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Constructing a Quantitative Correlation between N-Substituent Sizes of Chiral Ligands and Enantioselectivities in Asymmetric Addition Reactions of Diethylzinc with Benzaldehyde

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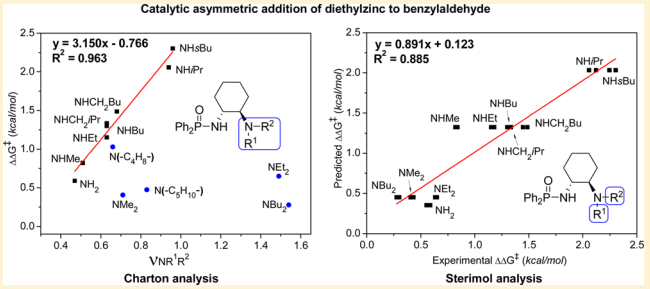
Supporting Information

ABSTRACT: Using the asymmetric addition reaction of diethylzinc with benzylaldehyde as a model, we have demonstrated that excellent correlations exist between steric reference parameters (Charton and Sterimol values) for appropriate sets of substituents present on chiral 1,2-amino-phosphoramide ligands and the enantiomeric ratios of alcohol products produced in this process.



Developing chiral ligands that promote formation of products with excellent levels of enantioselectivity has been the focus of intensive studies in the area of metal-catalyzed asymmetric reactions.[1−4] Despite the well-known influence of steric factors on enantioselectivity, thus far ligand optimization has for the most part focused on qualitative rather than quantitative observations. The major reason for this lies in the fact that most transition states for asymmetric catalytic reactions involving metals are highly complicated and difficult to analyze. Although significant progress has been made in the design of ligands that optimize the stereochemical courses of asymmetric reactions by using computational methods,[5−20] further advances are made difficult because these methods cannot be easily applied to metal-catalyzed reactions that proceed via complicated or unidentified mechanisms.

Sigman and his co-workers have demonstrated that steric parameters can be employed to quantitatively correlate substituent sizes and enantiomeric ratios in cases where the catalytic nature of an asymmetric reaction is not considered.[21−26] Indeed, steric parameter based quantitative methods targeted at optimizing chiral ligands are very attractive, and some successful applications have been reported using this approach.[27−29] However, additional systematic studies aimed at obtaining quantitative correlations between steric effects of ligand-substituents and enantioselectivities of catalytic asymmetric reactions are needed in order to develop a detailed understanding of and predictive powers for these processes. Herein, we report the results of an investigation in which steric parameters are used to quantitatively analyze the steric effects of the N-substituents of chiral phosphoramide ligands on the enantioselectivities of catalytic asymmetric addition reactions of diethylzinc with benzylaldehyde. The results of this effort show that appropriately chosen substituent steric parameters can be used to develop a quantitative correlation between substituent sizes and product enantiomeric ratios.

Compared to other classical steric parameters, such as A-values[30,31] and interference values,[32] Charton values[33,34] (ν), which are derived from van der Waals radii and for which an extensive library exists, have been widely used in QSAR (quantitative structure−activity relationship) studies in both the chemical and biological sciences. Consequently, we have utilized Charton values as steric reference parameters in the first phase of the investigation described below.

Although a long list of the Charton values for C-substituents based on a modified Taft treatment[35,36] ($\log k_R = \psi\nu_R + h$) of the rate constants for ester hydrolysis (Figure 1a) exists, only a very limited number of Charton values for N-substituents ($\nu_{NR^1R^2}$) have come from studies of N-substituted amide hydrolysis reactions (Figure 1b). However, Charton did quantitatively correlate $\nu_{NR^1R^2}$ to $\nu_{CHR^1R^2}$ as a linear relationship

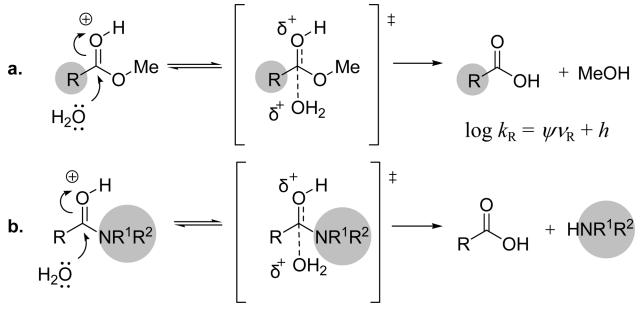


Figure 1. Charton steric parameters.

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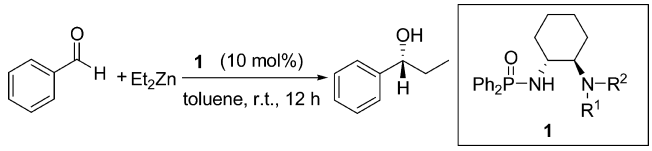
Table 1. Charton Values Used in Our Investigation

entry	NR^1R^2	$\nu_{NR^1R^2}$ [a]	CHR^1R^2	$\nu_{CHR^1R^2}$ [b]	R	ν_R [b]
1	NH_2	0.47	CH_3	0.52	H	0
2	NHMe	0.51	CH_2Me	0.56	Me	0.52
3	NHEt	0.63	CH_2Et	0.68	Et	0.56
4	NHBu	0.63	CH_2Bu	0.68	Bu	0.68
5	$NHCH_2iPr$	0.63	CH_2CH_2iPr	0.68	CH_2iPr	0.98
6	$NHCH_2Bu$	0.68	CH_2CH_2Bu	0.73	CH_2Bu	0.68
7	NH*i*Pr	0.94	CH_2iPr	0.98	*i*Pr	0.76
8	NH*s*Bu	0.96	CH_2sBu	1.00	*s*Bu	1.02
9	NMe_2	0.71	$CHMe_2$	0.76		
10	NEt_2	1.49	$CHEt_2$	1.28		
11	NBu_2	1.54	$CHBu_2$	1.56		
12	$N(-C_4H_8-)$	0.66	$CH(-C_4H_8-)$	0.71		
13	$N(-C_5H_{10}-)$	0.83	$CH(-C_5H_{10}-)$	0.87		

[a]See ref 37. Calculated from $\nu_{CHR^1R^2}$ by using the equation of $\nu_{NR^1R^2} = 1.03(\nu_{CHR^1R^2}) - 0.0691$. [b]See refs 33, 34.

Table 2. Asymmetric Addition Reactions of Diethylzinc with Benzaldehyde Catalyzed by Chiral Phosphoramides 1



entry	ligand	NR^1R^2	CHR^1R^2	yield[a] (%)	er[b] (*R*/*S*)	$\Delta\Delta G^{\ddagger}$[c] kcal/mol
1	**1a**	NH_2	CH_3	72	73:27	0.589
2	**1b**	NHMe	CH_2Me	71	80:20	0.820
3	**1c**	NHEt	CH_2Et	76	87.5:12.5	1.152
4	**1d**	NHBu	CH_2Bu	99	90:10	1.300
5	**1e**	$NHCH_2iPr$	CH_2CH_2iPr	99	90.5:9.5	1.334
6	**1f**	$NHCH_2Bu$	CH_2CH_2Bu	90	92.5:7.5	1.487
7	**1g**	NH*i*Pr	CH_2iPr	99	97:3	2.057
8	**1h**	NH*s*Bu	CH_2sBu	99	98:2	2.303
9	**1i**	NMe_2	$CHMe_2$	95	66.5:33.5	0.406
10	**1j**	NEt_2	$CHEt_2$	98	75:25	0.650
11	**1k**	NBu_2	$CHBu_2$	99	61.5:38.5	0.277
12	**1l**	$N(-C_4H_8-)$	$CH(-C_4H_8-)$	99	85:15	1.027
13	**1m**	$N(-C_5H_{10}-)$	$CH(-C_5H_{10}-)$	95	69:31	0.474

[a]Isolated yields. [b]Determined by using chiral GC analysis. [c]Estimated at 298 K (25 °C), $\Delta\Delta G^{\ddagger} = -RT\ln(S/R)$, $R = 0.001986$ kcal K^{-1} mol^{-1}.

on the basis of available $\nu_{NR^1R^2}$ and $\nu_{CHR^1R^2}$ values to lead the equation of $\nu_{NR^1R^2} = m\nu_{CHR^1R^2} + c$, where $m = 1.03$ and $c = -0.0691$.[37] As a result, $\nu_{NR^1R^2}$ can be directly calculated by using the corresponding $\nu_{CHR^1R^2}$ values (see Table 1).

Our initial studies focused on an assessment of the possibility that a linear free energy relationship (LFER) exists between Charton values of N-substituents ($\nu_{NR^1R^2}$) on chiral 1,2-amino-phosphoramide ligands and enantiomeric ratios in products of the catalytic asymmetric addition of diethylzinc to benzylaldehyde. For this purpose five chiral 1,2-amino-phosphoramide ligands, containing NH_2, NEt_2, $N(-C_5H_{10}-)$, NHBu, $NHCH_2Bu$ amine substituents with different Charton values, were prepared. Although all of these ligands were observed to catalyze enantioselective diethylzinc to benzaldehyde addition reactions, no LFER was observed between the Charton values and enantiomeric ratios. In order to further explore this issue, a larger group of chiral phosphoramides, containing NMe_2, $N(-C_4H_8-)$, NBu_2, NHMe, NHEt, $NHCH_2iPr$, NH*i*Pr and NH*s*Bu substituted amine groups, was synthesized, and the enantioselectivies of asymmetric diethylzinc to benzylaldehyde addition reactions that they catalyze were determined (see Table 2).

As can be seen from viewing the data in Table 2 and the corresponding plot in Figure 2a (plotted as $\Delta\Delta G^{\ddagger}$, which is derived from enantiomeric ratios), no LFER occurs between the Charton values and enantiomeric ratios when all mono- and disubstitued ligands are taken into account. However, a definite LFER was found between the ν_{NHR} values of mono-N-substituted ligands (Table 2, entry 1−8), which corresponds to the equation $\Delta\Delta G^{\ddagger} = 3.150(\nu_{NHR}) - 0.766$ with $R^2 = 0.963$. The large slope ($\Psi = 3.15$) seen in this correlation indicates that enantioselectivities are highly sensitive to changes in the nature of alkyl groups on the monosubstituted amino groups in the 1,2-amino-phosphoramides. It should be noted that the lack of an LFER that incorporates both mono- and di-N-substituents may be a consequence of the limitations of applying Charton parameters of sterically large groups.[25,26]

On the basis of the earlier observation that a linear relationship exists between $\nu_{CHR^1R^2}$ and $\nu_{NR^1R^2}$ along with the results of this study, which show that some of $\nu_{NR^1R^2}$ values linearly correlate with $\Delta\Delta G^{\ddagger}$ associated with the enantioselectivities of diethylzinc additions to benzaldehyde, we expected that $\Delta\Delta G^{\ddagger}$ and Charton values of C-substituents ($\nu_{CHR^1R^2}$) that correspond to those present on amino groups of 1,2-amino-

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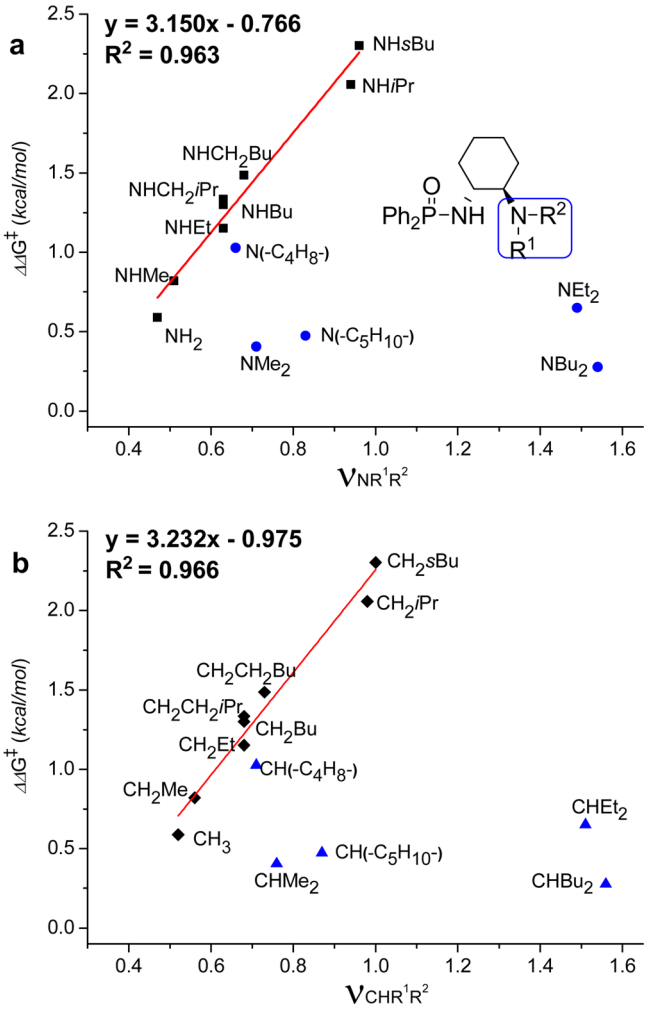

Figure 2. Quantitative correlations between Charton N- and C-substitutent size parameters, $\nu_{NR^1R^2}$ (a) and $\nu_{CHR^1R^2}$ (b), respectively, and enantioselectivities of catalyzed diethylzinc addition reactions with benzaldehyde.

phosphoramides would be linearly correlated. This expectation is a consequence of the fact that the two linear mathematical expressions shown in eqs 1 and 2 can be combined to create the relationship between $\Delta\Delta G^{\ddagger}$ and $\nu_{CHR^1R^2}$ shown in eq 3.

$$\nu_{NR^1R^2} = 1.03(\nu_{CHR^1R^2}) - 0.0691 \quad (1)$$

$$\Delta\Delta G^{\ddagger} = 3.150(\nu_{NR^1R^2}) - 0.766 \ (R^1 = H) \quad (2)$$

$$\Delta\Delta G^{\ddagger} = 3.245(\nu_{CHR^1R^2}) - 0.984 \ (R^1 = H) \quad (3)$$

As inspection of this expectation, the plot in Figure 2b demonstrates that an excellent linear relationship does indeed exist ($R^2 = 0.966$) between ν_{CH_2R} and enantiomeric ratios of the catalyzed addition reactions. Therefore, this linear relationship enables a LFER analysis to be carried out between N-substituent sizes and enantioselectivities by simply using the extensive list of Charton values of the corresponding C-substituents.

Because the mono-N-substituted ligands employed in the above analysis contain only one R-group, we determined if a correlation would occur between enantioselectivities and the Charton ν_R values (see Table 1).[33,34] However, compared with the excellent linear correlation seen when ν_{NHR} values were utilized, the one obtained using ν_R was poor ($R^2 = 0.557$) (Figure 3). Because ν values correspond to the influence of

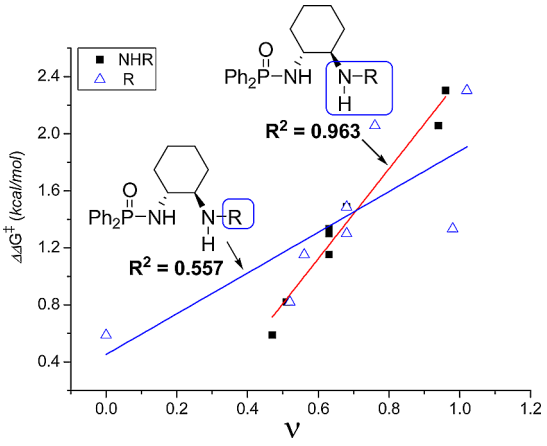

Figure 3. LFERs between substituent sizes and enantiomeric ratios using $\nu_{NR^1R^2}$ (red line) and ν_R (blue line) values.

substituents that are directly adjacent to the carbonyl carbon in esters undergoing hydrolysis, we believed that the use of ν values of the amino-groups (NHR) in the 1,2-amino-phosphoramides that are directly adjacent to zinc in the transition state of the addition reaction would lead to an even more accurate correlation than one derived by employing ν values of R groups that are one nitrogen atom away from the zinc center. On the basis of this reasoning, $\Delta\Delta G^{\ddagger}$ values were calculated from the linear equation constructed using ν_{NHR} values. The results along with experimental $\Delta\Delta G^{\ddagger}$ values and errors are tabulated in Table 3 and plotted in Figure 4.

Table 3. Comparison of Experimentally Determined and Calculated $\Delta\Delta G^{\ddagger}$ Values

entry	ligand	experimental $\Delta\Delta G^{\ddagger}$	predicted $\Delta\Delta G^{\ddagger}$[a]	error[b]
1	NH_2	0.5886	0.7145	0.1762
2	NHMe	0.8204	0.8405	0.0239
3	NHEt	1.1516	1.2185	0.0549
4	NHBu	1.3004	1.2185	0.0672
5	$NHCH_2$*i*Pr	1.3340	1.2185	0.0948
6	$NHCH_2$Bu	1.4869	1.3760	0.0806
7	NH*i*Pr	2.0573	2.1950	0.0627
8	NH*s*Bu	2.3033	2.2580	0.0201

[a]Calculated from $\Delta\Delta G^{\ddagger} = 3.150(\nu_{NHR}) - 0.766$. [b]Error = (|Experimental $\Delta\Delta G^{\ddagger}$ − Predicted $\Delta\Delta G^{\ddagger}$|)/Predicted $\Delta\Delta G^{\ddagger}$.

Sigman pointed out earlier that identifying appropriate reference parameters is an important component of a successful quantitative correlation analysis of asymmetric catalyzed processes.[25,26] More recently, by using Verloop's multidimensional Sterimol parameters[38−40] (B_1, B_5 and L) (Figure 5), Sigman was able to demonstrate that quantitative correlations exist between small and large substituents, located at various distances from the reaction centers, and enantioselectivities of asymmetric catalytic reactions. However, plots using Charton parameters for both small and large substituents display only partial linearity and breaks in linearity.

Inspired by Sigman's observations, we engaged in an effort to determine if a quantitative correlation occurs between N-substituent sizes and enantioselectivities by using the Steimol

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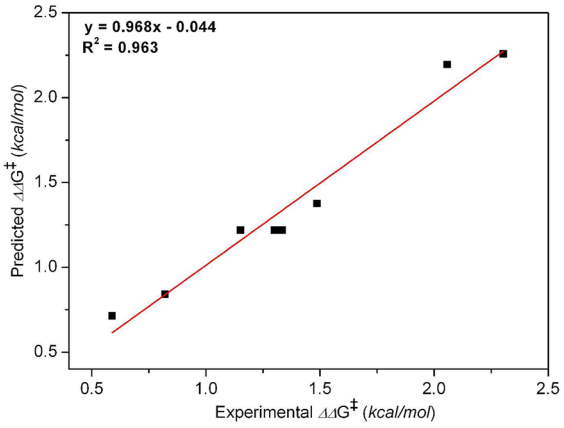

Figure 4. Plot of experimentally determined vs predicted $\Delta\Delta G^{\ddagger}$ values (Table 3).

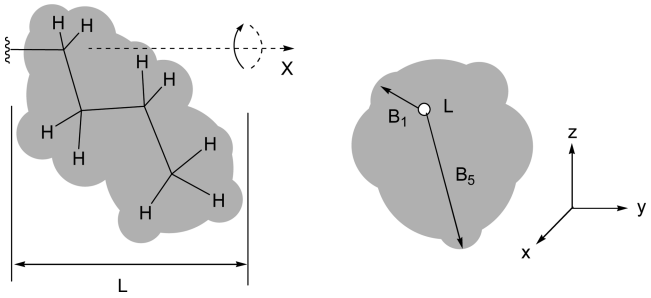

Figure 5. Sterimol parameters: B_1 (minimal width of substituent), B_5 (maximal width of substituent), and L (maximal length of substituent).

parameters listed in Table 4. In this treatment, it is possible to use Sterimol parameters for either the NR^1R^2 groups or the individual R^1 and R^2 substiuents of NR^1R^2 in the phosphoramide ligands (see Figure 6). When Sterimol parameters of NR^1R^2 groups were used, no quantitative relationship was observed in the case (see the Supporting Information for details). Therefore, our attention turned to utilizing Sterimol parameters of the individual R^1 and R^2 groups. Because two sets of three-dimensional Sterimol parameters should be evaluated simultaneously, the base model included all Sterimol subparameters of substituents (R^1, R^2) and cross-terms relating each R^1-Sterimol subparameter to the R^2-Sterimol subparameter. A stepwise regression analysis was then performed on the system to generate the correlation represented by eq 4, in which X and Y represent the respective R^1 and R^2 substituents.

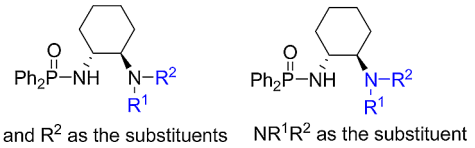

Figure 6. Substituent assignment for phosphoramide ligand.

$$\Delta\Delta G^{\ddagger} = 0.163 - 1.678X_{B1} + 1.867Y_{B1} \quad (4)$$

Analysis of the Sterimol-based model shows that $\Delta\Delta G^{\ddagger}$ strongly depends on the X_{B1} terms for both the R^1 and R^2 substituents (see the Supporting Information for details). The negative coefficient relating the X_{B1} term indicates that a larger proximal steric bulk of the R^1 group will lead to an increase in the transition state bond distance between the carbonyl and the zinc active center and a corresponding decrease in the level of enantioselectivity. In contrast, the positive coefficient related to the Y_{B1} term indicates that a large proximal steric bulk of the R^2 group is required to generate higher enantioselectivities. As predicted, the NH*s*Bu group, which has the largest calculated Y_{B1} value and the smallest calculated X_{B1} value, is present in the ligand that promotes the highest enantioselectivity for the catalyzed addition reaction. Indeed, a plot of the predicted and experimentally determined $\Delta\Delta G^{\ddagger}$ values (Figure 7) is linear

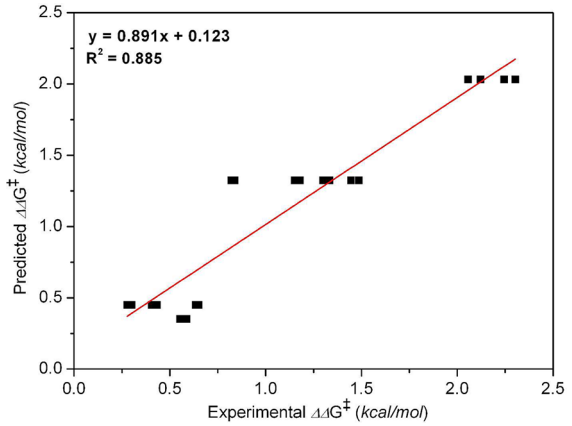

Figure 7. Plot of experimentally determined vs predicted $\Delta\Delta G^{\ddagger}$ values based on a Sterimol analysis.

with R^2 = 0.885. Because the N atom of the NR^1R^2 amino substituent in the 1,2-amino-phosphoramides directly coordinates with zinc, the steric repulsive effect of NR^1R^2 on the degree of enantioselectivity is mainly contributed by the R^1 and

Table 4. Sterimol Parameters[a] (B_1, B_5, L) of NR^1R^2 and R Groups

entry	substituent	B_1	B_5	L	entry	substituent	B_1	B_5	L
1	NH_2	1.35	1.97	2.78	11	$N(-C_4H_8-)$	1.90	4.09	4.90
2	NHMe	1.35	3.08	3.53	12	$N(-C_5H_{10}-)$	1.91	3.49	6.17
3	NHEt	1.35	3.42	4.83	13	H	1	1	2.06
4	NHBu	1.35	4.87	6.88	14	Me	1.52	2.04	2.87
5	$NHCH_2$*i*Pr	1.35	4.47	6.07	15	Et	1.52	3.17	4.11
6	$NHCH_2$Bu	1.35	5.89	8.13	16	Bu	1.52	4.54	6.17
7	NH*i*Pr	1.35	4.13	4.83	17	CH_2*i*Pr	1.52	4.45	4.92
8	NH*s*Bu	1.35	4.47	6.07	18	CH_2Bu	1.52	4.94	6.97
9	NMe_2	1.35	2.56	3.53	19	*i*Pr	1.90	3.17	4.11
10	**NEt_2**	1.35	4.39	4.83	20	*s*Bu	1.90	3.49	4.92

[a]See refs 38–40.

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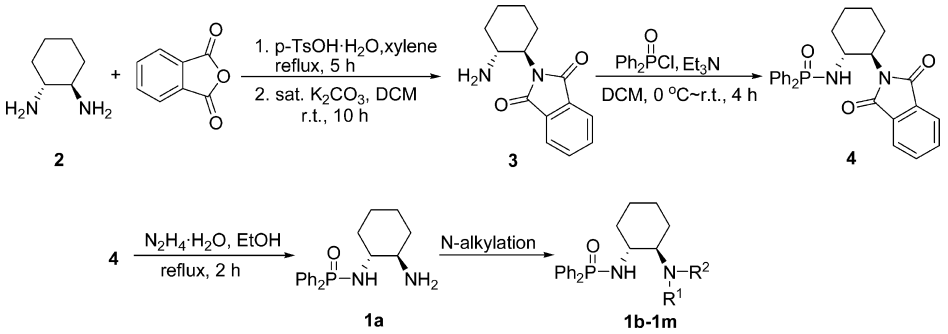

R^2 groups. Thus, using the Sterimol parameters of R^1 and R^2 groups for quantitative correlation analysis leads to a more accurate prediction of the levels of enantioselectivity of the catalyzed asymmetric addition reaction than using those of NR^1R^2 groups.

In summary, in the effort described above, we have thoroughly investigated quantitative correlations between Charton and Sterimol steric parameters associated with steric sizes of N-substituents in the amino groups of chiral phosphoramide ligands and the levels of enantioselectivity in asymmetric catalytic addition reactions of diethylzinc to benzaldehyde. When Charton values of NR^1R^2 groups were employed, a LFER was found to exist only between the size of the N-substituent in chiral mono-N-substituted ligands and enantioselectivity. In contrast, Sterimol parameters of R^1 and R^2 groups of all N-substituents were observed to quantitatively correlate with enantiomeric ratios. The different quantitative relationships obtained by using the Charton and Sterimol analytical methods can perhaps be attributed to the different nature of these steric reference parameters. Significantly, this investigation has demonstrated that choosing appropriate sets of substituents in chiral ligands and reference parameters is important for successfully constructing quantitative steric correlations between ligand substituents and enantioselectivities of catalytic asymmetric reactions.

EXPERIMENTAL SECTION

General Methods. All experiments were carried out in dried glassware with magnetic stirring under an atmosphere of dry nitrogen. ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz) and ^{31}P NMR (162 MHz) spectra were recorded in $CDCl_3$ solutions using a 400 MHz spectrometer. Chemical shifts were reported in parts per million (ppm, δ) relative to $CDCl_3$ (δ 7.26 for ^{1}H NMR), or $CDCl_3$ (δ 77.0 for ^{13}C NMR). Multiplicities are indicated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and br (broad). Commercial reagents were used as received unless otherwise indicated. All solvents were purified and dried prior to use according to standard methods.[41] Optical rotations were measured on a polarimeter and reported as follows: $[\alpha]_D^T$ (c g/100 mL, solvent). GC analysis was performed on a gas chromatograph with a FID detector on fused silica chiral capillary column (Chirasil Dex CB column, 25 m length × 0.32 mm ID × 0.25 mm film thickness).

Representative Procedure for Preparing Chiral Ligands 1a–1m. *(1R,2R)-N-Phthaloyl-1,2-diaminocyclohexane (**3**).* Prepared following the procedure described previously.[42]

*(1R,2R)-N-[2-(N′-Phthaloyl)cyclohexyl]diphenylphosphinic amide (**4**).* To a solution of **3** (7.33 g, 30 mmol) in dry CH_2Cl_2 (100 mL), Et_3N (7.58 g, 75 mmol) was added at room temperature. After being stirred for 10 min, diphenylphosphinic chloride (10.64 g, 45 mmol) in dry CH_2Cl_2 (50 mL) was added dropwise to the solution at 0 °C. The mixture was stirred for 4 h at room temperature, cooled in ice bath and diluted with water (20 mL). Extraction with CH_2Cl_2 gave combined organic layers that were washed with brine, dried over $MgSO_4$ and concentrated in vacuo to give a residue that was subjected to silica gel column chromatography (EtOAc/hexane = 1/1), which afforded 11.33 g (85%) of **4** as a white solid: mp 193–194 °C; $[\alpha]_D^{22.0}$ −41.5 (c 2.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20–1.40 (m, 3H), 1.65–1.85 (m, 3H), 2.26–2.42 (m, 2H), 2.90–3.00 (m, 1H), 3.50–3.68 (m, 1H), 3.85–4.00 (m, 1H), 7.00–7.13 (m, 2H), 7.23–7.31 (m, 1H), 7.32–7.39 (m, 2H), 7.40–7.53 (m, 3H), 7.65–7.75 (m, 4H), 7.75–7.85 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.8, 25.2, 28.7, 37.0 (d, J = 2.5 Hz), 51.6, 56.2 (d, J = 5.9 Hz), 122.9, 128.0 (d, J = 12.8 Hz), 128.2 (d, J = 12.6 Hz), 131.4 (d, J = 38.4 Hz), 131.5 (d, J = 9.5 Hz), 131.7 (d, J = 7.6 Hz), 131.8 (d, J = 9.1 Hz), 133.0 (d, J = 5.8 Hz), 133.6, 168.3, 168.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.0. Elemental Analysis, Anal. Calcd. for $C_{26}H_{25}N_2O_3P$: C 70.26, H 5.67, N 6.30 Found: C 70.15, H 5.77, N 6.25.

*(1R,2R)-1-N-(Diphenylphosphoroso)cyclohexane-1,2-diamide (**1a**, Entry 1 in Table 2).*[43] A solution of **4** (11.33 g, 25.5 mmol) in ethanol (5 mL) containing hydrazine monohydrate (1.0 mL) was stirred at reflux for 2 h. The mixture was then cooled to room temperature and diluted with diethyl ether, forming a precipitate that was removed by filtration. The filtrate was dried over $MgSO_4$ and concentrated in vacuo to afford 7.62 g (95%) **1a** as a light yellow solid, which was used in the following step without further purification: mp 152–153 °C; $[\alpha]_D^{21.3}$ −5.8 (c 2.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.80–0.95 (m, 1H), 0.95–1.22 (m, 3H), 1.44–1.55 (m, 2H), 1.62–1.74 (br, 2H), 1.74–1.85 (m, 1H), 1.87–2.02 (m, 1H), 2.18–2.31 (m, 1H), 2.36–2.52 (m, 1H), 3.40–3.52 (m, 1H), 7.22–7.42 (m, 6H), 7.70–7.89 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.6, 25.0, 34.6, 34.8 (d, J = 4.5 Hz), 56.4 (d, J = 4.0 Hz), 58.6 (d, J = 2.0 Hz), 128.3 (d, J = 12.5 Hz), 131.6 (d, J = 2.4 Hz), 131.8, 131.9, 132.2 (d, J = 9.4 Hz), 132.8 (d, J = 129.9 Hz), 133.4 (d, J = 128.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.2. Elemental Analysis, Anal. Calcd. for $C_{18}H_{23}N_2OP$: C 68.77, H 7.37, N 8.91 Found: C 68.92, H 7.54, N 8.64.

*(1R,2R)-1-N-(Diphenylphosphoroso)-2-N-(2-methyl)cyclohexane-1,2-diamine (**1b**, Entry 2 in Table 2).* To a solution of **1a** (314 mg, 1.0 mmol) in dry CH_2Cl_2 (5 mL) at room temperature was added Et_3N (202 mg, 2.0 mmol). After being stirred for 10 min, di-*tert*-butyl dicarbonate (262 mg, 1.2 mmol) in dry CH_2Cl_2 (4 mL) was added dropwise to the solution at 0 °C, and then the reaction mixture was stirred at room temperature for 12 h and concentrated in vacuo to give an oil. To a solution of the oil in THF (4 mL) was added $LiAlH_4$ (156 mg, 4.0 mmol) in THF (5 mL). The mixture was stirred at reflux for 4 h, cooled to 0 °C, diluted with 15 mL ice water and extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated in vacuo, giving a residue that was subjected to silica gel column chromatography (MeOH/CH_2Cl_2 = 1/20), which afforded 253 mg (77%) of **1b** as a white solid: mp 171–172 °C; $[\alpha]_D^{29.8}$ −21.3 (c 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92–1.06 (m, 1H), 1.09–1.23 (m, 2H), 1.27–1.36 (m, 1H), 1.55–1.76 (m, 2H), 2.05–2.15 (m, 2H), 2.16–2.24 (m, 1H), 2.24–2.28 (br, 1H), 2.41 (s, 3H), 2.76–2.93 (m, 1H), 3.33–3.47 (m, 1H), 7.38–7.56 (m, 6H), 7.86–7.98 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.5, 25.0, 30.4, 33.3, 35.0, 55.3 (d, J = 1.9 Hz), 64.4 (d, J = 5.0 Hz), 128.3, 128.5, 128.6, 131.7, 131.8, 131.9, 132.1, 132.2, 132.4, 132.6, 133.7, 133.9; ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.6. Elemental Analysis, Anal. Calcd. for $C_{19}H_{25}N_2OP$: C 69.49, H 7.67, N 8.53 Found: C 69.69, H 7.70, N 8.55.

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*(1R,2R)-1-N-(Diphenylphosphoroso)-2-N-(2-ethyl)cyclohexane-1,2-diamine (**1c**, Entry 3 in Table 2).* To a solution of **1a** (314 mg, 1.0 mmol) in dry CH_2Cl_2 (5 mL) at room temperature was added Et_3N (253 mg, 2.5 mmol). After being stirred for 10 min, acetyl chloride (118 mg, 1.5 mmol) in dry CH_2Cl_2 (4 mL) was added dropwise to the solution at 0 °C, and the resulting mixture was stirred for 2 h, diluted with water (20 mL), and extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated in vacuo to give 320 mg of a yellow solid. To a solution of this solid in THF (4 mL) was added $LiAlH_4$ (117 mg, 3.0 mmol) in THF (5 mL). The mixture was stirred at reflux for 4 h, cooled to 0 °C, diluted with 15 mL of ice water and extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated in vacuo to give a residue that was subjected to silica gel column chromatography (MeOH/CH_2Cl_2 = 1/30), which afforded 287 mg (84%) of **1c** as a white solid: mp 123−125 °C; $[\alpha]_D^{27.6}$ −30.9 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.03−1.11 (m, 1H), 1.15−1.20 (m, 3H), 1.21−1.36 (m, 2H),1.59−1.73 (m, 2H), 2.02−2.17 (m, 2H), 2.30−2.49 (m, 2H), 2.49−2.62 (m, 2H), 2.74−2.97 (m, 2H), 3.51−3.65 (m, 1H), 7.41−7.60 (m, 6H), 7.80−8.00 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.3, 24.6, 24.9, 31.1, 35.0 (d, *J* = 3.43 Hz), 40.9, 55.4, 62.8 (d, *J* = 5.29 Hz), 128.5 (q, *J* = 6.35 Hz), 131.7, 131.8, 132.1, 132.2,132.4, 132.6, 133.7, 133.8; ^{31}P NMR (162 MHz, $CDCl_3$) δ 26.6. Elemental Analysis, Anal. Calcd. for $C_{20}H_{27}N_2OP$: C 70.15, H 7.95, N 8.18 Found: C 70.12, H 7.99, N 8.20.

*(1R,2R)-1-N-Butyl-2-N-(diphenylphosphoroso)cyclohexane-1,2-diamine (**1d**, Entry 4 in Table 2).* To a solution of **1a** (314 mg, 1.0 mmol) in CH_3CN (5 mL) at room temperature was added K_2CO_3 (276 mg, 2.0 mmol) and butyl iodide (239 mg, 1.3 mmol). The resulting mixture was stirred at reflux overnight, cooled to room temperature and concentrated in vacuo to give an oil. The residue oil was diluted with CH_2Cl_2 (20 mL) and water (20 mL). The organic layer was separated, and the aqueous layer (pH ∼ 10) was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated in vacuo, giving a residue that subjected to silica gel column chromatography (MeOH/CH_2Cl_2 = 1/40), which afforded 274 mg (74%) of **1d** as a white solid: mp 133−134 °C; $[\alpha]_D^{20}$ −16.7 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (d, *J* = 7.4 Hz; 3H), 1.10−1.29 (m, 4H), 1.30−1.43 (m, 3H), 1.57−1.72 (m, 4H), 2.02−2.09 (m, 1H), 2.10−2.8 (m, 1H), 2.54−2.71 (m, 2H), 2.78−2.87 (m, 1H), 2.92−3.06 (m, 1H), 3.96−4.11 (br, 1H), 7.40−7.55 (m, 6H), 7.82−7.94 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 20.3, 24.4, 24.8, 30.2, 31.2, 34.6 (d, *J* = 3.4 Hz), 46.0, 54.6, 62.6 (d, *J* = 4.8 Hz), 128.4 (d, *J* = 12.6 Hz), 131.5, 131.6, 131.7, 132.0 (d, *J* = 9.8 Hz), 132.7 (d, *J* = 130.0 Hz), 133.3; ^{31}P NMR (162 MHz, $CDCl_3$) δ 24.1. Elemental Analysis, Anal. Calcd. for $C_{22}H_{31}N_2OP$: C 71.32, H 8.43, N 7.56 Found: C 71.16, H 8.18, N 7.36.

*(1R,2R)-1-N-(Diphenylphosphoroso)-2-N-(2-methylpropyl)-cyclohexane-1,2-diamine (**1e**, Entry 5 in Table 2).* The title compound was prepared following the general procedure described for **1d** on the same scale and was obtained as a white solid with the yield of 289 mg (78%): mp 116−117 °C; $[\alpha]_D^{23.0}$ −19.7 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (d, *J* = 6.6 Hz, 3H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.94−1.04 (m, 1H), 1.08−1.30 (m, 4H), 1.52−1.59 (m, 3H), 2.00−2.10 (m, 2H), 2.19−2.27(m, 2H), 2.52−2.60 (m, 1H), 2.80−2.93 (m, 1H), 3.78−3.96 (m, 1H), 7.36−7.50 (m, 6H), 7.80- 7.95 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7 (d, *J* = 4.0 Hz), 24.8 (d, *J* = 6.2 Hz), 28.7, 31.2, 34.6, 34.7, 54.8, 55.6 (d, *J* = 1.9 Hz), 63.0 (d, *J* = 6.6 Hz), 128.2 (d, *J* = 10.7 Hz), 128.4 (d, *J* = 10.5 Hz), 131.5 (d, *J* = 2.5 Hz), 131.6, 131.7, 132.0 (d, *J* = 9.5 Hz), 133.5 (d, *J* = 126.9 Hz), 133.6 (d, *J* = 130.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.6. Elemental Analysis, Anal. Calcd. for $C_{22}H_{31}N_2OP$: C 71.32, H 8.43, N 7.56 Found: C 71.14, H 8.30, N 7.38.

*(1R,2R)-1-N-(Diphenylphosphoroso)-2-N-pentylcyclohexane-1,2-diamine (**1f**, Entry 6 in Table 2).* The title compound was prepared following the general procedure described for **1d** on the same scale and was obtained as a white solid with the yield of 315 mg (82%): mp 146−147 °C; $[\alpha]_D^{20.9}$ −33.3 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, *J* = 6.4 Hz; 3H), 1.01−1.20 (m, 3H), 1.21−1.41 (m, 6H), 1.48−1.63 (m, 3H), 1.64−1.72 (m, 1H), 2.03−2.14 (m, 2H), 2.33−2.44 (m, 1H), 2.45−2.55 (m, 1H), 2.69−2.84 (m, 2H), 3.67−3.81 (m, 1H), 7.36−7.56 (m, 6H), 7.82−7.95 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.6, 24.7, 24.9, 29.6, 29.9, 31.1, 34.8 (d, *J* = 2.9 Hz), 46.6, 55.5, 62.8 (d, *J* = 6.1 Hz), 128.4 (d, *J* = 12.6 Hz), 128.5 (d, *J* = 12.4 Hz), 131.6 (d, *J* = 2.7 Hz), 131.7, 131.7, 132.1(d, *J* = 9.5 Hz), 133.3 (d, *J* = 127.2 Hz), 133.4 (d, *J* = 129.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.3. Elemental Analysis, Anal. Calcd. for $C_{23}H_{33}N_2OP$: C 71.85, H 8.65, N 7.29 Found: C 71.77, H 8.52, N 7.16.

*(1R,2R)-1-N-(Diphenylphosphoroso)-2-N-(propan-2-yl)-cyclohexane-1,2-diamine (**1g**, Entry 7 in Table 2).* The title compound was prepared following the general procedure described for **1d** on the same scale and was obtained as a white solid with the yield of 303 mg (85%): mp 113−114 °C; $[\alpha]_D^{22.0}$ −42.4 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91−1.00 (m, 1H), 1.02−1.06 (d, *J* = 6.1 Hz, 3H), 1.06−1.11 (d, *J* = 6.3 Hz, 3H), 1.16−1.30 (m, 3H), 1.54−1.72 (m, 3H), 2.01−2.11 (m, 2H), 2.27−2.38 (m, 1H), 2.77−2.88 (m, 1H), 2.88−3.00 (septet, *J* = 6.2, 1H), 3.83−4.08 (br, 1H), 7.39−7.56 (m, 6H), 7.80−8.00 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.8, 24.5, 24.8, 24.9, 32.4, 34.4, 45.7, 56.0, 60.0 (d, *J* = 6.8 Hz), 128.3 (d, *J* = 12.8 Hz), 128.5 (d, *J* = 12.5 Hz), 131.5 (d, *J* = 2.7 Hz), 131.6, 131.7, 132.0 (d, *J* = 9.5 Hz), 133.7 (d, *J* = 125.7 Hz), 134.0 (d, *J* = 130.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.4. Elemental Analysis, Anal. Calcd. for $C_{21}H_{29}N_2OP$: C 70.76, H 8.20, N 7.86 Found: C 70.80, H 8.03, N 7.86.

*(1R,2R)-1-N-(Butan-2-yl)-2-N-(diphenylphosphoroso)-cyclohexane-1,2-diamine (**1h**, Entry 8 in Table 2).* The title compound was prepared following the general procedure described for **1d** on the same scale and was obtained as a white solid with the yield of 252 mg (68%): mp 97−99 °C; $[\alpha]_D^{23.0}$ −41.4 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.80−0.95 (m, 3H), 0.95−1.15 (m, 4H), 1.15−1.33 (m, 4H), 1.34−1.74 (m, 4H), 1.97−2.13 (m, 2H), 2.27−2.45 (m, 1H), 2.65−2.79 (m, 1H), 2.80−2.97 (m, 1H), 3.98−4.14 (m, 1H), 7.36−7.54 (m, 6H), 7.82−7.98 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.7, 10.4, 20.1, 21.2, 24.6, 24.7, 24.9, 25.0, 28.9, 30.9, 32.1, 32.5, 34.2, 34.3, 51.3, 51.7, 56.1, 56.2, 59.7, 59.8, 60.3, 60.4, 128.2 (d, *J* = 13.0 Hz), 128.3 (d, *J* = 12.8 Hz), 131.5, 131.6, 131.7, 132.0 (d, *J* = 9.5 Hz), 133.3 (d, *J* = 125.7 Hz), 134.0 (d, *J* = 129.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.3. Elemental Analysis, Anal. Calcd. for $C_{22}H_{31}N_2OP$: C 71.32, H 8.43, N 7.56 Found: C 71.36, H 8.41, N 7.44.

*(1R,2R)-2-N-(Diphenylphosphoroso)-1-N,1-N-dimethylcyclohexane-1,2-diamine (**1i**, Entry 9 in Table 2).* To a solution of **1a** (314 mg, 1.0 mmol) in CH_3CN (5 mL) at room temperature was added K_2CO_3 (690 mg, 5.0 mmol) and methyl iodide (710 mg, 5.0 mmol). The resulting mixture was stirred at reflux overnight, cooled to room temperature and concentrated in vacuo to give an oil. The residue oil was diluted with CH_2Cl_2 (20 mL) and water (20 mL). The organic layer was separated, and the aqueous layer (pH ∼ 10) was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated in vacuo, giving a residue that subjected to silica gel column chromatography (MeOH/CH_2Cl_2 = 1/40), which afforded 277 mg (81%) of **1i** as a white solid: mp 103−105 °C; $[\alpha]_D^{23.0}$ −36.6 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.00−1.25 (m, 4H), 1.44−1.54 (m, 1H), 1.68−1.80 (m, 2H), 1.89−1.99 (m, 1H), 2.21 (s, 6H), 2.23−2.31 (m, 1H), 3.07−3.19 (m, 1H), 4.73 (d, *J* = 6.8 Hz, 1H), 7.38−7.50 (m, 6H), 7.75−7.95 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 24.5, 25.3, 34.2, 39.9, 52.3 (d, *J* = 1.9 Hz), 68.0 (d, *J* = 8.4 Hz), 128.2 (d, *J* = 12.5 Hz), 128.4 (d, *J* = 12.5 Hz), 131.3 (d, *J* = 3.3 Hz), 131.4, 131.5, 132.1 (d, *J* = 9.5 Hz), 134.4 (d, *J* = 123.2 Hz), 134.8 (d, *J* = 130.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.3. Elemental Analysis, Anal. Calcd. for $C_{20}H_{27}N_2OP$: C 70.15, H 7.95, N 8.18 Found: C 70.08, H 7.86, N 8.14.

*(1R,2R)-2-N-(Diphenylphosphoroso)-1-N,1-N-diethylcyclohexane-1,2-diamine (**1j**, Entry 10 in Table 2).* The title compound was prepared following the general procedure described for **1i** on the same scale and was obtained as a white solid with the yield of 293 mg (79%): mp 112−113 °C; $[\alpha]_D^{23.0}$ −62.5 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.00 (t, *J* = 7.0 Hz, 6H), 1.06−1.26 (m, 4H),

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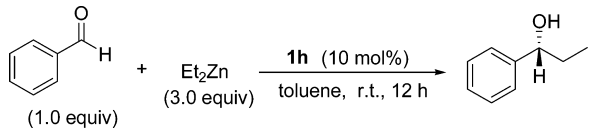
1.45−1.53 (m, 1H), 1.68−1.81 (m, 2H), 1.92−2.03 (m, 1H), 2.26−2.44 (m, 3H), 2.53−2.68 (m, 2H), 3.11−3.22 (m, 1H), 4.97 (d, J = 7.6 Hz, 1H), 7.35−7.52 (m, 6H), 7.72−7.83 (m, 2H), 7.86−7.98 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.8, 23.2, 24.5, 25.8, 34.0, 42.9, 52.0, 64.6 (d, J = 8.9 Hz), 128.1 (d, J = 12.6 Hz), 128.3 (d, J = 12.2 Hz), 131.1, 131.2, 132.0 (d, J = 9.4 Hz), 134.5 (d, J = 123.0 Hz), 135.0 (d, J = 130.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.6. Elemental Analysis, Anal. Calcd. for $C_{22}H_{31}N_2OP$: C 71.32, H 8.43, N 7.56 Found: C 71.54, H 8.28, N 7.49.

*(1R,2R)-2-N-(Diphenylphosphoroso)-1-N,1-N- dibutylcyclohexane-1,2-diamine (**1k**, Entry 11 in Table 2).* The title compound was prepared following the general procedure described for **1i** on the same scale and was obtained as a white solid with the yield of 332 mg (78%): mp 82−83 °C; $[\alpha]_D^{23.0}$ −81.2 (c 0.50, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82 (t, J = 7.2 Hz, 6H), 1.06−1.38 (m, 12H), 1.46−1.49 (m, 1H), 1.68−1.77 (m, 2H), 1.95−1.98 (m, 1H), 2.27−2.34 (m, 3H), 2.41−2.48 (m, 2H), 3.12−3.23 (m, 1H), 4.94 (d, J = 8.0 Hz, 1H), 7.37−7.45 (m, 6H), 7.76−7.81 (m, 2H), 7.88−7.93 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 20.5, 22.7, 24.3, 25.6, 29.5, 31.2, 33.6, 52.0, 65.0 (d, J = 8.9 Hz), 128.1 (d, J = 12.7 Hz), 128.2 (d, J = 12.5 Hz), 131.0, 131.1, 131.7 (d, J = 9.5 Hz), 134.2 (d, J = 123.0 Hz), 134.9 (d, J = 131.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.5. Elemental Analysis, Anal. Calcd. for $C_{26}H_{39}N_2OP$: C 73.21, H 9.22, N 6.57 Found: C 73.34, H 9.18, N 6.50.

*1-[(1R,2R)-2-[(Diphenylphosphoroso)amino]cyclohexyl]-pyrrolidine (**1l**, Entry 12 in Table 2).* The title compound was prepared following the general procedure described for **1i** on the same scale and was obtained as a white solid with the yield of 262 mg (71%): mp 99−101 °C; $[\alpha]_D^{23.0}$ −31.8 (c 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91−1.41 (m, 5H), 1.44−1.60 (m, 1H), 1.63−1.88 (m, 6H), 1.92−2.06 (m, 1H), 2.44−2.84 (m, 4H), 3.11−3.29 (m, 1H), 4.62−4.98 (br, 1H), 7.36−7.62 (m, 6H), 7.72−8.02 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.8, 23.6, 24.1, 24.8, 33.8, 47.1, 53.0, 63.3 (d, J = 8.1 Hz), 128.1 (d, J = 12.7 Hz), 128.3 (d, J = 12.4 Hz), 131.2 (d, J = 9.7 Hz), 131.3 (d, J = 5.7 Hz), 131.4 (d, J = 11.1 Hz), 132.1(d, J = 9.4 Hz), 134.2 (d, J = 124.2 Hz), 134.4 (d, J = 130.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.7. Elemental Analysis, Anal. Calcd. for $C_{22}H_{29}N_2OP$: C 71.71, H 7.93, N 7.60 Found: C 71.81, H 7.73, N 7.93.

*1-[(1R,2R)-2-[(Diphenylphosphoroso)amino]cyclohexyl]-piperidine (**1m**, Entry 13 in Table 2).* The title compound was prepared following the general procedure described for **1i** on the same scale and was obtained as a white solid with the yield of 294 mg (77%): mp 117−118 °C; $[\alpha]_D^{22.0}$ −36.8 (c 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.03−1.25 (m, 4H), 1.37−1.63 (m, 7H), 1.70−1.76 (m, 1H), 1.80−1.87 (m, 1H), 1.96−2.05 (m, 1H), 2.19−2.39 (m, 3H), 2.60−2.75 (m, 2H), 3.14−3.28 (m, 1H), 4.96−5.04 (d, J = 7.6 Hz, 1H), 7.34−7.59 (m, 6H), 7.72−7.86 (m, 2H), 7.88−8.00 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.7, 24.4, 24.8, 25.6, 26.9, 34.2, 51.6, 69.3, 69.4, 128.2 (d, J = 12.6 Hz), 128.3 (d, J = 12.5 Hz), 131.1, 131.2, 131.3 (d, J = 9.0 Hz), 132.1 (d, J = 9.4 Hz), 134.5 (d, J = 122.6 Hz), 134.7 (d, J = 144.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.1. Elemental Analysis, Anal. Calcd. for $C_{23}H_{31}N_2OP$: C 72.23, H 8.17, N 7.32 Found: C 72.40, H 8.15, N 7.31.

General Procedure for the Enantioselective Addition of Diethylzinc to Benzaldehyde. To a solution of the chiral ligand **1h**



(37 mg, 0.10 mmol) in toluene (0.5 mL), diethylzinc (2.0 mL of 1.5 M solution in toluene, 3.0 mmol) was slowly added at 0 °C under nitrogen atmosphere and stirred for 30 min, and then benzaldehyde (106 mg, 1.0 mmol) in toluene (0.5 mL) was added dropwise. The mixture was stirred for 12 h at room temperature, cooled in ice bath and quenched with aqueous HCl (10%, 10 mL). Extraction with EtOAc (10 mL × 3) gave combined organic layers, which were washed with brine (10 mL), dried over $MgSO_4$ and concentrated in vacuo to give a residue that was subjected to silica gel column chromatography (EtOAc/hexane = 1/10), which afforded 135 mg (99%, 96% *ee*) of (*R*)-1-phenylpropan-1-ol as a colorless oil: $[\alpha]_D^{20.9}$ +20.3 (c 1.00, $CHCl_3$) (Lit.[44] $[\alpha]_D^{26.0}$ +40.3 (c 1.21, $CHCl_3$) for 96% *ee* (*R*); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (t, 3H), 1.71−1.92 (m, 2H), 1.96 (br, 1H), 4.51−4.72 (m, 1H), 7.25−7.40 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.1, 31.8, 75.9, 125.9, 127.4, 128.4, 144.6. The *ee* value was determined by Chiral GC Chirasil Dex CB [Inlet temperature: 130 °C, t_R = 6.9 min (major, *R*), t_R = 7.2 min (minor, *S*)].

■ ASSOCIATED CONTENT

Supporting Information

Detailed information of the Sterimol analysis, copies of ^{1}H and ^{13}C NMR spectra of products, and GC data of chiral 1-phenylpropan-1-ol are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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