Articles

Stereoselective Hydride Reductions of Cyclic *N*-Diphenylphosphinyl Imines. Highly Diastereoselective Syntheses of Protected Primary Amines

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Reduction of *N*-diphenylphosphinyl imines of variously substituted cyclohexanones, cyclopentanones, and bicyclic ketones with lithium tri-*sec*-butylborohydride provides highly diastereoselective procedures for the syntheses of *N*-diphenylphosphinyl amines which represent protected primary amines that can be unmasked by mild acidic cleavage. Attack of cyclohexyl derivatives occurs almost exclusively via equatorial approach to yield axial amine derivatives while cyclopentyl and bicyclic imines are attacked from the less sterically encumbered faces.

While considerable effort has been focused on uncovering synthetically useful and stereocontrollable reductions of cyclic ketones to diastereomeric alcohols,[1] a relative paucity of investigations has centered on processes for the corresponding stereoselective reductions of cyclic imines to amines.[2] Furthermore, most of the available studies have concentrated on providing secondary and tertiary amines since these are available from reduction of readily available imines, iminium salts, or enamines. In general, although there are differences introduced by nitrogen substituents, the available studies[2a,d] indicate that the stereochemical profiles of cyclic imine reductions roughly parallel results observed for cyclic ketones. Thus, reductions of such cyclohexyl intermediates with "small" reagents such as $NaBH_4$ and $LiAlH_4$ provides respectable stereoselective conversion to equatorial secondary and tertiary amines. Conversely, use of hindered trialkylborohydrides to reduce imines or iminium salts provides the corresponding axial amines with exceptional stereoselectivity. However, the preparation of cyclic primary amines with stereochemical control via reductive protocols introduces complications in that requisite imines of ammonia are not normally suitably stable to serve as viable intermediates for reduction. In addition, oximes (the simplest, stable ammonia derivatives) are inert toward trialkylborohydrides.[3] Axial primary amines have been secured via hydrogenation of oximes (Ni or Pd catalysts)[4] or by reduction of benzylamine imines and subsequent removal of the benzyl group by catalytic hydrogenolysis.[2c,f–h,5] Unfortunately, many functionalities are not stable toward catalytic hydrogenation, and thus mild, convenient and noncatalytic hydrogenation processes are desirable. The problem is partly resolved by reduction of imines derived from 4,4′-dimethoxybenzhydrylamine with tri-*sec*-butylborohydride (and cleavage of the benzylamine products with formic acid), but these hindered and relatively unreactive intermediates give poor yields with this bulky hydride reagent if the imine is flanked by additional alkyl groups.[2e]

As alternative imine intermediates, *N*-diphenylphosphinyl imines **1** attractively appeared to provide reductive entries to primary amines which are more convenient than catalytic hydrogenation. Thus, derivatives **1** are easily prepared, often stable, but highly reactive intermediates[6] which are readily reduced to *N*-diphenylphosphinyl amines by most hydride reagents including tri-*sec*-butylborohydride. These latter derivatives represent

[⊗] Abstract published in *Advance ACS Abstracts,* November 1, 1995.

(1) For reviews of stereoselective results, mechanistic considerations and the steric and electronic factors responsible for the stereochemistry of cyclic ketone reductions, see: (a) Greeves, N. *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: New York, 1991; Vol. 8, Chapter 1.1. (b) Wigfield, D. C. *Tetrahedron* **1979**, *35*, 449. (c) Boone, J. R.; Ashby, E. C. *Top. Stereochem.* **1979**, *11*, 53 (Allinger, N. L., Eliel, E. L., Eds.). (d) Hajos, A. *Complex Hydrides*; Elsevier: New York, 1979; Chapter 12. See, also: (e) Cherest, M. *Tetrahedron* **1980**, 1593. (f) Ahn, N. T.; Eisenstein, O. *Tetrahedron Lett.* **1976**, 155. (g) Huet, J.; Maroni Barnaud, Y.; Ahn, N. T.; Seyden-Penne, J. *Tetrahedron Lett.* **1976**, 159. (h) Klein, J. *Tetrahedron Lett.* **1973**, 4307. (i) Klein, J. *Tetrahedron* **1974**, 3349. (j) Wigfield, D. C.; Gowland, F. W. *J. Org. Chem.* **1977**, *42*, 1108. (k) Cieplak, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 4540. (l) Shi, Z.; Boyd, R. J. *J. Am. Chem. Soc.* **1993**, *115*, 9614. (m) Coxon, J. M.; Liubrand, R. T. *Tetrahedron Lett.* **1993**, *34*, 7093. (n) Johnson, C. R.; Tait, B. D.; Cieplak, A. S. *J. Am. Chem. Soc.* **1987**, *109*, 5875. (o) Cieplak, A. S.; Tait, B. D.; Johnson, C. R. *J. Am. Chem. Soc.* **1989**, *111*, 8447. (p) Haltermann, R. L.; McEvoy, M. A. *J. Am. Chem. Soc.* **1990**, *112*, 6690. (q) Cheung, C.; Tseng, L. T.; Lin, M. H.; Srivastava, S.; Le Noble, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 1598. (r) Meyers, A. I.; Wallace, R. H. *J. Org. Chem.* **1989**, *54*, 2509. (s) Vedejas, E.; Dent, W. H., III. *J. Am. Chem. Soc.* **1989**, *111*, 6861. (t) Coxon, J. M.; McDonald, D. Q. *Tetrahedron* **1992**, *48*, 3353. (u) Wu, Y. D.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 908. (v) Wu, Y. D.; Houk, K. N.; Trost, B. M. *J. Am. Chem. Soc.* **1987**, *109*, 5560. (w) Mukherjee, D.; Wu, Y. D.; Fronczek, F. R.; Houk, K. N. *J. Am. Chem. Soc.* **1988**, *110*, 3328. (x) Wu, Y. D.; Tucker, J. A.; Houk, K. N. *J. Am. Chem. Soc.* **1991**, *113*, 5018.

(2) For a review of metal hydride reductions of imines, iminium salts and enamines, including stereochemical considerations, see: (a) Hutchins, R. O.; Hutchins, M. K. *Comprehensive Organic Synthesis*; Trost, B., Ed.; Pergamon: New York, 1991; Vol. 8, Chapter 1.2; other reductive protocols are discussed in chapters 1.3–1.8. See, also: (b) de Savignac, M. A.; Bon, M.; Mazarguil, H.; Lattes, A. *Bull. Chim. Soc. Fr.* **1975**, 2057. (c) Wrobel, J. E.; Ganem, B. *Tetrahedron Lett.* **1981**, *22*, 3447. (d) Hutchins, R. O.; Su, W.-Y.; Sivakumar, R.; Cistone, F.; Stercho, Y. P. *J. Org. Chem.* **1983**, *48*, 3412. (e) Hutchins, R. O.; Su, W.-Y. *Tetrahedron Lett.* **1984**, *25*, 695. (f) Knupp, G.; Frahm, A. W. *J. Chem. Res. (S)* **1981**, 164. (g) Knupp, G.; Frahm, A. W. *Chem. Ber.* **1984**, *117*, 2076. (h) Wiehl, W.; Frahm, A. W. *Chem. Ber.* **1986**, *119*, 2668.

(3) Treatment of 4-*tert*-butylcyclohexanone oxime (or the corresponding oxime methyl ether) with $LiBH(sec\text{-}C_4H_9)_3$ in THF (reflux) returned only starting material. See, also: Brown, H. C.; Kim, S. C.; Krishnamurthy, S. J. *J. Org. Chem.* **1980**, *45*, 1. Reductions of cyclic oximes with other reagents (e.g. Na/ethanol) provides equatorial cyclohexyl amines; see, for example, ref 2d.

(4) Rausser, R.; Weber, L.; Herschberg, E. B.; Oliveto, E. P. *J. Org. Chem.* **1966**, *31*, 1342; *J. Org. Chem.* **1966**, *31*, 1346.

(5) The process has been utilized to produce chiral, optically active axial amines using chiral, nonracemic benzyl imines; see ref 2f–h.

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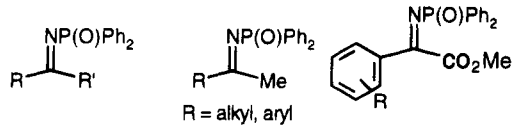


1 2 3

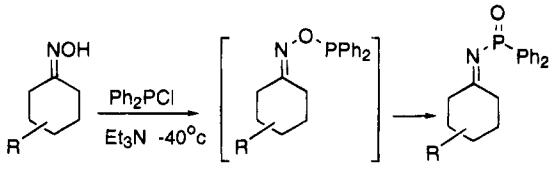
protected versions of primary amines that are easily cleaved in acidic media to the free amine salts.[7]

Intermediates **1** have been previously successfully utilized for enantiomeric reductions of methyl aryl and methyl alkyl *N*-diphenylphosphinyl imines **2** (2 to ca. 100% ee)[6b,c] and substituted α-*N*-diphenylphosphinyl imino acid esters **3** (51–95% ee).[8] These sucessful endeavors prompted an investigation of the application to diastereoselective reductions of cyclic systems, and, indeed, preliminary studies indicated that further exploration of such reductions would be fruitful.[9] This article presents a systematic investigation to uncover viable diastereoselective reduction methodologies for cyclohexyl and other cyclic *N*-diphenylphosphinyl imines.

Results and Discussion

The requisite imines **6** were prepared from the corresponding oximes **4** via reaction with chlorodiphenylphosphine followed by free radical rearrangement of the initially formed phosphorus(III) oxime ester **5** (Scheme 1).[6,10] The cyclic *N*-diphenylphosphinyl imines were utilized without further purification to avoid hydrolysis of these potentially sensitive intermediates. Notably, the reductions were normally conducted at ambient temperature and conveniently monitored by TLC which indicated that the reactions were frequently complete in <30 min although the reactions were continued for a total of 2 h to ensure completeness. Diastereomer ratios were determined by ^{31}P NMR.

Scheme 1



4 5 6

Effect of Reagent on Stereoselectivity of Reductions of Cyclohexyl *N*-Diphenylphosphinyl Imines. In order to search for effective stereoselective reductive protocols to cyclic amine derivatives, our initial studies focused on uncovering reagents capable of providing high levels of diastereoselective discrimination leading to either axial or equatorial isomers. Thus, several model cyclohexyl phosphinyl imines were reduced with a variety of reagents and the results presented in Table 1. Examination reveals that moderate to good yields (overall from the oximes) were procured with a variety of structural types and reagents. Of particular importance are the results obtained with lithium tri-*sec*-butylborohydride [LiBH(*s*-Bu)$_3$, L-Selectride]. In all cases the axial isomer was produced with a diastereoselectivity of >97%. This mimics the results obtained in the reductions of other carbon–nitrogen π-systems.[2c,d] The successful reduction of the 2-methylcyclohexyl derivative solves the problem previously mentioned[2d,e] in the quest for a practical synthesis of primary axial 2-substituted cyclohexyl amines.

The results with tri-*sec*-butylborohydride suggested a comprehensive investigation into the generality of such highly stereoselective processes. Before proceeding with a systematic study of tri-*sec*-butylborohydride, however, a more in depth examination and discussion of results with the other reducing agents (Table 1) may be fruitful. Again, in all cases, diastereomer ratios were determined by ^{31}P NMR.

Results with lithium aluminum hydride (LAH), sodium borohydride ($NaBH_4$), and sodium cyanoborohydride ($NaBH_3CN$) reveal an interesting trend. On the basis of the stereoselectivities displayed by these reagents in the reductions of 2-methyl, 4-*tert*-butyl, and *cis*-3,5-dimethylcyclohexyl systems (Table 1), the relative "sizes" of these reducing reagents with these substrates are: $NaBH_3CN$ > $NaBH_4$ > LAH; however, the differences are not spectacular. Indeed, LAH frequently gives a greater percentage of axial attack relative to $NaBH_4$.[1c] Also, as indicated, $NaBH_3CN$ is larger than $NaBH_4$.

Reductions with (*tert*-butylamino)borane in methanol solvent have a strong preference for axial approach to give the opposite isomer (equatorial) to that obtained with tri-*sec*-butylborohydride. For instance, the 4-*tert*-butyl phosphinyl imine afforded a 95:5 *trans/cis* ratio (Table 1), comparable to 4-*tert*-butylcyclohexanone (90:10 *trans/cis*).[11] Likewise, the 2-methylcyclohexyl phosphinyl imine gave a 79:21 *trans/cis* ratio. Thus, this reagent/solvent system behaves as a "small" reducing agent with the phosphinyl imine system. However, others[2c] have used this reagent (in THF) to obtain a 90:10 *cis/trans* ratio with (2-methylcyclohexylidene)benzylamines. Thus, with this system, opposite stereoselectivity was observed, the reason(s) for which are not obvious.

The results with (*tert*-butylamino)borane in acetic acid indicate increasing attack from the equatorial face. Indeed, in two cases, the axial product predominated. This is a radical reversal of stereoselectivity when compared with the results in methanol. However, these results were not unexpected. The amine borane was stirred overnight in acetic acid to ensure the formation of diacetoxyborohydride **7** [*t*-$BuNH_2BH(OAc)_2$]. This preformed reagent has been shown to act as a relatively bulky reducing reagent.[2d]

From the preliminary exploration above, a systematic exploration was pursued concerning the utility and scope of the L-Selectride reductive protocol for the stereoselective production of not only axial cyclohexyl amines but also other cyclic diastereomers. For comparison (and to ensure that both possible diastereomers provided separate ^{31}P signals), the phosphinyl imines were also reduced

(6) (a) Krzyzanowska, B.; Stec, W. J. *Synthesis* **1978**, 521. (b) Krzyzanowska, B.; Stec, W. J. *Synthesis* **1982**, 270. (c) Hutchins, R. O.; Abdel-Magid, A. F.; Stercho, Y. P.; Wambsgans, A. *J. Org. Chem.* **1987**, *52*, 702. The highly electron-withdrawing diphenylphosphinyl moiety greatly augments the electrophilicity of the imine carbon such that nucleophilic attack by hydride reagents is rapid.

(7) Greene, T. W.; Wuts, G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; Wiley: New York, 1991; p 375. Kenner, G. W.; Moore, G. A.; Ramage, R. *Tetrahedron Lett.* **1976**, 4005. Koziara, A.; Olejniczak, B.; Osowska, K.; Zwierzak, A. *Synthesis* **1982**, 918.

(8) Zhu, Q.-C. Ph.D. Thesis, Drexel University, 1992; manuscript in preparation.

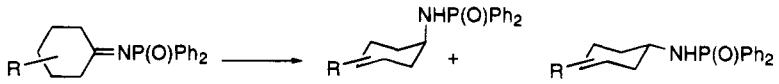
(9) Hutchins, R. O.; Rutledge, M. C. *Tetrahedron Lett.* **1987**, *28*, 5619.

(10) Hudson, R. F.; Brown, C.; Maron, A. *Chem. Ber.* **1982**, *115*, 2560.

(11) Andrews, G. C.; Crawford, T. L. *Tetrahedron Lett.* **1980**, *21*, 693.

Table 1. Reduction of Cyclohexylidene-*N*-(diphenylphosphinyl)amines with Hydride Reagents

Hydride Reagents

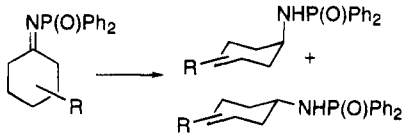


6 8

	ratio of equatorial/axial attack of **6** (% yield)[a]					
R	$LiAlH_4$	$NaBH_4$	$NaBH_3CN$	*t*-$BuNH_2BH_3$ HOAc	*t*-$BuNH_2BH_3$ MeOH	$LiBH(s\text{-}Bu)_3$
2-Me	44/66 (69)	50/50 (63)	52/48 (40)	77/23 (61)	21/79 (63)	>97/3 (64)
4-*t*-Bu	16/84 (56)	26/74 (65)	30/70 (56)	33/67 (60)	5/95 (65)	>97/3 (64)
c-3,5-diMe	35/65 (64)	40/60 (70)	47/53 (56)	54/46 (66)	3/97 (74)	>97/3 (57)
t-3,4-diMe					13/87 (72)	>97/3 (73)
4-Ph					72/28 (50)	>97/3 (59)

[a] Yields are for isolated, purified products calculated from oxime.

Table 2. Reduction of 3- and 4-Substituted Cyclohexylidene-*N*-(diphenylphosphinyl)amines



6 8

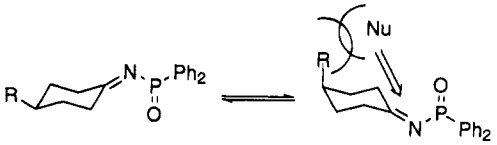
			ratio of equatorial/axial attack of **6**[a]	
entry	**6**	R	$LiBH(s\text{-}Bu)_3$ (% yield)[a]	$NaBH_4$ (% yield)[a]
1	**a**	4-*t*-Bu	>97/3 (64)	26/74 (65)
2	**b**	4-*i*-Pr	>97/3 (58)	32/68 (60)
3	**c**	4-Et	>97/3 (65)	34/66 (64)
4	**d**	4-Me	>97/3 (72)	41/59 (72)
5	**e**	4-Ph	95/5 (59)	52/48 (55)
6	**f**	*t*-3,4-diMe	>97/3 (69)	37/63 (73)
7	**g**	*c*-3,5-diMe	>97/3 (70)	40/60 (57)
8	**h**	3,3,5-triMe	>97/3 (71)	94/6 (66)
9	**i**	3-Me	>97/3 (63)	42/58 (79)

[a] Yields are for isolated, purified products calculated from oxime.

with $NaBH_4$ in THF. The results and data are given in Tables 2–5.

3- and 4-Substituted Cyclohexylidine-*N*-(diphenylphosphinyl)amines. Table 2 presents the results and stereoselective outcomes for a series of 3- and 4-substituted derivatives **6** to the corresponding phosphinyl amines **8**. As can be seen, *in all cases*, reductions with tri-*sec*-butylborohydride gave the axial isomers in >97%. In actuality, since the method utilized to determine the diastereomer ratio (^{31}P NMR) precluded accurate measurement or, in some cases, even the detection of trace amounts of the minor equatorial isomer, the actual discrimination for equatorial approach was probably greater so that the reported >97% diastereoselections are conservative estimates. In any event, the near exclusive attack from the equatorial face by the extremely bulky tri-*sec*-butylborohydride parallels or exceeds results with other cyclic imines[2c,d] and cyclohexanones.[12]

Examination of the results with sodium borohydride reveals that as the steric bulk of a 4-substituent increases, the amount of axial approach increases. We can interpret these observations with two different, but complementary rationals. Thus, a 4-*tert*-butyl group is known to be highly conformationally biased in cyclohexane systems with the equatorial orientation population >99% ($-\Delta G° > 4.2-4.9$ kcal/mol;[13ac] calculated 4.7 kcal/mol[14]). As the steric bulk of the 4-substituent decreases, there is a concomitant increase in the population of the axial conformer. For example, at 25 °C, an approximately 5% population of this conformer should be present when the group is methyl ($-\Delta G°$ value = 1.70[13a] to 1.74[13b] kcal/mol). The presence of this conformer, therefore, will influence the stereochemical outcome of any approaches to the diastereotopic faces. In equatorial approach, the reagent experiences steric interactions with the axial group. Thus, as the population of axial conformer **9** increases, the amount of equatorial attack on **9** (resulting in *trans* products) is expected to decrease leading to an overall increase in *cis* products, as observed in Table 2. However, the magnitude of the increase cannot be accounted for by the above explanation since the populations of the **9** conformers are low.



9

Distortion of the cyclohexane ring may also result in changes in stereoselectivity. Ahn[15] has observed that ring flattening causes an increase in axial attack while ring puckering decreases the amount of axial attack. This is presumably due to a decrease in steric interactions with the axial C_3 and C_5 hydrogens in the flattened ring. Cauletti and co-workers[16] have examined substituent effects on the ionization energies of 4-substituted cyclohexanones and found that ionization energies increase with an increase in the electronegativity of the 4-substituent. More significantly for our purposes, the series H–Me–Et–*t*-Bu gave a straight line plot for conformational energies, thus indicating that the observed differences are mainly due to ring flattening. Others[1x] have also implicated ring distortions to explain the variations of stereoselectivities observed in the reductions of cyclohexanones.

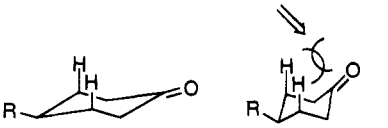
The results of Cauletti[16] imply that ring flattening increases along the series H–Me–Et–*t*-Bu. A 4-*tert*-

(12) (a) Brown, H. C.; Krisnamurthy, S. *J. Am. Chem. Soc.* **1972**, *94*, 7159. (b) Brown, H. C.; Krisnamurthy, S.; Kim, S. C. *J. Chem. Soc., Chem. Commun.* **1973**, 391.

(13) (a) Hirsch, J. A. *Top. Stereochem.* **1967**, *1*, 199 (Allinger, N. L., Eliel, E. L., Eds.). (b) Booth, H.; Everett, J. R. *J. Chem. Soc., Perkin Trans. 2* **1980**, 255. (c) Monoharan, M.; Eliel, E. L. *Tetrahedron Lett.* **1984**, *25*, 3267.

(14) van de Graff, B.; Baas, J. M. A.; Webster, B. M. *Rec. Trav. Chim. Pays-Bas* **1978**, *97*, 268.

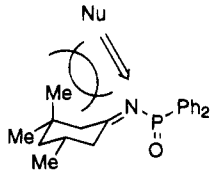
(15) Ahn, N. T.; Eisenstein, O. *Nouv. J. Chem.* **1977**, 61.



butyl is also known to substantially flatten a cyclohexane ring.[17] On the basis of these observations, a reasonable conclusion is that distortion of the cyclohexyl ring resulting in ring flattening or puckering is an important factor in causing the trends that are seen in the phosphinyl imine derivatives. The increase in axial attack from the 4-Me through the 4-*t*-Bu series matches these observations. Probably, a combination of conformational effects and ring distortions are responsible for the observed trend with the latter playing the predominate role.

An apparently anomalous example is the case of the 4-phenyl substituted derivative (**6e**, entry 5), the reductive result of which is difficult to explain. A phenyl substituent is highly biased toward an equatorial orientation ($-\Delta G°$ = 2.8[18] to 3.0[13a] kcal/mol) and therefore might be expected to behave stereochemically as a *tert*-butyl (or isopropyl; $-\Delta G°$ = 2.21 kcal/mol[13b]). However, this group does not cause the same ring distortions that are observed with the *tert*-butyl group.[18a] Thus, one would expect a decrease in the amount of axial attack relative to the 4-*tert*-butyl example. However, the magnitude of the observed change was not expected. Ring distortions have been implicated in observed radical changes in stereoselectivities with similar systems.[1u]

The results for reduction of the 3,3,5-trimethyl derivative (**6h**, entry 8) with $NaBH_4$ provided the expected predominant equatorial attack to give the axial product of **8** as observed with other imine derivatives[2d] and 3,3,5-trimethylcyclohexanone.[13a,19a] In this system, the axial C_3 methyl severely enhances hindrance toward axial attack of **6h**, even with "small" reagents such as $NaBH_4$.

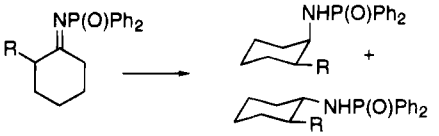


6h

2-Substituted Cyclohexylidine-*N*-(diphenylphosphinyl)amines. Table 3 presents results and stereochemical outcomes for the reductions of a selection of 2-substituted *N*-diphenylphosphinyl imines **10** to the corresponding phosphinyl amines **11**. Again, all reductions with tri-*sec*-butylborohydride afforded the cis diastereomers almost exclusively in line with previous results with other imines[2c,d] and iminium salts[2d] (and 2-methylcyclohexanone[12]).

It should be pointed out that the conformational situation leading to the high stereoselective production of *cis* isomers with 2-substituted phosphinyl imines is quite different than with the 3- and 4-substituted derivatives. Thus, in the latter, expected equatorial attack on the principal conformation (equatorial alkyl group orientation) affords the observed *cis* diastereomers as described above.

Table 3. Reduction of 2-Substituted Cyclohexylidene-*N*-(diphenylphosphinyl)amines



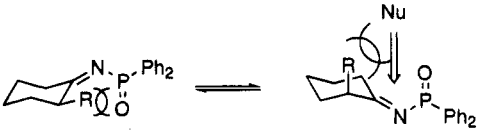
10 **11**

			equatorial/axial attack of **10**	
entry	**10**	R	$LiBH(s\text{-}Bu)_3$ (% yield)[a]	$NaBH_4$ (% yield)[a]
1	**a**	2-Me	>97/3 (64)	50/50 (63)
2	**b**	2-Et	>97/3 (67)	58/42 (63)
3	**c**	*t*-2-*i*-Pr-5-Me	>97/3 (60)	60/40 (60)
4	**d**	2-Ph	>97/3 (63)	40/60 (57)
5	**e**	2-tBu	>97/3 (57)	>97/3 (79)
6	**f**	2-MeO	>97/3 (71)	75/25 (71)

[a] Yields are for isolated, purified products calculated from oxime.

However, the conformational situation is modified with 2-substituted derivatives. Apparently, 1,3-allylic strain[2d,20] (especially with iminium systems) caused by eclipsing interactions between an equatorial alkyl group and any N-substituent (**12a**) favors an increase in the population of the 2-axial conformer **12b**. Equatorial approach to this conformer (leading to the *trans* isomer) is hindered by the axial alkyl group, thus leading to enhanced axial attack on **12b**, *even by tri-sec-butylborohydride*. This reversal of the normally highly favored equatorial approach by this latter reagent results from severe steric interactions between the axial alkyl substituent and the very bulky tri-*sec*-butylborohydride which overwhelms any steric encumbrance experienced in axial attack. Evidence for such reversal has been demonstrated in the reduction of *trans*-4-*tert*-butyl-2-*n*-propylcyclohexanone (axial propyl group) which afforded 87% of the alcohol isomer resulting from axial approach.[2d]

In addition to the above, axial approach to the conformer **12a** is also hindered by what amounts to a third *syn*-axial interaction[13a,19b] and, thus, the normally favored equatorial attack by tri-*sec*-butylborohydride is even further increased. Both effects then lead to a net increase in the amount of *cis* diastereoisomer formed and accounts for the relatively high stereoselection observed with carbon–nitrogen π systems[2d] compared to 2-methylcyclohexanone.[13a]



12a **12b**

Reductions with $NaBH_4$ also provided a predominance of axial (*cis*) amine diastereomers, albeit with much less diastereoselectivity. The results are in contrast to those observed with 3- and 4-substituted cases (Table 2) and

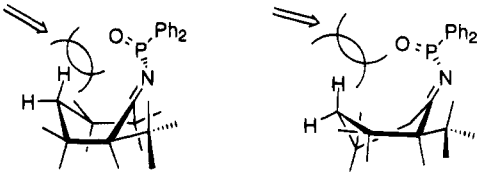
(16) Cauletti, C.; Di Maio, G.; Li, W.; Vecchi, E.; Vondrak, T. *Tetrahedron* **1986**, *42*, 3677.
(17) Abraham, R. J.; Bergen, H.; Chadwick, D. *Tetrahedron Lett.* **1981**, *22*, 2807.
(18) (a) Squillacote, M. E.; Neth, J. M. *J. Am. Chem. Soc.* **1987**, *109*, 198. (b) Eliel, E. L.; Manoharan, M. *J. Org. Chem.* **1981**, *46*, 1959.
(19) (a) Ashby, E. C.; Boone, J. R. *J. Org. Chem.* **1976**, *41*, 2890. (b) Wigfield, D. C.; Phelps, D. J. *J. Am. Chem. Soc.* **1974**, *96*, 543.
(20) (a) Johnson, F.; Malhotra, S. K. *J. Am. Chem. Soc.* **1965**, *87*, 5492. (b) Malhotra, S. K.; Johnson, F. *J. Am. Chem. Soc.* **1965**, *87*, 5493. (c) Johnson, F. *Chem. Rev.* **1968**, *68*, 375.

with 2-alkylcyclohexanones, but were not unexpected in view of the above discussion, and the fact that reductions of other 2-substituted cyclohexyl imine or iminium derivatives give mostly *cis* stereoisomers even with small reagents.[2c,d]

The percentage of equatorial attack observed for most 2-substituted *N*-diphenylphosphinyl cyclohexyl imines (40–60% for alkyl, except *tert*-butyl, Table 3) is much less than that obtained with other imines (74–85%)[2d] and iminium ions (82–98%).[2d] In general, imines give similar results to that of iminium systems. This may appear surprising since an imine, unlike an iminium ion, does not have a second group attached to nitrogen and can, thus, exist in a conformation that minimizes allylic strain (i.e. with the N-substituent anti to the equatorial 2-alkyl group). The observed increase in *cis* products in the reduction of imines relative to ketones may be explained by the greater complexing ability of imines since complexation creates a steric situation similar to that in iminium systems. Similar results have been observed in the reduction of 2-alkylcyclohexanones with complexing hydrides (e.g. $ClMgAlH_4$ and $Mg(AlH_4)_2$).[19a] Presumably, with phosphinyl imines the lessened amount of *cis* product (compared to imine and iminium cases) occurs because the complexing ability of the imine nitrogen is diminished by the strongly electron-withdrawing phosphinyl group.

A perusal of the data in Table 3 indicates another interesting feature exhibited in the borohydride reductions, namely that as the bulkiness of the 2-alkyl group increases, the amount of *cis* product increases. Thus, less of the axial conformer **12b** may be expected as the 2-substituent size increases giving, therefore, less *cis* diastereomer. However, the $-\Delta G^\circ$ values for the series 2-methyl, 2-ethyl, 2-isopropyl in cyclohexanone systems actually decreases (CH_3, 1.56 kcal/mol; C_2H_5, 1.09 kcal/mol; $(CH_3)_2CH$, 0.56 kcal/mol)[21a] indicating that, as the substituent becomes larger, the populations of axial conformers actually increases, probably because of less destabilizing interactions in the axial conformation for ethyl and isopropyl coupled with more destabilization of isopropyl in the equatorial form. This "2-alkyl ketone effect"[21a,22] presumably applies to (and is probably enhanced by allylic strain) cyclohexyl imines leading to the observed trend for 2-methyl (**10a**), 2-ethyl (**10b**), and 2-isopropyl (**10c**).[21b]

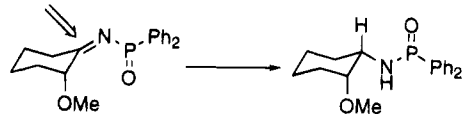
The 2-*tert*-butyl example **10e** (entry 5) is more complex and requires additional considerations and explanations. The energy difference between the "axial" and "equatorial" *tert*-butyl conformers of 2-*tert*-butylcyclohexanone is only 1.62 kcal/mol[21a] (*vs* >4.2 kcal/mol for cyclohexane[13a,c]) and the molecule actually probably exists in a nonchair conformer(s) to minimize unfavorable interactions.[21a,23] With the phosphinyl analog **10e**, the equatorial 2-*tert*-butyl conformer corresponding to **12a** should experience considerable allylic strain while the alternate conformer **12b** with an axial *tert*-butyl orientation experiences severe repulsive interactions. The likely result is that the 2-*tert*-butyl phosphinyl imine **10e** resides predominantly in nonchair conformations such as **13** ("boat") and/or **14** ("twist") both of which are concave and present incoming reagents with bowl-like conformations.



13 14

Thus, attack by both large and small hydride reagents suffers severe steric interactions in approach from inside the "bowl" (leading to the *trans* diastereomer) while attack from outside the "bowl" (which provides the *cis* isomer) is relatively unencumbered and leads almost exclusively to the *cis* product as observed (>97% equatorial attack). The "twist" conformation **14** is probably preferred because it minimizes eclipsing interactions between the *tert*-butyl group and the vicinal hydrogen (both in the "gunwale" position).

Reduction of the 2-methoxy derivative (**10f**, entry 6) with $NaBH_4$ provides a substantial increase in the *cis* diastereomer produced (75% equatorial attack) relative to the previously discussed 2-methyl through 2-isopropyl examples (50–60%, entries 1–3). In this case conformer **12a** is probably destabilized not only by 1,3-allylic strain as discussed above, but also by electrostatic dipole–dipole repulsions between the eclipsing imine and methoxy groups (or by axial stabilization by orbital interactions). Indeed, because of such electrostatic interactions, electronegative groups in 2-substituted cyclohexanones exist significantly in the axial orientations.[16,24] Recent reports[24e] indicate that 2-methoxy- and 2-(methylthio)cyclohexanone have significant percentages of the axial conformer (28% and 85%, respectively, in $CDCl_3$). Thus, given the previously discussed greater propensity for 2-substituents to favor axial positions in imines compared with ketones, (2-methoxycyclohexylidene)-*N*-(diphenylphosphinyl)-amine probably exists substantially in conformation **15** (corresponding to **12b**). Axial attack opposite the methoxy group gives the observed predominance of the *cis* diastereomer.



15

Additionally, 2-methylthio and probably 2-methoxy exhibits a stereoelectronic effect arising from the heteroatom lone pairs which slow equatorial attack of **15a** and axial attack of **15b** to give the *trans* isomer.[24f] Thus, the high stereoselective formation of the *cis* isomer may be attributed to a combination of both alterations of conformer populations by steric and electronic factors and impedement of reagent approach from directions leading to *trans* isomers. Indeed, although not tested with

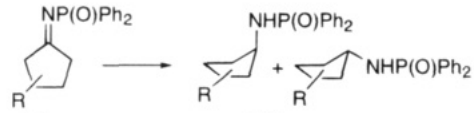
(21) (a) Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; Wiley: New York, 1994; p 732. (b) The situation for 2-isopropyl is more complicated since the compound studied was the *trans*-2-isopropyl-5-methyl isomer (**10c** entry 3, Table 2) and thus not as mobile as the other mono substituted derivatives.

(22) Allinger, N. L.; Blatter, H. M.; Freiberg, L. A.; Karkowski, F. M. *J. Am. Chem. Soc.* **1966**, *88*, 2999.

(23) (a) Rickborn, B. *J. Am. Chem. Soc.* **1962**, *84*, 2414. (b) Djerassi, C.; Hart, P. A.; Warawa, E. J. *J. Am. Chem. Soc.* **1964**, *86*, 78.

(24) (a) Pan, Y.-H.; Stothers, J. B. *Can. J. Chem.* **1967**, *45*, 2943. (b) Kirk, D. N. *Tetrahedron Lett.* **1969**, 1727. (c) Dosen-Micovic, L.; Jeremic, D.; Allinger, N. L. *J. Am. Chem. Soc.* **1983**, *105*, 1723. (d) Kirby, A. J. *The Anomeric Effect and Related Effects at Oxygen*; Springer-Verlag: Berlin, 1983; p 20. (e) Basso, E. A.; Kaiser, C.; Rittner, R.; Lambert, J. B. *J. Org. Chem.* **1993**, *58*, 7865. (f) Carreno, M. C.; Dominguez, E.; Garcia-Ruano, J. L.; Rubio, A. *J. Org. Chem.* **1987**, *52*, 3619.

Table 4. Reduction of Cyclopentylidene-*N*-(diphenylphosphinyl)amines

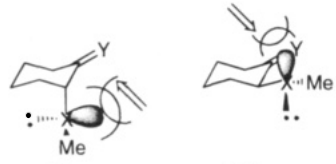


16 **17**

			% *cis* attack of **16**[a]	
entry	**16**	R	$LiBH(s\text{-}Bu)_3$ (% yield)[b]	$NaBH_4$ (% yield)[b]
1	**a**	2-Me	<3 (64)	73 (65)
2	**b**	2-Et	<3 (60)	66 (62)
3	**c**	3-Me	37 (62)	36 (66)
4	**d**	3-Et	39 (66)	40 (75)
5	**e**	*c*-3,4-diMe	<3 (66)	10 (62)

[a] *Cis* attack is approach from the same side of the ring as the substituent(s). [b] Yields are for isolated, purified products calculated from oxime.

2-methoxy, reduction of analogous, rigid 4-*tert*-butyl-2-(methylthio)cyclohexanones[24f] revealed that axial 2-substituents can cause dramatic reversal of facial selectivity of both bulky and small hydride reagents.

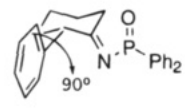


15a **15b**

X = S, Y = O

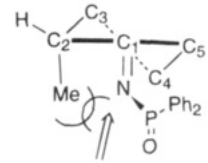
X = O, Y = $NP(O)Ph_2$ (**10e**)

Finally, the 2-phenyl derivative (**10d**, entry 4, Table 3) shows a difference in stereoselective sense upon reduction with sodium borohydride when compared to the other examples. Thus, with **10d** the *trans* isomer product is predominant (60% axial attack) which is a similar stereochemical outcome as observed in reductions of 2-alkyl-substituted cyclohexanones[1c] (results of reduction of 2-phenylcyclohexanone are apparently unknown). This predominance of axial attack of **12a** suggests that 1,3-allylic strain is not as severe as in the other examples, and, therefore, conformer **12b** is not as populated. This may imply that preferential attack occurs on a conformer in which the phenyl ring is perpendicular to the cyclic imine ring, thus exposing a flat surface toward the imine π bond and lessening repulsive interactions (this is the preferred conformation for an equatorial phenyl substituent on a cyclohexane ring[18a]). Additionally, the high conformational energy value for phenyl (2.7[18a] to 3.0[13a] kcal/mol in cyclohexane) suggests that, in the absence of other influences, equatorial orientations will be greatly favored.



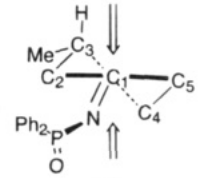
Alkyl-Substituted Cyclopentyl and Other Cyclic *N*-Diphenylphosphinyl Imines. The excellent stereoselective outcomes obtained with tri-*sec*-butylborohydride reductions of cyclohexyl phosphinyl imines prompted an extension of the methodology to cyclopentyl and other cyclic analogs. Table 4 presents data obtained for substituted cyclopentyl derivatives. As evident from this table, reductions of 2-substituted examples afforded excellent stereoselections for the *cis* diastereomers with tri-*sec*-butylborohydride (entries 1 and 2) which parallels results with 2-methylcyclopentanone.[12a] Here again, as discussed for 2-alkylcyclohexyl derivatives, allylic strain may force a normally pseudo equatorial[1c] group to adopt a pseudo axial orientation (**18**), thus favoring approach of the bulky reagent from the face opposite the alkyl group.

Contrary to the results with 2-substituted cyclohexyl examples (except 2-phenyl), attack by $NaBH_4$ occurs principally from the same side as the alkyl group (*cis* attack) to afford predominately the *trans* isomers (**17a**, 73%; **17b**, 66%). This closely mimics reductions of 2-methylcyclopentanone with other small reagents (e.g. $LiAlH_4$).[1c,19] The reversal may be caused either by less steric encumberance offered by a pseudo axial 2-substituent (compared to an axial 2-group in cyclohexyl cases) or by orbital overlap (antiperiplaner stabilization), or some other electronic considerations.[1c,f,k,15]



18

Reductions of the 3-alkyl derivatives (entries 3 and 4) were problematic with tri-*sec*-butylborohydride and $NaBH_4$ in that low levels of stereoselection were obtained. This, however, was not unexpected, and reductions of 3-methylcyclopentanone parallel these results.[20,1c] The preferred half-chair conformation of cyclopentyl systems provides essentially no bias for attack at either face (C_2 symmetry axis), unlike the situation in cyclohexyl systems. The 3-alkyl substituents probably reside in pseudo equatorial positions[1c] and thus offer no steric resistance to an incoming reagent. (See **19**.)



19

Stereochemical identities for the isomers produced in 3-methyl- and 3-ethylcyclopentyl imine reductions (**16c,d**) are not secure. Proton NMR analysis of the ring hydrogens adjacent to the nitrogen indicates that $NaBH_4$ and tri-*sec*-butylborohydride give the same major isomer for both cases. These isomers' above-mentioned protons resonates at a higher field than the minor ones indicating a pseudo axial orientation and thus, the major isomers are tentatively assigned as *cis*. This assignment and stereochemical profile parallels the results obtained in the reduction of 3-methylcyclopentanone which was attributed to nonsteric influences.[19a] In any case, the results demonstrate that stereochemical control in the reductions of simple 3-substituted cyclopentyl systems is not obtainable with hydrides.

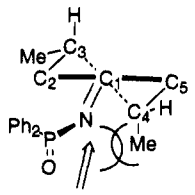
The *cis*-3,4-dimethylcyclopentyl derivative **16e** is another story (entry 5) in that essentially one diastereomer (*cis*) was obtained upon reduction with tri-*sec*-butylboro-

Table 5. Reduction of Norbornyl- and Camphoryl-*N*-(diphenylphosphinyl)amines

entry	R	% of the indicated predominant isomer: $LiBH(s\text{-}Bu)_3$ (% yield)[a]	% of the indicated predominant isomer: $NaBH_4$ (% yield)[a]
21	norbornyl	>97 endo (68)	80 endo (77)
22	camphoryl	>97 exo (63)	90 exo (70)

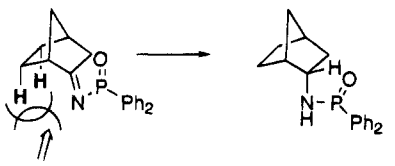
[a] Yields are for isolated, purified products calculated from oxime.

hydride and a high predominance (90%) of the same isomer with $NaBH_4$. This is again similar to results with *cis*-3,4-dimethylcyclopentanone[1c,19a,25] and may be ascribed to twisting of the methyls to minimize eclipsing. Thus, a conformation (**20**) is favored that contains one methyl group in a pseudo axial position. This blocks approach and leads to attack from the face opposite this methyl to give the all *cis* diastereomer.

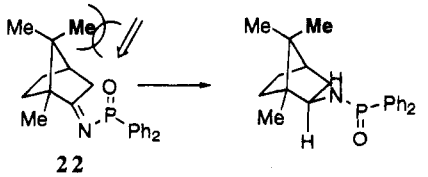


20

The *N*-diphenylphosphinyl imines derived from norbornanone and camphor were also subjected to the reductive protocol. The results are listed in Table 5 and closely parallel observations observed with the corresponding ketones.[1c] Thus, norbornyl imine **21** experiences predominant exo attack with both reagents, believed to result from steric hindrance from the endo hydrogens. The camphor imine **22** is attacked mainly from the endo face by both large and small reagents. Steric hindrance to exo attack provided by the syn C_7 methyl group is more severe than the encumbrance to endo attack provided by the endo hydrogens (Table 5).



21



22

In summary, tri-*sec*-butylborohydride reductions of a wide variety of cyclohexyl phosphinyl imines including 2-, 3-, and 4-substituted derivatives (**6** and **10**) provide excellent stereoselective entries to the corresponding axial phosphinyl amines resulting from equatorial attack. Likewise, similar reductions of 2-alkyl- and 3,4-dialkylcyclopentyl derivatives (**16a,b,e**) are also highly stereoselective with the directions of approach controlled by steric impedence to attack by pseudo axial alkyl groups. Steric effects also seem to control the high diastereoselectivities observed in reductions of norbornyl and camphor phosphinyl imines **21** and **22**, with the former giving nearly exclusive *exo* attack and the latter almost entirely *endo* approach. Reductions with $NaBH_4$ are generally less stereoselective with most examples,[26] as expected with this "small" reagent.

(25) Ashby, E. C.; Boone, J. R. *J. Am. Chem. Soc.* **1976**, *98*, 5524.

Experimental Section

General Information. ^1H nuclear magnetic resonance spectra were recorded at either 250, 300, or 400 MHz with deuteriochloroform as solvent and tetramethylsilane as an internal reference. ^{31}P nuclear magnetic resonance spectra were recorded at 36.23 MHz with deuteriochloroform as solvent and phosphoric acid (H_3PO_4) as an external reference (0 ppm). Mass spectra were recorded on either a FABS or EI/CI instrument. Infrared spectra were recorded on either a grating or FT instrument. Elemental Analyses were performed by either Micro-Analysis Inc. of Wilmington, DE, Wyeth-Ayerst Laboratories in Princeton, NJ, or the University of Pennsylvania. Gas chromatographic analyses were performed with a SUPELCO SP-35 capillary column. Melting points are uncorrected.

Materials. All solvents were freshly distilled under an atmosphere of argon prior to use. Tetrahydrofuran was distilled from sodium/benzophenone ketyl. Methylene chloride was distilled from phosphorus pentoxide (P_2O_5). Petroleum ether was distilled from calcium hydride (CaH_2). Chlorodiphenylphosphine was fractionally distilled under reduced pressure and stored under argon. Triethylamine was distilled from calcium hydride (CaH_2) and stored under argon. All reducing agents used were purchased from Aldrich Chemical Company and used as supplied. Ketones were purchased from either Aldrich or Lancaster. All organic solutions were dried with magnesium sulfate unless otherwise specified.

General Procedure for the Preparation of Oximes. Hydroxyamine hydrochloride (40 mmol 2.78 g), sodium acetate trihydrate (40 mmol 5.44 g), and water (50 mL) were heated to 60 °C and the appropriate ketone (20 mmol) in methanol (10 mL) was added. Enough additional methanol was then added to give a clear solution and stirring at 60 °C was continued overnight. The resulting solution was cooled to room temperature, added to water (100 mL) and extracted with ether. The combined organic phases were washed with saturated sodium bicarbonate and brine, and then dried. The crude oximes were purified either by recrystallization or distillation. Final purity of the oxime was determined by gas chromatography (SUPELCO SP-35 capillary column) and found to be >98% in all cases.

4-*tert*-Butylcyclohexanone oxime: yield 88%; mp 136–137.5 °C (lit.[2d] 138–139 °C).

4-Phenylcyclohexanone oxime: yield 74%; mp 110–111 °C (lit.[26a] mp 110 °C).

4-Isopropylcyclohexanone oxime: yield 74%; bp 93–94.5 °C (0.9 Torr) [lit.[26b] bp 117 °C (6 Torr)].

4-Ethylcyclohexanone oxime: yield 72%; bp 92–95 °C (0.8 Torr) [lit.[26c] bp 96 °C (1.2 Torr)].

4-Methylcyclohexanone oxime: yield 81%; mp 35.5–37 °C (lit.[26d] mp 37 °C).

***trans*-3,4-Dimethylcyclohexanone oxime**: yield 83%; bp 84 °C (0.9 Torr); ^1H NMR 9.75 (bs 1H), 3.30–3.24 (m 1H),

(26) (a) *CRC Handbook of Tables for Organic Compound Identification*, 3rd ed.; CRC Publications: Boca Raton, FL, 1972; Table 10. (b) Harvill, E. K.; Roberts, C. W.; Herbst, R. M. *J. Org. Chem.* **1950**, 58. (c) Mighton, H.; Wolinski, L. *J. Polymer Science* **1961**, *49*, 217. (d) Shriner, R. C.; Fuson, R. C.; Curtin, D. Y.; Morrill, T. C. *The Systematic Identification of Organic Compounds*, 6th ed.; Wiley and Sons: New York, 1980; pp 558–559. (e) Schultz, A. G.; Harrington, R. E. *J. Am. Chem. Soc.* **1991**, *113*, 4926. (f) Booth, H.; Gidley, G. C.; Franklin, N. C. *Tetrahedron* **1967**, *23*, 2421. (g) Vogel, A. I. *Textbook of Practical Organic Chemistry*, 4th ed.; Longman House: Harlow, 1978; p 1194. (h) Jackman, L. M.; Webb, R. L.; Yick, H. C. *J. Org. Chem.* **1982**, *47*, 1824. (i)Wallach, O. *Justus Liebigs Ann. Chem.* **1900**, *312*, 183. (j) *Dictionary of Organic Compounds*, 5th ed., 7th supplement; Chapman and Hall: New York, 1989; B-70098. (k) Suginome, H.; Kaji, M.; Yamada, S. *J. Chem. Soc., Perkin Trans. 1* **1988**, 321.

2.42–2.32 (m 1H), 2.14–2.07 (m 1H), 1.86–1.71 (m 2H), 1.50–1.40 (m 1H), 1.23–1.13 (m 2H), 1.01 and 0.99 (s 3H), 0.95 and 0.93 (s 3H); IR (cm^{-1}) 3280, 2960, 1670, 1455, 950; MS (EI) 67, 73, 82, 98 (base), 112, 126, 141 (M^+). Anal. Calcd for $C_8H_{15}NO$: C, 68.04; H, 10.71; N, 9.92. Found: C, 68.15; H, 10.50; N, 9.70.

***cis*-3,5-Dimethylcyclohexanone oxime**: yield 85%; mp 71–73 °C (lit.[26a] mp 74 °C).

3,3,5-Trimethylcyclohexanone oxime: yield 90%; mp 76–78 °C (lit.[2d] mp 86–87 °C; lit.[26b] mp 72–73 °C).

3-Methylcyclohexanone oxime: yield 76%; bp 70–71 °C (0.8 Torr); ^1H NMR identical to that reported in the literature.[26e]

2-Methylcyclohexanone oxime: yield 83%; mp 38.5–41 °C (lit.[26d] mp 43 °C).

2-Ethylcyclohexanone oxime: yield 79%; bp 76–77 °C (1.95 Torr) [lit.[2d] bp 67–69 °C (3 Torr)].

2-Phenylcyclohexanone oxime: yield 71%; mp 150.5–153 °C (lit.[26a] mp 169 °C).

2-*tert*-Butylcyclohexanone oxime: yield 88%; mp 71–72 °C (lit.[26f] mp 71–72 °C).

2-Methoxycyclohexanone oxime: yield 81%; bp 76–77 °C (0.9 Torr); ^1H NMR 9.26 (bs 1H), 3.75–3.73 (m 1H), 3.26 (s 3H), 3.09–3.01 (m 1H), 2.11–1.99 (m 2H), 1.88–1.78 (m 2H), 1.73–1.38 (m 3H); IR (cm^{-1}) 3360, 2950, 2840, 1670, 1445, 1090; MS (EI) 67, 81, 113 (base), 126, 144 (M + 1). Anal. Calcd for $C_7H_{13}NO_2$: C, 58.72; H, 9.15; N, 9.78. Found: C, 59.01; H, 9.29; N, 9.65.

(−)-2-Isopropyl-5-methylcyclohexanone oxime: yield 85%; mp 55–57 °C (lit.[26g] mp 59 °C).

2-Methylcyclopentanone oxime: yield 72%; bp 63–64 °C (0.75 Torr) [lit.[2d] bp 82–83 °C (3 Torr)].

2-Ethylcyclopentanone oxime: yield 80%; bp 56–57 °C (0.75 Torr); ^1H NMR 9.12 (bs 1H), 2.61–2.56 (m 1H), 2.47–2.33 (m 2H), 2.02–1.90 (m 1H), 1.87–1.55 (m 3H), 1.45–1.29 (m 2H), 0.98–0.92 (t 3H); IR (cm^{-1}) 3300, 2970, 2880, 1680, 1450, 1200, 925; MS (EI) 67, 99 (base), 127 (M^+). Anal. Calcd for $C_7H_{13}NO$: C, 66.11; H, 10.30; N, 11.01. Found: C, 65.86; H, 9.85; N, 11.31.

3-Methylcyclopentanone oxime: yield 84%; mp 85–87 °C (lit.[26h] mp 78–79 °C; lit.[26i] mp 86 °C).

3-Ethylcyclopentanone oxime: yield 86%; bp 69–70 °C (0.8 Torr); ^1H NMR 9.31 (bs 1H), 2.81–2.25 (m 3H), 2.03–1.81 (m 3H), 1.46–1.30 (m 3H), 0.95–0.92 (t 3H); IR (cm^{-1}) 3280, 2970, 1695, 1460, 1430, 920; MS (EI) 67, 98 (base), 112, 127 (M^+). Anal. Calcd for $C_7H_{13}NO$: C, 66.11; H, 10.30; N, 11.01. Found: C, 65.95; H, 10.20; N, 11.09.

***cis*-3,4-Dimethylcyclopentanone oxime**: yield 81%; mp 31–33.5 °C; ^1H NMR 9.26 (bs 1H), 2.63–2.44 (m 2H), 2.25–2.10 (m 4H), 0.93–0.90 (t 6H); IR (cm^{-1}) 3280, 2970, 1690, 1450; MS (EI) 69, 95 (base), 112, 127 (M^+). Anal. Calcd for C7H13NO: C, 66.11; H, 10.30; N, 11.01. Found: C, 66.19; H, 10.15; N, 10.97.

Norbornanone oxime: yield 76%; bp 74–75 °C (0.7 Torr) [lit.[26j] bp 114–116 °C (12 Torr)].

(1*R*)-(+)-Camphor oxime: yield 82%; mp 116.5–117.5 °C (lit.[26g] mp 119 °C).

General Procedure for the Synthesis of *N*-Diphenylphosphinyl Imines. The appropriate oxime (2.4 mmol) was dissolved in dry methylene chloride (30 mL), dry petroleum ether (30 mL), and triethylamine (2.4 mmol) and the resulting solution was cooled to −50 °C. Chlorodiphenylphosphine (2.4 mmol) was added via syringe and the mixture was allowed to stir at −50 °C for 1.5–2 h (white precipitate of triethylamine hydrochloride observed). The mixture was then cooled to −78 °C and transferred via cannula (positive argon or nitrogen pressure) to a filter under the inert atmosphere. The resulting clear colorless solution was carefully evaporated (high vacuum bled through a $CaSO_4$ drying tube) at 0 °C. The crude phosphinylimines were immediately subjected to the appropriate reducing agent (see below for experimental details).

General Procedure for Reduction of *N*-Diphenylphosphinyl Imines with Lithium Aluminum Hydride (LAH). To the appropriate phosphinyl imine (2.4 mmol) under argon in dry tetrahydrofuran (15 mL) at room temperature was added LAH (6 mmol 1.0 M in THF). The resulting solution was stirred for 2 h at room temperature. The reaction was then quenched with water (0.2 mL) followed by 15% sodium hydroxide (0.2 mL) and finally additional water (ca. 4 mL) until a white gum precipitated. The organic layer was decanted, diluted with ether (50 mL), washed with water and brine, and dried. Flash chromatography (15% THF/CH_2Cl_2) afforded the pure *N*-diphenylphosphinyl amines.

General Procedure for Reduction of *N*-Diphenylphosphinyl Imines with Diisobutyl Aluminum Hydride (DIBALH). To the appropriate phosphinyl imine (1.8 mmol) under argon in dry tetrahydrofuran (15 mL) at room temperature was added DIBALH (3.9 mmol 1.0 M in THF). The resulting solution was stirred overnight at room temperature. The reaction was quenched with water (2 mL) and 15% sodium hydroxide (2 mL) and allowed to stir for 30 min. Water (30 mL) was then added and the solution was extracted with ether (3 × 25 mL). The combined organics were washed with water and brine and dried. Flash chromatography (15% THF/CH_2Cl_2) afforded the products.

General Procedure for Reduction of *N*-Diphenylphosphinyl Imines with Sodium Borohydride ($NaBH_4$). To the appropriate phosphinyl imine (1.6 mmol) under argon in dry tetrahydrofuran (15 mL) at room temperature was added sodium borohydride (0.16 g, 3.6 mmol) and the resulting slurry was stirred for 2 h at room temperature. The reaction was filtered to remove excess sodium borohydride and allowed to stir with saturated ammonium chloride (10 mL) for 30 min. This mixture was extracted with ether and the combined organic phase was washed with water and brine and dried. Flash chromatography (15% THF/CH_2Cl_2) afforded the products.

General Procedure for Reduction of *N*-Diphenylphosphinyl Imines with Sodium Cyanoborohydride ($NaBH_3CN$). To the appropriate phosphinyl imine (2.3 mmol) under argon in dry tetrahydrofuran (15 mL) was added $NaBH_3CN$ (0.36 g, 5.7 mmol) and the resulting solution stirred overnight at room temperature. Saturated ammonium chloride (5 mL) was then added and the mixture stirred for 30 min. Water (25 mL) was added and the mixture extracted with ether (2 × 25 mL). The combined organic phase was washed with water and brine and dried. Flash chromatography (15% THF/CH_2Cl_2) afforded the products.

General Procedure for Reduction of *N*-Diphenylphosphinyl Imines with (*tert*-Butylamino)borane in Acetic Acid. (*tert*-Butylamino)borane (0.40 g, 4.6 mmol) was dissolved in dry acetic acid (15 mL, distilled from CrO_3 and cat. Ac_2O) and allowed to stir overnight at room temperature. This solution of acetoxyborohydride was then added to the crude phosphinyl imine (2.2 mmol) and allowed to stir overnight at room temperature under argon. The reaction was quenched with water (2 mL) and allowed to stir for 15 min. Ether was added (25 mL) followed by 15% sodium hydroxide (20 mL), and the resulting mixture was vigorously stirred for 20 min. The layers were separated, and the aqueous layer was extracted with ether (2 × 20 mL). The combined organic layers were washed successively with saturated sodium bicarbonate, water, and brine and then dried. Flash column chromatography (15% THF/CH_2Cl_2) yielded the desired products.

General Procedure for Reduction of *N*-Diphenylphosphinyl Imines with (*tert*-Butylamino)borane in Methanol. (*tert*-Butylamino)borane (0.38 g 4.4 mmol) was dissolved in methanol (15 mL, distilled from Mg/I_2) and stirred for 20 min. This suspension was then added to the crude phosphinyl imine (2.1 mmol) and allowed to stir overnight at room temperature under argon. The reaction mixture was quenched with water (5 mL) and 15% sodium hydroxide (5 mL) and stirred for 45 min. Ether (30 mL) was added, and the layers were separated. The aqueous layer was extracted with ether (2 × 15 mL) and the combined organic phase was washed with water and brine and dried. Flash column chromatography (15% THF/CH_2Cl_2) afforded the desired products.

General Procedure for Reduction of *N*-Diphenylphosphinyl Imines with Lithium Tri-*sec*-butylborohydride (L-Selectride). To a solution of crude phosphinyl imine (1.5 mmol) in dry tetrahydrofuran (15 mL) was added L-Selectride (3.2 mmol 3.2 mL of 1.0 M in THF). The resulting yellow

solution was allowed to stir for 2 h at room temperature under argon and was then quenched with water (2 mL). The organoboranes were decomposed with one of two methods: **Method A.** The solution was cooled to 0 °C and 15% sodium hydroxide (0.5 mL) added followed by slow addition of 30% hydrogen peroxide (0.5 mL). The cooling bath was removed and the solution stirred for 30 min. Water (15 mL) and ether (25 mL) were then added. The layers were separated and the aqueous layer extracted with ether (2 × 15 mL). The combined organics were washed with 30% sodium bisulfite (2 × 20 mL) and brine and then dried. **Method B.** Sodium perborate tetrahydrate, $NaBO_3 \cdot 4H_20$, (1.48 g 9.6 mmol), was added and the mixture stirred at room temperature for 2 h. Water (15 mL) and ether (30 mL) were added, and the layers were separated. The aqueous layer was extracted with ether (2 × 25 mL). The combined organic phase was washed with brine and dried. Evaporation and flash column chromatography yielded the desired products.

Diastereoselective Reduction Results of Cyclic *N*-Diphenylphosphinyl Imines with L-Selectride and Sodium Borohydride. Experimental procedures are as given in the previous section. Axial amine isomers from the reductions with L-Selectride were fully characterized as given below. Equatorial amine isomers were identified via ^1H and ^{31}P NMR of the axial/equatorial mixture resulting from sodium borohydride reductions. Elemental analysis of the axial/equatorial mixture provided further confirmation for the equatorial isomer. The ^1H chemical shift of the amine proton and proton geminal to the nitrogen are listed for the equatorial isomer as well as the ^{31}P chemical shift and elemental analysis.

N*-(Diphenylphosphinyl)-4-*tert*-butylcyclohexylamine (8a).** ***cis: Yield 64%; mp 167–169 °C; ^1H NMR 7.96–7.88 (m 4H), 7.48–7.42 (m 6H), 3.50–3.42 (m 1H), 3.23–3.16 (m 1H), 1.94–1.02 (m 9H), 0.82 (s 9H); ^{31}P NMR 22.28; IR (cm^{-1}, KBr) 3400, 3060, 2940, 1440, 1200; MS (EI) 77, 155, 201 (base), 256, 355 (M^+). Anal. Calcd for $C_{22}H_{30}NPO$: C, 74.33; H, 8.51; N, 3.94. Found: C, 74.12; H, 8.53; N, 3.77

trans: ^1H NMR 3.10–3.03 (m 1H CH–N), 2.79–2.73 (m 1H NH); ^{31}P NMR 22.08. Anal. Calcd for $C_{22}H_{30}NPO$: C, 74.33; H, 8.51. Found: C, 74.18; H, 8.44.

N*-(Diphenylphosphinyl)-4-isopropylcyclohexylamine 8b.** ***cis: yield 58%; mp 148–149.5 °C; ^1H NMR 7.94–7.87 (m 4H), 7.46–7.43 (m 6H), 3.41–3.32 (m 1H), 3.18–3.13 (m 1H), 1.81–1.18 (m 10H), 0.87–0.85 (d 6H); ^{31}P NMR 22.11; IR (cm^{-1}, KBr) 3380, 3060, 2940, 1440, 1190; MS (EI) 77, 140 (base), 201, 256, 341 (M^+). Anal. Calcd for $C_{21}H_{28}NPO$: C, 73.87; H, 8.27; N, 4.10. Found: C, 73.71; H, 8.32; N, 4.39.

trans: ^1H NMR 2.98–2.88 (m 1H CH–N), 2.75–2.67 (m 1H NH); ^{31}P NMR 21.74. Anal. Calcd for $C_{21}H_{28}NPO$: C, 73.87; H, 8.27; N, 4.10. Found: C, 73.68; H, 8.40; N, 4.12

N*-(Diphenylphosphinyl)-4-ethylcyclohexylamine (8c).** ***cis: yield 65%; mp 107–110 °C; ^1H NMR 7.96–7.87 (m 4H), 7.52–7.40 (m 6H), 3.37–3.29 (m 1H), 3.16–3.09 (m 1H), 1.72–1.54 (m 6H), 1.28–1.14 (m 5H), 0.88–0.83 (t 3H); ^{31}P NMR 22.35; IR (cm^{-1}, thin film) 3120, 3070, 2940, 2870, 1440, 1180, 1110; MS (EI) 77, 84, 126 (base), 201, 256, 327 (M^+). Anal. Calcd for $C_{20}H_{26}NPO$: C, 73.37; H, 8.00; N, 4.28. Found: C, 73.11; H, 8.08; N, 4.08.

trans: ^1H NMR 2.97–2.88 (m 1H CH–N), 2.75–2.68 (m 1H NH); ^{31}P NMR 22.11. Anal. Calcd for $C_{20}H_{26}NPO$: C, 73.37; H, 8.00; N, 4.28. Found: C, 73.11; H, 8.12; N, 4.06.

N*-(Diphenylphosphinyl)-4-methylcyclohexylamine (8d).** ***cis: yield 72%; mp 152–153 °C; ^1H NMR 7.93–7.86 (m 4H), 7.50–7.39 (m 6H), 3.32–3.28 (m 1H), 3.11–3.03 (m 1H), 1.71–1.50 (m 7H), 1.27–1.17 (m 2H), 0.81–0.79 (d 2H); ^{31}P NMR 22.35; IR (cm^{-1}, KBr) 3120, 3060, 2930, 1440, 1200; MS (CI) 314 (M + H). Anal. Calcd for $C_{19}H_{24}NPO$: C,72.82; H, 7.72. Found: C, 72.79; H, 7.59.

trans: ^1H NMR 2.96–2.87 (m 1H CH–N), 2.71–2.61 (m 1H NH); ^{31}P NMR 22.11. Anal. Calcd for $C_{19}H_{24}NPO$: C, 72.82; H, 7.72. Found: C, 72.86; H, 7.91.

N*-(Diphenylphosphinyl)-4-phenylcyclohexylamine (8e).** ***cis: yield 59%; mp 116.5–118 °C; ^1H NMR 7.97–7.91 (m 4H), 7.54–7.44 (m 6H), 7.32–7.17 (m 5H), 3.55–3.52 (m 1H), 3.30 (bs 1H), 2.60–2.52 (m 1H), 1.97–1.68 (m 8H); ^{31}P NMR 22.72; IR (cm^{-1}, KBr) 3220, 3060, 3040, 2935, 1440, 1190, 1025; MS (FABS) 201 (base), 218, 376 (M + H). Anal. Calcd for $C_{24}H_{26}NPO$: C, 76.78; H, 6.97. Found: C, 76.35; H, 6.91.

trans: ^1H NMR 3.09–3.02 (m 1H CH–N), 2.77–2.71 (m 1H NH), 2.47–2.39 (m 1H CH–Ph); ^{31}P NMR 22.31. Anal. Calcd for $C_{24}H_{26}NPO$: C, 76.78; H, 6.97. Found: C, 76.91; H, 6.90.

***N*-(Diphenylphosphinyl)-*trans*-3,4-dimethylcyclohexylamine (8f).** **Axial**: yield 69%; mp 122–123.5 °C; ^1H NMR 7.91–7.76 (m 4H), 7.53–7.44 (m 6H), 3.56–3.44 (m 1H), 3.28–3.18 (m 1H), 1.78–1.34 (m 6H), 1.22–1.09 (m 2H), 0.87–0.79 (m 6H); ^{31}P NMR 22.58; IR (cm^{-1}, KBr) 3180, 3055, 2920, 1435, 1180; MS (CI) 328 (M + H) also EI 77, 127 (base), 202, 271, 328 (M + H). Anal. Calcd for $C_{20}H_{26}NPO$: C, 73.37; H, 8.00; N, 4.28. Found: C, 73.83; H, 8.06; N, 4.69.

Equatorial: ^1H NMR 3.08–2.99 (m 1H), 2.81–2.69 (m 1H); ^{31}P NMR 22.21. Anal. Calcd for $C_{20}H_{26}NPO$: C, 73.37; H, 8.00; N, 4.28. Found: C, 73.40; H, 8.15; N, 4.11.

***N*-(Diphenylphosphinyl)-*cis*-3,5-dimethylcyclohexylamine (8g).** **Axial**: yield 70%; mp 165–168 °C; ^1H NMR 7.95–7.09 (m 4H), 7.52–7.44 (m 6H), 3.60–3.56 (m 1H CH–N), 3.25–3.16 (m 1H NH), 1.86–1.78 (m 2H) 1.70–1.62 (m 4H), 1.04–0.98 (m 2H), 0.90–0.88 (d 6H); ^{31}P NMR 22.38; IR (cm^{-1}, KBr) 3220, 3060, 2920, 1435, 1180; MS (EI) 77, 126 (base), 201, 216, 270, 327 (M^+). Anal. Calcd for $C_{20}H_{26}NPO$: C, 73.37; H, 8.00; N, 4.28. Found: C, 73.08; H, 8.01; N, 4.15.

Equatorial: ^1H NMR 3.07–2.93 (m 1H CH–N), 2.72–2.63 (m 1H NH); ^{31}P NMR 22.14. Anal. Calcd for $C_{20}H_{26}NPO$: C, 73.37; H, 8.00; N, 4.28. Found: C, 73.40; H, 8.22; N, 4.04.

***N*-(Diphenylphosphinyl)-3,3,5-trimethylcyclohexylamine (8h).** **Axial**: yield 71%; mp 120–121 °C; ^1H NMR 7.92–7.85 (m 4H), 7.50–7.40 (m 6H), 3.55–3.49 (m 1H), 3.16–3.09 (m 1H), 1.83–1.73 (m 2H), 1.59–1.53 (m 1H), 1.41–1.30 (m 2H), 1.16–1.10 (m 1H), 1.08 (s 3H), 0.86 (s 3H), 0.84 (s 3H), 0.81–0.78 (m 1H); ^{31}P NMR 22.38; IR (cm^{-1}, KBr) 3200, 3050, 2940, 1430, 1180; MS (EI) 77, 140 (base), 201, 216, 270, 341 (M^+). Anal. Calcd for $C_{21}H_{28}NPO$: C, 73.87; H, 8.27; N, 4.10. Found: C, 73.47; H, 8.18; N, 3.76.

Equatorial: ^1H NMR 2.66–2.60 (m 1H CH–N), 2.17–2.11 (m 1H NH); ^{31}P NMR 22.18. Anal. Calcd for $C_{21}H_{28}NPO$: C, 73.87; H, 8.27; N, 4.10. Found: C, 73.71; H, 8.34; N, 4.06.

N*-(Diphenylphosphinyl)-3-methylcyclohexylamine (8i).** ***trans: yield 63%; mp 106.5–107.5 °C; ^1H NMR 7.94–7.87 (m 4H), 7.52–7.41 (m 6H), 3.46–3.42 (m 1H), 3.10–3.05 (m 1H), 1.75–1.48 (m 7H), 1.32–1.22 (m 1H), 1.00–0.92 (m 1H), 0.86–0.84 (d 3H); ^{31}P NMR 22.24; IR (cm^{-1}, KBr) 3230, 3050, 2910, 1430, 1180; MS (CI) 314 (M + H). Anal. Calcd for $C_{19}H_{24}NPO$: C, 72.82; H, 7.72; N, 4.47. Found: C, 72.61; H, 7.75; N, 4.34.

cis: ^1H NMR 3.00–2.95 (m 1H CH–N), 2.80–2.76 (m 1H NH); ^{31}P NMR 21.98. Anal. Calcd for $C_{19}H_{24}NPO$: C, 72.82; H, 7.72; N, 4.47. Found: C, 73.00; H, 7.66; N, 4.40.

N*-(Diphenylphosphinyl)-2-methylcyclohexylamine (11a).** ***cis: yield 64%; mp 122–123 °C; ^1H NMR 7.94–7.87 (m 4H), 7.51–7.40 (m 6H), 3.21–3.18 (m 1H), 2.92–2.84 (m 1H), 1.85–1.24 (m 9H), 0.98–0.96 (d 3H); ^{31}P NMR 21.98; IR (cm^{-1}, KBr) 3180, 3040, 2920, 1430, 1180; MS (EI) 77, 112 (base), 201, 313 (M^+). Anal. Calcd for $C_{19}H_{24}NPO$: C, 72.82; H, 7.72; N, 4.47. Found: C, 72.52; H, 7.68; N, 4.20.

trans: ^1H NMR 2.63–2.55 (m 1H), 2.27–2.20 (m 1H); ^{31}P NMR 21.37. Anal. Calcd for $C_{19}H_{24}NPO$: C, 72.82; H, 7.72. Found: C, 72.76; H, 7.77.

N*-(Diphenylphosphinyl)-2-ethylcyclohexylamine (11b).** ***cis: yield 67%; mp 142–143.5 °C; ^1H NMR 7.93–7.86 (m 4H), 7.49–7.40 (m 6H), 3.33–3.27 (m 1H), 2.95–2.88 (m 1H), 1.78–1.73 (m 2H), 1.56–1.40 (m 7H), 1.32–1.20 (m 2H), 0.85–0.81 (t 3H); ^{31}P NMR 21.81; IR (cm^{-1}, KBr) 3220, 2920, 1435, 1185; MS (EI) 77, 126, 201 (base), 218, 256, 327 (M^+). Anal. Calcd for $C_{20}H_{26}NPO$: C, 73.37; H, 8.00; N, 4.28. Found: C, 73.11; H, 7.86; N, 4.34.

trans: ^1H NMR 2.70–2.61 (m 1H CH–N), 2.24–2.18 (m 1H NH); ^{31}P NMR 21.44. Anal. Calcd for $C_{20}H_{26}NPO$: C, 73.37; H, 8.00; N, 4.28. Found: C, 73.26; H, 8.10; N, 4.11.

***N*-(Diphenylphosphinyl)menthylamine (*trans*-2-isopropyl-5-Me) (11c).** **Axial**: yield 60%; mp 160–161.5 °C; ^1H NMR 7.94–7.82 (m 4H), 7.50–7.41, (m 6H), 3.46–3.42 (m 1H), 2.91–2.86 (m 1H), 1.80–1.72 (m 2H), 1.63–1.54 (m 4H), 1.43–1.39 (m 2H), 0.86–0.79 (dd 6H), 0.72–0.70 (d 3H); ^{31}P NMR

21.71; IR (cm^{-1}, KBr) 3220, 3060, 2930, 1440, 1185; MS (EI) 77 (base), 201, 270, 355 (M^+). Anal. Calcd for $C_{22}H_{30}NPO$: C, 74.34; H, 8.51; N, 3.94. Found: C, 74.02; H, 8.43; N, 3.92.

Equatorial: ^1H NMR 2.70–2.64 (m 1H CH–N), 2.46–2.40 (m 1H NH); ^{31}P NMR 21.34. Anal. Calcd for $C_{22}H_{30}NPO$: C, 74.34; H, 8.51; N, 3.94. Found: C, 73.98; H, 8.61; N, 3.76.

N*-(Diphenylphosphinyl)-2-phenylcyclohexylamine (11d).** ***cis: yield 63%; mp 105–108 °C; ^1H NMR 7.92–7.82 (m 4H), 7.44–7.38 (m 6H), 7.14–7.06 (m 5H), 3.50–3.42 (m 1H), 3.22–3.15 (m 1H) 2.52–2.43 (m 1H CH–Ph), 1.90–1.50 (m 8H); ^{31}P NMR 21.71; IR (cm^{-1}, thin film) 3130, 3070, 3040, 2940, 2870, 1440, 1185, 1105, 1120; MS (EI) 77, 91, 174, 201 (base), 256, 375. Anal. Calcd for $C_{24}H_{26}NPO$: C, 76.78; H, 6.98. Found: C, 77.16; H, 7.31.

trans: ^1H NMR 3.07–3.00 (m 1H), 2.90–2.83 (m 1H), 2.65–2.58 (m 1H CH–Ph); ^{31}P NMR 21.37. Anal. Calcd for $C_{24}H_{26}NPO$: C, 76.78; H, 6.98; N, 3.73. Found: C, 76.88; H, 7.15; N, 3.70.

N*-(Diphenylphosphinyl)-2-*tert*-butylcyclohexylamine (11e).** ***cis: yield 57%; mp 157.5–158.5 °C; ^1H NMR 7.87–7.81 (m 2H), 7.71–7.66 (m 2H), 7.54–7.42 (m 6H), 3.63–3.59 (m 1H), 3.01–2.94 (m 1H), 1.71–1.45 (m 5H), 1.28–1.02 (m 4H), 0.91 (s 9H); ^{31}P NMR 21.23; IR (cm^{-1}, KBr) 3320, 3080, 2940, 1435, 1200; MS (EI) 77 (base), 155, 201, 355 (M^+). Anal. Calcd for $C_{22}H_{30}NPO$: C, 74.34; H, 8.51; N, 3.94. Found: C, 74.03; H, 8.47; N, 3.84.

N*-(Diphenylphosphinyl)-2-methoxycyclohexylamine (11f).** ***cis: yield 71%; mp 113–114 °C; ^1H NMR 7.95–7.85 (m 4H), 7.48–7.43 (m 6H), 3.64–3.52 (m 2H CH–N and CH–O), 3.35 (s 3H), 3.13–3.02 (m 1H NH), 2.02–1.93 (m 1H), 1.69–1.53 (m 4H), 1.34–1.08 (m 3H); ^{31}P NMR 22.58; MS (EI, 35ev) 77, 96, 128, 201 (base), 218, 297, 314, 329 (M^+). Anal. Calcd for $C_{19}H_{24}NPO_2$: C, 69.28; H, 7.34; N, 4.25. Found: C, 68.89; H, 7.30; N, 4.30.

trans: ^1H NMR 3.43–3.35 (m 2H CH–N and CH–O), 3.13–3.02 (ca. peak overlaps with NH of *cis* product); ^{31}P NMR 22.35. Anal. Calcd for $C_{19}H_{24}NPO_2$: C, 69.28; H, 7.34; N, 4.25. Found: C, 69.29; H, 7.28; N, 4.22.

N*-(Diphenylphosphinyl)-2-methylcyclopentylamine (16a).** ***cis: yield 44%; mp 129.5–131.5 °C; ^1H NMR 7.94–7.86 (m 4H), 7.50–7.40 (m 6H), 3.52–3.36 (m 1H), 2.81–2.74 (m 1H), 2.07–1.46 (m 7H), 1.05–1.03 (d 3H); ^{31}P NMR 22.35; IR (cm^{-1}, KBr) 3190, 3060, 2970, 2880, 1440, 1180, 1100; MS (EI) 77, 98 (base), 142, 201, 299 (M^+). Anal. Calcd for $C_{18}H_{22}NPO$: C, 72.22; H, 7.41; N, 4.68. Found: C, 72.44; H, 7.87; N, 4.83.

trans: ^1H NMR 2.92–2.84 (m 1H), 2.77–2.68 (m 1H); ^{31}P NMR 21.98. Anal. Calcd for $C_{18}H_{22}NPO$: C, 72.22; H, 7.41; N, 4.68. Found: C, 72.02; H, 7.38; N, 4.60.

N*-(Diphenylphosphinyl)-2-ethylcyclopentylamine (16b).** ***cis: yield 60%; mp 146.5–147.5 °C; ^1H NMR 7.93–7.86 (m 4H), 7.50–7.40 (m 6H), 3.52–3.44 (m 1H), 2.76–2.69 (m), 2.04–1.44 (m 7H), 1.12–1.04 (m 2H), 0.87–0.84 (t 3H); ^{31}P NMR 22.18; IR (cm^{-1}, KBr) 3190, 3060, 2960, 2880, 1440, 1175, 1100; MS (EI) 77, 112 (base), 201, 313 (M^+). Anal. Calcd for $C_{19}H_{24}NPO$: C, 72.82; H, 7.72; N, 4.47. Found: C, 72.62; H, 7.77; N, 4.30.

trans: ^1H NMR 3.02–2.95 (m 1H CH–N), 2.71 (bs NH); ^{31}P NMR 21.81. Anal. Calcd for $C_{19}H_{24}NPO$: C, 72.82; H, 7.72; N, 4.47. Found: C, 73.00; H, 7.80; N, 4.41.

***N*-(Diphenylphosphinyl)-3-methylcyclopentylamine (mixture of *cis* and *trans*, 16c).** Yield: 62% (L-Selectride); mp145–148 °C; ^1H NMR 7.91–7.85 (m 4H), 7.50–7.40 (m 6H), 3.63–3.56 (minor m CH–N), 3.48–3.43 (major m CH–N), 2.88–2.77 (m 1H NH), 2.23–2.17 (m 1H), 2.10–1.47 (m 5H), 1.25–1.16 (m 1H), 0.97–0.96 (major d 3H), 0.91–0.90 (minor d 3H); ^{31}P NMR 22.14 (diastereomers were unresolved); IR (cm^{-1}, KBr) 3120, 3050, 2950, 1435, 1200; MS (EI) 77, 98 (base), 142, 201, 299 (M^+). Anal. Calcd for $C_{18}H_{22}NPO$: C, 72.22; H, 7.41; N, 4.68. Found: C, 72.02; H, 7.42; N, 4.41.

***N*-(Diphenylphosphinyl)-3-ethylcyclopentylamine (mixture of *cis* and *trans*, 16d).** Yield: 66% (L-Selectride); mp 102.5–105.5 °C; ^1H NMR 7.92–7.85 (m 4H), 7.50–7.40 (m 6H), 3.58–3.51 (minor m CH–N), 3.49–3.40 (major m CH–N), 2.78 (bs 1H NH), 2.27–2.19 (m 1H), 2.08–1.43 (m 6H), 1.35–1.20 (m 2H), 0.84–0.80 (m 3H); ^{31}P NMR 22.28 (diastereomers were unresolved); IR (cm^{-1}, thin film) 3180, 3060, 2960, 2870, 1440, 1175, 1100; MS (EI) 77, 112 (base), 142, 201, 313 (M^+). Anal. Calcd for $C_{19}H_{24}NPO$: C, 72.82; H, 7.72; N, 4.47. Found: C, 72.43; H, 8.08; N, 4.78.

N*-(Diphenylphosphinyl)-*cis*-3,4-dimethylcyclopentylamine (16e).** ***cis: yield 66%; mp 90–91 °C; ^1H NMR 7.92–7.85 (m 4H), 7.50–7.40 (m 6H), 3.43–3.28 (m 1H CH–N), 2.72–2.64 (m 1H), 2.19–2.10 (m 2H), 1.85–1.78 (m 2H), 1.18–1.06 (m 2H), 0.81–0.77 (d 6H); ^{31}P NMR 22.18; IR (cm^{-1}, thin film) 3180, 3060, 2960, 1440, 1180, 1100; MS (EI) 77, 112 (base), 201, 313 (M^+). Anal. Calcd for $C_{19}H_{24}NPO$: C, 72.82; H, 7.72; N, 4.47. Found: C, 73.11; H, 7.78; N, 4.10

trans: ^1H NMR 3.67–3.57 (m 1H CH–N), 2.82–2.73 (m 1H NH); ^{31}P NMR 22.18 (diastereomers were unresolved). Anal. Calcd for $C_{19}H_{24}NPO$: C, 72.82; N, 7.72; N, 4.47. Found: C, 72.89; H, 7.99; N, 4.30.

N*-(Diphenylphosphinyl)norbornylamine.** From **21**, ***endo: yield 68%; mp 145–147 °C; ^1H NMR 7.93–7.86 (m 4H), 7.51–7.41 (m 6H), 3.55–3.44 (m 1H), 2.98–2.90 (m 1H NH), 2.24–2.22 (m 1H), 2.14–2.13 (d 1H), 2.08–2.00 (m 1H), 1.75–1.67 (m 1H), 1.57–1.48 (m 2H), 1.26–1.19 (m 3H), 0.86–0.81 (m 1H); ^{31}P NMR 22.85; IR (cm^{-1}, KBr) 3170, 3030, 2950, 1440, 1200; MS (EI) 77, 110 (base), 201, 311 (M^+). Anal. Calcd for $C_{19}H_{22}NPO$: C, 73.29; H, 7.12. Found: C, 73.02; H, 7.18.

N*-(Diphenylphosphinyl)camphorylamine.** From **22**, ***exo: yield 63%; mp 96–97 °C; ^1H NMR 7.95–7.82 (m 4H), 7.51–7.39 (m 6H), 3.36–3.25 (m 1H CH–N), 2.94–2.86 (m 1H NH), 1.90–1.67 (m 2H), 1.62–1.52 (m 2H), 1.47–1.39 (m 1H), 1.23–1.13 (m 1H), 1.01 (s 3H), 0.86 (s 3H), 0.72 (s 3H); ^{31}P NMR 23.09; IR (cm^{-1}) 3240, 2960, 2890, 1440, 1180, 1110; MS (EI) 77 (base), 95, 152, 201, 217, 353 (M^+). Anal. Calcd for $C_{22}H_{28}NPO$: C, 74.76; H, 7.98. Found: C, 74.50; H, 7.41.

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