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Asymmetric Michael Addition Reaction of Phosphorus-Stabilized Allyl Anions with Cyclic Enones

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The asymmetric Michael addition reaction of chirally modified *P*-allyl anions derived from enantiomerically enriched 2-allyl-1,3,2-oxazaphosphorinane 2-oxides has been investigated with cyclic enones. The racemic 1,3,2-oxazaphosphorinane 2-oxide **3** has been shown to be extremely diastereoselective in the Michael addition to 5-, 6-, and 7-ring enones. With the enantiomerically enriched 2-allyl-1,3,2-oxazaphosphorinane 2-oxides, high regio- and diastereoselectivities (88−90% diastereomeric excess) have been achieved in the Michael addition reaction of one of the diastereomers (cis series). The Michael reaction of the anions derived from the trans series were not diastereoselective (~10% diastereomeric excess). The origin of the addition selectivity can be rationalized by (1) consideration of the structure and conformational preferences of the allyl anion (parallel conformation, s-trans, no lithium contact), (2) conformational analysis of the 1,3,2-oxazaphosphorinane 2-oxide ring (chair, equatorial allyl group) and (3) assumption of a 10-membered ring transition state structure with lithium coordination of the enone.

Introduction and Background

Over the past 30 years, the development of new reagents based on acceptor-substituted organolithium compounds and the diversification and development of heteroatom-stabilized anions as reagents in organic synthesis have expanded dramatically.[1] Stabilizing groups based on many different elements at various oxidation states have shown significant potential for synthetic application. An important subset of these reagents is the class of heteroatom-stabilized allyl anions.[1,2] A variety of heteroatom-stabilized allyl anions have been described which employ many different elements, but among them, sulfur[3] and phosphorus[4] have attracted more interest due to their versatility and synthetic potential for asymmetric modification.

One of the most fundamental questions surrounding the use of stabilized allyl anions in their reaction with electrophiles is the α/γ-regioselectivity. This sense of selectivity has been found to be highly dependent on the steric bulk and electronic nature of stabilizing groups as well as the nature of the electrophile.[5−8] The γ-selective reagents have found use in the preparation of γ-substituted carbonyl compounds and are thus homoenolate equivalents.[9] Earlier investigations from these laboratories clarified these effects in the electrophilic substitutions of phosphonamide-stabilized allyl anions.[10a] In addition, a spectroscopic and theoretical study of the structure and dynamics of the allyl anion derived from *P*-allylphosphonamide was carried out to elucidate the conformational and regiochemical (α/γ) behavior of the anions. Subsequently, higher level ab initio calculations with and without a lithium counterion have shown that the *E*-conformation of the anion as depicted in Figure 1 is a local minimum which corresponds remarkably well to an X-ray crystallographic analysis of a related benzylic anion.[10c]

However, the most synthetically useful application of the allyl anions is the Michael addition reaction.[11] A variety of reports have appeared on the reaction of sulfur-stabilized allyl anions with Michael acceptors.[12] Both allylic sulfones and the more synthetically useful chiral allylic sulfoxides have been utilized to afford Michael addition products with high γ-selectivity. Similarly,

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

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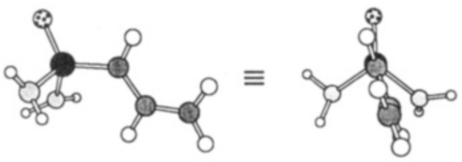
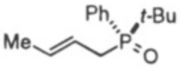


Figure 1. Calculated ground state conformation of *P*-allylphosphonamide anions.

Haynes et al.[12a,b,13] have shown that anions derived from allylic diphenylphosphine oxides react with a variety of Michael acceptors by 1,4-addition through the γ-carbon of the reagent.

Haynes[14] has since described the enantioselective γ-1,4-addition of individual enantiomers of (*E*)-2-butenyl-*tert*-butylphenylphosphine oxide (**i**) to 2-methyl-2-cyclopentenone and formulated a model for the asymmetric induction. In addition, a practical method for the preparation of *(S)*- and *(R)*-allyl-*tert*-butylphenylphosphine oxide has been developed.[14b]



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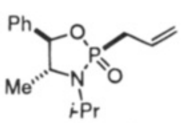
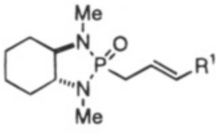


ii



iii

Hua et al.[15] demonstrated that the reactions of anions derived from various chiral 2-allyl-1,3,2-oxazaphospholidine 2-oxides prepared from ephedrine provided high yields of γ-1,4-adducts with 2-cyclopentenone or 2-cyclohexenone. The selectivity of the additions is dependent on the configuration at the phosphorus center and the N-substituent. For one of the phosphorus stereoisomers, the enantioselectivity of the conjugate addition reaction was 88–98% de, whereas low selectivity was observed for the other isomer. The sense of selectivity in this case was similar to that observed by Haynes with the phosphinoyl allyl anions.

In an adaptation of bicyclic phosphonamide methodology, Hanessian[16] has demonstrated the excellent versatility and generality of control offered by anions derived from *P*-allyl- and *P*-2-butenylphosphonamides **iii**. The reagents gave high yields of γ-1,4-addition products in reactions with cyclic α,β-unsaturated ketones, α,β-unsaturated lactones and lactams, and acyclic, α,β-unsaturated *tert*-butyl esters and remarkably high diastereoselectivities (>90/10 and >99/1 in several cases).

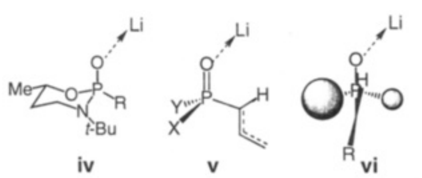


Figure 2. Design of 1,3,2-oxazaphosphorinane 2-oxide auxiliary.

In recent years, we have been extensively involved in the evaluation and development of chiral prosthetic groups for the asymmetric modulation of carbanions. One of the most studied phosphorus modifier groups is the 1,3,2-oxazaphosphorinane 2-oxide **iv** shown in Figure 2. This auxiliary has been used successfully as an asymmetric modifier in (1) the carbanionic Claisen rearrangement,[17] (2) the [2,3]-Wittig rearrangement,[18] (3) alkylations of benzyl and alkyl anions,[19] (4) aminations of anions,[20] (5) alkylation of anions derived from the 2-sulfide,[19c] and (6) asymmetric alkylidenation reactions.[21] The general design of this auxiliary is illustrated for the specific case of an allyl anion, **v**, in Figure 2. Given the preferred conformation of the anion (planar anion, parallel to P=O, no lithium contact), the control of diastereofacial selectivity is expected to arise from shielding of the anion faces by sterically disparate groups (see **vi**, Figure 2). The 1,3,2-oxazaphosphorinane 2-oxide provides a "tunable" environment by balancing the size difference between the N-substituents and the oxygen. Indeed, in a recent study of alkylation behavior we demonstrated a significant dependence of alkylation selectivity on the size of the *N*-alkyl group.[19b]

The *P*-allyl compound **iv** (R = allyl) is an appropriate starting substrate for a general investigation of the Michael reaction of *P*-allyl anions since it allows a number of important questions to be addressed. For example, on the basis of simple molecular model considerations, we suspected that a 6-membered platform would provide a greater dissymmetric influence on carbanion reaction selectivity compared to the 5-ring system reported by Hua. The origin of this effect was seen in the proximity of the *N*-alkyl group to the anion in the phosphorinane compared to the phospholidine. We describe below, in full, our studies on the asymmetric Michael addition of phosphorus-stabilized anions in the 1,3,2-oxazaphosphorinane 2-oxide series.

Results

Preparation of 2-Allyl-1,3,2-oxazaphosphorinane 2-Oxide 3. Previous studies from these laboratories on

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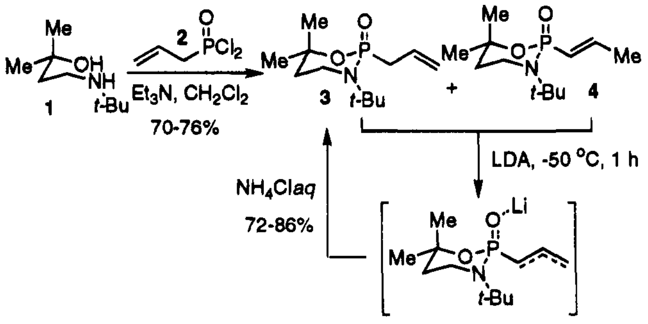
Scheme 1



the asymmetric alkylation of chiral phosphorus-stabilized anions employed the amino alcohol **1** to construct the auxiliary. Although the resulting phosphorinanes are racemic, the ease of synthesis allowed ready survey of reaction variables. Thus, treatment of **1** with allylphosphonic dichloride (**2**) in the presence of 2.1 equiv of triethylamine in dichloromethane afforded a 3–4/1 mixture of the 1,3,2-oxazaphosphorinane 2-oxide **3** along with its vinyl analog **4** in 70–76% yield. The ratio of the two tautomers depended on the reaction time and the amount of base used. (The proportion of **4** increased with greater amounts of base and at longer reactions times.) To make the isomerically pure *P*-allyl derivative **3**, the isomeric mixture of **3** and **4** was treated with LDA at −50 °C for 1 h followed by quenching with saturated aqueous ammonium chloride solution at −78 °C to produce the isomerically pure **3** in 72–86% yield, Scheme 1. The γ-deprotonation of **4** was very slow at lower temperature (−78 °C), and even after 1 h the isomeric composition was not changed. Bases such as *n*-BuLi and *t*-BuLi could not be employed mainly due to nucleophilic addition to the double bond.[10b]

The success of the coupling reaction of amino alcohols and alkylphosphonic dichlorides was highly dependent on the size of the alkylphosphonic dichloride. It has been shown that the more sterically demanding benzylphosphonic dichloride required elevated temperature together with slow addition of substrates. On the other hand, the allylphosphonic dichloride **2** reacted at low temperature (from −40 °C to rt) in high yield. The structure of 2-allyl-1,3,2-oxazaphosphorinane **3** was ascertained by its characteristic allylic resonances in the ^{1}H NMR spectrum and C(1′) resonance (37.95 ppm, J_{CP} = 129.8 Hz) in the ^{13}C NMR spectrum. The structure of the corresponding vinylic derivative **4** was secured by appearance of the characteristic ^{1}H NMR resonances of trans-related olefinic protons.

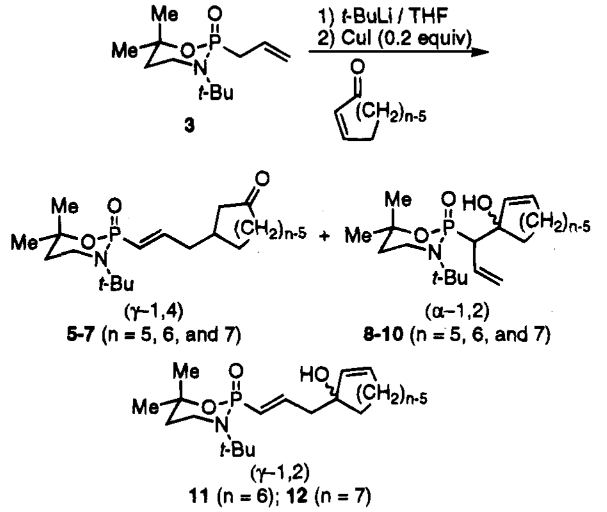
Michael Addition Reactions of Racemic 2-Allyl-1,3,2-oxazaphosphorinane 2-Oxide 3. The orienting reactions of Li^+3^- with Michael acceptors were designed to address a number of key questions including (1) the regioisomeric composition (α/γ) of 1,2- and 1,4-addition products, (2) the diastereoselectivity of the desired γ-1,4-addition product, and (3) the olefin geometry of the desired γ-1,4-addition products. Thus, when the pale yellow solution of Li^+3^-, generated by treatment with *t*-BuLi at low temperature (−78 °C), was transferred to a suspension of copper(I) iodide (0.2 equiv) and various cyclic enones in tetrahydrofuran, the yellow color immediately dissipated to give the Michael adducts (γ-1,4) **5–7** in 63–80% yield (Table 1). The reaction was strongly dependent upon the ring size of the cyclic enones employed, Scheme 2.

Table 1. Michael Reaction of Racemic 3

entry	n[a]	T, °C	time, min	α/γ[b]	product	yield, %[c]
1	5	−45	30	1/99	**5**	73–80
2	6	−45	30	1/49	**6**	70–73
3	7	−40	60	1/3.6	**7**	63

[a] *n* is the ring size of the cycloalkenone. [b] Ratio determined by ^{1}H NMR. [c] Only one diastereomer was observed for the γ-1,4-addition product by ^{31}P NMR.

Scheme 2



The regioselectivity was high in most cases favoring the γ-1,4-addition products **5–7** rather than the α-1,2-addition products **8–10**. The regioisomeric ratio was highly dependent on the ring size of the electrophile. Less than 2% of α-1,2-addition product has been detected except when 2-cycloheptenone was used for which the α-1,2-addition product **10** was isolated in 13% yield. The other regioisomeric products, derived from α-1,4- and γ-1,2-addition, were not detected in the reaction with cyclopentenone. Only trace amounts of the (inseparable) γ-1,2-addition products **11** and **12** were observed as contaminants with the desired γ-1,4-addition product in the reactions with 2-cyclohexenone and 2-cycloheptenone. Moreover, the γ-1,4-addition product has exclusively an *E*-olefinic bond suggesting that the allyl anion also possesses the *E*-configuration.

In general, the stoichiometric, base-promoted Michael reaction is reversible for highly stabilized anions under aprotic conditions.[11] However, the pK_a difference between the α-protons next to the phosphorus-stabilizing group (pK_a ~ 30–32)[22] and the α-protons next to the carbonyl (pK_a ~24) suggests that the reaction is kinetically controlled. Variation of reaction time and temperature did not affect the regioselectivity or the diastereoselectivity.

The diastereoselectivity for the desired γ-1,4-Michael addition manifold is beyond the limits of NMR or HPLC detection. Each of the regioisomerically pure addition products **5–7** gave a single peak on a variety of HPLC columns under a variety of conditions. A careful examination of the ^{1}H and ^{31}P NMR spectra also showed a single set of resonances and single peak, respectively. Even the ^{13}C NMR spectra, though complicated due to extensive phosphorus couplings, indicated single diastereomers. Encouraged by the preliminary results for the Michael addition of the racemic model **3**,

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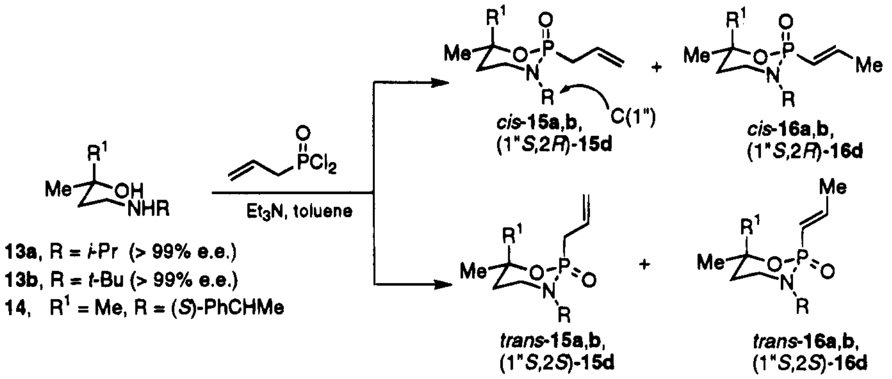
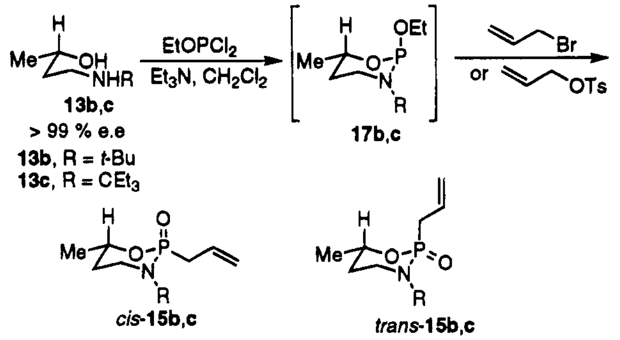
Scheme 3



Scheme 4



we next examined the reactions of the enantiomerically enriched 2-allyl-1,3,2-oxazaphosphorinane 2-oxides.

Preparation of Enantiomerically Enriched 2-Allyl-1,3,2-oxazaphosphorinane 2-Oxides. To assay the influence of the nitrogen substituent on the regio- and stereoselectivity of Michael addition, a variety of enantiomerically enriched 1,3,2-oxazaphosphorinane 2-oxides were prepared from the corresponding amino alcohols **13a–c** and **14**. Either of two reaction protocols were employed (1) direct condensation with allylphosphonic dichloride (Scheme 3) or (2) a two-step procedure involving cyclic phosphite formation followed by Michaelis–Arbuzov reaction with allyl bromide or allyl tosylate in acetonitrile (Scheme 4).[23] For the amino alcohols **13a,b** and **14**, the former procedure could be used; however, a mixture of phosphorus epimers and olefin isomers was obtained (Table 2). Thus, slow addition of allylphosphonic dichloride **2** to a mixture of triethylamine and the appropriate amino alcohol afforded a mixture of *cis*- and *trans*-**15** together with their corresponding (*E*)-2-propenyl analogs *cis*- and *trans*-**16**, Table 2. The phosphorus epimers were easily separable, but olefinic isomers were not. The tertiary amino alcohol **14** behaved like the achiral amino alcohol **3**. The reaction was slower and produced a mixture with a high (33%) proportion of the propenyl isomers (entry 9). On the other hand, the sterically demanding amino alcohol **13c** (NCEt$_3$) did not provide the cyclized product.

While the formation of the propenyl isomers could be eliminated by running the reaction in toluene, the ratio of the cis/trans phosphorus epimers was still poor. To improve the cis/trans selectivity, a two-step protocol was employed, Scheme 4. This reaction protocol has previously been shown to provide *cis*-2-benzyl-1,3,2-oxazaphosphorinane 2-oxides with high selectivity.[19b,21] Thus, treatment of a solution of amino alcohol **13b** and triethylamine in refluxing dichloromethane with ethyl dichlorophosphite (EtOPCl$_2$) produced the cyclic phosphite as a highly acid and water sensitive, colorless, oil. The diastereomeric ratio of the phosphite **17b** was determined by ^{31}P NMR to be >28/1. This oil was purified by distillation prior to the Arbuzov reaction. Treatment of phosphite **17b** with allyl bromide in acetonitrile at 60 °C produced a 6.7/1 mixture of *cis*-**15b**/*trans*-**15b**. The ratio could be improved to 9/1 by the use of allyl tosylate[24] (Table 2).

This two-step protocol was successful with the sterically hindered amino alcohol **13c** to generate phosphite **17c** in a >28/1 ratio. Treatment of the phosphite **17c** with allyl bromide or allyl tosylate gave *cis*-**15c**/*trans*-**15c** in a ratio of 7.3/1 and 10.1/1, respectively. Unfortunately, the separation of the *N*-*tert*-heptyl derivatives *cis*- and *trans*-**15c** was troublesome, and even repeated purification by MPLC yielded a 32/1 mixture of *cis*-**15c**/*trans*-**15c**. Thus, *cis*- and *trans*-**15a**, *cis*- and *trans*-**15b**, and *cis*-**15c** were available in the isomerically pure state while (*S,S*)- and (*S,R*)-**15d** were isomerically contaminated with 5% of the corresponding (2*E*)-propenyl analogs.

The assignment of the allylic structure for the desired *P*-allyl compounds was established using a similar analysis that was applied to identify **3**, i.e., the observation of diagnostic olefinic protons resonances in the ^{1}H NMR spectrum and the characteristic phosphorus-coupled α-methylene carbon resonance. The cis and trans configuration of the 1,3,2-oxazaphosphorinanes was established by spectroscopic and conformational analysis. In the ^{1}H NMR spectrum of the cis isomer, the methine proton on C(6) shifts downfield due to the anisotropic effect of the P=O bond. The cis compound also is generally more retained than the trans compound on silica gel.[19a]

Michael Reaction of 2-Allyl-1,3,2-oxazaphosphorinane 2-Oxides 15. The first issue to address was the influence of phosphorus configuration on the scope and selectivity of the reaction. Thus, the cis and trans isomers of the *tert*-butyl derivatives **15b** were selected. Second, variation in *N*-alkyl substituents (N-*i*-Pr, N-CEt$_3$) of 2-allyl-1,3,2-oxazaphosphorinanes was expected to be

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[23] (a) Wadsworth, W. S.; Emmons, W. D. *J. Am. Chem. Soc.* **1962**, *84*, 610. (b) Bentrude, W. G.; Hargis, J. H. *J. Am. Chem Soc.* **1970**, *92*, 7136. (c) Van Der Berg, G. R.; Platenburg, D. H. J. M.; Benschop, H. P. *J. Chem. Soc., Chem. Commun.* **1971**, 606. (d) Bodkin, L. L.; Simpson, P. *J. Chem. Soc., Perkin Trans. 2* **1972**, 2049. (e) Bodkin, C. L.; Simpson, P. *J. Chem. Soc., Chem. Commun.* **1970**, 1579. (f) Stec, W. J.; Lesiak, K.; Mielczarek, D.; Stec, B. *Z. Naturforch B: Org. Chem.* **1975**, *30*, 710. (g) Adamcik, R. D.; Chang, L. L.; Dennney, D. B. *J. Chem. Soc., Chem. Commun.* **1974**, 986. (h) Michalaiczyk, M. *Pure Appl. Chem.* **1980**, *52*, 959.

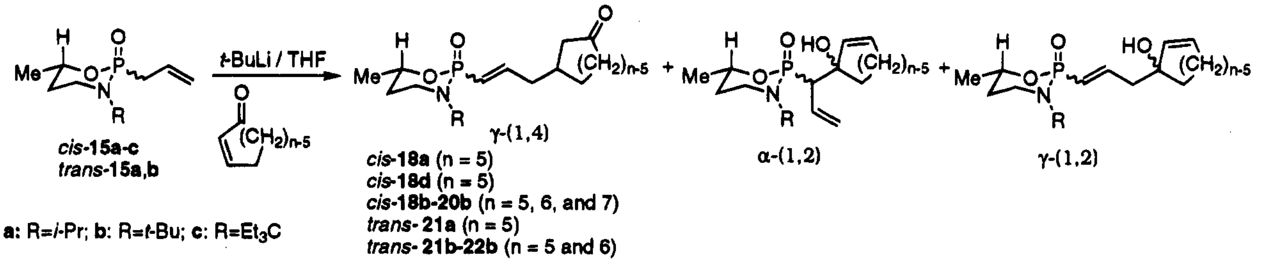
[24] (a) Johnson, C. R.; Dutra, G. A. *J. Am. Chem. Soc.* **1973**, *95*, 7777. (b) MacDowell, D. W. H.; Purpura, J. M. *J. Org. Chem.* **1986**, *51*, 183.

Table 2. Preparation of 2-Allyl-1,3,2-oxazaphosphorinanes

entry	amino alcohol	R	R^1	method^a	product	yield, %	cis/trans^b
1	**13a**	*i*-Pr	H	B	**15a**	70–80	1/1.2^d
2	**13b**	*t*-Bu	H	A	**15b**	66–71	1/1^d
3	**13b**	*t*-Bu	H	B	**15b**	72–81	1.5/1^d
4	**13b**	*t*-Bu	H	C	**15b**	74	6.7/1
5	**13b**	*t*-Bu	H	D	**15b**	72	9/1
6	**13c**	CEt_3	H	B	**15**^{c}		
7	**13c**	CEt_3	H	C	**15c**	89	7.3/1
8	**13c**	CEt_3	H	D	**15c**	83	8.1/1
9	**14**	(*S*)-PhCHMe	Me	A	**15d**	74	1.2/1^e
10	**14**	(*S*)-PhCHMe	Me	B	**15d**	55	1/1.3^f

[a] Method is depicted as A, allylphosphonic dichloride/Et_3N/CH_2Cl_2; B, allylphosphonic dichloride/Et_3N/toluene; C, $EtOPCl_2/Et_3N$ followed by allyl bromide in acetonitrile; or D, $EtOPCl_2/Et_3N$ followed by allyl tosylate in acetonitrile. [b] Ratio determined by ^{31}P NMR. [c] None of cyclized products were isolated. [d] Averaged ratio. [e] Each isomer was contaminated with 33% of **16d**. [f] Each isomer was contaminated with 5% of **16d**.

Table 3. Michael Addition Reactions of *cis*- and *trans*-15



entry	reactant	R	CuI, equiv	n^a	T, °C	time, min	α-1,2/γ-1,4^b	product, yield (%)	ds^c
1	*cis*-**15b**	*t*-Bu	0.2	5	−60 to −45	30–60	1/99	**18b**, 78	19/1
2	*cis*-**15b**	*t*-Bu	0.2	6	−60 to −45	30–60	1/32	**19b**, 68	13.3/1
3	*cis*-**15b**	*t*-Bu	0.2	7	−60 to −45	30–60	1/6.7	**20b**, 41	19/1
4	*cis*-**15b**	*t*-Bu		5	−78	5	1/99	**18b**, 77	19/1
5	*cis*-**15b**	*t*-Bu	0.5	6	−45	30	d	**19b**, 38	d
6	*cis*-**15b**	*t*-Bu	1.0	6	−45	30	d	**19b**, 38	d
7	*cis*-**15a**	*i*-Pr		5	−78	30	1/99	**18a**, 81	11.5/1
8	*cis*-**15c**	CEt_3		5	−78	30	1/99	**18c**, 92	15.7/1
9	*trans*-**15b**	*t*-Bu	0.2	5	−60 to −45	30–60	1/49	**21b**, 77	1.2/1
10	*trans*-**15b**	*t*-Bu		5	−78	5	1/49	**21b**, 76	1.2/1^e
11	*trans*-**15b**	*t*-Bu	0.2	6	−60 to −45	30–60	1/24	**22b**, 72	1.1/1
12	*trans*-**15b**	*t*-Bu	0.5	6	−45	30	d	**22b**, 55	d
13	*trans*-**15b**	*t*-Bu	1.0	6	−45	30	d	**22b**, 22	d
14	*trans*-**15a**	*i*-Pr		5	−78	30	1/99	**21a**, 85	1.2/1

[a] n is the ring size of the cycloalkenone. [b] Ratio determined by ^1H NMR. [c] ds derived from ee of the degradation product. [d] Not determined. [e] Determined by ^{31}P NMR.

significant on the basis of substituent effects in the reaction of *P*-alkyl-1,3,2-diazaphosphorinane[25] and -1,3,2-oxazaphosphorinane 2-oxide anions.[19b]

Representative substrates *cis*- and *trans*-**15b** were lithiated as described for **3** by addition of *t*-BuLi at low temperature to afford in each case a pale yellow solution. The yellow anion was either treated with various cyclic enones or transferred to a heterogeneous mixture of copper(I) iodide and cyclic enone in tetrahydrofuran to afford the 1,4-addition product, Table 3. Catalytic amounts of copper(I) iodide were used to suppress enolization of the cyclic enone and favor the Michael addition pathway. The use of more than 0.2 equiv of copper(I) iodide lowered the yield of the 1,4-addition product due to the preferential formation of the less reactive alkylcopper rather than the reactive cuprate.[26] When the Michael addition was conducted without copper(I) iodide, the reaction took place within 30 min although the yield was somewhat lower. The results for reactions of *cis*- and *trans*-**15** with cyclic enones are summarized in Table 3.

As was found for racemic **3**, the regioselectivity for the reaction of enantiomerically enriched 2-allyl-1,3,2-oxazaphosphorinane **15b** was very high in both the cis and trans series. The γ-1,4-adducts were obtained as the major products, and small amounts of α-1,2-addition products (<3% with 2-cyclopentenone and 2-cyclohexenone and 13% with 2-cycloheptenone) were observed. The major γ-1,4-addition products were contaminated with a trace amount of the inseparable γ-1,2-addition product for the reaction with 2-cyclohexenone and 2-cycloheptenone. The reaction without copper(I) iodide still gave mainly the γ-1,4-addition product with same regioselectivity and comparable chemical yield in both series (entries 4 and 10).

The diastereomeric composition of the isomerically pure γ-1,4-addition products could not be determined in a straightforward manner with routine techniques such as HPLC, ^1H NMR, ^{31}P NMR, and even ^{13}C NMR. Since the newly formed stereogenic center was remote from the phosphorus stereogenic center, all the analytical and spectroscopic methods mentioned above were unable to resolve the two diastereomers of γ-1,4-addition products in both the cis and trans series. To unambiguously establish the identity of the products, each γ-1,4-addition

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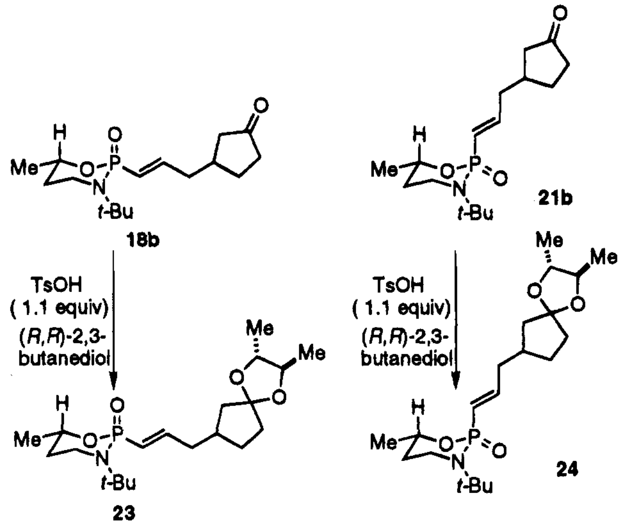
(25) Denmark, S. E.; Kim, J.-H. *J. Org. Chem.*, manuscript submitted.

(26) Review: Yamamoto, Y. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 947.

Scheme 5



product **18b** and **21b** was transformed to a chiral ketal with (*R*,*R*)-2,3-butanediol, Scheme 5.[27] When a catalytic amount of TsOH was used, the reaction did not occur presumably due to preferential protonation on the basic phosphonoyl oxygen. The reaction occurred in the presence of 1.1 equiv of TsOH in refluxing benzene to produce the chiral ketals **23** and **24** in low yield (~20%) due to unfavorable side reactions, such as the acid-catalyzed ring opening of the oxazaphosphorinane ring. Nevertheless, the ^{13}C NMR spectra of the chiral ketals **23** and **24** were clearly resolved to show almost a single set of resonances for **23** and double sets of resonances for **24**. Thus, the Michael reaction of *cis*-**15b** was shown to be highly selective, whereas the Michael reaction of *trans*-**15b** was shown to be unselective.

Since the direct protection of the Michael adducts with the optically active diol was plagued by low yields, we sought a more efficient method to determine the diastereoselectivity of the γ-1,4-addition process. We therefore resorted to a determination of the enantiomeric purity of a degradation product as described in the following section (Scheme 6). The subsequent enantiomeric ratio reflects ultimately the diastereomeric ratio of the Michael addition product since the starting amino alcohols **13a**–**c** were greater than 99% enantiomerically pure (assuming that the stereochemical integrity of the product is retained during the further manipulation).

The diastereoselectivity of the Michael reactions of *cis*- and *trans*-**15b** is presented in Table 3. Interestingly, the reaction of *cis*-**15b** with three different cyclic enones was highly selective (13.3/1–19/1, entries 1–4 in Table 3). Unfortunately, *trans*-**15b** did not provide the Michael adduct selectively (10–15% de, entries 9–11). The effect of the *N*-alkyl substituent on the selectivity of the reaction was next examined. Variation of the *N*-alkyl substituent from *N*-isopropyl to the sterically demanding *N*-*tert*-heptyl (NCEt$_3$) derivative did not significantly influence the diastereoselectivity. The reaction of *cis*-**15a** and *cis*-**15c** with cyclic enones produced the major γ-1,4-addition products **18a,c** in high yield (entries 7 and 8, Table 3). A small erosion in diastereoselectivity was found for these systems, (*cis*-**15a**, 11.5/1, entry 7; *cis*-**15c**, 15.7/1, entry 8). Not surprisingly, *trans*-**15a** exhibited very low diastereoselectivity (~10% de) similar to *trans*-**15b**.

Scheme 6

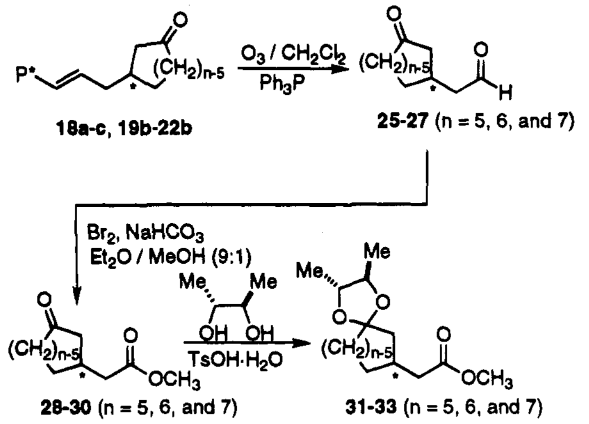


Table 4. Cleavage of Michael Addition Products and Determination of Optical Purity

entry	reactant	n	keto ester, yield (%)	[α]D, deg	ketal, yield (%)	e.e., %[a]
1	**18a**	5	**28**, 69	−99.7 (*S*)	**31**, 67	84
2	**18b**	5	**28**, 59	−107.8 (*S*)	**31**, 81	89
3	**19b**	6	**29**, 68	−8.7 (*S*)	**32**, 81	87
4	**20b**	7	**30**, 72	−54.8 (*S*)	**33**, 71	89
5	**21b**	5	**28**, 70	−8.3 (*S*)		10
6	**18c**	5	**28**, 71	−96.0 (*S*)	**31**, 65	89
7	(*S*,*S*)-**34**	5	**28**, 72	−106.1 (*S*)		88
8	(*S*,*R*)-**34**	5	**28**, 69	+46.8 (*R*)		39

[a] Determined by ^{13}C NMR.

Absolute Configuration and Enantiomeric Excess of the Products. The 1,4-addition products were degraded by ozonolysis in dichloromethane followed by workup with triphenylphosphine to produce oxocycloalkane-3-carboxaldehydes **25**–**27** which are also useful synthetic intermediates (Scheme 6). For the determination of enantiomeric purity, keto aldehydes were transformed into the stable keto esters **28**–**30** by oxidative esterification[28] using bromine in Et$_2$O/MeOH (9/1) followed by derivatization to the chiral ketal derivatives **31**–**33** with (*R*,*R*)-2,3-butanediol in benzene or toluene in the presence of a catalytic amount of *p*-toluenesulfonic acid. The enantiomeric ratio was determined from the optical rotation data of the keto aldehydes **28**–**30** and the integration of diagnostic resonances in the ^{13}C NMR spectra for the diastereomeric ketals **31**–**33**. The enantiomeric ratios for the cis series were high ranging from 84% to 89% ee, but those for the trans series were much lower (~10 ee). The absolute configuration of the newly created stereogenic center of the Michael adducts from *cis*-**15** was unambiguously established as *S* by comparison of specific rotation of the keto esters (*S*)-**28**–**30** with the literature values (Table 4).[15a,27]

Formal Resolution of Racemic 3. Since the racemic 1,3,2-oxazaphosphorinane 2-oxide **3** derived from the achiral amino alcohol **1** gave highly diastereoselective Michael additions while only the cis diastereomers of the enantiomerically enriched analogs **15** were useful, it would be synthetically advantageous to resolve the oxazaphosphorinane **3**. Since the direct resolution of **3**

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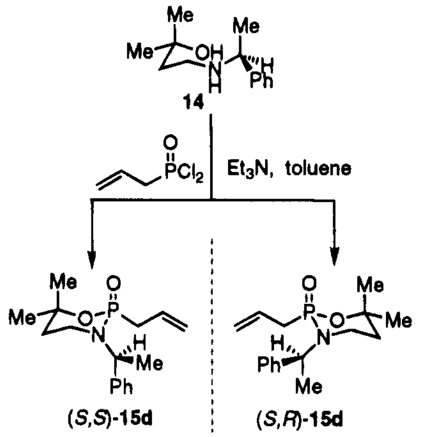
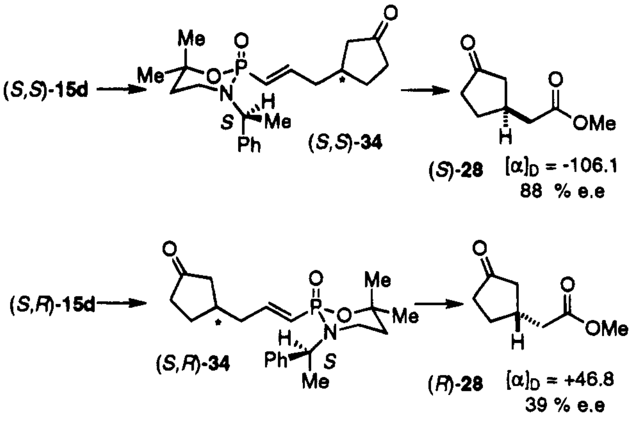
[27] (a) Posner, G. H.; Asirvatham, E. *J. Org. Chem.* **1985**, *50*, 2589. (b) Kuritani, H.; Takaoka, Y.; Shingu, K. *J. Org. Chem.* **1979**, *44*, 452.

[28] (a) Willams, D. R.; Klingler, F. D.; Allen, E. E.; Lichtenthaler, F. W. *Tetrahedron Lett.* **1988**, *29*, 5087. (b) Lichtenthaler, F. W.; Jarglis, P.; Lorenz, K. *Synthesis* **1988**, 790.

Scheme 7



Scheme 8



is practically impossible, we envisioned a formal resolution by the introduction of another stereogenic center on the nitrogen substituent. This additional stereogenic center then creates a pair of two diastereomers (enantiomorphic pair pertaining to the phosphorus heterocycle). If the selectivity of the reaction of each oxazaphosphorinane diastereomer is dependent primarily on the phosphorus stereogenic center and the *N*-alkyl group exerts only a generic steric effect of its configuration, this effective resolution of the enantiomorphic pair can be used as an alternative to the resolution of enantiomers (±)-**3**.

We thus searched for enantiomerically pure tertiary amines which have similar steric bulk to that of *tert*-butylamine, but such amines are not commercially available and not easy to prepare. Therefore, commercially available (*S*)-1-phenylethylamine was used to assay the formal resolution concept in the utilization of amino alcohol **14**.[20] The reaction of amino alcohol **14** with allylphosphonic dichloride afforded the heterocycles (*S,S*)- and (*S,R*)-**15d** in high yield which proved to be easily separable as mixtures with small amounts of their corresponding 2-propenyl analogs (Scheme 7; entries 9 and 10, Table 2). The relative configurations of the two diastereomers could not be determined but were temporarily assigned as (*S,S*)-**15d** the more polar major product and (*S,R*)-**15d** for the less polar isomer.

2-Cyclopentenone was chosen as a representative electrophile to explore the selectivity for the Michael reactions of (*S,S*)- and (*S,R*)-**15d** due to the large value of the specific rotation of the corresponding keto ester **28**. Thus, (*S,S*)- and (*S,R*)-**15d** were subjected to the Michael reaction conditions with 2-cyclopentenone using *n*-BuLi as the base to produce adducts (*S,S*)- and (*S,R*)-**34** in high yield (Scheme 8). The regioselectivity was again high (99/1 for γ-1,4/α-1,2), and other regioisomeric products were not observed. Subsequent ozonolytic cleavage of each adduct, (*S,S*)- and (*S,R*)-**34**, afforded keto aldehyde **28** in 72% and 69% yields, respectively. Both cleaved products showed some diastereoselection. Keto aldehyde **28** originating from the polar diastereomer (*S,S*)-**34** was shown to be 88% enantiomerically enriched, but the other from the less polar isomer (*S,R*)-**34** was only 39% enantiomerically enriched in opposite absolute configuration (Scheme 8).

Discussion

Preparation of 2-Allyl-1,3,2-oxazaphosphorinane 2-Oxides. The Michael addition reagents were prepared either by a coupling reaction of allylphosphonic dichloride with the requisite amino alcohol or by a two-step protocol involving trivalent phosphite formation followed by Arbuzov reaction. The former coupling method was less advantageous since chiral amino alcohols produced almost equal amounts of cis and trans phosphorus epimers sometimes along with the corresponding 2-propenyl isomers, while the latter method was better suited for the preparation of cis derivatives selectively. However, the high level of enrichment in the mixture of ethyl phosphites (>28/1) was not preserved during the Arbuzov reaction affording the cis isomer in a ratio of <9/1. The erosion of the selectivity during the Arbuzov reaction has often been seen and can be explained by formation of a pentacoordinate trigonal bipyramidal intermediate followed by pseudorotation.[23] The selectivity is also substrate and electrophile dependent (allyl bromide, 6–7/1, versus allyl tosylate, 9/1); the nucleophilic bromide counterion leads to the formation of pentacoordinate phosphoranes more so than does the tosylate. It has also been reported that less reactive electrophiles such as simple alkyl halides lead to erosion of selectivity in the reaction.[23]

Origin of Diastereoselectivity. Any attempt to rationalize the stereochemical outcome of the reaction must take into account a number of critical structural issues pertaining to the phosphorus-stabilized anion: (1) anion aggregation state, (2) ring conformation, (3) allyl anion conformation, and (4) association of the anion with the acceptor. While only a limited number of structural studies have yet been carried out on the allyl anions themselves,[10a] we have a considerable body of information on related benzyl anions for which a close analogy may be argued.[29]

Aggregation State. The lithium salts derived from the benzyl-1,3,2-oxazaphosphorinane 2-oxides and -1,3,2-diazaphosphorinane 2-oxides have been found by both solid state and solution analyses to exist as dimers.[10c,29] The existence of dimeric species in the lithium salts of P=O compounds is so pervasive as to suggest an extremely high enthalpy of dimerization. In the absence of accurate kinetic data, we cannot be certain if the dimer is also the reactive species. However, two experimental

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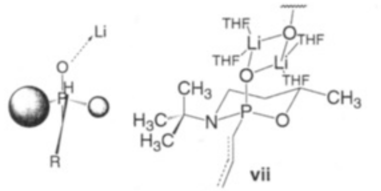
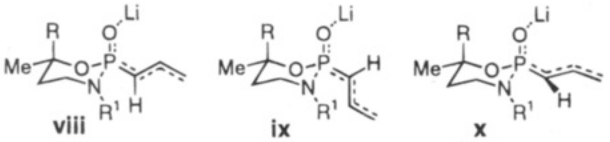
(29) (a) Denmark, S. E.; Dorow, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 864. (b) Denmark, S. E.; Miller, P. C.; Wilson, S. R. *J. Am. Chem. Soc.* **11991**, *113*, 1468. (c) Dorow, R. L. Ph.D. Thesis, University of Illinois-Urbana, IL, 1990. (d) Denmark, S. E.; Swiss, K. A.; Dorow, R. L.; Miller, P. C.; Wilson, S. R. Manuscript submitted. (e) The X-ray structure of a diethyl lithiobenzylphosphonate DABCO complex has been reported; see: Zarges, W.; Marsch, M.; Harms, K.; Haller, F.; Frenking, G.; Boche, G. *Chem. Ber.* **1991**, *124*, 861.



vii

Figure 3. Ring and anion conformation of Li$^+$*cis*-**15b**$^-$.



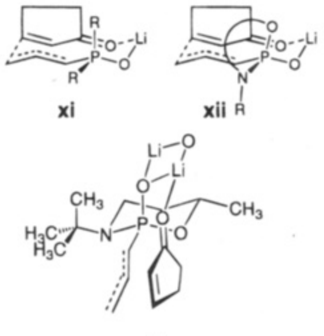
viii ix x

Figure 4. Limiting conformers of the *P*-allyl anion derived from 2-Allyl-1,3,2-oxazaphosphorinanes.

facts support the hypothesis that the monomer is in fact the reactive species. First, the addition of copper(I) iodide does not influence the selectivity, and second, the racemic compound **3** reacted with comparable or better selectivity. While the structure of the copper species is also not known, it is unlikely that two different aggregates would have the same selectivity. Moreover, in (±)-**3**, one would expect homochiral and heterochiral dimers. If these dimers were equally reactive, there should be a difference in reaction selectivity between racemic and enantiomerically enriched compounds. For simplicity we will analyze the monomers and comment on the differences a dimeric structure could introduce.

Ring and Anion Conformation. The conformation of phosphorus-containing heterocycles has been extensively investigated including the 1,3,2-oxazaphosphorinane 2-oxide system used herein.[30] However, outside of our own studies, there is little information on the conformation of the derived anions. The picture which emerges from extensive solution NMR investigations[29c] and an X-ray crystal structure analysis[31] of the *P*-isopropyl analog of *cis*-**15b** is that the anions exist as both chairs and twist boats depending on the configuration at phosphorus and the substituent on nitrogen. The ring conformation we propose for Li$^+$*cis*-**15b**$^-$ maintains a basic chairlike shape placing all the carbon substituents in equatorial positions (vii, Figure 3). Also depicted in vii is the s-trans, *E*-configuration of the allyl anion. The *E*-configuration is deduced from the corresponding *E*-configuration of the γ-substitution products,[10a,b] while the s-trans conformation is proposed on the basis of steric crowding around the phosphoryl unit.

Three limiting parallel (viii, ix) and orthogonal (x) conformers for the *P*-allyl anion derived from 2-allyl-1,3,2-oxazaphosphorinane 2-oxides are depicted in Figure 4. The conformational preference will clearly influence the diastereoselectivity of reaction as the opposite face of the anion is exposed in structures viii and ix. The conformer ix resembles most closely the solid state structure of the *P*-benzyl anion derived from 2-benzyl-1,3,2-diazaphosphorinane 2-oxide.[29a] In fact, in all anions studied to date which bear a hydrogen on the α-carbon, the preferred if not exclusive conformation is the parallel, s-trans as shown. This is most certainly due to the reduced steric interactions between the anion substituents and the lithio phosphoryl unit. Orthogonal conformations related to x have never been detected and generally constitute barriers or high energy minima on calculated rotational energy coordinates.[10c,d] It is however, important to keep in mind that the rotational barrier of the P$-$C bond in benzyl and other anions is extremely low.[10c,29] Thus, the anion conformers can interconvert even at low temperature.



xi xii xiii

Figure 5. *trans*-Decalyl-type transition structures for Michael additions.

Michael Reaction of 2-Allyl-1,3,2-oxazaphosphorinanes with Cyclic Enones. To rationalize the high diastereoselectivity in the Michael reaction of *P*-allyl- and *P*-butenylphosphine oxides and phosphonates, Haynes et al. invoked a 10-membered transition state structure (xi) which is proposed to resemble a *trans*-decalyl-like chair$-$chair structure (Figure 5).[7,8] Hanessian has adapted this model to explain the high selectivities observed with his chiral diazaphospholidine-based anions. We have incorporated this model in the formulation of the transition state model xii derived from Li$^+$**3**$^-$ and Li$^+$*cis*-**15a$-$c**$^-$ with cyclic enones, Figure 5. The salient features of the hypothesis are the coordination of the enone oxygen to the lithium by displacement of a THF molecule or scission of the dimer and minimization of transannular interactions in the pseudo 10-membered ring. The hypothetical transition structure xiii illustrates all of the key controlling features. To accommodate the incorporation of the enone in a 10-membered ring, the carbonyl group must be complexed by lithium anti to the enone double bond on the sterically unhindered side of the allyl anion. This presents the *si*-face of the cyclic enones toward the anion away from the bulky *N*-alkyl group. This would lead to the preferential formation of the *S*-configuration at the newly created stereogenic center as was observed with Li$^+$*cis*-**15a$-$c**$^-$.

It is difficult to formulate a transition state structure for the reaction of Li$^+$*trans*-**15a,b**$^-$. Spectroscopic studies of the anion suggest that the ring exists in a twist boat conformation, most likely with the anionic allyl group axially oriented and perhaps even in an orthogonal orientation to avoid 1,3-interactions. It is interesting to note that intramolecular reactions of phosphorus-stabilized anions (Claisen rearrangement[17] and the [2,3]-Wittig rearrangement[18]) derived from the similar 1,3,2-oxazaphosphorinane 2-oxides have shown comparable selectivities in the cis and trans series.

Formal Resolution. The highly selective Michael additions of Li$^+$**3**$^-$ and Li$^+$*cis*-**15b**$^-$ suggested that the reactive conformation for the two substrates is similar. The "resolution" of the enantiomers of (±)-**3** by installation of a spectator stereogenic center on the nitrogen was

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(30) For leading references on the conformational analysis of 1,3,2-oxazaphosphorinanes, see: Bentrude, W. G.; Setzer, W. N.; Khan, M.; Sopchik, A. E.; Ramli, E. *J. Org. Chem.* **1991**, *56*, 6127.

(31) Miller, P. C.; Wilson, S. R. Unpublished work from these laboratories.

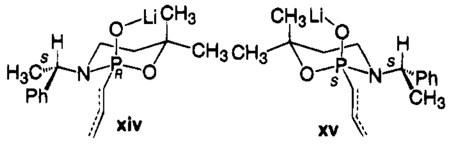

Figure 6. Enantiomorphic anions from (*S*,*R*)- and (*S*,*S*)-**15d**.

successful. However, the separated diastereomers did not behave like enantiomorphs as was hoped which implied that the stereogenic center on the nitrogen was not a simple spectator. This can be explained by difference in steric encumbrance in the transition states with preferred rotamers around the C−N bond, Figure 6. The rotational preference around C−N bond is controlled in large part by the steric interactions between the substituents on the *N*-(*S*)-phenylethyl group with the phosphorus heterocycle which tends to minimize gauche interactions in a staggered conformation. In the reactive conformation xiv, which represents the anions derived from (*S*,*R*)-**15d**, the phenyl group is located in an advantageous position to shield the allyl group and thus gives rise to a Michael addition which is as selective as that with the *tert*-butyl analog *cis*-**15b**. However, as shown in Figure 6, the methyl is a stereocontrolling element in the reactive conformer xv resulting in the formation of the antipodal product in 39% ee mainly due to steric attenuation from phenyl to methyl. We cannot rule out the intermediacy of the ring-flipped conformer of xv since, a priori, reaction via xv should have similar diastereoselectivity as the isopropyl analog *cis*-**15a**. The fact that the selectivity is lower argues against a strict extrapolation from analogy.

Conclusion

High diastereoselectivity was observed for the Michael addition reaction of racemic 1,3,2-oxazaphosphorinane 2-oxide **3** with cyclic enones. The diastereoselectivity and the regioselectivity of Michael reaction of enantiomerically enriched *cis*-**15a**−**c** were also high giving rise to γ-1,4-addition products with 5-, 6-, and 7-membered enones. The results can be rationalized by assuming that the s-trans, *E*-conformation of the anion reacts through a favored 10-membered transition state in the conjugate addition reaction. The reaction with enantiomerically enriched *trans*-**15** was not selective most likely due to a change in conformation of the ring of the auxiliary and a lesser shielding of the anion by the *N*-*tert*-butyl group. The size of the nitrogen substituent was shown to be of minor significance in controlling the stereochemical outcome of this reaction. Thus the utility of the 1,3,2-oxazaphosphorinane 2-oxide ring system and the design of a chiral auxiliary have been demonstrated.

A variety of *P*-allyl substrates derived from C_2-symmetric diamine auxiliaries, varying the ring size, phosphorus substituent, *N*-alkyl substituent, and nature of *P*-allyl unit, will be reported in the future.

Experimental Section

General Methods. See the supporting information. *J* values are reported in hertz (Hz).

Starting Materials. The amino alcohols **1**, **13a**−**c**,[10,19] and allylphosphonic dichloride[32] were prepared by literature procedures.

6,6-Dimethyl-3-(1,1-dimethylethyl)-2-(2-propenyl)-1,3,2-oxazaphosphorinane 2-Oxide (3) and 6,6-Dimethyl-3-(1,1-dimethylethyl)-2-(1(*E*)-propenyl)-1,3,2-oxazaphosphorinane 2-Oxide (4). To a solution of Et_3N (6.56 mL, 47.1 mmol) in CH_2Cl_2 (50 mL) were added simultaneously a solution of amino alcohol **1** (3.0 g, 18.8 mmol) in CH_2Cl_2 (25 mL) and a solution of allylphosphonic dichloride **2** (3.14 g, 19.8 mmol) in CH_2Cl_2 (25 mL) over 40 min. The reaction mixture was stirred at rt overnight. The reaction mixture was poured into H_2O (50 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated to give an oil, which was purified by SiO_2 column chromatography (hexane/EtOAc/*i*-PrOH, 35/62/3) to give 3.21 g (70%) of a mixture of **3** and **4**.

A solution of LDA prepared from diisopropylamine (1.46 mL, 10.4 mmol) and *n*-BuLi (6.57 mL, 9.98 mmol, 1.52 M in hexane) in 30 mL of THF at −23 to −20 °C for 30 min was cooled to −50 °C. To the LDA solution was added dropwise 2.13 g (8.68 mmol) of the mixture of **3** and **4** in 10 mL of THF dropwise. After being stirred at −50 °C for 1 h, the reaction mixture was cooled to −78 °C, and the reaction was quenched with saturated aqueous NH_4Cl solution. After 30 mL of water was added, the mixture was extracted with EtOAc (3 × 70 mL), washed with brine (50 mL), dried (Na_2SO_4), filtered, and concentrated. The crude product was distilled under reduced pressure to afford 1.53 g (72%) of isomerically pure **3** as a colorless oil. The pot residue was repurified by column chromatography (hexane/EtOAc/*i*-PrOH, 35/62/3) and distillation to give an additional 230 mg (10%) of **3** as an oil: bp 167−170 °C (0.2 Torr) (combined yield, 82%); ^1H NMR (300 MHz) δ 5.82−5.66 (m, 1 H), 5.12−5.05 (m, 2 H), 3.21−3.03 (m, 2 H), 2.80−2.30 (m, 2 H), 1.98−1.79 (m, 2 H), 1.50 (s, 3 H), 1.35 (s, 9 H), 1.29 (s, 3 H); ^{13}C NMR (75.5 MHz) δ 129.81 (J_{CP} = 11.2), 117.63 (J_{CP} = 14.6), 78.65 (J_{CP} = 9.7), 54.33 (J_{CP} = 5.2), 39.11, 39.02, 38.92, 37.95 (J_{CP} = 129.8), 28.96, 28.89, 28.63; ^{31}P NMR (121.6 MHz) δ 23.33; IR (CCl_4) 2938 s, 1253 s, 1199 s; MS (70 eV) 245 (M^+, 4), 148 (100); TLC R_f 0.31 (hexane/EtOAc/*i*-PrOH, 35/62/3). Anal. Calcd for $C_{12}H_{24}NO_2P$ (245.30): C, 58.76; H, 9.86; N, 5.71; P, 12.63. Found: C, 58.75; H, 9.87; N, 5.70; P, 12.60.

4: ^1H NMR (300 MHz) δ 6.60 (ddq, J_d = 18, J_d = 24, J_q = 6, 1 H), 5.74 (ddq, J_d = 18, J_d = 24, J_q = 3, 1 H), 3.17−3.10 (m, 2 H), 2.03−1.96 (m, 1 H), 1.83 (dd, *J* = 9, *J* = 3, 3 H), 1.80−1.70 (m, 4 H), 1.49 (s, 3 H), 1.31 (s, 9 H); ^{13}C NMR (75 MHz) δ 143.60 (J_{CP} = 5.7 Hz), 126.38 (J_{CP} = 176.7), 78.92 (J_{CP} = 7.3), 54.48, 39.34, 39.25, 38.59, 29.20, 28.80, 19.32 (J_{CP} = 17.9).

General Procedure for the Michael Reaction of 3. To a well-stirred solution of **3** in THF (0.1−0.2 M) was added *t*-BuLi (1.0−1.1 equiv) at −78 °C under N_2 atmosphere. After stirring for 15 min at −78 °C, the cold yellow solution was transferred via cannula to a cold (−78 °C) suspension of the cycloalkenone (1.05 equiv) and CuI (0.2 equiv) in THF over 3 min. The yellow color completely faded within 5 min. After the mixture was stirred for 30 min, the reaction mixture was quenched with aqueous NH_4Cl and the mixture poured into brine and extracted with EtOAc three times. The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated to give a colorless oil. The crude oil was purified by SiO_2 column chromatography.

(1′*E*)-2-[3′-(3″-Oxocyclopentyl)-1′-propenyl]-6,6-dimethyl-3-(1,1-dimethylethyl)-1,3,2-oxazaphosphorinane 2-Oxide (5). **5** was from 181 mg (0.738 mmol) of **3**, 1.41 mL (0.73 mmol, 1.78 M in pentane) of *t*-BuLi, 74 μL (0.886 mmol) of cyclopentenone, and 34 mg (0.18 mmol, 0.2 equiv) of CuI. ^1H NMR analysis of the crude product showed only the γ-addition product. Purification by column chromatography (hexane/EtOAc/*i*-PrOH, 49/50/1 to 35/51/4) afforded 194 mg (80%) of **5** as a colorless oil. The diastereomeric ratio was beyond limits of detection. An analytical sample of **5** was obtained by distillation: bp 171 °C (0.05 Torr); ^1H NMR (300 MHz) δ 6.59 (ddt, *J* = 21.5, 16.6, 7.2, 1 H), 5.79 (dd, *J* = 21.0, 16.6, 1 H), 3.24−3.11 (m, 2 H), 2.45−1.69 (m, 11 H), 1.51 (s, 3 H), 1.33 (s,

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[32] Bhongle, N. N.; Notter, R. H.; Turcotte, J. G. *Synth. Commun.* **1987**, *17*, 1071. (b) Morita, T.; Okamoto, Y.; Sakurai, H. *Chem. Lett.* **1980**, 435. (c) Morita, T.; Okamoto, Y.; Sakurai, H. *Tetrahedron Lett.* **1978**, 2523. (d) Stowell, M. H. B.; Ueland, J. M.; McClard, R. W. *Tetrahedron Lett.* **1990**, *31*, 3261.

12 H); ^{13}C NMR (75.5 MHz) δ 218.67, 145.89, 127.08 (J_{CP} = 174.4), 79.46 (J_{CP} = 8.7), 54.82, 44.47, 39.64, 39.43 (J_{CP} = 20.4), 38.84, 38.09, 35.92, 29.52, 29.45, 29.38, 29.08, 29.04; ^{31}P NMR (121.6 MHz) δ 12.02; IR (CCl$_4$) 2974 s, 1716 s, 1250 s, 1225 s; MS (70 eV) 327 (M$^+$), 312 (100); TLC R_f 0.22 (hexane/EtOAc/*i*-PrOH, 34/59/7). Anal. Calcd for $C_{17}H_{30}NO_3P$ (327.42): C, 62.37; H, 9.24; N, 4.28; P, 9.46. Found: C, 62.27; H, 9.26; N, 4.27; P, 9.58.

(1′*E*)-2-[3′-(3″-Oxocyclohexyl)-1′-propenyl]-6,6-dimethyl-3-(1,1-dimethylethyl)-1,3,2-oxazaphosphorinane 2-Oxide (6). **6** was from 110 mg (0.448 mmol) of **3**, 1.9 mL (0.493 mmol, 0.26 M in pentane) of *t*-BuLi, 46 μL (0.47 mmol) of cyclohexenone, and 17 mg (0.09 mmol, 0.2 equiv) of CuI. ^{1}H NMR analysis of the crude product showed 49/1 ratio of γ-1,4/α-1,2-addition product. Purification by column chromatography (hexane/EtOAc/*i*-PrOH, 34/59/7) afforded 112 mg (73%) of **6** as a colorless oil. The diastereomeric ratio of the γ-1,4-addition product was beyond limits of detection. An analytical sample of **6** was obtained by distillation: bp 200 °C (0.2 Torr); ^{1}H NMR (300 MHz) δ 6.51 (ddt, J = 23.7, 16.6, 7.0, 1 H), 5.73 (dd, J = 21.3, 16.6, 1 H), 3.14 (m, 2 H), 2.41–1.09 (m, 13 H), 1.47 (s, 3 H), 1.29 (s, 12 H); ^{13}C NMR (75.5 MHz) δ 210.64, 145.18 (J_{CP} = 3.8), 127.42 (J_{CP} = 175.2), 79.30 (J_{CP} = 7.1), 54.64 (J_{CP} = 4.9), 47.43, 40.93, 40.25 (J_{CP} = 20.1), 39.38 (J_{CP} = 7.8), 38.70, 37.99, 30.42, 29.34, 29.27, 29.23, 28.90, 24.60; ^{31}P NMR (121.6 MHz) δ 12.06; IR (CCl$_4$) 2942 m, 1717 m, 1250 m; MS (70 eV) 341 (M$^+$, 1), 70 (100); HRMS calcd for $C_{18}H_{32}NO_3P$ 341.2140, found 341.2102; TLC R_f 0.23 (hexane/EtOAc/*i*-PrOH, 34/59/7).

(1′*E*)-2-[3′-(3″-Oxocycloheptyl)-1′-propenyl]-6,6-dimethyl-3-(1,1-dimethylethyl)-1,3,2-oxazaphosphorinane 2-Oxide (7). **7** was from 182 mg (0.742 mmol) of **3**, 0.47 mL (0.742 mmol, 1.59 M in pentane) of *t*-BuLi, 91 μL (0.816 mmol) of cycloheptenone, and 28 mg (0.148 mmol, 0.2 equiv) of CuI. ^{1}H NMR analysis of the crude product showed a 3.6/1 ratio of γ-1,4/α-1,2-addition products. Purification by SiO$_2$ column chromatography (hexane/EtOAc/*i*-PrOH, 34/59/7) afforded 166 mg (63%) of **7** as a viscous oil. The diastereomeric ratio of the γ-1,4-addition product was beyond limits of detection. An analytical sample of **7** was obtained by Kugelrohr distillation: bp 183 °C (0.4 Torr); ^{1}H NMR (300 MHz) δ 6.54 (ddt, J = 21.6, 16.6, 7.8, 1 H), 5.76 (dd, J = 21.8, 16.6, 1 H), 3.16 (m, 2 H), 2.51–1.29 (m, 15 H), 1.61 (s, 3 H), 1.49 (s, 3 H), 1.33 (s, 9 H); ^{13}C NMR (75.5 MHz) δ 213.53, 145.76 (J_{CP} = 4.4), 127.53 (J_{CP} = 175.1), 79.43 (J_{CP} = 9.8), 54.78 (J_{CP} = 4.3), 49.52, 43.62, 41.36 (J_{CP} = 21.0), 39.52 (J_{CP} = 7.1), 38.79, 36.12, 35.20, 29.44, 29.37, 29.02, 28.19, 27.16, 24.03; ^{31}P NMR (121.6 MHz) δ 11.86; IR (CCl$_4$) 2974 s, 1716 s, 1275 s, 1250 s; MS (70 eV) 355 (M$^+$, 1), 70 (100); HRMS calcd for $C_{19}H_{34}NO_3P$ 355.2276, found 355.2264; TLC R_f 0.25 (hexane/EtOAc/*i*-PrOH, 34/59/7).

General Procedure for the Preparation of Scalemic 2-Allyl-1,3,2-oxazaphosphorinane 2-Oxides 15. Method A (Coupling with allylphosphonic dichloride): To a mixture of amino alcohol **13** (>99% ee) and triethylamine (2.1–2.5 equiv) in dichloromethane (0.5 M) was added a solution of allylphosphonic dichloride **2** (1.05 equiv) in toluene using the pressure-equalizing dropping funnel at −40 °C over 30 min. The cooling bath was removed, and the reaction mixture was stirred at rt overnight. The precipitate was filtered off, and the filtrate was washed with water. The aqueous layer was extracted with EtOAc three times. The combined organic extracts were washed with brine, dried (MgSO$_4$), filtered, and concentrated to give a pale yellow oil. The mixture of two diastereomers *cis*- and *trans*-**15** was purified by column chromatography and/or MPLC to give isomerically pure *cis*- and *trans*-**15**.

Method B: Same as method A but replacing dichloromethane with toluene.

Method C (Two-step protocol of phosphite formation followed by Arbuzov reaction): To a refluxing mixture of ethyl chlorophosphite and triethylamine in CH$_2$Cl$_2$ was slowly added amino alcohol **13** using syringe pump over 1 h. The reaction mixture was heated to reflux overnight. After the oil bath was removed, the reaction mixture was diluted with 5 vol of dry hexane. The triethylamine hydrochloride salt was removed by filtration under a N$_2$ blanket. The filtrate was concentrated, and the residue was distilled under reduced pressure to give a colorless liquid. The diastereomeric ratio of the two phosphite diastereomers was determined by ^{31}P NMR to be >28/1 in every case. The phosphite intermediate was treated with allyl bromide in acetonitrile at 60 °C for 6–10 h to give *cis*- and *trans*-**15**. The distereomeric mixture was purified by SiO$_2$ column chromatography.

Method D: Same as method C but replacing allyl bromide with allyl tosylate.

***(S)*-(2*u*,6*l*)-3-(1-Methylethyl)-6-methyl-2-(2-propenyl)-1,3,2-oxazaphosphorinane 2-Oxide (*cis*-15a) and *(S)*-(2*l*,6*l*)-3-(1-Methylethyl)-6-methyl-2-(2-propenyl)-1,3,2-oxazaphosphorinane 2-Oxide (*trans*-15a). Method B:** From 568 mg (4.33 mmol) of **13a**, 0.54 mL (4.55 mmol) of **2**, and 1.33 mL (9.54 mmol) of Et$_3$N followed by purification by SiO$_2$ column chromatography (EtOAc/*i*-PrOH, 49/1) were obtained 414 mg (44%) of *cis*-**15a** and 321 mg (34%) of *trans*-**15a** as colorless oils. Analytical samples of each were obtained by Kugelrohr distillation. *cis*-**15a**: bp 145–150 °C (0.5 Torr); [α]$_D$ = +0.45° (*c* 1.02, CHCl$_3$); ^{1}H NMR (300 MHz) δ 5.86–5.70 (m, 1 H), 5.17–5.09 (m, 2 H), 4.57–4.47 (m, 1 H), 3.85–3.72 (m, 1 H), 3.16–2.92 (m, 2 H), 2.75–2.59 (m, 2 H), 1.93–1.84 (m, 1 H), 1.69 (ddt, J = 14.0, 10.5, 5.7, 1 H), 1.30 (dd, J = 6.0, 1.2, 3 H), 1.22 (d, J = 6.6, 3 H), 1.11 (d, J = 6.7, 3 H); ^{13}C NMR (75.5 MHz) δ 129.20 (J_{CP} = 11.0), 118.39 (J_{CP} = 14.1), 72.15 (J_{CP} = 7.7), 45.77, 36.82, 34.22 (J_{CP} = 130.0), 32.77 (J_{CP} = 3.6), 21.84 (J_{CP} = 8.2), 20.31, 20.19 (J_{CP} = 5.6); ^{31}P NMR (121.6 MHz) δ 26.47; IR (CCl$_4$) 2975 m, 1256 s; MS (70 eV) 217 (M$^+$, 6), 134 (100); TLC R_f 0.25 (EtOAc/*i*-PrOH, 19/1). Anal. Calcd for $C_{10}H_{22}NO_2P$ (217.15): C, 55.29; H, 9.28; N, 6.45; P, 14.26. Found: C, 55.01; H, 9.34; N, 6.35; P, 14.03.

***trans*-15a:** bp 150–155 °C (0.5 Torr); [α]$_D$ = −48.7° (*c* 1.38, CHCl$_3$); ^{1}H NMR (300 MHz) δ 5.92–5.78 (m, 1 H), 5.21–5.13 (m, 2 H), 4.38–4.30 (m, 1 H), 4.00–3.85 (m, 1 H), 3.15 (ddt, J = 18.6, 12.9, 4.0, 1 H), 3.03–2.93 (m, 1 H), 2.75–2.56 (m, 2 H), 1.83–1.72 (m, 2 H), 1.34 (dd, J = 6.5, 1, 1, 3 H), 1.15 (d, J = 6.6, 3 H), 1.07 (d, J = 6.8, 3 H); ^{13}C NMR (75.5 MHz) δ 128.57 (J_{CP} = 10.6), 118.60 (J_{CP} = 13.5), 72.68 (J_{CP} = 7.8), 45.31 (J_{CP} = 4.0), 37.94 (J_{CP} = 2.8), 33.92 (J_{CP} = 5.6), 31.77 (J_{CP} = 119.4), 22.31 (J_{CP} = 7.1), 20.95 (J_{CP} = 1.7), 20.02 (J_{CP} = 2.8); ^{31}P NMR (121.6 MHz) δ 23.20; IR (CCl$_4$) 2975 m, 1256 s; MS (70 eV) 217 (M$^+$, 5), 134 (100); HRMS calcd for $C_{10}H_{20}NO_2P$ 217.1232, found 217.1223; TLC R_f 0.35 (EtOAc/*i*-PrOH, 19/1).

***(S)*-(2*u*,6*l*)-3-(1,1 Dimethylethyl)-6-methyl-2-(2-propenyl)-1,3,2-oxazaphosphorinane 2-Oxide (*cis*-15b) and *(S)*-(2*l*,6*l*)-3-(1,1-Dimethylethyl)-6-methyl-2-(2-propenyl)-1,3,2-oxazaphosphorinane 2-Oxide (*trans*-15b). Method A:** From 1.2 g (8.26 mmol) of **13b**, 1.31 g (8.26 mmol) of **2**, and 2.9 mL (20.8 mmol) of Et$_3$N followed by purification by SiO$_2$ column chromatography/MPLC (hexane/EtOAc/*i*-PrOH, 35/62/3) were obtained 635 mg (33%) of *trans*-**15b** and 625 mg (33%) of *cis*-**15b** as colorless oils. An analytical sample of each was obtained by Kugelrohr distillation. Other preparations were accomplished by method B, 70–80% (cis/trans, 3/2); method C, 74% (cis/trans, 6.7/1); and method D, 72% (cis/trans, 9/1). *cis*-**15b**: bp 135 °C (0.2 Torr); [α]$_D$ = +18.3° (*c* 1.0, CHCl$_3$); ^{1}H NMR (300 MHz) δ 5.76 (m, 1 H), 5.13–5.06 (m, 2 H), 4.52, (m, 1 H), 3.08 (m, 2 H), 2.66 (m, 2 H), 1.98 (m, 1 H), 1.59 (m, 1 H), 1.34 (s, 9 H), 1.28 (d, J = 6.7, 3 H); ^{13}C NMR (75.5 MHz) δ 129.22 (J_{CP} = 10.7), 118.37 (J_{CP} = 13.9), 75.25 (J_{CP} = 8.3), 55.27, 41.73, 35.24 (J_{CP} = 3.1), 34.67 (J_{CP} = 118.9), 29.28 (J_{CP} = 6.7), 22.60 (J_{CP} = 5.4); ^{31}P NMR (121.6 MHz) δ 26.90; IR (CCl$_4$) 2975 m, 1256 s; MS (70 eV) 231 (M$^+$, 2), 216 (100); TLC R_f 0.15 (hexane/EtOAc/*i*-PrOH, 34/59/7). Anal. Cacld for $C_{11}H_{22}NO_2P$ (231.37): C, 57.13; H, 9.59; N, 6.06; P, 13.39. Found: C, 56.95; H, 9.57; N, 5.92; P, 13.31.

***trans*-15b:** bp 150 °C (0.3 Torr); [α]$_D$ = −39.4° (*c* 1.0, CHCl$_3$); ^{1}H NMR (300 MHz) δ 5.85 (m, 1 H), 5.17 (m, 2 H), 4.31 (m, 1 H), 3.01 (ddt, J = 17.6, 13.4, 4.0, 1 H), 3.01 (ddt, J = 17.6, 10.5, 3.2, 1 H), 2.72 (dd, J = 19.6, 7.3, 2 H), 1.91–1.75 (m, 2 H), 1.35 (d, J = 6.6, 3 H), 1.34 (s, 9 H); ^{13}C NMR (75.5 MHz) δ 129.44 (J_{CP} = 11.4), 117.84 (J_{CP} = 14.0), 69.86 (J_{CP} = 6.5), 54.27, 40.05, 36.70 (J_{CP} = 129.6), 34.04, 28.89 (J_{CP} = 7.0), 21.75 (J_{CP} = 7.2); ^{31}P NMR (121.6 MHz) δ 22.21; IR (CCl$_4$) 2977 m, 1256 s; MS (70 eV) 231 (M$^+$, 6), 216 (100); TLC R_f 0.20 (hexane/EtOAc/*i*-PrOH, 34/59/7). Anal. Calcd for $C_{11}H_{22}NO_2P$

(231.37): C, 57.13; H, 9.59; N, 6.06; P, 13.39. Found: C, 56.92; H, 9.63; N, 5.92; P, 13.36.

***(S)*-(2*u*,6*l*)-3-(1,1-Diethylpropyl)-6-methyl-2-(2-propenyl)-1,3,2-oxazaphosphorinane 2-Oxide (*cis*-15c) and *(S)*-(2*l*,6*l*)-3-(1,1-Diethylpropyl)-6-methyl-2-(2-propenyl)-1,3,2-oxazaphosphorinane 2-Oxide (*trans*-15c). Method D:** From 1.02 g (5.45 mmol) of **13c**, 1.60 mL (11.45 mmol) of Et_3N, and 653 μL (5.72 mmol) of $EtOPCl_2$ was obtained 1.42 g of phosphite. Treatment of the phosphite with 2.89 g (13.6 mmol) of allyl tosylate followed by SiO_2 column chromatography (hexane/EtOAc, 1/1) afforded 1.25 g (83%) of **15c** (8.1/1 cis/trans mixture by ^{31}P NMR) as a colorless oil. Further purification by MPLC (hexane/EtOAc, 1/1) afforded 1.05 g (70%) of *cis*-**15c** (41/1 cis/trans mixture) and 89 mg (6%) of *trans*-**15c** (45/1 trans/cis mixture) as colorless oils. An analytical sample of *cis*-**15c** was obtained by Kugelrohr distillation. Similarly, **15c** was obtained by method C in 89% yield with 7.3/1 ratio of cis/trans mixture. *cis*-**15c**: bp 160 °C (0.2 Torr); ^1H NMR (300 MHz) δ 5.93−5.82 (m, 1 H, HC(2′)), 5.16−5.09 (m, 2 H), 4.26 (m, 1 H), 3.11−2.93 (m, 2 H), 2.80−2.57 (m, 2 H), 2.13−2.03 (m, 1 H), 1.79 (dq, J = 14.8, 7.4, 3 H), 1,57 (ddd, J = 17.7, 8.6, 4.4, 1 H), 1.42 (dq, J = 14.7, 7.4, 3 H), 1.31 (dd, J = 5.8, 0.9, 3 H), 0.85 (t, J = 7.4, 9 H); ^{13}C NMR (75.5 MHz) δ 129.36 (J_{CP} = 11.0), 118.23 (J_{CP} = 14.3), 68.47 (J_{CP} = 7.2), 64.66 (J_{CP} = 2.1), 38.48 (J_{CP} = 2.7), 36.93 (J_{CP} = 129.2), 34.67 (J_{CP} = 2.8), 26.31 (J_{CP} = 1.6), 22.09 (J_{CP} =8.3), 7.98; ^{31}P NMR (121.6 MHz) δ 27.25; IR (CCl_4) 2973 s, 1246 s; MS (70 eV) 273 (M^+, 1), 244 (100); TLC R_f 0.27 (hexane/EtOAc, 1/1). Anal. Calcd for $C_{14}H_{28}NO_2P$ (273.35): C, 61.51; H, 10.32; N, 5.12; P, 11.33. Found: C, 61.23; H, 10.38; N, 5.19; P, 11.10.

***trans*-15c:** ^1H NMR (300 MHz) δ 5.96−5.79 (m, 1 H), 5.18−5.06 (m, 2 H), 4.31−4.20 (m, 1 H), 3.35−3.18 (m, 1 H), 2.99−2.85 (m, 1 H), 2.82−2.59 (m, 2 H), 1.81−1.56 (m, 4 H), 1.46−1.18 (m, 4 H), 1.32 (dd, J = 6.1, 0.9, 3 H), 0.80 (t, J = 7.2, 9 H); ^{31}P NMR (121.6 MHz) δ 22.49; MS (70 eV) 273 (M^+, 1), 244 (100); TLC R_f 0.29 (hexane/EtOAc, 1/1).

***(S)*-(1″*l*,2*l*)-6,6-Dimethyl-3-(1-phenylethyl)-2-(2-propenyl)-1,3,2-oxazaphosphorinane 2-Oxide ((*S*,*S*)-15d) and (*S*)-(1″*l*,2*u*)-6,6-Dimethyl-3-(1-phenylethyl)-2-(2-propenyl)-1,3,2-oxazaphosphorinane 2-Oxide ((*S*,*R*)-15d).** To a mixture of (*S*)-**14** (745 mg, 3.59 mmol) and triethylamine (1.0 mL, 7.18 mmol) in toluene (20 mL) was added allylphosphonic dichloride **2** (656 mg, 4.13 mmol) in toluene (10 mL) at −40 °C over 30 min. The cooling bath was removed, and the reaction mixture was stirred at room temperature overnight. The triethylamine hydrochloride salt formed was filtered off, and the filtrate was diluted with 30 mL of water. The mixture was extracted with EtOAc (3 × 50 mL) and then washed with brine (30 mL), dried over $MgSO_4$, and concentrated to afford a yellow oil. The crude oily product was purified by SiO_2 column chromatography (hexane/EtOAc/*i*-PrOH, 38/59/3) to give 324 mg (31%) of the nonpolar (*S*,*R*)-**15d** and 258 mg (24%) of the polar (*S*,*S*)-**15d** as colorless oils. (*S*,*S*)-**15d**: ^1H NMR (300 MHz) δ 7.38−7.25 (m, 5 H), 5.74 (m, 1 H), 5.13−5.03 (m, 2 H), 4.84 (m, 1 H), 3.15 (m, 1 H), 2.80−2.66 (m, 3 H), 1.90−1.62 (m, 2 H), 1.68 (d, J = 6.9, 3 H), 1.52 (s, 3 H), 1.35, (d, J = 1.0, 3 H); TLC R_f 0.25 (hexane/EtOAc/*i*-PrOH, 38/59/3).

(*S*,*R*)-15d: ^1H NMR (300 MHz) δ 7.60−7.23 (m, 5 H), 5.82 (m, 1 H), 5.22−5.15 (m, 2 H), 5.02 (m, 1 H), 2.98 (m, 1 H), 2.76−2.58 (m 3 H), 1.84−1.20 (m, 2 H), 1.54 (d, J = 7.0, 3 H), 1.32 (s, 3 H), 1.30 (s, 3 H); TLC R_f 0.48 (hexane/EtOAc/*i*-PrOH, 38/59/3).

General Procedure of the Michael Addition Reaction of Scalemic 2-Allyl-1,3,2-oxazaphosphorinanes 15. Method A: To a well-stirred solution of **15** in THF (0.1−0.2 M) was added *n*-BuLi (1.0−1.1 equiv) at −78 °C under N_2 atmosphere. After stirring for 15 min at −78 °C, the cold yellow solution was transferred via cannula over 3 min to a cold (−40 °C) suspension of the cycloalkenone (1.05 equiv) and CuI (0.2 equiv) in THF. The yellow color completely faded within 5 min. After the reaction mixture was stirred for 30 min, the reaction was quenched with aqueous NH_4Cl and the mixture poured into brine and extracted with EtOAc three times. The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated to give a colorless oil. The crude oil was purified by SiO_2 column chromatography.

Method B: Method A was followed without CuI, and the reaction was preformed at −78 °C.

(*S*)-(2*u*,6*l*,3″*x*)-(1′*E*)-2-[3′-(3″-Oxocyclopentyl)propenyl]-3-(1-methylethyl)-6-methyl-1,3,2-oxazaphosphorinane 2-Oxide (18a). Method B: From 149 mg (0.685 mmol) of *cis*-**15a**, 0.51 mL (0.754 mmol) of *n*-BuLi (1.47 M in hexane), and 60 μL (0.719 mmol) of cyclopentenone, followed by purification by SiO_2 column chromatography (EtOAc/*i*-PrOH, 9/1), was obtained 166 mg (81%) of **18a** as a colorless oil: bp 165−170 °C (0.15 Torr); ^1H NMR (300 MHz) δ 6.84−6.67 (m, 1 H), 5.66 (dd, J = 19.8, 17.0, 1 H), 4.63−4.53 (m, 1 H), 3.72−3.60 (m, 1 H), 3.17 (ddd, J = 16.7, 11.1, 5.6, 1 H), 3.07−2.95 (m, 1 H), 2.45−2.11 (m, 6 H), 1.96−1.53 (m, 5 H), 1.34 (d, J = 6.0, 3 H), 1.22 (d, J = 6.7, 3 H), 1.07 (d, J = 6.7, 3 H); ^{13}C NMR (75.5 MHz) δ 218.02, 149.18 (J_{CP} = 4.6), 122.33 (J_{CP} = 178.3), 72.12 (J_{CP} = 7.0), 45.46 (J_{CP} = 5.0), 44.03, 39.13 (J_{CP} = 21.6), 37.67, 36.59, 35.35, 32.84 (J_{CP} = 3.4), 28.47, 21.0 (J_{CP} = 8.4), 19.95, 19.84; ^{31}P NMR (121.6 MHz) δ 16.48; IR (CCl_4) 2970 m, 1744 s, 1223 s; MS (70 eV) 284 ($M^+ - CH_3$, 100); HRMS calcd for $C_{16}H_{28}NO_3P$ 299.1650, found 299.1638; TLC R_f 0.34 (EtOAc/*i*-PrOH, 9/1).

(*S*)-(2*u*,6*l*,3″*x*)-(1′*E*)-2-[3′-(3′-Oxocyclopentyl)-1′-propenyl]-3-(1,1-dimethylethyl)-6-methyl-1,3,2-oxazaphosphorinane 2-Oxide (18b). Method A: From 236 mg (1.02 mmol) of *cis*-**15b**, 0.64 mL (1.02 mmol, 1.59 M in pentane) of *t*-BuLi, 94 μL (1.12 mmol) of cyclopentenone, and 39 mg (0.20 mmol) of CuI followed by purification by SiO_2 column chromatography (hexane/EtOAc/*i*-PrOH, 34/59/7) was obtained 249 mg (78%) of **18b** as a colorless oil. An analytical sample was obtained by Kugelrohr distillation: bp 175 °C (0.05 Torr); $[\alpha]_D = -47.1°$ (*c* 1.07, CH_2Cl_2); ^1H NMR (300 MHz) δ 6.65 (ddt, J = 21.5, 16.5, 7.2, 1 H), 5.83 (dd, J = 20.6, 16.5, 1 H), 4.58 (m, 1 H), 3.15 (m, 2 H), 2.44−1.18 (m, 11 H), 1.33 (s, 12 H); ^{13}C NMR (75.5 MHz) δ 218.29, 146.72, 125.20 (J_{CP} = 175.9), 70.46 (J_{CP} = 7.0), 54.60, 44.24, 39.94, 39.28 (J_{CP} = 22.0), 37.84, 35.67, 34.44 (J_{CP} = 4.1), 29.06, 28.75, 22.11 (J_{CP} = 7.3); ^{31}P NMR (121.6 MHz) δ 16.68; IR (CCl_4) 2973 m, 1746 s; MS (70 eV) 299 (18), 298 ($M^+ - CH_3$, 99), 58 (100); TLC R_f 0.14 (hexane/EtOAc/*i*-PrOH, 34/59/7). Anal. Calcd for $C_{16}H_{28}NO_3P$ (313.37): C, 62.32; H, 9.01; N, 4.47; P, 9.88. Found: C, 61.43; H, 9.03; N, 4.51; P, 9.79.

(*S*)-(2*u*,6*l*,3″*x*)-(1′*E*)-2-[3′-(3-Oxoyclopentyl)-1′-propenyl]-3-(1,1-dimethylethyl)-6-methyl-1,3,2-oxazaphosphorinane 2-Oxide (18c). Method B: From 415 mg (1.52 mmol) of *cis*-**18c**, 1.15 mL (1.67 mmol) of *n*-BuLi (1.45 M in hexane), and 134 μL (1.60 mmol) of cyclopentenone followed by purification by SiO_2 column chromatography (hexane/EtOAc/*i*-PrOH, 35/62/3) was obtained 495 mg (92%) of **18c** as a colorless oil. An analytical sample was obtained by Kugelrohr distillation: bp 190 °C (0.1 Torr); ^1H NMR (300 MHz) δ 6.76−6.59 (m, 1 H), 5.84 (dd, J = 20.8, 16.6, 1 H), 4.69−4.60 (m, 1 H), 3.13−2.94 (m, 2 H), 2.43−2.07 (m, 8 H), 1.87−1.55 (m, 6 H), 1.43 (dq, J = 14.6, 7.3, 3 H), 1.33 (dd, J = 6.0, 0.8, 3 H), 0.83 (t, J = 7.3, 9 H); ^{13}C NMR (75.5 MHz) δ 218.50, 146.09 (J_{CP} = 3.8), 124.91 (J_{CP} = 176.2), 69.14 (J_{CP} = 6.8), 64.70 (J_{CP} = 1.9), 44.40, 39.42 (J_{CP} = 21.3), 38.34 (J_{CP} = 2.8), 37.95, 35.79, 34.88 (J_{CP} = 2.9), 28.81, 26.08 (J_{CP} = 2.0), 22.38 (J_{CP} = 8.4), 8.05; ^{31}P NMR (121.6 MHz) δ 16.48; IR (CCl_4) 2973 s, 1746 s, 1239 s; MS (70 eV) 327 ($M^+ + 1 - C_2H_5$, 21), 325 ($M^+ - C_2H_5$, 100); TLC R_f 0.32 (hexane/EtOAc, 2/1). Anal. Calcd for $C_{19}H_{34}NO_3P$ (355.46): C, 64.20; H, 9.64; N, 3.94; P, 8.71. Found: C, 64.02; H, 9.67; N, 3.86; P, 8.80.

(*S*)-(2*u*,6*l*,3″*x*)-(1′*E*)-2-[3′-(3″-Oxocyclohexyl)-1′-propenyl]-3-(1,1-dimethylethyl)-6-methyl-1,3,2-oxazaphosphorinane 2-Oxide (19b). Method A: From 253 mg (1.09 mmol) of *cis*-**15b**, 0.69 mL (1.09 mmol, 1.59 M in pentane) of *t*-BuLi, 111 μL (1.15 mmol) of cyclohexenone, and 42 mg (0.20 mmol) of CuI followed by purification by SiO_2 column chromatography (hexane/EtOAc/*i*-PrOH, 34/59/7) was obtained 243 mg (68%) of **19b** as a colorless oil. An analytical sample was obtained by Kugelrohr distillation: bp 182 °C (0.1 Torr); ^1H NMR (300 MHz) δ 6.62 (ddt, J = 21.2, 16.7, 7.4, 1 H), 5.79 (dd, J = 21.0, 16.7, 1 H), 4.57 (m, 1 H), 3.14 (m, 2 H), 2.43−1.20 (m, 13 H), 1.32 (s, 9 H), 1.31 (d, J = 3.7, 3 H); ^{13}C NMR (75.5 MHz) δ 210.27, 146.06 (J_{CP} = 3.4), 125.47 (J_{CP} = 175.0), 70.29 (J_{CP} = 7.1), 54.38, 47.22, 40.71, 40.21 (J_{CP} = 21.6), 39.76, 37.74, 34.26, 30.23, 28.89, 24.40, 21.94 (J_{CP} = 7.2); ^{31}P NMR (121.6 MHz) δ 16.07; IR (CCl$_4$) 2976 m, 1747 s, 1228 s; MS (70 eV) 327 (M^+, 0.8), 312 (100); TLC R_f 0.21 (hexane/EtOAc/*i*-PrOH, 34/59/7). Anal. Calcd for $C_{17}H_{30}NO_3P$ (327.40): C, 62.37; H, 9.24; N, 4.28; P, 9.46. Found: C, 62.35; H, 9.32; N, 4.27; P, 9.42.

***(S)*-(2*u*,6*l*,3″*x*)-(1′*E*)-2-[3′-(3″-Oxocyloheptyl)-1′-propenyl]-3-(1,1-dimethylethyl)-6-methyl-1,3,2-oxazaphosphorinane 2-Oxide (20b). Method A:** From 235 mg (1.02 mmol) of *cis*-**15b**, 0.64 mL (1.02 mmol, 1.59 M in pentane) of *t*-BuLi, 119 μL (1.07 mmol) of cycloheptenone, and 39 mg (0.20 mmol) of CuI followed by purification by SiO$_2$ column chromatography (hexane/EtOAc/*i*-PrOH, 34/59/7) was obtained 142 mg (41%) of **20b** as a colorless oil. An analytical sample was obtained by Kugelrohr distillation: bp 191 °C (0.1 Torr); ^{1}H NMR (300 MHz) δ 6.61 (ddt, *J* = 21.3, 16.6, 7.2, 1 H), 5.77 (dd, *J* = 21.0, 16.6, 1 H), 4.56 (m, 1 H), 3.14 (m, 2 H), 2.50−1.20 (m, 15 H), 1.32 (s, 9 H), 1.31 (d, *J* = 5.1, 3 H); ^{13}C NMR (75.5 MHz) δ 218.10, 146.60, 125.11 (J_{CP} = 175.6), 70.37 (J_{CP} = 7.0), 54.43, 44.11, 39.84, 39.15 (J_{CP} = 21.3), 37.74, 35.55, 34.33 (J_{CP} = 4.9), 28.92, 28.62, 22.04, 22.94; ^{31}P NMR (121.6 MHz) δ 16.19; IR (CCl$_4$) 2976 m, 1703 s, 1250 s; MS (70 eV) 341 (M^+, 0.4), 326 (100); TLC R_f 0.25 (hexane/EtOAc/*i*-PrOH, 34/59/7). Anal. Calcd for $C_{18}H_{32}NO_3P$ (341.43): C, 63.32; H, 9.45; N, 4.10; P, 9.07. Found: C, 63.24; H, 9.49; N, 4.15; P, 9.17.

***(S)*-(2*l*,6*l*,3″*x*)-(1′*E*)-2-[3′-(3″-Oxocyclopentyl)-1′-propenyl]-3-(1-methylethyl)-6-methyl-1,3,2-oxazaphosphorinane 2-Oxide (21a). Method B:** From 280 mg (1.29 mmol) of *trans*-**15a**, 0.97 mL (1.42 mmol) of *n*-BuLi (1.47 M in hexane), and 113 μL (1.35 mmol) of cyclopentenone followed by purification by SiO$_2$ column chromatography (EtOAc/*i*-PrOH, 9/1) was obtained 330 mg (85%) of **21a** as a colorless oil. ^{31}P NMR analysis of the product showed ca. 55/45 mixture of diastereomers: bp 170 °C (0.15 Torr); ^{1}H NMR (300 MHz) δ 6.68−6.53 (m, 1 H), 5.82 (dd, *J* = 22.2, 16.9, 1 H), 4.34−4.25 (m, 1 H), 3.95−3.83 (m, 1 H), 3.17 (ddt, *J* = 18.4, 12.6, 4.1, 1 H), 3.03−2.93 (m, 1 H), 2.42−2.14 (m, 6 H), 1.90−1.57 (m, 5 H), 1.37 (dd, *J* = 6.1, 1.2, 3 H), 1.18 (d, *J* = 6.6, 3 H), 1.07 (d, *J* = 6.8, 3 H); ^{13}C NMR (75.5 MHz) δ 217.90, 146.38 (J_{CP} = 2.8), 120.54 (J_{CP} = 162.3), 74.86 (J_{CP} = 7.4), 45.04 (J_{CP} = 5.0), 43.91 (J_{CP} = 1.9), 39.24 (J_{CP} = 20.4), 39.21 (J_{CP} = 20.8), 37.76, 35.63, 34.53 (J_{CP} = 5.1), 29.03, 28.64 (J_{CP} = 1.5), 22.27 (J_{CP} = 7.0); ^{31}P NMR (121.6 MHz) δ 14.65 (major) 14.61 (minor); IR (CCl$_4$) 2971 s, 1746 s, 1250 s; MS (70 eV) 299 (M^+, 1), 284 (100); HRMS calcd for $C_{15}H_{26}NO_3$ P 299.1650, found 299.1641; TLC R_f 0.24 (EtOAc/*i*-PrOH, 9/1).

***(S)*-(2*l*,6*l*,3″*x*)-(1′*E*)-2-[3′-(3″-Oxocyclopentyl)-1′-propenyl]-3-(1,1-dimethylethyl)-6-methyl-1,3,2-oxazaphosphorinane 2-Oxide (21b). Method A:** From 226 mg (0.997 mmol) of *trans*-**15b**, 0.56 mL (1.03 mmol, 1.59 M in pentane) of *t*-BuLi, 92 mL (1.10 mmol) of cyclopentenone, and 37 mg (0.20 mmol) of CuI followed by purification by SiO$_2$ column chromatography (hexane/EtOAc/*i*-PrOH, 35/62/3 to 33/55/12) was obtained 218 mg (71%) of **21b** as a colorless oil. An analytical sample was obtained by Kugelrohr distillation: bp 182 °C (0.05 Torr); ^{1}H NMR (300 MHz) δ 6.66−6.51 (m, 1 H), 5.89 (dd, *J* = 2.5, 16.8, 1 H), 4.30−4.22 (m, 1 H), 3.29 (ddt, *J* = 17.3, 13.0, 4.3, 1 H), 3.01 (ddd, *J* = 13.0, 7.9, 4.4, 1 H), 2.41−2.13 (m, 7 H), 1.89−1.79 (m, 1 H), 1.57−1.55 (m, 1 H), 1.34 (dd, *J* = 6.7, 5.7, 3 H), 1.36−1.23 (m, 2 H), 1.31 (s, 9 H); ^{13}C NMR (75.5 MHz) δ 218.09, 145.93, 123.02 (J_{CP} = 162.9), 74.28 (J_{CP} = 8.6), 55.00 (J_{CP} = 3.1), 44.11, 41.21 (J_{CP} = 1.8), 39.34 (J_{CP} = 20.8), 37.76, 35.63, 34.53 (J_{CP} = 5.1), 29.03, 28.64 (J_{CP} = 1.5), 22.27 (J_{CP} = 7.0); ^{31}P NMR (121.6 MHz) δ 13.19; IR (CCl$_4$) 2975 s, 1744 s, 1252 s; MS (70 eV) 299 (17), 298 (M^+ − CH$_3$, 100); TLC R_f 0.35 (hexane/EtOAc/*i*-PrOH, 34/59/7). Anal. Calcd for $C_{16}H_{28}NO_3P$ (313.37): C, 61.32; H, 9.01; N, 4.47; P, 9.88. Found: C, 61.28; H, 8.95; N, 4.46; P, 9.93.

***(S)*-(1‴*l*,2*l*,3″*x*)-(1′*E*)-2-[3′-(3″-Oxocyclopentyl)-1′-propenyl]-6,6-dimethyl-3-(1-phenylethyl)-1,3,2-oxazaphosphorinane 2-Oxide ((*S*,*S*)-34). Method A:** From 128 mg (0.436 mmol) of (*S*,*S*)-**15d**, 0.28 mL (0.436 mmol, 1.57 M in pentane) of *t*-BuLi, 38 μL (0.458 mmol) of cyclopentenone, and 17 mg (0.087 mmol) of CuI followed by purification by column chromatography (hexane/EtOAc/*i*-PrOH, 35/62/3) was afforded 125 mg (76%) of (*S*,*S*)-**34** as a colorless oil: ^{1}H NMR (300 MHz) δ 7.38−7.24 (m, 5 H), 6.76 (m, 1 H), 6.74 (dd, *J* = 21.5, 16.5, 1 H), 4.72 (dq, *J* = 9.5, 7.0, 1 H), 3.22 (m, 1 H), 2.73 (m, 1 H), 2.41−1.40 (m, 11 H); 1.66 (d, *J* = 7.0, 3 H), 1.55 (s, 3 H), 1.37 (d, *J* = 1.0, 3 H); ^{13}C NMR (75.5 MHz) δ 218.22, 148.91 (J_{CP} = 3.7), 140.93 (J_{CP} = 3.7), 127.98, 126.78, 123.43 (J_{CP} = 190.9), 80.41 (J_{CP} = 7.8), 52.49 (J_{CP} = 4.2), 44.18, 39.24 (J_{CP} = 22.0), 37.76, 36.73 (J_{CP} = 4.7), 36.18, 35.47, 29.90 (J_{CP} = 5.2), 28.58, 27.04, 16.88; TLC R_f 0.10 (hexane/EtOAc/*i*-PrOH, 35/62/3).

***(S)*-(1‴*l*,2*u*,3″*x*)-(1′*E*)-2-[3′-(3″-Oxocyclopentyl)-1′-propenyl]-6,6-dimethyl-3-(1-phenylethyl)-1,3,2-oxazaphosphorinane 2-Oxide ((*S*,*R*)-34). Method A:** From 200 mg (0.682 mmol) of (*S*,*R*)-**15d**, 0.43 mL (0.682 mmol, 1.57 M in pentane) of *t*-BuLi, 60 μL (0.716 mmol) of cyclopentenone, and 26 mg (0.136 mmol) of CuI followed by purification by column chromatography (hexane/EtOAc/*i*-PrOH, 35/62/3) was obtained 182 mg (71%) of (*S*,*R*)-**34** as a colorless oil: ^{1}H NMR (300 MHz) δ 7.56−7.23 (m, 5 H), 6.71 (m, 1 H), 5.77 (dd, *J* = 21.9, 16.5, 1 H), 4.86 (dq, *J* = 9.7, 7.2, 1 H), 3.03 (m, 1 H), 2.67 (m, 1 H), 2.47−1.40 (m, 9 H), 1.76 (t, *J* = 6.3, 2 H), 1.48 (d, *J* = 7.0, 3 H), 1.38 (s, 3 H), 1.37 (s, 3 H); ^{13}C NMR (75.5 MHz) δ 218.26, 147.03 (J_{CP} = 4.9), 140.29, 127.76, 127.64, 127.50, 126.76, 124.40 (J_{CP} = 175.3), 80.67 (J_{CP} = 9.4), 51.46 (J_{CP} = 4.1), 44.18 (J_{CP} = 4.1), 39.28 (J_{CP} = 22.0), 37.84, 36.64, 36.56, 35.61, 28.97 (J_{CP} = 3.9), 28.73, 28.29, 16.03; TLC R_f 0.21 (hexane/EtOAc/*i*-PrOH, 35/62/3).

General Procedure for the Cleavage of the Michael Adducts Followed by Oxidation to the Corresponding Methyl Esters. The Michael adduct was dissolved in dry CH$_2$Cl$_2$ (10−15 mL) and placed in a 25-mL three-necked round bottomed flask equipped with a gas diffusion inlet tube, a thermometer, and a gas outlet tube. Ozone was bubbled into the reaction vessel in the dry ice−isopropyl alcohol cool bath (−75 °C) for 3−5 min until a sky blue color persisted. Excess ozone was expelled off by bubbling O$_2$ and N$_2$, consecutively. Immediate addition of triphenylphosphine followed by further stirring for 5−6 h gave the keto aldehyde (**25−27**) which was purified by SiO$_2$ column chromatography (Et$_2$O/pentane, 2/1). Keto aldehydes were used in next reaction without further purification.

To a solution of keto aldehyde (**25−27**) (~0.1 mmol) in 2 mL of MeOH/H$_2$O (9/1) were added NaHCO$_3$ (20 equiv) and 3−5 equiv of bromine in MeOH/H$_2$O (9/1) over 10 min in sequence. The heterogeneous mixture was stirred at room temperature for 9−12 h. After the reaction was complete, excess bromine was destroyed by addition of solid sodium thiosulfate, and 5 mL of water was added to the reaction mixture. The reaction mixture was extracted with Et$_2$O (3 × 10 mL), and the combined organic extracts were dried (MgSO$_4$), filtered, and concentrated. Purification of the residue by column chromatography gave keto esters **28−30** as a colorless liquid which was further purified by distillation under reduced pressure.

Methyl (3-Oxocyclopentyl)acetate (28). From 249 mg (0.795 mmol) of **18a**, ozone, and 208 mg (0.793 mmol) of Ph$_3$P followed by purification by SiO$_2$ column chromatography (Et$_2$O/pentane, 2/1) was obtained the crude keto aldehyde which was oxidized using 1.4 g (15.9 mmol) of NaHCO$_3$ and 1.6 mL (3.2 mmol) of 2 M Br$_2$ in MeOH/H$_2$O (9/1). Purification by column chromatography (ether/pentane, 2/1) followed by Kugelrohr distillation afforded 85 mg (69%) of **28** as a colorless oil. Similarly, other degradations were accomplished, 59% (from **18b**) 71% (from **18c**) 70% (from **21b**), 72% (from (*S*,*S*)-**34**), and 69% (from (*S*,*R*)-**34**): bp 131 °C (10 Torr); ^{1}H NMR (300 MHz) δ 3.63 (s, 3 H), 2.60−2.00 (m, 7 H), 1.87 (dd, *J* = 15.0, 8.0, 1H), 1.53 (m, 1 H); $[\alpha]_D$ = −107.8° (*c* 1.39, CHCl$_3$); TLC R_f 0.5 (Et$_2$O/pentane, 2,1).

Methyl (3-Oxocyclohexyl)acetate (**29**). From 226 mg (0.69 mmol) of **19b**, ozone, and 200 mg (0.763 mmol) of Ph$_3$P followed by purification by SiO$_2$ column chromatography (Et$_2$O/pentane, 2/1) was obtained a crude keto aldehyde which was oxidized using 1.16 g (13.8 mmol) of NaHCO$_3$ and 1.4 mL (2.76 mmol) of 2 M Br$_2$ in MeOH/H$_2$O, 9/1. Purification by SiO$_2$ column chromatography (Et$_2$O/pentane, 2/1) followed by Kugelrohr distillation afforded 77 mg (68%) of **29** as a colorless oil: bp 148 °C (10 Torr); ^{1}H NMR (300 MHz) δ 3.66 (s, 3 H), 2.50−1.20 (m, 11 H); $[\alpha]_D$ = −8.7° (*c* 0.96, CHCl$_3$); TLC R_f 0.52 (Et$_2$O/pentane, 2/1).

Methyl (3-Oxocycloheptyl)acetate (30). From 105 mg (0.308 mmol) of **20b**, ozone, and 80 mg (0.305 mmol) of Ph_3P followed by purification by column chromatography (Et_2O/pentane, 2/1) was obtained a crude keto aldehyde which was oxidized using 0.6 g (6.1 mmol) of $NaHCO_3$ and 0.77 mL (1.53 mmol) of 2 M Br_2 in $MeOH/H_2O$, 9/1. Purification by SiO_2 column chromatography (Et_2O/pentane, 2/1) followed by Kugelrohr distillation afforded 41 mg (72%) of **30** as a colorless oil: bp 148 °C (8 Torr); ^1H NMR (300 MHz) δ 3.64 (s, 3 H), 2.60–2.20 (m, 7 H), 1.86–1.79 (m, 3 H), 1.57–1.21 (m, 3 H); $[\alpha]_D = -54.8°$ (*c* 1.16, $CHCl_3$); TLC R_f 0.55 (Et_2O/pentane, 2/1).

General Procedure for the Protection of Keto Esters 28–30 with (*R,R*)-2,3-Butanediol. To a well-stirred suspension of $MgSO_4$ (10.0 equiv) in 5 mL of dry benzene were added keto ester (0.2 mmol) and (*R,R*)-2,3-butanediol (1.2 equiv). The catalytic amount of $TsOH \cdot H_2O$ was added, and the reaction mixture was heated to reflux for 10–12 h. After the reaction was complete, 30 mL of Et_2O was added, and the solids were filtered off. The filtrate was concentrated, and the residue was directly purified by SiO_2 column chromatography (hexane/EtOAc, 5/1) to afford the protected keto esters **31–33** as a colorless oil, which was further purified by Kugelrohr distillation under reduced pressure.

Methyl (*R*)-(2′*l*,3′*l*,7′*u*)-(2′,3′-Dimethyl-1′,4′-dioxaspiro[4.4]cyclonon-7′-yl)acetate (31). From 85 mg (0.544 mmol) of **28**, 59 mg (0.65 mmol) of (*R,R*)-2,3-butanediol, $TsOH \cdot H_2O$, and 2.0 g of $MgSO_4$ followed by purification by SiO_2 column chromatography (hexane/EtOAc, 5/1) was obtained 100 mg (81%) of **31** as a colorless oil. The ee was determined by ^{13}C NMR analysis (84% ee from **18a** 89% ee from **18b**, 89% ee from **18c**, 10% ee from **21b**): bp 105 °C (0.8 Torr); ^1H NMR (300 MHz) δ 3.59 (s, 3 H), 3.56–3.47 (m, 2 H), 2.38–2.28 (m, 3 H), 2.03 (dd, J = 13.4, 7.5, 1 H), 1.90–1.71 (m, 3 H), 1.45 (dd, J = 13.4, 8.5, 1 H), 1.29 (m, 1 H), 1.17 (d, J = 5.6, 6 H); ^{13}C NMR (75.5 MHz) δ 173.80, 116.55, 78.23, 78.10, 51.25, 43.88, 39.96, 37.25, 33.53, 29.68, 16.97; IR (CCl_4) 1740 s; MS (70 eV) 228 (M^+, 5), 127 (100); TLC R_f 0.40 (hexane/EtOAc, 5/1). Anal. Calcd for $C_{12}H_{20}O_4$ (228.29): C, 63.14; H, 8.83. Found: C, 63.17; H, 8.85.

Methyl (*R*)-(2′*l*,4′*l*,7′*u*)-(2′,3′-Dimethyl-1′,4′-dioxaspiro[4.5]cyclodec-7′-yl)acetate (32). From 77 mg (0.452 mmol) of **29**, 49 mg (0.542 mmol) of (*R,R*)-2,3-butanediol, $TsOH \cdot H_2O$, and 2.0 g of $MgSO_4$ followed by purification by SiO_2 column chromatography (hexane/EtOAc, 5/1) was obtained 78 mg (81%) of **32** as a colorless oil. The ee was determined by ^{13}C NMR analysis (87% ee from **19b**): bp 110 °C (0.5 Torr); ^1H NMR (300 MHz) δ 3.60 (s, 3 H), 3.54 (m, 2 H), 2.18–2.03 (m, 4 H), 1.77–1.22 (m, 6 H), 1.18 (d, J = 5.5, 3 H), 1.27 (d, J = 4.3, 3 H), 0.89–0.84 (m, 1 H); ^{13}C NMR (75.5 MHz) δ 172.91, 107.80, 78.04, 77.68, 51.26, 43.21, 41.17, 35.63, 32.11, 31.30, 22.76, 16.90; IR (CCl_4) 1740 s; MS (70 eV) 242 (M^+, 10), 127 (100); TLC R_f 0.43 (hexane/EtOAc, 5/1). Anal. Calcd for $C_{13}H_{22}O_4$ (242.31): C, 64.44; H, 9.15. Found: C, 64.46; H, 9.20.

Methyl (*R*)-(2′*l*,4′*l*,7′*u*)-(2′,4′-Dimethyl-1′,5′-dioxaspiro[4.6]cyclododec-7′-yl)acetate (33). From 41 mg (0.223 mmol) of **30**, 24 mg (0.268 mmol) of (*R,R*)-2,3-butanediol, $TsOH \cdot H_2O$, and 2.0 g of $MgSO_4$ followed by purification by SiO_2 column chromatography (pentane/Et_2O, 2/1) was obtained 40 mg (71%) of **33** as a colorless oil. The ee was determined by ^{13}C NMR analysis (89% ee from **20b**): bp 120 °C (0.8 Torr); ^1H NMR (300 MHz) δ 3.62 (s, 3 H), 3.54 (m, 2 H), 2.21 (s, 2 H), 1.85–1.24 (m, 11 H), 1.19 (d, J = 5.0, 3 H), 1.18 (d, J = 5.0, 3 H); ^{13}C NMR (75.5 MHz) δ 173.19, 110.36, 78.00, 77.73, 51.29, 45.41, 42.26, 40.29, 34.59, 30.45, 26.79, 22.31, 16.90, 16.77; IR (CCl_4) 1740 s; MS (70 eV) 256 (M^+, 7), 127 (100); TLC R_f 0.41 (pentane/Et_2O, 2/1). Anal. Calcd for $C_{14}H_{24}O_4$ (256.34): C, 65.60; H, 9.44. Found: C, 65.60; H, 9.47.

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Supporting Information Available: General experimental procedures along with complete ^1H and ^{13}C NMR assignments and IR and MS data for all characterized compounds (11 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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