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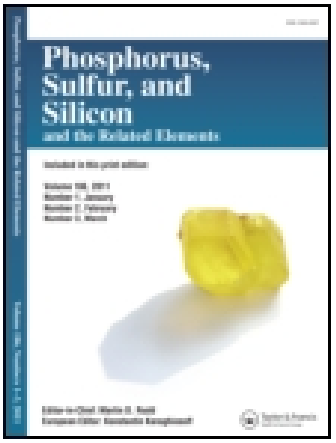

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Stereochemistry of the Three-Component Reaction Between the Ley′S Aldehyde, Benzyl Amines, and Trialkyl Phosphites. A New Approach to the Protected Enantiomerically Pure 1-Amino-2,3-Dihydroxypropylphosphonates

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STEREOCHEMISTRY OF THE THREE-COMPONENT REACTION BETWEEN THE LEY'S ALDEHYDE, BENZYL AMINES, AND TRIALKYL PHOSPHITES. A NEW APPROACH TO THE PROTECTED ENANTIOMERICALLY PURE 1-AMINO-2,3-DIHYDROXYPROPYLPHOSPHONATES

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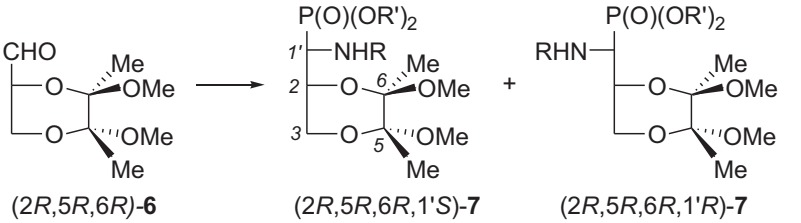
GRAPHICAL ABSTRACT



(2*R*,5*R*,6*R*)-**6** (2*R*,5*R*,6*R*,1'*S*)-**7** (2*R*,5*R*,6*R*,1'*R*)-**7**

Abstract *Enantiomerically pure orthogonally protected dimethyl 1-aminophosphonates (2R,5R,6R,1′R)- and (2R,5R,6R,1′S)-**10**, phosphonate analogs of 4-hydroxythreonine, were prepared employing the three-component reaction between trimethyl phosphite, (2R,5R,6R)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxane-2-carbaldehyde (Ley's aldehyde), and benzhydrylamine. Since both aminophosphonates **10** exist in a chloroform solution as single rotamers, the absolute configurations at C1′ were unequivocally established based on ^{1}H and ^{13}C NMR spectral data. Studies on stereochemistry of the addition of trialkyl phosphites showed that in chloroform in all cases the nucleophile preferentially attacks the si-face of the C=N bond, while in alcohols the 1,2-stereoinduction is negligible, and sense of chirality of phenylethylamines is solely responsible for a π-facial discrimination in the 1,3-asymmetric inductions.*

Keywords Chiral auxiliaries; conformation; configuration; reaction mechanism; Schiff bases

INTRODUCTION

Several polyhydroxy α-amino acids have been found as components of natural products. Polyoxamic acid [(2*S*,3*S*,4*S*)-2-amino-2,3,4-trihydroxypentanoic acid] (2*S*,3*S*,4*S*)-**1**

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Dedicated to Professor Louis D. Quin on the occasion of his 85th birthday.

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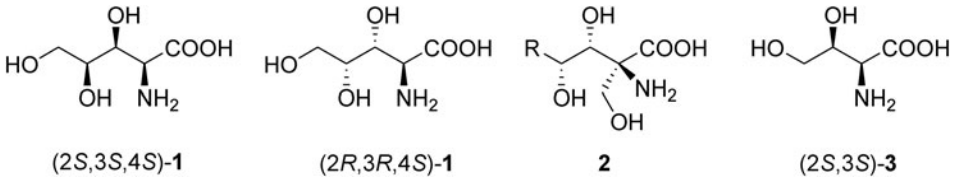

Figure 1 Polyoxamic acid and related polyhydroxy amino acids.

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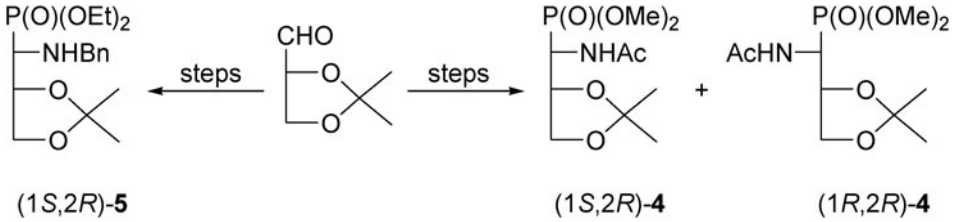
(Figure 1)[1–6] seems to be the best recognized among them since this molecule is incorporated into peptidyl nucleoside antibiotics, called polyoxins.[7] Less known antifungal sphingofungins A–D contain 3,4-diepipolyoxamic acid (2*S*,3*R*,4*R*)-**1**.[1,2,6] On the other hand, in sphingofungins E and F,[8–10] potent immunosuppressants mycestericins A–G[11–15] and myriocin[16–18] various α-branched polyhydroxy α-amino acid moieties **2** serve as a polar end of long chain molecules.

Also 4-hydroxy-L-threonine [(2*S*,3*S*)-2-amino-3,4-dihydroxybutyric acid] (2*S*,3*S*)-**3** and its stereoisomers (Figure 1) were found as constituents of natural products (e.g., Lobocyclamide B, Actinomycin Z1)[19,20] or were produced by several species.[19–24] It is firmly established that 4-hydroxy-L-threonine is a precursor of vitamin B_6[25] in *Rhizobium*[26] and in *Escherichia coli*.[27] The interest in syntheses of 4-hydroxy-L-threonine[19,28–33] is stimulated not only by its occurrence in nature but also by its intermediacy in biosynthesis of vitamin B_6 and chemical synthesis of the monobactam antibiotic carumonam.[34] Stereochemistry of 2-amino-3,4-dihydroxybutyric acids, including 4-hydroxy-L-threonine, was established by the correlation with D-glyceraldehyde.[35]

Studies on biological activity of aminophosphonates as bioisosters of amino acids are still an active field of research.[36] For this reason, the demand for new enantiomerically pure aminoalkylphosphonates continues.[37,38] The first synthesis of phosphonate analogs of 4-hydroxythreonines took advantage of the HO–C1 for H_2N–C1 replacement in diastereoisomeric adducts of dimethyl hydrogen phosphonate to 2,3-*O*-isopropylidene-D-glyceraldehyde via triflation, nucleophilic substitution with azide, and reduction and made both phosphonates (1*R*,2*R*)- and (1*S*,2*R*)-**4** synthetically available (Scheme 1).[39] In a recent approach, addition of diethyl hydrogen phosphonate to *N*-benzyl nitrone derived from 2,3-*O*-isopropylidene-D-glyceraldehyde in the presence of *tert*-butyldimethylsilyl triflate (TBDMSOTf) followed by the reduction of the respective hydroxylamine led to the formation of phosphonate (1*S*,2*R*)-**5** as a single diastereoisomer (Scheme 1).[40]

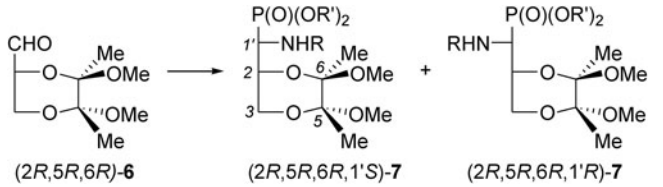


Scheme 1 The existing methods for the synthesis of the phosphonate analogs of 4-hydroxytheonines.

Table 1 Stereochemistry of the formation of 1-aminophosphonates **8**

		1-aminophosphonates, **8**					
		^{31}P NMR shifts			Stereochemistry		
Entry	Amine R	Major	Minor	Ratio of diastereoisomers	Major	Minor	**9**,%
a	$PhCH_2$	26.03	25.62	55:45	(1′*R*)	(1′*S*)	7
b	Ph_2CH	27.03	25.80	52:48	(1′*R*)	(1′*S*)	25
c	(*S*)-1-phenylethyl	27.43	25.33	81:19	(1′*R*)	(1′*S*)	6
d	(*R*)-1-phenylethyl	27.05	25.74	60:40	(1′*S*)	(1′*R*)	6
e	(*R*)-1-(1-naphthyl)ethyl	26.70	26.10	60:40	(1′*S*)	(1′*R*)	9

Our successful preparation of enantiomerically pure protected 1,2,3-trihydroxypropylphosphonates[41] employing (2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxane-2-carbaldehyde **6** (the Ley's aldehyde) easily prepared from D-mannitol in two steps[42–44] has prompted us to apply this aldehyde in the synthesis of the phosphonate analogs of 4-hydroxytheonines. Herein, we wish to describe our studies on the synthesis and separation of diastereoisomeric 1-aminophosphonates (2*R*,5*R*,6*R*,1′*S*)-**7** and (2*R*,5*R*,6*R*,1′*R*)-**7** prepared from the aldehyde **6**, selected primary amines and trialkyl phosphites (Scheme 2).



Scheme 2 Addition of trialkyl phosphites to a mixture of the aldehyde (2*R*,5*R*,6*R*)-**6** and amines RNH_2 in 2,2,2-trifluoroethanol.

RESULTS AND DISCUSSION

Synthesis

In search for the conditions to successfully accomplish the three-component reaction between aldehydes, primary amines, and trialkyl phosphites, the methodology elaborated by Heydari[45] was selected since by application of 2,2,2-trifluoroethanol the synthesis is carried out at room temperature, which we consider as a prerequisite for the future studies on protected sugar aldehydes. The preliminary studies on the three-component reaction between the aldehyde **6**, triethyl phosphite, and selected primary amines in 2,2,2-trifluoroethanol showed the formation of the expected diethyl 1-aminophosphonates (2*R*,5*R*,6*R*,1′*R*)-**8** and (2*R*,5*R*,6*R*,1′*S*)-**8** (Scheme 3), which were contaminated with the respective 1-hydroxyphosphonates (2*R*,5*R*,6*R*,1′*R*/*S*)-**9**[41] (Table 1) and, in consequence, with the unreacted amines.

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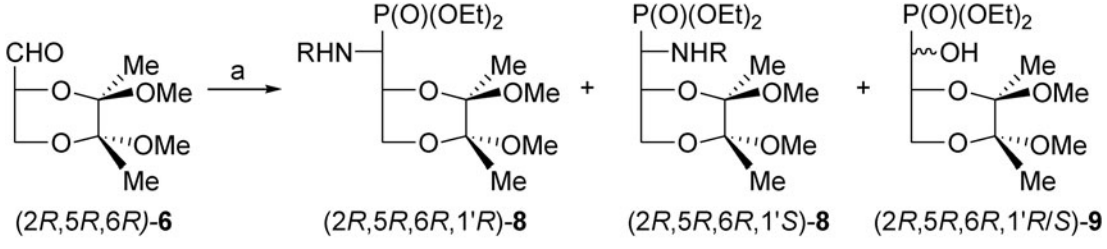

Scheme 3 Synthesis of diethyl 1-aminophosphonates (2*R*,5*R*,6*R*,1′*R*)-**8** and (2*R*,5*R*,6*R*,1′*S*)-**8**. Reaction conditions: (a) **6** (1.0 equiv.), $(EtO)_3P$ (1.0 equiv.), RNH_2 (1.0 equiv.), 2,2,2-trifluoroethanol, r.t., 24 h.

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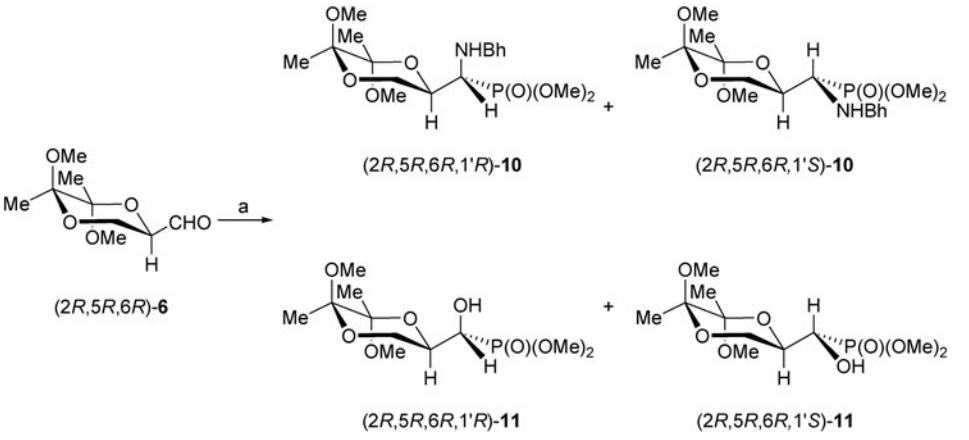
The addition of triethyl phosphite to the aldehyde **6** in the presence of the selected substituted benzyl amines (Table 1) was accompanied by the formation of up to 25% of diastereoisomeric 1-hydroxyphosphonates **9** when benzhydrylamine was used. The significant increase in the amount of 1-hydroxyphosphonates in the latter reaction results from the bulkiness of the diphenylmethylamino group making the competing Abramov reaction more feasible. Moreover, when tritylamine was applied only 1-hydroxyphosphonates **9** were produced.

Diastereoselectivity of the additions performed in the presence of benzylamine or benzhydrylamine appeared to be very low, and the respective 1-aminophosphonates (2*R*,5*R*,6*R*,1′*R*)-**8a** and (2*R*,5*R*,6*R*,1′*R*)-**8b** were formed as major products. To improve diastereoselectivity double asymmetric induction was tried with (*S*)- and (*R*)-1-phenylethylamine and (*R*)-1-(1-naphthyl)ethylamine. Good diastereoisomeric excess (62%) was noticed when (*S*)-1-phenylethylamine was applied, and 1-aminophosphonate (2*R*,5*R*,6*R*,1′*R*)-**8c** was obtained as a major product. On the other hand, reactions carried out with (*R*)-1-phenyl- and (*R*)-1-(1-naphthyl)ethylamines again showed poor diastereoselectivities (20%) but in these cases the 1-aminophosphonates (2*R*,5*R*,6*R*,1′*S*)-**8d** and (2*R*,5*R*,6*R*,1′*S*)-**8e** were formed preferentially. All attempts to purify the crude reaction mixtures failed to give pure compounds as well as to separate diastereoisomeric 1-aminophosphonates **8**.

Application of trimethyl phosphite in the reaction with the aldehyde **6** and benzhydrylamine led to the formation of a 56:44 mixture of dimethyl 1-aminophosphonates (2*R*,5*R*,6*R*,1′*R*)- and (2*R*,5*R*,6*R*,1′*S*)-**10** (Scheme 4). After careful optimization of the reaction condition it was established that application of 0.9 equivalent of trialkyl phosphite and 0.85 equivalent of benzyl amines minimized the formation of unwanted 1-hydroxyphosphonates and facilitated the purification of the reaction mixtures especially the separation of the aminophosphonates and unreacted benzyl amines. The crude product contained up to 25% of the respective dimethyl 1-hydroxyphosphonates (2*R*,5*R*,6*R*,1′*R*/*S*)-**11**. Diastereoisomeric 1-aminophosphonates (2*R*,5*R*,6*R*,1′*R*)-**10** and (2*R*,5*R*,6*R*,1′*S*)-**10** were successfully separated on silica gel columns to give both pure compounds as colorless oils in 20% yields.



Scheme 4 Synthesis of dimethyl 1-aminophosphonates (2*R*,5*R*,6*R*,1′*S*)- and (2*R*,5*R*,6*R*,1′*R*)-**10**. Reaction conditions: (a) **6** (1.0 equiv.), $(MeO)_3P$ (0.9 equiv.), Ph_2CHNH_2 (0.85 equiv.), 2,2,2-trifluoroethanol, r.t., 24 h.

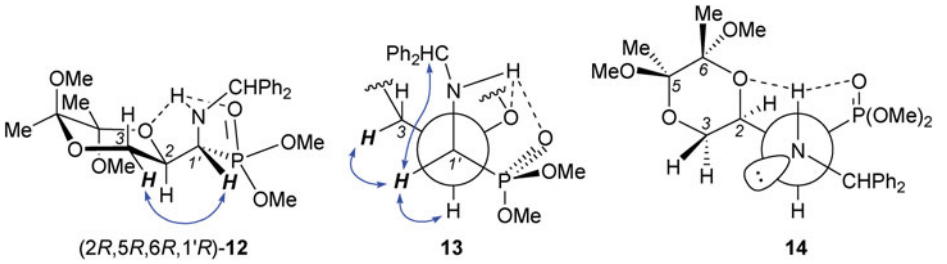


Figure 2 The preferred conformation **12** of the major phosphonate (2*R*,5*R*,6*R*,1′*R*)-**10**.

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Configurational Studies

The absolute configurations at C1′ in dimethyl 1-aminophosphonates (1′*S*)-**10** and (1′*R*)-**10** were established based on detailed analysis of ^{1}H and ^{13}C NMR spectral data. In a chloroform solution, the major 1-aminophosphonate (1′*R*)-**10** exits as a single rotamer in a conformation **12** (Figure 2). The antiperiplanar orientation of the phosphorus atom and C3 (projection **13**) is proved by the value of ^{3}J(PC1′C2C3) = 14.0 Hz,[46,47] while the gauche arrangements of the hydrogen atoms *H*C1′–C2*H* and the phosphorus atom and HC2 (*P*C1′–C2*H*) can be concluded from the values of ^{3}J(HC1′C2H) = 3.2 Hz[48] and ^{3}J(PC1′C2H) = 10.6 Hz,[49,50] respectively. Undoubtedly, this conformation is stabilized by a strong intramolecular hydrogen bond.[41] These conclusions received additional support by the observation of NOESY correlation signals between hydrogen atoms *H*C1′ and *H*C3eq, *H*C1′ and *H*C2, *H*C1′ and *H*CPh$_2$, but not between *H*C1′ and *H*C3ax (Figure 2, blue arrows). Furthermore, from the value of ^{3}J(PC1′NC) = 3.1 Hz one may suggest the gauche orientation **14** of the diphenylmethyl and the dimethoxyphosphoryl groups and, in consequence, the restricted rotation along the C1′–N bond. This conclusion receives further support by lack of shielding effects by the aromatic rings on the hydrogen atoms attached to the 1,3-dioxane ring.

The same approach was applied in configurational studies of diastereoisomeric diethyl 1-aminophosphonates **8a**–**f**. The absolute stereochemistry (2*R*,5*R*,6*R*,1′*R*) was assigned to the diastereoisomers (Table 1) displaying the following values of ^{3}J(PC1′C2C3) = 12.8–14.6 Hz and ^{3}J(HC1′C2H) = 2.4–4.0 Hz in their ^{1}H and ^{13}C NMR spectra.

On the other hand, in a chloroform solution the minor 1-aminophosphonate (1′*S*)-**10** exists almost exclusively in a conformation **15** (Figure 3) in which the phosphorus atom and C3 adopt the gauche-orientation **16**, since the following values of ^{3}J(PC1′C2C3) = 4.3 Hz,[46,47] ^{3}J(HC1′C2H) = 4.4 Hz,[48] and ^{3}J(PC1′C2H) = 14.2 Hz[49,50] were observed in

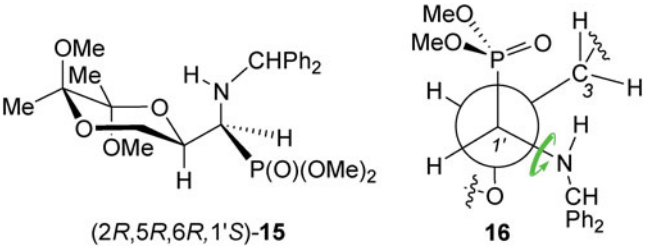
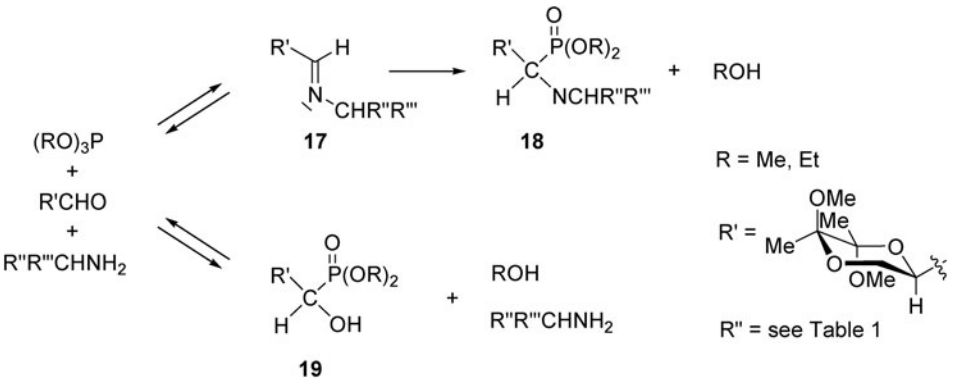


Figure 3 The preferred conformation **15** of the minor phosphonate (2*R*,5*R*,6*R*,1′*S*)-**10**.

the respective ^{1}H and ^{13}C NMR spectra. Opposite to the restricted rotation of the diphenylmethylamino group along the C1′–N bond observed in the major 1-aminophosphonate (1′*R*)-**10**, in the minor diastereoisomer (1′*S*)-**10** this group freely rotates, since the value of $^{3}J(PC1'NC) = 7.7$ Hz was observed.

Mechanistic Considerations

The accepted mechanism of the three-component reaction between trialkyl phosphites, aldehydes, and amines relies on the nucleophilic addition of the phosphorus nucleophiles to the preformed imines **17** or the respected iminium ions to produce 1-aminoalkylphosphonates **18** (Scheme 5).[51–57] The alternative mechanistic pathway to phosphonates **18** involves formation of 1-hydroxyalkylphosphonates **19**, which in the presence of amines are supposed to undergo a retro-Abramov reaction affording 1-aminophosphonates **18** through imines **17**.[52,55,57]



Scheme 5 Mechanisms of the three-component reaction between trialkyl phosphites, aldehydes, and amines.

To verify the latter pathway diethyl (*R*)-hydroxy-[(2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl]methylphosphonate (2*R*,5*R*,6*R*,1′*R*)-**9c**[41] was treated with (*S*)-1-phenylethylamine in 2,2,2-trifluoroethanol at room temperature. After 48 h the ^{1}H and ^{31}P NMR spectra showed the presence of a 1:1 mixture of the starting materials and no traces of diastereoisomeric diethyl 1-aminophosphonates (2*R*,5*R*,6*R*,1′*R*)-**8c** and (2*R*,5*R*,6*R*,1′*S*)-**8c** were detected. Since 1-hydroxyphosphonate (1′*R*)-**9c** remained unchanged, these observations exclude the reversibility of the Abramov reaction (Scheme 5), which would provide an equilibrium mixture of (1′*R*)-**9c** and (1′*S*)-**9c**.

To get further insight into the mechanism of the investigated reaction, imine **20**[58] was synthesized from the aldehyde (2*R*,5*R*,6*R*)-**6** and (*S*)-1-phenylethylamine and further subjected to the reaction with triethyl phosphite in 2,2,2-trifluoroethanol (Scheme 6). After 48 h the formation of a 77:23 mixture of diethyl 1-aminophosphonates (1′*R*)-**8c** and (1′*S*)-**8c** was observed by the ^{31}P NMR spectroscopy, while the respective diethyl 1-hydroxyphosphonates (1′*R*)-**9c** and (1′*S*)-**9c** were not detected in the crude reaction mixture. The similar reactivity pattern was found for trimethyl phosphite. These observations clearly showed that application of pre-formed imines **17** (Scheme 5) is a better approach in the synthesis of 1-aminoalkylphosphonates **18** than conducting a three-component reaction.

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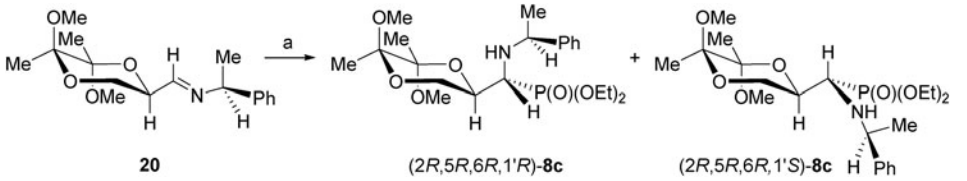


Scheme 6 Addition of triethyl phosphite to the imine **20**. Reaction conditions: (a) **20** (1.0 equiv.), $(EtO)_3P$ (1.0 equiv.), 2,2,2-trifluoroethanol, r.t., 48 h.

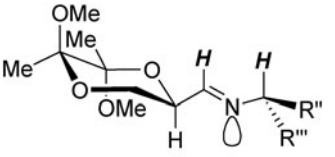
Replacement of 2,2,2-trifluoroethanol with anhydrous ethanol significantly slowed the three-component reaction down, which was complete in about 2 weeks. Under the same conditions, addition of triethyl phosphite to the imine **20** was even slower. In both cases, a 7:3 diastereoselectivity was observed, and 1-aminophosphonate (1′*R*)-**8c** was formed as a major product.

When the reaction between the aldehyde (2*R*,5*R*,6*R*)-**6**, benzylamine, and triethyl phosphite was performed in chloroform at room temperature, a 20:80 mixture of the expected diethyl 1-aminophosphonates (1′*R*)-**8a** and (1′*S*)-**8a** was obtained in less than 4 days. Similar diastereoselectivity (25:75) was noticed in the three-component reaction when benzylamine was replaced with benzhydrylamine. Application of (*R*)-1-phenylethylamine instead of benzylamine led to the formation of a 13:87 mixture of phosphonates (1′*R*)-**8d** and (1′*S*)-**8d** while with (*S*)-1-phenylethylamine the 1-aminophosphonates (1′*R*)-**8c** and (1′*S*)-**8c** were produced in a 31:69 ratio.

Transition State Models for the Addition of Trialkyl Phosphites to C=N Bonds

It is firmly established that imines exist in a preferred conformation in which hydrogen atoms within a ***H***–C=N–C–***H*** fragment are eclipsed to minimize the 1,3-allylic strain.[59] For this reason, aldimines formed from the aldehyde (2*R*,5*R*,6*R*)-**6** and benzylamines (Table 1) would adopt a conformation **21** (Figure 4) in which rotation around the N–CHR″R‴ is restricted. Thus, any π-facial discrimination resulted from the additions of trialkyl phosphites to the C=N bond would incorporate the 1,2-asymmetric induction generated by the chirality at C2 and the 1,3-asymmetric induction if chiral amines are employed.

In attempts at rationalizing the stereochemical outcome of the three-component reactions performed in chloroform transition states without chelation can be only considered. However, the nonchelation transition state models for nucleophilic additions to imines are rarely discussed in the literature[31,60] although sound evidence was gathered in favor



21

Figure 4 The preferred conformation **21** of imines formed from the aldehyde (2*R*,5*R*,6*R*)-**6** and benzylamines.

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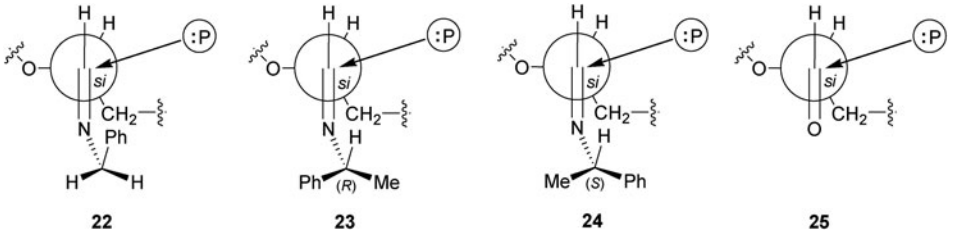

Figure 5 Transition state models of additions to the C=N bond in the three-component reactions without chelation (**22**–**24**) and to the C=O bond in the Abramov reaction (**25**).

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of the "Felkin-Ahn polar model" in which the incoming nucleophile enters from the opposite side of the electronegative substituent at the stereogenic center.[61] We suggest that triethyl phosphite preferentially approaches the *si* face of the C=N bond in the imine **21** (R″ = H, R‴ = Ph) on a Bürgi–Dunitz trajectory[62,63] in a transition state **22** resembling the Felkin-Ahn polar model in which the oxygen atom (O1) serves as the largest substituent to give (1′*S*)-aminophosphonates **8** as major diastereoisomers (Figure 5). The stereogenic centers present in the imine obtained from the aldehyde (2*R*,5*R*,6*R*)-**6** and (*R*)-1-phenylethylamine form a "matched-pair" (TS **23**) since better diastereoselectivity (13:87) is observed in comparison to the 1,2-asymmetric induction (20:80) found in the former case. Because the diastereoselectivity of the addition to the imine produced from the aldehyde (2*R*,5*R*,6*R*)-**6** and (*S*)-1-phenylethylamine drops down significantly (31:69), a "mismatched-pair" of stereogenic centers (TS **24**) is characteristic of this diastereoisomer. In support to these conclusions, it was noticed that a similar Felkin-Ahn model **25** acknowledges the sense of 1,2-stereoinduction of dialkyl hydrogen phosphonates to the aldehyde (2*R*,5*R*,6*R*)-**6**.[41]

Opposite to the preferential formation of (1′*S*)-aminophosphonates **8** in reactions conducted in chloroform regardless of the structural features of amines used, the absolute configuration of major 1-aminophosphonates **8** obtained in additions carried out in 2,2,2-trifluoroethanol (Table 1) or in ethanol strongly depends on the structure of amines used. To accommodate the observed results, we suggest that in alcohols (e.g., 2,2,2-trifluoroethanol; $pK_a = 12.4$) the respective iminium ions are subjected to the nucleophilic attack by triethyl phosphite. However, in order to avoid the 1,3-allylic strain, protonated imines are expected to adopt a conformation **26** (Figure 6) in which hydrogen atoms in the ***H***–C2–C=N$^+$–***H*** moiety are eclipsed.

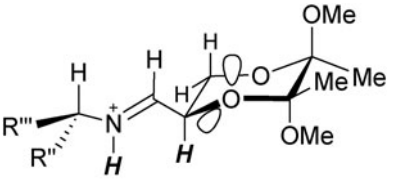

Figure 6 The preferred conformation **26** of protonated imines formed from the aldehyde (2*R*,5*R*,6*R*)-**6** and benzylamines.

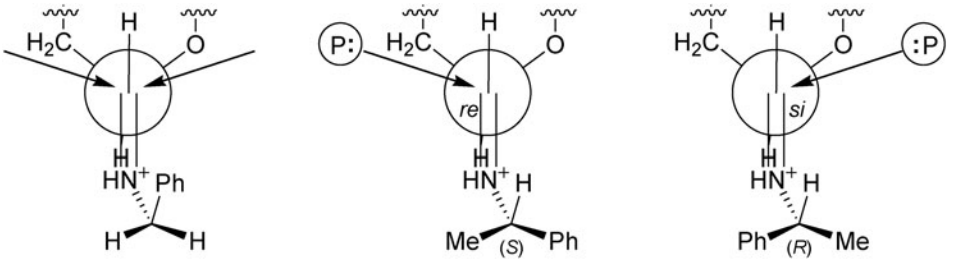

Figure 7 Transition state models of additions to the C = N bond in the three-component reactions performed in alcohols (**27**–**29**).

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Thus, a negligible diastereoselectivity observed in addition of trialkyl phosphites to imines formed from the aldehyde (2*R*,5*R*,6*R*)-**6** and benzylamine as well as benzhydrylamine reflects lack of facial discrimination as depicted in a TS model **27** ($H_{ax}C3H_{eq}$ vs. lone pairs at O1) (Figure 7).

A significant diastereoselectivity observed in the reaction of triethyl phosphite with the imine prepared from the aldehyde (2*R*,5*R*,6*R*)-**6** and (*S*)-1-phenylethylamine providing (2*R*,5*R*,6*R*,1′*R*)-**8c** as a major diastereoisomer can be explained by the preferential attack of the nucleophile at the less hindered *re* face (TS **28**) as a result of the 1,3-asymmetric induction only. For the same reason, the approaching nucleophile favors the *si* face (TS **29**) of the imine prepared from the aldehyde (2*R*,5*R*,6*R*)-**6** and (*R*)-1-phenylethylamine as well as from (*R*)-1-(1-naphthyl)ethylamine thus leading to the formation of (1′*S*)-**8e** and (1′*S*)-**8f** as major products.

CONCLUSIONS

(2*R*,5*R*,6*R*)-5,6-Dimethoxy-5,6-dimethyl-1,4-dioxane-2-carbaldehyde (Ley's aldehyde) was efficiently employed in the three-component reaction with trimethyl phosphite and benzhydrylamine to give enantiomerically pure dimethyl 1-aminophosphonates (2*R*,5*R*,6*R*,1′*R*)-**10** (20%) and (2*R*,5*R*,6*R*,1′*S*)-**10** (20%) after chromatographic separation on silica gel columns.

The absolute configurations at C1′ in 1-aminophosphonates (2*R*,5*R*,6*R*,1′*R*)-**10** (major) and (2*R*,5*R*,6*R*,1′*S*)-**10** (minor) were unequivocally established based on ^{1}H and ^{13}C NMR spectral data since in chloroform they exist as single rotamers, and the major diastereoisomer is additionally stabilized by a strong intramolecular hydrogen bond. Generally, for other 1-aminophosphonates, the (2*R*,5*R*,6*R*,1′*R*) absolute stereochemistry is assigned to the diastereoisomer having ^{3}J(HC1′C2H) = 2.4–4.0 Hz and ^{3}J(PC1′C2C3) = 12.8–14.6 Hz.

Diastereoselectivity of the additions of trialkyl phosphites to the C = N bond of intermediate imines (iminium ions) formed in the three-component reactions strongly depends on the solvent. Regardless the amine used in reactions carried out in chloroform, diethyl (2*R*,5*R*,6*R*,1′*S*)-1-aminophosphonates are formed as major products with d.e. up to 74%. The sense of chirality of major 1-aminophosphonates produced in alcohols solely depends on the configuration of the amines. When (*S*)-1-phenylethylamine was applied, (2*R*,5*R*,6*R*,1′*R*)-1-aminophosphonate was obtained as a major diastereoisomer (d.e. 62%),

while from (*R*)-1-phenylethylamine (2*R*,5*R*,6*R*,1′*S*)-1-aminophosphonate (d.e. 20%) was formed.

The Felkin-Ahn polar models of transition states proposed for the addition of trialkyl phosphites in chloroform account for preferential attack on the *si* face of the C=N bond and the 1,2-asymmetric induction is found more influential than the 1,3-asymmetric induction. The transition state models suggested for the reactions performed in alcohols well correlate with the negligible 1,2-diastereoselection and invoke the 1,3-asymmetric induction to rationalize the observed π-facial discrimination.

EXPERIMENTAL

General

^{1}H NMR spectra were recorded with a Varian Mercury-300 spectrometer; chemical shifts δ in ppm with respect to tetramethylsilane (TMS); coupling constants J in Hz. ^{13}C and ^{31}P NMR spectra were recorded on a Varian Mercury-300 machine at 75.5 and 121.5 MHz, respectively. Two-dimensional NMR (COSY and NOE) measurements were performed on a Bruker Avance III (600 MHz) spectrometer. IR spectral data were measured on an Infinity MI-60 FT-IR spectrometer. Melting points were determined on a Boetius apparatus and are uncorrected. Elemental analyses were performed by the Microanalytical Laboratory of this Faculty on a Perkin Elmer PE 2400 CHNS analyzer and their results were found to be in good agreement (±0.3%) with the calculated values. Polarimetric measurements were conducted on an Optical Activity PolAAr 3001 apparatus. The following absorbents were used: column chromatography, Merck silica gel 60 (70−230 mesh), cat.#1.07734.9025 (Darmstadt, Germany); analytical TLC, Merck TLC plastic sheets silica gel 60 F_{254}, cat.#1.05735.0001 (Darmstadt, Germany).

The Three-component Reaction of (2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxane-2-carboxaldehyde (2*R*,5*R*,6*R*)-6 with Benzhydrylamine and Trimethyl Phosphite

To a solution of the aldehyde (2*R*,5*R*,6*R*)-**6** (3.30 g, 16.6 mmol) in 2,2,2-trifluoroethanol (3 mL), benzhydrylamine (2.52 g, 13.7 mmol) was added followed by trimethyl phosphite (1.85 g, 14.9 mmol) and the reaction mixture was stirred at room temperature for 24 h. After removal of all volatiles in vacuum (0.1 mm Hg), the oily residue was analyzed by ^{1}H and ^{31}P NMR spectroscopy and subjected to chromatographic purification to give of dimethyl 1-aminophosphonates (2*R*,5*R*,6*R*,1′*S*)-**10** (1.26 g, 20%) and (2*R*,5*R*,6*R*,1′*R*)-**10** (1.22 g, 20%) as colorless oils.

Dimethyl (*S*)-[(2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl](diphenylmethylamino)methylphosphonate (2*R*,5*R*,6*R*,1′*S*)-10

$[\alpha]_D^{20} = -72.7$ (c 0.9, $CHCl_3$). IR (film): ν [cm^{-1}] 3480, 3335, 2992, 2952, 1599, 1493, 1453, 1374, 1245, 1142, 1037, 879, 827, 749, 705. ^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm]: 7.45–7.40 (m, 4H), 7.40–7.19 (m, 6H), 5.41 (s, 1H, HCPh$_2$), 4.29 (dddd, J_{2-P} = 14.2, J_{2-3ax} = 11.3, J_{2-1} = 4.4, J_{2-3eq} = 3.3 Hz, 1H, HCCP), 3.93 (t, $J_{3ax-3eq} = J_{3ax-2}$ = 11.3 Hz, 1H, H_{ax}CCCP), 3.83 (d, J = 10.7 Hz, 3H, POCH$_3$), 3.79 (d, J = 10.7 Hz, 3H, POCH$_3$), 3.62 (dd, $J_{3eq-3ax}$ = 11.3, J_{3eq-2} = 3.3 Hz, 1H, H_{eq}CCCP), 3.30 (s, 3H, OCH$_3$), 3.25 (s, 3H, OCH$_3$), 3.04 (dd, J_{1-P} = 17.7, J_{1-2} = 4.4 Hz, 1H, HCP), 2.09 (very br s,

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1H, NH), 1.29 (s, 3H, CH_3), 1.28 (s, 3H, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ [ppm]: 143.1, 143.1, 128.4, 128.4, 127.8, 127.4, 127.3, 127.1, 99.4, 97.3, 67.7 (d, $J = 6.6$ Hz), 65.0 (d, $J = 7.7$ Hz), 60.6 (d, $J = 4.3$ Hz, *C*CCP), 53.5 (d, $J = 148.3$ Hz, CP), 53.1 (d, $J = 6.6$ Hz), 52.7 (d, $J = 6.9$ Hz), 48.3, 48.0, 17.9, 17.7. ^{31}P NMR (121.5 MHz, $CDCl_3$) δ [ppm]: 28.58 ppm. Anal. Calcd. for $C_{24}H_{34}NO_7P$: C, 60.12; H, 7.15; N, 2.92. Found: C, 59.90; H, 7.19; N, 2.86.

Dimethyl (*R*)-[(2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl](diphenylmethylamino)methylphosphonate (2*R*,5*R*,6*R*,1′*R*)-10

$[\alpha]_D^{20} = -110.5$ (c 1.0, $CHCl_3$). IR (film): ν [cm^{-1}] 3480, 3355, 2990, 2951, 1599, 1493, 1454, 1374, 1248, 1142, 1033, 878, 813, 747, 700. ^1H NMR (300 MHz, $CDCl_3$) δ [ppm]: 7.48–7.44 (m, 2H), 7.42–7.38 (m, 2H), 7.34–7.21 (m, 6H), 5.25 (d, $J = 3.2$ Hz, 1H, *H*CPh_2), 4.32 (dddd, $J_{2-3ax} = 11.3$, $J_{2-P} = 10.6$, $J_{2-1} = 3.2$, $J_{2-3eq} = 3.2$ Hz, 1H, HCCP), 4.20 (t, $J_{3ax-3eq} = J_{3ax-2} = 11.3$ Hz, 1H, H_{ax}CCCP), 3.82 (d, $J = 10.6$ Hz, 3H, CH_3OP), 3.73 (d, $J = 10.7$ Hz, 3H, CH_3OP), 3.36 (s, 3H, OCH_3), 3.33 (s, 3H, OCH_3), 3.30 (dd, $J_{3eq-3ax} = 11.1$, $J_{3eq-2} = 3.2$ Hz, 1H, H_{eq}CCCP), 2.85 (dd, $J_{1-P} = 15.0$, $J_{1-2} = 3.2$ Hz, 1H, HCP), 1.90–1.30 (br s, 1H, NH), 1.29 (s, 3H, CH_3), 1.28 (s, 3H, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ [ppm]: 143.7, 142.5, 128.4, 127.7, 127.2, 127.2, 127.1, 99.4, 97.7, 68.9 (d, $J = 1.7$ Hz), 65.2 (d, $J = 3.1$ Hz), 60.8 (d, $J = 14.0$ Hz, *C*CCP), 53.0 (d, $J = 6.3$ Hz), 52.9 (d, $J = 142.8$ Hz, CP), 51.9 (d, $J = 6.6$ Hz), 48.38, 48.0, 17.8, 17.7. ^{31}P NMR (121.5 MHz, $CDCl_3$): δ [ppm]: 30.24 ppm. Anal. Calcd. for $C_{24}H_{34}NO_7P$: C, 60.12; H, 7.15; N, 2.92. Found: C, 60.01; H, 6.99; N, 2.72.

The Three-component Reaction (General Procedure)

To a solution of the aldehyde (2*R*,5*R*,6*R*)-**6** (1.00 mmol) in appropriate solvent: 2,2,2-trifluoroethanol, ethanol, or chloroform-*d* (0.5 mL), substituted benzylamine (1.00 mmol) was added followed by trialkyl phosphite (1.00 mmol) and the progress of the reaction was monitored by ^1H and ^{31}P NMR spectra until signals of the starting aldehyde or the respective imines disappeared. For the reactions performed in 2,2,2-trifluoroethanol, the crude products were subjected to chromatography on silica gel columns to give mixtures of the respective diastereoisomers usually contaminated with traces of unreacted amines. The spectral data (vide infra) were calculated from mixtures of diastereoisomers.

Diethyl (*R*)-[(2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl](phenylmethylamino)methylphosphonate (2*R*,5*R*,6*R*,1′*R*)-8a

^1H NMR (300 MHz, $CDCl_3$) δ [ppm]: 7.40–7.21 (m, 5H), 4.35–3.65 (m, 9H), 3.35 (s, 3H, OCH_3), 3.28 (s, 3H, OCH_3), 2.83 (dd, $J_{1-P} = 14.3$, $J_{1-2} = 4.0$ Hz, 1H, HCP), 2.20–1.90 (br s, 1H, NH), 1.40–1.20 (m, 12H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ [ppm]: 140.0, 128.5, 128.3, 127.1, 99.5, 97.9, 67.1 (d, $J = 3.6$ Hz, *C*CP), 62.5 (d, $J = 6.9$ Hz), 61.8 (d, $J = 7.5$ Hz), 61.1 (d, $J = 12.8$ Hz, *C*CCP), 55.2 (d, $J = 148.4$ Hz, CP), 52.9 (d, $J = 3.2$ Hz, NCH_2Ph), 48.6, 48.2, 18.0, 17.9, 16.9, and 16.8 (2 × d, $J = 6.3$ Hz). ^{31}P NMR (121.5 MHz, $CDCl_3$) δ [ppm]: 26.03 ppm.

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Diethyl (*S*)-[(2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl](phenylmethylamino)methylphosphonate (2*R*,5*R*,6*R*,1′*S*)-8a

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm]: 7.40–7.20 (m, 5H), 4.35–3.65 (m, 9H), 3.32 (s, 3H, OCH_3), 3.25 (s, 3H, OCH_3), 3.04 (dd, $J_{1-P} = 15.5$, $J_{1-2} = 5.7$ Hz, 1H, HCP), 2.20–1.90 (br s, 1H, NH), 1.40–1.20 (m, 12H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ [ppm]: 139.9, 128.5, 128.3, 127.1, 99.5, 98.0, 67.0 (d, $J = 7.3$ Hz, *C*CP), 62.2 (d, $J = 7.0$ Hz), 62.2 (d, $J = 7.0$ Hz), 61.0 (d, $J = 4.5$ Hz, *C*CCP), 56.2 (d, $J = 149.1$ Hz, CP), 52.9 (d, $J = 6.7$ Hz, NCH_2Ph), 48.4, 48.2, 18.0, 17.8, 16.8, and 16.8 (2 × d, $J = 6.3$ Hz). ^{31}P NMR (121.5 MHz, $CDCl_3$) δ [ppm]: 25.62 ppm.

Diethyl (*R*)-[(2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl](diphenylmethylamino)methylphosphonate (2*R*,5*R*,6*R*,1′*R*)-8b

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm]: 7.50–7.15 (m, 10H), 5.30 (d, $J = 3.2$ Hz, 1H, *H*CPh_2), 4.35–3.60 (m, 6H), 3.34 (s, 3H, OCH_3), 3.32 (s, 3H, OCH_3), 3.31 (dd, $J_{3eq-3ax} = 10.9$, $J_{3eq-2} = 3.0$ Hz, 1H, H_{eq}CCCP), 2.83 (dd, $J_{1-P} = 16.9$, $J_{1-2} = 2.4$ Hz, 1H, HCP), 2.20–1.90 (br s, 1H, NH), 1.40–1.20 (m, 12H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ [ppm]: 143.9, 142.6, 128.4, 127.8, 127.3, 127.3, 127.2, 127.0, 99.4, 97.8, 67.0 (d, $J = 2.3$ Hz, *C*CP), 65.0 (d, $J = 3.4$ Hz, CPh_2), 62.2 (d, $J = 6.5$ Hz), 61.5 (d, $J = 6.4$ Hz), 61.0 (d, $J = 14.0$ Hz, *C*CCP), 53.2 (d, $J = 143.6$ Hz, CP), 48.5, 48.1, 17.8, 17.8, 16.8 (d, $J = 6.7$ Hz), 16.7 (d, $J = 6.5$ Hz). ^{31}P NMR (121.5 MHz, $CDCl_3$) δ [ppm]: 27.03 ppm.

Diethyl (*S*)-[(2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl](diphenylmethylamino)methylphosphonate [(2*R*,5*R*,6*R*,1′*S*)-8b

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm]: 7.50–7.15 (m, 10H), 5.47 (s, 1H, *H*CPh_2), 4.35–3.60 (m, 5H), 3.92 (t, $J_{3ax-3eq} = J_{3ax-2} = 11.3$ Hz, 1H, H_{ax}CCCP), 3.67 (dd, $J_{3eq-3ax} = 11.3$, $J_{3eq-2} = 3.3$ Hz, 1H, H_{eq}CCCP), 3.27 (s, 3H, OCH_3), 3.24 (s, 3H, OCH_3), 3.01 (dd, $J_{1-P} = 18.0$, $J_{1-2} = 4.2$ Hz, 1H, HCP), 2.20–1.90 (br s, 1H, NH), 1.40–1.20 (m, 12H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ [ppm]: 143.3, 143.2, 128.4, 127.8, 127.4, 127.3, 127.2, 127.1, 99.4, 97.9, 67.7 (d, $J = 7.5$ Hz, *C*CP), 64.9 (d, $J = 8.1$ Hz, CPh_2), 62.4 (d, $J = 6.5$ Hz), 62.0 (d, $J = 7.2$ Hz), 60.6 (d, $J = 4.0$ Hz, *C*CCP), 53.7 (d, $J = 149.3$ Hz, CP), 48.3, 48.1, 17.9, 17.7, 16.8 (d, $J = 6.0$ Hz), 16.7 (d, $J = 6.0$ Hz). ^{31}P NMR (121.5 MHz, $CDCl_3$) δ [ppm]: 25.80 ppm.

Diethyl (*R*)-[(2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl][(*S*)-1-phenylethylamino]methylphosphonate (2*R*,5*R*,6*R*,1′*R*)-8c

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm]: 7.30–7.20 (m, 5H), 4.35–4.00 (m, 7H), 3.34 (s, 3H, OCH_3), 3.30 (s, 3H, OCH_3), 3.06 (dd, $J_{3eq-3ax} = 11.3$, $J_{3eq-2} = 3.5$ Hz, 1H, H_{eq}CCCP), 2.63 (dd, $J_{1-P} = 14.6$, $J_{1-2} = 2.8$ Hz, 1H, HCP), 2.05–1.85 (br s, 1H, NH), 1.40–1.20 (m, 15H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ [ppm]: 144.8, 128.3, 127.3, 127.2, 99.48, 97.9, 67.1 (d, $J = 1.5$ Hz, *C*CP), 62.1 (d, $J = 6.3$ Hz), 61.4 (d, $J = 7.1$ Hz), 60.8 (d, $J = 14.6$ Hz, *C*CCP), 56.5 (CPh), 53.7 (d, $J = 152.6$ Hz, CP), 48.6, 48.1, 25.2, 17.9, 16.9 (d, $J = 5.7$ Hz), 16.8 (d, $J = 5.7$ Hz). ^{31}P NMR (121.5 MHz, $CDCl_3$) δ [ppm]: 27.43 ppm.

Diethyl (*S*)-[(2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl][(*S*)-1-phenylethylamino]methylphosphonate (2*R*,5*R*,6*R*,1′*S*)-8c

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm]: 7.30–7.20 (m, 5H), 4.35–4.0 (m, 7H), 3.60 (dd, $J_{3eq-3ax} = 11.3$, $J_{3eq-2} = 3.1$ Hz, 1H, H_{eq}CCCP), 3.30 (s, 3H, OCH_3), 3.29 (s, 3H, OCH_3), 2.91 (dd, $J_{1-P} = 20.8$, $J_{1-2} = 3.6$ Hz, 1H, HCP), 2.05–1.85 (br s, 1H, NH), 1.40–1.20 (m, 15H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ [ppm]: 144.7, 128.3, 127.2, 127.1, 99.5, 97.9, 66.7 (d, $J = 6.3$ Hz, *C*CP), 62.6 (d, $J = 6.3$ Hz), 61.9 (d, $J = 6.9$ Hz), 60.6 (d, $J = 2.9$ Hz, *C*CCP), 56.0 (d, $J = 12.0$ Hz, CPh), 53.5 (d, $J = 141.4$ Hz, CP), 48.2, 48.1, 24.6, 17.9, 16.8 (d, $J = 6.3$ Hz), 16.6 (d, $J = 6.3$ Hz). ^{31}P NMR (121.5 MHz, $CDCl_3$) δ [ppm]: 25.33 ppm.

Diethyl (*R*)-[(2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl][(*R*)-1-phenylethylamino]methylphosphonate (2*R*,5*R*,6*R*,1′*R*)-8d

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm]: 7.40–7.15 (m, 5H), 4.30–3.60 (m, 7H), 3.46 (dd, $J_{3eq-3ax} = 11.1$, $J_{3eq-2} = 3.2$ Hz, 1H, H_{eq}CCCP), 3.35 (s, 3H, OCH_3), 3.27 (s, 3H, OCH_3), 2.85 (dd, $J_{1-P} = 18.6$, $J_{1-2} = 3.6$ Hz, 1H, HCP), 2.50–1.90 (br s, 1H, NH), 1.40–1.20 (m, 15H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ [ppm]: 145.1, 128.3, 127.1, 127.0, 99.4, 97.9, 67.2 (d, $J = 4.7$ Hz, *C*CP), 62.5 (d, $J = 6.9$ Hz), 61.5 (d, $J = 7.3$ Hz), 61.2 (d, $J = 13.8$ Hz, *C*CCP), 57.1 (d, $J = 10.3$ Hz, CPh), 53.3 (d, $J = 152.9$ Hz, CP), 48.4, 48.0, 23.9, 17.9, 17.7, 16.7 (d, $J = 6.3$ Hz), 16.6 (d, $J = 6.3$ Hz). ^{31}P NMR (121.5 MHz, $CDCl_3$) δ [ppm]: 25.74 ppm.

Diethyl (*S*)-[(2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl][(*R*)-1-phenylethylamino]methylphosphonate (2*R*,5*R*,6*R*,1′*S*)-8d

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm]: 7.40–7.15 (m, 5H), 4.35–4.0 (m, 6H), 3.29 (s, 3H, OCH_3), 3.16 (s, 3H, OCH_3), 3.64 (dd, $J_{3eq-3ax} = 11.3$, $J_{3eq-2} = 3.3$ Hz, 1H, H_{eq}CCCP), 3.51 (t, $J_{3ax-3eq} = J_{3ax-2} = 11.3$ Hz, 1H, H_{ax}CCCP), 2.80 (dd, $J_{1-P} = 13.4$, $J_{1-2} = 6.6$ Hz, 1H, HCP), 2.50–1.90 (br s, 1H, NH), 1.43–1.21 (m, 15H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ [ppm]: 144.6, 128.2, 127.4, 127.1, 99.3, 97.8, 67.8 (d, $J = 5.7$ Hz, *C*CP), 62.1 (d, $J = 7.5$ Hz), 61.8 (d, $J = 7.9$ Hz), 61.3 (d, $J = 8.2$ Hz, *C*CCP), 56.9 (d, $J = 1.7$ Hz, CPh), 54.1 (d, $J = 145.5$ Hz, CP), 48.3, 48.0, 24.4, 17.8, 17.7, 16.8 (d, $J = 6.3$ Hz), 16.7 (d, $J = 6.3$ Hz). ^{31}P NMR (121.5 MHz, $CDCl_3$) δ [ppm]: 27.05 ppm.

Diethyl (*R*)-[(2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl][(*R*)-1-(1-naphthyl)ethylamino]methylphosphonate [(2*R*,5*R*,6*R*,1′*R*)-8e

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm]: 8.30–7.40 (m, 7H), 5.07 (q, $J = 7.1$ Hz, 1H, HCNh), 4.40–3.30 (m, 7H), 3.37 (s, 3H, OCH_3), 3.29 (s, 3H, OCH_3), 2.94 (dd, $J_{1-P} = 18.3$, $J_{1-2} = 3.7$ Hz, 1H, HCP), 2.50–1.90 (br s, 1H, NH), 1.40–1.20 (m, 15H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ [ppm]: 140.8, 133.9, 131.3, 128.9, 127.3, 125.7, 124.1, 123.8, 123.3, 123.3, 99.5, 97.9, 66.9 (d, $J = 4.7$ Hz, *C*CP), 62.6 (d, $J = 6.8$ Hz), 61.7 (d, $J = 7.0$ Hz), 61.6 (d, $J = 12.8$ Hz, *C*CCP), 53.2 (d, $J = 153.1$ Hz, CP), 52.2 (d, $J = 10.0$ Hz, CNh), 48.4, 48.2, 23.2, 17.9, 17.8, 16.7 (d, $J = 6.0$ Hz), 16.7 (d, $J = 6.0$ Hz). ^{31}P NMR (121.5 MHz, $CDCl_3$) δ [ppm]: 26.10 ppm.

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Diethyl (*S*)-[(2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl][(*R*)-1-(1-naphthyl)ethylamino]methylphosphonate (2*R*,5*R*,6*R*,1′*S*)-8e

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm]: 8.30–7.40 (m, 7H), 5.20 (q, $J = 6.1$ Hz, 1H, HCNh), 4.40–3.30 (m, 7H), 3.30 (s, 3H, OCH_3), 3.14 (s, 3H, OCH_3), 2.93 (dd, $J_{1-P} = 14.3$, $J_{1-2} = 5.5$ Hz, 1H, HCP), 2.50–1.90 (br s, 1H, NH), 1.40–1.20 (m, 15H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ [ppm]: 144.7, 133.9, 131.8, 128.8, 127.3, 125.7, 125.7, 125.5, 125.3, 125.3, 99.4, 97.9, 68.1 (d, $J = 7.0$ Hz, *C*CP), 62.2 (d, $J = 7.0$ Hz), 62.0 (d, $J = 7.0$ Hz), 61.0 (d, $J = 6.3$ Hz, *C*CCP), 54.5 (d, $J = 145.0$ Hz, CP), 51.9 (d, $J = 1.5$ Hz, CPh), 48.3, 48.0, 24.1, 17.9, 17.8, 16.8 (d, $J = 6.0$ Hz), 16.7 (d, $J = 6.0$ Hz). ^{31}P NMR (121.5 MHz, $CDCl_3$) δ [ppm]: 26.70 ppm.

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