Supporting Information for
Stereochemical Memory Effects in Alkene Radical Cation – Anion Contact Ion Pairs: Effect of
Substituents, and Models for Diastereoselectivity¹

David Crich and Krishnakumar Ranganathan*

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

	Page
<hr/>	
Substrate Preparation	
Discussion of Substrate Preparation and Configurational Assignment	S-5
Discussion of Configurational Assignment of Products from Radical Reactions	S-14
General Experimental	S-15
General Procedure A. Boc Protection.	S-15
General Procedure B. Henry Reaction.	S-16
General Procedure C. Swern Oxidation.	S-16
General Procedure D. Alkylation α - to a Nitroketone.	S-16
General Procedure E. Reduction of Nitroketones with Tetrabutylammonium Borohydride.	S-17
General Procedure F. Oxazaborolidine-Mediated Reduction of Nitroketones.	S-17
General Procedure G. Phosphorylation of Nitro Alcohols with Ethyl Diphenyl Phosphite.	S-18
General Procedure H. Phosphorylation of Nitro Alcohols with Diphenyl Chlorophosphate.	S-18
General Procedure I. Removal of Boc Groups with Trimethylsilyl Trifluoromethanesulfonate.	S-18
General Procedure J. Removal of Boc Groups with Trifluoroacetic Acid.	S-19
4-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]aminobutanal (B).	S-19
6-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-3-hydroxy-2-methyl-2-nitrohexane (C).	S-20

6-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2-methyl-2-nitro-3-hexanone (D).	S-20
6-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2,4-dimethyl-2-nitro-3-hexanone (E).	S-20
6-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2,4-dimethyl-2-nitro-3-hexanol (<i>syn/anti</i> - F).	S-20
<i>anti</i> -6-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2,4-dimethyl-2-nitro-3-(diphenylphosphatoxy)hexane (<i>anti</i> - G).	S-21
<i>syn</i> -6-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2,4-dimethyl-2-nitro-3-(diphenylphosphatoxy)hexane (<i>syn</i> - G).	S-21
<i>anti</i> -6-(Benzylamino)-2,4-dimethyl-2-nitro-3-(diphenylphosphatoxy)hexane (<i>anti</i> - I).	S-21
<i>syn</i> -6-(Benzylamino)-2,4-dimethyl-2-nitro-3-(diphenylphosphatoxy)hexane (<i>syn</i> - I).	S-22
4(<i>R</i>)-5-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-4-methyl-1-pentene (H).	S-22
3(<i>R</i>)-4-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-3-methyl-1-butanal (I).	S-23
5(<i>R</i>),3(<i>R</i>)-6-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2,5-dimethyl-2-nitro-3-hexanol (<i>anti</i> - J).	S-23
5(<i>R</i>),3(<i>S</i>)-6-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2,5-dimethyl-2-nitro-3-hexanol (<i>syn</i> - J).	S-24
5(<i>R</i>)-6-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2,5-dimethyl-2-nitro-3-hexanone (K).	S-24
5(<i>R</i>),3(<i>R</i>)-6-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2,5-dimethyl-2-nitro-3-(diphenylphosphatoxy)hexane (<i>anti</i> - L).	S-24
5(<i>R</i>),3(<i>S</i>)-6-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2,5-dimethyl-2-nitro-3-(diphenylphosphatoxy)hexane (<i>syn</i> - L).	S-24
5(<i>R</i>),3(<i>R</i>)-6-Benzylamino-2,5-dimethyl-2-nitro-3-(diphenylphosphatoxy)hexane (<i>anti</i> - 2).	S-25
5(<i>R</i>),3(<i>S</i>)-6-Benzylamino-2,5-dimethyl-2-nitro-3-(diphenylphosphatoxy)hexane (<i>syn</i> - 2).	S-25
Methyl 4(<i>S</i>)-[<i>N</i> -benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]aminopentanoate (M).	S-25
4(<i>S</i>)-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]aminopentanal (N).	S-26
3(<i>R</i>),6(<i>S</i>)-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2-methyl-2-nitro-3-heptanol. (<i>anti</i> - O).	S-26
3(<i>S</i>),6(<i>S</i>)-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2-methyl-2-nitro-3-heptanol. (<i>syn</i> - O).	S-27
6(<i>S</i>)-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2-methyl-2-nitro-3-heptanone (P).	S-27
3(<i>R</i>),6(<i>S</i>)-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2-methyl-2-nitro-3-(diphenylphosphatoxy)heptane (<i>anti</i> - Q).	S-27
3(<i>S</i>),6(<i>S</i>)-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2-methyl-2-nitro-3-(diphenylphosphatoxy)heptane (<i>syn</i> - Q).	S-28

3(<i>R</i>),6(<i>S</i>)-Benzylamino-2-methyl-2-nitro-3-(diphenylphosphatoxy)heptane (<i>anti</i> - 3).	S-28
3(<i>S</i>),6(<i>S</i>)-Benzylamino-2-methyl-2-nitro-3-(diphenylphosphatoxy)heptane (<i>syn</i> - 3).	S-28
(4 <i>R</i>),(5 <i>R</i>)-6-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2,4,5-trimethyl-2-nitro-3-hexanone (<i>syn</i> - R).	S-29
3(<i>R</i>),4(<i>R</i>),(5 <i>R</i>)-6-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2,4,5-trimethyl-2-nitro-3-hexanol and 3(<i>S</i>),4(<i>R</i>),(5 <i>R</i>)-6-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]-amino-2,4,5-trimethyl-2-nitro-3-hexanol (<i>anti</i> , <i>syn</i> - and <i>syn</i> , <i>syn</i> - S).	S-29
3(<i>R</i>),4(<i>R</i>),(5 <i>R</i>)-6-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2,4,5-trimethyl-2-nitro-3-(diphenylphosphatoxy)hexane and 3(<i>S</i>),4(<i>R</i>),(5 <i>R</i>)-6-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2,4,5-trimethyl-2-nitro-3-(diphenylphosphatoxy)hexane (<i>anti</i> , <i>syn</i> - and <i>syn</i> , <i>syn</i> - T).	S-29
3(<i>R</i>),4(<i>R</i>),(5 <i>R</i>)-6-Benzylamino-2,4,5-trimethyl-2-nitro-3-(diphenylphosphatoxy)hexane (<i>anti</i> , <i>syn</i> - 4).	S-30
3(<i>S</i>),4(<i>R</i>),(5 <i>R</i>)-6-Benzylamino-2,4,5-trimethyl-2-nitro-3-(diphenylphosphatoxy)hexane (<i>syn</i> , <i>syn</i> - 4).	S-30
<i>trans</i> - <i>N</i> -Benzyl-3,4-dimethylpyrrolidin-2-one (<i>trans</i> - U).	S-31
4(<i>R</i>),6(<i>S</i>)-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2,4-dimethyl-2-nitro-3-heptanone (<i>syn</i> - V).	S-31
4(<i>R</i>),3(<i>R</i>),6(<i>S</i>)-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2,4-dimethyl-2-nitro-3-heptanol and 4(<i>S</i>),3(<i>R</i>),6(<i>S</i>)-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2,4-dimethyl-2-nitro-3-heptanol (<i>anti</i> , <i>syn</i> - and <i>syn</i> , <i>syn</i> - W).	S-31
4(<i>R</i>),3(<i>R</i>),6(<i>S</i>)-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2,4-dimethyl-2-nitro-3-(diphenylphosphatoxy)heptane (<i>anti</i> , <i>syn</i> - X).	S-32
4(<i>S</i>),3(<i>R</i>),6(<i>S</i>)-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-2,4-dimethyl-2-nitro-3-(diphenylphosphatoxy)heptane (<i>syn</i> , <i>syn</i> - X).	S-32
4(<i>S</i>),3(<i>R</i>),6(<i>S</i>)-Benzylamino-2,4-dimethyl-2-nitro-3-(diphenylphosphatoxy)heptane (<i>anti</i> , <i>syn</i> - 5).	S-33
4(<i>S</i>),3(<i>S</i>),6(<i>S</i>)-Benzylamino-2,4-dimethyl-2-nitro-3-(diphenylphosphatoxy)heptane (<i>syn</i> , <i>syn</i> - 5).	S-33
<i>cis</i> - <i>N</i> -Benzyl-3,5-dimethyl-2-pyrrolidinone (<i>cis</i> - Y).	S-33
<i>cis</i> -Dimethyl-2-pyrrolidinone (<i>cis</i> - Z).	S-34
3(<i>S</i>),4(<i>S</i>)-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-3-methyl-pentanal (Ab)	S-34
3(<i>S</i>),5(<i>S</i>),6(<i>S</i>)-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-3-hydroxy-2,5-dimethyl-2-nitroheptane (<i>anti</i> , <i>anti</i> - Ac).	S-35
3(<i>R</i>),5(<i>S</i>),6(<i>S</i>)-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butyloxycarbonyl)]amino-3-hydroxy-2,5-dimethyl-2-nitroheptane (<i>syn</i> , <i>anti</i> - Ac).	S-35

5(<i>S</i>),6(<i>S</i>)-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butoxycarbonyl)]amino-2,5-dimethyl-2-nitro-3-heptanone (<i>anti</i> - Ad).	S-36
--	------

5(<i>S</i>),3(<i>S</i>),6(<i>S</i>)-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butoxycarbonyl)]amino-2,5-dimethyl-2-nitro-3-(diphenylphosphatoxy)heptane (<i>anti</i> , <i>anti</i> - Ae).	S-36
---	------

5(<i>S</i>),3(<i>R</i>),6(<i>S</i>)-[<i>N</i> -Benzyl- <i>N</i> -(<i>tert</i> -butoxycarbonyl)]amino-2,5-dimethyl-2-nitro-3-(diphenylphosphatoxy)heptane (<i>syn</i> , <i>anti</i> - Ae).	S-36
--	------

5(<i>S</i>),3(<i>S</i>),6(<i>S</i>)-Benzylamino-2,5-dimethyl-2-nitro-3-(diphenylphosphatoxy)heptane (<i>anti</i> , <i>anti</i> - 6).	S-37
---	------

5(<i>S</i>),3(<i>R</i>),6(<i>S</i>)-Benzylamino-2,5-dimethyl-2-nitro-3-(diphenylphosphatoxy)heptane (<i>syn</i> , <i>anti</i> - 6).	S-37
--	------

General Procedure for Radical Ionic Cyclizations	S-37
---	------

<i>trans</i> -(<i>N</i> -Benzyl)-2-isopropyl-3-methylpyrrolidine (<i>trans</i> - 7).	S-38
--	------

<i>cis</i> -(<i>N</i> -Benzyl)-2-isopropyl-3-methylpyrrolidine (<i>cis</i> - 7).	S-38
--	------

<i>cis</i> -(<i>N</i> -Benzyl)-2-isopropyl-4-methylpyrrolidine (<i>cis</i> - 8).	S-38
--	------

<i>trans</i> -(<i>N</i> -Benzyl)-2-isopropyl-4-methylpyrrolidine (<i>trans</i> - 8).	S-39
--	------

<i>cis</i> -(<i>N</i> -Benzyl)-2-isopropyl-5-methylpyrrolidine (<i>cis</i> - 9).	S-39
--	------

<i>trans</i> -(<i>N</i> -Benzyl)-2-isopropyl-5-methylpyrrolidine (<i>trans</i> - 9).	S-39
--	------

3(<i>S</i>),10a(<i>S</i>)-3,10,10-Trimethyl-1,2,3,5,10,10a-hexahydropyrrolo[1,2- <i>b</i>]isoquinoline (10).	S-40
--	------

2,3- <i>cis</i> -3,4- <i>trans</i> -(<i>N</i> -Benzyl)-2-isopropyl-3,4-dimethylpyrrolidine (<i>cis</i> , <i>trans</i> - 11).	S-40
--	------

2,3- <i>trans</i> -3,4- <i>trans</i> -(<i>N</i> -Benzyl)-2-isopropyl-3,4-dimethylpyrrolidine (<i>trans</i> , <i>trans</i> - 11).	S-40
--	------

2,3- <i>cis</i> -3,5- <i>cis</i> -(<i>N</i> -Benzyl)-2-isopropyl-3,5-dimethylpyrrolidine (<i>cis</i> , <i>cis</i> - 12).	S-41
--	------

2,3- <i>trans</i> -3,5- <i>cis</i> -(<i>N</i> -Benzyl)-2-isopropyl-3,5-dimethylpyrrolidine (<i>trans</i> , <i>cis</i> - 12).	S-41
--	------

2,4- <i>cis</i> -4,5- <i>cis</i> -(<i>N</i> -Benzyl)-2-isopropyl-4,5-dimethylpyrrolidine and (<i>cis</i> , <i>cis</i> - 13).	S-41
--	------

2,4- <i>trans</i> -4,5- <i>cis</i> -(<i>N</i> -Benzyl)-2-isopropyl-4,5-dimethylpyrrolidine (<i>trans</i> , <i>cis</i> - 13).	S-42
--	------

2(<i>S</i>),3(<i>S</i>),10a(<i>S</i>)-2,3,10,10-Tetramethyl-1,2,3,5,10,10a-hexahydropyrrolo[1,2- <i>b</i>]isoquinoline (14).	S-42
--	------

References and Footnotes	S-43
---------------------------------	------

Copies of Spectra

<i>anti</i> - 1	S-45	Ab	S-66
<i>syn</i> - 1	S-46	<i>anti,anti</i> - Ac	S-67
I	S-47	<i>syn,anti</i> - Ac	S-68
<i>anti</i> - 2	S-48	Ad	S-69
<i>syn</i> - 2	S-49	<i>anti,anti</i> - Ae	S-70
N	S-50	<i>syn,anti</i> - Ae	S-71
<i>anti</i> - 3	S-51	<i>anti,anti</i> - 6	S-72
<i>syn</i> - 3	S-52	<i>syn,anti</i> - 6	S-73
<i>syn</i> - R	S-53	<i>trans</i> - 7	S-74
<i>anti, syn</i> - and <i>syn, syn</i> - S	S-54	<i>cis</i> - 8	S-75
<i>anti, syn</i> - and <i>syn, syn</i> - T	S-55	<i>trans</i> - 8	S-76
<i>anti, syn</i> - 4	S-56	<i>cis</i> - 9	S-77
<i>syn, syn</i> - 4	S-57	<i>trans</i> - 9	S-78
U	S-58	10	S-79
<i>syn</i> - V	S-59	<i>cis, trans</i> - 11	S-80
<i>anti, syn</i> - and <i>syn, syn</i> - W	S-60	<i>trans, trans</i> - 11	S-81
<i>anti, syn</i> - X	S-61	<i>cis, cis</i> - 12	S-82
<i>syn, syn</i> - X	S-62	<i>trans, cis</i> - 12	S-83
<i>anti, syn</i> - 5	S-63	<i>cis, cis</i> - 13	S-84
<i>syn, syn</i> - 5	S-64	<i>trans, cis</i> - 13	S-85
<i>cis</i> - Y	S-65	14	S-86

Discussion of Substrate Preparation and Assignment of Configuration

An initial pair of diastereomeric substrates bearing a methyl group adjacent to the anticipated alkene radical cation was prepared from the known alcohol **A**² which we obtained in a straightforward manner by

opening of γ -butyrolactone with benzylamine followed by reduction with lithium aluminum hydride and standard Boc protection. Henry reaction of the aldehyde **B** derived from **1** afforded the adduct **C** which, after Swern oxidation to **D**, underwent alkylation to give **E**. Reduction of **E** to the desired diastereomeric alcohols **F** was complicated by retro-Henry fragmentation in protic solvents but could be accomplished smoothly with tetrabutylammonium borohydride in dichloromethane when an inseparable 1:1 mixture of *syn*- and *anti*-**F** was obtained. Phosphorylation of this pair of highly sterically congested alcohols was best achieved with diphenylphosphoryl iodide, generated in situ from ethyl diphenylphosphite and iodine.³ The diastereomeric phosphates **G** were conveniently separated by chromatography at this stage and then treated separately with trimethylsilyl triflate in the presence of 2,6-lutidine to effect cleavage of the Boc group, so giving the desired diastereomers, *syn*- and *anti*-**1** (Scheme 1).⁴

Scheme 1. Preparation of *syn*- and *anti*-**1**

The presence of rotamers in the carbamate group of isomers **G** complicated configurational assignment, but this was readily achieved at the level of the amines **1**. Fortuitously, both isomers of **1** exhibited $^3J_{\text{H3,H4}}$

coupling of ~ 0 Hz indicating orthogonality of the C3-H3 and C4-H4 bonds in the predominant conformation.⁵ Together with NOESY data (Fig. 1), this absence of coupling was sufficient for the assignment of relative stereochemistry in this pair of diastereomers.

Figure 1. Assignment of Relative Configuration in Diastereomeric 2,4-Dimethyl-2-nitro-3-(diphenylphosphatoxy)alkanes

Problems both with separation of isomers and configurational assignment quickly eliminated the use of related simple schemes involving the synthesis and late stage separation of diastereomers for systems bearing methyl groups more remote from the phosphate ester. We were forced, therefore, to develop stereocontrolled syntheses in which a key feature was the Corey oxazaborolidine-directed reduction of nitroketones. As we have described elsewhere⁶ these reductions proceed with high degrees of asymmetric induction and follow the standard Corey model⁷ with the bulky 1-methyl-1-nitroethyl group serving as the large substituent. The synthesis of a pair of diastereomeric substrates carrying methyl groups two carbons removed from the phosphate ester began with the known 4-(*R*)-4-methylpent-1-en-5-ol,⁸ which was processed by Swern oxidation, reductive amination, and Boc protection to **H**. After ozonolysis to aldehyde **I**, this material was taken forward to the nitroketone **K** in a straightforward manner (Scheme 2). Interestingly, the nitroalcohols **J** were obtained with a 2.5/1 *anti/syn* ratio which was assigned with the benefit of the subsequent oxazaborolidine reductions. Oxazaborolidine-mediated borane reduction with the (*R*)-catalyst gave a 2.4:1 *syn/anti* ratio of alcohols **J**, while use of the (*S*) gave a much improved 10:1

ratio in favor of *anti*-**J** (Scheme 2, Table 1). The discrepancy between the two series is a clear indication of the influence of the stereogenic center in the substrate and is suggestive of stereochemical mismatching⁹ in the case of the (*R*)-catalyst. As several examples of the influence of remote stereogenic centers on the oxazaborolidine reduction were observed in the course of this study they have been collected in Table 1 for ease of comparison. Finally, the separate *syn* and *anti*-alcohols **J** were taken forward to the cyclization substrates by standard protocols, with diphenylphosphoryl chloride being sufficient for derivatization in this less hindered series (Scheme 2).

Scheme 2. Preparation of *syn*- and *anti*-**2**

A third pair of diastereomers with a single methyl group adjacent to the amine was obtained (Scheme 3, Table 1) from **M**, which itself was accessed by reduction of L-alanine-derived methyl 4(*S*)-4-(*N*-benzyl-*N*-*tert*-butoxycarbonyl)amino-2*E*-pentenoate.¹⁰

Scheme 3. Preparation of *syn*- and *anti*-3

Turning to the preparation of a series of dimethyl substituted substrates, ketone **K** was deprotonated with LiHMDS and the enolate quenched with methyl iodide resulting in an 82% yield of the dimethyl ketone **R**. Reduction with tetrabutylammonium borohydride then afforded alcohol **S** as an inseparable 1:3 mixture of the *syn,syn* and *anti,syn*-isomers.¹¹ Phosphorylation with ethyl diphenylphosphite and iodine gave the phosphates **T** in 48% yield with a *syn,syn:anti,syn* ratio of 1:4.7 which suggests that the *anti,syn*-isomer of alcohol **S** has the more accessible hydroxyl group. Separation being difficult, **T** was taken forward as a mixture of diastereomers and the Boc group removed with trifluoroacetic acid after which, fortuitously, the isomers of **4** could be separated by chromatography on silica gel (Scheme 4).

Scheme 4. Preparation of *syn,syn*- and *anti,syn*-4

The stereochemical assignment of **R** was greatly facilitated by a serendipitous observation whereby exposure of this ketone to TMSOTf and lutidine resulted in the isolation of the lactam **U** in 89% yield. Presumably, this product arises by a retro-Henry type reaction following cleavage of the Boc group and cyclization of the resulting amine onto the ketone to give a cyclic aminol. The *syn*-stereochemistry of **R** is inferred directly from the *trans*-nature of **U** which, itself, rests on NOESY measurements (Fig 2). The stereochemistry of *syn,syn*-4, like that of *syn* and *anti*-1, reposes on a combination of coupling constant and NOESY data (Fig. 1). Interestingly, only *syn,syn*-4, and not the corresponding *anti,syn*-isomer exhibits the ~ 0 Hz coupling for $^3J_{\text{H}_3,\text{H}_4}$, unlike the situation with *syn* and *anti*-1, leading to the conclusion that the extra methyl group has a significant influence on the backbone conformation of *anti,syn*-4.

Figure 2. Retro-Henry Derived Lactams¹²

A further pair of probes, with two methyl groups in a *syn*-1,3-relationship, was obtained in comparable manner from ketone **P** (Scheme 5). In this series, alkylation again afforded a major diastereomer and separation of the final *syn,syn* and *anti,syn* stereodiads was effected after phosphorylation, before final removal of the Boc group.

Scheme 5. Preparation of *syn,syn*- and *anti,syn*-**5**

The relative stereochemistry of *syn-V* was again facilitated by formation of a cyclic lactam *cis-Y* on exposure to TMSOTf. As there were no particularly diagnostic cross peaks in the NOESY spectrum of the *cis*-disubstituted lactam **Y**, it was subjected to debenzylation with sodium in liquid ammonia to give **Z** whose stereochemistry was assigned by correlation with the literature data.¹³ The stereochemical relationship between carbons 3 and 4 was again assigned on the basis of NOESY and coupling constant data in both the *syn,syn*- and *anti,syn*-isomers of **5** (Fig 1). It is noteworthy that five of the six compounds prepared in this study with the 3-(diphenylphosphatoxy)-4-methyl system adopt the related conformations in the region of the phosphate group (Figs 1). Only one, *anti,syn-4*, displayed a significantly different conformation.

The synthesis of a final pair of diastereomers began with dimethyl cuprate addition to L-alanine derived methyl 4(*S*)-4-(*N*-benzyl-*N*-tert-butoxycarbonyl)amino-2*E*-pentenoate which afforded **Aa**. This material

was then processed according Scheme 6 ultimately giving *anti,anti*- and *syn,anti*-**6** in which the configuration of the third stereogenic center reposes on the oxazaborolidine-mediated borane reduction (Table 1).

Scheme 6. Preparation of *anti,anti*- and *syn,anti*-**6**

Table 1. Diastereoselective Reduction of Nitroketones by Borane-Dimethyl Sulfide with Oxazaborolidine Catalysis.

Entry	Substrate	Catalyst	Major Product	(S):(R)-Alcohol ratio, (% yield)
1	K	(R)	syn-J	2.4:1 (78)

2	K	(S)	<i>anti</i> - J	1:10 (87)
3	P	(R)	<i>syn</i> - O	15:1 (77)
4	P	(S)	<i>anti</i> - O	1:25 (70)
5	Ad	(R)	<i>anti,anti</i> - Ac	10:1 (76)
6	Ad	(S)	<i>syn,anti</i> - Ac	1:2 (84)

One possible explanation for the poor stereoselectivity observed in the oxazaborolidine reductions of Table 1, entries 1 and 6, both of which result in the formation of *syn*-3-methyl alcohols, is the nascent *syn*-pentane type interaction¹⁴ between the methyl group and the hydroxyl O-B bond at the reaction center at the transition state for reduction. This is illustrated in Fig. 3 for the reduction of **K** with the (*R*)-enantiomer of the catalyst (Table 2, entry 1). In this model the carbon chain of the ketone is represented in an extended conformation to minimize steric clashes with the bulky 1-methyl-1-nitroethyl group and to present the methyl group away from the concave face of the catalyst. When the enantiomer of the catalyst is employed steric interactions between the carbonyl group and the methyl group diminish as the reaction proceeds to the *anti*- β -methyl alcohol.

Figure 3. Model for the Reductions Leading to *syn*- β -Methyl Alcohols

Assignment of Product Configuration

The stereochemical assignment of most products was made on the basis of diagnostic NOESY correlations on at least one member of each pair of stereoisomers and on both where ever possible (Figure 4).

Stereochemical assignment of *cis*- and *trans*-**8** was made by correlation of the data for the *cis*-isomer with that reported in the literature.¹⁵ The stereochemistry of **14**, for which NOESY measurements were complicated by the presence of minor inseparable quantities of **13**, rests on the close congruity of its ¹³C-NMR spectral data with that of **10** (Table 3) and on analogy with the stereochemistry of **10**.

Figure 4. Diagnostic NOESY Correlations for Product Assignment.

Table 3. Diagnostic ^{13}C -NMR Data for **10** and **14**

10: R = H
14: R = Me

	δ C3	δ C5	δ C10	δ C10a
10	62.3	56.2	38.1	70.3
14	64.7	56.5	37.8	70.6

General Experimental. All the reactions were performed under a dry argon atmosphere in solvents dried and distilled by standard procedures. Extracts were dried over Na_2SO_4 and concentrated under vacuum at room temperature. Melting points were recorded on a hotstage microscope and are uncorrected. Unless otherwise stated, ^1H , ^{13}C and ^{31}P NMR spectra were run in CDCl_3 at 300, 75 and 121 MHz respectively. ^1H and ^{13}C chemical shifts are downfield from tetramethylsilane as internal standard. ^{31}P chemical shifts are quoted with respect to external H_3PO_4 . DEPT, COSY, HMQC and NOESY spectra were acquired at 500 MHz. For compounds containing the Boc group spectra were recorded at 50 $^\circ\text{C}$.

General Procedure A. Boc Protection. A solution of substrate (2.9 mmol) in CH_2Cl_2 (11 mL) was treated at 0 $^\circ\text{C}$ with triethylamine (1.0 mL, 7.3 mmol) then di-*tert*-butyl dicarbonate (0.83 g, 3.8 mmol) and the resulting mixture was stirring for 12 h at room temperature before the reaction mixture was diluted with ethyl acetate (150 mL). The organic layer was washed with water (2×50 mL) and brine (2×50 mL), dried and concentrated to give a crude product. Purification by silica gel column chromatography, eluting with mixtures of hexanes and ethyl acetate, then afforded the product.

General Procedure B. Henry Reaction. 2-Nitropropane (11.2 mL, 130 mmol) and the substrate (6.5 mmol) were dissolved in a 1/1 mixture of acetonitrile and *tert*-butanol (35 mL). After cooling to 0 °C, potassium *tert*-butoxide (0.72 g, 6.5 mmol) was added and the reaction mixture stirred for 24 h with gradual warming to room temperature. Saturated ammonium chloride solution (30 mL) and ethyl acetate (75 mL) were then added, the organic layer was separated, and the aqueous layer extracted with ethyl acetate (2 × 35 mL). The combined organic layers were washed with water (2 × 50 mL) and brine, dried and concentrated to afford the crude product. Purification by silica gel column chromatography, eluting with mixtures of hexanes and ethyl acetate afforded the products.

General Procedure C. Swern Oxidation. A solution of oxalyl chloride (0.43 mL, 5.1 mmol) in CH₂Cl₂ (30 mL) was cooled to -78 °C and a solution of DMSO (0.71 mL, 10.2 mmol) in CH₂Cl₂ (7 mL) was added dropwise. After stirring for 15 min a solution of substrate (2.5 mmol) in CH₂Cl₂ (7 mL) was added drop wise and the stirring continued for at -78 °C for 1 h. Triethylamine (2.1 mL, 15.3 mmol) was then added over 5 min, during which time the reaction mixture became a colorless solution. After stirring for 20 min, the reaction mixture was allowed to warm to room temperature over 1.5 h. Water (75 mL) was then added and the resulting mixture washed with 10% aqueous sodium acetate (3 x 30 mL) and brine (2 x 30 mL), dried and concentrated. Purification by silica gel column chromatography, eluting with hexanes/ethyl acetate mixtures afforded the products.

General Procedure D. Alkylation α - to a Nitroketone. To a solution of LHMDs (1.0M in THF, 6.9 mL, 6.9 mmol) in THF (20 mL) at -78 °C, was added dropwise, a solution of nitroketone (3.8 mmol) in THF (50 mL) over 1 h through a pressure equalizing addition funnel. Stirring was then maintained for 0.5 h maintaining at -78 °C before iodomethane (0.75 mL, 11.4 mmol) was added, following which the

reaction mixture was allowed to come to room temperature with stirring over night. The reaction mixture was then diluted with ethyl ether (100 mL) and washed with saturated sodium bicarbonate (2×50 mL), water (2×50 mL) and brine (2×50 mL), dried and concentrated. Purification by silica gel column chromatography, eluting with mixtures of hexanes and ethyl acetate afforded the products.

General Procedure E. Reduction of Nitroketones with Tetrabutylammonium Borohydride. To a solution of substrate (1.3 mmol) dissolved in dry CH_2Cl_2 (20 mL) at 0°C , was added tetrabutylammonium borohydride (0.82 g, 3.2 mmol) in one portion. The reaction mixture was stirred for 5 h at the same temperature, then was quenched by dropwise addition of saturated aqueous ammonium chloride (5 mL). The reaction mixture was further stirred for 15 min. and diluted with CH_2Cl_2 (50 mL). The organic layer was washed with saturated ammonium chloride (2×25 mL), water (2×50 mL) and brine (2×25 mL), dried, and concentrated. Purification by silica gel column chromatography, eluting with hexanes/ethyl acetate mixtures afforded the products.

General Procedure F. Oxazaborolidine-Mediated Reduction of Nitroketones. Borane dimethyl sulfide (1.0 M in CH_2Cl_2 , 2.6 mL, 2.6 mmol) was added at room temperature to a solution of (*S*)-(-)- or (*R*)-(+)- α,α -diphenyl-2-pyrrolidinemethanol (0.015 g, 0.06 mmol) in THF/toluene (1/1, 3.0 mL). The reaction mixture was then heated to 45°C with stirring for 17 h before a solution of nitroketone (0.9 mmol) in THF (3 mL) was added over 0.5 h. The reaction mixture was maintained at 45°C for an additional 1.5-5 h (TLC control), then cooled to room temperature and quenched by drop wise addition of methanol (1.5 mL) until the vigor of the reaction subsided. The reaction mixture was then diluted with ethyl acetate (70 mL) and the organic layer washed with 1M HCl (2×25 mL), water (2×25 mL), saturated sodium bicarbonate solution (2×25 mL) and brine (25 mL), dried and concentrated to give the crude product.

Purification by silica gel chromatography, eluting with hexane/ethyl acetate mixtures, afforded the products.

General Procedure G. Phosphorylation of Nitro Alcohols with Ethyl Diphenyl Phosphite. To a stirred solution of ethyl diphenyl phosphite (0.448 g, 1.7 mmol) in dry CH_2Cl_2 (10 mL) at -15°C , iodine (0.43 g, 1.7 mmol) was added in one portion. After 0.5 h, a solution of nitroketone (0.8 mmol) and pyridine (0.3 mL, 3.4 mmol) in CH_2Cl_2 (20 mL) was added dropwise, after which the reaction was allowed to come to room temperature with stirring over 18 h. The reaction mixture was then poured into ethyl acetate (100 mL) and the organic layer was washed with 10 % $\text{Na}_2\text{S}_2\text{O}_3$ solution (2 x 50 mL), water (2 x 50 mL), and brine (2 x 50 mL), dried, and concentrated. Purification by silica gel column chromatography, eluting with mixtures of hexanes and ethyl acetate, afforded the phosphorylated nitro alcohols.

General Procedure H. Phosphorylation of Nitro Alcohols with Diphenyl Chlorophosphate. Diphenyl chlorophosphate (1.5 mL, 7.5 mmol) was added to a solution of substrate (4.4 mmol) and DMAP (0.90 g, 7.7 mmol) in CH_2Cl_2 (40 mL) at room temperature. The reaction mixture was stirred overnight, then diluted with ethyl acetate (80 mL). The organic layer was washed with saturated aqueous ammonium chloride (2×25 mL), water (2×25 mL), and brine (2×25 mL), dried, and concentrated to afford the crude product. Purification by silica gel column chromatography, eluting with hexanes/ethyl acetate mixtures gave the phosphorylated nitroalcohols.

General Procedure I. Removal of Boc Groups with Trimethylsilyl Trifluoromethanesulfonate. TMSOTf (0.3 mL, 1.6 mmol) was added to a solution of substrate (1.0 mmol) and 2,6-lutidine (0.25 mL, 2.1 mmol) in dry CH_2Cl_2 (20 mL) and the reaction mixture stirred at room temperature for 0.5 h.

Saturated aqueous ammonium chloride (30 mL) was then added and the aqueous layer was extracted with ethyl acetate (3 × 25 mL). The combined organic layer was washed with saturated sodium bicarbonate solution (2 × 25 mL), water (2 × 25 mL) and brine (2 × 25 mL), dried, and concentrated. Chromatography on silica gel column, eluting with mixtures of hexanes, ethyl acetate and methanol containing 1% triethylamine, then afforded the free amines.

General Procedure J. Removal of Boc Groups with Trifluoroacetic Acid. TFA (0.70 mL, 9.4 mmol) was added at room temperature to a stirred solution of substrate (1.9 mmol) in CH₂Cl₂ (25 mL), followed by stirring for 16 h. The reaction mixture was then taken-up in ethyl acetate (80 mL) and washed well with saturated aqueous NaHCO₃ (3 × 25 mL), water (2 × 25 mL), and brine (25 mL), dried, and concentrated to afford the crude product. Purification by silica gel column chromatography, eluting with mixtures of hexanes, ethyl acetate and methanol containing 1% triethylamine, then afforded the free amines.

4-[N-Benzyl-N-(*tert*-butyloxycarbonyl)]aminobutanal (B). 4Å Molecular sieves (4.50 g) were added to a stirred solution of **A**² (2.75 g, 10.5 mmol) in CH₂Cl₂ (150 mL) followed, after cooling to 0 °C, by PCC (4.5 g, 21 mmol). After stirring for 2 h, the reaction mixture was concentrated to 75% of the initial volume and loaded onto a silica gel column. Elution with hexanes and ethyl acetate (5/1) afforded **B** as a colorless oil (2.24 g, 77%). ¹H NMR δ: 9.68 (t, *J* = 1.5 Hz, 1H), 7.28- 7.18 (m, 5H), 4.39 (s, 2H), 3.19 (t, *J* = 7.2 Hz, 2H), 2.35 (br. t, *J* = 7.2 Hz, 2H), 1.83- 1.74 (m, *J* = 7.2 Hz, 2H), 1.44 (br. s, 9H); ¹³C NMR δ: 201.2, 155.9, 138.5, 128.5, 127.5, 126.4, 79.9, 50.5, 45.9, 41.1, 28.5, 20.7. Anal. Calcd for C₁₆H₂₃NO₃: C, 69.29; H, 8.36. Found: C, 69.58; H, 8.34.

6-[*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)]amino-3-hydroxy-2-methyl-2-nitrohexane (C). White solid. M.p. 64- 66 °C; ¹H NMR δ: 7.33- 7.19 (m, 5H), 4.44 (br. d, *J* = 15.6 Hz, 1H), 4.35 (br. d, *J* = 16.0 Hz, 1H), 3.96 (br. d, *J* = 10.2 Hz, 1H), 3.27- 3.10 (m, 2H), 1.77- 1.23 (m, 19H); ¹³C NMR δ: 156.2, 138.5, 128.6, 127.5, 127.3, 92.1, 80.1, 75.9, 50.6, 46.3, 28.5, 25.2, 23.0, 20.9. Anal. Calcd. for C₁₉H₃₀N₂O₅: C, 62.27; H, 8.25. Found: C, 61.99; H, 8.25.

6-[*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)]amino-2-methyl-2-nitro-3-hexanone (D). Pale yellow solid. M.p. 75- 77 °C. ¹H NMR δ: 7.31- 7.19 (m, 5H), 4.39 (s, 2H), 3.18 (br. t, *J* = 6.7 Hz, 2H), 2.44 (br. t, *J* = 6.9 Hz, 2H), 1.82- 1.73 (m, 2H), 1.68 (s, 6H), 1.45 (s, 9H); ¹³C NMR δ: 201.3, 155.9, 138.5, 128.8, 127.6, 127.3, 94.1, 79.9, 50.6, 45.8, 33.5, 28.5, 26.3, 22.3. Anal. Calcd. for C₁₉H₂₈N₂O₅: C, 62.62; H, 7.74. Found: C, 62.41; H, 7.68.

6-[*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)]amino-2,4-dimethyl-2-nitro-3-hexanone (E). Colorless oil. ¹H NMR δ: 7.33- 7.19 (m, 5H), 4.44 (br. d, *J* = 15.3 Hz, 1H), 4.33 (br. d, *J* = 15.3 Hz, 1H), 3.12 (br. m, 2H), 2.71 (br. m, 1H), 1.86- 1.77 (m, 1H), 1.69 (s, 6H), 1.58- 1.40 (m, 10H), 1.10 (d, *J* = 6.9 Hz, 3H); ¹³C NMR δ: 205.4, 155.7, 138.4, 128.6, 127.7, 127.4, 94.4, 80.1, 50.5, 44.3, 38.7, 32.4, 28.6, 23.5, 18.2. Anal. Calcd. for C₂₀H₃₀N₂O₅: C, 63.47; H, 7.99. Found: C, 63.34; H, 7.96.

6-[*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)]amino-2,4-dimethyl-2-nitro-3-hexanol (*syn/anti*-F). Colorless oil (1/1 *syn/anti* mixture). ¹H NMR δ: 7.33- 7.20 (m, 10H), 4.46- 4.33 (br. m, 4H), 3.89 (br. d, 2H), 3.40- 3.0 (br. m, 4H), 2.8 (br. 1H), 1.71- 1.34 (br. m, 36H), 0.96 (br. d, *J* = 6.6 Hz, 3H), 0.90 (br. d, *J* = 6.6 Hz, 3H); ¹³C NMR δ: 156.1, 155.9, 138.6, 138.5, 128.6, 128.3, 127.5, 127.3, 127.1, 92.2, 92.0, 80.1, 79.9, 79.7,

77.8, 50.8, 50.6, 45.1, 44.6, 34.8, 32.8, 32.0, 30.8, 28.6, 28.5, 24.0, 23.1, 22.6, 22.2, 18.8, 13.3. Anal. Calcd. for C₂₀H₃₂N₂O₅: C, 63.13; H, 8.48. Found: C, 63.18; H, 8.64.

***anti*-6-[*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)]amino-2,4-dimethyl-2-nitro-3-**

(diphenylphosphatoxy)hexane (*anti*-G). ¹H NMR δ: 7.32- 7.18 (m, 15H), 5.03 (d, *J* = 9.8 Hz, 1H), 4.45 (br. s, 1H), 4.23 (d, *J* = 15.4 Hz, 1H), 3.14 (br. s, 2H), 1.72 (br. s, 2H), 1.59 (s, 3H), 1.55 (s, 3H), 1.46 (br. s, 9H), 1.32- 1.26 (m, 1H), 1.11 (d, *J* = 6.9 Hz, 3H); ¹³C NMR δ: 156.1, 151.0, 138.7, 130.2, 128.9, 127.9, 127.6, 125.8, 120.4, 90.9, 87.5, 80.2, 50.6, 45.1, 32.7, 29.8, 28.8, 23.7, 22.7, 19.8; ³¹P NMR δ: -11.96. Anal. Calcd. for C₃₂H₄₁N₂O₈P: C, 62.73; H, 6.75. Found: C, 62.29, H; 6.62 (determined on a mixture of syn- and anti-isomers).

***syn*-6-[*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)]amino-2,4-dimethyl-2-nitro-3-**

(diphenylphosphatoxy)hexane (*syn*-G). ¹H NMR: δ 7.32- 7.17 (m, 15H), 5.09 (d, *J* = 8.9 Hz, 1H), 4.41 (br. d, *J* = 15.5 Hz, 1H), 4.32 (br. d, *J* = 15.5 Hz, 1H), 3.21 (br. s, 2H), 1.77 (br. s, 2H), 1.62- 1.53 (br. m, 7H), 1.45 (br. s 9H) 0.85 (d, *J* = 6.4 Hz, 3H); ¹³C NMR δ: 156.1, 150.9, 138.8, 130.1, 128.8, 127.9, 127.5, 125.7, 120.4, 91.3, 86.2, 80.2, 50.5, 44.6, 35.0, 32.5, 28.8, 23.3, 14.2; ³¹P NMR δ: -11.97. Anal. Calcd. for C₃₂H₄₁N₂O₈P: C, 62.73; H, 6.75. Found: C, 62.29, H; 6.62 (determined on a mixture of syn- and anti-isomers).

***anti*-6-(Benzylamino)-2,4-dimethyl-2-nitro-3-(diphenylphosphatoxy)hexane (*anti*-1).** Pale yellow oil.

¹H NMR δ: 7.32- 7.19 (m, 15H), 5.09 (d, *J* = 9.9 Hz, 1H), 3.76 (d, *J* = 14.4 Hz, 1H), 3.72 (d, *J* = 13.2 Hz, 1H), 2.68- 2.51 (m, 3H), 1.97- 1.92 (m, 1H), 1.75- 1.73 (m, 1H), 1.63, (s, 3H), 1.60 (s, 3H), 1.35- 1.30, (m, 1H), 1.08 (d, *J* = 6.9 Hz, 3H); ¹³C NMR δ: 150.9, 140.2, 130.2, 128.8, 128.6, 127.5, 125.9, 120.5,

90.1, 87.5, 54.2, 47.2, 32.9, 31.5, 23.7, 22.8, 19.7; ^{31}P NMR δ : -11.77. ESIHRMS Calcd for $\text{C}_{27}\text{H}_{34}\text{N}_2\text{O}_6\text{P}$: 513.2155. Found: 513.2164 $[\text{M}+\text{H}]^+$.

***syn*-6-(Benzylamino)-2,4-dimethyl-2-nitro-3-(diphenylphosphatoxy)hexane (*syn*-1).** Pale yellow oil.

^1H NMR δ : 7.33- 7.17 (m, 15H), 5.22 (d, J = 9.87 Hz, 1H), 3.76 (d, J = 13.1 Hz, 1H), 3.73 (d, J = 13.2 Hz, 1H), 2.69- 2.62 (br, m, 3H), 1.99- 1.94 (m, 1H), 1.77- 1.73 (m, 1H), 1.63 (s, 3H), 1.58 (s, 3H), 1.56- 1.53 (m, 1H), 0.92 (d, J = 6.7 Hz, 3H); ^{13}C NMR δ : 150.9, 140.1, 130.2, 128.8, 128.7, 127.5, 125.9, 120.5, 91.4, 85.7, 54.1, 46.8, 36.3, 32.3, 23.6, 22.9, 14.9; ^{31}P NMR δ : -11.70. ESIHRMS Calcd for: $\text{C}_{27}\text{H}_{34}\text{N}_2\text{O}_6\text{P}$: 513.2155. Found: 513.2179 $[\text{M}+\text{H}]^+$.

4(*R*)-5-[*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)]amino-4-methyl-1-pentene (H**).** 2(*R*)-2-Methyl-4-pentenol⁸ (1.67 g) was subjected to the general procedure for Swern oxidation. After work-up, the solution of resulting aldehyde in CH_2Cl_2 (100 mL) was concentrated (bath temperature 25 °C) under reduced pressure (20 mm.Hg) to a final volume of 15 mL the treated sequentially with benzylamine (2.9 mL, 26.3 mmol) in THF (40 mL) and sodium triacetoxyborohydride (5.24 g, 24.7 mmol). The resulting mixture was stirred at room temperature for 8 h, then was taken up in ethyl acetate (100 mL) and washed with 3M NaOH (3 $\times$ 30 mL), water (3 $\times$ 30 mL) and brine (50 mL), dried and concentrated. Purification of the residue by silica gel column chromatography (eluent: hexanes/ethyl acetate 3/1) afforded 4(*R*)-5-(benzylamino)-4-methylpent-1-ene¹⁶ (1.05 g, 39%) as a colorless oil. ^1H NMR δ : 7.34-7.23 (m, 5H), 5.86- 5.72 (m, 1H), 5.06- 4.98 (m, 2H), 3.78 (s, 2H), 2.57 (dd, J = 6.3 Hz, 11.7 Hz, 1H), 2.45 (dd, J = 6.9 Hz, 11.4 Hz, 1H), 2.22- 2.13 (m, 1H), 1.97- 1.87 (m, 1H), 1.77- 1.71 (m, 1H), 1.30 (br. s, 1H), 0.93 (d, J = 6.6 Hz, 3H); ^{13}C NMR δ : 140.8, 137.4, 128.5, 128.2, 126.9, 116.0, 55.6, 54.3, 39.6, 33.4, 18.1. Following the general procedure A for Boc protection, this amine was then converted to **H** (1.40 g, 88%) as colorless oil.

^1H NMR δ : 7.33- 7.20 (m, 5H), 5.75- 5.69 (m, 1H), 5.02- 4.98 (m, 2H), 4.45 (s, 2H), 3.11- 3.04 (br. m, 2H), 2.12- 2.06 (br. m, 1H), 1.89- 1.83 (m, 2H), 1.46 (br. s, 9H), 0.87 (d, $J = 6$ Hz, 3H); ^{13}C NMR δ : 156.3, 138.7, 136.8, 128.5, 127.5, 127.1, 116.0, 79.6, 52.5, 50.9, 38.9, 32.2, 28.5, 17.4. Anal. Calcd. for $\text{C}_{18}\text{H}_{27}\text{NO}_2$: C, 74.70; H, 9.40. Found: C, 74.85; H, 9.20.

3(R)-4-[N-Benzyl-N-(tert-butyloxycarbonyl)]amino-3-methyl-1-butanal (I). Ozone was bubbled into a solution of **H** (0.83 g, 2.9 mmol) in dry methanol (25 mL) at -78°C for 10 min until the solution turned blue. Oxygen was then bubbled until the solution turned colorless before dimethyl sulfide (2.1 mL, 28.7 mmol) was added. The contents allowed to come to room temperature with stirring overnight after which the reaction mixture was concentrated and purified by silica gel column chromatography (eluent: hexanes/ethyl acetate 7/1) to afford **I** (0.72 g, 86%) as a colorless oil. ^1H NMR δ : 9.67- 9.65 (br. m, 1H), 7.31- 7.18 (m, 5H), 4.46- 4.34 (br. m, 2H), 3.17- 2.98 (br. m, 2H), 2.42- 2.38 (br. m, 2H), 2.23- 2.14 (m, 1H), 1.44 (br. s, 9H), 0.91 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR δ : 200.5, 156.1, 138.4, 128.6, 127.5, 127.3, 80.0, 52.3, 50.9, 48.7, 28.5, 27.6, 17.9. ESIHRMS Calcd. for $\text{C}_{17}\text{H}_{25}\text{NO}_3\text{Na}$: 314.1732. Found: 314.1721 $[\text{M}+\text{Na}]^+$.

5(R),3(R)-6-[N-Benzyl-N-(tert-butyloxycarbonyl)]amino-2,5-dimethyl-2-nitro-3-hexanol (*anti*-J). Colorless, viscous oil with a 10/1 anti/syn ratio. ^1H NMR δ : 7.34- 7.19 (m, 5H), 4.42 (br. s, 2H), 4.05 (br. d, $J = 10.2$ Hz, 1H), 3.24- 3.04 (br. m, 2H), 2.07- 1.98 (m, 1H), 1.52 (s, 3H), 1.50 (s, 3H), 1.45 (br. s, 9H), 1.40- 1.23 (m, 1H), 1.10- 0.95 (m, 1H), 0.91 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR δ : 156.4, 138.6, 128.6, 127.5, 127.3, 92.3, 80.1, 74.1, 53.2, 51.3, 35.8, 29.6, 28.6, 23.3, 20.6, 17.6. Anal. Calcd for $\text{C}_{20}\text{H}_{32}\text{N}_2\text{O}_5$: C, 63.13; H, 8.48. Found: C, 63.27; H, 8.36.

5(R),3(S)-6-[N-Benzyl-N-(tert-butyloxycarbonyl)]amino-3-hydroxy-2,5-dimethyl-2-nitrohexane (*syn*-J). Colorless, viscous oil with a 2.4/1 *syn/anti* ratio. ^1H NMR δ : 7.34- 7.18 (m, 5H), 4.58 (br. d, $J = 15.9$ Hz, 1H), 4.28 (br. d, $J = 15.9$ Hz, 1H), 4.12- 4.10 (m, 1H), 3.57-3.53 (br. m, 1H), 2.78- 2.72 (br. m, 1H), 2.08- 2.01 (m, 1H), 1.56 (s, 3H), 1.48 (s, 3H), 1.44 (br. s, 9H), 1.35- 1.22 (m, 2H), 0.98 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR δ : 156.7, 138.3, 128.5, 127.2, 127.1, 92.2, 80.5, 73.6, 52.1, 51.5, 34.8, 29.7, 28.5, 22.5, 21.4, 18.3. Anal. Calcd for $\text{C}_{20}\text{H}_{32}\text{N}_2\text{O}_5$: C, 63.13; H, 8.48. Found: C, 63.25; H, 8.27.

5(R)-6-[N-Benzyl-N-(tert-butyloxycarbonyl)]amino-2,5-dimethyl-2-nitro-3-hexanone (K). Pale yellow oil. ^1H NMR δ : 7.33- 7.19 (m, 5H), 4.48 (d, $J = 15.6$ Hz, 1H), 4.35 (d, $J = 15.6$ Hz, 1H), 3.11- 2.97 (br. m, 2H), 2.53- 2.20 (m, 3H), 1.68 (s, 6H), 1.45 (br. s, 9H), 0.87 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR δ : 206.7, 156.2, 138.4, 128.6, 127.6, 127.3, 94.2, 80.0, 51.2, 50.6, 40.8, 28.5, 28.2, 23.3, 17.6. Anal. Calcd for $\text{C}_{20}\text{H}_{30}\text{N}_2\text{O}_5$: C, 63.47; H, 7.99. Found: C, 63.20; H, 8.21.

5(R),3(R)-6-[N-Benzyl-N-(tert-butyloxycarbonyl)]amino-2,5-dimethyl-2-nitro-3-(diphenylphosphatoxy)hexane (*anti*-L). Pale yellow oil. ^1H NMR δ : 7.34- 7.08 (m, 15H), 5.26 (br. t, $J = 9.25$ Hz, 1H), 4.43- 4.39 (br. d, 1H), 4.14 (d, $J = 15.6$ Hz, 1H), 3.13- 2.92 (m, 2H), 2.3- 2.23 (m, 1H), 1.82- 1.73 (m, 1H), 1.60 (s, 3H), 1.54 (s, 3H), 1.44 (br. s, 9H), 1.2- 1.16 (m, 1H), 0.98 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR δ : 156.2, 150.8, 138.2, 129.9, 129.8, 128.5, 127.4, 127.2, 125.5, 120.1, 90.4, 81.6, 79.8, 52.2, 49.8, 36.1, 28.4, 28.1, 22.3, 16.6; ^{31}P NMR δ : -12.12. Anal. Calcd for: $\text{C}_{32}\text{H}_{41}\text{N}_2\text{O}_8\text{P}$: C, 62.73; H, 6.75. Found: C, 62.47; H, 6.51.

5(R),3(S)-6-[N-Benzyl-N-(tert-butyloxycarbonyl)]amino-2,5-dimethyl-2-nitro-3-(diphenylphosphatoxy)hexane (*syn*-L). Colorless oil. ^1H NMR δ : 7.34- 7.17 (m, 15H), 5.18 (br. s, 1H),

4.44- 4.32 (br. m, 2H), 3.12 (br. s, 2H), 2.04- 2.01 (m, 1H), 1.65- 1.36 (br. m, 17H), 0.87 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR δ : 156.3, 150.7, 138.7, 129.9, 128.5, 127.6, 127.1, 125.5, 120.2, 90.4, 82.5, 79.9, 51.8, 50.4, 37.2, 29.3, 28.5, 22.9, 21.6, 19.0; ^{31}P NMR δ : -12.20. Anal. Calcd. for $\text{C}_{32}\text{H}_{41}\text{N}_2\text{O}_8\text{P}$: C, 62.73; H, 6.75. Found: C, 62.92; H, 6.87.

5(R),3(R)-6-Benzylamino-2,5-dimethyl-2-nitro-3-(diphenylphosphatoxy)hexane (*anti*-2). Pale yellow oil. ^1H NMR δ : 7.34- 7.18 (m, 15H), 5.29 (t, $J = 9.3$ Hz, 1H), 3.66 (s, 2H), 2.42 (dd, $J = 11.4$ Hz, 6.3 Hz, 1H), 2.32 (dd, $J = 11.7$ Hz, 7.2 Hz, 1H), 2.0- 1.91 (m, 1H), 1.85- 1.78 (m, 1H), 1.62 (s, 3H), 1.56 (s, 3H), 1.17- 1.07 (m, 1H), 0.99 (d, $J = 6.3$ Hz, 3H); ^{13}C NMR δ : 150.6, 140.7, 129.9, 128.5, 128.2, 127.0, 125.6, 120.2, 90.5, 82.0, 56.1, 53.9, 36.6, 29.5, 22.6, 22.0, 17.4; ^{31}P NMR δ : -11.81. Anal. Calcd for $\text{C}_{27}\text{H}_{33}\text{N}_2\text{O}_6\text{P}$: C, 63.27; H, 6.49. Found: C, 63.40; H, 6.54.

5(R),3(S)-6-Benzylamino-2,5-dimethyl-2-nitro-3-(diphenylphosphatoxy)hexane (*syn*-2). Pale yellow oil. ^1H NMR δ : 7.38- 7.15 (m, 15H), 5.57- 5.5 (m, 1H), 3.76 (d, $J = 13.5$ Hz, 1H), 3.71 (d, $J = 13.5$ Hz, 1H), 2.61- 2.5 (m, 2H), 1.89- 1.85 (m, 1H), 1.63- 1.38 (m, 8H), 0.85 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR δ : 150.6, 140.9, 129.9, 128.4, 128.3, 126.8, 125.6, 120.3, 90.6, 82.6, 54.8, 54.4, 37.4, 29.5, 23.2, 21.3, 20.0; ^{31}P NMR δ : -11.69. ESIHRMS Calcd. for $\text{C}_{27}\text{H}_{34}\text{N}_2\text{O}_6\text{P}$: 513.2155. Found: 513.2167 $[\text{M}+\text{H}]^+$.

Methyl 4(S)-[N-benzyl-N-(*tert*-butoxycarbonyl)]aminopentanoate (M). Magnesium granules (0.56 g, 22.9 mmol, ~20 mesh) were added to a stirred solution of methyl (4S)-4-[N-benzyl-N-(*tert*-butoxycarbonyl)]amino-2(*E*)-pentenoate¹⁰ (2.09 g, 6.6 mmol) at 0 °C in dry methanol (40 mL). The reaction mixture was stirred for 4 h at 0 °C then was poured into a rapidly stirred solution of HCl (1M, 30 mL). After stirring for 20 min, the aqueous layer was extracted with ethyl acetate (3 × 30 mL) and the

combined organic layer washed with saturated sodium bicarbonate solution (2 × 25 mL), water (2 × 25 mL) and brine (50 mL), dried and concentrated to give the crude product. Purification by silica gel column chromatography (eluent: hexanes/ethyl acetate 7/1) then afforded **M** (1.73 g, 82%) as pale yellow oil. ¹H NMR δ: 7.30- 7.17 (m, 5H), 4.39-4.25 (br. m, 2H), 4.21-3.91 (br. m, 1H), 3.62 (s, 3H), 2.22 (br. t, *J* = 7.3 Hz, 2H), 1.96- 1.86 (m, 1H), 1.78- 1.69 (m, 1H), 1.42 (br. s, 9H), 1.08 (d, *J* = 6.3 Hz, 3H); ¹³C NMR δ: 173.6, 155.9, 139.9, 128.3, 127.2, 126.8, 79.8, 52.0, 51.4, 47.6, 31.3, 30.1, 28.5, 19.2. Anal. Calcd for: C₁₈H₂₇NO₄; C, 62.76; H, 8.47. Found: C, 67.07; H, 8.47.

4(S)-[N-Benzyl-N-(tert-butyloxycarbonyl)]aminopentanal (N). DIBAL-H (1M in hexanes, 15.9 mL, 15.9 mmol) was added dropwise to a stirred solution of **M** (4.27 g, 13.3 mmol) in toluene (25 mL) at -78 °C. Stirring was maintained at -78 °C for 45 min before the reaction mixture was poured into a rapidly stirred HCl (1M, 30 mL). After stirring for 0.5 h. the layers were separated and the aqueous layer extracted with ethyl acetate (3 × 30 mL). The combined organic layer was then washed with saturated sodium bicarbonate solution (2 × 25 mL), water (2 × 25 mL) and brine (50 mL), dried and concentrated to give the crude product. Purification by silica gel column chromatography (eluent: hexanes/ethyl acetate 5:1) afforded **N** (3.11 g, 80%) as colorless oil. ¹H NMR δ: 9.59 (s, 1H), 7.29- 7.16 (m, 5H), 4.34 (d, *J* = 15.6 Hz, 1H), 4.27 (d, *J* = 16.2 Hz, 1H), 4.11- 3.92 (m, 1H), 2.28 (br. s, 2H), 1.92- 1.79 (m, 1H), 1.74- 1.62 (m, 1H), 1.43 (br. s, 9H), 1.12 (d, *J* = 6.9 Hz, 3H); ¹³C NMR δ: 201.3, 155.9, 139.8, 128.4, 127.2, 126.9, 79.9, 51.7, 47.7, 41.1, 28.5, 27.3, 19.2. ESIHRMS Calcd for C₁₇H₂₅NO₃K: 330.1472. Found: 330.1469 [M+K]⁺.

3(R),6(S)-[N-Benzyl-N-(tert-butyloxycarbonyl)]amino-2-methyl-2-nitro-3-heptanol. (anti-O).⁴

Colorless, viscous oil with a 25/1 anti/syn ratio (determined by NMR spectroscopy after phosphorylation

and removal of the Boc group). ^1H NMR δ : 7.31- 7.20 (m, 5H), 4.36 (d, J = 15.9 Hz, 1H), 4.29 (d, J = 16.0 Hz, 1H), 4.15- 4.04 (br. m, 1H), 3.91 (br. d, J = 10 Hz, 1H), 2.20- 2.00 (br. s, 1H), 1.85- 1.76 (m, 1H), 1.54- 1.42 (br. m, 17H), 1.17- 1.04 (m, 4H); ^{13}C NMR δ : 156.2, 140.2, 128.3, 127.4, 126.9, 92.1, 79.9, 75.6, 51.6, 46.9, 31.7, 28.5, 28.3, 23.5, 20.6, 19.4. ESIHRMS Calcd. for $\text{C}_{20}\text{H}_{32}\text{N}_2\text{O}_5\text{Na}$: 403.2209. Found: 403.2225 $[\text{M}+\text{Na}]^+$. Anal. Calcd for: $\text{C}_{20}\text{H}_{32}\text{N}_2\text{O}_5$; C, 63.13; H, 8.48. Found: C, 63.15; H, 8.27 (determined on a mixture of *syn* and *anti*-isomers).

3(*S*),6(*S*)-[*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)]amino-3-hydroxy-2-methyl-2-nitroheptane. (*syn*-O).⁴
Colorless, viscous oil with a 15/1 *syn*/*anti* ratio (determined by NMR spectroscopy after phosphorylation and removal of the Boc group). ^1H NMR δ : 7.30- 7.18 (m, 5H), 4.38- 4.01 (br. m, 3H), 3.92- 3.85 (br. s, 1H), 1.64- 1.59 (br. m, 2H), 1.49- 1.20 (br. m, 16H), 1.19- 1.03 (br. m, 4H); ^{13}C NMR δ : 156.5, 140.0, 128.4, 127.2, 126.9, 92.13, 80.3, 76.4, 51.6, 46.8, 32.5, 28.4, 27.8, 22.8, 20.9, 19.3. ESIHRMS Calcd. for $\text{C}_{20}\text{H}_{32}\text{N}_2\text{O}_5\text{Na}$: 403.2209. Found: 403.2227 $[\text{M}+\text{Na}]^+$. Anal. Calcd for: $\text{C}_{20}\text{H}_{32}\text{N}_2\text{O}_5$; C, 63.13; H, 8.48. Found: C, 63.15; H, 8.27 (determined on a mixture of *syn* and *anti*-isomers).

6(*S*)-[*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)]amino-2-methyl-2-nitro-3-heptanone (P). Pale yellow oil. ^1H NMR δ : 7.30- 7.17 (m, 5H), 4.33 (d, J = 15.9 Hz, 1H), 4.26 (d, J = 15.6 Hz, 1H), 4.10- 3.97 (br. m, 1H), 2.31- 2.22 (br. s, 2H), 1.84- 1.62 (br. m, 8H), 1.42 (br. s, 9H), 1.09 (d, J = 6.3 Hz, 3H); ^{13}C NMR δ : 201.4, 156.0, 139.8, 128.4, 127.2, 127.0, 94.1, 80.0, 51.7, 47.4, 33.4, 28.8, 28.5, 23.3, 19.2. Anal. Calcd for: $\text{C}_{20}\text{H}_{30}\text{N}_2\text{O}_5$; C, 63.47; H, 7.99. Found: C, 63.43, H, 8.03.

3(*R*),6(*S*)-[*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)]amino-2-methyl-2-nitro-3-(diphenylphosphatoxy)-heptane (*anti*-Q).⁴ Colorless oil. ^1H NMR δ : 7.34- 7.14 (m, 15H), 5.20- 5.14 (br. m, 1H), 4.33- 4.09 (br.

m, 3H), 1.87- 1.74 (br. m, 1H), 1.55- 1.40 (br. m, 18H), 1.01 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR δ : 156.1, 150.7, 140.0, 129.8, 128.3, 127.3, 126.8, 125.5, 120.2, 90.3, 83.4, 79.9, 51.5, 46.9, 30.9, 28.4, 28.3, 23.1, 21.7, 19.5; ^{31}P NMR δ : -12.11. Anal Calcd. for: $\text{C}_{32}\text{H}_{41}\text{N}_2\text{O}_8\text{P}$; C, 62.73; H, 6.75. Found: C, 63.02; H, 6.72.

3(S),6(S)-[N-Benzyl-N-(tert-butyloxycarbonyl)]amino-2-methyl-2-nitro-3-(diphenylphosphatoxy)-heptane (*syn-Q*).⁴ Colorless oil. ^1H NMR δ : 7.33- 7.14 (m, 15H), 4.95- 4.90 (br. m, 1H), 4.31- 4.16 (br. m, 2H), 4.10- 3.6 (br. m, 1H), 1.65- 1.27 (br. m, 19H), 0.98 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR δ : 156.1, 150.7, 139.9, 129.8, 128.3, 127.4, 126.9, 125.5, 120.2, 90.3, 84.2, 79.9, 52.3, 47.4, 31.6, 28.8, 28.5, 22.7, 21.7, 19.2; ^{31}P NMR δ : -12.19. Anal. Calcd for: $\text{C}_{32}\text{H}_{41}\text{N}_2\text{O}_8\text{P}$; C, 62.73; H, 6.75. Found: C, 62.86; H, 6.91.

3(R),6(S)-Benzylamino-2-methyl-2-nitro-3-(diphenylphosphatoxy)heptane (*anti-3*).⁴ Yellow oil. ^1H NMR δ : 7.30- 7.19 (m, 15H), 5.17- 5.13 (m, 1H), 3.74 (d, $J = 13.0$ Hz, 1H), 3.63 (d, $J = 13.0$ Hz, 1H), 2.67 (m, 1H), 1.69- 1.50 (m, 10H), 1.00 (d, $J = 6.3$ Hz, 3H); ^{13}C NMR: δ 150.8, 141.1, 130.2, 128.8, 128.6, 127.3, 125.8, 120.6, 90.7, 84.4, 51.9, 51.4, 33.1, 27.6, 23.2, 22.1, 20.6; ^{31}P NMR δ : -11.93. Anal. Calcd for: $\text{C}_{27}\text{H}_{33}\text{N}_2\text{O}_6\text{P}$; C, 63.27; H, 6.49. Found: C, 63.42, H, 6.55.

3(S),6(S)-Benzylamino-2-methyl-2-nitro-3-(diphenylphosphatoxy)heptane (*syn-3*).⁴ Yellow oil. ^1H NMR: δ 7.32- 7.18 (m, 15H), 5.21 (dt, $J = 9.0$ Hz, 2.5 Hz, 1H), 3.75 (d, $J = 13.0$ Hz, 1H), 3.65 (d, $J = 13.0$ Hz, 1H), 2.64- 2.6 (m, 1H), 1.66- 1.52 (m, 10H), 0.99 (d, $J = 6.3$ Hz, 3H); ^{13}C NMR δ : 150.9, 141.1, 130.2, 128.7, 128.5, 127.3, 125.8, 120.5, 90.7, 84.5, 52.3, 51.5, 33.3, 28.0, 23.2, 22.1, 20.6; ^{31}P NMR δ : -11.86. ESIHRMS Calcd. for $\text{C}_{27}\text{H}_{34}\text{N}_2\text{O}_6\text{P}$: 513.2155. Found: 513.2167 $[\text{M}+\text{H}]^+$.

(4R),(5R)-6-[N-Benzyl-N-(tert-butyloxycarbonyl)]amino-2,4,5-trimethyl-2-nitro-3-hexanone (*syn*-R).

Colorless oil (16/1 *syn/anti*-mixture). ^1H NMR δ : 7.32-7.19 (m, 5H), 4.44 (d, $J = 15.6$ Hz, 1H), 4.34 (d, $J = 15.6$ Hz, 1H), 3.02 (d, $J = 6.3$ Hz, 2H), 2.81 (br. s, 1H), 2.13- 2.09 (br. m, 1H), 1.69 (s, 3H), 1.68 (s, 3H), 1.46 (br. s, 9H), 1.04 (d, $J = 6.6$ Hz, 3H), 0.85 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR δ : 205.2, 156.1, 138.2, 128.6, 127.7, 127.2, 94.7, 80.1, 50.6, 50.3, 41.8, 34.0, 28.5, 23.8, 23.5, 12.7. ESIHRMS Calcd. for $\text{C}_{21}\text{H}_{32}\text{N}_2\text{O}_5\text{Na}$: 415.2209. Found: 415.2208 $[\text{M}+\text{Na}]^+$.

3(R),4(R),(5R)-6-[N-Benzyl-N-(tert-butyloxycarbonyl)]amino-2,4,5-trimethyl-2-nitro-3-hexanol and 3(S),4(R),(5R)-6-[N-Benzyl-N-(tert-butyloxycarbonyl)]-amino-2,4,5-trimethyl-2-nitro-3-hexanol

(*anti,syn*- and *syn,syn*-S). The data for *syn,syn/anti,syn*-S are taken from a 1/3 mixture of diastereomers favoring the *anti,syn*-isomer. *anti,syn*-S ^1H NMR δ : 7.32- 7.19 (m, 5H), 4.48 (br. d, 1H), 4.35 (d, $J = 15.6$ Hz, 1H), 3.96 (d, $J = 7.8$ Hz, 1H), 3.24- 3.16 (m, 1H), 2.97- 2.91 (br. m, 1H), 2.36- 2.32 (br. m, 2H), 1.62- 1.45 (br. m, 16H), 0.78 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR δ : 156.3, 138.5, 128.6, 127.6, 127.3, 92.2, 79.9, 78.0, 50.9, 50.8, 36.0, 31.3, 28.5, 23.2, 22.7, 12.3, 11.7. The diagnostic peaks of the minor isomer are as follows; *syn,syn*-S ^1H NMR δ : 1.95- 1.92 (br. m, 1H) 0.88- 0.84 (br. m, 3H). ^{13}C NMR δ : 138.4, 92.7, 80.1, 50.3, 37.7, 35.4, 31.6, 23.4, 22.6, 21.8, 14.0, 9.5. ESIHRMS Calcd. for $\text{C}_{21}\text{H}_{34}\text{N}_2\text{O}_5\text{Na}$: 417.2365. Found: 415.2375 $[\text{M}+\text{Na}]^+$.

3(R),4(R),(5R)-6-[N-Benzyl-N-(tert-butyloxycarbonyl)]amino-2,4,5-trimethyl-2-nitro-3-(diphenylphosphatoxy)hexane and 3(S),4(R),(5R)-6-[N-Benzyl-N-(tert-butyloxycarbonyl)]amino-2,4,5-trimethyl-2-nitro-3-(diphenylphosphatoxy)hexane (*anti,syn*- and *syn,syn*-T). The data for *anti,syn/syn,syn*-T are taken from a 1/4.7 mixture of diastereomers favoring the *anti,syn*-isomer. *anti,syn*-T ^1H NMR (500 MHz) δ : 7.25- 7.12 (m, 15H), 5.30- 5.27 (m, 1H), 4.47- 4.44 (br. m, 1H), 4.22 (d, $J = 15.5$ Hz,

1H), 3.21- 3.17 (br. m, 1H), 2.94 (br. s, 1H), 2.50- 2.44 (br. m, 1H), 1.97- 1.94 (br. m, 1H), 1.70 (s, 3H), 1.61 (br. s, 3H), 1.45 (s, 9H), 0.91- 0.85 (br. m, 6H); ^{13}C NMR (125 MHz) δ : 156.1, 150.7, 138.2, 129.7, 128.4, 127.4, 127.1, 125.4, 119.9, 90.2, 86.3, 79.9, 50.2, 49.8, 35.8, 30.7, 28.4, 22.6, 21.2, 12.5, 11.9. ^{31}P NMR δ : -12.10, -12.43. The diagnostic peaks of the minor isomer are as follows: *syn,syn-T* ^1H NMR (500 MHz) δ : 5.16- 5.10 (m, 1H), 1.85 (br. s, 1H) 1.54 (s, 3H); ^{13}C NMR (125 MHz) δ : 86.1, 36.5, 35.3, 26.2, 22.4, 11.0, 9.9. ESIHRMS Calcd. for $\text{C}_{33}\text{H}_{43}\text{N}_2\text{O}_8\text{PNa}$: 649.2655. Found: 649.2657 $[\text{M}+\text{Na}]^+$.

3(R),4(R),(5R)-6-Benzylamino-2,4,5-trimethyl-2-nitro-3-(diphenylphosphatoxy)hexane (*anti,syn-4*).

^1H NMR (500 MHz) δ : 7.31- 7.17 (m, 15H), 5.33 (dd, $J = 7.5$ Hz, 10.2 Hz, 1H), 3.70 (AB, $J = 13.3$ Hz, 2H), 2.46- 2.37 (m, 2H), 2.26- 2.19 (m, 1H), 2.09- 2.06 (m, 1H), 1.72 (s, 3H), 1.66 (s, 3H), 0.87 (d, $J = 6.8$ Hz, 3H), 0.77 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (125 MHz) δ : 150.5, 140.6, 129.7, 128.3, 127.9, 126.8, 125.4, 119.9, 90.1, 86.2, 53.7, 36.2, 32.4, 25.8, 21.0, 12.6, 10.3; ^{31}P NMR δ : -12.01. ESIHRMS Calcd. for $\text{C}_{28}\text{H}_{36}\text{N}_2\text{O}_6\text{P}$: 527.2311. Found: 527.2304 $[\text{M}+\text{H}]^+$.

3(S),4(R),(5R)-6-Benzylamino-2,4,5-trimethyl-2-nitro-3-(diphenylphosphatoxy)hexane (*syn,syn-4*).

Data taken from a 5.7:1 mixture with the *anti,syn*-isomer. *syn,syn-4* ^1H NMR (500 MHz) δ : 7.33- 7.16 (m, 15H), 5.33 (dd, $J = 2.3$ Hz, 9.8 Hz, 1H), 3.72 (AB, $J = 13.3$ Hz, 2H), 2.55 (d, $J = 2.55$ Hz, 2H), 2.10- 2.00 (m, 1H), 1.76- 1.66 (m, 1H), 1.63 (s, 3H), 1.59 (s, 3H), 0.92 (d, $J = 6.8$ Hz, 3H), 0.83 d, $J = 7.0$ Hz, 3H); ^{13}C NMR (125 MHz) δ : 150.5, 139.5, 129.7, 128.4, 128.3, 127.1, 125.4, 120.0, 91.3, 84.8, 53.7, 53.3, 37.2, 35.7, 23.1, 22.1, 14.5, 10.5; ^{31}P NMR δ : -12.12. ESIHRMS Calcd. for $\text{C}_{28}\text{H}_{36}\text{N}_2\text{O}_6\text{P}$: 527.2311. Found: 527.2310 $[\text{M}+\text{H}]^+$.

***trans*-N-Benzyl-3,4-dimethylpyrrolidin-2-one (*trans*-U).** A solution of *syn*-**R** (0.38 g, 1.0 mmol) in CH₂Cl₂ (15 mL) was treated with 2,6-lutidine (0.25 mL, 2.8 mmol) and then TMSOTf (0.3 mL, 2.8 mmol) and stirred at room temperature for 1 h, followed by dilution with ethyl acetate (50 mL). The organic layer washed well with saturated aqueous ammonium chloride solution (2 × 25mL), water and brine and dried. The volatiles were removed to afford a mixture of diastereomers in the ratio 1/17.2 favoring *trans*-U. Chromatography over silica gel (eluent: hexanes/ethyl acetate 1/1) afforded pure *trans*-U (0.15 g, 74%) as a colorless oil. ¹H NMR (500 MHz) δ: 7.30- 7.18 (m, 5H), 4.38 (d, *J* = 14.5 Hz, 1H), 4.42 (d, *J* = 14.5 Hz, 1H), 3.21 (dd, *J* = 7.8 Hz, 9.5 Hz, 1H), 2.73 (t, *J* = 9.2 Hz, 1H), 2.04- 1.97 (m, 1H), 1.90- 1.84 (m, 1H), 1.18 (d, *J* = 7.0 Hz, 3H), 1.04 (d, *J* = 6.6 Hz, 3H); ¹³C NMR (125 MHz) δ: 177.4, 137.1, 129.1, 128.4, 127.8, 52.4, 46.9, 45.0, 36.3, 17.7, 14.8. ESIHRMS Calcd. for C₁₃H₁₇NONa: 226.1208. Found: 226.1209 [M+Na]⁺.

4(*R*),6(*S*)-[N-Benzyl-N-(*tert*-butoxycarbonyl)]amino-2,4-dimethyl-2-nitro-3-heptanone (*syn*-V).⁴
 The data for this compound are taken from a 1/9 mixture favoring the *syn*-isomer. ¹H NMR δ: 7.32- 7.21 (m, 5H), 4.43 (br. d, *J* = 16.5 Hz, 1H), 4.13 (br. d, *J* = 15.3 Hz, 1H), 4.01 (br. s, 1H), 2.65-2.6 (m, 1H), 2.03-1.93 (m, 1H), 1.67 (s, 6H), 1.43 (br. m, 10H), 1.08 (d, *J* = 6.6 Hz, 3H), 1.06 (d, *J* = 6.6 Hz, 3H); ¹³C NMR δ: 205.8, 155.9, 139.7, 128.4, 127.2, 126.9, 94.4, 80.1, 49.9, 47.8, 38.9, 38.7, 28.5, 23.7, 19.7, 17.9. The minor isomer *anti*-V was characterized by the following signals. ¹H NMR δ: 0.90 (br. m, 6H); ¹³C NMR δ: 39.2, 38.7, 31.7, 23.6, 22.6, 23.6, 18.4, 14.0. ESIHRMS Calcd. for C₂₁H₃₂N₂O₅Na: 415.2209 Found: 415.2226 [M+Na]⁺.

4(*R*),3(*R*),6(*S*)-[N-Benzyl-N-(*tert*-butoxycarbonyl)]amino-2,4-dimethyl-2-nitro-3-heptanol and 4(*S*),3(*R*),6(*S*)-[N-Benzyl-N-(*tert*-butoxycarbonyl)]amino-2,4-dimethyl-2-nitro-3-heptanol (*anti*,*syn*-

and *syn,syn-W*).⁴ Following the general procedure E for reduction of carbonyl group, **V** (0.75 g, 1.88 mmol) afforded a 1.6/1 mixture of *anti,syn-* and *syn,syn-W* (0.6 g, 79%) as pale yellow oil. The minor diastereomeric pair *syn,anti-* and *anti,anti-W* was separated during the purification of the crude reaction mixture by silica gel column chromatography (eluent: hexanes/ethyl acetate 5/1). ¹H NMR δ: 7.31- 7.21 (br. m, 5H), 4.32 (s, 2H), 4.01- 4.03 (br. m, 1H), 3.82- 3.80 (br. m, 1H), 2.72 (br. s, 1H), 2.02- 1.99 (br. m, 1H), 1.71- 1.31 (br. m 17H), 1.12- 1.07 (br. m 6H); ¹³C NMR δ: 156.2, 140.1, 128.4, 127.3, 126.9, 92.2, 80.0, 78.3, 50.6, 47.3, 42.2, 32.7, 28.5, 23.8, 22.5, 19.9, 18.4; *syn,syn-W* ¹H NMR δ: 4.42 (br. d, *J* = 16 Hz, 1H), 4.22- 4.16 (br. m, 2H), 3.70 (br. s 1H), 0.87 (d, *J* = 6.9 Hz, 3H), 0.82 (d, *J* = 6.9 Hz, 3H); ¹³C NMR δ: 139.9, 91.9, 79.8, 49.8, 48.1, 37.5, 31.4, 23.0, 22.7, 12.9. ESIHRMS Calcd. for C₂₁H₃₄N₂O₅Na: 417.2365. Found: 417.2350.

4(*R*),3(*R*),6(*S*)-[*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)]amino-2,4-dimethyl-2-nitro-3-(diphenylphosphoxy)heptane (*anti,syn-X*).⁴ Pale yellow oil. ¹H NMR δ: 7.36- 7.14 (m, 15H), 5.04 (dd, *J* = 2.7 Hz, 9.9 Hz, 1H), 4.43-4.25 (br. m, 1H), 4.11 (d, *J* = 16.5 Hz, 1H), 3.95 (br. s, 1H), 2.04- 1.96 (br. m, 1H), 1.87- 1.81 (br. m, 1H), 1.59- 1.42 (br. m, 16H), 1.10 (d, *J* = 7.2 Hz, 3H), 1.01 (d, *J* = 6.6 Hz, 3H); ¹³C NMR δ: 155.2, 151.2, 139.8, 129.8, 128.4, 127.4, 126.9, 125.5, 120.1, 90.9, 87.6, 50.4, 48.4, 36.2, 31.7, 28.5, 23.1, 22.6, 20.2, 19.6; ³¹P NMR δ: -11.95. ESIHRMS Calcd. for C₃₃H₄₃N₂O₈NaP: 649.2655. Found: 649.2625 [M+Na]⁺.

4(*S*),3(*R*),6(*S*)-[*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)]amino-2,4-dimethyl-2-nitro-3-(diphenylphosphoxy)heptane (*syn,syn-X*).⁴ Pale yellow oil. ¹H NMR δ: 7.34- 7.14 (m, 15H), 4.82 (d, *J* = 10.3 Hz, 1H), 4.38- 4.14 (br. m, 3H), 1.86-1.78 (br. m 1H), 1.66- 1.34 (br. m, 16H), 1.01-0.99 (br. m, 4H), 0.90 (br. s, 3H); ¹³C NMR δ: 156.1, 150.7, 139.9, 129.9, 128.4, 127.3, 126.9, 125.4, 120.1, 91.0, 87.0, 79.9, 49.5,

46.9, 31.3, 28.4, 23.0, 22.8, 19.9, 13.4. ^{31}P NMR δ : -12.04 ESIHRMS Calcd. for $\text{C}_{33}\text{H}_{43}\text{N}_2\text{O}_8\text{NaP}$: 649.2655. Found: 649.2649 $[\text{M}+\text{Na}]^+$.

4(*S*),3(*R*),6(*S*)-Benzylamino-2,4-dimethyl-2-nitro-3-(diphenylphosphatoxy)heptane (*anti,syn*-5).⁴

Pale yellow oil. ^1H NMR (500 MHz) δ : 7.33- 7.18 (m, 15H), 5.11- 5.08 (dd, $J = 2.2$ Hz, 9.8 Hz, 1H), 3.88 (d, $J = 13.1$ Hz, 1H), 3.62 (d, $J = 13.1$ Hz, 1H), 2.55- 2.52 (m, 1H), 2.18- 2.16 (m, 1H), 1.65 (s, 3H), 1.62 (s, 3H), 1.47- 1.42 (m, 1H), 1.12- 1.07 (m, 1H), 1.04 (d, $J = 6.2$ Hz, 3H), 0.98 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (125 MHz) δ : 150.5, 140.9, 129.8, 128.3, 128.1, 126.8, 125.4, 120.1, 90.7, 87.6, 51.2, 49.4, 39.4, 31.1, 22.9, 22.7, 21.4, 19.5; ^{31}P NMR δ : -11.87. ESIHRMS Calcd. for $\text{C}_{28}\text{H}_{36}\text{N}_2\text{O}_6\text{P}$: 527.2311. Found: 527.2314 $[\text{M}+\text{H}]^+$.

4(*S*),3(*S*),6(*S*)-Benzylamino-2,4-dimethyl-2-nitro-3-(diphenylphosphatoxy)heptane (*syn,syn*-5).⁴

Pale yellow oil. ^1H NMR (500 MHz) δ : 7.33- 7.16 (m, 15H), 5.26 (d, $J = 9.9$ Hz, 1H), 3.86 (d, $J = 13.0$ Hz, 1H), 3.67 (d, $J = 13.0$ Hz, 1H), 2.69- 2.65 (m, 1H), 2.11- 2.06 (m, 1H), 1.65 (s, 3H), 1.63- 1.58 (m, 4H), 1.35- 1.31 (m, 1H), 1.06 (d, $J = 6.2$ Hz, 3H), 0.87 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (125 MHz) δ : 150.5, 140.9, 129.8, 128.3, 128.2, 126.8, 125.4, 120.2, 91.0, 86.1, 51.1, 49.8, 44.3, 31.1, 23.5, 22.5, 20.7, 14.4; ^{31}P NMR δ : -11.54. ESIHRMS Calcd. for $\text{C}_{28}\text{H}_{36}\text{N}_2\text{O}_6\text{P}$: 527.2311. Found: 523.2314 $[\text{M}+\text{H}]^+$.

***cis*-N-Benzyl-3,5-dimethyl-2-pyrrolidinone (*cis*-Y).** Treatment of *syn*-V with 2,6-lutidine and TMSOTf as described above for the formation of *trans*-U afforded, after silica gel column chromatography (eluent: hexanes/ethyl acetate 1/1), a 1/6.2 mixture of *trans*-Y and *cis*-Y (0.23 g, 84%), as colorless oil. *cis*-Y: ^1H NMR (500 MHz) δ : 7.31- 7.20 (m, 5H), 4.96 (d, $J = 15.0$ Hz, 1H), 4.01 (d, $J = 15.0$ Hz, 1H) 3.43- 3.38 (m, 1H), 2.48- 2.45 (m, 1H), 2.39- 2.35 (m, 1H), 1.25 (d, $J = 7.0$ Hz, 3H), 1.19- 1.17 (m, 1H), 1.16 (d, $J =$

6.2 Hz, 3H); ^{13}C NMR (125 MHz) δ : 178.1, 137.4, 128.9, 128.5, 127.8, 51.3, 44.4, 37.2, 36.9, 20.6, 16.9.

The minor isomer *trans*-**Y** was characterized by the following signal. ^1H NMR (500 MHz) δ : 3.94 (d, J = 15 Hz, 1H), 3.50- 3.44 (m, 1H), 2.65- 2.60 (m, 1H), 1.85- 1.72 (m, 2H), 1.22 (d, J = 7.0 Hz, 3H), 1.12 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz) δ : 177.6, 50.8, 35.5, 35.4, 19.3, 16.9. ESIHRMS Calcd. for $\text{C}_{13}\text{H}_{17}\text{NONa}$: 226.1192. Found: 226.1198 $[\text{M}+\text{Na}]^+$.

***cis*-Dimethyl-2-pyrrolidinone (*cis*-**Z**).** Ammonia (4 mL) was condensed in a flask fitted with a cold finger condenser (dry ice/acetone) and treated at $-78\text{ }^{\circ}\text{C}$ with sodium (0.13 g, 5.9 mmol), resulting in a dark blue solution. To this solution was added a mixture of *cis*- and *trans*-**Y** (0.12 g, 0.59 mmol) in THF (1mL) at the same temperature, after which the reaction mixture was warmed to $-40\text{ }^{\circ}\text{C}$ and stirred for 2 h before solid NH_4Cl (0.5 g) was added slowly and the volatiles allowed to evaporate. Water (5 mL) was added to the residue and extracted with ethyl acetate ($3 \times 25\text{ mL}$). The combined organic layer was washed with water ($2 \times 25\text{ mL}$) and brine (25mL), dried and concentrated to afford a crude product which was purified by silica gel column chromatography (eluent: hexanes/ethyl acetate 1/1 with 5% MeOH) to afford **31** as a 6.6/1 mixture of diastereomers (40 mg, 61%) favoring the *cis*-**Z**-isomer as a pale yellow solid. *cis*-**Z** $^{13}\text{ }^1\text{H}$ NMR (500 MHz) δ : 6.7 (br. s, 1H) 3.65- 3.61 (m, 1H), 2.55- 2.47 (m, 2H), 1.24- 1.18 (m, 4H), 1.16 (d, J = 6.7 Hz, 3H); ^{13}C NMR (125 MHz) δ : 180.9, 48.5, 39.3, 37.7, 22.6, 16.4. The minor isomer *trans*-isomer was characterized by the following signals. ^1H NMR (500 MHz) δ : 6.94 (br. s, 1H), 3.74- 3.68 (m, 1H), 2.59- 2.54 (m, 1H), 1.89- 1.85 (m, 2H); ^{13}C NMR (125 MHz) δ : 181.3, 48.1, 37.6, 35.6, 22.5, 16.6.

3(*S*),4(*S*)-[*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)]amino-3-methyl-pentanal (Ab**)** DIBAL-H (1.5M in toluene, 3.34 mL, 5.02 mmol) was added dropwise to a solution of **Aa**¹⁰ (1.35 g, 3.9 mmol) in toluene (25 mL) at $-78\text{ }^{\circ}\text{C}$ and stirred for 45 min. at this temperature. The reaction was then quenched by pouring the

cold reaction mixture into a rapidly stirred solution of HCl (1M, 30 mL). After stirring for 0.5 h, the layers were separated and the aqueous layer extracted with ethyl acetate (3 × 30 mL). The combined organic layer was then washed with saturated sodium bicarbonate solution (2 × 25 mL), water (2 × 25 mL) and brine (50 mL), dried and concentrated to give the crude product which was purified by silica gel column chromatography (eluent: hexanes/ethyl acetate 5/1) to afford **Ab** (0.98g, 80%) as a colorless oil. ¹H NMR δ: 9.72 (br. s, 1H), 7.31- 7.17 (m, 5H), 4.40 (d, *J* = 15.9 Hz, 1H), 4.32- 4.27 (br. m, 1H), 3.76- 3.72 (br. s, 1H), 2.50- 2.35 (m, 2H), 2.22- 2.12 (m, 1H), 1.44 (s, 9H), 1.10 (d, *J* = 6.6 Hz, 3H), 0.91 (d, *J* = 7.2 Hz, 3H); ¹³C NMR δ: 201.5, 156.1, 139.7, 128.3, 127.2, 126.8, 79.9, 56.9, 48.8, 48.4, 32.8, 28.5, 17.4, 16.9. ESIHRMS Calcd. for C₁₈H₂₇NO₃Na: 328.1889. Found: 328.1881 [M+Na]⁺.

3(*S*),5(*S*),6(*S*)-[*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)]amino-3-hydroxy-2,5-dimethyl-2-nitroheptane (*anti,anti*-Ac).⁴ The data for this compound are taken from a 10/1 mixture with the *syn,anti*-isomer. ¹H NMR: δ 7.30- 7.17 (m, 5H), 4.42 (d, *J* = 15.9 Hz, 1H), 4.35 (d, *J* = 15.6 Hz, 1H), 4.10- 4.04 (br. m, 1H), 2.02- 1.97 (br. m, 1H), 1.55 (s, 3H), 1.51 (s, 3H), 1.46- 1.37 (br. m, 10H), 1.14- 1.03 (br. m, 4H), 0.89 (d, *J* = 6.9 Hz, 3H); ¹³C NMR: δ 156.5, 139.9, 128.3, 127.0, 126.7, 92.3, 79.9, 74.4, 56.7, 48.5, 35.7, 35.3, 28.4, 23.1, 21.0, 17.1, 16.2. ESIHRMS Calcd. for C₂₁H₃₄N₂O₅Na: 417.2365. Found: 417.2369 [M+Na]⁺.

3(*R*),5(*S*),6(*S*)-[*N*-Benzyl-*N*-(*tert*-butyloxycarbonyl)]amino-3-hydroxy-2,5-dimethyl-2-nitroheptane (*syn,anti*-Ac).⁴ The data for this compound are taken from a 2/1 mixture with the *anti,anti*-isomer. ¹H NMR: δ 7.31- 7.17 (m, 5H), 4.39 (d, *J* = 16.2 Hz, 1H), 4.26 (d, *J* = 16.2 Hz, 1H), 4.15- 4.06 (br. m, 1H), 3.98- 3.92 (br. m, 1H), 2.52 (br. s, 1H), 2.02- 1.93 (br. m, 1H), 1.55 (s, 3H), 1.53 (s, 3H), 1.38 (br. s, 9H), 1.27- 1.20 (br. m, 2H), 1.14 (d, *J* = 6.9 Hz, 3H), 0.96 (d, *J* = 6.9 Hz, 3H); ¹³C NMR: δ 156.2, 139.9, 128.3,

127.1, 128.7, 92.5, 79.8, 74.9, 56.3, 48.8, 36.5, 35.8, 28.5, 23.5, 20.8, 17.6, 17.4. ESIHRMS Calcd. for $C_{21}H_{34}N_2O_5Na$: 417.2365. Found: 417.2371 $[M+Na]^+$.

5(S),6(S)-[N-Benzyl-N-(tert-butyloxycarbonyl)]amino-2,5-dimethyl-2-nitro-3-heptanone (*anti*-Ad).⁴

White solid. M.p 60 °C; 1H NMR δ : 7.29- 7.18 (m, 5H), 4.40- 4.32 (br. m, 2H), 3.79 (br. s, 1H), 2.58- 2.53 (br. m, 1H), 2.38- 2.25 (br. m, 2H), 1.70 (s, 3H), 1.68 (s, 3H), 1.39 (s, 9H), 1.06 (d, $J = 7.2$ Hz, 3H), 0.82 (d, $J = 6.3$ Hz, 3H); ^{13}C NMR δ : 200.9, 156.1, 139.8, 128.4, 127.3, 126.8, 94.4, 79.9, 56.2, 48.5, 40.8, 33.5, 28.5, 23.3, 17.1, 16.9. ESIHRMS Calcd. for $C_{21}H_{32}N_2O_5Na$: 415.2216 Found: 415.2209 $[M+Na]^+$.

5(S),3(S),6(S)-[N-Benzyl-N-(tert-butyloxycarbonyl)]amino-2,5-dimethyl-2-nitro-3-(diphenylphosph-

atoxy)heptane (*anti,anti*-Ae).⁴ Colorless oil. 1H NMR: δ 7.33- 7.11 (m, 15H), 5.24 (t, $J = 9.3$ Hz, 1H), 4.33 (d, $J = 15.6$ Hz, 3H), 3.99- 3.85 (br. m, 2H), 2.05- 2.01 (br. m, 1H), 1.83 (t, $J = 12.3$ Hz, 1H), 1.62 (s, 3H), 1.55 (s, 3H), 1.34 (s, 9H), 1.17 (br. t, 1H), 0.99- 0.96 (br. m, 6H); ^{13}C NMR δ : 156.2, 150.7, 140.1, 129.9, 128.2, 126.9, 126.6, 125.5, 120.1, 90.4, 81.9, 79.7, 56.8, 47.5, 36.3, 36.2, 34.0, 28.4, 22.5, 17.2, 15.6; ^{31}P NMR δ : -11.98. ESIHRMS Calcd. for $C_{33}H_{43}N_2O_8Na$ $[M+Na]^+$: 649.2655. Found: 649.2672 $[M+Na]^+$.

5(S),3(R),6(S)-[N-Benzyl-N-(tert-butyloxycarbonyl)]amino-2,5-dimethyl-2-nitro-3-(diphenylphosph-

atoxy)heptane (*syn,anti*-Ae).⁴ Colorless oil. 1H NMR δ : 7.34- 7.17 (m, 15H), 5.34 (br. s, 1H), 4.34 (d, $J = 16.2$, Hz, 1H), 4.22- 4.01 (br. m, 2H), 1.90- 1.72 (br. m, 2H), 1.63 (s, 3H), 1.59 (s, 3H), 1.46- 1.34 (br. m, 10H), 1.10 (d, $J = 7.5$ Hz, 3H), 0.86 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR δ : 156.2, 150.8, 140.2, 129.8, 128.2, 127.0, 126.6, 125.5, 120.3, 90.5, 82.9, 79.7, 56.5, 48.3, 36.4, 35.1, 28.4, 22.9, 21.9, 17.6, 17.2. ^{31}P NMR δ : -12.12. ESIHRMS Calcd. for $C_{33}H_{43}N_2O_8Na$: 649.2655. Found: 649.2633 $[M+Na]^+$.

5(*S*),3(*S*),6(*S*)-Benzylamino-2,5-dimethyl-2-nitro-3-(diphenylphosphatoxy)heptane (*anti,anti*-6).⁴

Pale yellow oil. ¹H NMR δ: 7.33- 7.10 (m, 15H), 5.28 (t, *J* = 10.2 Hz, 1H), 3.66 (AB, *J* = 13.2 Hz, 2H), 2.54- 2.49 (m, 1H), 1.93- 1.83 (m, 2H), 1.62 (s, 3H), 1.56 (s, 3H), 1.28- 1.18 (m, 1H), 0.96 (d, *J* = 6.9 Hz, 3H), 0.89 (d, *J* = 6.6 Hz, 3H); ¹³C NMR δ: 150.5, 141.0, 129.9, 128.4, 128.2, 126.9, 125.6, 120.1, 90.6, 82.4, 56.5, 51.4, 33.4, 32.6, 22.7, 22.1, 15.8, 15.1; ³¹P NMR δ: -11.78. ESIHRMS Calcd. for C₂₈H₃₆N₂O₆: 527.2311 Found: 527.2307 [M+H]⁺.

5(*S*),3(*R*),6(*S*)-Benzylamino-2,5-dimethyl-2-nitro-3-(diphenylphosphatoxy)heptane (*syn,anti*-6).⁴

Pale yellow oil. ¹H NMR δ: 7.33- 7.10 (m, 15H), 5.35- 5.28 (m, 1H), 3.84 (d, *J* = 12.9 Hz, 1H), 3.64 (d, *J* = 12.9 Hz, 1H), 2.83- 2.80 (m, 1H), 1.99- 1.91 (m, 1H), 1.76- 1.70 (m, 1H), 1.60 (s, 3H), 1.50 (s, 3H), 1.33- 1.24 (m, 1H), 0.99 (d, *J* = 6.3 Hz, 3H), 0.72 (d, *J* = 6.9 Hz, 3H); ¹³C NMR δ: 150.6, 141.2, 129.9, 128.5, 126.9, 125.6, 125.5, 120.5, 90.6, 82.8, 53.6, 52.0, 34.6, 33.9, 23.4, 21.1, 17.3, 15.6; ³¹P NMR: δ - 11.67. ESIHRMS Calcd. for C₂₈H₃₆N₂O₆: 527.2311. Found: 527.2294 [M+H]⁺.

General Procedure for Radical Ionic Cyclizations. Tributyltin hydride (0.38 mL, 1.39 mmol) and AIBN (0.04 g, 0.28 mmol) were added to a solution of substrate (0.49 g, 0.93 mmol) in degassed benzene (46 mL) and the mixture heated to reflux for 40 h with addition of further AIBN (5 mol %) every 12 h. The reaction mixture was then cooled to room temperature and the solvent removed under reduced pressure. HCl (1M in ether, 20 mL) was added to the residue and the contents stirred for 30 min. The organic layer was then extracted with dilute HCl (3 × 25 mL) and the combined aqueous layers washed well with petroleum ether (4 × 25 mL), then basified with NaOH (5M, 40 mL). The basic aqueous phase was extracted with diethyl ether (4 × 25 mL) and the combined organic layers washed with water (3 × 25

mL), brine (25 mL), dried, and concentrated to afford the crude product. Purification by alumina or silica gel column chromatography (eluting with mixtures of hexanes with ethyl acetate and MeOH) afforded the products described below in the yields and ratios set out in Table 2. Product ratios were determined by careful integration of the crude reaction mixtures.

***trans*-(*N*-Benzyl)-2-isopropyl-3-methylpyrrolidine (*trans*-7).** ^1H NMR (500 MHz, C_6D_6) δ : 7.46-7.21 (m, 5 H), 4.02 (d, $J = 13.28$ Hz, 1H), 3.21 (d, $J = 13.28$ Hz, 1H), 2.94 (t, $J = 8$ Hz, 1H), 2.29- 2.19 (m, 1H), 2.00- 1.95 (m, 2H), 1.90- 1.86 (m, 1H), 1.84- 1.80 (m, 1H), 1.18- 1.15 (m, 1H), 1.09 (d, $J = 6.81$ Hz, 3H) 1.00 (d, $J = 6.9$ Hz, 3H), 0.97 (d, $J = 6.85$ Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ : 141.2, 129.0, 128.6, 127.2, 77.9, 60.2, 52.8, 33.1, 32.9, 30.1, 22.9, 20.2, 17.1. ESIHRMS Calcd for $\text{C}_{15}\text{H}_{24}\text{N}$: 218.1909. Found: 218.1919 $[\text{M}+\text{H}]^+$.

***cis*-(*N*-Benzyl)-2-isopropyl-3-methylpyrrolidine (*cis*-7).** The data for this minor compound are taken from a 1:2.4 mixture with the *trans* isomer. ^1H NMR (500 MHz, C_6D_6) δ : 7.53- 7.19 (m, 5H), 4.10 (d, $J = 14.0$ Hz, 1H), 3.34 (d, $J = 13.5$ Hz, 1H), 3.11- 3.06 (m, 1H), 2.43 (dd, $J = 8.0$ Hz, 5.0 Hz, 1H), 2.24- 2.12 (m, 2H), 1.91- 1.79 (m, 1H), 1.71- 1.65 (m, 1H), 1.42- 1.35 (m, 1H), 1.14 (d, $J = 6.75$ Hz, 3H), 1.08 (d, $J = 6.91$ Hz, 3H), 1.04 (d, $J = 7.07$ Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ : 141.7, 128.7, 128.5, 127.0, 71.9, 62.6, 53.8, 36.8, 33.4, 30.3, 21.5, 19.8, 16.1. ESIHRMS Calcd. for $\text{C}_{15}\text{H}_{24}\text{N}$: 218.1909. Found: 218.1904 $[\text{M}+\text{H}]^+$.

***cis*-(*N*-Benzyl)-2-isopropyl-4-methylpyrrolidine (*cis*-8).** The data for this compound, which corresponded with the literature,¹⁵ are taken from a 13:1 mixture with the *trans* isomer. ^1H NMR (500 MHz, C_6D_6) δ : 7.48- 7.20 (m, 5H), 4.01 (d, $J = 13.4$ Hz, 1H), 3.04 (d, $J = 13.4$ Hz, 1H), 2.65 (dd, $J = 9.5$

Hz, 3.5 Hz, 1H), 2.38- 2.34 (m, 1H), 2.30- 2.26 (m, 1H), 1.87- 1.75 (m, 2H), 1.80- 1.75 (m, 1H) 1.19- 1.12 (m, 1H), 1.08 (d, $J = 7.0$ Hz, 3H), 1.01 (d, $J = 6.0$ Hz, 3H), 0.97 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ : 141.4, 129.1, 128.6, 127.1, 70.6, 62.1, 59.1, 34.2, 30.1, 28.7, 21.5, 20.7, 15.7.

***trans*-(*N*-Benzyl)-2-isopropyl-4-methylpyrrolidine (*trans*-8).** The data for this compound are taken from a 18:1 mixture with the *cis* isomer. ^1H NMR (500 MHz, C_6D_6) δ : 7.46- 7.20 (m, 5H), 4.02 (d, $J = 13.1$ Hz, 1H), 3.10 (d, $J = 13.2$ Hz, 1H), 3.07- 3.05 (m, 1H), 2.48- 2.44 (m, 1H), 2.08- 1.97 (m, 1H), 1.94- 1.84 (m, 1H), 1.80- 1.68 (m, 2H), 1.18 (dd, $J = 19.9$ Hz, 10.9 Hz, 1H), 1.07 (d, $J = 6.7$ Hz, 3H), 0.97 (d, $J = 6.9$ Hz, 3H), 0.89 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ : 141.2, 128.9, 128.6, 127.1, 69.4, 63.3, 59.7, 33.9, 30.1, 28.7, 20.5, 19.0, 16.0. ESIHRMS Calcd. for $\text{C}_{15}\text{H}_{24}\text{N}$: 218.1909. Found: 218.1899 $[\text{M}+\text{H}]^+$.

***cis*-(*N*-Benzyl)-2-isopropyl-5-methylpyrrolidine (*cis*-9).** The data for this compound are taken from a 5.9:1 mixture with the *trans* isomer. ^1H NMR (500 MHz, C_6D_6) δ : 7.43-71.9 (m, 5H), 3.75 (d, $J = 14.5$ Hz, 1H), 3.64 (d, $J = 14.5$ Hz, 1H), 2.7- 2.64 (m, 1H), 2.60 (ddd, $J = 11.5$ Hz, 7.0 Hz, 4.0 Hz, 1H), 1.79- 1.67 (m, 2H), 1.54- 1.47 (m, 2H), 1.36- 1.29 (m, 1H), 1.05 (d, $J = 6.1$ Hz, 3H), 1.00 (d, $J = 6.77$ Hz, 3H), 0.89 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ : 141.7, 129.2, 128.6, 126.9, 71.1, 61.4, 58.3, 33.2, 30.2, 23.5, 21.5, 20.5, 15.9. ESIHRMS Calcd for $\text{C}_{15}\text{H}_{24}\text{N}$: 218.1909. Found: 218.1898 $[\text{M}+\text{H}]^+$.

***trans*-(*N*-Benzyl)-2-isopropyl-5-methylpyrrolidine (*trans*-9).** The data for this compound are taken from a 3.3:1 mixture with the *cis* isomer. ^1H NMR (500 MHz, C_6D_6) δ : 7.51- 7.19 (m, 5H), 3.84 (d, $J = 14$ Hz, 1H), 3.50 (d, $J = 14.5$ Hz, 1H), 3.33 (quintet, $J = 6.27$ Hz, 1H), 2.73- 2.68 (m, 1H), 1.89- 1.79 (m, 2H), 1.75- 1.67 (m, 1H), 1.59- 1.53 (m, 1H), 1.30- 1.25 (m, 1H), 1.03 (d, $J = 6.5$ Hz, 3H), 0.94 (d, $J = 7.0$

Hz, 3H), 0.84 (d, $J = 6.5$ Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ : 141.2, 128.8, 128.6, 126.9, 65.1, 55.1, 52.2, 31.5, 29.1, 23.2, 20.5, 15.4, 13.4. ESIHRMS Calcd. for $\text{C}_{15}\text{H}_{24}\text{N}$: 218.1909. Found: 218.1904.

3(*S*),10a(*S*)-3,10,10-Trimethyl-1,2,3,5,10,10a-hexahydropyrrolo[1,2-*b*]isoquinoline (10). ^1H NMR (500 MHz, C_6D_6) δ : 7.38- 6.99 (m, 4H), 4.13 (d, $J = 14.4$ Hz, 1H), 3.25 (d, $J = 14.3$ Hz, 1H), 2.36 (t, $J = 8.4$ Hz, 1H), 2.28- 2.24 (m, 1H), 1.83- 1.77 (m, 1H), 1.73- 1.64 (m, 1H), 1.63- 1.56 (m, 1H), 1.42- 1.38 (m, 4H), 1.26 (s, 3H), 1.20 (d, $J = 6.0$ Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6): δ 146.1, 134.9, 127.1, 126.8, 126.6, 125.9, 71.3, 62.3, 56.2, 38.1, 32.0, 26.3, 25.7, 23.5, 19.2. ESIHRMS Calcd for $\text{C}_{15}\text{H}_{22}\text{N}$: 216.1752. Found: 216.1705 $[\text{M}+\text{H}]^+$.

2,3-*cis*-3,4-*trans*-(*N*-Benzyl)-2-isopropyl-3,4-dimethylpyrrolidine (*cis,trans*-11).¹⁷ ^1H NMR (500 MHz, C_6D_6) δ : 7.53 (d, $J = 7.5$ Hz, 2H), 7.32 (t, $J = 7.5$ Hz, 2H), 7.24- 7.22 (m, 1H), 4.15 (d, $J = 13$ Hz, 1H), 3.42 (d, $J = 13.5$ Hz, 1H), 3.14 (dd, $J = 5.9$ Hz, 8.7 Hz, 1H), 2.65 (dd, $J = 3.1$ Hz, 8.8 Hz, 1H), 1.86- 1.80 (m, 2H), 1.77- 1.71 (m 1H), 1.67- 1.59 (m, 1H), 1.15 (d, $J = 6.5$ Hz, 3H), 1.12 (d, $J = 7$ Hz, 3H), 0.99 (d, $J = 7$ Hz, 3H), 0.85 (d, $J = 6$ Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6): δ 141.2, 128.4, 128.2, 126.6, 71.5, 62.9, 62.6, 44.3, 39.4, 30.4, 21.9, 18.8, 16.8, 13.4. ESIHRMS Calcd. for $\text{C}_{16}\text{H}_{26}\text{N}$: 232.2065. Found: 232.2060 $[\text{M}+\text{H}]^+$.

2,3-*trans*-3,4-*trans*-(*N*-Benzyl)-2-isopropyl-3,4-dimethylpyrrolidine (*trans,trans*-11).¹⁷ The data for this compound are taken from a 16:1 mixture with the *cis,trans* isomer. ^1H NMR (500 MHz, C_6D_6) δ : 7.49- 7.20 (m, 5H), 3.97 (d, $J = 13.5$ Hz, 1H), 3.17 (d, $J = 13.5$ Hz, 1H), 2.6 (dd, $J = 3.5$ Hz, 9.5 Hz, 1H), 2.39 (dd, $J = 6.5$ Hz, 9.5 Hz, 1H), 2.05- 2.03 (m, 1H), 1.96- 1.87 (m, 1H), 1.52- 1.49 (m, 2H), 1.12 (d, $J = 7.5$ Hz, 3H), 1.05- 1.00 (m, 9H); ^{13}C NMR (125 MHz, C_6D_6) δ : 141.7, 128.5, 128.3, 126.6, 78.0, 59.8,

59.7, 41.9, 39.3, 29.1, 20.9, 19.7, 19.4, 17.5. ESIHRMS Calcd. for C₁₆H₂₆N: 232.2065 Found: 232.2057 [M+H]⁺.

2,3-*cis*-3,5-*cis*-(*N*-Benzyl)-2-isopropyl-3,5-dimethylpyrrolidine (*cis,cis*-12).¹⁷ The data for this compound are taken from a 1:1 inseparable mixture with the 2,3-*trans* isomer. ¹H NMR (C₆D₆, 500 MHz) δ: 7.52- 7.20 (m, 5H), 3.97 (d, *J* = 14 Hz, 1H), 3.72 (d, *J* = 14 Hz, 1H), 2.82- 2.80 (m, 1H), 2.75- 2.73 (dd, *J* = 3.5 Hz, 8.5 Hz, 1H), 2.12- 2.07 (m, 1H), 1.78- 1.75 (m, 2H), 1.26- 1.23 (m, 1H), 1.10 (d, *J* = 6.5 Hz, 3H), 1.06 (d, *J* = 7.0 Hz, 3H), 1.02 (d, *J* = 7.5 Hz, 3H), 1.05 (d, *J* = 6.5 Hz, 3H); ¹³C NMR (C₆D₆, 125 MHz) δ: 141.4, 129.1, 128.1, 126.7, 72.6, 61.4, 60.6, 42.8, 35.8, 30.2, 21.7, 21.4, 19.1, 15.4. ESIHRMS Calcd. for C₁₆H₂₆N: 232.2065. Found: 232.2070 [M+H]⁺.

2,3-*trans*-3,5-*cis*-(*N*-Benzyl)-2-isopropyl-3,5-dimethylpyrrolidine (*trans,cis*-12).¹⁷ The data for this compound are taken from a 29:1 inseparable mixture with the 2,3-*cis* isomer. ¹H NMR (C₆D₆, 500 MHz) δ: 7.52- 7.19 (m, 5H), 3.85 (d, *J* = 14 Hz, 1H), 3.53 (d, *J* = 14 Hz, 1H), 3.30- 3.27 (m, 1H), 2.47 (t, *J* = 4.4 Hz, 1H), 2.14- 2.08 (m, 1H), 2.00- 1.95 (m, 2H), 1.13 (d, *J* = 7.0 Hz, 3H), 1.06- 1.01 (m, 1H) 1.04 (d, *J* = 7.0 Hz, 3H), 0.97 (d, *J* = 6.6 Hz, 3H), 0.95 (d, *J* = 7.0 Hz, 3H); ¹³C NMR (C₆D₆, 125 MHz) δ: 140.9, 128.3, 128.7, 126.5, 72.4, 55.0, 51.3, 40.6, 31.6, 28.3, 24.1, 19.9, 15.9. ESIHRMS Calcd for C₁₆H₂₆N: 232.2065. Found: 232.2066 [M+H]⁺.

2,4-*cis*-4,5-*cis*-(*N*-Benzyl)-2-isopropyl-4,5-dimethylpyrrolidine and (*cis,cis*-13).¹⁷ The data for this compound are taken from a 12.5:1 inseparable mixture with the 2,4-*trans* isomer. ¹H NMR (500 MHz, C₆D₆) δ: 7.46- 7.18 (m, 5H), 3.82 (d, *J* = 14.3 Hz, 1H), 3.54 (d, *J* = 14.3 Hz, 1H), 2.73 (quintet, *J* = 6.9 Hz, 1H), 2.54- 2.49 (m, 1H), 2.03- 1.93 (m, 1H), 1.86- 1.78 (m, 1H), 1.68- 1.63 (m, 1H), 1.23- 1.17 (m,

1H), 1.03 (d, $J = 7$ Hz, 3H), 0.97 (d, $J = 7$ Hz, 3H), 0.92 (d, $J = 7$ Hz, 3H), 0.88 (d, $J = 6.5$ Hz, 3H); ^{13}C NMR (C_6D_6 , 125 MHz) δ : 141.4, 129.1, 128.4, 70.7, 63.4, 59.4, 34.6, 32.9, 30.3, 20.8, 17.6, 16.6, 16.0. ESIHRMS Calcd. for $\text{C}_{16}\text{H}_{26}\text{N}$: 232.2065. Found: 232.2055 $[\text{M}+\text{H}]^+$.

2,4-*trans*-4,5-*cis*-(*N*-Benzyl)-2-isopropyl-4,5-dimethylpyrrolidine (*trans,cis*-13).¹⁷ The data for this compound are taken from a 9.1:1 inseparable mixture with the 2,4-*cis* isomer. ^1H NMR (500 MHz, C_6D_6) δ : 7.51- 7.21 (m, 5H), 3.83 (d, $J = 13.9$ Hz, 1H), 3.54 (d, $J = 13.9$ Hz, 1H), 3.12 (quintet, $J = 6.5$ Hz, 1H), 2.74- 2.70 (m, 1H), 2.24- 2.13 (m, 1H), 1.91-1.81 (m, 1H), 1.70-1.65 (m, 1H), 1.34- 1.27 (m, 1H), 1.07 (d, $J = 6.7$ Hz, 3H), 0.95 (d, $J = 6.9$ Hz, 3H), 0.83 (d, $J = 6.9$ Hz, 3H), 0.71 (d, $J = 6.5$ Hz, 3H); ^{13}C NMR (C_6D_6 , 125 MHz) δ : 141.5, 128.9, 128.6, 128.0, 65.7, 58.1, 52.5, 35.8, 31.6, 29.2, 20.5, 15.8, 15.5, 7.0. ESIHRMS Calcd. for $\text{C}_{16}\text{H}_{26}\text{N}$: 232.2065 Found: 232.2066 $[\text{M}+\text{H}]^+$.

2(*S*),3(*S*),10a(*S*)-2,3,10,10-Tetramethyl-1,2,3,5,10,10a-hexahydropyrrolo[1,2-*b*]isoquinoline (14). The spectral data for this compound, which could not be obtained completely pure, are taken from a sample contaminated with approximately 10% of a mixture of the two isomers of **13**. ^1H NMR (500 MHz, C_6D_6) δ : 7.37 (d, $J = 8$ Hz, 1H), 7.23- 7.20 (m, 1H), 7.13 (t, $J = 8$ Hz, 1H), 7.00 (d, $J = 7.5$ Hz, 1H), 4.1 (d, $J = 14.3$ Hz, 1H), 3.23 (d, $J = 14.3$ Hz, 1H), 2.33- 2.29 (m, 2H), 2.04- 1.98 (m, 1H), 1.94- 1.88 (m, 1H), 1.37 (s, 3H), 1.26 (s, 3H), 1.09 (d, $J = 7.5$ Hz, 3H), 1.02 (d, $J = 7$ Hz, 3H); ^{13}C NMR (C_6D_6 , 125 MHz) δ : 146.1, 134.9, 127.0, 126.7, 126.6, 125.9, 70.6, 64.7, 56.5, 37.8, 34.3, 33.1, 26.3, 26.1, 17.4, 14.7. ESIHRMS Calcd. for $\text{C}_{16}\text{H}_{24}\text{N}$: 230.1909. Found: 230.1899 $[\text{M}+\text{H}]^+$.

References and Footnotes

1. Arabic numbers refer to cmpds in the Article. Cmpds **A-Ae** are found only in this Supporting Information.
2. Mournier, N.; Camplo, M.; Schiopacassi della Bruna, G.; Pellacini, F.; Ungheni, D.; Chermann, J.-C.; Kraus, J.-L. *Nucleosides & Nucleotides* **2000**, *19*, 1057.
3. a) Crich, D.; Jiao, X.-Y. *J. Am. Chem. Soc.* **1996**, *118*, 6666. b) Stowell, J. K.; Widlanski, T. S. *Tetrahedron Lett.* **1995**, *36*, 1825. c) Forsman, J. P.; Lipkin, D. *J. Am. Chem. Soc.* **1953**, *75*, 3145.
4. Nitrophosphates and their precursors are numbered as indicated. The *N*-benzyl group is considered part of the extended conformation backbone and all methyl groups are considered substituents. For consistency this system is applied even to cmpds **20**, **29**, and **37** which would be more correctly shown with the methyl group as part of the backbone and the amine as a substituent.

5. Substantial precedent exists for eclipsed or near-eclipsed conformations in highly substituted systems:
a) Forsyth, D. A.; Johnson, S. M. *J. Am. Chem. Soc.* **1994**, *116*, 11481. b) Gordillo, B.; Juaristi, E.; Martínez, R.; Toscano, R. A.; White, P. S.; Eliel, E. L. *J. Am. Chem. Soc.* **1992**, *114*, 2157. c) Anderson, J. E.; Casarini, D.; Ijeh, A. I.; Lunazzi, L. *J. Am. Chem. Soc.* **1997**, *119*, 8050. d) Anderson, J. E.; Tocher, D. A.; Corrie, J. E. T.; Lunazzi, L. *J. Am. Chem. Soc.* **1993**, *115*, 3494, and references therein..
6. Crich, D.; Ranganathan, K.; Rumthao, S.; Shirai, M. *J. Org. Chem.* **2003**, *68*, 2034.
7. a) Corey, E. J.; Helal, C. J. *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 1987. b) Glushkov, V. A.; Tolstikov, A. G. *Russ. Chem. Rev.* **2004**, *73*, 632. c) Wallbaum, S.; Martens, J. *Tetrahedron: Asymmetry* **2003**, *3*, 1475.

-
8. Lin, N. H.; Overman, L. E.; Rabinowitz, M. H.; Robinson, L. A.; Sharp, M. J.; Zablocki, J. *J. Am. Chem. Soc.* **1996**, *118*, 9062.
9. Masamune, S.; Choy, W.; Peterson, J. S.; Sita, L. R. *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 1.
10. Hanessian, S.; Sumi, K. *Synthesis* **1991**, 1083.
11. The oxazaborolidine reduction could not be successfully applied to ketones **R** and **V**, presumably for reasons of steric hindrance.
- 12 The possibility that lactams **U** and **Y** were equilibrated products, and so not reliable gauges of stereochemistry, was excluded by a control experiment in which *N*-benzylpyrrolidinone was exposed to TMSOTf and lutidine under the conditions applied for the retro-Henry reaction followed by quenching with D₂O, when no measurable incorporation of deuterium was observed.
13. Armstrong, R. W.; Ogawa, A. K.; DeMattei, J. A.; Scarlato, G. R.; Tellew, J. E.; Chong, L. S. *J. Org. Chem.* **1996**, *61*, 6153.
14. For discussions of the *syn*-pentane effect on stereoselectivity and conformation see: a) Roush, W. R. *J. Org. Chem.* **1991**, *56*, 4151. b) Hoffmann, R. W.; Stahl, M.; Schopfer, U.; Frenking, G. *Chem. Eur. J.* **1998**, *4*, 559.
15. Coldham, I.; Hufton, R.; Price, K. N.; Rathmell, R. E.; Snowden, D. J.; Vennall, G. P. *Synthesis* **2001**, 1523.
- 16 Lorthiois, E.; Marek, I.; Normant, J. F. *J. Org. Chem.* **1998**, *63*, 556.
- 17 In the trisubstituted pyrrolidines **11**, **12**, and **13** the first stereochemical descriptor refers to the relationship between the isopropyl group on the 2-position and the next substituent around the ring. The second stereochemical descriptor applies to the relationship between the two methyl groups thus, for example, *cis,trans*-**11** refers to 2,3-*cis*-3,4-*trans*-1-benzyl-2-isopropyl-3,4-dimethylpyrrolidine.

anti-1

I

anti-3

T

syn-V
(9:1 with *anti*-isomer)

cis-**Y**
(6.2/1 with *trans*-isomer)

S-70

trans-**7**
(containing *cis*-isomer)

cis-**8**
(13:1 with *trans*-isomer)

***trans*-8**
(18:1 with *cis*-isomer)

cis-9
(5.9:1 with *trans*-isomer)

trans-9
(3.3:1 with *cis*-isomer)

cis,trans-11

trans,trans-11
(16/1 with *cis,trans*-isomer)

***cis,cis*-12**
(1/1 with *trans,cis*-isomer)

trans,cis-12
(29/1 with *cis,cis*-isomer)

***cis,cis*-13**
(12.5/1 with *trans,cis*-isomer)

***trans,cis*-13**
(9.1/1 with *cis,cis*-isomer)

14
(containing minor amounts of both isomers of **13**)