# The Stereochemical Dichotomy in Palladium(0)- and Nickel(0)-Catalyzed Allylic Substitution

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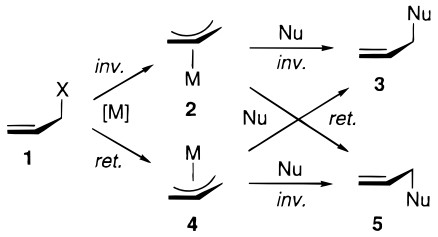
**Abstract:** The steric course of the first step of Pd(0)-catalyzed allylic substitution with stabilized C-nucleophiles can be completely reversed by a suitably positioned coordinating $Ph_2P$ group, resulting in an overall inversion (**1** → **4** → **5**), as opposed to the normally observed retention (**1** → **2** → **3**). Thus, on reaction with $NaCH(CO_2Me)_2$, the allylic acetate **10**, containing a phosphinous amide moiety, gives **24** as a result of *ret.*−*inv.* pathway, whereas **9**, lacking the coordinating group, affords the "normal" *inv.*−*inv.* product **23**. The intermediate $\eta^3$-complex **32**, generated in the former reaction, has been characterized by $^1H$ and $^{31}P$ NMR spectroscopy. While this stereochemical control is highly successful with cyclic substrates, it does not operate in acyclic series, as documented by the reactivity of the *anti*-configured 1,4-functionalized hexenes **14** and **15**, which both give the product of *inv.*−*inv.* pathway, i.e., **35** and **36**, respectively. The *syn*-configured allylic substrates **21** and **22** exhibit the same pattern, irrespective of the presence of the coordinating neighboring group. The lack of overriding control in the latter instances has been attributed to a rotation about the C−C bond connecting the coordinating group to the allylic system, which allows the precoordinated Pd(0) to approach the allylic moiety from the face opposite to the leaving group (**15** → **41** → **42**). Precoordination of the catalyst to the $Ph_2P$ group is evidenced by substantial acceleration of the reaction in all cases studied. For the Ni(0)-catalyzed reaction of the allylic methoxy derivatives with MeMgBr, precoordination proved to be the prerequisite for the reaction to occur (**50** → **51** → **52**); *ret.*−*ret.* pathway was observed.

## Introduction

Palladium(0)-catalyzed allylic substitution is known to proceed via $\eta^3$-complexes **2** that arise from allylic esters, such as the acetate **1** (X = OAc), with inversion of configuration (Scheme 1).[1] The subsequent reaction of **2** with malonate anions and other stabilized C-nucleophiles again proceeds with inversion (**2** → **3**),[1] giving overall retention. By contrast, organometallics and nonstabilized nucleophiles react with retention in the second step (**2** → **5**).[1,2] The analogous molybdenum(0)-catalyzed reaction with malonate-type nucleophiles also leads to an overall retention of configuration.[3] However, the mechanism has been shown to involve double retention (**1** → **4** → **3**).[4,5]

**Scheme 1**




Although the Pd(0)-catalyzed reaction is dominated by inversion in the first step (**1** → **2**), the retention pathway (**1** → **4**) is also known.[6,7] In the two examples published to date, this reversal was enforced by coordination of the catalyst to the leaving group.[6,7] However, none of these approaches is overwhelmingly practical, for in one case (**1**; X = $Ph_2PCH_2CO_2$) the retention pathway operates only if the normal route is precluded (i.e., with sterically biased substrates),[6] whereas the other protocol requires allylic chlorides[7] (**1**; X = Cl), which are generally less stable than the esters and more difficult to

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(1) (a) Trost, B. M.; Strege, P. E. *J. Am. Chem. Soc.* **1975**, *97*, 2534. (b) Trost, B. M.; Verhoeven, T. R. *J. Org. Chem.* **1976**, *41*, 3215. (c) Hayashi, T.; Hagihara, T.; Konishi, M.; Kumada, M. *J. Am. Chem. Soc.* **1983**, *105*, 7767. For reviews, see: (d) Trost, B. M. *Tetrahedron* **1977**, *33*, 371. (e) Trost, B. M. *Acc. Chem. Res.* **1980**, *13*, 385. (f) Tsuji, J. *Tetrahedron* **1986**, *42*, 4361. (g) Frost, C. G.; Howarth, J.; Williams, J. M. J. *Tetrahedron: Asymmetry* **1992**, *3*, 1089. (h) Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395. (i) Trost, B. M. *Acc. Chem. Res.* **1996**, *29*, 355.

(2) (a) Temple, J. S.; Schwartz, J. *J. Am. Chem. Soc.* **1980**, *102*, 7381. (b) Matsushida, H.; Negishi, E. *J. Chem. Soc., Chem. Commun.* **1982**, 160. (c) Temple, J. S.; Riediker, M.; Schwartz, J. *J. Am. Chem. Soc.* **1982**, *104*, 1310. (d) Labadie, J. W.; Stille, J. K. *J. Am. Chem. Soc.* **1983**, *105*, 6129. (e) Goliaszewski, A.; Schwartz, J. *J. Am. Chem. Soc.* **1984**, *106*, 5028. (f) Keinan, E.; Roth, Z. *J. Org. Chem.* **1983**, *48*, 1769. (g) Fiaud, J.-C.; Legros, J.-Y. *J. Org. Chem.* **1987**, *52*, 1907.

(3) (a) Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1982**, *104*, 5543. (b) Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1983**, *105*, 3343. (c) Trost, B. M.; Lautens, M. *Organometallics* **1983**, *2*, 1687. (d) Trost, B. M.; Lautens, M.; Peterson, B. *Tetrahedron Lett.* **1983**, *24*, 4525. (e) Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1987**, *109*, 1469. (f) Trost, B. M.; Lautens, M. *Tetrahedron* **1987**, *43*, 4817. (g) Trost, B. M.; Merlic, C. A. *J. Am. Chem. Soc.* **1990**, *112*, 9590.

(4) Dvořák, D.; Starý, I.; Kočovský, P. *J. Am. Chem. Soc.* **1995**, *117*, 6130.

(5) The stoichiometric reaction mediated by Mo(0), involving the isolation of the $\eta^3$-complex, proceeds with inversion in the second step (**1** → **4** → **5**): (a) Faller, J. W.; Linebarrier, D. *Organometallics* **1988**, *7*, 1670. (b) Ward, Y. D.; Villanueva, L. A.; Allerd, G. D.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1996**, *118*, 897.

(6) (a) Starý, I.; Kočovský, P. *J. Am. Chem. Soc.* **1989**, *111*, 4981. (b) Starý, I.; Zajíček, J.; Kočovský, P. *Tetrahedron* **1992**, *48*, 7229.

(7) (a) Kurosawa, H.; Ogoshi, S.; Kawasaki, Y.; Murai, S.; Miyoshi, M.; Ikeda, I. *J. Am. Chem. Soc.* **1990**, *112*, 2813. (b) Kurosawa, H.; Kajimaru, H.; Ogoshi, S.; Yoneda, H.; Miki, K.; Kasai, N.; Murai, S.; Ikeda, I. *J. Am. Chem. Soc.* **1992**, *114*, 8417.

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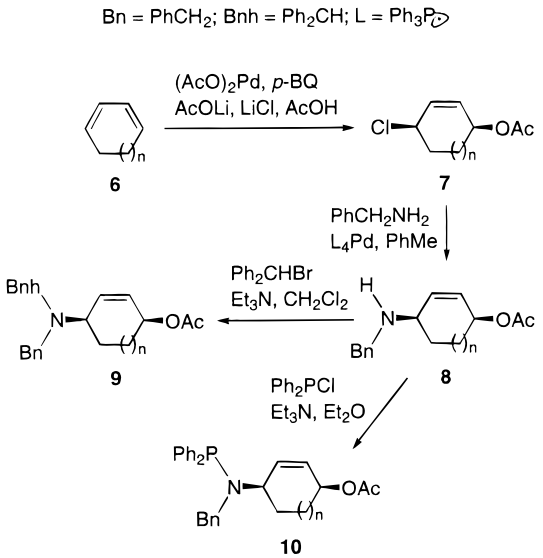
**Scheme 2**[a]




[a] **a**, $n = 1$; **b**, $n = 2$. Bn = $PhCH_2$; Bnh = $Ph_2CH$; L = $Ph_3P$.

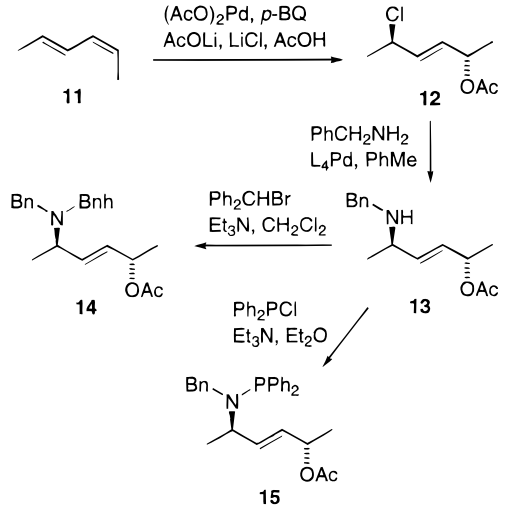
prepare stereostructurally pure.[8] Herein, we report on unprecedented methodology for *altering the stereochemistry of the first step* of the Pd(0)-catalyzed allylic substitution *by precoordination of the catalyst to a neighboring group* rather than to the leaving group.

## Results and Discussion

**Synthesis of Model Compounds.** To examine the potential steering effect of a neighboring group on the formation of the $\eta^3$-complex, we required 1,4-disubstituted olefins with one substituent serving as a leaving group (AcO) and the other capable of coordinating to the catalyst prior to the reaction. To this end, we prepared the *cis*-allylic acetates **8a** and **8b** (Scheme 2), using the Bäckvall *cis*-chloroacetoxylation of 1,3-cyclohexadiene and 1,3-cycloheptadiene, respectively (**6** → **7**),[9,10] followed by the $(Ph_3P)_4Pd$-catalyzed replacement of the allylic chlorine with benzylamine (**7**→ **8**).[11]

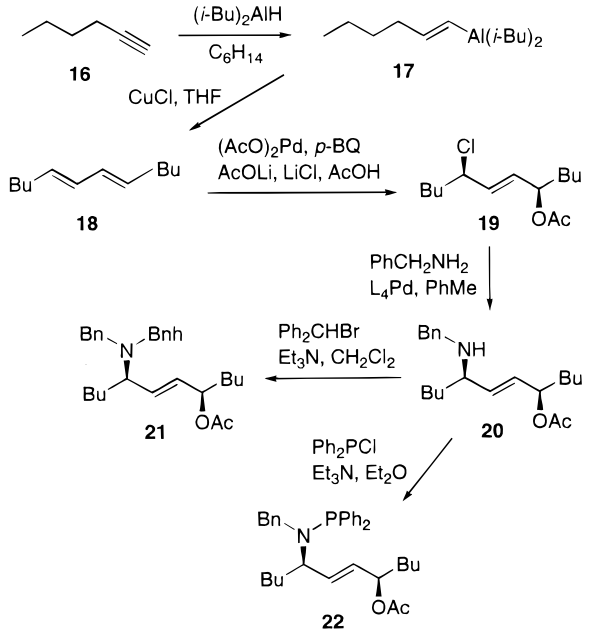
We reasoned that appending a phosphine group to the nitrogen atom might lead to precoordination of the catalyst[6,12] and, consequently, to altering the stereochemistry of the $\eta^3$-complex

**Scheme 3**[a]




[a] For the legend, see Scheme 2.

**Scheme 4**[a]




[a] For the legend, see Scheme 2.

formation. The $Ph_2P$ derivative **10a**, identified as a suitable candidate, was prepared from **8a** by reaction with $Ph_2PCl$ ($Et_3N$, $Et_2O$, reflux 18 h, 68%);[13] the homologue **10b** was obtained from **8b** in a similar manner (85%). For comparison, the *N*-benzhydryl derivatives **9a** and **9b** (Bnh = $Ph_2CH$), were prepared from **8a** and **8b** in 58% and 81% yield, respectively, on reaction with $Ph_2CHBr$ and $Et_3N$ in refluxing $CH_2Cl_2$. The latter substituent can be assumed to have steric demands similar to those of $Ph_2P$ but to lack its coordinating capability.

In addition to the cyclic derivatives **9a**, **9b**, **10a**, and **10b**, acyclic model compounds were also synthesized (Schemes 3 and 4) to explore the scope of this methodology. Thus, (*E*,*Z*)-hexa-2,4-diene (**11**) was stereospecifically functionalized under the Bäckvall conditions[9,10] to afford the *anti*-chloroacetate **12**[9,10] (Scheme 3), which was converted into the benzylamine derivative **13** (84%) by Pd(0)-catalyzed reaction with $PhCH_2NH_2$. Reaction of the latter product with $Ph_2CHBr$ ($Et_3N$, $CH_2Cl_2$, reflux, 44 h) afforded the *N*-benzhydryl derivative **14** (53%),

(8) In another example of formal retention, reported for **1** (X = $CF_3CO_2$), the mechanism apparently involves the usual inversion **1** → **2** followed by thermodynamic equilibration **2** → **4**: Vitagliano, A.; Åkermark, B.; Hanson, S. *Organometallics* **1991**, *10*, 2592.

(9) (a) Bäckvall, J.-E.; Nordberg, R. E. *J. Am. Chem. Soc.* **1981**, *103*, 4959. (b) Bäckvall, J.-E.; Byström, S. E.; Nordberg, R. E. *J. Org. Chem.* **1984**, *49*, 4619. (c) Bäckvall, J.-E.; Nyström, J.-E.; Nordberg, R. E. *J. Am. Chem. Soc.* **1985**, *107*, 3676. (d) Bäckvall, J.-E.; Nordberg, R. E.; Wilhelm, D. *J. Am. Chem. Soc.* **1985**, *107*, 6892. For reviews, see: (e) Bäckvall, J.-E. *Acc. Chem. Res.* **1983**, *16*, 335. (f) Bäckvall, J.-E. *Pure Appl. Chem.* **1992**, *64*, 429; *Pure Appl. Chem.* **1996**, *68*, 535. (g) Bäckvall, J.-E. *Acta Chem. Scand.* **1996**, *50*, 661.

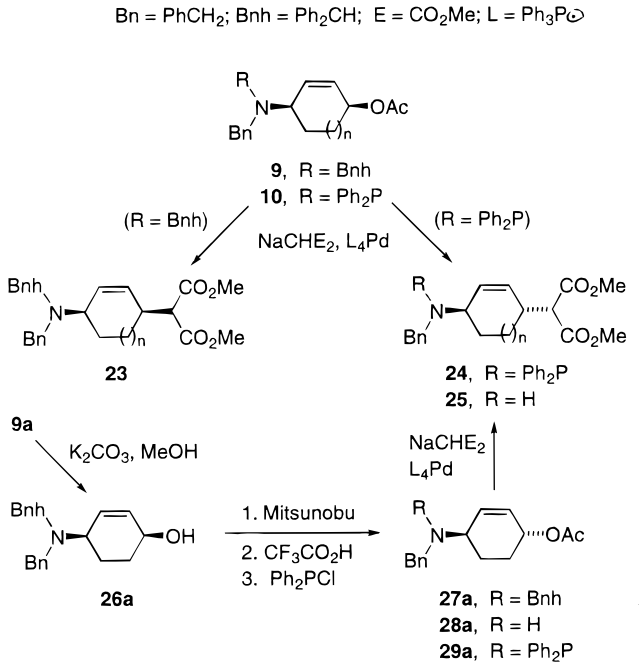
(10) (a) Nyström, J.-E.; Rein, T.; Bäckvall, J.-E. *Org. Synth.* **1989**, *67*, 105. (b) Bäckvall, J.-E.; Granberg, K. L.; Hopkins, R. B. *Acta Chem. Scand.* **1990**, *44*, 492.

(11) While this work was in progress, Bäckvall published the same transformation in the cyclohexane series (**7a** → **8a**): Gatti, R. G. P.; Carson, A. L. E.; Bäckvall, J.-E. *J. Chem. Soc., Perkin Trans. 1* **1997**, 577.

(12) For reviews on steering the reagent/catalyst by a neighboring group, see: (a) Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307. (b) Brown, J. M. *Angew. Chem., Int Ed. Engl.* **1987**, *26*, 190. See also: (c) Crabtree, R. H.; Davis, M. W. *J. Org. Chem.* **1986**, *51*, 2655. (d) Burk, M. J.; McGrath, M. P.; Wheeler, R.; Crabtree, R. H. *J. Am. Chem. Soc.* **1988**, *110*, 5034. For recent examples, see, e.g.: (e) Kočovský, P. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1759 and references therein. (f) Breit, B. *J. Chem. Soc., Chem. Commun.* **1997**, 591. (g) Breit, B. *Angew. Chem., Int. Ed.* **1997**, *35*, 2835.

(13) All yields refer to "isolated" yields.

**Scheme 5**[a]



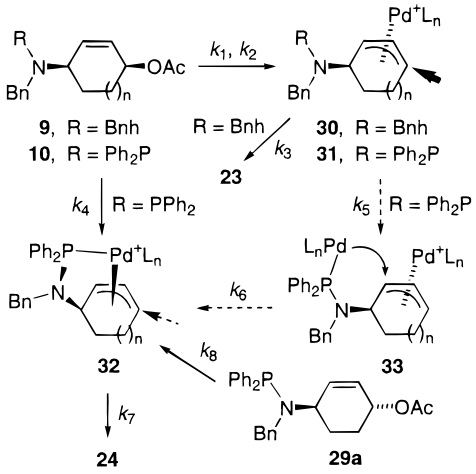

[a] **a**, $n = 1$; **b**, $n = 2$. Bn = $PhCH_2$; Bnh = $Ph_2CH$; E = $CO_2Me$; L = $Ph_3P$.

whereas treatment with $Ph_2PCl$ ($Et_3N$, $Et_2O$, reflux, 18 h) furnished the desired phosphinous amide **15** (68%).

The *syn*-diastereoisomeric series could be analogously prepared from (*E*,*E*)-hexa-2,4-diene.[9,10,14] However, this diene is no longer commercially available and would have to be synthesized, so, for practical reasons, we selected the less volatile (*E*,*E*)-diene **18**[15] (Scheme 4) as the starting material. The latter diene was readily obtained from 1-hexyne via alumination with DIBAH (hexane, 40 °C, 16 h), followed by the CuCl-mediated dimerization[16] in THF at room temperature for 4 h (**16** → **17** → **18**). Bäckvall functionalization[9,10] of the resulting diene **18** readily afforded the *syn*-chloroacetate **19** (21% overall from **16**),[17] which was then converted into the required *N*-benzhydryl and *N*-phosphinous derivatives **21** (48%) and **22** (50%) via the amine **20** in the same manner as shown for the previous series.

**Palladium(0)-Catalyzed Allylic Substitution in the Cycloalkane Series.** As expected, the *N*-benzhydryl derivatives **9a** and **9b** reacted with $NaCH(CO_2Me)_2$ in the presence of $(Ph_3P)_4Pd$ (7 mol %) at reflux in THF for 22 h to give rise to the *cis*-derivatives **23a** (73%) and **23b** (66%), respectively (Scheme 5).[13] By contrast, treatment of the phosphinous amide **10a** with $NaCH(CO_2Me)_2$ and $(Ph_3P)_4Pd$ (7 mol %) in THF at room temperature for 22 h furnished the *trans*-derivative **24a** (76%); no trace of its epimer was detected (by $^1H$ NMR of the crude product). The homologue **10b** followed the same pattern, giving exclusively **24b** (62%) at room temperature. In addition to the 2D-NMR data for **24a** and **24b**, which were fully compatible with their structures,[18] a chemical correlation was carried out for **24a** via the amine **25a**, obtained from **24a** by removal of the $Ph_2P$ group ($CF_3CO_2H$, rt, 3 h, 68%). An authentic sample of **25a** was prepared from **9a** as follows: saponification ($K_2CO_3$, MeOH, THF, $H_2O$, 40 °C, 26 h) afforded the alcohol **26a** (91%), which was converted into the *trans*-acetate **27a** via the Mitsunobu reaction ($Ph_3P$, DEAD, rt, 20 h, 82%).[19] Selective removal of the *N*-benzhydryl group ($CF_3CO_2H$, reflux, 18 h) furnished **28a** (52%), which was submitted to the Pd(0)-catalyzed reaction with $NaCH(CO_2Me)_2$ (reflux in THF for 22 h). The resulting product **25a** (58%) proved to be identical with the compound obtained from **24a** (vide supra). Interestingly, the removal of the bulky *N*-benzhydryl group (**27a** → **28a**) proved to be necessary since attempted Pd(0)-catalyzed substitution failed with **27a**. On the other hand, the phosphinous amide **29a**, obtained from **28a** on reaction with $Ph_2PCl$ (33%), reacted rapidly (rt, 15 min!) to afford **24a** (64%).

**Scheme 6**[a]




[a] For the legend, see Scheme 5.

The *cis*-derivative **23a** is obviously formed by the standard double inversion via the $\eta^3$-complex **30a** (Scheme 6); the same mechanism applies to the cycloheptane series (**9b** → **30b** → **23b**). On the other hand, the overall inversion in the case of the $Ph_2P$ derivatives **10a** and **10b** can be rationalized by the sought after *ret.*−*inv.* pathway involving precoordination of the catalyst to the neighboring phosphine group (**10** → **32**); inversion in the final step would then lead to **24a** and **24b**, respectively. To gain further support in favor of this mechanism, we endeavored to intercept the intermediate $\eta^3$-complex **32**. To this end, **10a** was treated with a stoichiometric amount of $(Ph_3P)_4Pd$ in the absence of the nucleophile and the reaction

(14) The Mitsunobu reaction using the alcohol obtained on saponification of either acetate **13** or **14** failed to produce the required *syn*-epimer, giving mainly elimination products.

(15) Yamamoto, Y.; Yatagai, H.; Maruyama, K.; Sonoda, A.; Murahashi, S. *J. Am. Chem. Soc.* **1977**, *99*, 5652.

(16) For the method, see: Zweifel, G.; Miller, R. L. *J. Am. Chem. Soc.* **1970**, *92*, 6678.

(17) In this case, a slow addition of a dilute, hexane solution of **18** into a mixture of $(AcO)_2Pd$, *p*-benzoquinone, LiCl, and AcOLi in an AcOH-hexane mixture proved essential for the reaction to proceed with acceptable efficiency, with the formation of the products of the competing Diels−Alder addition of *p*-BQ to the diene **18** being substantially reduced.

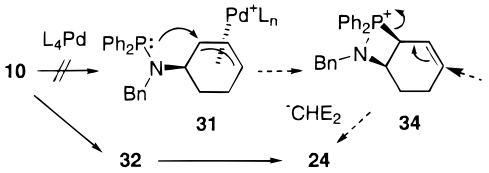
(18) For the *cis*/*trans* assignment of 1,4-disubstituted cycloalkenes by $^1H$ NMR, as derived from a large series of compounds, see: Nordberg, R. Thesis, Royal Institute of Technology, Stockholm, 1982. The characteristic features are as follows: chemical shifts of the corresponding allylic protons are consistently higher for the *trans*-series by ~0.1 ppm and their *W*/2 values (width at half-height of the multiplet) are typically twice as large. Thus, (*E*)-1,4-diacetoxycyclohex-2-ene shows C*H*-OAc at $\delta$ 5.32 (m, $W/2 = 11$ Hz), whereas its *Z*-counterpart exhibits this proton at $\delta$ 5.23 (m, $W/2 = 8$ Hz). Analogously, the products of monosubstitution of the latter diacetates with malonate give the following values for the allylic protons: 2.98 (m) and 5.28 (m, $W/2 = 16$ Hz) for the *E*-isomer and 2.88 (m) and 5.19 (m, $W/2 = 9$ Hz) for the *Z*-isomer. The data obtained for our compounds are in line with this generalization.

(19) (a) Mitsunobu, O. *Synthesis* **1981**, 1. (b) Shull, B. K.; Sakai, T.; Nichols, J. B.; Koreeda, M. *J. Org. Chem.* **1997**, *62*, 8294. (c) The *trans*-configuration of **27a** was corroborated by the $^1H$ NMR spectrum:[18] whereas the C*H*-OAc in **9a** is characterized by a very narrow multiplet centered at 5.02 ppm (partly overlapped with the $Ph_2CH_2$ singlet at 5.00 ppm), the corresponding proton in **27a** appears at 5.17 ppm as ddd ($J = 3$, 5.5, and 9 Hz).

was monitored by NMR. Whereas the $^{31}$P signal of the free $Ph_2P$ group of **10a** appears at 51.7 ppm, two signals were observed in the $^{31}$P NMR spectrum of the $\eta^3$-complex generated from **10a**, namely at 29.1 and 103.3 ppm. While the former signal is characteristic for the $Ph_3P$ associated with Pd, the latter peak can be attributed to the $Ph_2P$−N coordinated to Pd, as in **32a**.[20] The complex generated from **29a** and $(Ph_3P)_4Pd$ exhibited the same $^{31}$P signals (at 29.1 and 103.4 ppm) and the same $^1$H NMR spectrum[21−23] as that of the species generated from **10a**, demonstrating their identity. Hence, these results strongly support the participation of the $\eta^3$-chelate **32** in the formation of the *trans*-product **24**.

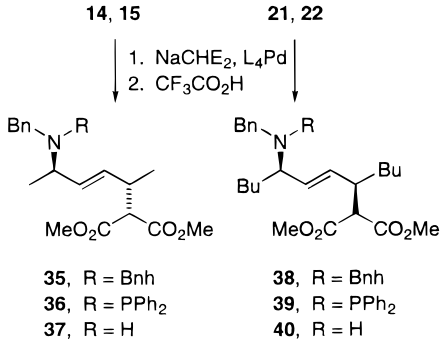
Although the above experiments demonstrated the formation of the chelate **32**, the overall outcome can also be considered to originate from a competing process: thus, if the first step occurred without coordination, i.e., in the *inv.* fashion, the resulting complex **31** might coordinate another Pd (**31** → **33**), and the Bosnich-type inversion of the latter species[23−26] (**33** → **32**), followed by reaction with the nucleophile, would then give the same product **24** (Scheme 6). To address this issue, let us analyze the kinetics of these reactions. The reaction of an $\eta^3$-complex with malonate anion is usually faster than its formation from the corresponding allylic acetate,[23,26] so that for the sequence **9** → **30** → **23** in the *N*-benzhydryl series we can assume $k_3 > k_1$.[27] Should the phosphinous derivative **10** react via **31**, followed by isomerization to **32** (via **33**), we can further assume that the rate of the first step would not differ dramatically from that of the generation of **30** from **9**.[28] In other words, **10** would be likely to react with a rate comparable to that of **9**, i.e., $k_1 \approx k_2$. However, it required an overnight reflux in THF to convert **9** into **23**, whereas **10** is consumed over the same period of time at room temperature (vide supra). Moreover, the *trans*-isomer **29a**, which must react via **32a**, gives **24a** at room temperature in 15 min, showing that both $k_7$ and $k_8$ are relatively large and, therefore, $k_7 > k_4$. The isomerization pathway **33** → **32**, being an intramolecular process, would presumably be fast so that the rate-limiting step for generating **32** should either involve $k_4$ (if formed directly from **10**) or $k_2$ (if generated by the diastereofacial isomerization). Since we argued that $k_2 \approx k_1$, the isomerization path can be excluded in view of the substantial difference in the reaction rates of **9** vs **10**. Hence, these results support the *ret.*−*inv.* pathway **10** → **32** → **24**.

**Scheme 7**[a]




[a] For the legend, see Scheme 5.

**Scheme 8**[a]




[a] Bn = $PhCH_2$; Bnh = $Ph_2CH$; E = $CO_2Me$; L = $Ph_3P$.

Yet another mechanism for the overall inversion in the case of the $Ph_2P$ derivatives **10** can be considered (Scheme 7): if the first step occurred without coordination, the resulting complex **31** might undergo an intramolecular attack by the phosphorus atom to generate the phosphonium ion **34**, whose reaction with the nucleophile would then give the same product **24**. However, this mechanism can be excluded in view of the kinetic arguments (vide supra) and the actual observation of the Pd chelate **32a** by NMR (in the stoichiometric experiment), whereas the phosphonium ion **34a** could not be detected.

**Palladium(0)-Catalyzed Allylic Substitution in the Acyclic Series.** In the Pd(0)-catalyzed reaction with dimethyl sodiomalonate, the *anti*-configured *N*-benzhydryl derivative **14** (Scheme 8) afforded the expected substitution product **35** with *anti*-configuration of the substituents (66 °C, 16 h, 61%). In contrast to the alicyclic series, its phosphinous analogue **15** also gave the product corresponding to overall retention, namely the *anti*-configured **36** (rt, 22 h, 58%), as evidenced by converting both **35** and **36** into the same amine **37** on treatment with $CF_3CO_2H$ (in 85% and 77% yield, respectively). Similarly, the *syn*-configured derivatives **21** and **22** furnished the *syn*-products **38** (66 °C, 42 h, 25%) and **39** (rt, 1.5 h, 57%), respectively; in the former case, the reaction turned out to be extremely slow and a substantial amount of the unreacted starting material (69%) was recovered. Again, the relative configuration was established by converting both **38** and **39** into the amine **40** on reaction with $CF_3CO_2H$.

The striking difference between the cyclic and noncyclic series can be understood in terms of the possibility of rotation about the C−C bond connecting the allylic moiety to the neighboring group. Whereas such rotation is precluded in the cyclic systems, it can take place with **15** (Scheme 9). In this instance, precoordination of the catalyst to the phosphorus atom of the neighboring group can still be assumed (**15** → **41**), followed by the normal inversion to generate the $\pi$-allyl complex **42**. This latter reaction is, apparently, lower in activation energy than that proceeding with retention of configuration. Subsequent

(20) For comparison, the following $^{31}$P NMR signals have been observed: free $Ph_3P$ at −5.1 ppm; $(Ph_3P)_4Pd$ at 24.0 ppm; ($\eta^3$-cinnamyl)-$Pd^+(PPh_3)_n$ at 26.0 ppm; (*N*-piperidinyl)$PPh_2$ at 62.8 ppm; $[Ph_2(N\text{-piperidinyl})P]_mPd(PPh_3)_n$ at 29.3, 127.3, and 129.4 ppm.

(21) The $^1$H NMR spectrum of **32a** exhibited $\sigma$ 4.15−4.28 (m, 1 H), 5.43−5.59 (m, 1 H), and 6.01−6.16 (m, 1 H) ppm, which are all typical of the palladium $\eta^3$-complex protons.[22]

(22) For $^1$H NMR spectra of related $\eta^3$-complexes of Pd, see ref 23.

(23) Granberg, K. L.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **1992**, *114*, 6858. For correction, see: *J. Am. Chem. Soc.* **1994**, *116*, 10853.

(24) (a) Auburn, P. R.; Mackenzie, P. B.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2033. (b) Mackenzie, P. B.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2046.

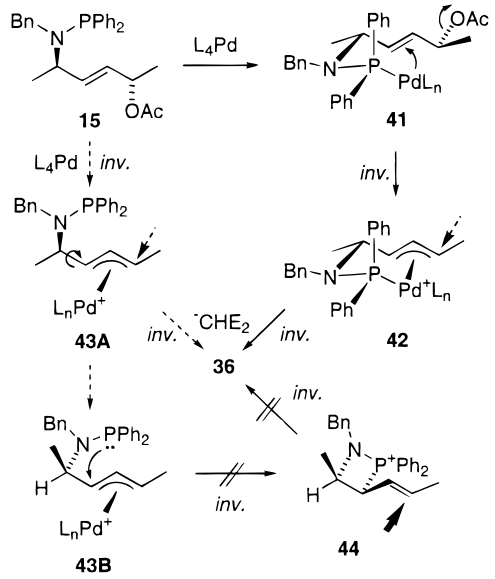
(25) The "Bosnich mechanism" was actually first proposed by Collman and Hegedus: (a) Collman, J. P.; Hegedus, L. S. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1980; p 692. For further examples, see refs 6b, 8, 23, 26, and (b) Bäckvall, J.-E.; Vågberg, J. O.; Zercher, G.; Genêt, J. P.; Denis, A. *J. Org. Chem.* **1987**, *52*, 5430. (c) Moreno-Mañas, M.; Ribas, J.; Virgili, A. *J. Org. Chem.* **1988**, *53*, 5328. (d) Kurosawa, H.; Ogoshi, S.; Chatani, N.; Kawasaki, Y.; Murai, S.; Ikeda, I. *Chem. Lett.* **1990**, 1745.

(26) Bäckvall, J.-E.; Granberg, K. L.; Heumann, A. *Isr. J. Chem.* **1991**, *31*, 17.

(27) With sterically hindered substrates, the nucleophilic attack can be dramatically slowed (i.e., $k_3 < k_1$), which is known to be manifested by (partial) loss of stereoselectivity.[23,26] However, the reaction of **9** with malonate anion proved to be highly stereoselective (vide supra) so that this possibility can be ruled out.

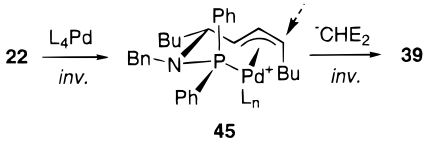
(28) Although $Ph_2P$ may seem to be much larger than $Ph_2CH$, their steric effect on the ultimate environment of the double bond is, in fact, similar, as revealed by molecular modeling. Therefore, if only the steric effect of the *N*-substituent were taken into account, little difference in reactivity (i.e., in the reaction rate) would be anticipated for **9** and **10**.

**Scheme 9**[a]



[a] For the legend, see Scheme 8.

**Scheme 10**[a]



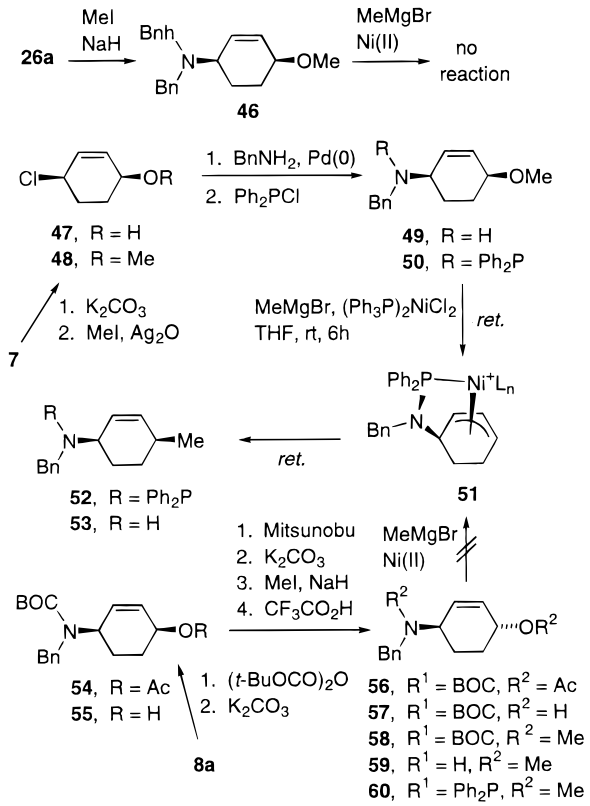
[a] For the legend, see Scheme 5.

second inversion on reaction with malonate anion then gives rise to **36**. An alternative route, not involving the precoordination, i.e., generating the $\eta^3$-complex **43**, followed by its reaction with malonate, would also produce **36**. However, this mechanism can be ruled out in view of the substantial acceleration of the reaction in the case of the phosphinous amide **15** (rt, 22 h) as compared to its *N*-benzhydryl counterpart **14** (66 °C, 16 h), which can only be attributed to the entropic factor associated with the precoordination (**15** → **41** → **42**). Nucleophilic participation of the phosphorus atom (**43A** → **43B** → **44**) can also be excluded, since this pathway would comprise a triple inversion that could not produce the *anti*-isomer **36**.[29]

Apparently, the *syn*-derivative **22** behaves similarly to **15** (Scheme 10); the precoordination of Pd (**22** → **45**) is supported by a substantial acceleration of the reaction (rt, 1.5 h) as compared to the benzhydryl derivative **21** (66 °C, >42 h).

**Nickel(0)-Catalyzed Allylic Substitution.** Consiglio has shown that allylic ethers undergo a nickel(0)-catalyzed reaction with Grignard reagents, which follows the *inv.*−*ret.* mechanism (**1** → **2** → **5**).[30] Hoveyda has recently reported on the stereocontrol of this process by a coordinating group located in the vicinity of the allylic moiety.[31] It was therefore desirable to investigate the reactivity of our model compounds in this context, to which end we prepared the *cis*- and *trans*-derivatives **46**, **50**, and **60**. The *cis*-configured *N*-benzhydryl derivative **46** was readily obtained on methylation of the alcohol **26a** (42%) (Scheme 11). Its $Ph_2P$ analogue **50** was synthesized as

**Scheme 11**[a]



[a] For the legend, see Scheme 8.

follows: the *cis*-chloroacetate **7**[9,10] was saponified (26−66%)[32] and the resulting alcohol **47** was methylated to afford the *cis*-chloromethoxycyclohexene **48** (87%).[33] The latter product was then treated with $PhCH_2NH_2$/Pd to give **49** (93%),[34,35] followed by the reaction with $Ph_2PCl$, which furnished the desired model compound **50** (85%). A rather elaborate scheme was adopted for the *trans*-derivative **60** since alternative, seemingly simpler, approaches failed. The successful route commenced with protection of **8a** as the BOC derivative **54**, which was then selectively hydrolyzed. The resulting *cis*-alcohol **55** (61% overall) was submitted to Mitsunobu reaction, and the *trans*-acetate **56** thus obtained was saponified to give the alcohol **57** (24% overall), methylation of which produced the *trans*-methyl ether **58**. Removal of the BOC group from **58**, followed by reaction of the resulting amine **59** (68% overall from **57**) with $Ph_2PCl$ produced the required *trans*-methoxy derivative **60** (69%).

As expected in view of Hoveyda's report,[31] the *cis*-methyl ether **46** proved inert, presumably due to the lack of a strongly coordinating group. By contrast, the $Ph_2P$ derivative **50** of the same configuration readily reacted with MeMgBr in the presence of $(Ph_3P)_2NiCl_2$ (3 mol %) to afford the *cis*-derivative **52** (THF, 0 → 15 °C, 6 h, 74%), which is consistent with double retention (**50** → **51** → **52**). The activating $Ph_2P$ group was then removed under mild conditions ($CF_3CO_2H$, rt, 2 h) to produce **53** (80%).

(29) Note that this analysis lends further credence to the rejection of a similar mechanism for the cyclic series (Scheme 7).

(30) (a) Consiglio, G.; Morandini, F.; Piccolo, O. *J. Am. Chem. Soc.* **1981**, *103*, 1846. (b) Consiglio, G.; Piccolo, O.; Roncetti, L.; Morandini, F. *Tetrahedron* **1986**, *41*, 2043.

(31) (a) Didiuk, M. T.; Morken, J. P.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1995**, *117*, 7273. (b) Didiuk, M. T.; Morken, J. P.; Hoveyda, A. H. *Tetrahedron* **1998**, *54*, 1117.

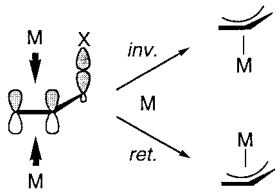
(32) This reaction, carried out with $K_2CO_3$ in THF, MeOH, and $H_2O$ at room temperature for 2 h, is capricious and the procedure shown in the Experimental Section represents the most successful batch.

(33) For an alternative synthesis of **48**, see: Rabasco, J.; Kass, S. R. *J. Org. Chem.* **1993**, *58*, 2633.

(34) On a small scale, **49** was synthesized on reaction of (*E*)-bis[(4-methoxy-1,3-$\eta^3$-cyclohexenyl)palladium chloride][35] with $PhCH_2NH_2$. However, in view of the stoichiometric nature of this reaction, it was only used in order to obtain an authentic sample of **49**.

(35) Bäckvall, J.-E.; Nordberg, R. E.; Zetterberg, K.; Åkermark, B. *Organometallics* **1983**, *2*, 1625.

**Scheme 12**




Rather surprisingly, the *trans*-epimer **60** failed to react in the expected manner: instead of the formation of **52**, a mixture of compounds was obtained on prolonged reaction time (rt, 48 h), in which a substantial amount of the starting material could still be detected; the crude reaction mixture did not exhibit the characteristic methyl doublet at 0.9 ppm in the $^1$H NMR spectrum, demonstrating that the partial conversion of the starting material did not give rise to even a detectable amount of **52**.

**Stereochemical and Mechanistic Considerations.** The prerequisite for the allylic substitution to occur is the ability of the system to attain a conformation in which the $\pi$-orbitals of the double bond and the $\sigma$-bond connecting the leaving group to the allylic carbon are aligned (Scheme 12).[36] According to this picture, there seems to be little stereoelectronic preference for the metal approach, so that both *inv.* and *ret.* pathways can be, a priori, expected.[37,38]

The *inv.* mechanism appears to be preferred on purely steric grounds (less steric hindrance) and in view of the possible interaction of the occupied d-orbital of the metal with the empty, antibonding orbitals of C=C ($\pi$*) and C−X ($\sigma$*), as in the case of Cu[39] and Pd[6b] (Figure 1). On the other hand, the *ret.* pathway may be encouraged by precoordination of the metal to the leaving group, which seems to be the case with Mo[4,5b] and, exceptionally, with Pd.[6,7] In this paper we have clearly demonstrated that the precoordination can also be effected by a neighboring group (rather than the leaving group), thereby opening the application of this methodology to further transition metals, namely Pd and Ni.

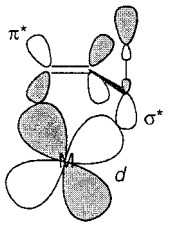
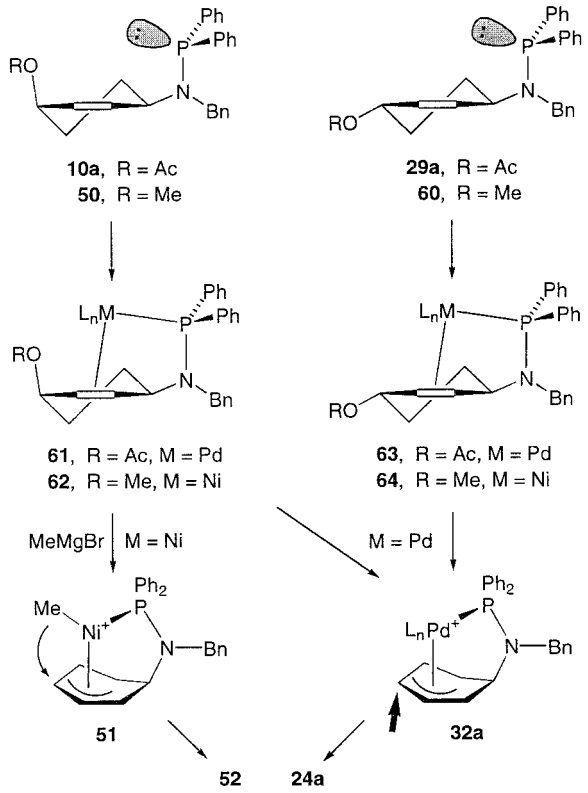



**Figure 1.** Interaction of the d-orbital of the metal with the $\pi$*- and $\sigma$*-orbitals of the allylic substrate.

**Scheme 13**[a]




[a] L = $Ph_3P$.

The required allylic alignment can easily be attained with the *cis*-configured cyclic substrates, such as **10a**; here, the bulky neighboring group can be assumed to be pseudoequatorial, forcing the leaving group into a pseudoaxial position (Scheme 13). As a result, the palladium chelated by the $Ph_2P$ group and the double bond can form the $\pi$-complex (**61** → **32a**), attack on which by malonate anion leads to the product of overall inversion (**24a**). In the *trans*-series (**29a**), the alignment is more difficult to attain; however, the entropic factor apparently compensates for the increased energy demand associated with the conformational change required for the alignment, so that the $\pi$-complex is also generated (**29a** → **63** → **32a**). Therefore, both **10a** and **29a** react readily at room temperature, furnishing the same product **24a**.

The Ni(0)-catalyzed reaction can be assumed to share the features of the $\eta^3$-complex formation with Pd(0). In fact, Hoveyda[31] has demonstrated the *inv.* mechanism for the complex formation in the acyclic series. Therefore, it may seem rather surprising to find **60** essentially inert despite the conceivable chelation in **64**. A possible rationalization of this discrepancy is that changing the conformation of **64** into the reactive one (with a pseudoaxial MeO group) is rather too costly energetically (in conjunction with the poor leaving capability of $MeO^-$), whereas in Hoveyda's example, the flexible aliphatic chain can assume the conformation required for the *inv.* mechanism relatively easily (as it did in our examples with Pd).

The very high regioselectivity, i.e., the exclusive nucleophilic attack at the distal position with respect to the bulky amino group, can be understood in terms of steric hindrance at the proximal position and is in line with Bäckvall observations.[9,10] The attack on the proximal position is rare and has only been reported either with nucleophiles other than $\beta$-dicarbonyls (e.g., $Et_2NH$)[11,35] or when $PhSO_2$ was employed as the leaving group

(36) The maximum deviation from the perfect alignment that is tolerated, seems to be ∼30°, as derived from the investigation of Wagner−Meerwein rearrangements in a series of rigid, polycyclic skeletons: Saunders: M.; Chandrasekhar, J.; Schleyer, P. v. R. Rearrangements of Carbocations. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic: New York, 1980; Vol. 1, pp 24−34.

(37) This scenario parallels the occurrence of both *anti*- and *syn*-mechanisms for the E2 elimination reactions. For leading reviews, see: (a) Sicher, J. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 200. (b) Sicher, J. *Pure Appl. Chem.* **1971**, *22*, 655. (c) Bartsch, R. A.; Závada, J. *Chem. Rev.* **1980**, *80*, 453.

(38) For stereoelectronic effects in general, see: (a) Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon: Oxford, 1983. For the stereochemical dichotomy in allylic substitution ($S_N2'$), see: (b) Magid, R. M. *Tetrahedron* **1980**, *36*, 1901. (c) Paquette, L. A.; Stirling, C. J. M. *Tetrahedron* **1992**, *48*, 7383.

(39) (a) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1984**, *25*, 3063. (b) Corey, E. J.; Hannon, F. J. *Tetrahedron Lett.* **1990**, *31*, 1393. (c) Hill, R. S.; Becalska, A.; Chiem, N. *Organometallics* **1991**, *10*, 2104.

(40) Bäckvall, J.-E.; Juntunen, S. K. *J. Am. Chem. Soc.* **1987**, *109*, 6396.

(rather than AcO).[40] While this manuscript was undergoing a referee review, another example has been published by Krafft, in which the regioslectivity of the nucleophilic attack on the $\eta^3$-Pd-complex is controlled by the neighboring, small to medium size amino group.[41] In some examples, this effect also led to the overall inversion of configuration with malonate nucleophile.[41]

## Conclusions

We have demonstrated, for the first time, that the steric course of the $\eta^3$-Pd−complex formation from allylic acetates can be altered by a neighboring group capable of precoordinating the catalyst (**10** → **32** → **24** in Scheme 6). This new approach appears to be more general than the previously reported methods relying on precoordination to the leaving group,[6,7] thereby offering a substantially broader application, especially for the construction of cyclic, polyfunctional molecules. The versatility of this method is enhanced by the ready introduction of the coordinating $Ph_2P$ group ($Ph_2PCl$, 35 °C) and its removal ($CF_3CO_2H$, rt). The related, Ni(0)-catalyzed reaction with a Grignard reagent (**50** → **51** → **52** in Scheme 11) extends the scope of this methodology as it broadens the choice of the nucleophile and the stereochemical outcome.

This investigation has demonstrated that the retention mechanism **1** → **4** may be more common than originally thought, since it has now been observed for three transition metals: Pd, Mo, and Ni.[42] Our new findings have also helped to fill a few gaps in the C−C bond-forming methodology via allylic substitution (Scheme 1) in terms of the choice of the nucleophile, stereochemistry, and the catalyst. The updated menu can be summarized as follows: (1) The *inv.*−*inv.* mechanism is the classical one for the combination of Pd and stabilized C-nucleophiles, such as malonates.[1] (2) The *inv.*−*ret.* path is typical for Pd and nonstabilized nucleophiles and organometallics,[2] and does also occur with Ni and organometallics.[30,31] (3) The *ret.*−*inv.* route requires precoordination of the catalyst either to the leaving group[6,7] or to a neighboring group (as shown in this paper) and has been demonstrated for Pd and stabilized C-nucleophiles. This sequence also works for stoichiometric, Mo(0)-mediated reactions involving isolation of the $\eta^3$-complex, followed by its reaction with malonate anions and the like.[5] (4) The *ret.*−*ret.* mechanism has been demonstrated for Mo(0)-catalyzed reactions with malonates as nucleophiles,[4] and for Ni with a Grignard reagent (this paper); again, the prerequisite for the latter reaction to occur is the precoordination of the catalyst to a neighboring group.

The *ret.* mechanism (**1** → **4**) is currently limited to those allylic systems, which cannot attain a conformation suitable for the *inv.* mechanisms (e.g., by rotation). Since we have demonstrated the stereochemical switch (**1** → **2**/**4**) with the aid of 1,4-heterodisubstituted cycloalkenes, this protocol can be regarded as an extension of the Bäckvall[9,10] methodology; however, further applications beyond this framework can easily be envisaged. One such example is the stereodirection of the organocuprate attack on the enone system by means of a neighboring *o*-(diphenylphosphino)benzoyloxy group,[43,44] published while this paper was undergoing a reviewing process.

(41) Krafft, M. E.; Wilson, A. M.; Fu, Z.; Procter, M. J.; Dasse, O. A. *J. Org. Chem.* **1998**, *63*, 1748.

(42) For a similar stereochemical switch in the cuprate-mediated allylic substitution, see: (a) Gallina, C.; Ciattini, P. G.; *J. Am. Chem. Soc.* **1979**, *101*, 1035. (b) Goering, H. L.; Kantner, S. S.; Tseng, C. C. *J. Org. Chem.* **1983**, *48*, 715. (c) Tseng, C. C.; Yen, S. J.; Goering, H. L. *J. Org. Chem.* **1986**, *51*, 2892 and refs given therein. (d) Valverde, S.; Bernabé, M.; Garcia-Ochoa, S.; Gómez, A. M. *J. Org. Chem.* **1990**, *55*, 2294 and refs given therein.

(43) Breit, B. *Angew. Chem., Int. Ed.* **1998**, *37*, 525.

## Experimental Section

**General Methods.** Melting points were determined on a Kofler block and are uncorrected. The NMR spectra were recorded in $CDCl_3$, $^1H$ at 250 MHz, $^{13}C$ at 62.9 MHz, and $^{31}P$ at 101.3 MHz with chloroform-$d_1$ ($\delta$ 7.26, $^1H$; $\delta$ 77.0, $^{13}C$) as internal standard. The IR spectra were recorded for a thin film between KBr plates unless otherwise stated. The mass spectra (EI and/or CI) were measured on a dual sector mass spectrometer using direct inlet and the lowest temperature enabling evaporation. The GC−MS analysis was performed with RSL-150 column (25 m × 0.25 mm). All reactions were performed under an atmosphere of dry, oxygen-free nitrogen in oven-dried glassware twice evacuated and filled with the nitrogen. Solvents and solutions were transferred by syringe-septum and cannula techniques. All solvents for the reactions were of reagent grade and were dried and distilled immediately before use as follows: diethyl ether and tetrahydrofuran (THF) from sodium/benzophenone; dichloromethane from calcium hydride. All reagents were purchased at highest commercial quality and used without further purification, unless otherwise stated. Yields are given for isolated product showing one spot on a TLC plate and no impurities detectable in the NMR spectrum. The identity of the products prepared by different methods was checked by comparison of their NMR, IR, and MS data and by the TLC behavior. Detailed experimental procedures, $R_f$ values, HRMS, and elemental analyses are given in the Supporting Information.

**General Procedure for the Preparation of Benzylamines from the Corresponding Chlorides via Pd(0)-Catalyzed Allylic Substitution (Method I).** To a solution of the allylic chloride (5.47 mmol) and benzylamine (2.00 g, 18.7 mmol) in toluene (40 mL) was added tetrakis(triphenylphosphine)palladium(0) (300 mg, 261 $\mu$mol, 4.8 mol %) in one portion, and the solution was allowed to stir at room temperature for 18−58 h. The mixture was then concentrated by evaporation to ~5 mL and purified by chromatography ($SiO_2$, petroleum ether−ether 1:1 or 1:2) to give the allylic amine.

**General Procedure for Derivatization of Amines with Benzhydryl (Method II).** To a solution of the amine (1.26 mmol) and triethylamine (600 $\mu$L, 436 mg, 4.30 mmol) in dichloromethane (5 mL) was added diphenylmethyl bromide (1.00 g, 4.05 mmol) in a single portion. The mixture was heated to reflux and stirred for 40−88 h. Water (10 mL) was then added, the layers were separated, and the aqueous phase was extracted with dichloromethane (2 × 15 mL). The organic portions were combined, and the solvent was evaporated. Chromatography ($SiO_2$, petroleum ether−ether 20:1, 15:1, or 10:1) afforded the benzhydryl derivative.

**General Procedure for Derivatization of Amines with Chlorodiphenylphosphine (Method III).** Chlorodiphenylphosphine (300 $\mu$L, 369 mg, 1.67 mmol) was added dropwise to a solution of the amine (1.23 mmol) and triethylamine (250 $\mu$L, 182 mg, 1.80 mmol) in ether (6 mL), and the solution was brought to reflux and stirred for 14−22 h. The mixture was then cooled and filtered through a short plug of alumina, and the solvent was evaporated. The crude product was purified on an aluminum oxide column (petroleum ether−ether 4:1 or 1:1) to afford the diphenylphosphinous amide.

**General Procedure for the Pd(0)-Catalyzed Allylic Substituion with Dimethyl Sodiomalonate (Method IV).** Dimethyl malonate (150 $\mu$L, 173 mg, 1.31 mmol) was added dropwise to a suspension of sodium hydride (50 mg, 60% suspension in mineral oil, 1.25 mmol) in THF (3 mL). After 5 min of stirring, tetrakis(triphenylphosphine)palladium-(0) (40 mg, 35 $\mu$mol, 11 mol %) was added, followed by a solution of the allylic acetate (315 $\mu$mol) in THF (2 mL). The mixture was either refluxed for 16−42 h, or stirred at room temperature for 20 h or 15−90 min. The solution was then cooled, poured into water (5 mL), and extracted with $CH_2Cl_2$ (2 × 10 mL). The organic portions were combined, and the solvent was evaporated. Chromatography ($SiO_2$, petroleum ether−ether 6:1 or 5:1 or $Al_2O_3$, petroleum ether−ether 4:1 or 3:1 or ether) furnished the substitution product.

(44) Our attempts at controlling the cuprate addition in the case of the conjugated ketone, prepared by oxidation of the allylic alcohol **26a**, were unsuccessful. Therefore, it appears that this type of control, as demonstrated by Breit,[43] requires the coordinating group to be located at the carbon more distant than in the $\delta$-position.

**General Procedure for Removal of the $Ph_2P$ Group (Method V).** Trifluoracetic acid (2 mL) was added to the phosphinous amide (223 mmol), and the solution was allowed to stir at room temperature for 1.5−14 h. The mixture was then evaporated, treated with $NaHCO_3$ (saturated, aqueous, 5 mL), and extracted with $CH_2Cl_2$ (3 × 5 mL). The combined organic extracts were evaporated, and the residue was purified by chromatography ($SiO_2$, petroleum ether−ether 1:1 or 1:2) to give the amine.

**(*Z*)-1-Acetoxy-4-(benzylamino)cyclohex-2-ene (8a)** was obtained from (*Z*)-1-acetoxy-4-chlorocyclohex-2-ene (**7a**)[10] using method I (rt, 24 h) as a colorless oil (88%), whose spectral data are identical to those described in the literature:[11] IR (film) $\nu$ 3320, 3021, 2942, 2859, 1745, 1450, 1367, 1240, 1025 $cm^{-1}$; $^1H$ NMR $\delta$ 1.28−1.82 (m, 4 H, $CH_2$-$CH_2$), 1.96 (s, 3 H, $CH_3$), 3.05−3.15 (m, 1 H, C*H*N), 3.71 and 3.73 (AB system, $J$ = 13 Hz, 2 × 1 H, C$H_2$Ph), 5.06−5.14 (m, 1 H, C*H*OAc), 5.68 and 5.92 (2 × br d, 2 × $J$ = 11 Hz, 2 × 1 H, CH═CH), 7.11−7.28 (m, 5 H, Ar); $^{13}C$ NMR $\delta$ 21.7 ($CH_3$), 25.6 and 26.5 ($CH_2CH_2$), 51.4 ($CH_2$Ph), 52.8 (*C*HN), 67.7 (*C*HOAc), 126.8 (CH, Ph), 127.4 (olefinic *C*HCHOAc), 128.5 (2 × CH of Ph) and 135.9 (olefinic *C*HCHN), 140.8 (Ar *ipso* C), 171.1 (C═O); MS (CI) *m*/*z* (%) 246 (100, $MH^+$), 186 (25), 159 (25), 91 (50).

**(*Z*)-1-Acetoxy-4-(benzylamino)cyclohept-2-ene (8b)** was obtained from (*Z*)-1-acetoxy-4-chlorocyclohept-2-ene (**7b**)[10] using method I (rt, 20 h) as a colorless oil (90%): IR $\nu$ 3311, 3019, 2912, 2842, 1725, 1600, 1443, 1364, 1235, 1018, 725 $cm^{-1}$; $^1H$ NMR $\delta$ 1.21−1.88 (m, 6 H, $CH_2CH_2CH_2$), 1.91 (s, 3 H, $CH_3$), 3.19 (br d, $J$ = 12 Hz, 1 H, C*H*N), 3.61 and 3.67 (AB system, $J$ = 13 Hz, 2 × 1 H, C$H_2$Ph), 5.21 (br d, $J$ = 11.5 Hz, 1 H, C*H*OAc), 5.49−5.65 (m, 2 H, CH═CH), 7.06−7.19 (m, 5 H, Ar); $^{13}C$ NMR $\delta$ 21.7 ($CH_3$), 25.7 ($CH_2CH_2CH_2$), 32.9 and 33.8 ($CH_2CH_2CH_2$), 52.0 ($CH_2$Ph), 58.6 (*C*HN), 74.5 (*C*HOAc) 127.4, 128.6, 128.9, 133.3, and 136.3 (Ar *C*H's and *C*H═*C*H), 140.6 (Ar *ipso* C), 170.6 (*C*═O); MS (CI) *m*/*z* (%) 259 (5, $M^{\bullet+}$), 199 (40), 156 (20), 91 (100).

**(*Z*)-1-Acetoxy-4-[benzyl(diphenylmethyl)amino]cyclohex-2-ene (9a)** was obtained from **8a** using method II (40 °C, 88 h) as a colorless oil (58%): IR $\nu$ 3022, 2942, 2848, 1734, 1503, 1371, 1240, 1033, 900 $cm^{-1}$; $^1H$ NMR $\delta$ 1.01−1.74 (m, 4 H, $CH_2CH_2$), 1.92 (s, 3 H, $CH_3$), 3.49 (br t, $J$ = 8.5 Hz, 1 H, C*H*N), 3.64 and 3.65 (AB system, $J$ = 14 Hz, 2 × 1 H, C$H_2$Ph), 4.90−4.97 (m, 2 H, C*H*$Ph_2$ and C*H*OAc), 5.59−5.74 (m, 2 H, C*H*═C*H*), 7.05−7.32 (m, 15 H, Ar); $^{13}C$ NMR $\delta$ 21.7 ($CH_3$), 22.8 and 28.0 ($CH_2CH_2$), 51.9 ($CH_2$Ph), 55.5 (*C*HN), 66.4 (*C*HOAc), 69.0 (*C*H$Ph_2$), 126.8, 126.9, 127.2, 127.3, 127.4, 128.4, 128.5, 128.8, 129.2, 129.6 and 137.8 (Ar *C*H's and *C*H═*C*H), 142.1, 142.9, 143.8 (Ar *ipso* C), 171.0 (*C*═O); MS (EI) *m*/*z* (%) 411 (5, $M^{\bullet+}$), 383 (5), 351 (5), 325 (30), 167 (100), 91 (50).

**(*Z*)-1-Acetoxy-4-[benzyl(diphenylmethyl)amino]cyclohept-2-ene (9b)** was obtained from **8b** using method II (40 °C, 40 h) as a colorless oil (81%): IR (film) $\nu$ 3057, 3019, 2820, 2844, 1736, 1660, 1597, 1488, 1445, 1369, 1230, 1021 $cm^{-1}$; $^1H$ NMR $\delta$ 1.16−1.84 (m, 6 H, $CH_2CH_2CH_2$), 1.93 (s, 3 H, $CH_3$), 3.51 (br d, $J$ = 12 Hz, 1 H, C*H*N), 3.64 and 3.67 (AB system, $J$ = 13 Hz, 2 × 1 H, C$H_2$Ph), 4.82 (s, 1 H, C*H*$Ph_2$) 5.10 (br d, $J$ = 10.5 Hz, 1 H, C*H*OAc), 5.46 and 5.80 (2 × br d, 2 × $J$ = 12.5 Hz, 2 × 1 H, CH═CH), 7.05−7.32 (m, 15 H, Ar); $^{13}C$ NMR $\delta$ 21.8 ($CH_3$), 25.9 ($CH_2CH_2CH_2$), 32.4 and 32.9 ($CH_2$-$CH_2CH_2$), 51.9 ($CH_2$Ph), 59.4 (*C*HN), 68.5 (*C*H$Ph_2$), 74.8 (*C*HOAc), 127.0, 127.3, 127.4, 127.7, 128.5, 128.6, 128.9, 129.6, 129.6, 132.3, and 136.2 (Ar *C*H's and *C*H═*C*H), 141.6, 142.2, 142.5 (Ar *ipso* C), 170.7 (*C*═O); MS (EI) *m*/*z* (%) 425 (10, $M^{\bullet+}$), 365 (100), 274 (80).

**(*Z*)-1-Acetoxy-4-[benzyl(diphenylphosphinous)amidyl]cyclohex-2-ene (10a)** was obtained from **8a** using method III (34 °C, 18 h) as a clear oil (68%): IR (film) $\nu$ 3059, 2940, 2846, 1731, 1434, 1370, 1244, 1082, 1027 $cm^{-1}$; $^1H$ NMR $\delta$ 1.68−1.99 (m, 4 H, $CH_2CH_2$), 2.11 (s, 3 H, $CH_3$), 3.61−3.79 (m, 1 H, C*H*N), 4.22 and 4.33 (2 × dd, 2 × $J_{H,P}$ = 5 Hz, 2 × $J_{H,H}$ = 15 Hz, 2 × 1 H, C$H_2$Ph), 5.15 (br s, 1 H, C*H*OAc), 5.88 and 6.00 (2 × br d, 2 × $J$ = 11.5 Hz, 2 × 1 H, CH═CH), 7.10−7.66 (m, 15 H, Ar); $^{13}C$ NMR $\delta$ 21.8 ($CH_3$), 25.6 and 27.6 ($CH_2CH_2$), 53.6 ($CH_2$Ph), 56.4 (*C*HN), 66.4 (*C*HOAc), 126.5, 127.3, 128.5, 128.6, 128.7, 128.9, 129.1, 132.5, 132.8 and 133.2 (Ar *C*H's and *C*H═*C*H), 138.4 and 140.3 (2×) (Ar *ipso* C), 171.2 (*C*═O); $^{31}P$ NMR $\delta$ 51.68; MS (EI) *m*/*z* (%) 429 (10, $M^{\bullet+}$), 370 (50), 290 (40), 201 (35), 183 (75), 91 (100).

**(*Z*)-1-Acetoxy-4-[benzyl(diphenylphosphinous)amidyl]cyclohept-2-ene (10b)** was obtained from **8a** using method III (34 °C, 16 h) as a clear oil (85%): IR (film) $\nu$ 3051, 2924, 1743, 1591, 1438, 1370 $cm^{-1}$; $^1H$ NMR $\delta$ 1.30−1.95 (m, 6 H, $CH_2CH_2CH_2$), 2.05 (s, 3 H, $CH_3$), 3.72 (br d, $J$ = 18 Hz, 1 H, C*H*N), 4.11 and 4.22 (2 × dd, $J_{H,P}$ = 5.5 and 7 Hz, $J_{H,H}$ = 13 Hz, 2 × 1 H, C$H_2$Ph), 5.29 (br d, $J$ = 11 Hz, 1 H, C*H*OAc), 5.65 and 6.06 (2 × br d, 2 × $J$ = 12 Hz, 2 × 1 H, CH═CH), 7.18−7.65 (m, 15 H, Ar); $^{13}C$ NMR $\delta$ 21.8 ($CH_3$), 25.9 ($CH_2CH_2CH_2$), 32.9 and 33.6 ($CH_2CH_2CH_2$), 54.1 ($CH_2$Ph), 60.7 (*C*HN), 74.8 (*C*HOAc), 127.5, 128.7, 128.8, 128.9, 129.0, 129.3, 132.2, 132.6, 132.9, 133.5, and 137.3 (Ar *C*H's and *C*H═*C*H), 140.0, 140.2, 140.4 (Ar *ipso* C), 170.7 (*C*═O); $^{31}P$ NMR $\delta$ 50.33; MS (EI) *m*/*z* (%) 443 (35, $M^{\bullet+}$), 400 (35), 384 (60), 352 (100), 183 (95).

**(*E*)-(2*S**,5*R**)-2-Acetoxy-5-[benzyl(diphenylmethyl)amino]hex-3-ene (14)** was obtained from **13** using method II (40 °C, 44 h) as a colorless oil (53%): IR $\nu$ 3020, 2963, 1722, 1659, 1600, 1491, 1449, 1365, 1031 $cm^{-1}$; $^1H$ NMR $\delta$ 0.98 (d, $J$ = 8 Hz, 3 H, C$H_3$CHN), 1.06 (d, $J$ = 7.5 Hz, 3 H, C$H_3$CHO), 1.92 (s, 3 H, $CH_3CO$), 3.38−3.46 (m, 1 H, C*H*N), 3.48 and 3.62 (AB system, $J$ = 15 Hz, 2 × 1 H, C$H_2$Ph), 4.85 (s, 1 H, C*H*$Ph_2$), 5.10−5.28 (m, 2 H, C*H*OAc and C*H*═CH), 5.55 (dd, $J$ = 6, 14 Hz, CH═C*H*), 7.00−7.34 (m, 15 H, Ar); $^{13}C$ NMR $\delta$ 15.8, 19.3 and 20.4 (3 × $CH_3$), 49.9 ($CH_2$Ph), 53.7 (*C*HN), 68.9 and 69.7 (*C*HOAc and *C*H$Ph_2$), 125.1, 125.5, 125.8, 126.5, 126.9, 127.0, 127.1, 127.2, 127.5, 127.7, 127.8, 127.9, 129.0, 129.1 and 132.9 (Ar *C*H's and *C*H═*C*H), 141.0, 141.7, 141.9 (Ar *ipso* C), 169.2 (*C*═O); MS (EI) *m*/*z* (%) 413 (5, $M^{\bullet+}$), 398 (40), 167 (100).

**(*E*)-(2*S**,5*R**)-2-Acetoxy-5-[benzyl(diphenylphosphinous)amidyl]-hex-3-ene (15)** was obtained from **13** using method III (34 °C, 18 h) as a clear oil (68%): IR (film) $\nu$ 3082, 3021, 2971, 2920, 1744, 1602, 1584, 1491, 1450, 1369 $cm^{-1}$; $^1H$ NMR $\delta$ 1.14 (d, $J$ = 6.5 Hz, 3 H, C$H_3$CHN), 1.24 (d, $J$ = 7 Hz, 1 H, C$H_3$CHOAc), 1.94 (s, 3 H, $CH_3$-CO), 3.47 (ddq, $J$ = 6, 16.5, 6.5 Hz, 1 H, C*H*N), 3.90 and 4.07 (2 × dd, 2 × $J$ = 4, 15 Hz, 2 × 1 H, C$H_2$Ph), 5.15−5.34 (m, 2 H, C*H*OAc and C*H*═CH), 5.60 (dd, 2 × $J$ = 7.5, 14.5 Hz, 1 H, CH═C*H*), 6.85−7.36 (m, 15 H, Ar); $^{13}C$ NMR $\delta$ 20.7, 20.9 and 21.8 (3 × $CH_3$), 53.7 ($CH_2$Ph), 56.0 (*C*HN), 70.9 (*C*HOAc), 127.2, 128.6, 128.7, 128.8, 129.0, 130.2, 132.7, 133.0, 133.3 and 135.2 (Ar *C*H's and *C*H═*C*H), 140.3 (2×) and 140.5 (Ar *ipso* C), 170.6 (*C*═O); $^{31}P$ NMR $\delta$ 47.83; MS (EI) *m*/*z* (%) 431 (5, $M^{\bullet+}$), 372 (15), 344 (100), 298 (25), 256 (50).

**(*E*)-(5*R**,8*R**)-5-Acetoxy-8-chlorododec-6-ene (19).** To a solution of hex-1-yne **16** (4.10 g, 50.0 mmol) in hexanes (25 mL) at 0 °C was added diisobutylaluminum hydride (1 M in hexanes, 50 mL, 50.0 mmol). The solution was warmed to 40 °C and stirred for 16 h. Volatile components were then evaporated, and the residue (**17**) was dissolved in THF (50 mL) and cooled to 0 °C. CuCl (5.50 g, 55.5 mmol) was then added in portions over 10 min, and the suspension allowed to warm to room temperature and stir for 4 h. The black suspension was then poured onto a stirred mixture of $H_2SO_4$ (5%, 100 mL) and petroleum ether (100 mL), the phases were separated, and the aqueous layer further extracted with ether−petroleum ether 1:1 (2 × 100 mL). The combined organic layers were then evaporated to give **18** as a clear oil (3.20 g). A solution of the latter oil in hexanes (50 mL) was added dropwise over 12 h to a vigorously stirred suspension of $(AcO)_2Pd$ (500 mg, 2.30 mmol), *p*-benzoquinone (10.0 g, 91.0 mmol), LiCl (4.00 g, 92.0 mmol), $LiOAc·2H_2O$ (9.00 g, 86.0 mmol), and acetic acid (50 mL) in hexanes (50 mL). The reaction mixture was stirred at room temperature for a further 42 h, and then AcOEt (300 mL) was added. The solution was extracted with NaOH (2M, 2 × 100 mL), $NaHCO_3$ (saturated, aqueous, 2 × 100 mL) and water, and then the combined aqueous extracts were further extracted with ether (2 × 200 mL). The combined organic layers were evaporated, and purified by chromatography ($SiO_2$, petroleum ether−ether 40:1) to afford **19** as a pale red oil (1.07 g, 4.10 mmol, 21%): $R_f$ (petroleum ether−ether 15:1) 0.60; IR (film) $\nu$ 2957, 2929, 2860, 1740, 1468, 1239, 1020 $cm^{-1}$; $^1H$ NMR $\delta$ 0.75−0.88 (m, 6 H, 2 × $CH_2CH_3$), 1.15−1.75 (m, 12 H, $CH_2CH_2CH_2$), 1.98 (s, 3 H, $CH_3CO$), 4.26 (q, $J$ = 7 Hz, 1 H, C*H*Cl), 5.17 (q, $J$ = 6 Hz, 1 H, C*H*OAc), 5.57 and 5.61 (2 × dd, $J$ = 5.5, 15.5 and 7, 15.5 Hz, 2 × 1 H, C*H*═C*H*); $^{13}C$ NMR $\delta$ 14.3 (2 × $CH_2CH_3$), 22.5 and 22.8 (3 × $CH_2CH_3$), 27.6 and 29.0 (2 × $CH_2Et$), 34.3 ($CH_2CHCl$), 37.4 ($CH_2CHOAc$), 62.3 (*C*HCl), 73.7

(*C*HOAc), 131.0 and 137.3 (*C*H═*C*H), 170.6 (C═O); MS [CI($NH_3$)] *m*/*z* (%) 278 (100, $MNH_4^+$), 225 (45), 183 (15), 182 (15), 165 (20).

**(*E*)-(5*R**,8*R**)-5-Acetoxy-8-(benzylamino)dodec-6-ene (20)** was obtained from **19** using method I (rt, 58 h) as a pale pink oil (72%): IR (film) $\nu$ 3320, 2958, 2930, 2857, 1737, 1370, 1238, 1019, 972 $cm^{-1}$; $^1H$ NMR $\delta$ 0.77−0.85 (m, 6 H, 2 × $CH_2CH_3$), 1.25−1.80 (m, 12 H, $CH_2CH_2CH_2$), 1.99 (s, 3 H, $CH_3CO$), 2.89−3.08 (1 H, m, C*H*N), 3.54 and 3.72 (AB system, $J$ = 13 Hz, 2 H, $CH_2Ph$), 5.13−5.21 (m, 1 H, C*H*OAc), 5.34−5.47 (m, 2 H, 1 H, CH═CH), 7.16−7.27 (5H, m, Ar); $^{13}C$ NMR $\delta$ 14.4 (2 × $CH_2CH_3$), 21.7 ($CH_3C$═O), 22.8 and 23.1 (2 × $CH_2CH_3$), 27.8 and 28.5 (2 × $CH_2Et$), 34.6 ($CH_2CHN$), 35.9 ($CH_2$-CHOAc), 51.6 ($CH_2Ph$), 62.3 (*C*HN), 74.9 (*C*HOAc), 127.2, 128.6, 128.7, 130.7 and 136.5 (Ar *C*H's and *C*H═*C*H), 140.5 (Ar *ipso* C), 170.6 (C═O); MS (EI) *m*/*z* (%) 332 (100, $MH^+$), 274 (50), 272 (50), 225 (10), 183 (65).

**(*E*)-(5*R**,8*R**)-5-Acetoxy-8-[benzyl(diphenylmethyl)amino]dodec-6-ene (21)** was obtained from **20** using method II (40 °C, 72 h) as a colorless oil (48%): IR $\nu$ 3020, 2957, 2923, 1736, 1239 $cm^{-1}$; $^1H$ NMR $\delta$ 0.61−0.85 (m, 6 H, 2 × $CH_2CH_3$), 0.97−1.43 (m, 12 H, $CH_2CH_2$-$CH_2$), 1.95 (s, 3 H, $CH_3CO$), 3.09 (q, $J$ = 7.5 Hz, 1 H, C*H*N), 3.45 and 3.71 (AB system, $J$ = 15.5 Hz, 2 H, $CH_2Ph$), 4.80 (s, 1 H, C*H*$Ph_2$), 5.00−5.16 (m, 2 H, C*H*OAc and C*H*═CH), 5.42 (dd, $J$ = 9, 14.5 Hz, 1 H, CH═C*H*), 6.85−7.29 (m, 15 H, Ar); $^{13}C$ NMR $\delta$ 14.5 (2 × $CH_2CH_3$), 21.9 ($CH_3C$═O), 22.9 and 23.0 (2 × $CH_2CH_3$), 27.8 and 29.5 (2 × $CH_2Et$), 33.0 ($CH_2CHN$), 34.6 ($CH_2CHOAc$), 51.8 ($CH_2$-Ph), 61.4 (*C*HN), 70.6 (*C*H$Ph_2$), 75.2 (*C*HOAc), 126.4, 127.0, 127.2, 127.9, 128.2, 128.3, 128.4, 128.9, 129.0, 129.7, 131.7, and 132.7 (Ar *C*H's and *C*H═*C*H), 142.7, 143.1 and 143.9 (Ar *ipso* C), 170.7 (C═O).

**(*E*)-(5*R**,8*R**)-5-Acetoxy-8-[benzyl(diphenylphosphinous)amidyl]-dodec-6-ene (22)** was obtained from **20** using method III (34 °C, 20 h) as a clear oil (50%): $^1H$ NMR $\delta$ 0.61−0.78 (m, 6 H, 2 × $CH_2CH_3$), 0.91−1.87 (m, 12 H, $CH_2CH_2CH_2$), 1.91 (s, 3 H, $CH_3CO$), 2.96−3.15 (1 H, m, C*H*N), 3.76 and 4.05 (2 × dd, $J$ = 2, 15, and 2.5, 2 × 1 H, $CH_2Ph$), 5.03−5.18 (m, 2 H, C*H*OAc and C*H*═CH), 5.54 (dd, $J$ = 9, 14.5 Hz, 1 H, CH═C*H*), 6.72−7.43 (m, 15 H, Ar); $^{13}C$ NMR $\delta$ 14.8 (2 × $CH_2CH_3$), 21.8 ($CH_3C$═O), 22.9 (2 × $CH_2CH_3$), 27.8 and 29.2 (2 × $CH_2Et$), 34.6 ($CH_2CHN$), 34.9 ($CH_2CHOAc$), 53.7 ($CH_2Ph$), 61.3 (*C*HN), 74.6 (*C*HOAc), 127.2, 128.5, 128.6, 128.7, 128.8, 129.0, 130.4, 132.9, 133.2, 134.8 and 134.9 (Ar *C*H's and *C*H═*C*H), 140.2, 140.6 and 140.8 (Ar *ipso C*H's) 170.6 (C═O); $^{31}P$ NMR $\delta$ 46.47; MS (EI) *m*/*z* (%) 515 (25, $M^{\bullet+}$), 456 (70), 386 (100), 297 (30), 183 (65), 91 (60).

**(*Z*)-Dimethyl [4-[benzyl(diphenylmethyl)amino]cyclohex-2-en-1-yl]malonate (23a)** was obtained from **9a** using method IV (66 °C, 22 h, with 7.6 mol % of Pd) as a colorless oil (73%): IR (film) $\nu$ 3061, 3022, 2951, 1759, 1736, 1492, 1451, 1434, 1155, 1026 $cm^{-1}$; $^1H$ NMR $\delta$ 1.36−1.55 (m, 4 H, $CH_2CH_2$), 2.62−2.74 (m, 1 H, C*H*C$H(CO_2Me)_2$) 3.22 (d, $J$ = 11 Hz, 1 H, C*H*$(CO_2Me)_2$), 3.48−3.55 (m, 1 H, C*H*N), 3.60 (s, 6 H, 2 × $CH_3$), 3.64 and 3.68 (AB system, $J$ = 13 Hz, 2 × 1 H, $CH_2Ph$), 4.89 (s, 1 H, C*H*$Ph_2$), 5.52 and 5.53 (AB system, $J$ = 13 Hz, 2 H, C*H*═C*H*), 7.06−7.24 (m, 15 H, Ar); $^{13}C$ NMR $\delta$ 22.9 and 25.4 ($CH_2CH_2$), 34.2 (*C*HCH$(CO_2Me)_2$), 51.9 ($CH_2Ph$), 52.8 and 52.9 (2 × *C*$H_3$), 55.1 (*C*HN), 56.4 (*C*H$(CO_2Me)_2$), 69.0 (*C*H$Ph_2$), 126.8, 127.2, 128.5, 129.2, 129.6, 129.8, and 134.1 (Ar *C*H's and *C*H═*C*H), 142.1, 142.4, 143.0 (Ar *ipso* C), 169.0 and 169.2 (2 × *C*═O); MS (EI) *m*/*z* (%) 483 (10, $M^{\bullet+}$), 299 (10), 208 (50), 167 (100), 91 (45).

**(*Z*)-Dimethyl [4-[benzyl(diphenylmethyl)amino]cyclohept-2-en-1-yl]malonate (23b)** was obtained from **9b** using method IV (66 °C, 22 h, with 11 mol % of Pd) as a colorless oil (66%): IR (film) $\nu$ 3024, 2920, 2858, 1740, 1492 $cm^{-1}$; $^1H$ NMR $\delta$ 1.00−1.80 (m, 6 H, $CH_2$-$CH_2CH_2$), 2.63−2.73 (m, 1 H, C*H*C$H(CO_2Me)_2$) 3.26 (d, $J$ = 9.5 Hz, 1 H, C*H*$(CO_2Me)_2$), 3.60−3.75 (m, 3 H, $CH_2Ph$, C*H*N), 3.61 and 3.62 (2 × s, 2 × 3H, 2 × *C*$H_3$), 4.83 (s, 1 H, C*H*$Ph_2$), 5.37 and 5.79 (2 × br d, $J$ = 13.5 Hz, 2 × 1 H, CH═CH), 7.05−7.29 (m, 15 H, Ar); $^{13}C$ NMR $\delta$ 29.3 ($CH_2CH_2CH_2$), 30.9 and 32.0 ($CH_2CH_2CH_2$), 40.2 (*C*HCH$(CO_2Me)_2$), 51.7 ($CH_2Ph$), 52.8 and 53.0 (2 × *C*$H_3$), 57.3 (*C*HN), 58.9 (CH*C*H$(CO_2Me)_2$), 68.1 (*C*H$Ph_2$), 126.9, 127.1, 127.3, 128.3, 128.4, 128.5, 128.6, 129.6, 130.7, and 138.0 (Ar *C*H's and *C*H═*C*H), 141.7, 142.2, and 142.5 (Ar *ipso* C), 169.3 and 169.5 (2 × *C*═O); MS (EI) *m*/*z* (%) 497 (10, $M^{\bullet+}$), 406 (25), 167 (100).

**(*E*)-Dimethyl [4-[Benzyl(diphenylphosphinous)amidyl]cyclohex-2-en-1-yl]malonate (24a). Method A.** Compound **24a** was obtained from **10a** using method IV (rt, 22 h, with 4.4 mol % of Pd) as a colorless oil (76%): IR (film) $\nu$ 3024, 2951, 2857, 1741, 1436 $cm^{-1}$; $^1H$ NMR $\delta$ 1.50−1.82 (m, 4 H, $CH_2CH_2$), 2.76 (m, 1 H, C*H*C$H(CO_2Me)_2$) 3.03 (d, $J$ = 10 Hz, 1 H, C*H*$(CO_2Me)_2$), 3.42−3.58 (m, 1 H, C*H*N), 3.51 (s, 3 H, $CH_3O$), 3.53 (s, 3 H, $CH_3O$), 3.95 and 4.02 (2 × dd, 2 × $J_{H,P}$ = 6 Hz, 2 × $J_{H,H}$ = 13 Hz, 2 × 1 H, $CH_2Ph$), 5.42 and 5.53 (2 × br d, 2 × $J$ = 12.5 Hz, 2 × 1 H, CH═CH), 6.86−7.29 (m, 15 H, Ar); $^{13}C$ NMR $\delta$ 27.0 and 30.1 ($CH_2CH_2$), 36.4 (*C*HCH$(CO_2Me)_2$), 52.8 (*C*HN), 53.6 ($CH_2Ph$), 56.2 and 56.5 (2 × *C*$H_3$), 57.1 (*C*H$(CO_2Me)_2$), 127.2, 128.4, 128.6, 128.8, 129.0, 132.6, 132.9, 133.1, and 134.3 (Ar *C*H's and *C*H═*C*H), 140.2, 140.4 and 140.6 (Ar *ipso* C), 169.0 (2 × *C*═O); $^{31}P$ NMR $\delta$ 50.47; MS (EI) *m*/*z* (%) 501 (10, $M^{\bullet+}$), 442 (40), 370 (10), 290 (20), 186 (25).

**Method B.** Compound **24a** was obtained from **29a** using method IV (rt, 15 min, with 5.3 mol % of Pd) as a colorless oil (64%), identical with the compound prepared according to method A.

**(*E*)-Dimethyl [4-[benzyl(diphenylphosphinous)amidyl]cyclohept-2-en-1-yl]malonate (24b)** was obtained from **10b** using method IV (rt, 20 h, with 7 mol % of Pd) as a colorless oil (62%): IR (film) $\nu$ 3020, 2957, 2922, 2862, 1758, 1730, 1590, 1435 $cm^{-1}$; $^1H$ NMR $\delta$ 1.39−2.01 (m, 6 H, $CH_2CH_2CH_2$), 3.12−3.21 (m, 1 H, C*H*C$H(CO_2Me)_2$) 3.52 (d, $J$ = 9.5 Hz, 1 H, C*H*$(CO_2Me)_2$), 3.86 (s, 6 H, 2 × $CH_3$), 4.11 and 4.22 (2 × dd, $J$ = 6, 15.5, 6.5, and 15.5 Hz, 2 × 1 H, $CH_2Ph$), 3.72−3.88 (m, 1H, C*H*N), 5.60 and 5.79 (2 × br d, $J$ = 12.5 Hz, 2 × 1 H, CH═CH), 7.15−7.58 (m, 15 H, Ar); $^{13}C$ NMR $\delta$ 23.3 ($CH_2CH_2CH_2$), 29.9 and 33.3 ($CH_2CH_2CH_2$), 37.6 (*C*HCH$(CO_2Me)_2$), 52.8 (*C*HN), 53.8 ($CH_2Ph$), 56.5 (CH*C*H$(CO_2Me)_2$), 59.2 and 59.4 (2 × *C*$H_3$), 127.2, 128.6, 128.9, 130.9, 132.6, 132.9, 133.3, 137.6, and 137.7 (Ar *C*H's and *C*H═*C*H), 140.2, 140.4, and 140.5 (Ar *ipso* C), 169.1 and 169.2 (2 × *C*═O); $^{31}P$ NMR $\delta$ 50.31; MS (EI) *m*/*z* (%) 515 (40, $M^{\bullet+}$), 456 (70), 424 (100), 383 (80), 183 (80), 91 (90).

**(*E*)-Dimethyl [4-(Benzylamino)cyclohex-2-en-1-yl]malonate (25a). Method A.** Compound **25a** was obtained from **24a** using method V (rt, 3 h) as a colorless oil (68%): IR (film) $\nu$ 3340, 3030, 2942, 2859, 1756, 1739, 1453, 1436, 1155, 1029 $cm^{-1}$; $^1H$ NMR $\delta$ 1.31−1.48 and 1.80−2.06 (2 × m, 2 × 2 H, $CH_2CH_2$), 2.85−2.99 (m, 1 H, C*H*C$H(CO_2Me)_2$), 3.15−3.26 (m, 1 H, C*H*N), 3.21 (d, $J$ = 9 Hz, 1 H, C*H*$(CO_2Me)_2$), 3.70 (s, 6 H, 2 × $CH_3$), 3.81 (s, 2 H, $CH_2Ph$), 5.57 and 5.88 (2 × d, 2 × $J$ = 10.5 Hz, 2 × 1 H, CH═CH), 7.10−7.29 (m, 5 H, Ar); $^{13}C$ NMR $\delta$ 26.0 and 29.7 ($CH_2CH_2$), 36.4 (*C*HCH$(CO_2Me)_2$), 51.2 (*C*HN), 52.8 (2 × *C*$H_3$), 53.2 ($CH_2Ph$), 57.0 (*C*H$(CO_2Me)_2$), 127.3, 128.5, 128.8, 129.2, and 132.8 (Ar *C*H's and *C*H═*C*H), 140.9 (Ar *ipso* C), 169.1 (2 × C═O); MS (EI) *m*/*z* (%) 317 (10, $M^{\bullet+}$), 230 (20), 186 (25), 185 (15), 159 (55), 91 (100).

**Method B.** Compound **25a** was obtained from **28a** using method IV (66 °C, 22 h, with 11 mol % of Pd) as a colorless oil (58%), identical with the compound prepared according to method A.

**(*E*)-Dimethyl [4-(benzylamino)cyclohept-2-en-1-yl]malonate (25b)** was obtained from **25b** using method V (rt, 14 h) as a colorless oil (77%): IR (film) $\nu$ 3335, 3020, 2921, 2849, 1733, 1434, 1194, 1152, 1026, 699 $cm^{-1}$; $^1H$ NMR $\delta$ 1.55−1.78 (m, 6 H, $CH_2CH_2CH_2$), 2.20 (br s, 1 H, NH), 3.00−3.16 (m, 1 H, C*H*C$H(CO_2Me)_2$) 3.28−3.38 (m, 1 H, C*H*N), 3.44 (d, $J$ = 9 Hz, 1 H, C*H*$(CO_2Me)_2$), 3.65 (s, 6 H, 2 × $CH_3$), 3.72 (s, 2 H, $CH_2Ph$), 5.58 and 5.67 (2 × dd, $J$ = 4.5, 12, 3, and 12 Hz, 2 × 1 H, C*H*═C*H*), 7.12−7.35 (m, 5 H, Ar); $^{13}C$ NMR $\delta$ 23.6 ($CH_2CH_2CH_2$), 30.0 and 32.6 ($CH_2CH_2CH_2$), 38.8 (*C*HCH$(CO_2Me)_2$), 51.6 ($CH_2Ph$), 52.8 (*C*H$(CO_2Me)_2$), 56.2 and 56.4 (*C*HN and 2 × $CH_3$), 127.4, 128.6, 128.7, 128.8, 128.9, 131.9, and 136.4 (Ar *C*H's and *C*H═*C*H), 140.4 (Ar *ipso* C), 169.2 (2 × *C*═O); MS (EI) *m*/*z* (%) 331 (5, $M^{\bullet+}$), 300 (5), 224 (5), 200 (30), 108 (20), 91 (100).

**(*Z*)-1-[Benzyl(diphenylmethyl)amino]cyclohex-2-en-4-ol (26a).** To a solution of acetate **9a** (488 mg, 1.19 mmol) in a 1:1 THF−methanol mixture (6 mL) was added a solution of $K_2CO_3$ (500 mg, 3.62 mmol) in water (3 mL) in a single portion. The mixture was heated to 40 °C and stirred for 26 h. Water (10 mL) was then added, and the mixture was extracted with dichloromethane (2 × 20 mL). The organic portions were combined, and the solvent was evaporated. Chromatography ($SiO_2$, petroleum ether−ether 1:1) afforded **26a** as a colorless oil (398 mg, 1.08 mmol, 91%): $R_f$ (petroleum ether−ether 1:1) 0.30; IR (film)

$\nu$ 3340, 3024, 2932, 2838, 1603, 1494, 1454, 1072 cm$^{-1}$; $^1$H NMR $\delta$ 1.20−1.78 (m, 4 H, C$H_2$C$H_2$), 3.38−3.46 (m, 1H, C$H$N), 3.62 (s, 2H, C$H_2$Ph), 3.83 (m, 1 H, C$H$OH), 4.90 (s, 1 H, C$H$Ph$_2$), 5.61 (s, 2 H, C$H$═C$H$), 7.02−7.25 (m, 15 H, Ar); $^{13}$C NMR $\delta$ 21.3 and 30.9 (*C*H$_2$*C*H$_2$), 52.2 (*C*H$_2$Ph), 55.8 (*C*HN), 63.7 (*C*HOH), 69.4 (*C*HPh$_2$), 126.9, 127.3, 127.4, 128.5, 128.6, 129.1, 129.6, 130.2, and 137.8 (Ar *C*H's and *C*H═*C*H), 141.9, 142.4, and 143.2 (Ar *ipso* C); MS (EI) *m*/*z* (%) 369 (5, M$^{\bullet+}$), 346 (10), 325 (10), 200 (20), 167 (70), 91 (100).

**(*E*)-1-Acetoxy-4-[benzyl(diphenylmethyl)amino]cyclohex-2-ene (27a).** Acetic acid (15 $\mu$L, 16 mg, 262 $\mu$mol) was added to a solution of alcohol **26a** (36 mg, 97 $\mu$mol) and triphenylphosphine (69 mg, 363 $\mu$mol) in THF (1 mL) at 0 °C. Diethyl azodicarboxylate (41 $\mu$L, 45 mg, 260 $\mu$mol) was then added dropwise, and the solution allowed to stir at room temperature for 20 h. Water (5 mL) was then added, the solution was extracted with $CH_2Cl_2$ (2 × 15 mL), and the combined organic portions were evaporated. Chromatography ($SiO_2$, petroleum ether−ether 10:1) afforded **27a** as a colorless oil (33 mg, 80 $\mu$mol, 82%): $R_f$ (petroleum ether−ether 15:1) 0.30; IR (film) $\nu$ 3025, 2940, 1746, 1494, 1455, 1372, 1029 cm$^{-1}$; $^1$H NMR $\delta$ 1.18−2.00 (m, 4 H, $CH_2CH_2$), 1.90 (s, 3 H, $CH_3$), 3.51−3.63 (br t, $J$ = 8.5 Hz, 1 H, C$H$N), 3.64 and 3.65 (AB system, $J$ = 14 Hz, 2 × 1 H, C$H_2$Ph), 4.90−4.97 (m, 2 H, C$H$Ph$_2$ and C$H$OAc), 5.59−5.74 (m, 2 H, CH═CH), 7.05−7.33 (m, 15 H, Ar); $^{13}$C NMR $\delta$ 21.7 (*C*H$_3$), 26.3 and 29.1 (*C*H$_2$*C*H$_2$), 51.7 (*C*H$_2$Ph), 55.3 (*C*HN), 69.1 (*C*HPh$_2$), 70.5 (*C*HOAc), 126.9, 127.0, 127.3, 127.5, 127.6, 128.4, 128.5, 128.6, 128.7, 129.2, 129.3, 129.8, 129.7, 130.0, and 134.9 (Ar *C*H's and *C*H═*C*H), 141.9, 142.2, and 143.1 (Ar *ipso* C), 171.1 (*C*═O); MS [$^+$CI ($NH_3$)] *m*/*z* (%) 412 (15, MH$^+$), 272 (15), 244 (15), 182 (30), 167 (80), 106 (100), 91 (55).

**(*E*)-1-Acetoxy-4-(benzylamino)cyclohex-2-ene (28a).** A mixture of trifluoracetic acid (1 mL) and acetate **27a** (42 mg, 102 mmol) was refluxed while stirring for 18 h, then evaporated and treated with $NaHCO_3$ (saturated, aqueous, 2 mL). The resulting solution was extracted with $CH_2Cl_2$ (2 × 3 mL), and the combined organic extracts were evaporated. Chromatography ($SiO_2$, petroleum ether−ether 1:2) afforded the known[11] **28a** as a colorless oil (13 mg, 53 $\mu$mol, 52%), whose spectral characteristics were identical to those described in the literature:[11] IR (film) $\nu$ 3315, 3024, 2940, 2870, 1748, 1447, 1241 cm$^{-1}$; $^1$H NMR $\delta$ 1.32−2.09 (m, 4 H, $CH_2CH_2$), 1.95 (s, 3 H, $CH_3$), 3.12−3.20 (m, 1 H, C$H$N), 3.72 (br s, 2 H, C$H_2$Ph), 5.15−5.23 (m, 1 H, C$H$OAc), 5.60 and 5.83 (2 × br d, 2 × $J$ = 11 Hz, 2 × 1 H, CH═CH), 7.16−7.28 (m, 5 H, Ar); $^{13}$C NMR $\delta$ 21.7 (*C*H$_3$), 27.3 (*C*H$_2$CHOAc) and 28.0 (*C*H$_2$CHN), 51.3 (*C*H$_2$Ph), 52.7 (*C*HN), 69.6 (*C*HOAc), 127.4, 128.1 (olefinic *C*HCHOAc), 128.5 (CH in Ph), 128.8, and 134.6 (olefinic *C*HCHN), 140.8 (Ar *ipso* C), 171.1 (*C*═O); MS (EI) *m*/*z* (%) 245 (5, M$^{\bullet+}$), 217 (5), 185 (15), 159 (20), 106 (20), 91 (100).

**(*E*)-1-Acetoxy-4-[benzyl(diphenylphosphinous)amidyl]cyclohex-2-ene (29a)** was obtained from **28a** using method III (34 °C, 14 h) as a clear oil (33%): IR $\nu$ 3058, 3028, 2936, 2874, 1746, 1691, 1439, 1372, 1242, 1028, 699 cm$^{-1}$; $^1$H NMR $\delta$ 1.32−2.18 (m, 4 H, $CH_2$-$CH_2$) 1.91 (s, 3 H, $CH_3$) 3.51−3.71 (m, 1 H, C$H$N), 3.97 and 4.05 (2 × dd, 2 × $J_{H,P}$ = 5.5 Hz, 2 × $J_{H,H}$ = 13 Hz, 2 × 1 H, C$H_2$Ph), 5.20−5.31 (m, 1 H, C$H$OAc), 5.52 and 5.65 (2 × br d, 2 × $J$ = 10.5 Hz, 2 × 1 H, CH═CH), 6.92−7.39 (m, 15 H, Ar); $^{13}$C NMR $\delta$ 21.7 (*C*H$_3$), 28.7 and 29.1 (*C*H$_2$*C*H$_2$), 53.6 (*C*H$_2$Ph), 56.1 (*C*HN), 70.2 (*C*HOAc), 127.3, 128.5, 128.7, 128.8, 128.9, 129.0, 129.1, 132.5, 132.8, 132.9, 133.2, and 136.0 (Ar *C*H's and *C*H═*C*H), 140.1, 140.4, and 140.5 (Ar *ipso* C), 171.1 (*C*═O); $^{31}$P NMR $\delta$ 50.94; MS (EI) *m*/*z* (%) 429 (10, M$^{\bullet+}$), 386 (100), 370 (40), 290 (40), 201 (70), 183 (45), 149 (25), 91 (65).

**$\pi$-Allyl Complex (32a).** Tetrakis(triphenylphosphine)palladium(0) (26 mg, 23 $\mu$mol) was added to a solution of acetate **10a** (9 mg, 21 $\mu$mol) in deuteriochloroform (0.5 mL) and the solution was allowed to stand at room temperature for 30 min. After this time the following spectral data were recorded for the $\pi$-allyl complex **32a**: $^1$H NMR $\delta$ 1.50−2.16 (m, 4 H, $CH_2CH_2$) 2.71−3.03 (m, 1 H, C$H$N), 3.79 and 4.04 (2 × dd, $J_{H,P}$ = 6 and 8 Hz, $J_{H,H}$ = 15.5 Hz, 2 × 1 H, C$H_2$Ph), 4.15−4.28 and 5.43−5.59 (2 × m, 2 × 1 H, allyl C$H$CHC$H$), 6.01−6.16 (m, 1 H, allyl CHC$H$CH), 6.70−7.99 (m, 30 H, Ar); $^{31}$P NMR $\delta$ 29.3 (Pd*P*Ph$_3$), 103.7 (N*P*Ph$_2$).

**(*E*)-(2*S**,5*R**)-Dimethyl [5-[benzyl(diphenylmethyl)amino]hex-3-en-2-yl]malonate (35)** was obtained from **14** using method IV (66 °C, 16 h, with 8.6 mol % of Pd) as a colorless oil (61%): $^1$H NMR $\delta$ 0.95 (d, $J$ = 8 Hz, 3 H, $CH_3$), 0.99 (d, $J$ = 8 Hz, 3 H, $CH_3$), 2.72−2.86 (m, 1 H, C$H$CH(CO$_2$Me)$_2$) 3.15 (d, $J$ = 10 Hz, 1 H, C$H$(CO$_2$Me)$_2$), 3.46−3.64 (m, 3 H, C$H$N and C$H_2$Ph), 3.51 (s, 3 H, $CH_3$O), 3.63 (s, 3 H, $CH_3$), 4.85 (s, 1 H, C$H$Ph$_2$), 5.18 and 5.42 (2 × dd, $J$ = 8, 16 Hz, 2 H, CH═CH), 6.99−7.36 (m, 15 H, Ar); MS (EI) *m*/*z* (%) 485 (1, M$^{\bullet+}$), 470 (5), 325 (10), 167 (100).

**(*E*)-(2*S**,5*R**)-Dimethyl [5-[benzyl(diphenylphosphinous)amidyl]-hex-3-en-2-yl]malonate (36)** was obtained from **15** using method IV (rt, 22 h, with 7.2 mol % of Pd) as a colorless oil (58%): IR (film) $\nu$ 3051, 2963, 1755, 1735, 1436, 1196, 1024 cm$^{-1}$; $^1$H NMR $\delta$ 0.91 (d, $J$ = 7.5 Hz, 3 H, $CH_3$), 1.15 (d, $J$ = 7.5 Hz, 3 H, $CH_3$), 2.71−2.90 (m, 1 H, C$H$CCH(CO$_2$Me)$_2$) 3.12 (d, $J$ = 10 Hz, 1 H, C$H$(CO$_2$Me)$_2$), 3.23−3.43 (m, 1 H, C$H$N), 3.51 (s, 3 H, $CH_3$O), 3.60 (s, 3 H, $CH_3$O), 3.82 and 4.03 (2 × dd, 2 × $J_{H,P}$ = 3.5 Hz, 2 × $J_{H,H}$ = 14 Hz, 2 × 1 H, C$H_2$Ph), 5.14 and 5.43 (2 × dd, 2 × $J$ = 13, 7 Hz, 2 × 1 H, CH═CH), 6.81−7.40 (m, 15 H, Ar); $^{13}$C NMR $\delta$ 18.8 and 21.4 (*C*H*C*H$_3$), 37.4 (*C*HCH(CO$_2$Me)$_2$), 52.7 and 52.8 (2 × CO$_2$*C*H$_3$), 53.4 (*C*H$_2$Ph), 56.3 (*C*HN), 58.2 (*C*H(CO$_2$Me)$_2$), 127.1, 128.5, 128.6, 128.8, 128.9, 132.0, 132.7, 132.9, 133.1, 133.2, 134.9 and 135.0 (Ar*C*H and *C*H═*C*H), 140.3, 140.5 and 140.7 (Ar *ipso* C), 169.0 and 169.1 (2 × *C*═O); $^{31}$P NMR $\delta$ 46.80; MS (EI) *m*/*z* (%) 503 (2, M$^{\bullet+}$), 412 (10), 370 (25), 304 (25), 91 (100).

**(*E*)-(2*S**,5*R**)-Dimethyl [5-(Benzylamino)hex-3-en-2-yl]malonate (37).** Trifluoracetic acid (1 mL) was added to amine **35** (18 mg, 37 $\mu$mol), and the solution was brought to reflux and stirred for 16 h. The mixture was then evaporated, treated with $NaHCO_3$ (saturated, aqueous, 2 mL), and extracted with $CH_2Cl_2$ (2 × 3 mL). The combined organic extracts were evaporated, and the residue was purified by chromatography ($SiO_2$, petroleum ether−ether 1:2) to afford **37** as a colorless oil (10 mg, 31 $\mu$mol, 85%): IR (film) $\nu$ 3320, 2955, 1733, 1443, 1150, 1019 cm$^{-1}$; $^1$H NMR $\delta$ 1.11 (d, 6 H, $J$ = 7 Hz, 2 × CHC$H_3$), 1.25 (br s, 1H, N$H$), 2.80−2.96 (m, 1 H, C$H$CH(CO$_2$Me)$_2$), 3.12 (dt, $J$ = 14, 7 Hz, 1 H, C$H$N), 3.25 (d, $J$ = 9.5 Hz, 1 H, C$H$(CO$_2$Me)$_2$), 3.60 and 3.73 (AB system, $J$ = 12.5 Hz, 2 H, C$H_2$Ph), 3.63 (s, 3 H, $CH_3$O), 3.70 (s, 3 H, $CH_3$O), 5.35 and 5.45 (2 × dd, 2 × $J$ = 14, 7 Hz, 2 × 1 H, CH═CH), 7.15−7.29 (m, 5 H, Ar); $^{13}$C NMR $\delta$ 19.0 and 22.6 (2 × C*H*CH$_3$), 37.5 (*C*HCH(CO$_2$Me)$_2$), 51.2 (*C*H$_2$Ph), 52.5 and 52.6 (2 × *C*H$_3$), 55.4 (*C*HN), 58.3 (*C*H(CO$_2$Me)$_2$), 127.2, 132.4 and 136.1 (Ar *C*H's), 128.5 and 128.8 (*C*H═*C*H), 141.1 (Ar *ipso* C), 169.0 and 169.1 (*C*═O); MS (EI) *m*/*z* (%) 319 (5, M$^{\bullet+}$), 230 (20), 304 (40), 212 (15), 91 (100). Identical compound was also obtained from phosphinous amide **36** in 77% yield using method V (rt, 90 min).

**(*E*)-(5*R**,8*R**)-Dimethyl [8-[Benzyl(diphenylmethyl)amino]dodec-6-en-5-yl]malonate (38).** With **21** as the starting compound, method IV (66 °C, 42 h, with 6.1 mol % of Pd) gave the unreacted starting material **21** (69%) and the substitution product **38** as a colorless oil (25%): IR (film) $\nu$ 2951, 2936, 2857, 1738, 1721, 1491, 1454, 1432, 1028 cm$^{-1}$; $^1$H NMR $\delta$ 0.61−0.80 (m, 6 H, 2 × C$H_3$), 0.98−1.41 (m, 12 H, 2 × $CH_2CH_2CH_2$), 2.69 (br q, 1 H, C$H$CH(CO$_2$Me)$_2$) 3.09−3.22 (m, 1 H, C$H$N), 3.35 (d, $J$ = 9.5 Hz, C$H$(CO$_2$Me)$_2$), 3.43 and 3.68 (AB system, $J$ = 15.5 Hz, 2 ×1 H, C$H_2$Ph), 3.67 (s, 6 H, 2 × $CH_3$), 4.78 (s, 1 H, C$H$Ph$_2$), 5.07 and 5.37 (2 × dd, $J$ = 15, 9.5 Hz, 2 H, CH═CH), 6.93−7.34 (m, 15 H, Ar); $^{13}$C NMR $\delta$ 14.4 (2 × $CH_2CH_3$), 22.7 and 22.9 (2 × *C*H$_2$CH$_3$), 29.5 and 29.8 (2 × *C*H$_2$Et), 32.5 and 33.5 (2 × *C*H$_2$Pr), 43.6 (*C*HCH(CO$_2$Me)$_2$), 51.7 (*C*H$_2$Ph), 52.9 (*C*HN), 57.9 (*C*H(CO$_2$Me)$_2$), 61.6 (2 × CO$_2$*C*H$_3$), 70.8 (*C*HPh$_2$) 126.3, 127.0, 127.1, 127.7, 128.1, 128.2, 128.3, 128.7, 129.6, 132.5, and 133.4 (Ar *C*H's and *C*H═*C*H), 142.8, 143.2 and 144.3 (Ar *ipso* C), 169.1 and 169.4 (2 × *C*═O); MS (FAB) *m*/*z* (%) 570 (10, MH$^+$), 512 (65), 167 (100).

**(*E*)-(5*R**,8*R**)-Dimethyl [8-[benzyl(diphenylphosphinyl)amino]-dodec-6-en-5-yl]malonate (39)** was obtained from **22** using method IV (rt, 90 min, with 9 mol % of Pd) as a colorless oil (57%): IR (film) $\nu$ 2951, 2923, 1759, 1737, 1431, 1240, 1142 and 1024 cm$^{-1}$; $^1$H NMR $\delta$ 0.55−0.73 (m, 6 H, 2 × $CH_2CH_3$), 0.86−1.70 (m, 12 H, 2× $CH_2$-$CH_2CH_2$), 2.51−2.67 (m, 1 H, C$H$CCH(CO$_2$Me)$_2$), 2.90−3.07 (m, 1 H, C$H$N), 3.18 (d, $J$ = 9 Hz, 1 H, C$H$(CO$_2$Me)$_2$), 3.47 (s, 3 H, $CH_3$O), 3.53 (s, 3 H, $CH_3$O), 3.66 and 3.98 (2 × dd, $J$ = 15, 2.5 Hz, 2 × 1 H, C$H_2$Ph), 4.98 and 5.34 (2 × dd, 2 × $J$ = 9, 15.5 Hz, 2 × 1 H, CH═CH), 6.74−7.40 (m, 15 H, Ar); $^{13}$C NMR $\delta$ 14.4 and 14.5 (2 × $CH_2CH_3$),

22.8 and 22.9 (2 × $CH_2CH_3$), 29.5 and 29.7 (2 × $CH_2Et$), 35.0 and 35.2 (2 × $CH_2Pr$), 43.1 ($CHCH(CO_2Me)_2$), 52.8 (CHN), 53.3 ($CH_2$-Ph), 57.5 ($CH(CO_2Me)_2$), 61.5 and 61.8 (2 × $CO_2CH_3$), 127.1, 128.5, 128.6, 128.7, 128.8, 129.0, 132.2, 132.7, 133.0, 133.4, 134.3, 135.2, and 135.3 (Ar CH's and CH=CH), 140.3, 140.8 and 141.0 (Ar *ipso* C), 169.1 and 169.2 (2 × C=O); $^{31}$P NMR $\delta$ 45.92.

**(*E*)-(5*R**,8*R**)-Dimethyl [8-(Benzylamino)dodec-6-en-5-yl]malonate (40).** Trifluoracetic acid (0.5 mL) was added to amine **38** (14 mg, 25 $\mu$mol), and the solution was brought to reflux and stirred for 20 h. The mixture was then evaporated, treated with $NaHCO_3$ (saturated, aqueous, 3 mL), and extracted with $CH_2Cl_2$ (2 × 4 mL). The combined organic extracts were evaporated, and the residue was purified by chromatography ($SiO_2$, petroleum ether−ether 1:1) to afford **40** as a colorless oil (10 mg, 25 $\mu$mol, 99%): IR (film) $\nu$ 3320, 2925, 2856, 1735, 1433, 1041, 1026, 975 cm$^{-1}$; $^1$H NMR $\delta$ 0.95−1.07 (m, 6 H, 2 × $CH_3$), 1.31−1.70 (m, 12 H, $CH_2CH_2CH_2$), 2.90−3.03 (m, 1 H, $CHCH(CO_2Me)_2$) 3.07−3.16 (m, 1 H, CHN), 3.56 (d, $J$ = 9 Hz, $CH(CO_2Me)_2$), 3.71 and 3.90 (AB system, $J$ = 13 Hz, 2 H, $CH_2Ph$), 3.83 (s, 3 H, $CH_3O$), 3.85 (s, 3 H, $CH_3O$), 5.40−5.57 (m, 2 H, CH=CH), 7.33−7.50 (m, 15 H, Ar); $^{13}$C NMR $\delta$ 14.4 (2 × $CH_2CH_3$), 22.7 and 23.1 (2 × $CH_2CH_3$), 28.7 and 29.7 (2 × $CH_2Et$), 32.7 and 36.2 (2 × $CH_2Pr$), 43.3 ($CHCH(CO_2Me)_2$), 51.7 ($CH_2Ph$), 52.7 (CHN), 57.7 and 60.5 ($CH(CO_2Me)_2$ and 2 × $CO_2CH_3$), 127.2, 128.6, 128.8 and 132.2 (Ar CH's and CH=CH), 137.0 (Ar *ipso* C), 169.0 and 169.3 (2 × C=O); MS (FAB) *m*/*z* (%) 404 (100, MH$^+$), 346 (40), 297 (15), 165 (35), 154 (50). Identical compound was also obtained from phosphinous amide **39** in 83% yield using method V (rt, 2 h).

**(*Z*)-1-[Benzyl(diphenylmethyl)amino]-4-methoxycyclohex-2-ene (46).** To a solution of alcohol **26a** (95 mg, 257 $\mu$mol) in DMF (2 mL) was added NaH (15 mg, 60% in oil, 375 $\mu$mol), and the solution was allowed to stir for 5 min. MeI (40 $\mu$L, 642 $\mu$mol) was then added dropwise, and the solution was stirred at room temperature for 38 h. Ethyl acetate (10 mL) was then added, and the mixture was extracted with water (2 × 5 mL). The organic portion was evaporated, and the residue was purified by chromatography ($SiO_2$, petroleum ether−ether 15:1) to afford **46** as a colorless oil (41 mg, 107 $\mu$mol, 42%): IR (film) 3019, 2920, 1487, 1445, 1071, 692 cm$^{-1}$; $^1$H NMR $\delta$ 1.25−1.86 (m, 4 H, $CH_2CH_2$), 3.22 (s, 3 H, $CH_3$), 3.39−3.45 (m, 1 H, CHN), 3.69 (s, 2 H, $CH_2Ph$), 4.96 (s, 1 H, $CHPh_2$), 5.65 (d, $J$ = 12 Hz, 1 H, CH=CH), 5.78 (br d, $J$ = 12 Hz, 1 H, CH=CH), 7.05−7.27 (m, 15 H, Ar); $^{13}$C NMR $\delta$ 22.1 and 26.9 ($CH_2CH_2$), 51.8 ($CH_2Ph$), 55.8 and 56.6 (CHN and CHOMe), 68.8 ($CHPh_2$), 126.6, 127.1, 127.3, 128.3, 128.4, 128.5, 128.7, 129.3, 129.7, 130.5, 132.8, 136.1 (Ar CH's and CH=CH), 142.2, 142.3, and 143.0 (Ar *ipso* C); MS (EI) *m*/*z* 383 (5, MH$^+$), 355 (10), 325 (10), 182 (65), 167 (40), 105 (100), 84 (75).

**(*Z*)-1-Chlorocyclohex-2-en-4-ol (47).** Potassium carbonate (600 mg, 4.34 mmol) was added to a solution of **7** (450 mg, 2.59 mmol) in a mixture of THF (4 mL), methanol (4 mL), and water (4 mL), the mixture was stirred at room temperature for 2 h and then diluted with water (20 mL). The product was extracted with dichloromethane (3 × 20 mL); the organic layer was washed with water, dried, and evaporated. Chromatography ($SiO_2$, petroleum ether−ether 1:1) afforded the known[45] **47** (225 mg, 66%)[32] as a pure product: $^1$H NMR $\delta$ 1.60−1.82 (m, 2 H), 1.80−1.97 (m, 2 H), 2.37 (s, 1 H, OH), 4.02 (br t, 1 H, CHOH), 4.36 (m, 1 H, CHCl), 5.66 (s, 2 H, CH=CH); $^{13}$C NMR $\delta$ 29.2 (t), 30.3 (t), 54.5 (d, CHCl), 66.2 (d, CHOH), 130.0 (d), 134.3 (d).

**(*Z*)-1-Chloro-4-methoxycyclohex-2-ene (48).** A mixture of the alcohol **47** (59 mg, 445 $\mu$mol), methyl iodide (1 mL), and silver(I) oxide (120 mg, 518 $\mu$mol) in acetonitrile (1 mL) was refluxed for 14 h. The mixture was filtered through a small pad of aluminum oxide, solvent was evaporated in vacuo, and the residue was purified by chromatography ($SiO_2$, petroleum ether−ether 10:1) to give the known[33] **48** (57 mg, 87%): $^1$H NMR $\delta$ 1.70−1.82 (m, 2 H), 1.83−2.04 (m, 2 H), 3.22 (s, 3 H, MeO), 3.64 (m, 1 H, CHOMe), 4.40 (m, 1 H, CHCl), 5.75 (s, 2 H, CH=CH); $^{13}$C NMR $\delta$ 24.3 (t), 30.1 (t), 54.6 (d, CHCl), 56.2 (q, MeO), 74.5 (d, CHOMe), 130.5 (d), 131.7 (d).

**(*Z*)-1-(Benzylamino)-4-methoxycyclohex-2-ene (49)** was obtained from **48** using method I (rt, 18 h) as a colorless oil (93%): IR (film) $\nu$ 3305, 3019, 2915, 2813, 1446, 1392, 1185, 1079 cm$^{-1}$; $^1$H NMR $\delta$ 1.94−2.20 (m, 4 H, $CH_2CH_2$), 3.49 (br s, 1 H, CHN), 3.61 (s, 3 H, $CH_3$), 3.91 (br s, 1 H, CHOMe), 4.07 and 4.09 (AB system, $J$ = 14.5 Hz, 2 H, $CH_2Ph$), 6.13 and 6.17 (br AB system, $J$ = 11.5 Hz, 2 H, CH=CH), 7.47−7.66 (m, 5 H, Ar); $^{13}$C NMR $\delta$ 25.5 and 25.7 ($CH_2CH_2$), 51.3 ($CH_2Ph$), 52.8 (CHN), 56.5 ($OCH_3$), 73.9 (CHOMe), 127.3, 128.5, 128.7, 128.8, and 134.1 (Ar CH's and CH=CH), 141.1 (Ar *ipso* C); MS (EI) *m*/*z* (%) 217 (5, MH$^+$), 189 (60), 159 (60), 106 (55), 91 (100).

**(*Z*)-1-[Benzyl(diphenylphosphinous)amidyl]-4-methoxycyclohex-2-ene (50)** was obtained from **49** using method III (34 °C, 18 h) as a colorless oil (85%): IR (film) $\nu$ 2922, 2870, 1439, 1185, 1121 cm$^{-1}$; $^1$H NMR $\delta$ 1.10−1.82 (m, 4 H, $CH_2CH_2$), 3.18 (s, 3 H, $CH_3$), 3.32−3.45 (m, 2 H, CHN and CHOMe), 4.02 and 4.06 (2 × dd, $J$ = 6.5, 15.5 and 5.5, 15.5 Hz, 2 H, $CH_2Ph$), 5.62 (d, $J$ = 12 Hz, 1 H, CH=CH), 5.70 (br d, $J$ = 12 Hz, 1 H, CH=CH), 6.85−7.37 (m, 15 H, Ar); $^{13}$C NMR $\delta$ 25.5 and 26.6 ($CH_2CH_2$), 53.6 ($CH_2Ph$), 56.7 and 56.8 (CHN and $OCH_3$), 72.5 (CHOMe), 127.2, 128.6, 128.7, 128.8, 129.0, 129.2, 132.6, 132.8, 133.0, 133.3, 136.4 and 136.5 (Ar CH's and CH=CH), 140.4, 140.6 and 140.8 (Ar *ipso* C); $^{31}$P NMR $\delta$ 52.06.

**(*Z*)-1-[Benzyl(diphenylphosphinous)amidyl]-4-methylcyclohex-2-ene (52).** To a solution of methoxy derivative **50** (185 mg, 461 $\mu$mol) and bis(triphenylphosphine)nickel(II) chloride (10 mg, 15 $\mu$mol, 3.3 mol %) in THF (5 mL) at 0 °C was added methylmagnesium bromide (1.50 mL, 1.4 M in a 3:1 toluene−THF mixture, 2.10 mmol, 4.6 equiv) dropwise, and the reaction mixture was allowed to warm slowly. After 6 h, by which time the temperature had reached 15 °C, water (5 mL) was added cautiously, and the solution was extracted with dichloromethane (2 × 10 mL). The mixture was then concentrated by evaporation, and the residue was purified by chromatography ($Al_2O_3$, petroleum ether−ether 1:10) to afford **52** as a colorless oil (132 mg, 74%): $^1$H NMR $\delta$ 0.89 (d, $J$ = 8.5 Hz, 3 H, $CH_3$), 1.16−1.72 (m, 4 H, $CH_2CH_2$), 1.90−2.06 (m, 1 H, $CHCH_3$), 3.41−3.56 (m, 1 H, CHN), 4.07 and 4.11 (2 × dd, $J$ = 5, 14.5 and 6.5, 14.5 Hz, 2 H, $CH_2Ph$), 5.47 and 5.60 (2 × br d, $J$ = 11.5 Hz, 1 H, CH=CH), 6.84−7.45 (m, 15 H, Ar); $^{13}$C NMR $\delta$ 19.5 ($CH_3$), 25.1 ($CH_2CHMe$), 27.0 ($CH_2CHN$), 28.1 (CHMe), 52.1 ($CH_2Ph$), 54.3 (CHN), 125.6, 126.9, 127.0, 127.1, 127.4, 127.5, 127.6, 129.3, 129.4, 131.0, 131.3, 131.5, 131.8, 132.8, and 134.1 (Ar CH's and CH=CH), 139.3, 139.4, and 139.5 (Ar *ipso* C); $^{31}$P NMR $\delta$ 50.73; MS (EI) *m*/*z* (%) 385 (30), 290 (55), 277 (55), 183 (100), 91 (55).

**(*Z*)-1-(Benzylamino)-4-methylcyclohex-2-ene (53)** was obtained from **53** using method V (rt, 2 h) as a colorless oil (80%): IR (film) $\nu$ 3325, 3018, 2952, 2923, 2862, 1604, 1495, 1453, 730 cm$^{-1}$; $^1$H NMR $\delta$ 0.90 (d, $J$ = 8 Hz, 3 H, $CH_3$), 1.20−1.72 (m, 4 H, $CH_2CH_2$), 2.03−2.15 (m, 1 H, $CHCH_3$), 3.02−3.11 (m, 1 H, CHN), 3.74 and 3.77 (AB system, $J$ = 14.5 Hz, 2 H, $CH_2Ph$), 5.60 and 5.70 (2 × br d, $J$ = 12.5 Hz, 1 H, CH=CH), 7.13−7.35 (m, 15 H, Ar); $^{13}$C NMR $\delta$ 21.5 ($CH_3$), 27.1 ($CH_2CHMe$), 27.6 ($CH_2CHN$), 30.6 (CHMe), 51.7 ($CH_2Ph$), 52.0 (CHN), 127.2, 128.5, 128.8, 129.1, and 135.7 (Ar CH's and CH=CH), 141.2 (Ar *ipso* C); MS (CI) *m*/*z* (%) 201 (30), 173 (30), 159 (50), 144 (25), 91 (100).

**(*Z*)-1-[Benzyl(*tert*-butyloxycarbonyl)amino]cyclohex-2-en-4-ol (55).** To a solution of amino acetate **8a** (990 mg, 4.04 mmol) and 4-(*N*,*N*)-(dimethylamino)pyridine (50 mg, cat.) in dichloromethane (20 mL) was added di-*tert*-butyl dicarbonate (1.30 g, 5.96 mmol), and the solution was allowed to stir at room temperature for 14 h. The solution was then evaporated and loaded onto a flash column ($SiO_2$ prewashed with 1% triethylamine in petroleum ether), and the spot at 0.20 $R_f$ in petroleum ether−ether 2:1 was collected. This crude product (**54**) was then dissolved in a 1:1 THF−methanol mixture (6 mL), and $K_2CO_3$ (500 mg, 3.62 mmol) in water (3 mL) was added. The mixture was then stirred at room temperature for 72 h. Water (10 mL) was then added, and the mixture was extracted with dichloromethane (2 × 15 mL). The organic portions were combined, and the solvent was evaporated. Chromatography ($SiO_2$, petroleum ether−ether 1:1) afforded **55** as a colorless oil (710 mg, 2.47 mmol, 61%): IR (film) $\nu$ 3290, 2980, 2934, 1739, 1369, 1256, 1095, 1067 cm$^{-1}$; $^1$H NMR (all peaks broadened due to restricted rotation of BOC group) $\delta$ 1.15−1.68 (m, 4 H, $CH_2CH_2$), 1.27 (br s, 9 H, $C(CH_3)_3$), 2.31 (br s, 1 H, OH), 3.84−3.98 (m, 1 H, CHN), 4.13 and 4.28 (2 × br d, 2 × $J$ =

(45) Andersson, P. G. *J. Org. Chem.* **1996**, *61*, 4154.

15.5 Hz, 2 H, C$H_2$Ph), 4.34 (m, 1 H, C*H*OH), 5.53 (br d, $J$ = 11.5 Hz, 1 H, CH═C*H*CHN), 5.70 (br d, $J$ = 11.5 Hz, 1 H, CH═C*H*CHOH), 7.10−7.26 (m, 15 H, Ar); $^{13}$C NMR $\delta$ 23.0 (*C*$H_2$CHN), 28.7 (3 × *C*$H_3$), 30.4 (*C*$H_2$CHOH), 48.7 (*C*$H_2$Ph), 54.0 (*C*HN), 63.1 (*C*HOH), 80.5 (*C*(C$H_3$)$_3$), 127.1, 128.6, 131.6, and 133.2 (Ar *C*H's and *C*H═*C*H), 140.3 (Ar *ipso* C), 156.1 (*C*═O).

**(*E*)-1-[Benzyl(*tert*-butyloxycarbonyl)amino]cyclohex-2-en-4-ol (57).** To a solution of alcohol **55** (710 mg, 2.47 mmol), triphenylphosphine (2.35 g, 8.96 mmol), and acetic acid (535 mg, 8.90 mmol) in THF (15 mL) at 0 °C was added dropwise diethyl azodicarboxylate (1.40 mL, 8.94 mmol). The solution was warmed to 40 °C and stirring was continued for 22 h. The reaction mixture was then cooled, and water (10 mL) was added. The mixture was extracted with dichloromethane (2 × 20 mL), and the combined organic portions were evaporated. The residue was then loaded onto a flash column ($SiO_2$), and the spot at 0.40 $R_f$ in petroleum ether−ether 6:1 was collected. This crude product (**56**) was then dissolved in a 1:1 THF−methanol mixture (2 mL), $K_2CO_3$ (150 mg, 1.09 mmol) in water (1 mL) was added, and the mixture was stirred at room temperature for 96 h. Water (5 mL) was then added, and the mixture was extracted with dichloromethane (2 × 10 mL). The organic portions were combined, and the solvent was evaporated. Chromatography ($SiO_2$, petroleum ether−ether 1:1) afforded **57** as a colorless oil (169 mg, 595 $\mu$mol, 24%): $^1$H NMR (all peaks broadened due to restricted rotation of BOC) $\delta$ 1.12−1.40 (m, 4 H, $CH_2CH_2$), 1.17 (br s, 9 H, C(C$H_3$)$_3$), 2.14 (br s, 1 H, OH), 4.00−4.80 (m, 4 H, C*H*N, C*H*OH and C$H_2$Ph), 5.39 and 5.60 (br d, $J$ = 12.5 Hz, 2 × H, CH═CH), 7.05−7.23 (m, 15 H, Ar); $^{13}$C NMR $\delta$ 27.2 (*C*$H_2$CHN), 28.0 (3 × *C*$H_3$), 32.7 (*C*$H_2$CHOH), 47.7 (*C*$H_2$Ph), 53.6 (*C*HN), 67.0 (*C*HOH), 80.5 (*C*(C$H_3$)$_3$), 126.7, 127.0, 128.6, 130.9, and 135.5 (Ar *C*H's and *C*H═*C*H), 140.5 (Ar *ipso* C), 156.2 (*C*═O).

**(*E*)-1-(Benzylamino)-4-methoxycyclohex-2-ene (59).** To a solution of alcohol **57** (164 mg, 571 $\mu$mol) in DMF (4 mL) was added sodium hydride (35 mg, 60% in mineral oil, 875 $\mu$mol) and the reaction mixture was stirred for 5 min. Methyl iodide (100 $\mu$L, 1.61 mmol) was then added dropwise. After the mixture was stirred at room temperature for a further 18 h, ethyl acetate (10 mL) was added, and the solution was extracted with water (3 × 3 mL). The organic layer was then evaporated and loaded onto a flash column ($SiO_2$) and the spot at 0.30 $R_f$ in petroleum ether−ether 4:1 was collected. This clear oil **58** was then dissolved in trifluoracetic acid (2 mL) and the solution was stirred at room temperature for 3 h. The mixture was then evaporated, $NaHCO_3$ was added (saturated, aqueous, 5 mL), and the solution was extracted with dichloromethane (2 × 10 mL). The combined organic portions were then evaporated to afford **59** as a colorless oil (84 mg, 68%): IR (film) $\nu$ 3330, 2932, 1454, 1103 cm$^{-1}$; $^1$H NMR $\delta$ 1.42−1.65 and 2.14−2.30 (2 × m, 2 × 2 H, $CH_2CH_2$), 3.32−3.41 (m, 1 H, C*H*N), 3.43 (s, 3 H, $CH_3$), 3.86−3.95 (m, 1 H, C*H*OMe), 3.93 (s, 2 H, C$H_2$Ph), 5.92 (s, 2 H, CH═CH), 7.26−7.40 (m, 5 H, Ar); $^{13}$C NMR $\delta$ 27.5 and 28.4 (*C*$H_2$*C*$H_2$), 51.3 (*C*$H_2$Ph), 53.4 (*C*HN), 56.1 (O*C*$H_3$), 75.7 (*C*HOMe), 127.4, 128.6, 128.7, 128.9, and 135.1 (Ar *C*H's and *C*H═*C*H), 140.9 (Ar *ipso* C); MS (EI) *m*/*z* (%) 218 (100, MH$^+$), 185 (20), 159 (15), 110 (15), 91 (10).

**(*E*)-1-[Benzyl(diphenylphosphinous)amidyl]-4-methoxycyclohex-2-ene (60)** was obtained from **59** using method III (34 °C, 16 h) as a clear oil (69%): IR (film) $\nu$ 2926, 1439, 1180, 1120, 1101, 722 cm$^{-1}$; $^1$H NMR $\delta$ 1.15−2.02 (m, 4 H, $CH_2CH_2$), 3.21 (s, 3 H, $CH_3$), 3.50−3.69 (m, 1 H, C*H*N) 3.71−3.81 (m, 1 H, C*H*OMe), 3.95−4.12 (m, 2 H, C$H_2$Ph), 5.63 and 5.76 (2 × br d, 2 × $J$ = 11.5 Hz, 2 H, C*H*═C*H*), 6.87−7.80 (m, 15 H, Ar); $^{13}$C NMR $\delta$ 29.2 and 29.6 (*C*$H_2$*C*$H_2$), 53.7 (*C*$H_2$Ph), 56.0 (*C*HN), 56.6 (O*C*$H_3$), 76.0 (*C*HOMe), 127.3, 128.5, 128.6, 128.7, 128.8, 128.9, 129.0, 129.1, 130.6, 132.5, 132.8, 132.9, 133.3, 134.5, and 134.6 (Ar *C*H's and *C*H═*C*H), 140.1 (2 × C), 140.5 (Ar *ipso* C); $^{31}$P NMR $\delta$ 49.92.

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**Supporting Information Available:** Detailed experimental procedures, HRMS, and combustion analysis data (13 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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