New Homochiral Ligands Bearing Nonstereogenic Chirotopic Centers. Lithiated *N,N′*-Dialkylureas as Chiral Bases and Sterically Crowded Phosphines for Asymmetric Catalysis

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Received March 8, 1999

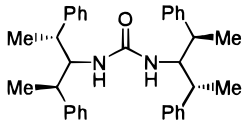
The synthesis of new homochiral pseudo-C_2-symmetrical ligands of type **1** bearing a nonstereogenic chirotopic center is reported. Two such structural units are combined in the ureas **2** and **10**, which proved to be useful for enantioselective deprotonation and alkylation of ketones (up to 88% *ee*). The monophosphine **3** induced a high enantiomeric excess in the Pd-catalyzed allylation of dimethyl malonate (up to 73% *ee*). Furthermore, we have shown that the achiral sterically crowded alkyl diphosphine **23** efficiently stabilized Pd(0) at high temperatures.

Introduction

During the last two decades, asymmetric synthesis has gained a great deal of attention.[1] Extensive effort has been devoted to the design of new chiral ligands, which were employed in enantioselective transformations in either a stoichiometric or a catalytic manner. A major drawback of many of these ligands is a challenging synthesis requiring the stereospecific linkage of a sterically demanding secondary carbon center to a heteroatom. Recently, we have introduced a new class of powerful homochiral ligands of type **1** bearing a nonstereogenic center at C(2).[2] According to the definition of Mislow,[3] C(2) can be described as a chirotopic center, i.e., a center in a chiral environment. By design, these pseudo-C_2-symmetrical ligands have the inherent synthetic advantage of avoiding the control of the stereochemistry at the secondary carbon atom C(2) (**1a** = **1b**).

1a **1b**

X = NH_2, PR_2, BH_2, Cl, Metal



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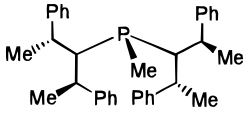

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Two such chiral backbones were combined in the urea **2** and the phosphine **3**. Herein, we wish to report the full details of our investigations concerning these two types of reagents.[2] The lithiated urea **2** proved to be useful as a chiral base for the enantioselective deprotonation[4,5] of conformationally locked prochiral cyclic ketones, as well as for the enantioselective alkylation[6] of cycloalkanones. For the first time, anions of chiral ureas[7] rather than lithium amides were employed in those reactions of considerable synthetic importance. Furthermore, the

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(1) (a) Nogradi, M. *Stereoselective Synthesis*; VCH: Weinheim, 1995. (b) Houben-Weyl, Methoden der Organischen Chemie. *Stereoselective Synthesis* Helmchen, G., Mulzer, J., Hoffmann, R. W., Schaumann, E., Eds.; Thieme: Stuttgart, 1995−1996; Vol. E21a−f. (c) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; Wiley: New York, 1994. (d) *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: Weinheim, 1993.

(2) Graf, C.-D.; Malan, C.; Knochel, P. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 3014.

(3) Mislow, K.; Siegel, J. *J. Am. Chem. Soc.* **1984**, *106*, 3319.

(4) Reviews: (a) O'Brien, P. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1439. (b) Gais, H.-J. In ref 1b; Vol. E21a, p 589. (c) Simpkins, N. S.; Cox, P. J. *Tetrahedron: Asymmetry* **1991**, *2*, 1. (d) Hodgson, D. M.; Gibbs, A. R.; Lee, G. P. *Tetrahedron* **1996**, *52*, 14361. (e) Simpkins, N. S. *Pure Appl. Chem.* **1996**, *68*, 691. (f) Koga, K. *Pure Appl. Chem.* **1994**, *66*, 1487.

(5) For some examples, see: (a) Vaulont, I.; Gais, H.-J.; Reuter, N.; Schmitz, E.; Ossenkamp, R. K. L. *Eur. J. Org. Chem.* **1998**, *805*, 5. (b) Gais, H.-J.; Ossenkamp, R. K. L. *Liebigs Ann.* **1997**, 2433. (c) Aoki, K.; Tomioka, K.; Noguchi, H.; Koga, K. *Tetrahedron* **1997**, *53*, 13641. (d) Shirai, R.; Sato, D.; Aoki, K.; Tanaka, M.; Kawasaki, H.; Koga, K. *Tetrahedron* **1997**, *53*, 5963. (e) Aoki, K.; Koga, K. *Tetrahedron Lett.* **1997**, *38*, 2505. (f) Majewski, M.; McKinnon, J. *Can. J. Chem.* **1994**, *72*, 1699. (g) Izawa, H.; Shirai, R.; Kawasaki, H.; Kim, H.; Koga, K. *Tetrahedron Lett.* **1989**, *30*, 7221. (h) Cain, C. M.; Cousins, R. P. C.; Coumbarides, G.; Simpkins, N. S. *Tetrahedron* **1990**, *46*, 523.

(6) (a) Imai, M.; Hagihara, A.; Kawasaki, H.; Manabe, K.; Koga, K. *J. Am. Chem. Soc.* **1994**, *116*, 8829. (b) Hasegawa, Y.; Kawasaki, H.; Koga, K. *Tetrahedron Lett.* **1993**, *34*, 1963. (c) Murakata, M.; Nakajima, M.; Koga, K. *J. Chem. Soc., Chem. Commun.* **1990**, 1657. (d) Ando, A.; Shioiri, T. *J. Chem. Soc., Chem. Commun.* **1987**, 656. (e) Yamashita, T.; Mitsui, H.; Watanabe, H.; Nakamura, N. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 961. (f) Yamashita, Y.; Odashima, K.; Koga, K. *Tetrahedron Lett.* **1999**, *40*, 2803.

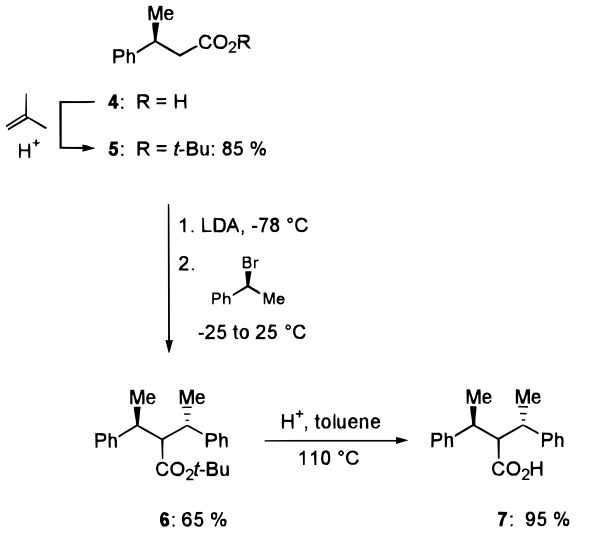
(7) To date, only a few reports describing the use of ureas as chiral auxiliaries have appeared. (a) Asymmetric Diels−Alder reactions: Kishikawa, K.; Yamamoto, M.; Kohmoto, S.; Yamada, K. *Chem. Lett.* **1988**, 1623. (b) Enantioselective Ru-catalyzed transfer hydrogenation: Touchard, F.; Fache, F.; Lemaire, M. *Tetrahedron: Asymmetry* **1997**, *8*, 3319. (c) Diastereoselective radical allylations: Curran, D. P.; Kuo, L. H. *J. Org. Chem.* **1994**, *59*, 3259. (d) For use as templates in supramolecular chemistry, see: Hamann, B. C.; Branda, N. R.; Rebek, J., Jr. *Tetrahedron Lett.* **1993**, *34*, 6837 and references cited therein.

(8) Reviews: (a) Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395. (b) Pfaltz, A. *Acc. Chem. Res.* **1993**, *26*, 339. (c) Hayashi, T. In ref 1d; p 325. (d) Frost, C. G.; Howarth, J.; Williams, J. M. J. *Tetrahedron: Asymmetry* **1992**, *3*, 1089. (e) Consiglio, G.; Waymouth, R. M. *Chem. Rev.* **1989**, *89*, 257.

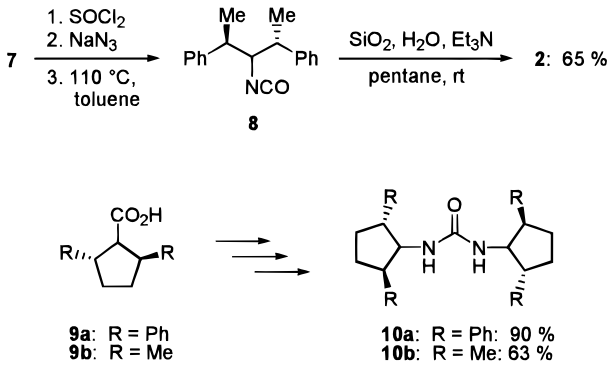
(9) For some examples, see: (a) Gläser, B.; Kunz, H. *Synlett* **1998**, 53. (b) Chen, Z.; Jiang, Q.; Zhu, G.; Xiao, D.; Cao, P.; Guo, C.; Zhang, X. *J. Org. Chem.* **1997**, *62*, 4521. (c) Hamada, Y.; Seto, N.; Ohmori, H.; Hatano, K. *Tetrahedron Lett.* **1996**, *37*, 7565. (d) Knühl, G.; Sennhenn, P.; Helmchen, G. *J. Chem. Soc., Chem. Commun.* **1995**, 1845. (e) Trost, B. M.; Bunt, R. C. *J. Am. Chem. Soc.* **1994**, *116*, 4089. (f) Brown, J. M.; Hulmes, D. I.; Guiry, P. J. *Tetrahedron* **1994**, *50*, 4493. (g) von Matt, P.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 566.

10.1021/jo990412u CCC: $18.00
Published on Web 06/24/1999

Scheme 1



Scheme 2



sterically crowded phosphine **3** was found to be an excellent ligand for Pd-catalyzed enantioselective allylations.[8,9]

Results and Discussion

As key intermediate for the preparation of ligands of type **1**, we chose the carboxylic acid **7**. The esterification of commercially available (*S*)-3-phenylbutyric acid **4** with isobutylene provided the *tert*-butyl ester **5**, which was alkylated with (*S*)-1-bromoethylbenzene[10] (88% ee), furnishing the desired (*S*,*S*)-*tert*-butyl ester **6** contaminated with 10% of the *meso*-isomers (Scheme 1). Simple recrystallization of **6** from pentane/acetone provided the ester **6** in diastereomerically and enantiomerically pure form. Subsequent acid-catalyzed cleavage of the ester function of **6** gave the desired carboxylic acid **7**. This convenient reaction sequence has been performed on a 10 g scale with an overall yield of ca. 50%.

Synthesis of the Urea 2. The carboxylic acid **7** underwent a straightforward Curtius rearrangement[11] leading to the intermediate isocyanate **8**, which was transformed to the chiral urea **2** simply by stirring a solution of **8** in pentane/ether with silica gel at room temperature (65% yield, Scheme 2). The same approach allowed the preparation in equally good yields of the ureas **10** (R = Ph, Me) bearing cycloalkyl groups.[12] The synthesis of the starting compounds **9a** and **9b** in enantiomerically pure form is described elsewhere.[13]

Scheme 3

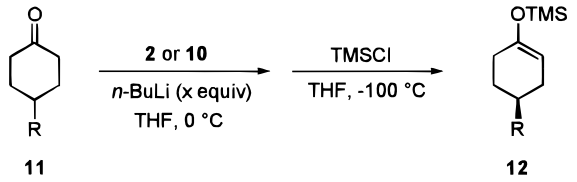


Table 1. Asymmetric Deprotonation of Prochiral Cyclic Ketones 11

entry	urea	x^a	R	**12**	yield^b (%)	ee^c (%)
1	**2**	1	*t*-Bu	**a**	45	33
2	**2**	2	*t*-Bu	**a**	85	87
3^d	**2**	2	*t*-Bu	**a**	40	67
4	**2**	2	Me	**b**	87	84
5	**2**	2	*i*-Pr	**c**	84	87
6	**2**	2	Ph	**d**	88	83
7	**2**	2	OTBS	**e**	85	88
8	**10a**	2	*t*-Bu	**a**	60	37^e
9^d	**10b**	2	*t*-Bu	**a**	20	7

^{a} Number of equivalents of *n*-BuLi added. ^{b} Isolated yield of analytically pure product. ^{c} The ee was determined by GC on a chiral phase. The absolute configuration was determined by comparing the optical rotation with literature values. ^{d} HMPA was added. ^{e} (*R*).

Asymmetric Deprotonation of Prochiral Cycloalkanones. We were interested to find whether the anions of the chiral ureas **2** and **10** obtained by abstraction of the acidic protons of **2** and **10** by 1 or 2 equiv of a strong base such as *n*-BuLi could act as chiral bases in the enantioselective deprotonation[4,5] of prochiral cycloalkanones such as **11** (Scheme 3). Over the past few years, this important reaction in the field of asymmetric synthesis has been thoroughly studied by the research groups of Koga[4f,5c−e,g] and Simpkins,[4c,e,5h] using exclusively lithium amides.

In a first experiment, we employed the weakly basic monolithiated urea **2**, using Corey's "in situ quench protocol".[14] The silyl enol ether **12a** (R = *t*-Bu) was obtained in moderate yield and low enantiomeric excess (Table 1, entry 1). We were delighted to find that the use of the strongly basic dianion of urea **2** resulted in better stereoselectivities. The product **12a** could be isolated in 85% yield and with 87% ee (entry 2).[15] We hoped that increasing the polarity of the reaction medium by adding HMPA would lead to improved enantioselectivities as observed by Koga[5c,d] in the case of lithium amides. In the case of dilithiated urea **2**, the reverse was observed: the yield and the enantiomeric excess decreased (entry 3). The enantioselective deprotonation mediated by the dianion of **2** is of broad scope. A variety of cyclohexanones **11a**−**e** bearing different groups R at C(4) (alkyl, aryl, $OSiR_3$) reacted well, leading to the corresponding silyl enol ethers **12a**−**e** in high yields (84−88%) and high

(10) (*S*)-1-bromoethylbenzene has been prepared by treatment of (*R*)-1-phenylethanol with Ph_3P/Br_2. The enantiomeric excess was determined directly by GC on a chiral support.

(11) Pfister, J. R.; Wymann, W. E. *Synthesis* **1983**, 38.

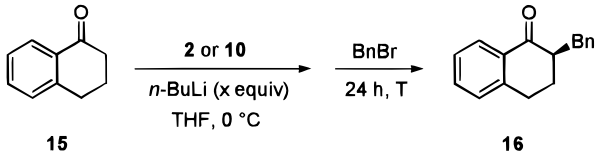
(12) Note that the ureas **2** and **10a**,**b** are the only possible stereoisomers that can be formed because the homochiral carbon backbones are attached to the nitrogen atoms by nonstereogenic (chirotopic) centers.

(13) Graf, C.-D.; Knochel, P. *Tetrahedron* **1999**, *55*, in press.

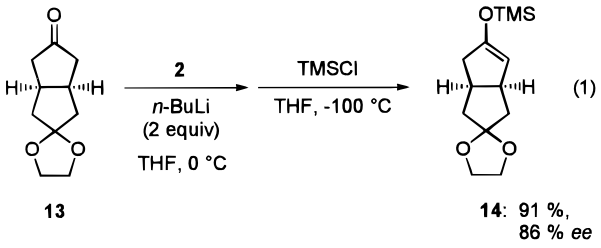
(14) Corey, E. J.; Gross, A. W. *Tetrahedron Lett.* **1984**, *25*, 495.

(15) Interestingly, the corresponding chiral urea derived from (*S*)-1-phenylethylamine afforded the silyl enol ether **12a** with only 40% ee (34% yield), showing the importance of the pseudo-C_2-symmetrical backbone.

Scheme 4



enantiomeric excesses (83−88%) (entries 4−7).[16] The reaction could be extended to the prochiral bicyclic cyclopentanone **13**, resulting in the silyl enol ether **14** in equally good yield and 86% ee (eq 1).[17]



Remarkably, the products **12c**, **12e**, and **14** are of synthetic interest, being already employed as enantiomerically enriched starting materials in natural product syntheses.[18] Disappointingly, the use of the dianions of ureas **10** bearing cycloalkyl groups (in which conformational flexibility should be reduced) led to lower yields and selectivities (Table 1, entries 8 and 9). Dilithiated **10b** (R = Me) was found to be almost unreactive probably as a result of its extremely low solubility in the reaction medium (despite the addition of HMPA).

Enantioselective Alkylation of 1-Tetralone (15). Another reaction of considerable synthetic importance is the enantioselective alkylation of ketones.[6] In this reaction, the ketone is first converted to a prochiral enolate, which is subsequently trapped by an alkyl halide in the presence of a chiral base. The latter is complexed to the enolate and thus directs the attack of the electrophile preferentially to one of the two enantiotopic faces of the molecule. Inspired by the successful application of the dilithiated urea **2** in the asymmetric deprotonation of prochiral cycloalkanones, we treated 1-tetralone (**15**) at room temperature with this reagent followed by benzyl bromide, which afforded benzyl tetralone **16** in good yield (74%) but only moderate enantiomeric excess (50%, Scheme 4 and Table 2, entry 1).

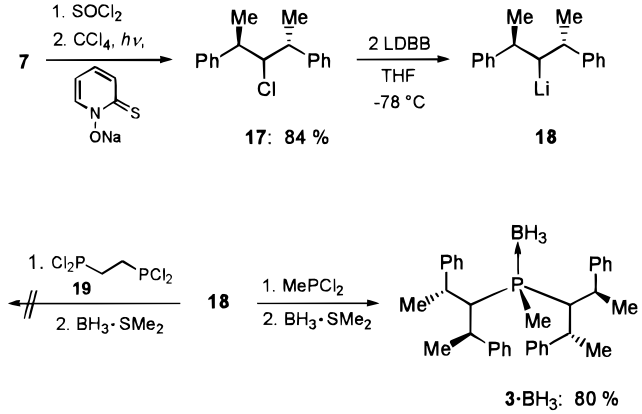
Alternatively, the benzylation could be carried out using the monoanion of **2** as the source of chirality. The yield of **16** was nearly the same (80%), but the enantiomeric excess increased to 76% (entry 2). Further investigation revealed that THF is the solvent of choice (compare entries 3 and 5), and the optimum reaction temperature turned out to be −20 °C (entries 2−4). Thus, performing the alkylation at −20 °C in THF furnished the product **16** in high yield (83%) and high enantiomeric excess (81%, entry 3).[19] We hoped that lowering the temperature and simultaneously increasing the reactivity of the electrophile would further improve the enantioselectivity. Disappointingly, the use of benzyl iodide at −40 °C resulted in both lower yield (25%) and reduced enantiomeric excess (41%, entry 6). As already observed in the case of the asymmetric deprotonation, the chiral ureas **10** (R = Ph, Me) bearing cycloalkyl groups were found to be much less efficient than **2**. Under the same reaction conditions, benzyl tetralone **16** was obtained in only modest optical purities (around 40% ee, entries 7 and 8).

Table 2. Enantioselective Benzylation of 1-Tetralone (15)

entry	urea	x^a	T (°C)	yield^b (%)	ee^c (%)
1	**2**	2	25	74	50
2	**2**	1	25	80	76
3	**2**	1	−20	83	81
4	**2**	1	−40	57	60
5^d	**2**	1	−20	69	40
6^e	**2**	1	−40	25	41
7	**10a**	1	−20	54	39
8^f	**10b**	1	−20	75	41

[a] Number of equivalents of *n*-BuLi added. [b] Isolated yield of analytically pure product. [c] The ee was determined by HPLC on a chiral phase. The absolute configuration was determined by comparing the optical rotation with literature values. [d] Toluene was used as solvent. [e] BnI was used. [f] HMPA was added to dissolve the anion of **10b**.

Scheme 5



Syntheses of Phosphines. Next, we turned our attention to the preparation of phosphines containing homochiral substituents with nonstereogenic chirotopic centers. The pseudo-C_2-symmetrical carboxylic acid **7** was readily transformed to the corresponding alkyl chloride **17** via a radical decarboxylation (Scheme 5).[20]

Thus, treatment of **7** with thionyl chloride followed by reaction with the sodium salt of 2-mercaptopyridine-*N*-oxide with simultaneous photolysis in CCl_4 furnished the alkyl chloride **17** in 84% yield. It was reductively lithiated using lithium 4,4′-di-*tert*-butylbiphenylide (LDBB, 2 equiv),[21] and the in situ generated alkyllithium reagent **18** was allowed to react with methyldichlorophosphine

(16) During the preparation of this manuscript, Koga reported the preparation of the silyl enol ethers **12a**−**d** in 92−95% ee using fluorine-containing chiral lithium amides; see: ref 5c.

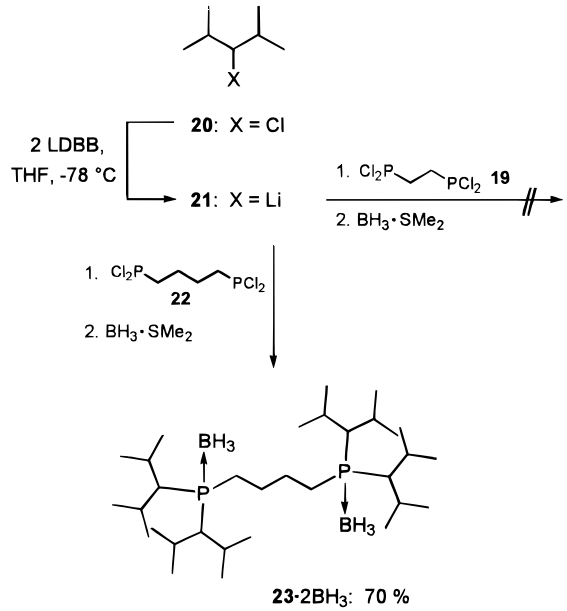
(17) Cyclopentanone **13** was chosen as one of the first substrates in the area of asymmetric deprotonation and converted to **14** by Koga with similar enantiomeric excess (87% ee); see: ref 5g. Recently, Gais et al. optimized the reaction by variation of the ketal protecting group of the starting compound; see: ref 5a,b.

(18) (a) The silyl enol ether **12c** served as starting compound for the synthesis of (+)-brasilenol; see: Greene, A. E.; Serra, A. A.; Barreiro, E. J.; Costa, P. R. R. *J. Org. Chem.* **1987**, *52*, 1169. (b) The silyl enol ether **12e** served as starting compound for the synthesis of derivatives of vitamine D; see: Parker, K. A.; Dermatakis, A. *J. Org. Chem.* **1997**, *62*, 6692. (c) The silyl enol ether **14** served as starting compound for the synthesis of carbacyclin and its derivatives; see: ref 5a,b,g.

(19) Recently, Koga has reported the catalytic enantioselective benzylation of 1-tetralone (**15**), leading to **16** with 96% ee (76% yield); see: ref 6a.

(20) Barton, D. H. R.; Crich, D.; Motherwell, W. B. *Tetrahedron* **1985**, *41*, 3901.

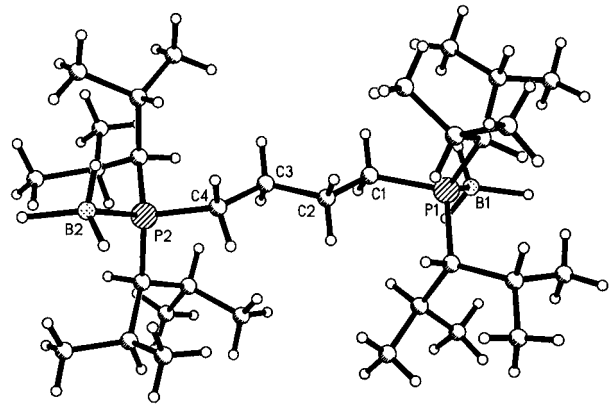
Scheme 6



affording the chiral monophosphine **3**, which was isolated and stored as its BH_3-complex (80% yield, Scheme 5).[22] Attempts to prepare a diphosphine by reacting **18** with 1,2-bis(dichlorophosphino)ethane (**19**) were unsuccessful probably as a result of extreme steric hindrance caused by the highly branched pentyllithium reagent **18**. To corroborate the latter hypothesis, we envisioned the synthesis of a 1,2-diphosphine starting from the less hindered achiral alkyl chloride **20** in which the two bulky phenyl groups of **17** were replaced by smaller methyl groups (Scheme 6).

Surprisingly, a similar reactivity pattern was observed, i.e., no diphosphine could be detected after reaction of the alkyllithium reagent **21** with the phosphorus electrophile **19**. Remarkably, treatment of **21** with 1,4-bis(dichlorophosphino)butane **22** smoothly furnished the expected 1,4-diphosphine **23**, which was isolated as its BH_3-complex (70% yield). An X-ray crystal structure analysis of the latter compound revealed the impressive crowding around each phosphorus center (Figure 1).[23]

Reducing the distance between the overcrowded phosphorus atoms by replacing the butano spacer by an ethano group would result in severe steric repulsion of the branched alkyl substituents, thereby explaining the experimental failures described above.[24]



23·2BH_3

Figure 1.

Scheme 7

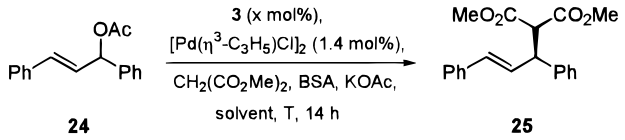


Table 3. Enantioselective Pd-Catalyzed Allylation

entry	solvent	x^a (mol %)	T (°C)	yield^b (%)	ee^c (%)
1	THF	6	25	93	25
2	toluene	6	25	96	43
3	CH_2Cl_2	6	25	94	56
4	DMF	6	25	88	72
5	DMF	3	25	90	73
6	DMF	9	25	93	69
7	DMF	3	0	67	73

[a] Amount of phosphine **3** added. [b] Isolated yield of analytically pure product. [c] The ee was determined by HPLC on a chiral phase. The absolute configuration was determined by comparing the optical rotation with literature values.

Enantioselective Pd-Catalyzed Allylation. To date, complexes of chiral phosphines with transition metals have found widespread use as catalysts for various enantioselective processes.[1] We chose Pd-catalyzed allylation[8,9] to test the effectiveness of the new monophosphine **3** as a chiral ligand. Although many palladium complexes of multidentate phosphine and nitrogen ligands are excellent catalysts for this reaction, palladium complexes of simple chiral monophosphines are normally not effective.[25] We were delighted to find that after deprotection[26] phosphine **3** proved to catalyze the enantioselective allylation of dimethyl malonate with the allylic acetate **24** in the presence of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$, leading to the malonate **25** in excellent yield and up to 73% ee (Scheme 7 and Table 3).[27]

The enantiomeric excess of **25** was strongly dependent on the choice of solvent, with DMF being superior to THF, toluene, or dichloromethane (Table 3, entries 1−4). Interestingly, variation of the ratio of phosphine to palladium (entries 4−6), as well as lowering of the

(21) (a) Freeman, P. K.; Hutchinson, L. L. *J. Org. Chem.* **1980**, *45*, 1924. (b) Yus, M. *Chem. Soc. Rev.* **1996**, 155.

(22) Note that phosphine−borane complex **3**·BH_3 is the only possible stereoisomer that can be formed because the homochiral carbon backbones are attached to the phosphorus atom by nonstereogenic (chirotopic) centers. Because the phosphorus atom is also nonstereogenic and chirotopic, **3**·BH_3 contains three contiguous tetrahedral nonstereogenic chirotopic atoms.

(23) The crystal data for **23**·2BH_3 are as follows: orthorhombic; *Pbca* with a = 1800.3(1) pm, b = 1447.4(1) pm, c = 2838.4(1) pm, V = 7.3962(7) nm^3, Z = 8, D_{calc} = 0.974 Mg/m^3, λ = 154.178 pm (Cu Kα) by Enraf Nonius CAD4 diffractometer. Final R value was 0.0491 for 5470 reflections. Atomic coordinates and esd values have been deposited at the Cambridge Crystallographic Data Center.

(24) The facile preparation of the 1,4-diphosphine **23** from the achiral alkyllithium compound **21** and the chlorophosphine **22** strongly suggests a clean reaction of the chiral organolithium reagent **18** with **22** to furnish an acyclic chiral 1,4-diphosphine. However, this reaction was not examined because there is no need for further development of new acyclic chiral 1,4-diphosphines. As a result of the presence of the butano spacer, they are too conformationally flexible and in the past, they have proven to be inferior to sterically more rigid (acyclic) 1,2-diphosphines in asymmetric transformations; see: ref 1.

(25) During the preparation of this manuscript, Hamada and Zhang independently presented two monophosphines with a rigid bicyclic structure that led to high enantioselectivities in Pd-catalyzed allylations; see: ref 9b,c.

(26) McKinstry, L.; Livinghouse, T. *Tetrahedron* **1995**, *51*, 7655.

(27) Over the past few years, this reaction was thoroughly studied, and enantiomeric excesses of >95% were achieved using a variety of different P,P- or P,N-ligands; see: refs 8 and 9.

reaction temperature (entry 7), did not significantly influence the enantioselectivity of the transformation. Thus, performing the allylation at room temperature using only 1 equiv of phosphine **3** gave 90% isolated yield of malonate **25** with 73% ee (entry 5).

Stabilization of Pd(0) by Complexation with the Sterically Crowded Diphosphine 23. During the past decade, significant progress for Pd-catalyzed cross-coupling reactions, olefin arylations ("Heck reactions") and carbonylation of aryl halides has been made, allowing the use of unreactive aryl chlorides as cheap starting materials in those processes.[28] The major problem associated with the use of aryl chlorides,[29] the fast decomposition of the catalyst at the high temperatures required for reaction, leading to the precipitation of inert Pd-black, was overcome by the stabilization of Pd(0) with sterically hindered chelating alkyl phosphines.[30,31] Inspired by the pioneering work of Milstein,[30e−i] we were interested to find whether the sterically crowded 1,4-diphosphine **23** could further improve the yields of the Heck reaction of even less reactive donor-substituted aryl chlorides. In a first experiment, chlorobenzene was sought to react with styrene in DMF in the presence of $Pd(OAc)_2$ (1 mol %), phosphine **23** (2 mol %), and NaOAc (1 equiv). Surprisingly, no reaction took place, even after 24 h at 140 °C. However, no precipitation of Pd-black could be observed. Reducing the amount of diphosphine **23** to only 1 mol % and replacing chlorobenzene by the more reactive bromobenzene did not change the outcome of the experiment; neither the desired product stilbene nor Pd-black could be detected. Obviously, the extremely bulky phosphine **23** efficiently stabilized Pd(0) through complexation, preventing at the same time an oxidative addition to an aryl halide by efficient shielding of the metal center.

Conclusion

In summary, we have shown that chiral nitrogen or phosphorus ligands in which the chiral group is attached to the heteroatom by a nonstereogenic chirotopic center can be used for asymmetric synthesis. The new chiral urea **2** proves to be useful for enantioselective deprotonations and for enantioselective alkylations. The bulky monophosphine **3** was found to be an excellent source of chirality in Pd-catalyzed allylations. Finally, we have demonstrated that the achiral sterically crowded diphosphine **23** efficiently stabilizes Pd(0) by complexation.

Experimental Section

General. Enantiomeric excesses were determined by HPLC. Chiralcel columns OD, OB, and OJ (Daicel Chemical Industries) were used at room temperature with *n*-heptane/2-propanol as mobile phase and detection by a diode array UV−vis detector. Alternatively, determination of optical purity was carried out by GC on a Chirasil-DEX CB column (Chrompak) with hydrogen as carrier gas. Racemic compounds were used to choose the operating conditions for the resolution of the enantiomer and diastereomer peaks. The absolute configurations of the silyl enol ethers **12a**−**e** and **14**, tetralone **16**, and malonate **25** were determined by comparing the optical rotation with literature values. Melting points are uncorrected.

THF was distilled from potassium, and Et_2O and toluene were distilled from sodium/benzophenone. CH_2Cl_2, DMF, HMPA, TMSCl, and *i*-Pr_2NH were distilled from CaH_2, and acetonitrile and CCl_4 were distilled from P_4O_{10}. Starting materials were purchased from commercial sources and used without further purification unless otherwise noted. The following starting materials were prepared according to literature procedures: (2*S*,5*S*)-2,5-diphenylcyclopentanecarboxylic acid (**9a**),[13] (2*S*,5*S*)-2,5-dimethylcyclopentanecarboxylic acid (**9b**),[13] 4-(*tert*-butyldimethylsiloxy)cyclohexanone (**11e**),[5f] 7,7-ethylenedioxybicyclo[3.3.0]octan-3-one (**13**),[32] 1,4-bis(dichlorophosphino)butane (**22**),[33] and *rac*-(*E*)-1,3-diphenyl-1-acetoxy-2-propene (**24**).[9f]

***tert*-Butyl (*S*)-3-Phenylbutanoate (5).** Concentrated H_2SO_4 (0.5 mL) was added at −15 °C to a well-stirred solution of (*S*)-3-phenylbutanoic acid (14.0 g, 85.3 mmol; 99% ee) in CH_2Cl_2 (120 mL), followed by liquid isobutylene (23.0 g, 410 mmol). The reaction mixture was allowed to warm to room temperature overnight and then stirred at 35 °C for 2 h. The solution was diluted with $CHCl_3$ (250 mL) and washed successively with saturated aqueous Na_2CO_3 and brine. The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by chromatography (pentane/Et_2O 10:1) yielding ester **5** (16.0 g, 85%) as a viscous oil: $[\alpha]^{25}_D = +23.5$ ($c = 3.6$, $CHCl_3$); IR (film) 1730 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.32−7.14 (m, 5H), 3.28−3.14 (m, 1H), 2.52 (dd, $J = 7.3$, 14.7 Hz, 1H), 2.44 (dd, $J = 8.1$, 14.7 Hz, 1H), 1.35 (s, 9H), 1.28 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.6, 145.9, 128.3, 126.8, 126.2, 80.1, 44.1, 36.8, 28.0, 21.9; MS (EI) *m*/*z* 220 (M^+, 1%). Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 75.96; H, 9.09.

(*S*)-1-Bromoethylbenzene.[34] Bromine (31.5 g, 197 mmol) was added at −20 °C to a vigorously stirred suspension of Ph_3P (52.0 g, 198 mmol) in acetonitrile (170 mL). The cooling bath was removed, and the mixture was stirred at room temperature for 50 min. After the mixture cooled back to −35 °C, a solution of (*R*)-1-phenylethanol (16.0 g, 131 mmol; 97% ee) in acetonitrile (19 mL) was slowly added while the temperature, which should not exceed −30 °C, was carefully controlled. The heterogeneous reaction mixture was warmed to −10 °C over 70 min (100% conversion) and subsequently poured into water (500 mL). The aqueous phase was extracted with pentane, and the combined organic phases were washed with water and brine and dried ($MgSO_4$). The solution was concentrated under reduced pressure (bath temperature < 40 °C), yielding (*S*)-1-bromoethylbenzene (quantitative; 88% ee) contaminated with small amounts of $Ph_3P(O)$. To prevent exhaustive racemization, this crude product was directly used for the next step within 20 min. GC (CB, 100 kPa, 50 °C (1 min) to 100 °C, 4 °C/min): t_R (min) = 15.4 (*S*), 16.1 (*R*).

***tert*-Butyl (*S*)-3-Phenyl-2-[(*S*)-phenylethyl]butanoate (6).** At −78 °C, *n*-BuLi (62.0 mL, 86.2 mmol, 1.4 M in *n*-hexane) was added to a solution of *i*-Pr_2NH (10.2 g, 101 mmol) in THF (70 mL). The cooling bath was removed, and the solution was stirred for 20 min at 0 °C. After the mixture cooled back to −78 °C, a solution of **5** (14.0 g, 63.6 mmol; 99% ee) in THF (18 mL) was dropwise added, and the solution was stirred for 1.5 h at this temperature before being quickly

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warmed to −25 °C. A solution of (*S*)-1-bromoethylbenzene (131 mmol; 88% ee; see above) and HMPA (19.0 g, 106 mmol) in THF (14 mL) was quickly added while the temperature, which should not exceed −20 °C, was carefully controlled. The dark-red solution was allowed to warm to room temperature over 3 h and poured into water. After separation of the organic layer, the volatiles were removed under reduced pressure. The residue was dissolved in $CHCl_3$ and washed successively with 10% aqueous HCl, 20% aqueous NaOH, and brine. The organic layer was dried ($MgSO_4$), and the solvent was removed in vacuo. The crude product was crystallized from pentane/acetone at room temperature, yielding ester **6** in diastereomerically and enantiomerically pure form (13.5 g, 65%; 100% ee) as colorless needles: mp 129−131 °C; $[\alpha]^{25}_D = -20.1$ (c = 1.7, $CHCl_3$); IR (KBr) 1710 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.25−7.02 (m, 10H), 3.12−3.01 (m, 1H), 2.99−2.88 (m, 1H), 2.71 (dd, J = 7.0, 9.5 Hz, 1H), 1.31 (d, J = 7.1 Hz, 3H), 1.14 (d, J = 7.1 Hz, 3H), 0.92 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.5, 145.2, 144.8, 128.3, 128.1, 127.9, 127.7, 126.2, 126.1, 79.7, 59.3, 40.7, 39.8, 27.5, 20.3, 16.7; MS (EI) m/z 324 (M^+, 1%); HRMS calcd for $C_{22}H_{28}O_2$ 324.2089, found 324.2088.

(*S*)-3-Phenyl-2-[(*S*)-phenylethyl]butanoic Acid (7). A solution of ester **6** (6.00 g, 18.5 mmol; 100% ee) and *p*-TsOH·H_2O (400 mg, 2.10 mmol) in toluene (30 mL) was refluxed overnight. The solvent was evaporated under reduced pressure, and the crude product was purified by chromatography (pentane/EtOAc 4:1, 1% AcOH added), yielding carboxylic acid **7** (4.70 g, 95%) as a colorless oil that slowly solidified upon standing: mp 89−91 °C; $[\alpha]^{25}_D = -12.5$ (c = 2.4, $CHCl_3$); IR (KBr) 2650, 1700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 10.2 (br, 1H), 7.42−7.10 (m, 10H), 3.20−3.05 (m, 2H), 2.98 (dd, J = 7.9, 8.0 Hz, 1H), 1.38 (d, J = 6.9 Hz, 3H), 1.35 (d, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 179.5, 144.7, 143.6, 128.6, 128.0, 127.9, 127.5, 126.6, 126.5, 58.7, 40.1, 39.8, 20.2, 18.9; MS (EI) m/z 268 (M^+, 8%). Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.54; H, 7.37.

***N,N′*-Bis{(2*R*)-phenyl-1-[(*R*)-phenylethyl]propyl}-urea (2).** The carboxylic acid **7** (4.00 g, 14.9 mmol) was refluxed with thionyl chloride (9.00 g, 75.7 mmol) for 3 h. Excess reagent was evaporated in vacuo, and the solid residue was dissolved in CH_2Cl_2 (16 mL) and cooled to 0 °C. After addition of *n*-Bu_4NBr (38 mg, 0.12 mmol), an ice-cold solution of sodium azide (1.50 g, 23.1 mmol) in water (3.5 mL) was dropwise added. The biphasic system was vigorously stirred at 0 °C for 2 h. The organic layer was separated, and the aqueous phase was extracted with ice-cold CH_2Cl_2. The combined organic phases were successively washed with ice-cold water and brine and dried ($MgSO_4$, 0 °C). After filtration, the solution of the carboxylic azide was quickly added via cannula to hot toluene (200 mL, 100 °C) under argon. The reaction mixture was refluxed for 1.5 h. After cooling to room temperature, the solution was concentrated in vacuo, and the brownish oil was dissolved in pentane/Et_2O (1:1; 40 mL). Silica gel (2.0 g), Et_3N (1 mL), and water (2 mL) were added, and the suspension was stirred at room temperature overnight. After evaporation of the volatiles under reduced pressure, the crude product was purified by chromatography (pentane/EtOAc/CH_2Cl_2 3:1:1) yielding urea **2** (2.45 g, 65%) as a colorless solid: mp 74−76 °C; $[\alpha]^{25}_D = -99.3$ (c = 1.5, $CHCl_3$); IR (KBr) 1670 cm^{-1}; ^1H NMR (DMSO-d_6, 110 °C, 500 MHz) δ 7.36−7.11 (m, 20H), 5.57 (m, 2H), 4.23 (m, 2H), 2.76 (m, 2H), 2.59 (m, 2H), 1.18 (d, J = 7.1 Hz, 6H), 1.08 (d, J = 7.0 Hz, 6H); ^{13}C NMR (DMSO-d_6, 110 °C, 125 MHz) δ 158.8, 146.7, 144.1, 129.0, 128.8, 128.3, 128.1, 126.4, 58.4, 43.4, 42.0, 20.2, 19.5; MS (EI) m/z 399 ($M^+ - C_8H_9$, 9%). Anal. Calcd for $C_{35}H_{40}N_2O$: C, 83.29; H, 7.99; N, 5.55. Found: C, 83.11; H, 8.02; N, 5.50.

***N,N′*-Bis[(2*R*,5*R*)-2,5-diphenylcyclopentyl]urea (10a).** The carboxylic acid **9a** (970 mg, 3.64 mmol) was first treated with thionyl chloride (3.00 g, 25.2 mmol) and then with a solution of sodium azide (370 mg, 5.69 mmol) and *n*-Bu_4NBr (20 mg, 0.06 mmol) in water (2 mL) as described for **2**. After completion of the Curtius rearrangement in hot toluene (100 mL), the solution was cooled to room temperature. Silica gel (2.0 g), Et_3N (2 mL), and water (2 mL) were added, and the suspension was stirred at 55 °C overnight. After evaporation of the volatiles in vacuo, the crude product was purified by chromatography (pentane/EtOAc/CH_2Cl_2 2:1:1), yielding urea **10a** (820 mg, 90%) as colorless needles: mp 180 °C; $[\alpha]^{25}_D = +222.8$ (c = 0.7, $CHCl_3$); IR (KBr) 1646 cm^{-1}; ^1H NMR (DMSO-d_6, 100 °C, 500 MHz) δ 7.30−7.06 (m, 20H), 5.06 (d, J = 8.7 Hz, 2H), 4.21 (q, J = 8.2 Hz, 2H), 3.37 (q, J = 7.6 Hz, 2H), 2.82 (q, J = 8.5 Hz, 2H), 2.24−2.14 (m, 4H), 1.99−1.91 (m, 2H), 1.78−1.70 (m, 2H); ^{13}C NMR (DMSO-d_6, 100 °C, 125 MHz) δ 156.2, 143.4, 141.1, 128.0, 127.5, 127.0, 126.6, 125.2, 125.0, 59.1, 49.3, 46.4, 30.3, 28.4; MS (EI) m/z 500 (M^+, 32%). Anal. Calcd for $C_{35}H_{36}N_2O$: C, 83.96; H, 7.25; N, 5.60. Found: C, 83.72; H, 7.27; N, 5.46.

***N,N′*-Bis[(2*S*,5*S*)-2,5-dimethylcyclopentyl]urea (10b).** The carboxylic acid **9b** (1.40 g, 9.85 mmol) was first treated with thionyl chloride (5.00 g, 42.0 mmol) and then with a solution of sodium azide (1.00 g, 15.4 mmol) and *n*-Bu_4NBr (30 mg, 0.09 mmol) in water (2 mL) as described for **2**. After completion of the Curtius rearrangement in hot toluene (100 mL), the solution was cooled to room temperature. Silica gel (2.0 g), Et_3N (2 mL), and water (2 mL) were added, and the suspension was stirred at 55 °C overnight. After evaporation of the volatiles in vacuo, the solid residue was refluxed with MeOH (30 mL) for 3 min, and the hot suspension was quickly filtered. The procedure was repeated once, and the combined filtrates were concentrated under reduced pressure. The crude product was crystallized from hot MeOH, yielding the urea **10b** (785 mg, 63%) as long needles: mp 240 °C; $[\alpha]^{25}_D = +117.8$ (c = 0.9, MeOH); IR (KBr) 1630 cm^{-1}; ^1H NMR (DMSO-d_6, 100 °C, 500 MHz) δ 5.45 (m, 2H), 3.47 (q, J = 8.3 Hz, 2H), 2.10 (sept, J = 7.0 Hz, 2H), 1.83−1.77 (m, 4H), 1.65 (sept, J = 7.1 Hz, 2H), 1.22−1.15 (m, 2H), 1.11−1.02 (m, 2H), 0.95 (d, J = 6.7 Hz, 6H), 0.80 (d, J = 7.1 Hz, 6H); ^{13}C NMR (DMSO-d_6, 100 °C, 125 MHz) δ 157.8, 59.5, 38.0, 34.5, 30.6, 30.1, 18.2, 14.8; MS (EI) m/z 252 (M^+, 14%); HRMS calcd for $C_{15}H_{28}N_2O$ 252.2202, found 252.2185.

Typical Procedure for the Enantioselective Deprotonation. (*S*)-4-*tert*-Butyl-1-trimethylsiloxy-1-cyclohexene (12a). At −78 °C, *n*-BuLi (0.58 mL, 0.94 mmol, 1.6 M in *n*-hexane) was dropwise added to a solution of urea **2** (236 mg, 0.47 mmol) in THF (10 mL). The solution was allowed to warm to 0 °C over 15 min and stirred for a further 15 min. After the solution cooled to −100 °C, TMSCl (0.24 mL, 1.89 mmol) was added, followed by a solution of 4-*tert*-butylcyclohexanone (58.0 mg, 0.38 mmol) in THF (0.8 mL). The reaction mixture was stirred for a further 50 min before the addition of Et_3N (2 mL) and saturated aqueous $NaHCO_3$ (2.5 mL). After the mixture warmed to room temperature, the aqueous phase was separated and extracted with Et_2O. The combined organic phases were washed with water and brine and dried (Na_2SO_4). The solvent was evaporated under reduced pressure, and the crude product was purified by bulb-to-bulb distillation (150 °C, 0.7 Torr), yielding the silyl enol ether **12a** [5h] (90 mg, 85%; 87% ee) as a colorless oil. The recovered urea **2** (205 mg, 87%) has been reused for further reactions. GC (CB, 100 kPa, 80 °C (1 min) to 120 °C, 2 °C/min): t_R (min) = 20.5 (*S*), 20.8 (*R*); $[\alpha]^{25}_{365} = -202$ (c = 1.5, benzene) [lit.[5c] (*R*), 92% ee: $[\alpha]^{25}_{365} = +217$ (c = 1.7, benzene)]; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.69 (m, 1H), 2.00−1.74 (m, 3H), 1.72−1.54 (m, 2H), 1.19−0.98 (m, 2H), 0.72 (s, 9H), 0.27 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 150.3, 104.0, 44.0, 32.1, 31.0, 27.3, 25.1, 24.4, 0.3.

(*S*)-4-Methyl-1-trimethylsiloxy-1-cyclohexene (12b). The reaction was carried out according to the typical procedure using 4-methylcyclohexanone (86.0 mg, 0.77 mmol), urea **2** (480 mg, 0.95 mmol), *n*-BuLi (1.20 mL, 1.92 mmol, 1.6 M in *n*-hexane), and TMSCl (0.50 mL, 3.94 mmol) to give silyl enol ether **12b** (123 mg, 87%; 84% ee) as a colorless oil: GC (CB, 100 kPa, 70 °C (1 min) to 140 °C, 2 °C/min): t_R (min) = 9.3 (*S*), 9.5 (*R*); $[\alpha]^{25}_{365} = -204$ (c = 1.5, benzene) [lit.[5c] (*R*), 94% ee: $[\alpha]^{25}_{365} = +224$ (c = 1.5, benzene)]; IR (film) 1670 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 4.78 (m, 1H), 2.19−1.84 (m, 2H), 1.74−1.45 (m, 2H), 1.39−1.11 (m, 2H), 0.91 (d, J = 6.2 Hz, 3H), 0.94−0.79 (m, 1H), 0.14 (s, 9H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 150.1, 103.6, 32.3, 31.2, 29.6, 28.3, 21.3, 0.3; MS (EI) m/z 184 (M^+, 25%). Anal. Calcd for $C_{10}H_{20}OSi$: C, 65.15; H, 10.93. Found: C, 64.99; H, 10.92.

(*S*)-4-Isopropyl-1-trimethylsiloxy-1-cyclohexene (12c). The reaction was carried out according to the typical procedure using 4-isopropylcyclohexanone (70.0 mg, 0.50 mmol), urea **2** (320 mg, 0.63 mmol), *n*-BuLi (0.80 mL, 1.28 mmol, 1.6 M in *n*-hexane), and TMSCl (0.32 mL, 2.52 mmol) to give silyl enol ether **12c** (90 mg, 84%; 87% ee) as a colorless oil: GC (CB, 100 kPa, 60 °C (1 min) to 140 °C, 2 °C/min): t_R (min) = 24.7 (*S*), 25.0 (*R*); $[\alpha]^{25}_{365} = -187$ (*c* = 1.0, benzene) [lit.[5c] (*R*), 95% ee: $[\alpha]^{25}_{365} = +217$ (*c* = 1.5, benzene)]; IR (film) 1671 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 4.83 (m, 1H), 2.11−1.86 (m, 2H), 1.85−1.64 (m, 2H), 1.56−1.36 (m, 1H), 1.34−1.11 (m, 3H), 0.88 (d, *J* = 6.8 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 3H), 0.16 (s, 9H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 150.3, 103.8, 40.0, 32.0, 30.3, 27.3, 26.5, 20.1, 19.9, 0.3; MS (EI) *m*/*z* 212 (M^+, 17%). Anal. Calcd for $C_{12}H_{24}OSi$: C, 67.85; H, 11.39. Found: C, 67.71; H, 11.29.

(*S*)-4-Phenyl-1-trimethylsiloxy-1-cyclohexene (12d). The reaction was carried out according to the typical procedure using 4-phenylcyclohexanone (90.0 mg, 0.52 mmol), urea **2** (325 mg, 0.64 mmol), *n*-BuLi (0.80 mL, 1.28 mmol, 1.6 M in *n*-hexane), and TMSCl (0.35 mL, 2.76 mmol) to give silyl enol ether **12d** (112 mg, 88%; 83% ee) as a colorless oil: GC (CB, 100 kPa, 70 °C (1 min) to 140 °C, 3 °C/min): t_R (min) = 32.8 (*S*), 33.2 (*R*); $[\alpha]^{25}_{365} = -120$ (*c* = 1.3, benzene) [lit.[5c] (*R*), 93% ee: $[\alpha]^{25}_{365} = +136$ (*c* = 1.5, benzene)]; IR (film) 1668 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.25−7.06 (m, 5H), 4.86 (m, 1H), 2.74−2.58 (m, 1H), 2.27−2.04 (m, 3H), 2.03−1.69 (m, 3H), 0.13 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 150.3, 146.7, 128.4, 126.9, 126.0, 103.6, 40.0, 32.0, 30.2, 0.4; MS (EI) *m*/*z* 246 (M^+, 44%). Anal. Calcd for $C_{15}H_{22}OSi$: C, 73.11; H, 9.00. Found: C, 73.02; H, 9.27.

(*S*)-4-*tert*-Butyldimethylsiloxy-1-trimethylsiloxy-1-cyclohexene (12e). The reaction was carried out according to the typical procedure using 4-*tert*-butyldimethylsiloxycyclohexanone (90.0 mg, 0.39 mmol), urea **2** (245 mg, 0.49 mmol), *n*-BuLi (0.60 mL, 0.96 mmol, 1.6 M in *n*-hexane), and TMSCl (0.25 mL, 1.97 mmol) to give silyl enol ether **12e** (101 mg, 85%; 88% ee) as a colorless oil: $[\alpha]^{25}_D = -31.7$ (*c* = 0.4, $CHCl_3$). The enantiomeric excess was determined by comparison of the optical rotation with literature data:[18b] (*S*), 80% ee: $[\alpha]^{25}_D = -28.8$ (*c* = 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 4.64 (m, 1H), 3.88−3.75 (m, 1H), 2.22−1.88 (m, 4H), 1.76−1.55 (m, 2H), 0.83 (s, 9H), 0.12 (s, 9H), 0.00 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.7, 101.3, 67.3, 33.3, 31.7, 28.1, 25.9, 18.1, 0.3, −4.6, −4.7.

(1*S*,5*R*)-7,7-Ethylenedioxy-3-trimethylsiloxybicyclo[3.3.0]oct-2-en (14). The reaction was carried out according to the typical procedure using 7,7-ethylenedioxybicyclo[3.3.0]-octan-3-one (**13**, 90.0 mg, 0.49 mmol), urea **2** (310 mg, 0.61 mmol), *n*-BuLi (0.76 mL, 1.22 mmol, 1.6 M in *n*-hexane), and TMSCl (0.30 mL, 2.36 mmol) to give silyl enol ether **14** (114 mg, 91%; 86% ee) as a colorless oil: GC (CB, 100 kPa, 80 °C (1 min) to 180 °C, 2 °C/min): t_R (min) = 25.1 (1*S*,5*R*), 25.4 (1*R*,5*S*); $[\alpha]^{25}_{365} = -31.4$ (*c* = 1.3, benzene) [lit.[5g] (1*S*,5*R*), 99% ee: $[\alpha]^{25}_{365} = -36.9$ (*c* = 3.1, benzene)]; IR (film) 1644 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.54 (m, 1H), 3.82 (m, 4H), 3.22−2.98 (m, 1H), 2.69−2.43 (m, 2H), 2.02−1.87 (m, 3H), 1.62−1.47 (m, 2H), 0.13 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 153.0, 117.9, 107.3, 64.6, 63.9, 43.2, 42.6, 41.4, 40.4, 35.8, 0.0; MS (EI) *m*/*z* 254 (M^+, 13%). Anal. Calcd for $C_{13}H_{22}O_3Si$: C, 61.38; H, 8.72. Found: C, 61.20; H, 8.40.

Typical Procedure for the Enantioselective Alkylation. (*R*)-2-Benzyl-3,4-dihydro-2*H*-naphthalen-1-one (16). At −78 °C, *n*-BuLi (0.67 mL, 1.00 mmol, 1.5 M in *n*-hexane) was dropwise added to a solution of urea **2** (505 mg, 1.00 mmol) in THF (7 mL). The solution was allowed to warm to 0 °C over 15 min and stirred for a further 15 min. After the mixture cooled to −40 °C, a solution of 1-tetralone (120 μL, 0.90 mmol) in THF (2 mL) was slowly added. The cooling bath was removed, and the homogeneous solution was stirred at room temperature for 40 min. After the mixture cooled back to −78 °C, a solution of benzyl bromide (1.20 mL, 10.1 mmol) in THF (2 mL) was dropwise added in 15 min. The reaction mixture was allowed to warm to −20 °C and stirred for a further 24 h before the addition of 1 M HCl (5 mL) and Et_2O (80 mL). The organic layer was separated, and the aqueous phase was extracted with Et_2O. The combined organic phases were washed with brine and dried (Na_2SO_4). The solvent was evaporated under reduced pressure, and the crude product was purified by chromatography (pentane/Et_2O 4:1 to 1:1), yielding benzyl tetralone **16** [6c] (180 mg, 83%; 81% ee) as colorless crystals (mp 54 °C). The recovered urea **2** (350 mg, 69%) has been reused for further reactions. HPLC (OD, 0.5% *i*-PrOH, 0.6 mL/min, 254 nm): t_R (min) = 22.7 (*R*), 25.3 (*S*); $[\alpha]^{25}_D = +15.1$ (*c* = 1.7, MeOH) [lit.[6c] (*R*), 92% ee: $[\alpha]^{25}_D = +17.8$ (*c* = 1.9, MeOH)]; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.98 (m, 1H), 7.40−7.32 (m, 1H), 7.27−7.09 (m, 7H), 3.40 (dd, *J* = 3.6, 13.3 Hz, 1H), 2.89−2.78 (m, 2H), 2.71−2.50 (m, 2H), 2.18−1.96 (m, 1H), 1.78−1.61 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 199.3, 144.0, 140.0, 133.2, 132.5, 129.2, 128.7, 128.4, 127.5, 126.6, 126.1, 49.4, 35.7, 28.6, 27.7.

(2*R*,4*R*)-3-Chloro-2,4-diphenylpentane (17). Carboxylic acid **7** (8.10 g, 30.2 mmol) was converted to the corresponding acid chloride by refluxing with thionyl chloride (18.0 g, 151 mmol) for 3 h. Excess reagent was evaporated in vacuo, and the solid residue was dissolved in CCl_4 (40 mL). This solution was dropwise added (syringe pump) to a refluxing suspension of the sodium salt of 2-mercaptopyridine-*N*-oxide (5.70 g, 36.3 mmol) and DMAP (380 mg, 3.11 mmol) in CCl_4 (35 mL) *under argon* while being irradiated with a photo lamp (300 W). After the addition of the acid chloride, the lamp was switched off. After refluxing for another 45 min, the brown reaction mixture was cooled, diluted with pentane, and poured into 10% aqueous HCl. The aqueous phase was extracted with pentane, and the combined organic phases were washed with water and brine and dried ($MgSO_4$). After evaporation of the solvent under reduced pressure, the crude product was purified by chromatography (pentane/Et_2O 40:1 to 10:1), yielding the alkyl chloride **17** (6.60 g, 84%) as a colorless, waxy solid: mp 46−48 °C; $[\alpha]^{25}_D = +17.3$ (*c* = 1.9, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.28−7.04 (m, 10H), 4.20 (dd, *J* = 5.7, 7.5 Hz, 1H), 2.99−2.85 (m, 2H), 1.31 (d, *J* = 7.1 Hz, 3H), 1.29 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 144.4, 142.4, 128.7, 128.5, 127.9, 127.7, 126.7, 126.6, 74.2, 43.5, 43.4, 20.7, 18.5; MS (EI) *m*/*z* 258 (M^+, 7%). Anal. Calcd for $C_{17}H_{19}Cl$: C, 78.90; H, 7.40. Found: C, 79.00; H, 7.50.

Bis{(2*R*)-phenyl-1-[(*R*)-phenylethyl]propyl}methylphosphine−Borane Complex (3·BH_3). At −78 °C, a solution of the alkyl chloride **17** (2.00 g, 7.73 mmol) in THF (4 mL) was added to a vigorously stirred solution of lithium 4,4′-di-*tert*-butylbiphenylide, prepared from 4,4′-di-*tert*-butylbiphenyl (4.60 g, 17.3 mmol) and lithium pieces (107 mg, 15.4 mmol) in THF (35 mL). Within 4 min, the blue color changed to dark red. A solution of methyldichlorophosphine (320 mg, 2.74 mmol) in THF (1 mL) was added at −78 °C, instantaneously causing discoloration. The cooling bath was removed, and the reaction mixture was stirred at room temperature for 3 h before $BH_3{\cdot}SMe_2$ (1.00 g, 13.2 mmol) was added. After the mixture stirred at room temperature overnight, water (7 mL) was carefully added, followed by Et_2O (250 mL). The organic layer was separated, and the aqueous phase was extracted with Et_2O. The combined organic phases were washed with 10% aqueous HCl and brine and dried ($MgSO_4$). The solvents were evaporated under reduced pressure, and the crude product was purified by chromatography (aluminum oxide, neutral, III; pentane/CH_2Cl_2 6:1, then pentane/Et_2O/CH_2Cl_2 10:1:2 to 1:1:1), followed by crystallization from EtOAc yielding phosphine−borane complex **3**·BH_3 (1.12 g, 80%) as colorless crystals: mp 136−138 °C; $[\alpha]^{25}_D = -161.8$ (*c* = 1.1, $CHCl_3$); IR (KBr) 2370 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.10−6.80 (m, 16H), 6.72−6.67 (m, 4H), 4.17−4.10 (m, 1H), 3.60−3.51 (m, 1H), 3.42−3.35 (m, 1H), 3.33−3.25 (m, 1H), 3.13−3.07 (m, 1H), 2.98−2.94 (m, 1H), 1.82 (d, *J* = 8.6 Hz, 3H), 1.61 (d, *J* = 7.3 Hz, 3H), 1.56 (d, *J* = 6.9 Hz, 3H), 1.49 (d, *J* = 7.2 Hz, 6H), 1.75−0.65 (br, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 146.0 (d, *J* = 13.8 Hz), 145.1 (d, *J* = 10.1 Hz), 144.8 (d, *J* = 11.3 Hz), 144.3 (d, *J* = 7.6 Hz), 127.9−127.6 (m), 127.4, 126.8 (m), 126.0, 125.7, 125.1, 124.9, 47.7 (d, *J* = 20.1 Hz), 47.2 (d, *J* = 21.4 Hz), 38.2−37.9 (m), 24.3−24.1 (m), 14.1 (m), 10.4 (d, *J* = 31.4 Hz); ^{31}P NMR ($CDCl_3$, 81 MHz) δ 34.5 (br); MS (FD) *m*/*z* 506

(M^+, 67%). Anal. Calcd for $C_{35}H_{44}BP$: C, 83.00; H, 8.76. Found: C, 83.09; H, 8.55.

Bis{(2*R*)-phenyl-1-[(*R*)-phenylethyl]propyl}methylphosphine (3). At −10 °C, HBF_4·OMe_2 (1.20 g, 8.97 mmol) was dropwise added to a well-stirred solution of phosphine−borane complex **3**·BH_3 (860 mg, 1.70 mmol) in CH_2Cl_2 (2 mL) under argon. The reaction mixture was warmed to room temperature overnight before dilution with CH_2Cl_2 (30 mL). The solution was basified with saturated aqueous $KHCO_3$, and the organic layer was separated. The aqueous phase was extracted with CH_2Cl_2, and the combined organic phases were dried ($MgSO_4$) under argon. After evaporation of the solvent in vacuo, the pure, air-sensitive phosphine **3** (750 mg, 90%) was dissolved in CH_2Cl_2 (11 mL). This stock solution was used for further experiments. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.42−7.19 (m, 16H), 6.96 (m, 2H), 6.77 (m, 2H), 3.45−3.37 (m, 1H), 3.35−3.25 (m, 1H), 3.03 (m, 1H), 2.84−2.70 (m, 2H), 1.89 (m, 1H), 1.79 (d, J = 7.3 Hz, 3H), 1.58 (d, J = 7.3 Hz, 3H), 1.40 (d, J = 7.1 Hz, 3H), 1.03 (d, J = 7.0 Hz, 3H), 0.64 (d, J = 5.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 148.5, 148.0, 146.6 (m), 143.4 (m), 128.8 (m), 128.4 (m), 128.1, 128.0, 127.9, 127.4, 127.2, 126.1 (m), 125.5 (m), 47.8 (d, J = 25.5 Hz), 43.3 (d, J = 25.9 Hz), 41.6 (m), 40.0 (d, J = 18.2 Hz), 39.8 (m), 35.5 (d, J = 18.4 Hz), 23.2 (m), 20.3 (d, J = 14.5 Hz), 16.6 (d, J = 25.0 Hz), 15.2 (m), 4.3 (d, J = 23.3 Hz); ^{31}P NMR ($CDCl_3$, 81 MHz) δ −37.1.

3-Chloro-2,4-dimethylpentane (20). At −15 °C, 2,4-dimethyl-3-pentanol (23.6 g, 203 mmol) was added to a vigorously stirred suspension of Ph_3P (200 g, 762 mmol) in acetonitrile (250 mL), dropwise followed by trichloroacetonitrile (44.1 g, 305 mmol). The orange suspension was allowed to warm to room temperature overnight. It was poured into water (500 mL), the organic layer was separated, and the aqueous phase was extracted with pentane. The combined organic phases were washed with brine and dried ($MgSO_4$). The solvent was distilled off through a Vigreux column at atmospheric pressure. The crude product was distilled to give the alkyl chloride **20**[35] (7.60 g, 28%) as a colorless, volatile liquid: bp 136 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.50 (t, J = 6.2 Hz, 1H), 2.06−1.91 (m, 2H), 0.98 (d, J = 5.4 Hz, 6H), 0.96 (d, J = 5.6 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 78.0, 32.0, 20.8, 18.2; MS (EI) m/z 99 (M^+ − Cl, 1%). Anal. Calcd for $C_7H_{15}Cl$: C, 62.44; H, 11.23. Found: C, 62.33; H, 10.98.

1,4-Bis[di(1′-isopropyl-2′-methylpropyl)phosphino]butane−Borane Complex (23·2BH$_3$). The alkyl chloride **20** (2.20 g, 16.3 mmol) was successively treated with lithium 4,4′-di-*tert*-butylbiphenylide, prepared from 4,4′-di-*tert*-butylbiphenyl (9.50 g, 35.7 mmol) and lithium pieces (226 mg, 32.6 mmol) in THF (70 mL), 1,4-bis(dichlorophosphino)butane (**22**, 890 mg, 3.42 mmol), and BH_3·SMe_2 (2.00 g, 26.3 mmol) as described for the preparation of **3**·BH_3. The crude product was purified by chromatography (aluminum oxide, neutral, III; pentane/CH_2Cl_2 6:1, then pentane/Et_2O/CH_2Cl_2 20:1:5), followed by crystallization from EtOAc yielding phosphine−borane complex **23**·2BH_3 (1.30 g, 70%) as colorless crystals: mp 101 °C; IR (KBr) 2380 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.32−2.02 (m, 8H), 1.82−1.62 (m, 12H), 1.18−1.14 (m, 48H), 1.02−0.20 (br, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 45.6 (d, J = 23.9 Hz), 28.3 (m), 28.2 (m), 26.1 (d, J = 13.0 Hz), 25.2 (d, J = 8.4 Hz), 24.2 (d, J = 9.7 Hz), 22.6 (d, J = 27.9 Hz), 21.7 (m), 21.5 (m); ^{31}P NMR ($CDCl_3$, 203 MHz) δ 34.2 (br); MS (FD) m/z 528 (M^+ − BH_3, 100%). Anal. Calcd for $C_{32}H_{74}B_2P_2$: C, 70.85; H, 13.75. Found: C, 70.68; H, 13.46.

(35) The preparation of **20** is already optimized; cf. the original procedure: Matveeva, E. D.; Yalovskaya, A. I.; Cherepanov, I. A.; Bundel, Y. G.; Kurts, A. L. *J. Org. Chem. USSR* **1989**, *25*, 587.

1,4-Bis[di(1′-isopropyl-2′-methylpropyl)phosphino]butane (23). The phosphine−borane complex **23**·2BH_3 (1.00 g, 1.84 mmol) was decomplexed using HBF_4·OMe_2 (2.50 g, 18.7 mmol) in CH_2Cl_2 (4 mL) as described for **3** to give the pure, air-sensitive diphosphine **23** (810 mg, 85%), which was dissolved in CH_2Cl_2 (5 mL). This stock solution was used for further experiments. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.10−1.90 (m, 8H), 1.53 (m, 8H), 1.46−1.40 (m, 4H), 1.06−0.94 (m, 48H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 47.4 (d, J = 22.6 Hz), 31.6−31.1 (m), 28.1 (m), 27.8 (m), 23.7 (m), 22.8 (m), 22.5 (m), 22.1 (m), 21.6 (d, J = 14.8 Hz); ^{31}P NMR ($CDCl_3$, 82 MHz) δ −21.5.

Typical Procedure for the Enantioselective Allylation. Methyl (*S*,*E*)-2-Methoxycarbonyl-3,5-diphenylpent-4-enoate (25). A three-necked flask under argon was charged with the phosphine **3** using a stock solution of **3** in CH_2Cl_2 (0.13 mL of a 0.14 M solution, 18.0 μmol). The solvent was evaporated, and DMF (1.5 mL) was added leading to a homogeneous solution. After the addition of [Pd(η^3-C_3H_5)Cl]$_2$ (3.0 mg, 8 μmol), the reaction mixture was stirred for 30 min at room temperature, leading to a yellow solution. (*E*)-1,3-Diphenyl-1-acetoxy-2-propene (**24**, 150 mg, 0.60 mmol) was added, and after 30 min *N*,*O*-bis(trimethylsilyl)acetamide (366 mg, 1.80 mmol), dimethyl malonate (238 mg, 1.80 mmol), and KOAc (3.0 mg, 0.03 mmol) were successively added. The reaction mixture was stirred at room temperature overnight before the addition of Et_2O and saturated aqueous NH_4Cl. The organic layer was separated, and the aqueous phase was extracted with Et_2O. The combined organic phases were washed with brine and dried ($MgSO_4$). The solvent was evaporated under reduced pressure, and the crude product was purified by chromatography (pentane/EtOAc 5:1), yielding malonate **25**[9f] (174 mg, 90%; 73% ee) as a colorless oil: HPLC (OD, 1% *i*-PrOH, 0.4 mL/min, 254 nm): t_R (min) = 32.3 (*R*), 34.3 (*S*); $[\alpha]^{25}_D$ = −12.9 (c = 1.3, EtOH) [lit.[9g] (*S*), 99% ee: $[\alpha]^{25}_D$ = −18.4 (c = 1.1, EtOH)]; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.27−7.06 (m, 10H), 6.40 (d, J = 15.8 Hz, 1H), 6.25 (dd, J = 8.4, 15.8 Hz, 1H), 4.19 (dd, J = 8.4, 10.9 Hz, 1H), 3.88 (d, J = 10.9 Hz, 1H), 3.61 (s, 3H), 3.43 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.1, 167.7, 140.2, 136.8, 131.8, 129.1, 128.7, 128.4, 127.8, 127.5, 127.1, 126.3, 57.6, 52.5, 52.3, 49.1.

Attempted Heck Reaction.[30e] A three-necked flask under argon was charged with the phosphine **23** using a stock solution of **23** in CH_2Cl_2 (0.65 mL of a 0.31 M solution, 0.20 mmol). The solvent was evaporated, and DMF (3.5 mL) was added, leading to a homogeneous solution. After the addition of chlorobenzene (1.00 g, 8.88 mmol), styrene (1.10 g, 10.6 mmol), $Pd(OAc)_2$ (20.0 mg, 0.09 mmol), and NaOAc (730 mg, 8.90 mmol), the yellowish reaction mixture was heated to 140 °C during 1 h and stirred further for 23 h at this temperature. The yellow color persisted, and neither Pd-black nor stilbene could be detected while chlorobenzene and styrene remained unchanged.

Acknowledgment. The authors thank BASF AG, Bayer AG and Degussa AG, for generous gifts of chemicals and the DFG (SFB 260 and Leibniz program) for financial support.

Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra of compounds **2**, **3**·BH_3, **3**, **5**−**7**, **10a**,**b**, **12b**−**d**, **14**, **17**, **20**, **23**·2BH_3, and **23**, ^{31}P NMR spectra of compounds **3**·BH_3, **3**, **23**·2BH_3, and **23**, and complete X-ray data for **23**·2BH_3. This material is available free of charge via the Internet at http://pubs.acs.org.

JO990412U