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Enantioselective alkene radical cations reactions

David Crich,* Michio Shirai, Franck Brebion and Sochanchingwung Rumthao

Department of Chemistry, University of Illinois at Chicago, 845 West Taylor Street, Chicago, IL 60607-7061, USA

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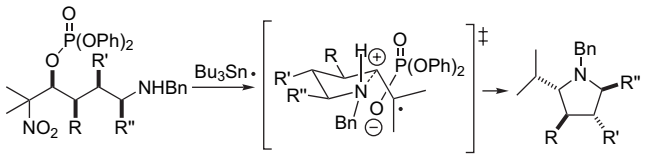
Abstract—The reaction of enantiomerically enriched 2-methyl-2-nitro-3-(diphenylphosphatoxy)alkyl radicals with tributyltin hydride and AIBN in benzene at reflux results in the formation of alkene radical cation/anion pairs, which are trapped intramolecularly by amine nucleophiles, leading to pyrrolidine and piperidine systems with memory of stereochemistry. The scope and limitations of the system are explored with respect to nucleophile, leaving group, and substituents within the substrate backbone.

1. Introduction

Alkene radical cations generated within the confines of contact ion pairs by the expulsion of leaving groups from the β-position of radicals participate in stereoselective cyclization reactions with suitably placed amines. This concept was demonstrated (Scheme 1) with an extensive series of substrates carrying methyl groups on the carbon backbone, with the results best accommodated by a chair-like transition state for cyclization with the maximum number of substituents pseudo-equatorial.[1]



Scheme 1. Preferred model for diastereoselective alkene radical cation cyclizations.[1]

In this paper we report in full on a parallel series of experiments in which all stereogenic centers are destroyed on formation of the alkene radical cation, leaving the operation of a memory effect as the only explanation for the observed enantioselectivity.[2]

2. Results and discussion

Working in collaboration with Newcomb we have established, using time resolved laser flash photolytic techniques, that alkyl radicals substituted with a leaving group in the β-position expel the leaving group to afford contact alkene radical cation/anion pairs even in nonpolar solvents.[3] In polar solvents supporting charge separation these contact ion pairs undergo equilibration with the medium leading to solvent separated ion pairs and even free radical cations and the corresponding anions. This type of behavior is seen under anaerobic conditions with DNA C′4 radicals when the C′3-phosphate group is expelled leading to the C3′C4′ alkene radical cation, such as has been so productively employed as a 'hole' source in the study of charge transfer through DNA by Giese.[4] In nonpolar solvents collapse of the contact alkene radical cation/anion pair to either the original radical or a rearranged radical is extremely rapid, typically out competing equilibration of the components of the contact ion pair. This extremely rapid recombination is now seen as the basis for a number of regio-[5] and stereoselective[5a,6] rearrangements that were originally interpreted as open-shell concerted processes (Schemes 2 and 3).[7] Computational work in this area, while originally supportive of the concerted mechanisms, has evolved and now points to the fragmentation/recombination mechanisms for these rearrangements.[8]

In parallel with the mechanistic studies we have developed a series of preparative methods in which nucleophilic attack, inter- or intramolecular, on the contact radical ion pair takes place in competition with collapse to a rearranged radical in nonpolar solvents. When this nucleophilic trapping is followed up by a radical cyclization the overall tandem polar/radical crossover sequence affords diverse bicyclic systems depending on the substitution pattern (Scheme 4).[9]

The combination of the stereoselectivity of the rearrangement reactions (Schemes 2 and 3), which implies rapid collapse of a highly ordered contact radical ion pair, coupled

* Corresponding author. Tel.: +1 312 996 5189; fax: +1 312 996 0431; e-mail: dcrich@uic.edu

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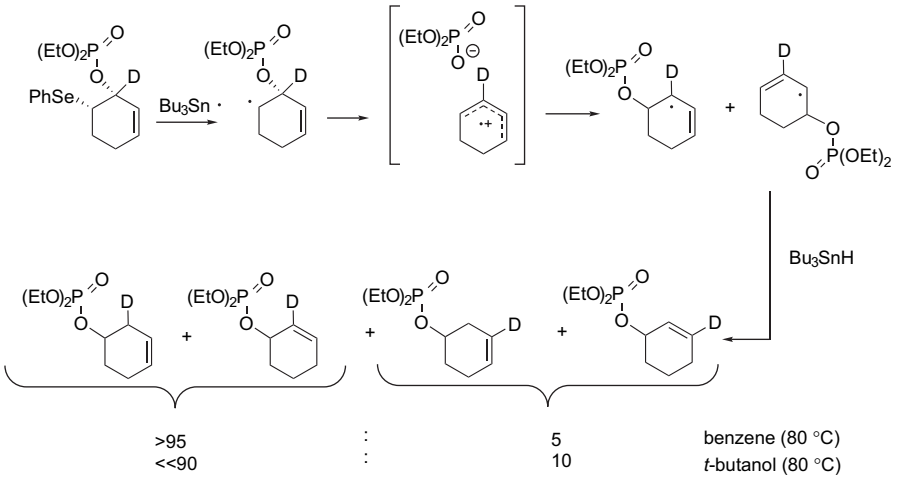
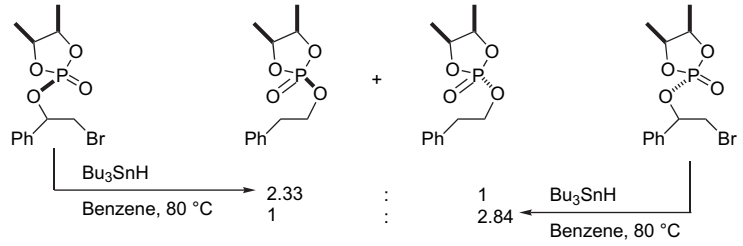
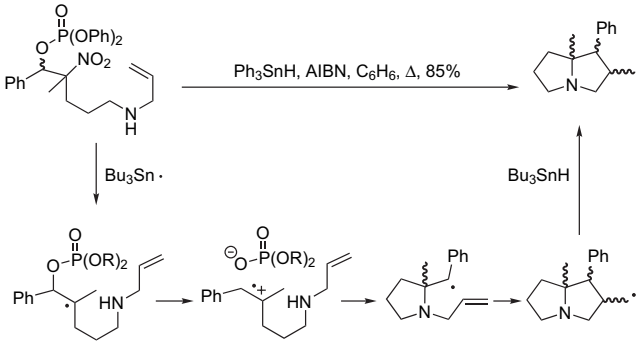


Scheme 2. Changing regioselectivity of a β-phosphatoxyalkyl radical rearrangement as a function of solvent.[5,6]



Scheme 3. Stereoselective rearrangement with predominant retention of configuration at phosphorus.[5]

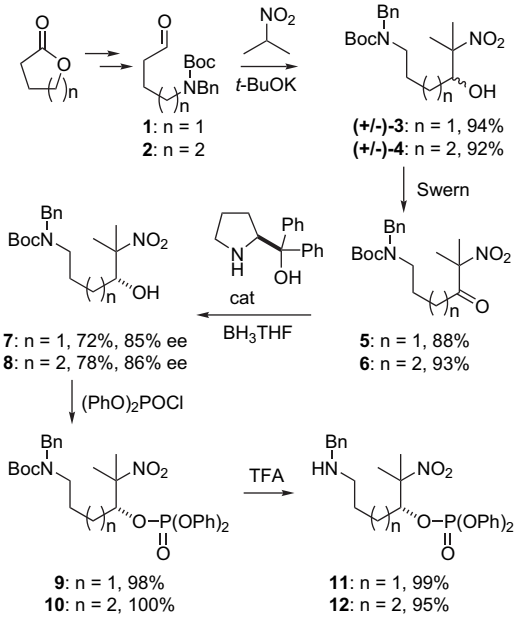
with the polar/radical crossover reactions (Scheme 4), and the implicit faster rates of nucleophilic trapping than ion pair collapse, lead directly to the hypothesis of stereoselective nucleophilic trapping reactions in which the order of the contact radical ion pair is reflected in the stereochemistry of the product.



Scheme 4. Example of a polar/radical crossover sequence.[9c,d]

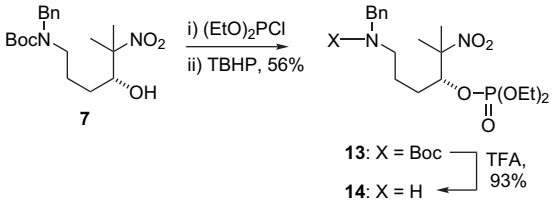
As discussed above, the hypothesis of memory effects in alkene radical cation reactions was first put to the test at the level of diastereoselectivity leading to the model of Scheme 1. In this system the amine attacks the face of the alkene radical cation opposite to that shielded by the just departed leaving group through a chair-like transition state with a maximum number of substituents pseudo-equatorial. The second generation system described here is enantioselective and requires the synthesis of a series of enantiomerically enriched β-(phosphatoxy)nitroalkanes, the precursors of choice in these tin hydride mediated polar radical crossover sequences, which we accessed by Corey oxazaborolidine-catalyzed reduction of α-nitroketones.[10]

The synthesis of a first pair of substrates, **11** and **12**, was accomplished as set out in Scheme 5.



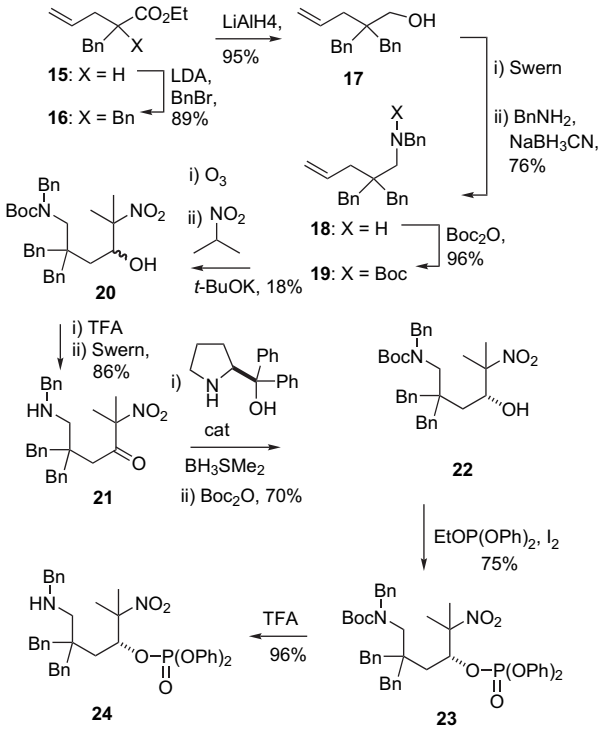
Scheme 5. Synthesis of substrates **11** and **12**.

In order to compare the effect of the leaving group the diethylphosphate analog **14** of one of these substrates was also prepared (Scheme 6).



Scheme 6. Synthesis of a diethylphosphate **14**.

With a view to determining the influence of the '*gem*-disubstituent' effect[11] on the diastereoselectivity substrate **24**, bearing a quaternary carbon center, was synthesized by the route outlined in Scheme 7.

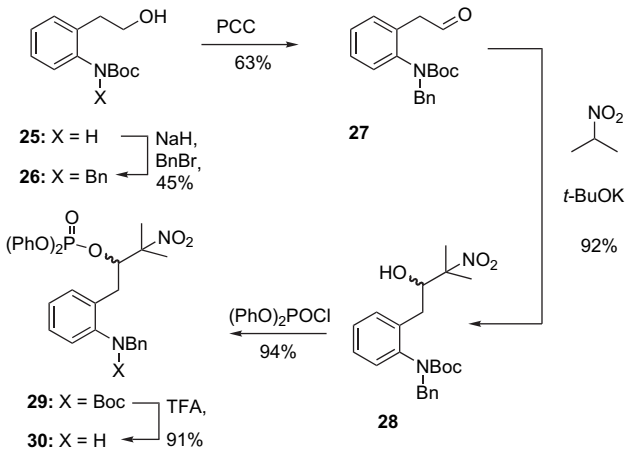


Scheme 7. Synthesis of substrate **24**.

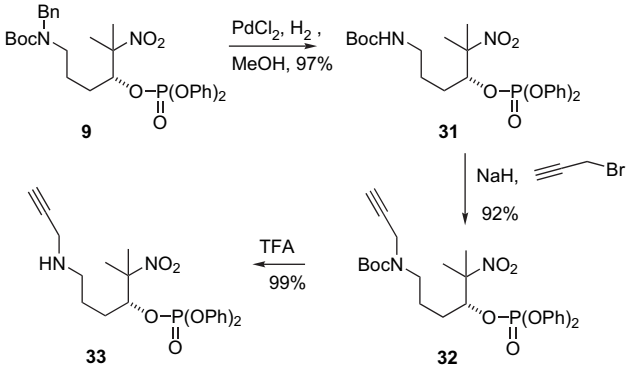
Yet another substrate, conformationally biased **30**, was obtained from the aniline derivative **25** (Scheme 8).[12] Substrate **30** was prepared only in racemic form, as a control experiment indicated that it did not undergo cyclization on treatment with tributyltin hydride under the usual conditions, as discussed below.

A substrate for a tandem polar/radical process in which the nucleophilic cyclization is followed by a radical cyclization was prepared from **9** by a process in which a benzyl group was exchanged for a propargyl moiety (Scheme 9).

Two substrates incorporating alcohol rather than amine nucleophiles were accessed as described in Schemes 10 and 11. Whereas the synthesis of the simple substrate **41** was straightforward (Scheme 10), that of the *gem*-dialkyl



Scheme 8. Preparation of an aniline-base substrate **30**.

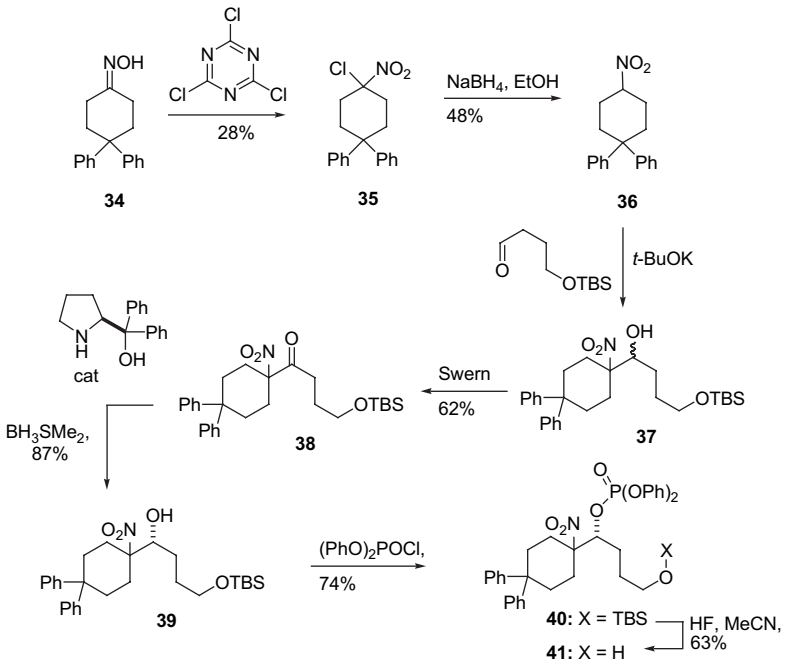


Scheme 9. Synthesis of a propargylic substrate.

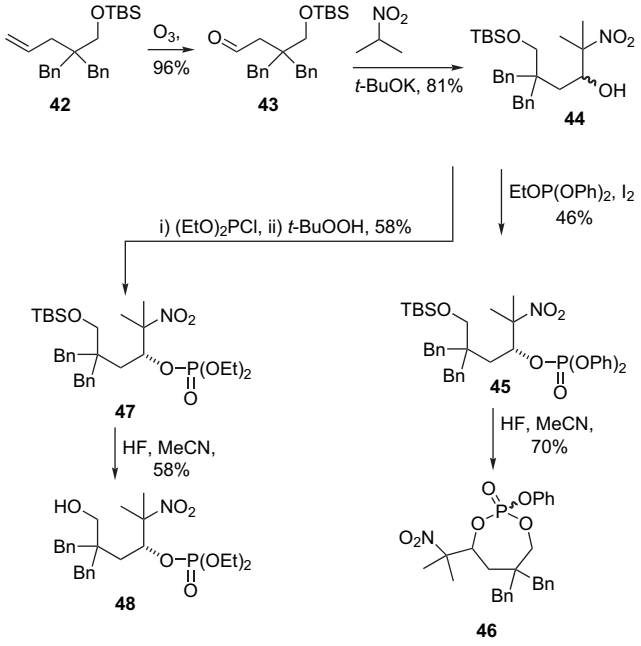
substituted variant proved more problematic owing to cyclization of the newly revealed alcohol onto the phosphate in the course of the final desilylation, with isolation of the 1,3,2-dioxaphosphepane **46** (Scheme 11). This problem, which could only be overcome by switching to the less electrophilic diethylphosphate, also reared its head in the attempted polar/radical cyclization of racemic **48**, as discussed below, and consequently no attempt was made to obtain this compound in enantiomerically enriched form.

A common feature of the above syntheses is the borane reduction of α-nitroketones catalyzed by the Corey oxazaborolidine catalyst. For ease of comparison the various reductions are presented in Table 1. The absolute stereochemistry of the nitroalcohols obtained from these reductions is assigned according to the standard model of Corey for the oxazaborolidine reduction of disymmetrically substituted ketones,[13] with the 1-methyl-1-nitroethyl group playing the role of the most bulky substituent. The applicability of this model to the α-nitroketones was rigorously established in our earlier model studies.[10] It is noteworthy that moderate to good enantioselectivities were obtained in all instances, with only a minor reduction due to the presence of the quaternary center in **21**.

The polar/radical crossover reactions were conducted with tributylstannane and AIBN in benzene at 80 °C leading to the results presented in Table 2. The enantioselectivities were determined by either chiral GC or HPLC as appropriate.

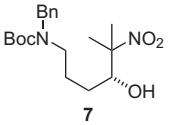
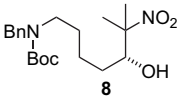
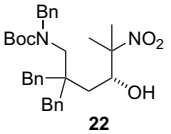
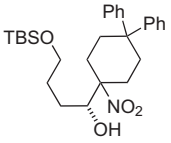


Scheme 10. Synthesis of substrate **41**.



Scheme 11. Preparation of substrate **48**.

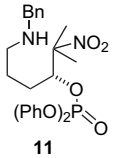
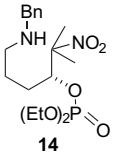
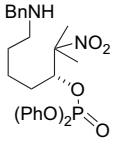
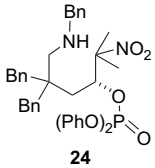
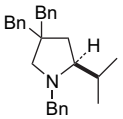
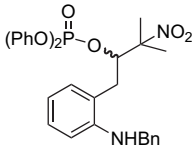
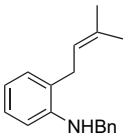
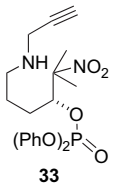
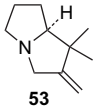
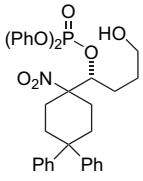
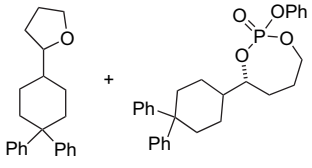
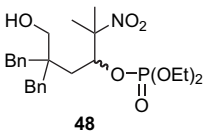
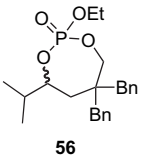
Table 1. Enantiomerically enriched nitro alcohols obtained by CBS reduction of α-nitroketones

Nitro alcohol	% Yield	% ee
 **7**	72	85
 **8**	78	86
 **22**	70	79
 **39**	87	96

The absolute configuration of pyrrolidine **49** was established by hydrogenolytic debenzylation and subsequent tosylation to give the sulfonamide **57**, whose specific rotation was compared to the literature value (Scheme 12).[14,15] As all successful cyclizations in Table 2, with the exception of alcohol **41**, gave comparable enantioselectivities it was not considered necessary to rigorously establish the configuration of all products, which consequently were assigned by analogy with **49**.

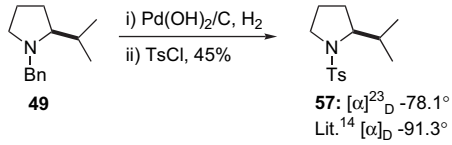
Comparison of entries 1–4 and 6 in Table 2 indicates that in the case of a secondary amine as nucleophile neither ring size (five or six), leaving group (diphenyl or diethylphosphate), nor the presence of a normally rate enhancing quaternary center has major significance on the enantioselectivity of these cyclizations. We interpret this result as arising from an extremely rapid trapping of the contact radical cation/anion pair once it is formed in what is probably the rate limiting radical ionic fragmentation step. This observation is consistent with the earlier study based on diastereoselectivity (Scheme 1) and the general rational presented above. This is entirely reasonable given the intramolecular nature of the attack on a simple trialkyl substituted alkene radical

Table 2. Enantioselective alkene radical cation cyclizations

Entry	Substrate	Substrate % ee	Product	% Yield	% ee[a]
1	 **11**	85	 **49**	43	61 (71)
2	 **14**	85	 **49**	45	62
3	 **12**	86	 **50**	41	60 (70)
4	 **24**	79	 **51**	44	60 (76)
5	 **30**	(+/−)[b]	 **52**	50	—
6	 **33**	85	 **53**	64	60 (71)
7	 **41**	94	 **54** **55**	**54**: 25 **55**: 52	0
8	 **48**	(+/−)[b]	 **56**	67	—

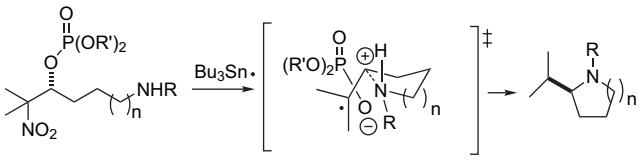
[a] Actual ee (ee predicated on enantiomerically pure substrate).
[b] Reactions conducted with racemic material.

cation in a nonpolar solvent, in view of the 2.5×10^9 M^{-1} s^{-1} rate constant determined for the intermolecular rate constant for the attack of butylamine on the stabilized *p*-methoxystyrene radical cation in the polar solvent acetonitrile at 25 °C.[16] Taking into account the absolute configurations of the substrates and products, we are led to propose a model for these cyclizations (Scheme 13) that is directly comparable to the one advanced earlier for the diastereoselective cyclizations. Thus, the initial radical undergoes rate determining fragmentation to give an ordered contact alkyl radical



Scheme 12. Establishment of absolute configuration.

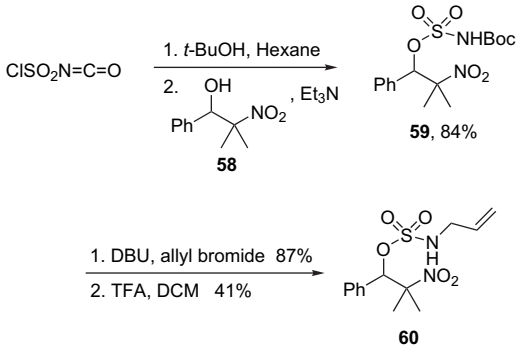
cation/anion pair that suffers extremely rapid collapse to the cyclized radical with attack of the nucleophile on the opposite face of the alkene radical cation to the one shielded by the counter-ion (Scheme 13). While this model bears some resemblance to the widespread Beckwith/Houk model for radical cyclization,[17] it differs fundamentally in one key aspect. The Beckwith/Houk model requires full conformation equilibration before cyclization through the most-favored chair-like transition state, while the model of Schemes 1 and 13 implies very rapid cyclization before solvation of the contact radical ion pair and conformational equilibration.[18]



Scheme 13. Preferred model for enantioselective alkene radical cation cyclizations.

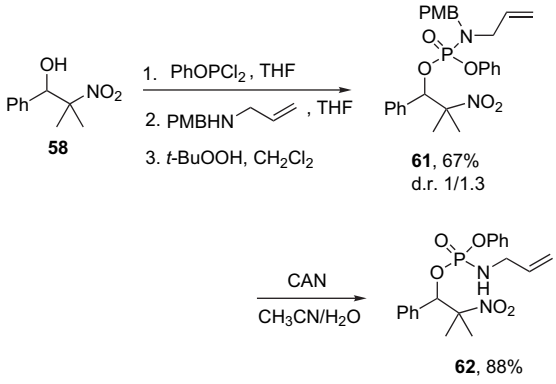
The remaining entries of Table 2 serve to illustrate the limitations of the method. Thus, with the much weaker aniline-based nucleophile (entry 5) no cyclization was seen, leading to decomposition of the alkene radical cation and the formation of a complex reaction mixture from which only the alkene **52** was isolated. Alcohols are generally much poorer nucleophiles than amines as is known to hold with alkene radical cations as electrophiles, with the rate constants for the attack of alcohols being slower than those of amines.[16] This leads to a reduced rate of cyclization, enabling solvation of the contact ion pair and conformational equilibration to become competitive, leading overall to a reduction in enantioselectivity (Table 2, entry 7). Finally, a significant limitation to the use of alcohols as nucleophiles in these cyclizations, at least when conducted under refluxing conditions in benzene, is seen in the formation of the 1,3,2-dioxaphosphepanes **55** and **56** (Table 2, entries 7 and 8). Given the reaction protocol, with dropwise addition of the stannane to a solution of the substrate in benzene at reflux, these cyclizations involving nucleophilic attack at phosphorus presumably take place before the radical reaction. The formation of the cyclic phosphepane ring should not prevent fragmentation to the alkene radical cation, as we have previously demonstrated that suitably substituted phosphepanes undergo a rearrangement analogous to the one in Scheme 3 with rate constants of 10^5–10^6 s^{-1} in benzene at 80 °C with a very high degree of retention of configuration at phosphorus.[19] However, the intramolecular nature of the contact radical cation/anion pair generated from expulsion of the phosphepane leaving group presumably accelerates internal return and thereby reduces the possibility of nucleophilic attack by the alcohol.

We considered an alternative approach to enantioselective alkene radical cation reactions in which the leaving group in the fragmentation step serves as source of chirality, thereby eliminating the need for the synthesis of enantiomerically enriched nitroalcohols. This approach, employing a stereogenic phosphorus or sulfur center, may be viewed as an extension of the diastereoselective probes of mechanism reported in Scheme 3. Before undertaking the synthesis of any enantiomerically enriched compounds a series of simple models were prepared to test the viability of such an approach in the context of a tandem polar/radical reaction. Thus, reaction of chlorosulfonyl isocyanate with nitroalcohol **58**[9b,20] afforded the sulfamate **59** which, following N-alkylation[21] and subsequent removal of the carbamate group, gave the radical precursor **60** (Scheme 14).



Scheme 14. Synthesis of an *N*-allyl sulfamate.

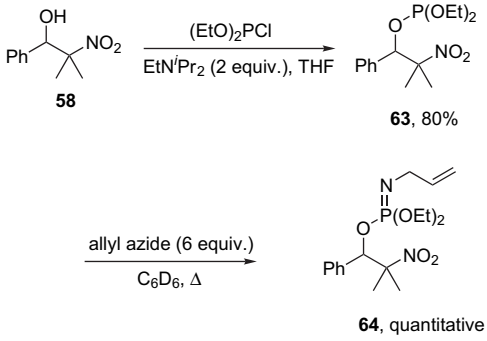
In the phosphorus series an *N*-allyl phosphoramide **62** was prepared in straightforward manner as outlined in Scheme 15.



Scheme 15. Synthesis of an *N*-allyl phosphoramide.

The synthesis of an *N*-allyl phosphorimidate **64**, after some experimentation, was also achieved in a straightforward manner employing the Staudinger reaction[22] of phosphite **63** with allyl azide (Scheme 16). In accordance with the precedent for the Staudinger reaction with phosphites,[23] as opposed to the more common phosphines, reaction of allyl azide with the diethylphosphite **63** proceeded according to plan to give the unstable **64**. However, reaction of allyl azide with the corresponding diphenylphosphite corresponding to **63** was prohibitively slow.

Compounds **60**, **62**, and **64** were treated with tin hydride and AIBN in benzene at reflux in the usual manner, unfortunately, no evidence was found for any of the anticipated



Scheme 16. Synthesis of an *N*-allyl phosphorimidate.

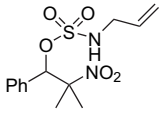
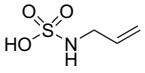
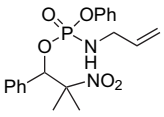
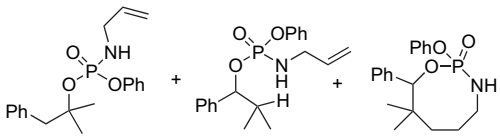
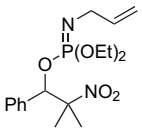
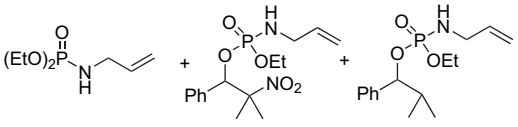
rearrangements. Nevertheless, as seen in Table 3, the results obtained are of more general interest in the context of the comportment of contact alkene radical cation/anion pairs. Blank experiments in benzene at reflux demonstrated the thermal stability of **60**, **62**, and **64**, in the absence of air and water.

With the sulfamate **60** the only isolated product was *N*-allyl sulfamic acid **65**, which was obtained in 48% yield (Table 3, entry 1). This material obviously derives from radical ionic fragmentation followed by cage escape and reflects the poor nucleophilicity of the sulfamate anion. With the phosphoramide **62**, the main product **66** was that of a 1,2-shift of the initial radical (Table 3, entry 2). This reflects the predominant 1,2-shift identified with simple phosphate esters either by stereochemical or isotopic labeling (Scheme 3).[5a] Aside from the simple reduction product **67**, which was isolated in 7% yield from this reaction, the phosphoramide **62** also gave rise to a very interesting minor product in the form of the 1,3,2-azoxaphosphocane **68** in 8% yield (Table 3, entry 2). This product, which appears to be the first example of its class,[24] and which was isolated as a single but unassigned diastereomer, is the apparent result of an 8-*endo-trig* cyclization of the initial radical. 8-*endo-trig* Cyclizations are relatively uncommon, usually involve conformationally constrained systems,[25] and have low rate constants,[26] and thus, the formation of **68** was somewhat unexpected as the 1,1-dimethyl-2-diphenylphosphatoxy-2-phenylethyl radical is known to rearrange in benzene at 20 °C with a rate constant of 1.2×10^6 s^{-1}.[3a] However, it should be noted that the rates of β-phosphatoxyalkyl rearrangement are severely influenced by substituents on phosphorus. For example, the 1,1-dimethyl-2-diethylphosphatoxy-2-phenylethyl radical rearranges too slowly to measure by time resolved laser flash photolysis in benzene ($k<10^4$ s^{-1}).[3a,k,27] The failure of **62** to rearrange in a formal 2,3-manner, preferring instead the 1,2-mode, led us to the phosphorimidate **64** with the hope that the exchange of a P=N double bond for a P=O would force the rearrangement into the formal 2,3-mode of rearrangement needed for the tandem polar/radical crossover process. We were encouraged in this direction by recent publication of the 3,3-sigmatropic rearrangements of *O*-allyl phosphorimidates by the Mapp group[23f,g] and by the formal analogy between open-shell 2,3-rearrangements and closed shell 3,3-sigmatropic rearrangements recognized by Zipse in his methyleneology principle.[28] Unfortunately, the major product isolated from this reaction was the simple phosphoramide **69**. This suggests that recombination within the ion pair formed on radical ionic fragmentation was not a viable reaction path. Two other minor products isolated, **70** and **71**, suggest that decomposition of the phosphorimidate is competitive with the radical ionic fragmentation under the reaction conditions employed, discouraging us from further work with this class of substrate.

3. Conclusion

The fragmentation of β-(phosphatoxy)alkyl radicals in benzene at reflux results in the formation of alkene radical cation/phosphate anion pairs. Amines trap these ion pairs intramolecularly to form five- and six-membered rings on a time scale that competes with equilibration of the ion pair with solvent, resulting in the observation of significant stereochemical memory effects. A chair-like transition state is proposed as a model for these cyclizations. Oxygen

Table 3. Radical reactions of sulfamates, phosphoramides, and phosphorimidates

Entry	Substrate	Products	% Yield
1	 **60**	 **65**	~48%
2	 **62**	 **66** + **67** + **68**	**66**: 42% **67**: 7% **68**: 8%
3	 **64**	 **69** + **70** + **71**	**69**: 40% **70**: 6% **71**: 5%

nucleophiles, on the other hand, are not sufficiently nucleophilic to achieve cyclization before solvent equilibration of the ion pair. Sulfamates, phosphoramides, and phosphorimidates were also explored as leaving groups for alkene radical formation and appear to function as such. However, it was not possible to achieve rearrangements akin to the β-(phosphatoxy)alkyl and β-(acetoxy)alkyl rearrangements with these groups.

4. Experimental

4.1. General

Unless otherwise stated, ^{1}H, ^{13}C and, ^{31}P NMR spectra were recorded in $CDCl_3$ solution. Specific rotations were recorded in $CHCl_3$ solution, unless otherwise stated. All solvents were dried and distilled by standard protocols. All reactions were conducted under a blanket of dry nitrogen or argon. All organic extracts were dried over sodium sulfate, and concentrated under aspirator vacuum at room temperature. Chromatographic purifications were carried out over silica gel. Room temperature is referred to as rt.

4.1.1. Typical protocol for the Henry reaction.

4.1.1.1. *N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)-4-hydroxy-5-methyl-5-nitrohexylamine (3).[1] 2-Nitropropane (1.97 g, 22.1 mmol) and aldehyde **1** (3.01 g, 10.9 mmol) were dissolved in a 1:1 mixture of acetonitrile and *tert*-BuOH (20 mL). To this solution was added potassium *tert*-butoxide (597 mg, 5.32 mmol) and the reaction mixture was stirred overnight. Satd aq NH_4Cl and ether were then added. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layer was washed with water and brine, then dried, and concentrated to dryness. Purification by column chromatography afforded the respective nitroaldol product **3**[1] (3.74 g, 94%).

4.1.2. Typical protocol for the Swern oxidation of nitroaldol adducts.

4.1.2.1. *N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)-5-methyl-5-nitro-4-oxo-hexylamine (5).[1] A solution of oxalyl chloride (1.3 mL, 14.9 mmol) in CH_2Cl_2 (50 mL) was cooled to −78 °C under N_2 followed by the dropwise addition of a solution of DMSO (1.5 mL, 21.1 mmol) in CH_2Cl_2 (7 mL), then the reaction mixture was stirred for 15 min. To this mixture was added dropwise a solution of nitroaldol adduct **3** (2.58 g, 7.04 mmol) in CH_2Cl_2 (17 mL) and stirred at −78 °C for 1 h. Triethylamine (7.4 mL, 53.1 mmol) was added dropwise. After stirring for 20 min, the reaction mixture was allowed to warm up to rt. Satd aq NH_4Cl was then added and the separated organic layer was washed with H_2O and brine, then dried and concentrated to dryness. Purification by column chromatography afforded **5**[1] (2.26 g, 88%).

4.1.3. Typical protocol for the CBS reduction of nitroketones.

4.1.3.1. (4*R*)-*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)-4-hydroxy-5-methyl-5-nitrohexylamine (7). To a solution of (*S*)-(−)-α,α-diphenyl-2-pyrrolidinemethanol (135 mg, 0.533 mmol, 9 mol %) in THF (4 mL) was added borane/dimethyl sulfide (2 M in THF, 7.20 mL, 14.4 mmol) under Ar. The mixture was stirred at 45–50 °C overnight. Ketone **5** (2.23 g, 6.12 mmol) in THF (35 mL) was added dropwise to the solution of the catalyst for 30 min at 45–50 °C, then the reaction mixture was stirred for 20 min. Then the reaction solution was cooled to rt and quenched by dropwise addition of satd aq NH_4Cl until the vigor of the reaction subsided. The aqueous layer was extracted with ethyl acetate and the combined organic layer was washed with water and brine, then dried and concentrated to dryness. Purification by column chromatography gave **7** (1.57 g, 72%, 85% ee) as colorless oil, $[\alpha]_D^{23}$ +12.2 (*c* 1.0) with spectral data identical to those of the racemate (**3**).[1]

4.1.4. Typical protocol for the phosphorylation of nitroaldols.

4.1.4.1. (4*R*)-*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)-4-diphenylphosphatoxy-5-methyl-5-nitrohexylamine (9). Diphenyl chlorophosphate (179 mg, 0.67 mmol) was added to nitroalcohol **7** (207 mg, 0.565 mmol) in CH_2Cl_2 (5 mL) followed by the addition of DMAP (91 mg, 0.74 mmol) in one portion at rt. The reaction mixture was stirred overnight, then quenched by satd aq NH_4Cl. The aqueous layer was extracted with CH_2Cl_2, the combined organic layer was washed with water and brine, then dried and concentrated to dryness. Purification by column chromatography afforded the corresponding phosphate **9** (331 mg, 98%) as colorless oil. $[\alpha]_D^{23}$ +0.16 (*c* 2.5); ^{1}H NMR: δ 7.34–7.14 (m, 15H), 5.10 (br t, J=6.9 Hz, 1H), 4.37 (d, J=15.6 Hz, 1H), 4.29 (d, J=15.6 Hz, 1H), 3.18 (m, 2H), 1.80 (m, 1H), 1.75–1.45 (m, 3H), 1.59 (s, 3H), 1.53 (s, 3H), 1.44 (s, 9H); ^{13}C NMR: δ 155.9, 138.5, 129.8, 128.5, 127.5, 127.2, 125.5, 120.2, 90.3, 83.6, 79.9, 50.2, 45.9, 28.8, 28.5, 24.7, 22.7; ^{31}P NMR: δ −12.2; ESIHRMS: Calcd for $C_{31}H_{39}N_2O_8PNa$ $[M+Na]^+$ 621.2342. Found 621.2344.

4.1.5. Typical protocol for the removal of Boc group.

4.1.5.1. (4*R*)-*N*-Benzyl-4-diphenylphosphatoxy-5-methyl-5-nitrohexylamine (11). Phosphate **9** (257 mg, 0.43 mmol) was stirred in 10% TFA/CH_2Cl_2 (10 mL) under N_2 at rt overnight. NaOH (15%) was then added to pH 11 and the aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with water and brine, then dried and concentrated to dryness. Column chromatography afforded the respective radical precursor **11** (207 mg, 99%) as colorless oil. $[\alpha]_D^{23}$ +3.2 (*c* 2.0); ^{1}H NMR: δ 7.37–7.14 (m, 15H), 5.19 (m, 1H), 3.69 (s, 2H), 2.58 (m, 2H), 1.74–1.64 (m, 4H), 1.61 (s, 3H), 1.56 (s, 3H); ^{13}C NMR: δ 150.5, 140.5, 131.0, 129.9, 128.5, 128.2, 127.0, 125.6, 120.4, 120.3, 120.2, 90.5, 83.9, 54.0, 48.6, 29.2, 26.3, 22.9, 21.8; ^{31}P NMR: δ −11.9; ESIHRMS: Calcd for $C_{26}H_{32}N_2O_6P$ $[M+H]^+$ 499.1998. Found 499.1991.

4.1.6. Determination of enantiomeric excess. The ee's of nitroalcohols and nitrophosphates were determined by chiral HPLC, whereas the ee's of the radical cyclization products were obtained by chiral GC. HPLC conditions: Chiralcel OD (250×4.6 mm) column; eluent: 0.5, 1.7 or 2.0% 2-propanol/hexanes with a flow rate 0.5 or 1.0 mL/min. UV Detector: 254 nm. GC conditions: Supelco ALPHA DEX 120 Capillary Column (α-cyclodextrin) (30 m×0.25 μm) or Supelco GAMMA DEX 120 Capillary Column (γ-cyclodextrin) (30 m×0.25 μm), with He as carrier gas, a flow rate of 20 or 30 cm/s, and FID detection.

4.1.6.1. *N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)-5-hydroxy-6-methyl-6-nitroheptylamine (4). Following the general procedure for Henry reaction, **2** (1.98 g, 6.79 mmol) was converted to **4** (2.37 g, 92%) as colorless oil. ^{1}H NMR: δ 7.32–7.19 (m, 5H), 4.41 (s, 2H), 3.91 (m, 1H), 3.18 (m, 2H), 1.61–1.47 (m, 6H), 1.54 (s, 3H), 1.51 (s, 3H), 1.45 (s, 9H); ^{13}C NMR: δ 156.1, 138.7, 128.5, 127.5, 1127.2, 92.2, 79.9, 77.3, 75.9, 50.6, 46.3, 31.3, 31.1, 28.5, 23.2, 20.8; ESIHRMS: Calcd for $C_{20}H_{32}N_2O_5$ [M+H]$^+$ 403.2209. Found 403.2227.

4.1.6.2. *N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)-6-methyl-6-nitro-5-oxo-heptylamine (6). Following the general procedure for Swern oxidation, **4** (1.26 g, 3.32 mmol) was converted to **6** (1.17 g, 93%) as colorless oil. ^{1}H NMR: δ 7.30–7.19 (m, 5H), 4.41 (s, 2H), 3.17 (t, J=6.6 Hz, 2H), 2.46 (t, J=6.8 Hz, 2H), 1.70 (s, 6H), 1.57 (m, 4H), 1.46 (s, 9H); ^{13}C NMR: δ 206.7, 188.5, 138.7, 128.5, 127.5, 127.20, 127.17, 94.1, 79.8, 77.3, 50.5, 46.2, 35.8, 28.5, 23.3, 21.0; ESIHRMS: Calcd for $C_{20}H_{30}N_2O_5$ Na [M+Na]$^+$ 401.2052. Found 401.2037.

4.1.6.3. (5*R*)-*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)-5-hydroxy-6-methyl-6-nitroheptylamine (8). Following the general procedure for CBS reduction, **6** (313 mg, 0.827 mmol) was converted to **8** (245 mg, 78%) as colorless oil. $[\alpha]_D^{23}$ +1.6 (*c* 1.0). Enantiomeric excess was determined by chiral HPLC after the derivatization to the phosphate **10**. The spectral data for this compound corresponded with those of the racemate (**4**).

4.1.6.4. (5*R*)-*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)-5-diphenylphosphatoxy-6-methyl-6-nitroheptylamine (10). Following the general procedure for phosphorylation, **8** (192 mg, 0.51 mmol) was converted to **10** (306 mg, 99%, 86% ee) as colorless oil. $[\alpha]_D^{23}$ +4.0 (*c* 1.0); ^{1}H NMR: δ 7.33–7.10 (m, 15H), 5.10 (m, 1H), 4.36 (s, 2H), 3.05 (m, 2H), 1.65–1.46 (m, 6H), 1.61 (s, 3H), 1.54 (s, 3H), 1.44 (s, 9H); ^{13}C NMR: δ 172.2, 138.7, 129.8, 129.4, 128.5, 127.4, 127.2, 125.4, 120.2, 100.2, 90.3, 83.7, 79.7, 77.3, 50.5, 46.3, 31.2, 28.5, 23.2, 22.6; ^{31}P NMR: δ −12.2; ESIHRMS: Calcd for $C_{32}H_{41}N_2O_8PNa$ [M+Na]$^+$ 635.2498. Found 635.2489.

4.1.6.5. (5*R*)-*N*-Benzyl-5-diphenylphosphatoxy-6-methyl-6-nitroheptylamine (12). Following the general procedure for removal of Boc group, **10** (231 mg, 0.38 mmol) was converted to **12** (183 mg, 95%) as colorless oil. $[\alpha]_D^{23}$ +3.1 (*c* 0.9); ^{1}H NMR: δ 7.35–7.12 (m, 15H), 5.14 (br t, J=9.0 Hz, 1H), 3.72 (s, 2H), 2.50 (m, 2H), 2.07 (m, 2H), 1.78–1.40 (m, 4H), 1.60 (s, 3H), 1.54 (s, 3H); ^{13}C NMR: δ 150.6, 129.9, 128.6, 128.3, 128.2, 127.1, 125.6, 120.32, 120.26, 120.2, 120.1, 90.3, 83.8, 54.0, 48.8, 31.3, 29.8, 29.6, 23.7, 22.8; ^{31}P NMR: δ –11.9; ESIHRMS: Calcd for $C_{27}H_{34}N_2O_6P$ [M+H]$^+$ 513.2155. Found 513.2167.

4.1.6.6. (4*R*)-*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)-4-diethylphosphatoxy-5-methyl-5-nitrohexylamine (13). Enantioenriched nitroalcohol **7** (385 mg, 1.05 mmol) and pyridine (0.2 mL, 2.5 mmol) were dissolved in dry CH_2Cl_2 (20 mL) and the solution was cooled to 0 °C. Chlorodiethylphosphite (0.30 mL, 2.1 mmol) was added dropwise. The reaction was stirred for 50 min, then *tert*-butyl hydroperoxide in decane (0.45 mL, 2.25 mmol) was added dropwise. After stirring overnight, the reaction was quenched with satd aq NH_4Cl, then separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with water and brine, then dried, and concentrated. Chromatographic purification gave the colorless oil **13** (294 mg, 56%) ^{1}H NMR: δ 7.33–7.22 (m, 5H), 4.83 (m, 1H), 4.46 (d, J=15.6 Hz, 1H), 4.38 (d, J=15.6 Hz, 1H), 4.09 (m, 4H), 3.23 (m, 2H), 1.86 (m, 1H), 1.66–1.40 (m, 3H), 1.60 (s, 3H), 1.52 (s, 3H), 1.46 (s, 9H), 1.32 (m, 6H); ^{13}C NMR ($CDCl_3$): δ 155.8, 138.4, 128.5, 127.7, 127.2, 90.4, 81.8, 80.5, 79.8, 64.1, 61.8, 50.2, 45.8, 29.8, 28.4, 25.8, 22.9, 16.3, 16.1; ESIHRMS: Calcd for $C_{23}H_{39}N_2O_8PNa$ [M+Na]$^+$ 525.2342. Found 525.2350.

4.1.6.7. (4*R*)-*N*-Benzyl-4-diethylphosphatoxy-5-methyl-5-nitrohexylamine (14). Following the general procedure for Boc group removal, **13** (258 mg, 0.513 mmol) afforded **14** (193 mg, 93%) as a colorless oil. ^{1}H NMR: δ 7.33–7.24 (m, 5H), 4.91 (m, 1H), 4.10 (m, 4H), 3.82 (s, 2H), 2.71 (br s, 2H), 1.95–1.69 (m, 4H), 1.63 (s, 3H), 1.56 (s, 3H), 1.32 (t, J=7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$): δ 130.1, 130.0, 129.5, 129.3, 127.3, 90.3, 81.9, 65.6, 65.4, 63.1, 52.3, 46.9, 30.3, 27.9, 23.4, 22.5, 19.6, 15.7; ESIHRMS: Calcd for $C_{18}H_{32}N_2O_6P$ [M+H]$^+$ 403.1998. Found 403.2002.

4.1.6.8. Ethyl 2,2-dibenzylpent-4-enoate (16). *n*-BuLi (2.4 M in hexanes, 1.0 mL, 2.4 mmol) was added dropwise to diisopropylamine (30 mg, 2.3 mmol) in THF (3 mL) over 5 min at −78 °C under N_2 followed by stirring for 30 min. To this LDA solution was added 2-benzyl-3-phenylpropionate[3] (406 mg, 1.86 mmol) in THF (3 mL) dropwise for 5 min. The reaction mixture was stirred for 45 min at −78 °C followed by dropwise addition of allyl bromide in THF (3 mL) at −78 °C. The reaction was slowly warmed up to 0 °C over a period of 2.5 h and quenched with satd aq NH_4Cl. The aqueous mixture was extracted with EtOAc, combined organic layer was washed with brine and dried and concentrated to dryness. Purification by column chromatography (hexanes/EtOAc, 9:1) provided **16** (510 mg, 89%). ^{1}H NMR: δ 7.31–7.17 (m, 10H), 6.08–5.94 (m, 1H), 5.28–5.16 (m, 2H), 4.09 (q, J=7.2, 2H), 3.13 (d, J=14.1 Hz, 2H), 2.92 (d, J=13.2 Hz, 2H), 2.35 (dd, J=7.2, 7.2 Hz, 2H), 1.190 (t, J=7.5 Hz, 3H); ^{13}C NMR: δ 175.4, 137.6, 134.4, 130.3, 128.2, 126.7, 119.1, 60.6, 51.8, 42.2, 36.0, 14.2; ESIHRMS: Calcd for $C_{21}H_{24}O_2Na$ [M+Na]$^+$ 331.1674. Found 331.1669.

4.1.6.9. 2,2-Dibenzylpent-4-en-1-ol (17). Ester **16** (51 mg, 0.17 mmol) in dry ether (2 mL) was added to a solution of $LiAlH_4$ (75 mg, 0.20 mmol) in dry ether (20 mL) at 0 °C under Ar. The resulting mixture was refluxed for 12 h and quenched by dropwise addition of 10% NaOH (1 mL) at rt. The organic layer was decanted off and the residue was washed with EtOAc. The combined organic layer was washed with water and brine and dried. Concentration and purification of the crude mixture by column chromatography (hexanes/EtOAc, 4:1) afforded the alcohol **17** (41 mg, 95%). ^{1}H NMR: δ 7.32–7.20 (m, 10H), 6.04 (m, 1H), 5.15 (m, 2H), 3.35 (s, 2H), 2.76 (d, J=13.2 Hz, 2H), 2.68 (d, J=13.2 Hz, 2H), 2.01 (d, J=6.9 Hz, 2H); ^{13}C NMR: δ 138.4, 135.0, 130.8, 128.2, 126.3, 118.3, 66.5, 43.0, 41.3, 38.2; EIHRMS: Calcd for $C_{19}H_{22}O$ [M]$^+$ 266.1671. Found 266.1688.

4.1.6.10. 5-Benzylamino-4,4-dibenzylpent-1-ene (18). Following the general procedure for Swern oxidation, alcohol **17** (4.77 g, 17.9 mmol) was converted to the corresponding aldehyde (5.23 g) as colorless oil, which was directly taken to the next reaction after the extraction. ^{1}H NMR: δ 9.71 (s, 1H), 7.33–7.12 (m, 10H), 5.91 (m, 1H), 5.22 (m, 2H), 3.02 (d, J=13.8 Hz, 2H), 2.85 (d, J=13.8 Hz, 2H), 2.29 (d, J=7.5 Hz, 2H); ^{13}C NMR: δ 206.6, 136.6, 133.4, 130.6, 128.5, 126.9, 119.5, 53.7, 40.3, 35.6; ESIHRMS: Calcd for $C_{19}H_{20}ONa$ $[M+Na]^+$ 287.1412. Found 287.1424. To a CH_3OH (50 mL) solution of crude aldehyde (5.23 g), benzylamine (3.86 g, 36.0 mmol) and CH_3CO_2H (1.10 mL, 18.5 mmol) was added sodium cyanoborohydride (1.48 g, 22.4 mmol) in portions at 0 °C under N_2. The reaction was stirred at rt for 2 h. Satd aq $NaHCO_3$ was added, then CH_3OH was removed by the evaporation. The aqueous layer was extracted with ether, the combined organic layer was washed with satd aq NH_4Cl, satd aq $NaHCO_3$, H_2O, and brine then dried. Concentration gave yellow oil which was purified by column chromatography giving amine **18** (4.84 g, 76% from alcohol) as a colorless oil. ^{1}H NMR: δ 7.42–7.12 (m, 15H), 6.03 (m, 1H), 5.13 (m, 2H), 3.70 (s, 2H), 2.77 (d, J=6.0 Hz, 2H), 2.70 (d, J=7.5 Hz, 2H), 2.34 (s, 2H), 2.03 (d, J=6.9 Hz, 2H); ^{13}C NMR: δ 138.7, 135.2, 130.9, 129.4, 128.8, 128.2, 128.0, 127.1, 126.2, 118.1, 68.1, 54.7, 54.3, 51.5, 42.1, 39.4; ESIHRMS: Calcd for $C_{26}H_{30}N$ $[M+H]^+$ 356.2378. Found 356.2376.

4.1.6.11. 5-[*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)] amino-4,4-dibenzyl-pent-1-ene (19). To the CH_2Cl_2 (50 mL) solution of **18** (4.552 g, 12.80 mmol) and TEA (2.8 mL, 20.1 mmol) was added Boc_2O (3.781 g, 17.32 mmol) in CH_2Cl_2 (7 mL) at 0 °C under N_2, then it was stirred for 19 h at rt. The reaction was quenched with satd aq NH_4Cl, then aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with satd aq NH_4Cl, H_2O, and brine, then dried and concentrated to dryness. Purification by column chromatography then afforded Boc-protected amine **19** (5.62 g, 96%) as a colorless oil. ^{1}H NMR: δ 7.31–7.04 (m, 15H), 5.99 (m, 1H), 5.09 (m, 2H), 4.49 (s, 2H), 3.42 (s, 2H), 2.82 (d, J=13.8 Hz, 2H), 2.74 (d, J=13.8 Hz, 2H), 2.19 (d, J=6.9 Hz, 2H), 1.39 (s, 9H); ^{13}C NMR: δ 157.1, 138.5, 135.5, 131.2, 130.8, 129.1, 128.5, 128.0, 127.1, 126.9, 126.2, 117.8, 80.1, 57.5, 43.0, 42.6, 40.1, 28.6, 28.4; ESIHRMS: Calcd for $C_{31}H_{37}NO_2Na$ $[M+Na]^+$ 478.2722. Found 478.2716.

4.1.6.12. *N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)-2,2-dibenzyl-4-hydroxy-5-methyl-5-nitrohexylamine (20). A solution of alkene **19** (5.05 g, 11.1 mmol) in CH_2Cl_2 (50 mL) was bubbled with O_3 at −78 °C until the solution turned blue. On complete disappearance of the starting material, N_2 gas was bubbled through the reaction mixture for 15 min at −78 °C. To the resulting mixture was added Ph_3P (3.33 g, 12.7 mmol) at −78 °C and the reaction was allowed to warm up to rt. After stirring the reaction mixture overnight, it was concentrated and purified by column chromatography to afford an aldehyde (1.74 g, 34%). ^{1}H NMR: δ 9.69 (t, J=1.5 Hz, 1H), 7.34–7.09 (m, 15H), 4.43 (s, 2H), 3.51 (s, 2H), 3.00 (d, J=13.8 Hz, 2H), 2.84 (d, J=13.8 Hz, 2H), 2.37 (d, J=1.5 Hz, 2H), 1.36 (s, 9H); ^{13}C NMR: δ 202.2, 157.0, 138.4, 137.3, 131.20, 131.15, 128.7, 128.6, 128.4, 128.3, 127.2, 126.7, 106.2, 80.6, 54.3, 53.5, 48.0, 43.9, 43.8, 28.3; ESIHRMS: Calcd for $C_{30}H_{35}NO_3Na$ $[M+Na]^+$ 480.2515. Found 480.2500. To a mixture of this aldehyde (1.30 g, 2.84 mmol) and 2-nitropropane (20 mL, 22 mmol) was added *t*-BuOK (177 mg, 1.58 mmol) at rt. After stirring for 12 h, the reaction was quenched with satd aq NH_4Cl, diluted with water, and the aqueous layer was extracted with Et_2O. The combined organic layer was washed with H_2O and brine, then dried and concentrated to dryness. Purification of the residue by column chromatography (Et_2O/CH_2Cl_2, 0.5:99.5) afforded nitroalcohol **20** (838 mg, 54%). ^{1}H NMR: δ 7.33–7.13 (m, 13H), 7.01 (m, 2H), 4.67 (d, J=15.9 Hz, 1H), 4.30 (br t, J=8.7 Hz, 1H), 4.10 (d, J=15.0 Hz, 1H), 4.03 (d, J=15.0 Hz, 1H), 3.03–2.07 (m, 5H), 1.64 (dd, J=12.0, 11.4 Hz, 1H), 1.55 (s, 3H), 1.49–1.41 (m, 1H), 1.38 (s, 12H); ^{13}C NMR: δ 158.4, 138.3, 138.1, 137.8, 131.2, 131.1, 128.6, 128.3, 128.24, 128.17, 127.3, 126.9, 126.6, 126.5, 92.8, 81.4, 77.2, 73.6, 43.0, 42.1, 28.3, 22.2, 21.8; ESIHRMS: Calcd for $C_{33}H_{42}N_2O_5Na$ $[M+Na]^+$ 569.2991. Found 569.2997.

4.1.6.13. *N*-Benzyl-2,2-dibenzyl-5-methyl-5-nitro-4-oxo-hexylamine (21). Following the general procedure for removal of Boc group, **20** (140 mg, 0.26 mmol) afforded the crude secondary amine, which was directly taken to the next step after the extraction. Following the general procedure for Swern oxidation, ketone **21** (97 mg, 86%) was obtained as colorless oil. ^{1}H NMR: δ 8.32 (br s, 1H), 7.47–7.06 (m, 15H), 4.05 (s, 2H), 3.35 (s, 2H), 3.11 (d, J=13.5 Hz, 2H), 3.00 (d, J=13.5 Hz, 2H), 2.37 (s, 2H), 1.67 (s, 6H); ^{13}C NMR: δ 202.1, 162.2, 138.2, 130.92, 130.90, 130.7, 130.6, 130.1, 129.0, 128.4, 128.3, 126.5, 94.9, 63.6, 57.5, 42.0, 40.5, 39.2, 23.8.

4.1.6.14. (4*R*)-*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)-2,2-dibenzyl-4-hydroxy-5-methyl-5-nitrohexylamine (22). Following the general procedure for CBS reduction, ketone **21** (95 mg, 0.21 mmol) was converted to alcohol. The colorless oil was obtained by the extraction, then Boc protection was directly accomplished. To the CH_2Cl_2 solution (15 mL) of obtained alcohol, Boc_2O (160 mg, 0.73 mmol) and TEA (0.5 mL, 3.6 mmol) were added. The reaction was stirred overnight and the solvent was removed by evaporation. Purification by column chromatography gave enantiomerically enriched alcohol **21** (80 mg, 70%) as colorless oil, which showed similar spectra to racemate **20**. The enantiomeric excess was determined after the derivatization to **24**.

4.1.6.15. (4*R*)-*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)-2,2-dibenzyl-4-diphenylphosphatoxy-5-methyl-5-nitrohexylamine (23). I_2 (306 mg, 1.21 mmol) was added to a stirred solution of ethyldiphenylphosphite (250 mg, 0.95 mmol) in CH_2Cl_2 (2 mL) at 0 °C under N_2. After 15 min, this solution was added to a mixture of nitroalcohol **22** (345 mg, 0.63 mmol), pyridine (0.120 mL, 1.48 mmol) in CH_2Cl_2 (3 mL) under N_2 at 0 °C. The reaction mixture was stirred at 0 °C for 1 h, then NH_4Cl was added. The aqueous layer was extracted with CH_2Cl_2, the combined organic layer was washed with 10% $Na_2S_2O_3$, H_2O, and brine, then dried and concentrated to dryness. Purification by column chromatography afforded phosphorylated product **23** (371 mg, 75%). ^{1}H NMR: δ 7.36–7.03 (m, 25H), 5.78 (t, J=9.0 Hz, 1H), 4.45 (d, J=16.2 Hz, 1H), 4.29 (d, J=16.2 Hz, 1H), 3.71 (d, J=14.7 Hz, 1H), 3.45 (d, J=14.7 Hz, 1H),

3.11 (d, J=14.7 Hz, 1H), 3.02 (d, J=14.4 Hz, 1H), 2.99 (d, J=14.7 Hz, 1H), 2.83 (d, J=14.4 Hz, 1H), 1.91 (dd, J=15.3, 10.8 Hz, 1H), 1.75 (dd, J=15.3, 4.5 Hz, 1H), 1.61 (s, 3H), 1.42 (s, 3H), 1.33 (s, 9H); ^{13}C NMR: δ 157.3, 138.8, 138.1, 131.5, 130.1, 129.7, 128.7, 128.5, 128.3, 128.2, 126.8, 126.4, 125.3, 120.2, 91.7, 82.1, 80.2, 53.2, 53.0, 42.3, 41.7, 41.3, 35.8, 28.4, 27.7, 24.4, 21.3; ^{31}P NMR: δ −12.9; ESIHRMS: Calcd for $C_{45}H_{51}N_2O_8PNa$ $[M+Na]^+$ 801.3281. Found 801.3263.

4.1.6.16. (4*R*)-*N*-Benzyl-2,2-dibenzyl-4-diphenylphosphatoxy-5-methyl-5-nitrohexylamine (24). Following the general procedure for removal of Boc group, phosphate **23** (294 mg, 0.38 mmol) gave the secondary amine **24** (245 mg, 96%, 79% ee). ^{1}H NMR: δ 7.33–7.09 (m, 25H), 5.96 (t, J=8.4 Hz, 1H), 3.67 (d, J=13.5 Hz, 1H), 3.61 (d, J=13.5 Hz, 1H), 3.01 (s, 2H), 2.77 (s, 2H), 2.73 (d, J=12.3 Hz, 1H), 2.63 (d, J=12.3 Hz, 1H), 1.76 (m, 2H), 1.65 (s, 3H), 1.46 (s, 3H); ^{13}C NMR: δ 150.7, 138.4, 138.0, 131.1, 131.0, 129.9, 128.8, 128.7, 128.2, 128.1, 127.7, 126.6, 126.4, 125.5, 120.2, 91.7, 82.2, 54.9, 54.6, 43.3, 42.4, 41.0, 35.7, 24.7, 20.8; ^{31}P NMR: δ −12.8; ESIHRMS: Calcd for $C_{40}H_{44}N_2O_6P$ $[M+H]^+$ 679.2937. Found 679.2943.

4.1.6.17. 2-{2-[*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)-amino]phenyl}ethanol (26). Carbamate **25**[12] (2.00 g, 8.45 mmol) was treated with NaH (60% in oil, 433 mg, 10.8 mmol) in DMF (80 mL) at 0 °C followed by dropwise addition of BnBr (1.10 mL, 9.25 mmol). After stirring overnight, the reaction was quenched with NH_4Cl and the separated aqueous layer was extracted with ether. The combined organic layer was washed with water and brine then dried. Purification by column chromatography gave **26** (1.39 g, 50%). ^{1}H NMR: δ 7.27–7.19 (m, 7H), 7.12 (m, 1H), 6.89 (br s, 1H), 4.91 (d, J=14.5 Hz, 1H), 4.50 (d, J=14.5 Hz, 1H), 3.75 (br s, 2H), 2.72 (m, 1H), 2.59 (m, 1H), 1.44 (s, 9H); ^{13}C NMR: δ 155.4, 141.3, 138.0, 136.8, 130.0, 129.1, 128.9, 128.3, 127.6, 127.4, 127.1, 80.6, 62.6, 54.3, 34.1, 28.3. Anal. Calcd for $C_{20}H_{25}NO_3$: C, 73.37; H, 7.70. Found: C, 73.27; H, 7.69.

4.1.6.18. 2-{2-[*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)-amino]phenyl}ethanal (27). Alcohol **26** (2.14 g, 6.52 mmol) was stirred in CH_2Cl_2 (40 mL) with PCC (98%, 1.74 g, 7.92 mmol) and 4 Å molecular sieves overnight. The resulting black suspension was filtered through silica gel pre-wetted by hexanes, eluting with Et_2O. Chromatographic purification gave **27** (1.326 g, 63%) as a colorless oil. ^{1}H NMR: δ 9.38 (s, 1H), 7.26–7.04 (m, 9H), 4.72 (m, 2H), 3.38 (d, J=16.5 Hz, 1H), 3.27 (d, J=16.5 Hz, 1H), 1.41 (s, 9H); ^{13}C NMR: δ 199.0, 154.7, 141.5, 137.6, 131.4, 130.7, 128.8, 128.4, 128.3, 127.6, 80.7, 54.2, 45.8, 28.3. Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12. Found C, 73.65; H, 7.11.

4.1.6.19. 1-{2-[*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)-amino]phenyl}-3-methyl-3-nitrobutan-2-ol (28). Following the general Henry reaction procedure, **27** (1.39 g, 4.28 mmol) afforded **28** (1.63 g, 92%). ^{1}H NMR: δ 7.32–6.90 (m, 9H), 4.79 (m, 1H), 4.60 (m, 1H), 4.37 (d, J=11 Hz, 0.5H), 4.24 (d, J=11 Hz, 0.5H), 2.58 (br s, 1H), 2.27–2.10 (m, 2H), 1.57 (s, 3H), 1.53 (s, 3H), 1.47 (s, 9H); ^{13}C NMR: δ 155.3, 141.3, 137.8, 137.4, 135.5, 131.0, 129.8, 129.5, 128.8, 128.4, 128.38, 128.2, 128.0, 127.8, 127.6, 91.6, 91.4, 81.9, 80.9, 74.4, 55.2, 54.3, 33.6, 32.1, 28.4, 28.3, 23.1, 20.9; ESIHRMS: Calcd for $C_{23}H_{30}N_2O_5Na$ $[M+Na]^+$ 437.2052. Found 437.2054.

4.1.6.20. 1-{2-[*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)-amino]phenyl}-3-methyl-3-nitro-2-(diphenylphosphatoxy)-butane (29). Following the general procedure for phosphorylation, **28** (198 mg, 0.48 mmol) afforded colorless oil **29** (291 mg, 94%). ^{1}H NMR: δ 7.50–6.80 (m, 19H), 5.61 (br s, 0.6H), 5.49 (m, 0.4H), 5.25 (m, 0.6H), 4.99 (d, J=14.5 Hz, 0.4H), 4.49 (d, J=15 Hz, 0.4H), 4.31 (d, J=14.5 Hz, 0.6H), 3.05 (d, J=15 Hz, 0.4H), 2.87 (m, 1.6H), 1.68 (s, 3H), 157 (s, 1H), 1.55 (s, 2H), 1.44 (s, 9H), 1.44; ^{13}C NMR: δ 155.1, 154.7, 150.52, 150.46, 150.4, 142.0, 141.6, 138.7, 138.0, 133.6, 133.4, 131.9, 130.1, 129.8, 129.6, 129.5, 129.49, 129.3, 128.8, 128.6, 128.4, 128.3, 128.1, 127.7, 127.6, 127.4, 127.3, 125.4, 125.3, 125.1, 120.2, 120.16, 120.1, 120.0, 90.5, 90.46, 90.38, 83.0, 82.98, 82.63, 82.6, 80.8, 80.7, 54.2, 53.3, 34.2, 32.3, 28.3, 23.4, 23.1, 21.8, 21.6; ^{31}P NMR: δ −12.4, −12.6; ESIHRMS: Calcd for $C_{35}H_{39}N_2O_8PNa$ $[M+Na]^+$ 669.2342. Found 669.2322.

4.1.6.21. 1-[2-Benzylaminophenyl]-3-methyl-3-nitro-2-(diphenylphosphatoxy)butane (30). Removal of the Boc group from **29** (685 mg, 1.06 mmol) according to the general procedure gave **30** (568 mg, 98%). ^{1}H NMR: δ 7.42–6.90 (m, 17H), 6.58 (m, 2H), 5.65 (m, 1H), 5.11 (br s, 1H), 4.41 (d, J=15 Hz, 1H), 4.35 (d, J=15 Hz, 1H), 3.15 (dd, J=15, 6 Hz, 1H), 2.86 (dd, J=15, 6 Hz, 1H), 1.68 (s, 3H), 1.42 (s, 3H); ^{13}C NMR: δ 150.4, 150.37, 150.3, 150.2, 146.4, 139.7, 131.5, 129.9, 129.0, 128.6, 127.3, 127.0, 125.6, 120.3, 120.2, 120.19, 119.1, 117.1, 111.6, 90.8, 90.75, 80.44, 80.40, 47.8, 35.5, 23.1, 21.7; ^{31}P NMR: δ −11.1; ESIHRMS: Calcd for $C_{30}H_{31}N_2O_6PNa$ $[M+Na]^+$ 569.1817. Found 569.1819.

4.1.6.22. (4*R*)-*N*-(*tert*-Butyloxycarbonyl)-4-diphenylphosphatoxy-5-methyl-5-nitrohexylamine (31). Phosphate **9** (103 mg, 0.17 mmol) was treated with $PdCl_2$ (64 mg, 0.36 mmol) in methanol (10 mL) under hydrogen atmosphere for 4 h. Satd aq $NaHCO_3$ was added, then it was extracted with EtOAc. The organic layer was washed with H_2O and brine, then dried and concentrated to dryness. Purification by column chromatography gave the secondary amine **31** (84 mg, 97%) as colorless oil. $[\alpha]_D^{23}$ +0.3 (c 0.94); ^{1}H NMR: δ 7.36–7.14 (m, 10H), 5.15 (m, 1H), 4.43 (br s, 1H), 3.06 (m, 2H), 1.75–1.48 (m, 4H), 1.61 (s, 3H), 1.56 (s, 3H), 1.43 (s, 9H); ^{13}C NMR: δ 155.6, 129.9, 129.3, 125.6, 120.4, 120.1, 90.3, 83.5, 39.8, 28.5, 26.5, 23.0, 21.5; ^{31}P NMR: δ −12.0; ESIHRMS: Calcd for $C_{24}H_{33}N_2O_8PNa$ $[M+Na]^+$ 531.1872. Found 531.1859.

4.1.6.23. (4*R*)-*N*-(*tert*-Butyloxycarbonyl)-*N*-prop-2-ynyl-4-diphenylphosphatoxy-5-methyl-5-nitrohexylamine (32). Secondary amine **31** (161 mg, 0.317 mmol) was treated with NaH (60% in oil, 37 mg, 0.93 mmol) in DMF (15 ml) at 0 °C under N_2 for 20 min, then propargyl bromide (75 mg, 0.63 mmol) was added dropwise. The reaction was stirred for 1 h, then quenched with H_2O. It was extracted with EtOAc then washed with H_2O and brine. It was dried

over Na_2SO_4 followed by the evaporation, which gave a brown oil. Purification by column chromatography gave **32** (160 mg, 92%) as a colorless oil. ^{1}H NMR: δ 7.34–7.18 (m, 10H), 5.15 (m, 1H), 3.92 (m, 2H), 3.31 (t, J=7.2 Hz, 2H), 2.13 (t, J=2.1 Hz, 1H), 1.90–1.78 (m, 2H), 1.75–1.65 (m, 2H), 1.62 (s, 3H), 1.57 (s, 3H), 1.45 (s, 9H); ^{13}C NMR: δ 155.1, 129.8, 125.5, 120.2, 83.6, 80.4, 71.7, 46.1, 36.3, 28.8, 28.4, 24.7, 23.8, 22.7, 22.2; ^{31}P NMR: δ −12.1; ESIHRMS: Calcd for $C_{27}H_{35}N_2O_8PNa$ $[M+Na]^+$ 569.2029. Found 569.2036.

4.1.6.24. (4*R*)-4-Diphenylphosphatoxy-*N*-prop-2-ynyl-5-methyl-5-nitrohexylamine (33). Following the general procedure for removal of Boc group, **32** (211 mg, 0.386 mmol) gave the precursor of radical cyclization **33** (170 mg, 99%). ^{1}H NMR: δ 7.33–7.17 (m, 10H), 5.17 (m, 1H), 3.36 (s, 2H), 2.66 (m, 2H), 2.52 (br s, 1H), 2.21 (s, 1H), 1.66–1.64 (m, 4H), 1.61 (s, 3H), 1.56 (s, 3H); ^{13}C NMR: δ 129.8, 125.5, 120.2, 106.2, 90.4, 83.7, 71.8, 47.7, 37.9, 29.2, 25.7, 22.7, 22.0; ^{31}P NMR: δ −11.9; ESIHRMS: Calcd for $C_{22}H_{28}N_2O_6P$ $[M+H]^+$ 447.1685. Found 447.1677.

4.1.6.25. 4,4-Diphenylcyclohexanone oxime (34). 4,4-Diphenylcyclohexanone[29] (4.70 g, 18.8 mmol) in EtOH (94 mL) was added to a stirred solution of hydroxylamine hydrochloride (6.25 g, 90.0 mmol) and sodium acetate (12.63 g, 154 mmol) in water (25 mL) at rt. The resulting milky white solution was stirred for 2 h and concentrated under rotary evaporation. The residue was extracted with EtOAc, dried by Na_2SO_4, and concentrated. Purification of the crude mixture by column chromatography (EtOAc/hexanes, 1:5) afforded oxime **34** (4.85 g, 97%). IR (film): 3243, 1446 cm^{-1}; ^{1}H NMR: δ 7.31–7.26 (m, 10H), 2.66 (t, J=6.9 Hz, 2H), 2.50–2.34 (m, 6H); ^{13}C NMR: δ 159.8, 146.6, 128.6, 127.0, 126.1, 46.3, 36.5, 35.5, 28.5, 21.4; ESIHRMS: Calcd for $C_{18}H_{19}NONa$ $[M+Na]^+$ 288.1364. Found 288.1360.

4.1.6.26. 1-Chloro-1-nitro-4,4-diphenylcyclohexane (35). Trichloroisocyanuric acid (20.41 g, 88 mmol) was added in five portions at 5 min intervals to a well stirred two phase mixture of EtOAc/H_2O (1:1, 1534 mL), oxime **34** (4.60 g, 17.5 mmol), and $NaHCO_3$ (36.4 g, 434 mmol). The reaction mixture developed a distinct blue color after 20 min and stirring was continued at rt until the organic layer became colorless for 24 h. The reaction mixture was transferred into a separatory funnel and 0.2 M aq NaOH solution (230 mL) was added. The aqueous layer was extracted with EtOAc. The combined organic layer was washed with water and brine and concentrated to dryness. Purification by column chromatography (EtOAc/hexanes, 1:5) afforded **35** (1.54 g, 28%). IR (film): 1555, 698 cm^{-1}; ^{1}H NMR: δ 7.38–7.18 (m, 10 H), 2.67–2.43 (m, 8H); ^{13}C NMR: δ 129.0, 128.84, 128.77, 126.9, 126.63, 126.60, 126.52, 126.49, 126.44, 35.8, 35.2, 33.2; EIHRMS: Calcd for $C_{18}H_{18}NO_2Cl$ $[M]^+$ 315.1.26. Found 315.1025.

4.1.6.27. 1-Nitro-4,4-diphenylcyclohexane (36). Ten percent Pd/C (106 mg, 5%) and $NaBH_4$ (337 mg, 8.9 mmol) were added to a solution of **35** (2.00 g, 6.3 mmol) in EtOH (33 mL) at rt. The reaction was stirred for 1 h after which it was filtered and concentrated. The residue was diluted with water and the aqueous layer was extracted with EtOAc. The combined organic layer was washed with brine, dried and concentrated. Purification of the crude mixture by column chromatography (EtOAc/hexanes, 1:4) afforded **36** (850 mg, 48%). IR (film): 1543 cm^{-1}; ^{1}H NMR: δ 7.38–7.14 (m, 10H), 4.52–4.48 (m, 1H), 2.78–2.71 (m, 2H), 2.26–2.14 (m, 6H); ^{13}C NMR: δ 149.6, 144.0, 128.9, 128.6, 127.3, 126.4, 126.3, 126.2, 83.8, 34.0, 27.2; EIHRMS: Calcd for $C_{18}H_{19}NO_2$ $[M]^+$ 281.1415. Found 281.1414.

4.1.6.28. 4-(*tert*-Butyldimethylsiloxy)-1-(1′-nitro-4′,4′-diphenylcyclohexyl)butan-1-ol (37). To a stirred solution of **36** (166 mg, 0.59 mmol) in THF (1 mL) was added 0.025 M aqueous NaOH (0.87 mL) at rt and further stirred for 2 min. 4-(*tert*-Butyldimethylsiloxy)butan-1-al (107 mg, 0.53 mmol) was added followed by cetyl ammonium bromide (21 mg, 0.059 mmol) at rt. After stirring the reaction for 12 h at ambient temperature, the reaction was quenched with satd aq NH_4Cl solution (5 mL) and the aqueous layer was extracted with EtOAc. The organic layer was washed with water and brine and dried. Concentration and purification of the residue by column chromatography (EtOAc/hexanes, 1:9) afforded nitro alcohol **37** (0.142 g, 50%) as a colorless oil. ^{1}H NMR: δ 7.38–7.10 (m, 10H), 3.68–3.57 (m, 3H), 3.39 (d, J=4.8 Hz, 1H), 2.67–2.53 (m, 4H), 2.09–1.60 (m, 8H), 0.87 (s, 9H), 0.03 (s, 6H); ^{13}C NMR: δ 149.6, 144.0, 128.8, 128.4, 127.5, 126.2, 126.1, 126.0, 94.9, 76.4, 63.2, 45.3, 32.4, 29.1, 28.8, 27.5, 27.1, 26.0, 18.4, −5.3; ESIHRMS: Calcd for $C_{28}H_{41}NO_4SiK$ $[M+K]^+$ 522.2442. Found 522.2437. Anal. Calcd for $C_{28}H_{41}NO_4Si$: C, 69.52; H, 8.54. Found: C, 69.78; H, 8.45.

4.1.6.29. 4-(*tert*-Butyldimethylsiloxy)-1-(1′-nitro-4′,4′-diphenylcyclohexyl)butan-1-one (38). Following the general procedure for Swern oxidation, nitroalcohol **37** (629 mg, 1.3 mmol) provided ketone **38** (388 mg, 62%). IR (film) 1725, 1542 cm^{-1}; ^{1}H NMR: δ 7.34–7.12 (m, 10H), 3.54 (t, J=6.3 Hz, 2H), 2.62 (d, J=11.4 Hz, 4H), 2.53 (t, J=6.9 Hz, 2H), 2.16 (d, J=10.5 Hz, 4H), 1.73 (quint, J=6.0 Hz, 2H), 0.87 (s, 9H), 0.01 (s, 6H); ^{13}C NMR: δ 201.7, 148.3, 144.1, 129.0, 128.5, 127.1, 126.5, 126.2, 98.4, 61.4, 44.9, 32.4, 32.1, 28.3, 26.4, 26.0, 18.4, −5.2. Anal. Calcd for $C_{28}H_{39}NO_4Si$: C, 69.82; H, 8.16. Found C, 69.74; H, 8.25.

4.1.6.30. (1*R*)-4-(*tert*-Butyldimethylsiloxy)-1-(1′-nitro-4′,4′-diphenylcyclohexyl)butan-1-ol (39). Following the general procedure for CBS reduction, ketone **38** (563 mg, 1.0 mmol) afforded alcohol **39** (420 mg, 87%, 96% ee). $[\alpha]_D^{23}$ +9.0 (c 1.0); with spectral data matching those of the racemate (**37**).

4.1.6.31. (1*R*)-4-(*tert*-Butyldimethyl-silyloxy)-1-(1′-nitro-4′,4′-diphenylcyclohexyl)-1-diphenylphosphatoxy butane (40). Following general procedure for phosphorylation, alcohol **39** (104 mg, 0.21 mmol) afforded phosphate **40** (109 mg, 74%). ^{1}H NMR: δ 7.37–7.08 (m, 20H), 4.73 (m, 1H), 3.64–3.48 (m, 2H), 2.69–2.60 (m, 4H), 2.05–1.82 (m, 5H), 1.63–1.51 (m, 3H), 0.86 (s, 9H), 0.00 (s, 6H); ^{13}C NMR: δ 150.5, 149.3, 143.5, 129.9, 129.8, 129.0, 128.8, 128.4, 127.5, 127.3, 126.4, 126.2, 126.1, 126.0, 125.5, 120.3, 120.2, 120.1, 93.5, 93.4, 84.4, 84.3, 76.4, 63.2, 61.9, 45.0,

32.2, 32.1, 29.2, 28.7, 27.8, 27.7, 27.5, 27.2, 27.1, 26.0, 18.4, −5.2; ^{31}P NMR: δ −11.80; ESIHRMS: Calcd for $C_{40}H_{50}NO_7PSiNa$ $[M+Na]^+$ 738.2992. Found 738.2984.

4.1.6.32. (4*R*)-4-Diphenylphosphatoxy-4-(1′-nitro-4′, 4′-diphenylcyclohexyl)butan-1-ol (41). To a solution of **40** (100 mg, 0.15 mmol) in acetonitrile (6 mL) at rt was added aqueous solution of HF (49%, 0.15 mmol, 4 mL). The reaction was further stirred for 5 min and diluted with EtOAc. The organic layer was washed with water and brine and dried over Na_2SO_4. Concentration and purification of the residue by column chromatography (EtOAc/hexanes, 1:1) afforded alcohol **41** (55 mg, 63%, 94% ee). ^{1}H NMR: δ 7.35–7.06 (m, 20H), 4.76 (t, J=7.6 Hz, 1H), 3.54–3.47 (m, 2H), 2.69–2.61 (m, 4H), 2.03–1.55 (m, 8H); ^{13}C NMR: δ 149.2, 143.4, 129.9, 129.0, 128.4, 127.4, 126.4, 126.1, 125.6, 120.2, 120.1, 93.5, 93.4, 84.2, 84.1, 62.0, 45.0, 32.1, 28.4, 27.8, 27.7, 27.5, 27.4; ^{31}P NMR: δ −11.72; ESIHRMS: Calcd for $C_{34}H_{38}NO_7P$ $[M+H]^+$ 602.2308. Found 602.2335.

4.1.6.33. 2,2-Dibenzyl-1-(*tert*-butyldimethylsiloxy)-pent-4-ene (42). Alcohol **17** (0.50 g, 1.87 mmol) in DMF (2 mL) was added slowly to a stirred solution of TBDMSCl (0.338 g, 2.24 mmol) and imidazole (0.317 g, 4.6 mmol) in DMF (15 mL) at 0 °C under Ar. The resulting mixture was warmed to rt and stirred for 2 h. Water (15 mL) was added and the aqueous layer was extracted with hexane (3×15 mL). The combined organic layer was washed with water and brine and dried. Concentration and purification of the crude mixture by column chromatography (hexanes/EtOAc, 9:1) afforded **42** (0.60 g, 79%). ^{1}H NMR: δ 7.28–7.17 (m, 10H), 6.08–5.99 (m, 1H), 5.17–5.03 (m, 2H), 3.18 (s, 2H), 2.69 (ABq, J=13.2, 13.2 Hz, 4H), 1.93 (d, J=7.2 Hz, 2H), 1.00 (s, 9H), 0.06 (s, 6H); ^{13}C NMR: δ 138.7, 134.9, 131.0, 127.8, 126.0, 117.9, 65.5, 42.9, 40.4, 37.1, 26.1, −5.3; ESIHRMS: Calcd for $C_{25}H_{36}OSiNa$ $[M+Na]^+$ 403.2433. Found 403.2452.

4.1.6.34. 3-Benzyl-3-(*tert*-butyldimethylsiloxymethyl)-4-phenylbutanal (43). A solution of olefin (6.0 g, 15.8 mmol) in DCM (180 mL) cooled to −78 °C was bubbled O_3 until the solution turned light blue. On complete disappearance of the starting material, N_2 gas was bubbled through the reaction mixture for 10 min at −78 °C. The resulting mixture was treated with Me_2S (4.89 g, 79 mmol) at −78 °C and slowly warmed to rt. After stirring for 6 h at rt, it was concentrated and purified by column chromatography (hexanes/EtOAc, 9:1) to afford **43** (5.77 g, 96%). IR (film): 1718, 1085 cm^{-1}; ^{1}H NMR: δ 9.86 (br s, 1H), 7.33–7.21 (m, 10H), 3.42 (s, 2H), 2.92 (s, 4H), 2.23 (d, J=2.1 Hz, 2H), 1.04 (s, 9H), 0.14 (s, 6H); ^{13}C NMR δ 202.6, 137.7, 130.9, 128.2, 126.6, 65.5, 47.6, 43.7, 41.1, 26.1, 18.4, −5.2; ESIHRMS: Calcd for $C_{24}H_{34}NO_2SiNa$ $[M+Na]^+$ 405.2226. Found 405.2224.

4.1.6.35. 5-Benzyl-5-(*tert*-butyldimethylsilyloxymethyl)-2-methyl-2-nitro-6-phenylhexan-3-ol (44). To a stirred solution of **43** (70 mg, 0.18 mmol) and 2-nitropropane (0.77 g, 2.6 mmol) was added *t*-BuOK (0.77 g, 2.6 mmol) at 0 °C. After stirring for 12 h at rt the reaction was quenched with satd solution of NH_4Cl, diluted with water and the aqueous layer was extracted with EtOAc. Concentration and purification of the residue by column chromatography (EtOAc/hexanes, 3:7) afforded **44** (70 mg, 81%). IR (film) 3394, 1543, 1082 cm^{-1}. ^{1}H NMR: δ 7.32–7.12 (m, 10H), 4.42–4.39 (m, 1H), 4.13 (d, J=3.0 Hz, 1H), 3.56 (d, J=9.9 Hz, 1H), 3.41 (d, J=9.9 Hz, 1H), 2.86 (d, J=13.5 Hz, 1H), 2.73 (m, 2H), 2.63 (d, J=13.5 Hz, 1H), 1.51 (s, 3H), 1.49–1.39 (m, 2H), 1.40 (s, 3H), 0.93 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); ^{13}C NMR: δ 137.6, 137.4, 131.0, 130.9, 128.2, 128.1, 126.6, 126.5, 92.4, 71.9, 68.5, 43.8, 40.8, 37.5, 26.0, 23.0, 20.8, 0.16, −5.3; ESIHRMS: Calcd for $C_{27}H_{41}NO_4SiNa$ $[M+Na]^+$ 494.2703. Found 494.2709.

4.1.6.36. 2,2-Dibenzyl-1-(*tert*-butyldimethylsiloxy)-5-methyl-5-nitro-4-(diphenylphosphatoxy)hexane (45). I_2 (0.0812 g, 0.32 mmol) was added to a stirred solution of ethyldiphenylphosphite (0.08 g, 0.31 mmol) in dichloromethane (9 mL) at −30 to −20 °C under Ar. After 15 min this solution was added to a mixture of **44** (0.15 g, 0.32 mmol), pyridine (0.10 g, 1.28 mmol) in dichloromethane (15 mL) under Ar at −30 to −20 °C. The reaction mixture was allowed to warm to 0 °C, diluted with dichloromethane, subsequently washed with NH_4Cl, satd $Na_2S_2O_3$, brine and dried. Concentration and purification by column chromatography (hexanes/EtOAc, 4:1) afforded **45** (100 mg, 46%). IR (film): 1548, 1010, 956 cm^{-1}; ^{1}H NMR: δ 7.29–7.12 (m, 20H), 5.78 (t, J=9.0 Hz, 1H), 3.42 (d, J=9.9 Hz, 1H), 3.19 (d, J=9.9 Hz, 1H), 2.99 (s, 2H), 2.94 (d, J=13.5 Hz, 1H), 2.65 (d, J=13.5 Hz, 1H), 1.65 (s, 3H), 1.47–1.68 (m, 2H), 1.25 (s, 3H), 0.94 (s, 9H), 0.25 (s, 3H), 0.21 (s, 3H); ^{31}P NMR: δ −13.07; ^{13}C NMR: δ 156.4, 150.6, 150.5, 138.0, 137.9, 131.3, 129.9, 129.5, 128.1, 128.0, 126.3, 125.6, 125.5, 120.2, 120.1, 120.0, 115.6, 91.5, 82.0, 66.0, 41.6, 40.1, 39.5, 33.2, 33.1, 26.1, 24.3, 21.2, 18.3, −5.2, −5.3; ESIHRMS: Calcd for $C_{39}H_{50}NO_{7}$-SiPNa $[M+Na]^+$ 726.2992. Found 726.2986.

4.1.6.37. 6,6-Dibenzyl-4-(1-methyl-1-nitroethyl)-2-phenoxy-[1,3,2]dioxaphosphepane 2-oxide (46). Forty-nine percent aqueous HF solution (2 mL) was added to a solution of **45** (0.086 g, 0.08 mmol) in CH_3CN (2 mL) at 0 °C. The reaction mixture was stirred for 5 min at rt followed by quenching with water (5 mL) at rt. The aqueous layer was extracted with EtOAc, washed with brine, and dried. Concentration and purification by column chromatography (EtOAc/hexanes, 1:1) provided **46** (0.049 g, 70%). IR (film): 1546 cm^{-1}; ^{1}H NMR: δ 7.36–6.89 (m, 15H), 5.26–5.19 (m, 1H), 3.94 (d, J=9.6 Hz, 1H), 3.44 (d, J=13.5 Hz, 1H), 2.61–2.45 (m, 4H), 1.90 (dd, J=11.1, 10.8 Hz, 1H), 1.68 (s, 3H), 1.54 (s, 3H), 1.53–1.46 (m, 1H); ^{31}P NMR: δ −4.48; ^{13}C NMR: δ 135.8, 135.4, 131.2, 131.0, 130.5, 129.9, 128.7, 128.6, 128.6, 128.5, 127.1, 127.0, 125.6, 120.0, 120.0, 89.8, 89.7, 75.9, 75.8, 72.1, 43.5, 40.75, 40.73, 40.6, 38.4, 24.5, 20.3; ESIHRMS: Calcd for $C_{27}H_{30}NO_6PNa$ $[M+Na]^+$ 518.1708. Found 518.1689.

4.1.6.38. 2,2-Dibenzyl-1-(*tert*-butyldimethylsiloxy)-4-(diethylphosphatoxy)-5-methyl-5-nitrohexane (47). To a solution of **44** (0.370 g, 0.79 mmol), pyridine (0.312 g, 3.95 mmol) in dichloromethane (11 mL) at 10 °C was added diethylchlorophosphite (0.37 g, 2.37 mmol) and stirred for 30 min at rt. When the starting material was consumed, *t*-BuOOH (0.79 mL, 3.95 mmol) was added into the reaction

flask at 10 °C over 5 min and continued stirring for 20 min at rt. EtOAc (20 mL) was added and the organic layer was washed with 5% $Na_2S_2O_3$, and dried. Concentration and purification of the crude mixture by column chromatography (EtOAc/hexanes, 3:2) gave **47** (0.233 g, 58%). IR (film): 1549, 1031, 1004 cm^{-1}; ^1H NMR: δ 7.37–7.18 (m, 10H), 5.51 (t, J=9.0 Hz, 1H), 4.20–4.13 (m, 4H), 3.41 (d, J=9.9 Hz, 1H), 3.19 (d, J=9.9 Hz, 1H), 3.07 (d, J=13.5 Hz, 1H), 2.98 (m, 1H), 2.93 (m, 1H), 2.69 (d, J=13.5 Hz, 1H), 1.61 (s, 3H), 1.57–1.40 (m, 2H), 1.42 (s, 3H), 1.39–1.28 (m, 6H), 0.98 (s, 9H), 0.10 (s, 3H), 0.04 (s, 3H); ^{31}P NMR: δ −1.99; ^{13}C NMR: δ 138.1, 131.2, 131.0, 127.8, 126.1, 91.5, 79.9, 79.8, 65.7, 64.4, 64.3, 64.2, 41.5, 39.8, 39.2, 32.6, 32.5, 26.0, 24.4, 20.7, 18.2, 16.2, 16.1, −5.3, −5.4; ESIHRMS: Calcd for $C_{31}H_{50}NO_7SiPNa$ $[M+Na]^+$ 630.2992. Found 630.2987.

4.1.6.39. 2,2-Dibenzyl-4-(diethylphosphatoxy)-5-methyl-5-nitrohexanol (48). To a solution of **47** (0.18 g, 0.29 mmol) in acetonitrile (2 mL) was added aq HF (49%, 1.02 mL, 29 mmol) at rt. After stirring for 5 min at rt, water (4 mL) was added and the aqueous mixture was extracted with EtOAc. The organic layer was washed with water and brine and dried. Concentration and purification of the crude mixture by column chromatography (EtOAc/hexanes, 3:2) afforded **48** (82 mg, 58%). ^1H NMR: δ 7.29–7.18 (m, 10H), 5.56 (m, 1H), 4.09 (m, 2H), 3.98 (m, 2H), 3.50 (s, 2H), 2.94 (d, J=13.2, 1H), 2.90 (m, 2H), 2.54 (d, J=13.2 Hz, 1H), 1.76 (dd, J=15.3, 8.4 Hz, 1H), 1.58 (s, 3H), 1.58–1.48 (m, 1H), 1.42 (s, 3H), 1.32 (t, J=6.0 Hz, 3H), 1.22 (t, J=6.0 Hz, 3H); ^{31}P NMR: δ −2.09; ^{13}C NMR: δ 138.0, 137.9, 131.1, 131.0, 128.3, 128.2, 126.5, 126.4, 91.7, 79.8, 65.6, 64.7, 64.3, 41.7, 41.6, 41.4, 36.9, 24.3, 20.4, 16.2, 16.1; ESIHRMS: Calcd for $C_{25}H_{36}NO_7PNa$ $[M+Na]^+$ 516.2127. Found 516.2113.

4.1.7. Typical protocol for the radical cyclization.

4.1.7.1. (*S*)-1-Benzyl-2-isopropylpyrrolidine (49). To the solution of the radical precursor **11** (200 mg, 0.40 mmol) and AIBN (14 mg, 0.085 mmol) in deoxygenated benzene (30 mL) was added tributyltin hydride (0.173 mL, 0.643 mmol). The reaction mixture was heated to reflux for 30 h with addition of further AIBN (8 mg, 0.05 mmol) twice in 12 h intervals. The reaction mixture was then cooled to rt, 2 M HCl (12 mL) was added, and the biphasic mixture was stirred for 20 min. The organic layer was washed with aq 2 M HCl and the combined aqueous layer was washed with hexane, then basified to pH 11 with 15% NaOH and extracted with ethyl ether. The combined organic layer was washed with water and brine then dried. Concentration under reduced pressure followed by chromatographic purification afforded **49** (35 mg, 43%, 61% ee) as colorless oil. $[\alpha]_D^{23}$ −32.4 (c 1.0); ^1H NMR: δ 7.38–7.22 (m, 5H), 4.04 (d, J=13.2 Hz, 1H), 3.10 (d, J=13.2 Hz, 1H), 2.88 (m, 1H), 2.34 (m, 1H), 2.03 (m, 1H), 1.95 (m, 1H), 1.61 (m, 4H), 0.94 (s, 3H), 0.92 (s, 3H); ^{13}C NMR: δ 131.4, 129.9, 129.2, 127.9, 78.2, 71.6, 52.3, 29.7, 28.7, 26.1, 22.1, 21.1; ESIHRMS: Calcd for $C_{14}H_{22}N$ $[M+H]^+$ 204.1752. Found 204.1747.

4.1.7.2. (*S*)-1-Benzyl-2-isopropylpiperidine (50). Following the general procedure for radical cyclization, **12** (180 mg, 0.351 mmol) afforded **50** (31 mg, 41%, 60% ee) as colorless oil. $[\alpha]_D^{23}$ −23.7 (c 0.27); ^1H NMR: δ 7.39–7.19 (m, 5H), 4.10 (d, J=13.5 Hz, 1H), 3.09 (d, J=13.5 Hz, 1H), 2.81 (m, 1H), 2.26 (m, 1H), 2.00 (m, 1H), 1.92 (m, 1H), 1.73 (m, 1H), 1.60 (m, 2H), 1.42 (m, 1H), 1.23 (m, 2H), 0.94 (d, J=3.0 Hz, 3H), 0.91 (d, J=3.0 Hz, 3H); ^{13}C NMR: δ 129.0, 128.2, 126.6, 124.4, 77.4, 66.6, 56.6, 27.7, 24.9, 24.7, 23.6, 20.3, 16.1; ESIHRMS: Calcd for $C_{15}H_{24}N$ $[M+H]^+$ 218.1909. Found 218.1911.

4.1.7.3. (*S*)-1,4,4-Tribenzyl-2-isopropylpyrrolidine (51). Following the general procedure for radical cyclization, **24** (205 mg, 0.30 mmol) afforded **51** (51 mg, 44%, 60% ee) as colorless oil. $[\alpha]_D^{23}$ −24.4 (c 1.0); ^1H NMR: δ 7.35–7.00 (m, 15H), 3.96 (d, J=13.5 Hz, 1H), 2.90–2.75 (m, 3H), 2.66–2.62 (m, 3H), 2.20 (td, J=8.6, 4.5 Hz, 1H), 2.02–1.88 (m, 2H), 1.70 (dd, J=12.6, 8.6 Hz, 1H), 1.57 (dd, J=12.6, 9.0 Hz, 1H), 0.91 (d, J=6.9 Hz, 3H), 0.85 (d, J=7.2 Hz, 3H); ^{13}C NMR: δ 140.1, 139.3, 131.0, 131.0, 128.8, 128.2, 128.0, 127.8, 126.7, 126.0, 125.9, 69.1, 62.8, 58.0, 46.1, 44.0, 35.0, 30.4, 27.8, 20.3, 15.3; ESIHRMS: Calcd for $C_{28}H_{34}N$ $[M+H]^+$ 384.2691. Found 384.2691.

4.1.7.4. *N*-Benzyl-2-(3-methyl-2-butenyl)aniline (52). Following the general procedure for radical cyclization, **30** (409 mg, 0.62 mmol) afforded **52** (80 mg, 50%) as a colorless oil. ^1H NMR: δ 7.38–7.34 (m, 3H), 7.31–7.26 (m, 2H), 7.14–7.08 (m, 2H), 6.73–6.67 (m, 2H), 5.21 (t, J=6.9 Hz, 1H), 4.33 (s, 2H), 3.22 (d, J=6.9 Hz, 2H), 1.69 (s, 3H), 1.58 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 133.7, 130.5, 129.3 129.1, 128.6, 127.8, 127.3, 121.9, 117.5, 111.0, 48.6, 31.2, 25.7, 17.7; ESIHRMS: Calcd for $C_{18}H_{21}N$ $[M]^+$ 251.1674. Found 251.1670.

4.1.7.5. (7*S*)-1,1-Dimethyl-2-methylenepyrrolizidine (53). The general procedure for radical cyclization was followed but extraction method was changed. On complete consumption of **33** (144 mg, 0.32 mmol) the reaction mixture was cooled to rt, then 2 M HCl (12 mL) was added, and stirred for 20 min. The aqueous layer was washed with hexane, then basified to pH 11 with 15% aq NaOH and extracted with ethyl ether. The combined organic layer washed with water and 2 M HCl (12 mL) was added again. After stirring for 30 min, aqueous layer was separated and concentrated to give the pure HCl salt of pyrrolizidine **53** (39 mg, 64%, 60% ee). $[\alpha]_D^{23}$ −9.2 (c 1.0); ^1H NMR: δ 12.8 (br s, 1H), 5.08 (br s, 1H), 5.06 (br s, 1H), 4.51 (dd, J=14.1, 6.3 Hz, 1H), 3.90 (m, 2H), 3.42 (d, J=15.6 Hz, 1H), 2.84 (m, 1H), 2.05 (m, 3H), 1.61 (m, 1H), 1.33 (s, 3H), 1.17 (s, 3H); ^{13}C NMR: δ 108.9, 100.2, 76.9, 57.9, 56.2, 33.0, 28.8, 27.4, 25.2, 21.5; ESIHRMS: Calcd for $C_{10}H_{18}N$ $[M+H]^+$ 152.1439. Found 152.1439.

4.1.7.6. 2-(4′,4′-Diphenylcyclohexyl)-tetrahydrofuran (54) and (7*R*)-7-(4′,4′-diphenylcyclohexyl)-2-phenoxy-[1,3,2]dioxaphosphepane-2-oxide (55). To the mixture of **41** (158 mg, 0.26 mmol), AIBN (22 mg, 0.14 mmol), and tributyltin hydride (169 mg, 0.58 mmol) was added deoxygenated benzene (6.5 mL) and refluxed for 12 h. The reaction mixture was cooled, concentrated, and purified by column chromatography to provide tetrahydrofuran **54** (20 mg, 25%) and the cyclic phosphate **55** (68 mg, 52%). **54**: ^1H NMR: δ 7.38–7.16 (m, 10H), 3.81–3.79 (m, 1H), 3.67–3.65

(m, 1H), 3.40–3.35 (m, 2H), 2.72 (d, J=12.4 Hz, 1H), 1.97–1.80 (m, 5H), 1.59–0.98 (m, 6H); ^{13}C NMR: δ 151.3, 146.1, 128.5, 128.2, 128.1, 126.3, 125.6, 125.5, 83.8, 67.8, 46.1, 43.1, 36.3, 29.4, 26.6, 25.9, 25.4; ESIHRMS: Calcd for $C_{22}H_{26}ONa$ $[M+Na]^+$ 329.1881. Found 329.1886. **55**: ^{1}H NMR: δ 7.37–7.06 (m, 15H), 4.23–4.05 (m, 3H), 2.79–2.74 (m, 2H), 1.95–1.91 (m, 5H), 1.73–1.67 (m, 4H), 1.41–1.36 (m, 2H); ^{13}C NMR: δ 151.1, 144.8, 129.8, 128.7, 128.3, 128.0, 126.3, 125.8, 125.7, 125.1, 120.2, 83.0, 82.9, 68.9, 68.8, 45.9, 43.0, 36.3, 36.2, 31.8, 29.2, 25.5, 24.5; ^{31}P NMR: δ −2.92; ESIHRMS: Calcd for $C_{28}H_{31}O_4PNa$ $[M+Na]^+$ 485.1858. Found 485.1838.

4.1.7.7. 6,6-Dibenzyl-2-ethoxy-4-(1-methyl-1-nitroethyl)[1,3,2]dioxaphosphepane 2-oxide (56). In a one necked 25 mL flask fitted with a condenser, and a septum was placed nitrophosphate **48** (0.082 g, 0.177 mmol), tributyltin hydride (0.77 g, 0.27 mmol), and AIBN (0.012 g, 0.071 mmol). Degassed benzene (18 mL) was added to the reaction mixture, which was then heated to reflux in an oil bath preheated at 100 °C for 15 h. The reaction mixture was cooled to rt and concentrated. Chromatographic purification (EtOAc/hexanes, 3:7) provided cyclic phosphates **56** (44 mg, 67%). IR (film): 1026, 992 cm^{-1}; ^{1}H NMR: δ 7.32–7.20 (m, 8H), 6.94 (d, J=6.9 Hz, 2H), 4.50–4.46 (m, 1H), 4.19–4.09 (m, 2H), 3.82–3.77 (m, 2H), 3.26 (d, J=13.8 Hz, 1H), 2.64 (d, J=13.8 Hz, 1H), 2.58 (d, J=13.5, 1H), 2.48 (d, J=13.5 Hz, 1H), 1.87–1.77 (m, 2H), 1.51 (d, J=15.1 Hz, 1H), 1.29 (t, J=7.2 Hz, 3H), 0.97 (d, J=6.9 Hz, 3H), 0.94 (d, J=6.6 Hz, 3H); ^{31}P NMR: δ 2.71; ^{13}C NMR: δ 136.7, 136.2, 131.3, 130.7, 128.4, 126.8, 126.7, 77.9, 71.4, 64.2, 43.7, 41.0, 40.8, 40.4, 33.8, 33.7, 19.0, 17.4, 16.3; ESIHRMS: Calcd for $C_{23}H_{32}O_2PNa$ $[M+Na]^+$ 425.1775. Found 425.1773.

4.1.7.8. (*S*)-1-*p*-Toluenesulfonyl-2-isopropylpyrrolidine (57). Pyrrolidine **49**(15 mg, 0.074 mmol) was treated in EtOAc (10 mL) with 20% $Pd(OH)_2$/C (18 mg) under a H_2 atmosphere for 4 h. The reaction mixture was carefully filtered through Celite and residue was washed with EtOAc (10 mL). The filtrate was treated with diisopropylethylamine (0.1 mL, 0.57 mmol) and TsCl (45 mg, 0.24 mmol), then stirred overnight at rt. The reaction was quenched with satd aq $NaHCO_3$ and aqueous layer was extracted with EtOAc. The combined organic layer was washed with H_2O and brine then dried. After the evaporation, the residue was purified by silica gel chromatography. The sulfonamide **57** (9 mg, 45%) was obtained as a colorless solid, $[\alpha]_D^{23}$ −78.1 (c 0.9), lit.[14] $[\alpha]_D^{23}$ −91.3 (c 1.0).

4.1.7.9. *N*-*tert*-Butyloxycarbonyl *O*-(2-methyl-2-nitro-1-phenylpropyl) sulfamate (59). A solution of chlorosulfonyl isocyanate (0.8 mL, 9.1 mmol) in hexanes (8 mL) was added dropwise to a solution of 2-methylpropan-2-ol (675 mg, 9.1 mmol) in hexane (17 mL) and the solution was stirred at rt for 45 min. Then a solution of alcohol **58**[20] (1.2 g, 6.07 mmol) and triethylamine (1.35 mL, 9.7 mmol) in THF (20 mL) was added dropwise. After 2 h, the reaction was quenched with water and extracted with CH_2Cl_2. The organic layer was washed with brine, dried, and concentrated. Chromatographic purification (hexanes/EA from 90:10 to 70:30) afforded **59** (1.914 g, 84%) as a colorless oil. IR (neat): 3255, 2987, 1757, 1550, 1456, 1147, 923 cm^{-1}; ^{1}H NMR: δ 7.39 (s, 5H), 7.30 (br s, 1H), 6.18 (s, 1H), 1.70 (s, 3H), 1.45 (s, 3H), 1.42 (s, 9H); ^{13}C NMR: δ 148.6, 133.1, 129.9, 128.8, 128.0, 90.5, 87.3, 84.9, 27.9, 23.9, 20.2.

4.1.7.10. *N*-Allyl *O*-(2-methyl-2-nitro-1-phenylpropyl) sulfamate (60). To a solution of **59** (1.0 g, 2.7 mmol) and allyl bromide (10 mL) in acetonitrile (16 mL) was added dropwise 1,8-diazabicyclo[5.4.0]undec-7-ene (0.52 mL, 3.5 mmol) at rt. The reaction mixture was stirred overnight and quenched with a satd aq NH_4Cl. The aqueous layer was extracted twice with CH_2Cl_2 and the resulting organic layer was washed with brine, dried, and concentrated. The residue was purified by flash chromatography (hexanes/EA from 95:5 to 85:15) to afford *N*-allyl *N*-*tert*-butyloxycarbonyl *O*-(2-methyl-2-nitro-1-phenylpropyl) sulfamate (962 mg, 87%) as a white solid. mp 68–70 °C; IR (neat): 3069, 2983, 1742, 1550, 1401, 1191, 1149, 958, 857, 843 cm^{-1}; ^{1}H NMR: δ 7.35–7.40 (s, 5H), 6.13 (s, 1H), 5.76 (m, 1H), 5.22 (d, J=18.1 Hz, 1H), 5.18 (d, J=11.1 Hz, 1H), 3.97–4.07 (ABX, J=16.5 Hz, 4H), 1.70 (s, 3H), 1.48 (s, 9H), 1.44 (s, 3H); ^{13}C NMR: δ 150.1, 133.3, 132.5, 130.0, 128.8, 128.0, 118.6, 90.4, 87.2, 85.2, 51.4, 28.1, 24.1, 20.3. Anal. Calcd for $C_{18}H_{26}N_2O_7S$: C, 52.16; H, 6.32. Found: C, 52.07; H, 6.29. To a solution of this sulfamate (207 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) was added at 0 °C trifluoroacetic acid (0.39 mL, 5 mmol). The reaction mixture was stirred at rt for 2 h and quenched with a 1 N NaOH solution. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was washed with brine, dried, and concentrated. Chromatographic purification (hexanes/EA from 100:0 to 80: 10) afforded **60** (64 mg, 41%) as a colorless oil. IR (neat): 3317, 3067, 1647, 1547, 1456, 1349, 1180, 963 cm^{-1}; ^{1}H NMR: δ 7.40 (s, 5H), 5.96 (s, 1H), 5.66 (ddt, J=16.9, 10.5, 5.0 Hz, 1H), 5.11–5.18 (m, 2H), 4.51 (t, J=5.9 Hz, 1H), 3.57–3.43 (m, 2H), 1.67 (s, 3H), 1.47 (s, 3H); ^{13}C NMR: δ 133.9, 132.5, 129.9, 128.8, 128.1, 118.6, 90.8, 85.7, 46.5, 24.3, 19.9. Anal. Calcd for $C_{13}H_{18}N_2O_5S$: C, 49.67; H, 5.77. Found: C, 49.77; H, 5.74.

4.1.7.11. *N*-Allyl *N*-(4-methoxybenzyl) *O*-(2-methyl-2-nitro-1-phenylpropyl) *O*-phenyl phosphoramidate (61). To a solution of phenylphosphorodichloridite (2.87 mL, 20.0 mmol) and *N*,*N*-diisopropylethylamine (11.6 mL, 66.8 mmol) in THF (40 mL) was added dropwise, at −78 °C, a solution of alcohol **58**[20] (3.26 g, 16.7 mmol) in THF (15 mL). The reaction mixture was warmed up to rt and stirred for 1 h. Then the solution was cooled to −78 °C and a solution of allyl-(4-methoxybenzyl)amine (5.33 g, 30.1 mmol) in THF (10 mL) was added dropwise. The reaction mixture was warmed up to rt and stirred for 2 h. The solid was filtrated and washed with EtOAc. The filtrate was concentrated in vacuo to give the phosphoramidite as oil. The crude reaction mixture was dissolved in CH_2Cl_2 (80 mL) and a solution of *tert*-butyl hydroperoxide (5–6 M in decane, 8 mL, 40 mmol) was added at 0 °C and the reaction mixture was stirred at rt for 1 h. The reaction was quenched with satd aq $NaHCO_3$, extracted with CH_2Cl_2, washed with water and brine, dried, and concentrated. Chromatographic purification (CH_2Cl_2/EA from 100:0 to 90:10) afforded the phosphate **61** (5.55 g, 67%) as a viscous oil. IR (neat): 3066, 1612, 1591, 1545, 1491, 1266, 1210, 1025,

926 cm^{-1}; ^1H NMR: δ 7.39–7.10 (m, 20H, two dias), 6.97 (m, 2H, one dias), 6.91 (m, 2H, one dias), 6.82 (m, 2H, one dias), 6.74 (m, 2H, one dias), 5.95 (d, J=8.5 Hz, 1H, one dias), 5.93 (d, J=8.6 Hz, 1H, one dias), 5.66 (m, 1H, one dias), 5.30 (m, 1H, one dias), 5.19–4.95 (m, 4H, two dias), 4.20–4.08 (m, 3H, two dias), 3.96 (dd, J=14.8, 10.1 Hz, 1H, one dias), 3.79 (s, 3H, one dias), 3.77 (s, 3H, one dias), 3.52 (m, 2H), 3.45 (m, 1H), 3.26 (m, 1H), 1.62 (s, 3H, one dias), 1.57 (s, 3H, one dias), 1.45 (s, 3H, one dias), 1.38 (s, 3H, one dias); ^{13}C NMR: δ 159.2, 159.1, 151.0 (d, J_{PC}=7.0 Hz), 150.9 (d, J_{PC}=6.8 Hz), 135.1, 135.0, 134.0, 133.8, 130.1 (2C), 129.8, 129.7, 129.5, 129.2, 129.0 (d, J_{PC}=3.4 Hz,), 128.6, 128.3, 128.2, 128.1, 125.0, 124.8, 120.5 (d, J_{PC}=4.6 Hz), 120.3 (d, J_{PC}=4.9 Hz), 119.0, 118.9, 114.0, 113.9, 91.2 (d, J_{PC}=4.7 Hz), 91.1 (d, J_{PC}=4.7 Hz), 82.6 (d, J_{PC}=5.2 Hz), 82.5 (d, J_{PC}=5.1 Hz), 60.6, 55.5, 48.2 (d, J_{PC}=3.5 Hz), 48.1 (d, J_{PC}=3.7 Hz), 47.7 (d, J_{PC}=2.7 Hz), 47.4 (d, J_{PC}=2.7 Hz), 24.1, 23.6, 20.4, 20.0; ^{31}P NMR: δ 4.78, 2.39. Anal. Calcd for $C_{27}H_{31}N_2O_6P$: C, 63.52; H, 6.12. Found: C, 63.40; H, 6.14.

4.1.7.12. *N*-Allyl *O*-(2-methyl-2-nitro-1-phenylpropyl) *O*-phenyl phosphoramidate (62). To a solution of phosphoramidate **61** (two dias ratio 1.7:1) (1 g, 1.96 mmol) in CH_3CN/H_2O (6:1, 19 mL) was added at rt cerium ammonium nitrate (3.22 g, 7.84 mmol). The mixture was stirred at rt for 1 h and then diluted with CH_2Cl_2 and quenched with satd aq $NaHCO_3$. The organic layer was washed with brine, dried and concentrated. Chromatographic purification (CH_2Cl_2/EA from 100:0 to 90:10) afforded **62** as an unassigned mixture of two diastereomers (670 mg, 88%) as a white solid. IR (neat): 3223, 1593, 1545, 1491, 1261, 1212, 1041, 1025, 934 cm^{-1}; ^1H NMR: δ 7.40–7.08 (m, 18H, major and minor), 7.00 (d, J=8.7 Hz, 2H, major), 5.95 (d, J=8.5 Hz, 1H, major), 5.92 (d, J=8.6 Hz, 1H, minor), 5.81 (m, 1H, major), 5.56 (m, 1H, minor), 5.20 (dq, J=17.1, 1.6 Hz, 1H, major), 5.10 (dq, J=10.3, 1.3 Hz, 1H, major), 5.01 (dq, J=17.0, 1.4 Hz, 1H, minor), 4.97 (dq, J=10.2, 1.3 Hz, 1H, minor), 3.62–3.49 (m, 2H, major), 3.40–3.30 (m, 2H, minor), 2.98 (dt, J=12.1, 6.8 Hz, 1H, major), 2.82 (dt, J=12.6, 6.9 Hz, 1H, minor), 1.60 (s, 3H, minor), 1.59 (s, 3H, major), 1.44 (s, 3H, major), 1.41 (s, 3H, minor); ^{13}C NMR: δ 159.9 (d, J_{PC}=6.5 Hz, major and minor), 135.7 (d, J_{PC}=6.3 Hz, major), 135.4 (d, J_{PC}=6.5 Hz, minor), 135.1 (major and minor), 129.8, 129.7, 129.6, 129.3 (major and minor), 128.1 (minor), 128.6 (minor), 128.4 (major), 128.0 (major), 125.1 (minor), 125.0 (major), 120.44 (d, J_{PC}=4.5 Hz, minor), 120.42 (d, J_{PC}=4.1 Hz, minor), 116.0 (minor), 116.2 (major), 91.4 (d, J_{PC}=8.6 Hz, major), 91.2 (d, J_{PC}= 8.2 Hz, minor), 84.5 (d, J_{PC}=4.7 Hz, major), 82.4 (d, J_{PC}=4.8 Hz, minor), 44.2 (major), 44.0 (minor), 24.4 (major), 23.5 (minor), 20.5 (minor), 19.4 (major); ^{31}P NMR: δ 3.45 (major), 2.39 (minor). ESIMS *m/z*: 413 ($[M+Na]^+$, 100), 803 ($[2M+Na]^+$, 65). Anal. Calcd for $C_{19}H_{23}N_2O_5P$: C, 58.46; H, 5.94. Found: C, 58.64; H, 6.00.

4.1.7.13. Diethyl 2-(ethyl-2-nitro-1-phenylpropyl) phosphite (63). To a solution of diethylchlorophosphite (0.9 mL, 6.3 mmol) and *N*,*N*-diisopropylethylamine (1.74 mL, 10 mmol) in THF (10 mL) was added dropwise at −78 °C a solution of alcohol **58**[20] (975 mg, 5 mmol) in THF (3 mL). The reaction mixture was warmed up to rt and stirred for 1 h. The solid was filtered off and washed with EtOAc. The filtrate was concentrated to give an oil, which was purified by column chromatography on neutral Al_2O_3 (hexane/EA from 90:10) to afford the phosphite **63** (1.28 g, 80%) as colorless oil. IR (neat): 2980, 1545, 1455, 1025, 924 cm^{-1}; ^1H NMR: δ 7.36–7.31 (m, 5H), 5.63 (d, J=8.7 Hz 1H), 3.77–3.58 (m, 4H), 1.41 (s, 3H), 1.59 (s, 3H), 1.10 (t, J=7.0 Hz, 3H), 1.07 (t, J=7.0 Hz, 3H); ^{13}C NMR: δ 137.4, 128.9, 128.3, 91.9 (d, J_{PC}=3.9 Hz), 78.8 (d, J_{PC}=13.1 Hz), 59.0 (d, J_{PC}=12.2 Hz), 58.7 (d, J_{PC}=10.6 Hz), 23.6, 19.1, 16.9, 16.8; ^{31}P NMR: δ 140.9. Anal. Calcd for $C_{14}H_{22}NO_5S$: C, 53.33; H, 7.03. Found: C, 53.60; H, 7.07.

4.1.7.14. *N*-Allyl *O*,*O*-diethyl *O*-2-(ethyl-2-nitro-1-phenylpropyl) phosphorimidate (64). To a solution of sodium azide (2 equiv) and tetrabutylammonium bromide (0.05 equiv) in water was added allyl bromide. The solution was heated at 50–60 °C for 2 h with a vigorous stirring. The aqueous layer was washed twice with benzene (C_6H_6 or C_6D_6). The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered to afford a solution of allyl azide in benzene (~0.5 M in C_6H_6; ~1.33 M in C_6D_6,), free from allyl bromide as determined by GC, which was stored over molecular sieves for 24 h prior to use. The 1.33 M solution of allyl azide in C_6D_6 (3.3 mL, 4.38 mmol) was added to a solution of phosphite **63** (230 mg, 0.73 mmol) in C_6D_6 (5 mL) and the solution was heated at reflux for 4 h. The NMR of the crude reaction mixture indicated quantitative conversion of **63** to **64**. ^1H NMR (C_6D_6): δ 7.26–7.22 (m, 2H), 7.12–7.08 (m, 3H), 6.19 (m, 1H), 6.10 (d, J=9.0 Hz 1H), 5.62 (dq, J=16.9, 2.4 Hz, 1H), 5.21 (dq, J=10.0, 2.4 Hz, 1H), 4.09–3.70 (m, 6H), 1.49 (s, 3H), 1.12 (s, 3H), 1.05 (br t, J=7.0 Hz, 3H), 1.01 (dt, J=7.0, 1.0 Hz, 3H); ^{13}C NMR (C_6D_6): δ 141.6 (d, J_{PC}=15.5 Hz), 136.4, 128.6, 128.1, 127.9, 111.6, 90.7 (d, J_{PC}=8.2 Hz), 82.1 (d, J_{PC}=7.2 Hz), 62.9 (d, J_{PC}=9.2 Hz), 62.8 (d, J_{PC}=7.8 Hz), 45.6, 23.6, 19.1, 15.8; ^{31}P NMR: (C_6D_6) δ −3.69.

4.1.7.15. *N*-Allyl sulfamic acid (65). A solution of **60** (229 mg, 0.73 mmol) in benzene (36 mL) was degassed by sparging with nitrogen for 40 min. Bu_3SnH (289 μL, 1.17 mmol) and AIBN (48 mg, 0.31 mmol) were added and the solution was heated at reflux for 6 h. Then, Bu_3SnH (96 μL, 0.39 mmol) and AIBN (18 mg, 0.11 mmol) were added and the solution was heated for 3 h. The solvent was evaporated and CH_2Cl_2 and water were added. The organic layer was concentrated but contained only thin residues. The aqueous layer was evaporated to give a gum (90 mg), which was washed with CH_3CN and hexanes to give **65** (80 mg, ~48%) contaminated by some tin residues. ^1H NMR: δ 5.94 (m, 1H), 5.23 (d, J=17.1 Hz, 1H), 5.08 (d, J=10.0 Hz, 1H), 3.60 (d, J=5.2 Hz, 2H); ^{13}C NMR: δ 135.1, 115.1, 46.2; ESIMS *m/z*: 136 (100).

4.1.7.16. *N*-Allyl *O*-(1,1-dimethyl-2-phenylethyl) *O*-phenyl phosphoramidate (66), *N*-allyl *O*-(2-methyl-1-phenylpropyl) *O*-phenyl phosphoramidate (67), and 7,7-dimethyl-2-phenoxy-8-phenyl-[1,3,2]oxazaphosphocane 2-oxide (68). A solution of **62** (195 mg, 0.5 mmol), AIBN (33 mg, 0.20 mmol), and Bu_3SnH (0.2 mL, 0.75 mmol) in degassed benzene (25 mL) was heated at reflux for 6 h. Then AIBN (8 mg, 0.05 mmol) and Bu_3SnH (50 μL,

0.18 mmol) were added and the mixture was heated for a further 15 h. The reaction mixture was concentrated and the residue was purified by column chromatography (CH_2Cl_2/EA from 100:0 to 70:30) to afford by order of elution **67** (12 mg, 7%), **66** (73 mg, 42%), and **68** (14 mg, 8%). Compound **66**: white solid. mp 40–41 °C. IR (neat): 3220, 1593, 1545, 1491, 1261, 1212, 1041, 1025, 934 cm^{-1}; ^1H NMR: δ 7.39–7.10 (m, 3H), 5.77 (m, 1H), 5.13 (dq, J=17.1, 1.5 Hz, 1H), 5.05 (dq, J=11.7, 1.4 Hz, 1H), 3.50 (m, 2H), 2.93–3.05 (m, 2H), 1.54 (s, 3H), 1.52 (s, 3H); ^{13}C NMR: δ 151.5 (d, J_{PC}=6.9 Hz), 137.2, 131.0 (d, J_{PC}=6.9 Hz), 131.0, 129.7, 128.4, 126.8, 124.7, 120.7 (d, J_{PC}=4.6 Hz), 115.8, 84.9 (d, J_{PC}=7.4 Hz), 49.5 (d, J_{PC}=6.4 Hz), 44.3, 28.0, 27.5; ^{31}P NMR: δ −0.18. Anal. Calcd for $C_{19}H_{22}NO_3P$: C, 66.07; H, 7.00. Found: C, 66.19; H, 7.02. Compound **67**: colorless oil. ^1H NMR: δ 7.37–6.97 (m, 20H, two dias), 5.81 (m, 1H, one dias), 5.47 (m, 1H, one dias), 5.23–5.03 (m, 4H, two dias), 4.91 (m, 1H, one dias), 3.58 (m, 2H, one dias), 3.35 (m, 1H, one dias), 3.17 (m, 1H, one dias), 2.17–2.07 (m, 2×1H, two dias), 1.03 (d, J=6.8 Hz, 3H, one dias), 0.93 (d, J=6.8 Hz, 3H, one dias), 0.83 (d, J=6.8 Hz, 3H, one dias), 0.74 (d, J=6.8 Hz, 3H, one dias); ^{13}C NMR: δ 151.3 (d, J_{PC}=6.7 Hz), 151.2 (d, J_{PC}=6.6 Hz), 139.9, 139.7, 136.0 (d, J_{PC}=6.4 Hz), 135.7 (d, J_{PC}=7.0 Hz), 129.8, 129.7, 128.5, 128.3 (2C), 128.1, 124.9, 124.6, 120.8 (d, J_{PC}=4.6 Hz), 120.3 (d, J_{PC}=4.8 Hz), 116.1, 115.9, 85.7 (d, J_{PC}=6.7 Hz), 85.2 (d, J_{PC}=5.4 Hz), 44.3, 44.1, 35.2 (d, J_{PC}=6.4 Hz), 35.1 (d, J_{PC}=6.1 Hz), 18.8 (2C), 18.6, 18.5; ^{31}P NMR: δ 3.82, 3.70; HRMS: Calcd for $C_{19}H_{24}NO_3NaP$ $[M+Na]^+$ 368.1392. Found 368.1397. Compound **68**: white solid. mp 132 °C; IR (neat): 3222, 2963, 1592, 1491, 1250, 1214, 936 cm^{-1}; ^1H NMR: δ 7.33–7.10 (m, 10H), 5.25 (d, J=11.8 Hz, 1H), 3.60 (br s, 1H), 3.15–3.10 (m, 1H), 3.05–2.95 (m, 1H), 2.00–1.93 (m, 1H), 1.90–1.60 (m, 3H), 0.82 (s, 3H), 0.80 (s, 3H); ^{13}C NMR: δ 151.4 (d, J_{PC}=6.0 Hz), 138.3, 129.8, 128.1, 127.9, 127.8, 124.8, 120.7 (d, J_{PC}=4.25 Hz), 84.5 (d, J_{PC}=3.6 Hz), 43.8, 41.5, 38.7 (d, J_{PC}=3.8 Hz), 26.7, 24.5, 21.1; ^{31}P NMR: δ 5.16; HRMS: Calcd for $C_{19}H_{24}NO_3P$ $[M+Na]^+$ 368.1392. Found 368.1388.

4.1.7.17. *N*-Allyl diethyl phosphoramidate (69), *N*-allyl *O*-ethyl *O*-(2-methyl-2-nitro-1-phenylpropyl) phosphoramidate (70), and *N*-allyl *O*-ethyl ester *O*-(2-methyl-1-phenylpropyl) phosphoramidate (71). The phosphorimidate **64** was prepared by reaction of **63** (450 mg, 1.4 mmol) and a 0.5 N solution of allyl azide in C_6H_6 (11.2 mL, 5.6 mmol) as described above. Benzene (60 mL) was added to the solution of **64** and the resulting solution was degassed for 30 min. Then AIBN (92 mg, 0.56 mmol) and Bu_3SnH (1.48 mL, 5.6 mmol) were added and the mixture heated at reflux for 10 h. The reaction mixture was concentrated and the residue was purified by column chromatography (CH_2Cl_2/EA from 100:0 to 50:50) to afford by order of elution **70** (30 mg, 6%), **71** (22 mg, 5%), and **69** (120 mg, 40%). Compound **69**: IR (neat): 3227, 3086, 2980, 1645, 1445, 1233, 1034, 965 cm^{-1}; ^1H NMR: δ 5.85 (m, 1H), 5.20 (dq, J=17.0, 1.6 Hz, 1H), 5.08 (dq, J=10.4, 1.6 Hz, 1H), 4.09–3.99 (m, 4H), 3.51 (m, 2H), 1.30 (t, J=7.0 Hz, 6H); ^{13}C NMR: δ 136.3 (d, J_{PC}=6.1 Hz), 115.6, 62.5 (d, J_{PC}=5.1 Hz), 44.0, 16.4 (d, J_{PC}=7.0 Hz); ^{31}P NMR: δ 9.40; HRMS: Calcd for $C_7H_{16}NO_3NaP$ $[M+Na]^+$ 216.0766. Found 216.0758. **70**: ^1H NMR: δ 7.38–7.35 (m, 10H, two dias), 5.85 (d, J=8.6 Hz, 1H, one dias), 5.81 (d, J=8.5 Hz, 1H, one dias), 5.82 (m, 1H, one dias), 5.61 (m, 1H, one dias), 5.19 (dq, J=17.0, 1.7 Hz, 1H, one dias), 5.10 (dq, J=10.1, 1.5 Hz, 1H, one dias), 5.03 (dq, J=17.2, 1.4 Hz, 1H, one dias), 4.98 (dq, J=10.4, 1.5 Hz, 1H, one dias), 4.05–3.80 (m, 4H, two dias), 3.52–3.38 (m, 2H, two dias), 3.38–3.20 (m, 2H, two dias), 1.64 (s, 3H, one dias), 1.62 (s, 3H, one dias), 1.45 (s, 3H, one dias), 1.44 (s, 3H, one dias), 1.26 (t, J=7.0 Hz, 3H, one dias), 1.12 (t, J=7.0 Hz, 3H, one dias); ^{13}C NMR: δ 136.1 (d, J_{PC}=6.4 Hz), 135.9 (d, J_{PC}=6.7 Hz), 135.6, 135.5, 129.5, 129.4, 128.6, 128.5, 128.2, 128.1, 115.9, 115.7, 91.4 (d, J_{PC}=8.6 Hz), 91.3 (d, J_{PC}=8.3 Hz), 82.1 (d, J_{PC}=4.9 Hz), 82.0 (d, J_{PC}=5.0 Hz), 63.2 (d, J_{PC}=5.4 Hz), 63.0 (d, J_{PC}=5.4 Hz), 44.0, 43.9, 24.1, 23.9, 19.6, 19.4, 16.3, 16.2; ^{31}P NMR: δ 8.44, 7.46; HRMS: Calcd for $C_{15}H_{23}N_2O_5NaP$ $[M+Na]^+$ 365.1243. Found 365.1238. Compound **71**: slightly yellow oil. ^1H NMR: δ 7.33–7.25 (m, 10H, two dias), 5.84 (m, 1H, one dias), 5.50 (m, 1H, one dias), 5.18 (dq, J=17.2, 1.6 Hz, 1H, one dias), 5.07 (dq, J=10.3, 1.3 Hz, 1H, one dias), 4.99–4.88 (m, 4H, two dias), 4.08 (m, 2H, one dias), 3.81 (m, 2H, one dias), 3.48 (m, 2H, one dias), 3.17 (m, 1H, one dias), 3.08 (m, 1H, one dias), 2.16–2.05 (m, 2H, two dias), 1.31 (t, J=7.1 Hz, 3H, one dias), 1.09 (t, J=7.1 Hz, 3H, one dias), 1.05 (d, J=6.7 Hz, 3H, one dias), 1.01 (d, J=6.6 Hz, 3H, one dias), 0.79 (d, J=6.7 Hz, 3H, one dias), 0.78 (d, J=6.7 Hz, 3H, one dias); ^{13}C NMR: δ 140.2, 136.5 (d, J_{PC}=7.0 Hz), 136.1 (d, J_{PC}=7.0 Hz), 128.4, 128.2, 128.0, 127.4, 127.3, 115.7, 115.5, 84.8 (d, J_{PC}=6.3 Hz), 84.4 (d, J_{PC}=5.2 Hz), 62.6 (d, J_{PC}=5.2 Hz), 62.5 (d, J_{PC}=5.3 Hz), 44.1, 43.9, 35.2 (d, J_{PC}=7.1 Hz), 35.1 (d, J_{PC}=7.1 Hz), 19.0, 18.8, 18.6, 16.5 (d, J_{PC}=7.1 Hz, one dias), 16.2 (d, J_{PC}=7.1 Hz, one dias); ^{31}P NMR: δ 8.75, 8.63; HRMS: Calcd for $C_{15}H_{24}NO_3NaP$ $[M+Na]^+$ 320.1392. Found 320.1403.

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