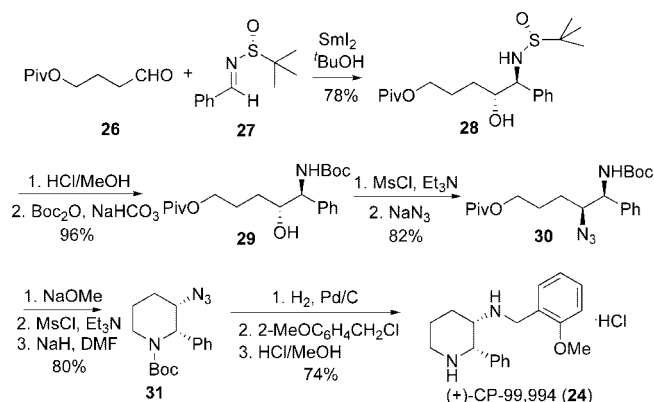
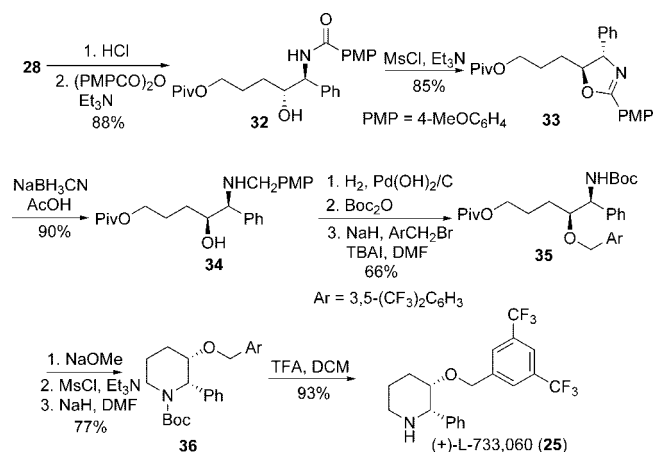
tiopure β -amino alcohols via the direct pinacol-type cross-coupling between carbonyls and imines.

The synthetic values were illustrated by the easy preparation of two biologically important compounds, (3*R*,4*S*)-statine **16** and *D*-*erythro*-sphinganine **17** (Scheme 4).¹⁶ The cross-coupling of aldehyde **18** (2 equiv) with *N*-sulfinylimine **19** was performed at -78 °C under standard conditions to provide **20** in 58% yield with 99% de. The *tert*-butyl ester and *N*-sulfinyl were then removed by hydrolysis in one step to afford enantiopure (3*R*,4*S*)-statine (**16**) in high yield. When palmitaldehyde **21** (4 equiv) was treated with imine **22** under similar reaction conditions, **23** was obtained as a single diastereomer in 64% yield. Removal of the benzyl and sulfinyl groups gave *D*-*erythro*-sphinganine (**17**) in 90% yield with 97% ee. To the best of our knowledge, this approach represents one of the most convenient syntheses of **16** and **17** reported to date.

(+)-CP-99,994 (**24**) and (+)-L-733,060 (**25**) are potent and selective human neuronkinin-1 substance P receptor antagonists.¹⁷ Their valuable biological properties have stimulated immense interest in their syntheses.¹⁸ The applications of the imine-aldehyde asymmetric cross-couplings are further demonstrated by total synthesis of two important 2,3-disubstituted piperidine derivatives (Schemes 5 and 6).¹⁹ Reductive coupling of 4-pivaloxybutanal **26** with (*R*)-imine **27** afforded **28** in 78% yield and >99% ee. The chiral auxiliary was removed, and the resulting amine was then protected with Boc to give **29**, which was subjected to mesylation and subsequent azide displacement to afford **30** in high yield. Deblocking of Piv with NaOMe, mesylation of the terminal hydroxyl, and ring closure gave 2,3-disubstituted piperidine **31** in a satisfactory yield. (+)-CP-99,994 (**24**) was finally obtained after reduction of the azide, attachment of the aromatic moiety, and deprotection of the Boc group.

The synthesis of (+)-L-733,060 (**25**) is outlined in Scheme 6. Amide **32**, which was obtained after simple transformations from the same adduct **28**, underwent an intramolecular cyclization in the presence of MsCl/Et₃N to give oxazoline **33**. Reductive ring-opening of **33** afforded *syn*-1,2-amino alcohol **34** in excellent yield with an inverted stereochemistry of the hydroxyl group. Switch of the protecting group of amine to Boc and subsequent O-benylation gave **35**, which was converted into **36** after routine deprotection of Piv and ring closure. (+)-L-733,060 (**25**) was then successfully obtained after the removal of Boc group.

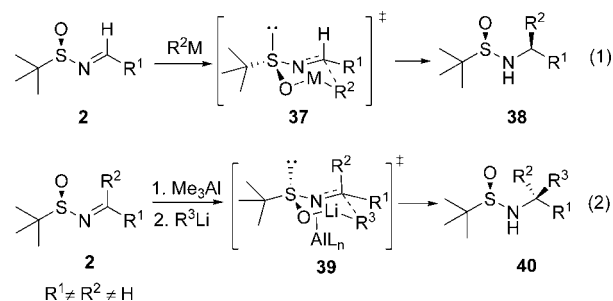
The syntheses of (+)-CP-99,994 (**24**) and (+)-L-733,060 (**25**) illustrated the vast utility of the Sml₂-induced reductive coupling of *N*-*tert*-butanesulfinyl imines with aldehydes. The *anti*-1,2-amino alcohols thus obtained can be favorably trans-

SCHEME 4. Synthesis of (3*R*,4*S*)-Statine (**16**) and *D*-*erythro*-Sphinganine (**17**)SCHEME 5. Synthesis of (+)-CP-99,994 (**24**)SCHEME 6. Synthesis of (+)-L-733,060 (**25**)

formed into *syn*-1,2-diamines, *syn*-1,2-amino alcohols, and 2,3-disubstituted piperidine derivatives. In this way, 2,3-disubstituted piperidine derivatives of all four possible configurations can be prepared.

Stereoselective Zn/In-Mediated Allylation of *N*-*tert*-Butanesulfinyl Imines—Reversal of Stereogenic Outcome and the Reaction Mechanism

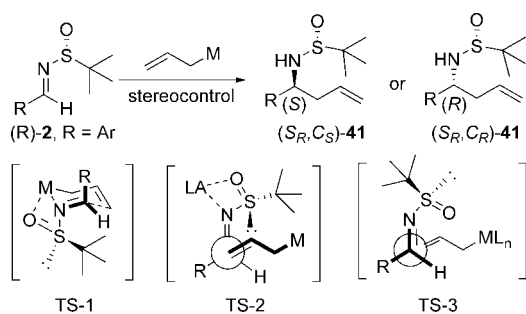
Following Ellman's pioneering work,²⁰ *N*-*tert*-butanesulfinyl imines **2** have been widely employed in the 1,2-nucleophilic addition by Grignards, organolithiums, and Reformatsky-type

SCHEME 7. 1,2-Nucleophilic Addition of Organometallic Reagents to *N*-*tert*-Butanesulfinyl Aldimines and Ketimines

and Barbier-type reagents (eq 1 in Scheme 7). In many cases, the products were obtained with high diastereoselectivities. A six-membered cyclic transition state **37** with metal (such as Mg) coordinating to the sulfinyl oxygen atom was proposed for the observed stereochemical outcome of the adduct **38**. In the case of *N*-*tert*-butanesulfinyl ketimines as substrates (eq 2 in Scheme 7), the Me₃Al-mediated 1,2-addition of organolithium reagent was found to provide higher levels of diastereoselectivity to form product **40**, where organolithium reagent subjected to 1,2-addition with the coordination of Me₃Al to nitrogen on the sulfinyl group formed a kind of transition state **39**.

Quite often, it is desirable to prepare enantiopure amines in both orientations. Therefore, the reversal of diastereoselectivity from the same enantiomer of either (*R*)- or (*S*)-sulfinyl imine by altering the reaction transition state would be a subject of great interest and significance.²¹ Inspired by the success of using *N*-*tert*-butanesulfinamide as chiral auxiliary in the Sml₂-mediated coupling reactions, we turned our attention to the Zn-mediated allylation of *N*-*tert*-butanesulfinyl imines. To our delight, a complete switchover of stereochemical outcome was realized in this reaction.

The diastereoselective additions of allylmagnesium and allyllithium to chiral *N*-*tert*-butanesulfinyl imines have been previously reported by Ellman²⁰ and Foubelo,²² respectively. In their studies, addition of allylmagnesium (Mg or In) to *N*-*tert*-butanesulfinyl imines was proposed to proceed via the six-mem-

SCHEME 8. Three Possible Transition States in the Allylation of *N-tert*-Butanesulfinyl Imines

bered chairlike transition state model (TS-1 in Scheme 8), in which allylmetal could coordinate to sulfinyl oxygen and the R group would take the pseudoaxial position. Thus, when (*R*)-*N-tert*-butanesulfinyl imine is employed, the *Si*-face addition will be favored to yield the (*S*)-amine as the major product. However, it can be assumed that an acyclic transition state, TS-2 in Scheme 8, might also be involved in the presence of a rather strong Lewis acid. The coordination of Lewis acid with nitrogen and sulfinyl oxygen of imine would direct the allyl attack predominately also from the *Si*-face to give (*S*)-amine. Additionally, another type of acyclic transition state model, TS-3, could be envisioned, which results in the allylic addition to the less-hindered *Re*-face of imine where the (*R*)-amine product would be preferably formed.

Gratifyingly, as shown in Table 4, the allylation of (*R*)-*N-tert*-butanesulfinyl aldimines **2** in two systems, with TS-2 and TS-3 model, went equally well.²³ All the reactions proceeded smoothly at room temperature to provide the corresponding homoallylic amines **41** in good yields as well as with high diastereoselectivities in both systems. Thus, the opposite stereocontrol was achieved. *N-tert*-Butanesulfinyl imines of aromatic aldehydes proved to be excellent substrates in both systems giving excellent dr in most cases. Taking into account the transition state model TS-2, $\text{In}(\text{OTf})_3$ was found to be the best additive among the screened ones. On the other hand, it seemed that chelation of Zn(II) with sulfinylimine was disrupted in HMPA in the presence of a small amount of H_2O where the reaction proceeded via transition state model TS-3, though the real role of H_2O in the system is not clear yet. For aliphatic imines (entries 11–14), the HMPA system gave even better diastereoselectivities.

N-tert-Butanesulfinyl ketimines **42** were also examined as substrates to produce the corresponding quaternary carbon-containing chiral homoallylic amines (Table 5). The asymmetric allylation of ketimines is a challenging topic in organic synthesis partially because ketimines are relatively less reactive than aldimines. In our case, ketimines **42** work equally

TABLE 4. Diastereoselective Allylation to (*R*)-*N-tert*-Butanesulfinyl Aldimines in Two Different Systems^a

entry	R	THF system ^b		HMPA system ^c	
		yield (%)	dr	yield (%)	dr
1	C ₆ H ₅	93	98:2	97	1:99
2	4-FC ₆ H ₄	98	98:2	97	1:99
3	4-ClC ₆ H ₄	98	98:2	96	3:97
4	4-BrC ₆ H ₄	93	97:3	99	2:98
5	4-MeC ₆ H ₄	95	96:4	88	3:97
6	4-MeOC ₆ H ₄	91	95:5	81	2:98
7	2-ClC ₆ H ₄	91	97:3	73	2:98
8	2-MeC ₆ H ₄	95	98:2	89	3:97
9	3-BrC ₆ H ₄	98	98:2	99	2:98
10	2-naphthyl	81	95:5	86	3:97
11	cyclopropyl	98	86:14	97	4:96
12	cyclohexyl	99	97:3	94	3:97
13	ethyl	93	88:12	92	5:95
14	propyl	96	94:6	94	2:98
15	phenethyl	92	90:10	93	4:96
16	phenethenyl	83	91:9	87	6:94

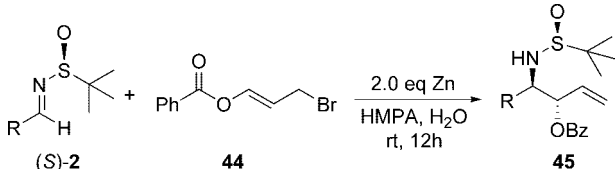
^a Reactions were carried out with 0.25 mmol of imine **2** and 0.5 mmol of Zn/allyl bromide in 5 mL of dry solvent at rt. ^b $\text{In}(\text{OTf})_3$ (0.275 mmol) was used as additive. ^c Water (10 μL) was used as additive.

TABLE 5. Diastereoselective Allylation to (*R*)-*N-tert*-Butanesulfinyl Ketimine in THF System^a

entry	R	yield (%)	dr
1	C ₆ H ₅	69	97:3
2	4-MeC ₆ H ₄	67	96:4
3	4-CF ₃ C ₆ H ₄	89	96:4
4	4-MeOC ₆ H ₄	76	95:5
5	4-ClC ₆ H ₄	83	97:3
6	4-BrC ₆ H ₄	85	97:3
7	4-FC ₆ H ₄	79	97:3
8	3-MeC ₆ H ₄	66	95:5
9	3-ClC ₆ H ₄	81	98:2

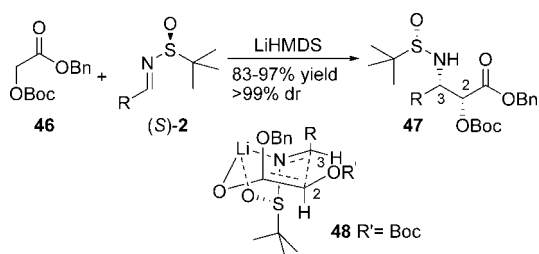
^a Reactions were carried out with 0.25 mmol of ketimine, 0.75 mmol of Zn/allyl bromide, and 0.325 mmol of $\text{In}(\text{OTf})_3$ in 5 mL of dry THF at rt.

well in the presence of $\text{In}(\text{OTf})_3$ giving the corresponding enantiopure homoallylic amines **43** in moderate yields and with excellent diastereomeric ratios. In most cases, >95:5 dr was observed. However, ketimines did not react with allylic bromide in THF in the absence of Lewis acid additive. This was one of the few reports of success and among the best in asymmetric induction in the allylation of aromatic ketimines.²⁴ In the optimized HMPA system, ketimines were not activated enough, and the allylation reaction did not take place.

TABLE 6. Preparation of Vicinal Amino Alcohols^a


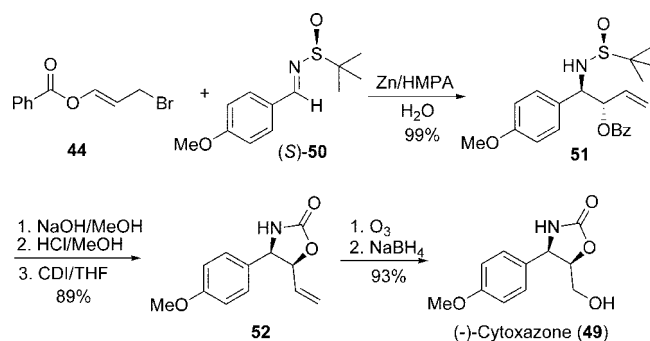
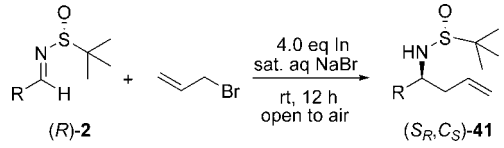
entry	R	yield (%)	dr
1	C ₆ H ₅	93	97:3
2	4-FC ₆ H ₄	98	97.5:2.5
3	4-BrC ₆ H ₄	93	97:3
4	3-ClC ₆ H ₄	98	98:2
5	4-ClC ₆ H ₄	85	96:4
6	2-CH ₃ C ₆ H ₄	98	98.5:1.5
7	2-naphthyl	96	96:4
8	3-methylbutyl	82	78:22
9	4-MeOC ₆ H ₄	99	96:4
10	4-CH ₃ C ₆ H ₄	96	96.5:3.5

^a Reactions were carried out with 0.25 mmol of imine **2**, 0.5 mmol of **44**, 10 μ L of water as additive, and 0.5 mmol Zn powder in 5 mL of dry HMPA at rt. *Caution*: HMPA is a suspected human carcinogen.

SCHEME 9. Addition of O-Protected α -Hydroxyacetate to *N-tert*-Butanesulfinyl Imine

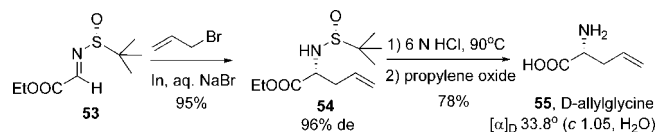
The Zn/HMPA system can be extended to set vicinal chiral centers simultaneously.²⁵ Reaction of (*S*)-*N-tert*-butanesulfinyl aldimines **2** with benzoyl-substituted allyl bromide **44** provided the β -amino alcohol derivatives **45** (Table 6), which are very useful building blocks for the preparation of natural and bioactive compounds. In most cases, the corresponding products were obtained in high yields and with excellent diastereoselectivities. This method provides a new alternative route to prepare various side chains of Taxol and its derivatives by subsequent conversion of the yielded amino alcohols.

Qin reported a different synthetic approach to the side chain of Taxol through an enolate addition of O-protected α -hydroxyacetate **46** to (*S*)-*N-tert*-butanesulfinylimine (Scheme 9).²⁶ The bulky protecting group in **46** improved the yield and stereoselectivity, leading to **47** as the sole adduct. Again, the reaction was rationalized as subject to six- and four-membered bicyclic transition state **48**, in which *cis* relationship between the R group in the axial position and the OR' group in the equatorial position may allow the easier access to C2 and C3. That could be the reason why the bulky R' group (such as Boc) favored the formation of **47** as the dominating adduct.

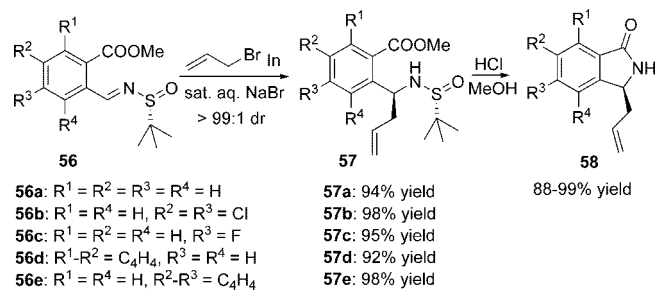
SCHEME 10. Synthesis of (–)-Cytozaxone (**49**)**TABLE 7.** Allylation in Aqueous Media^a


entry	R	yield (%)	dr
1	4-MeC ₆ H ₄	97	98:2
2	4-ClC ₆ H ₄	99	97:3
3	4-CF ₃ C ₆ H ₄	99	97:3
4	4-MeOC ₆ H ₄	85	98:2
5	4-PhC ₆ H ₄	93	99:1
6	3-ClC ₆ H ₄	98	99:1
7	3-MeOC ₆ H ₄	95	98:2
8	2-MeOC ₆ H ₄	94	>99:1
9	2-FC ₆ H ₄	92	>99:1
10	2-BrC ₆ H ₄	99	>99:1
11	2,4-Cl ₂ C ₆ H ₃	95	>99:1
12	2,4-(MeO) ₂ C ₆ H ₃	84	>99:1
13	3,4-(MeO) ₂ C ₆ H ₃	81	98:2
14	1-naphthyl	99	98:2
15	2-naphthyl	98	98:2
16	2-thiophenyl	98	94:6
17	3-furanyl	90	95:5
18	2-pyridyl	73	95:5
19	ferrocenyl	74	>99:1
20	propyl	84	92:8
21	isopropyl	82	96:4
22	cyclohexyl	87	96:4
23	phenethenyl	92	95:5

^a Reactions were carried out with 0.25 mmol of imine **2** and 1.0 mmol In/allyl bromide in 5 mL of saturated aq NaBr solution at rt.

SCHEME 11. Preparation of Enantiopure Allylglycine

The synthetic application of the allylation of *N-tert*-butanesulfinyl imine by the benzoyl-substituted allyl bromide **44** was illustrated by the total synthesis of (–)-cytozaxone (**49**) (Scheme 10),²⁷ a microbial metabolite isolated from *Streptomyces* sp. and a selective modulator of T_H2 cytokine secretion.²⁸ Allylation of imine (*S*)-**50** with **44** in the presence of Zn/HMPA provided **51** in excellent yield. Routine removal of the benzoyl group and chiral auxiliary followed by ring clo-

SCHEME 12. Synthesis of Chiral 3-Allyl Isoindolinones

sure in the presence of carbonyldiimidazole (CDI) gave oxazolidinone **52**. Ozonolysis of the double bond of **52** followed by reduction of the generated aldehyde with NaBH₄ completed the total synthesis of (–)-cytoxazone (**49**).

Notably, the additive-aided allylation reaction can even be performed in aqueous media in open air.²⁹ Among the screened media, such as aqueous NH₄Br, KBr, NaCl, NaBr, and NaOAc solutions, aqueous NaBr offered the best result, and the reaction proceeded well at room temperature even in open air. As shown in Table 7, both aryl and alkyl aldimines provided the corresponding homoallylic amines in high yields and with excellent stereoselectivities. To demonstrate the synthetic utility of this aqueous allylation, the enantiopure allylglycine **55** was conveniently prepared as shown in Scheme 11. This provides a novel and easy access to unnatural amino acids. This method could also be used to prepare chiral 3-substituted isoindolinones, which are valuable pharmacological compounds and important synthetic building blocks (Scheme 12).³⁰ Allylation of imine **56** proceeded smoothly at room temperature to give **57** in high yields and excellent diastereoselectivities. Treatment of **57** with HCl in CH₃OH led to the removal of chiral auxiliary and subsequent lactamization to a series of enantiopure 3-allyl isoindolinones **58**, which may be transformed into other chiral 3-substituted isoindolinones through elaboration of the allyl group.

Conclusion

We have developed several new and stereoselective reactions for the preparation of enantiopure amines as chiral building blocks, chiral ligands, and auxiliaries in organic chemistry. Sml₂-mediated homocoupling and cross-coupling of *N*-*tert*-butanesulfinylimines with nitrones and aldehydes provide an efficient way to synthesize enantiopure vicinal diamines and β-amino alcohols. This system is highlighted by its simplicity and high efficiency in stereochemical control. The successes of these reactions may greatly stimulate the investigation of *N*-*tert*-butanesulfonamides as chiral auxiliary in other Sml₂-mediated reactions. In the Zn-mediated allylation of *N*-*tert*-butanesulfinylimines, a stereoselectivity reversal can be realized by

simply alternating the reaction conditions. Even more, this reaction can be used to set up two chiral centers in one step by using the benzoyl-substituted allyl bromide as the nucleophile. Further studies found that this allylation mediated by In can be even carried out in aqueous media at room temperature and in open air. Applications of these synthetic methods have been demonstrated by the total synthesis of some biologically active molecules, which in turn contribute to the development of new synthetic methods.

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FOOTNOTES

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REFERENCES

- (a) Ellman, J. A.; Owens, T. D.; Tang, T. P. *N*-*tert*-Butanesulfinyl Imines: Versatile Intermediates for the Asymmetric Synthesis of Amines. *Acc. Chem. Res.* **2002**, *35*, 1984–1995. (b) Ellman, J. A. Application of *tert*-Butanesulfinamide in the

- Asymmetric Synthesis of Amines. *Pure Appl. Chem.* **2003**, *75*, 39–46. (c) Senanayake, C. H.; Krishnamurthy, D.; Lu, Z.-H.; Han, Z.; Gallon, E. Enantiopure Sulfoxides and Sulfinamides: Recent Developments in Their Stereoselective Synthesis and Application to Asymmetric Synthesis. *Aldrichim. Acta* **2005**, *38*, 93–103. (d) Daniel, M.; Stockman, R. A. Chiral Non-racemic Sulfinamides: Versatile Reagents for Asymmetric Synthesis. *Tetrahedron* **2006**, *62*, 8868–8905.
- 2 (a) Liu, G.; Cogan, D. A.; Owens, T. D.; Tang, T. P.; Ellman, J. A. Synthesis of Enantiomerically Pure *N*-*tert*-Butanesulfinyl Imines (*tert*-Butanesulfinimines) by the Direct Condensation of *tert*-Butanesulfinamide with Aldehydes and Ketones. *J. Org. Chem.* **1999**, *64*, 1278–1284. (b) Huang, Z.; Zhang, M.; Wang, Y.; Qin, Y. KHSO_4 -Mediated Condensation Reaction of *tert*-Butanesulfinamide with Aldehydes. Preparation of *tert*-Butanesulfinyl Aldimines. *Synlett* **2005**, 1334–1336.
 - 3 (a) Kochi, T.; Tang, T. P.; Ellman, J. A. Development and Application of a New General Method for the Asymmetric Synthesis of *syn*- and *anti*-1,3-Amino Alcohols. *J. Am. Chem. Soc.* **2003**, *125*, 11276–11282. (b) Kochi, T.; Ellman, J. A. Asymmetric α -Alkylation of *N*-*tert*-butanesulfinyl Aldimines. Application to the Total Synthesis of (6*R*,7*S*)-7-Amino-7,8-dihydro- α -bisabolene. *J. Am. Chem. Soc.* **2004**, *126*, 15652–15653.
 - 4 (a) Weix, D. J.; Shi, Y.; Ellman, J. A. Diastereoselective and Enantioselective Rh(II)-Catalyzed Additions of Arylboronic Acids to *N*-*tert*-butanesulfinyl and *N*-Diphenylphosphinoyl Aldimines. *J. Am. Chem. Soc.* **2005**, *127*, 1092–1093. (b) Beenen, M. A.; Weix, D. J.; Ellman, J. A. Asymmetric Synthesis of Protected Arylglycines by Rhodium-Catalyzed Addition of Arylboronic Acids to *N*-*tert*-butanesulfinyl Imino Esters. *J. Am. Chem. Soc.* **2006**, *128*, 6303–6305. (c) Dai, H.; Lu, X. Diastereoselective Synthesis of Arylglycine Derivatives by Cationic Palladium(II)-Catalyzed Addition of Arylboronic Acids to *N*-*tert*-butanesulfinyl Imino Esters. *Org. Lett.* **2007**, *9*, 3077–3080.
 - 5 (a) Huang, H.; Guo, X.; Hu, W. Efficient Trapping of Oxonium Ylides with Imines: A Highly Diastereoselective Three-Component Reaction for the Synthesis of β -Amino- α -hydroxyesters with Quaternary Stereocenters. *Angew. Chem., Int. Ed.* **2007**, *46*, 1337–1339. (b) Fur, N. L.; Mojovic, L.; Plé, N.; Turck, A.; Reboul, V.; Metzner, P. *ortho*-Metalation of Enantiopure Aromatic Sulfoxides and Stereocontrolled Addition to Imines. *J. Org. Chem.* **2006**, *71*, 2609–2616.
 - 6 (a) Xu, M.-H.; Wang, W.; Lin, G.-Q. A Highly Efficient Asymmetric Synthesis of Optically Active α,γ -Substituted γ -Butyrolactones Using a Chiral Auxiliary Derived from Isosorbide. *Org. Lett.* **2000**, *2*, 2229–2232. (b) Wang, W.; Xu, M.-H.; Lei, X.-S.; Lin, G.-Q. Chiral Sulfonamide Induced Enantioselective Protonation of Samarium Enolate in the Reaction of α,β -Unsubstituted Ester with Ketone. *Org. Lett.* **2000**, *2*, 3773–3776. (c) Xu, M.-H.; Wang, W.; Xia, L.-J.; Lin, G.-Q. Development of a New Reaction System for the Synthesis of Highly Optically Active α,γ -Substituted γ -Butyrolactones. *J. Org. Chem.* **2001**, *66*, 3953–3962.
 - 7 Kagan, H. B. Twenty-five Years of Organic Chemistry with Diodosamarium: An Overview. *Tetrahedron* **2003**, *59*, 10351–10372.
 - 8 (a) Viso, A.; de la Pradilla, R. F.; García, A.; Flores, A. α,β -Diamino Acids: Biological Significance and Synthetic Approaches. *Chem. Rev.* **2005**, *105*, 3167–3196. (b) Lucet, D.; Le Gall, T.; Mioskowski, C. The Chemistry of Vicinal Diamines. *Angew. Chem., Int. Ed.* **1998**, *37*, 2580–2627. (c) Bergmeier, S. C. The Synthesis of Vicinal Amino Alcohols. *Tetrahedron* **2000**, *56*, 2561–2576. (d) Trost, B. M.; Terrell, L. R. A Direct Catalytic Asymmetric Mannich-type Reaction to *syn*-Amino Alcohols. *J. Am. Chem. Soc.* **2003**, *125*, 338–339. (e) List, B.; Pojarliev, P.; Biller, W. T.; Martin, H. J. The Proline-Catalyzed Direct Asymmetric Three-Component Mannich Reaction: Scope, Optimization, and Application to the Highly Enantioselective Synthesis of 1,2-Amino Alcohols. *J. Am. Chem. Soc.* **2002**, *124*, 827–833. (f) Matsunaga, S.; Yoshida, T.; Morimoto, H.; Kumagai, N.; Shibasaki, M. Direct Catalytic Asymmetric Mannich-type Reaction of Hydroxyketone Using an Et_2Zn /Linked-BINOL Complex: Synthesis of Either *anti*- or *syn*- β -Amino Alcohols. *J. Am. Chem. Soc.* **2004**, *126*, 8777–8785.
 - 9 Recently, Shi reported a catalytic asymmetric diamination for a variety of conjugated alkenes in good yields with high regio-, diastereo-, and enantioselectivities. Du, H.-F.; Yuan, W.-C.; Zhao, B.-G.; Shi, Y. Catalytic Asymmetric Diamination of Conjugated Dienes and Trienes. *J. Am. Chem. Soc.* **2007**, *129*, 11688–11689.
 - 10 (a) Hatano, B.; Ogawa, A.; Hirao, T. Cp_2VCl_2 -Catalyzed Meso-Selective Pinacol Coupling Reaction of Aldimines in the Presence of Chlorosilane and Zinc Metal. *J. Org. Chem.* **1998**, *63*, 9421–9424. (b) Alexakis, A.; Aujard, I.; Mangeney, P. Practical and Efficient Synthesis of C_2 Symmetrical Diamines with $\text{Zn}/\text{Me}_2\text{SiCl}$. *Synlett* **1998**, 873–874. (c) Ortega, M.; Rodríguez, M. A.; Compos, P. J. Zn-Mediated Catalytic Photoreduction of Aldimines. One-Pot Synthesis and Separation of meso and *d,l* C_2 Symmetrical Diamines. *Tetrahedron* **2004**, *60*, 6475–6478.
 - 11 Shimizu, M.; Suzuki, I.; Makino, H. Highly Chemoselective Crossed Imino Pinacol Coupling Reaction Using the Synergistic Effect of Boron Trifluoride Etherate and Trichloromethylsilane. *Synlett* **2003**, 1635–1638.
 - 12 Zhong, Y.-W.; Izumi, K.; Xu, M.-H.; Lin, G.-Q. Highly Diastereoselective and Enantioselective Synthesis of Enantiopure C_2 -Symmetrical Vicinal Diamines by Reductive Homocoupling of Chiral *N*-*tert*-butanesulfinyl Imines. *Org. Lett.* **2004**, *6*, 4747–4750.
 - 13 Zhong, Y.-W.; Xu, M.-H.; Lin, G.-Q. Samarium Diodide-Induced Asymmetric Synthesis of Optically Pure Unsymmetrical Vicinal Diamines by Reductive Cross-Coupling of Nitrones with *N*-*tert*-butanesulfinyl Imines. *Org. Lett.* **2004**, *6*, 3953–3956.
 - 14 Zhong, Y.-W.; Dong, Y.-Z.; Fang, K.; Izumi, K.; Xu, M.-H.; Lin, G.-Q. A Highly Efficient and Direct Approach for Synthesis of Enantiopure β -Amino Alcohols by Reductive Cross-Coupling of Chiral *N*-*tert*-butanesulfinyl Imines with Aldehydes. *J. Am. Chem. Soc.* **2005**, *127*, 11956–11957.
 - 15 (a) Taniguchi, N.; Uemura, M. Asymmetric Synthesis of β -Amino Alcohols by Cross-Pinacol Coupling of Planar Chiral Ferrocenecarboxaldehyde with Imines. *J. Am. Chem. Soc.* **2000**, *122*, 8301–8302. (b) Tanaka, Y.; Taniguchi, N.; Uemura, M. Asymmetric Synthesis of β -Amino Alcohols by Reductive Cross-Coupling of Benzylideneamine with Planar Chiral Benzaldehydes. *Org. Lett.* **2002**, *4*, 835–838. (c) Chavarot, M.; Rivard, M.; Rose-Munch, F.; Rose, E.; Py, S. First Asymmetric SmI_2 -Induced Cross-Coupling of $\text{Cr}(\text{CO})_3$ Aromatic Nitronne Complexes with Carbonyl Compounds. *Chem. Commun.* **2004**, 2330–2331.
 - 16 (a) Pesenti, C.; Bravo, P.; Corradi, E.; Frigerio, M.; Meille, S. V.; Panzeri, W.; Viani, F.; Zanda, M. Synthesis of (+)- and (–)-Satine via Chiral Sulfoxide Chemistry. *J. Org. Chem.* **2001**, *66*, 5637–5640. (b) Andrés, J. M.; Pedrosa, R.; Pérez, A.; Pérez-Encabo, A. Diastereoselective Synthesis of Enantiopure β -Amino- β -hydroxy Acids by Reformatsky Reaction of Chiral α -Dibenzylamino Aldehydes. *Tetrahedron* **2001**, *57*, 8521–8530. (c) So, R. C.; Ndonye, R.; Izmirian, D. P.; Richardson, S. K.; Guerrero, R. L.; Howell, A. R. Straightforward Synthesis of Sphingamines via a Serine-Derived Weinreb Amide. *J. Org. Chem.* **2004**, *69*, 3233–3235. (d) Yun, J. M.; Sim, T. B.; Hahn, H. S.; Lee, W. K. Efficient Synthesis of Enantiomerically Pure 2-Acylaziridines: Facile Synthesis of *N*-Boc-safingol, *N*-Boc-*D*-erythro-sphinganine, and *N*-Boc-spisulosine from a Common Intermediate. *J. Org. Chem.* **2003**, *68*, 7675–7680.
 - 17 (a) Desai, M. C.; Lefkowitz, S. L.; Thadeio, P. F.; Longo, K. P.; Snider, R. M. Discovery of a Potent Substance P Antagonist: Recognition of the Key Molecular Determinant. *J. Med. Chem.* **1992**, *35*, 4911–4913. (b) Harrison, T.; Williams, B. J.; Swain, C. J.; Ball, R. G. Piperidine-Ether Based hNK₁ Antagonists 1: Determination of the Relative and Absolute Stereochemical Requirements. *Bioorg. Med. Chem. Lett.* **1994**, *4*, 2545–2550.
 - 18 (a) Takahashi, K.; Nakano, H.; Fujita, R. A Concise and Practical Catalytic Asymmetric Synthesis of (–)-CP-99,994 and (–)-L-733,061. *Tetrahedron Lett.* **2005**, *46*, 8927–8930. (b) Cherian, S. K.; Kumar, P. Enantioselective Synthesis of (+)-L-733,060. *Tetrahedron: Asymmetry* **2007**, *18*, 982–987, and references therein.
 - 19 Liu, R.-H.; Fang, K.; Wang, B.; Xu, M.-H.; Lin, G.-Q. Concise Asymmetric Synthesis of (+)-CP-99,994 and (+)-L-733,060 via Efficient Construction of Homochiral *syn*-1,2-Diamines and *syn*-1,2-Amino Alcohols. *J. Org. Chem.* **2008**, *73*, 3307–3310.
 - 20 Cogan, D. A.; Liu, G. C.; Ellman, J. A. Asymmetric Synthesis of Chiral Amines by Highly Diastereoselective 1,2-Additions of Organometallic Reagents to *N*-*tert*-butanesulfinyl Imines. *Tetrahedron* **1999**, *55*, 8883–8904.
 - 21 (a) Plobeck, N.; Powell, D. Asymmetric Synthesis of Diarylmethylamines by Diastereoselective Addition of Organometallic Reagents to Chiral *N*-*tert*-butanesulfinimines: Switchover of Diastereofacial Selectivity. *Tetrahedron: Asymmetry* **2002**, *13*, 303–310. (b) Colyer, J. T.; Anderson, N. G.; Tedrow, J. S.; Soukup, T. S.; Faul, M. M. Reversal of Diastereofacial Selectivity in Hydride Reductions of *N*-*tert*-butanesulfinyl Imines. *J. Org. Chem.* **2006**, *71*, 6859–6862. (c) Tanuwidjaja, J.; Peltier, H. M.; Ellman, J. A. One-Pot Asymmetric Synthesis of Either Diastereomer of *tert*-butanesulfinyl-Protected Amines from Ketones. *J. Org. Chem.* **2007**, *72*, 626–629.
 - 22 Foubelo, F.; Yus, M. Indium-Mediated Diastereoselective Addition of Allyl Bromides to Enantiomerically Pure *N*-*tert*-butanesulfinyl Aldimines. *Tetrahedron: Asymmetry* **2004**, *15*, 3823–3825.
 - 23 Sun, X.-W.; Xu, M.-H.; Lin, G.-Q. Room-Temperature Highly Diastereoselective Zn-Mediated Allylation of Chiral *N*-*tert*-butanesulfinyl Imines: Remarkable Reaction Condition Controlled Stereoselectivity Reversal. *Org. Lett.* **2006**, *8*, 4979–4982.
 - 24 (a) Wada, R.; Shibusuchi, T.; Makino, S.; Oisaki, K.; Kanai, M.; Shibasaki, M. Catalytic Enantioselective Allylation of Ketoinmines. *J. Am. Chem. Soc.* **2006**, *128*, 7687–7691. (b) Berger, R.; Duff, K.; Leighton, J. L. Enantioselective Allylation of Ketone-Derived Benzoylhydrazones: Practical Synthesis of Tertiary Carbinamines. *J. Am. Chem. Soc.* **2004**, *126*, 5686–5687.
 - 25 Sun, X.-W. Ph. D. Dissertation, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 2007.
 - 26 Wang, Y.; He, Q.-F.; Wang, H.-W.; Zhou, X.; Huang, Z.-Y.; Qin, Y. Highly Diastereoselective Enolate Addition of *O*-Protected α -Hydroxyacetate to (S_2)-*tert*-butanesulfinylimines: Synthesis of Taxol Side Chain. *J. Org. Chem.* **2006**, *71*, 1588–1591.
 - 27 Liu, M. M.S. Dissertation, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 2007.
 - 28 (a) Takeya, H.; Morishita, M.; Koshino, H.; Morita, T.-i.; Kobayashi, K.; Osaka, H. Cytosaxone: A Novel Cytokine Modulator Containing a 2-Oxazolidinone Ring

- Produced by *Streptomyces* sp. *J. Org. Chem.* **1999**, *64*, 1052–1053. (b) Mishra, R. K.; Coates, C. M.; Revell, K. D.; Turos, E. Synthesis of 2-Oxazolidinones from β -Lactams: Stereospecific Total Synthesis of (–)-Cytosaxone and All of Its Stereoisomers. *Org. Lett.* **2007**, *9*, 575–578; see references cited therein for related synthesis of (–)-cytosaxone.
- 29 Sun, X.-W.; Liu, M.; Xu, M.-H.; Lin, G.-Q. Remarkable Salt Effect on In-Mediated Allylation of *N-tert*-Butanesulfinyl Imines in Aqueous Media: Highly Practical Asymmetric Synthesis of Chiral Homoallylic Amines and Isoindolines. *Org. Lett.* **2008**, *10*, 1259–1262.
- 30 (a) Csende, F.; Stájer, G. Approaches to the Formation of Condensed Isoindolones. *Curr. Org. Chem.* **2005**, *9*, 1261–1276. (b) Wang, Z.-Q.; Feng, C.-Q.; Xu, M.-H.; Lin, G.-Q. Design of C_2 -Symmetric Tetrahydropentalenes as New Chiral Diene Ligands for Highly Enantioselective Rh-Catalyzed Arylation of *N*-Tosylarylimines with Arylboronic Acids. *J. Am. Chem. Soc.* **2007**, *129*, 5336–5337.