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Synthesis of New 1,3-Oxaphosphorinanium Salts. Stereochemistry of Hydroxide-Induced Displacement of Methoxide Ion

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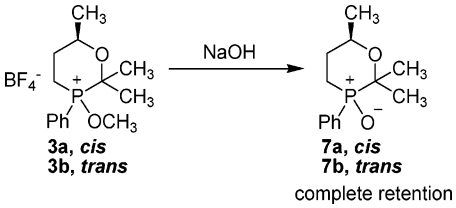

The synthesis of pure *cis*- and *trans*-3-methoxy-2,2,6-trimethyl-3-phenyl-1,3-oxaphosphorinanium tetrafluoroborate salts **3a** and **3b**, respectively, molecules designed to evaluate the effect of oxygen on the steric course of base-induced nucleophilic displacement of the methoxy group at phosphorus, was accomplished. It was found that these isomeric salts react with aqueous sodium hydroxide to produce the corresponding phosphine oxides **7a** and **7b** with complete retention of configuration at phosphorus.

Introduction

It has long been known that quaternary phosphonium salts undergo nucleophilic displacement reactions by aqueous hydroxide ion to produce phosphine oxides[1] and that the cleavage of acyclic phosphonium salts occurs with inversion of configuration at phosphorus.[2] In this regard, there has been considerable interest in the stereochemical behavior of phosphorus in cyclic systems in which phosphorus is the only heteroatom in the ring. In cyclic systems, however, ring size has been implicated as having a pronounced effect on the steric course of the nucleophilic displacement of exocyclic substituents at phosphorus. Phosphetanium salts have been shown to be converted to the corresponding phosphine oxides with complete retention of configuration at phosphorus.[3] On the other hand, depending on the specific compound, phospholanium salts have been observed to cleave with complete retention of configuration[4] or to produce mixtures of stereoisomers.[5] Both mechanistic and stereochemical arguments have been proposed to explain these differences.

In six-membered rings, the most studied leaving group has been the benzyl group attached to the phosphorus atom, and the base cleavage reaction with aqueous sodium hydroxide ion has been found to be nonstereospecific. When pure samples of cis and trans isomers (phenyl and methyl cis or trans) of 1-benzyl-4-methyl-1-phenyl phosphorinanium bromides **1a** and **1c** (Scheme 1) were reacted with aqueous NaOH under identical conditions, mixtures of different proportions of oxides **2a** and **2b** were obtained.[6] When a more electronegative group than benzyl was used (i.e., methoxy group), **1b** and **1d** reacted with base to produce the same phosphine oxides **2a** or **2b** with complete inversion of configuration at phosphorus.[5]

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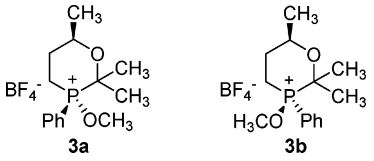
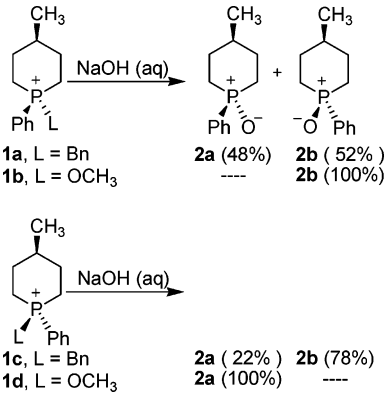


FIGURE 1. 1,3-Oxaphosphorinanium salts for stereochemical study.

SCHEME 1



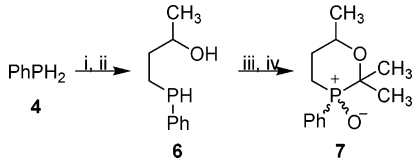
On the basis of the later study, we herein report our results on the hydroxide-induced displacement of the methoxide group from pure samples of cis and trans isomers of 3-methoxy-2,2,6-trimethyl-3-phenyl-1,3-oxaphosphorinanium tetrafluoroborate salts **3a** and **3b** (Figure 1), systems designed to study the effect of a second heteroatom in the cyclic system on the stereochemistry of this type of reactions. The literature contains a number of examples of six-membered rings containing both oxygen and phosphorus. These compounds, however, are of either the 1,2-oxaphosphorinane[7] or 1,3,2-dioxaphosphorinane type, where several stereochemical studies have been carried out on the latter.[8] The 1,3-oxaphosphorinane system is much more difficult to synthesize and therefore has not been studied as extensively.

In contrast to five-membered rings where the presence of the oxygen atom has no effect in the stereochemical course of the reaction,[4c] in our study the presence of oxygen on the ring does induce a different stereochemical outcome, and to our surprise, the reaction of **3a** and **3b** with base proceeds with complete retention of configuration at phosphorus to yield phosphine oxides **7a** and **7b**, instead of inversion (as in **1b** and **1d**).

Results and Discussions

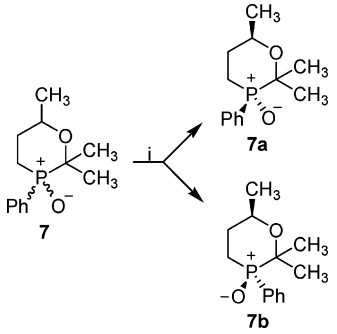
Of prime importance for the synthesis of **3a** and **3b** was the development of a synthetic route to the key intermediate 3-hydroxybutylphenylphosphine **6** (Scheme 2). It was anticipated that **6** could be prepared by the selective ring-opening reaction of 2-methyloxetane **5** (prepared following Searles' procedure[9]), by the lithium salt of phenylphosphine **4**, previously synthesized by reduction of dicholorophenylphosphine.[10] In fact, this procedure allowed us to obtain compound **6** as the major product of the reaction (54% yield). In the following steps, the cyclization toward oxides **7** was carried out following Marsi's adaptation of Oehme's procedure[4c,11] for the synthesis of 1,3-oxaphospholanes with the proper adjustment of the temperature and reaction time. Thus, when compound **6** was heated at temperatures below 100 °C with acetone and in the presence of *p*-toluenesulfonic acid during an 84 h period, followed immediately by treatment with *tert*-butylhydroperoxide in benzene, the desired cyclic phosphine oxides **7** were obtained as a mixture of the cis and trans diastereoisomers (13% yield from **6**).

SCHEME 2[a]



[a] Key: (i) *n*-BuLi, THF, 0 °C; (ii) 2-methyloxetane, **5**, −78 °C; (iii) *p*-TsOH, acetone, C_6H_6; (iv) *t*-BuOOH, C_6H_6.

SCHEME 3[a]



[a] Key: (i) column chromathography: silica gel (230−400), acetone.

The separation of the diastereomeric mixture of oxides **7** was accomplished by column chromatography leading to diastereoisomers **7a** and **7b** in a very pure form (Scheme 3).

Both compounds were fully characterized by NMR spectroscopy; however, to carry out the stereochemical study, it was necessary to establish the relative stereochemistry of these compounds. The assignment of the relative configurations of diastereoisomers **7a** and **7b** was unambiguously established by an X-ray crystal structure determination of **7a**.[12] Unfortunately, an appropriate crystal of **7b** could not be obtained for X-ray studies. Figure 2 shows the X-ray crystal structure of **7a** in which it can be observed that the six-membered ring adopts a flattened chair conformation where the methyl group at C(6) occupies an equatorial position and the phenyl substituent at phosphorus an axial position, establishing

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(12) Crystal structure of compound **7a** has been deposited at the Cambridge Crystallographic Data Centre (CCDC 270336).

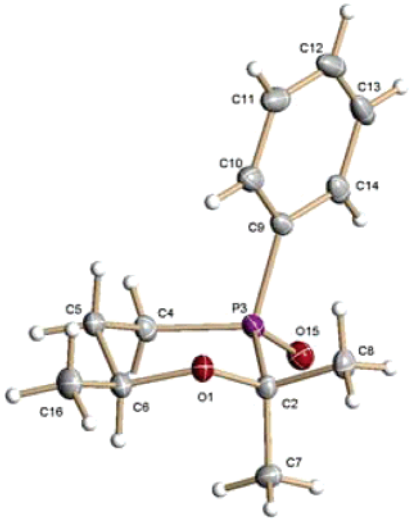
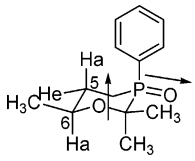


FIGURE 2. X-ray structure of phosphine oxide **7a**, cis configuration (CH_3−Ph).

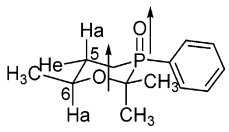
a cis relationship between them. It is then assumed that in diastereoisomer **7b**, the methyl and the phenyl groups must have a trans relationship. The fact that the ring system is appreciably flattened at the phosphorus end is suggested by the torsional angles involving the central fragment P(3)−C(2), Table 6s (Supporting Information). These angles are all far from the ideal angle of 60° for gauche conformations and the 180° angle for anti conformations by approximately 20°. In addition, the widening of the C(5)−C(4)−P(3) (115.2°), C(4)−P(3)−0(15) (113.2°), and C(2)−P(3)−O(15) (114°) bond angles and a diminished C(2)−P(3)−C(4) (103.5°) internal ring angle can be observed, Table 3s (Supporting Information). The net effect is to alleviate the crowding generated when the phosphorus substituent occupies an axial position, as has been reported for similar compounds.[13] In contrast, the O(1)−C(6)−C(5)−C(4) torsion angle at nearly 60° and the C(16)−C(6)−C(5)−C(4) torsion angle at nearly 180° show a normal chair conformation shape at C(6). Incidentally, this latter angle (178.43°) also proves that the methyl group at C(6) occupies an equatorial position in **7a**, and by analysis of its very similar proton (Table 1) and ^{13}C NMR signals, this methyl group also occupies an equatorial position in **7b**.

It has been known that an axial phenyl group assumes a conformation in which it is perpendicular to the symmetry plane of the chair-shaped cyclohexane ring, avoiding 1,3-syn diaxial repulsions between the aromatic ortho hydrogens and the cyclohexane ring hydrogens.[14] This also applies for some 1-phenyl-phosphorinane derivatives, based on X-ray studies.[15] In contrast, it is observed in the crystal structure of **7a** that the axial phenyl substituent bisects the phosphorinane ring as

TABLE 1. ^1H NMR Data of Isomers 7a and 7b



7a



7b

proton	δ, ppm (multiplicity, *J* (Hz)) for **7a**	δ, ppm (multiplicity, *J* (Hz)) for **7b**
$CH_{3(e)}$	1.26 (d,13.6)	1.38 (d, 12.0)
$CH_{3(a)}$	1.70 (d,11.6)	1.27 (d, 13.6)
$CH_{3(6)}$	1.29 (d, 6.0)	1.28 (d, 6.0)
CH_2−CH_2	2.12 (m)	2.22 (m)
CH	4.1 (ddq, 2.0, 11.1, 6.0)	4.0 (ddq, 2.0, 11.0, 6.0)
$C_6H_{5(meta)}$	7.51 (m)	7.48 (m)
$C_6H_{5(para)}$	7.57 (m)	7.55 (m)
$C_6H_{5(ortho)}$	8.11 (m)	7.78 (m)

confirmed by the torsion angles O(15)−C(14) (2.81°) and O(15)−C(10) (178.4°). The other four torsional angles involving the P(3)−C(9) fragment provide additional evidence for the observed orientation of the phenyl group. In support of this behavior, a parallel conformation of an axial phenyl group has been assumed for 5-phenyl-1,3-dioxanes.[16] Presumably, the methyl groups at C(2) and/or the absence of an axial hydrogen in the adjacent position (at the ring oxygen) cause the different conformational behavior of **7a**; however, this cannot be determined only on the basis of the data reported here.

Some independent facts support the stereochemical assignments given to the isomeric oxides **7a** and **7b**. The ^1H NMR spectra of these compounds support a configurational assignment (Table 1) in which the methyl group at C-6 occupies an equatorial position in both isomers since axial−axial three-bond coupling constants for the H_5−H_6 protons are observed with values of 11.1 Hz for **7a** and of 11.0 Hz for **7b**. In **7a**, there is a difference of 0.44 ppm in the proton shifts of the methyl groups at C(2), presumably due to the shielding exerted by the phenyl group on the equatorial methyl, rather than on the axial one. Thus, in the spectrum of **7b**, the difference in the chemical shifts of the methyl groups at C(2) (0.11 ppm) is less pronounced than in **7a**, due to the marked shielding effect of the phenyl substituent on the axial methyl. Therefore, when comparing the chemical shifts of the axial methyl group at C(2) on both isomers, a greater shielding effect of the phenyl group can be assumed when it occupies an equatorial position (**7b**) than when it is in an axial position (**7a)**. The relationship between the C(2) methyl groups and the P=O group provides additional support to our stereochemical assignment. The coupling constant (^3J) between these methyl groups and the phosphorus atom on the P=O function should have a lower magnitude when they have a cis disposition than when they have a trans disposition. In addition, the chemical shift of the methyl groups cis to the P=O functionality should be more downfield than the chemical shift of the methyl groups trans to the P=O group.[17] Moreover, the order of elution, **7a** > **7b**, is in accord with the predicted higher dipole moment of **7b**, which leads to stronger retention on the column. In

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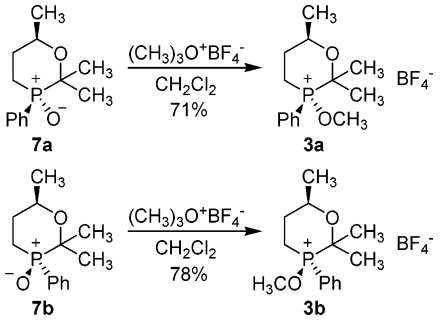
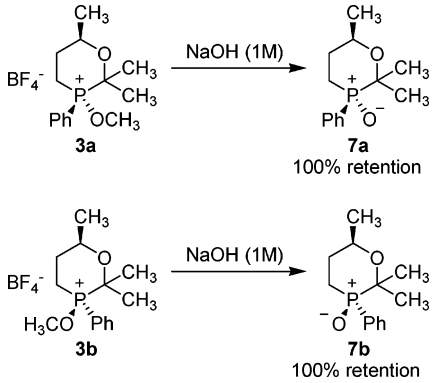
SCHEME 4



SCHEME 5



diasteroisomer **7a**, the dipoles are oriented in opposite directions, whereas in **7b**, the dipoles are oriented in the same direction.

Once the configurations of the phosphine oxides **7a** and **7b** were established, the required molecules for our study, **3a** and **3b**, were obtained by direct methylation of **7a** and **7b** with trimethyloxonium tetrafluoroborate. The configuration of **3a** and **3b** was assigned on the basis of the established configuration of their parents, **7a** and **7b**, respectively, and the known fact that methylation of phosphine oxides with trimethyloxonium tetrafluoroborate proceeds with retention of configuration at phosphorus (Scheme 4).[18] Some key NMR signals were used for the structural determination of these compounds; for example, the signals for the methoxy groups on both isomers appear as doublets centered around 4.0 ppm as a result of the coupling of these protons with the adjacent phosphorus atom. Likewise, the $^3J_{P-H(OCH_3)}$ coupling constants have similar values of 11.0 and 11.4 Hz and are in agreement with the values previously reported by Marsi[5] for phosphorus cyclic compounds. The signals of the methyl groups at C(2) of isomers **3a** and **3b** show similar chemical shifts according of these groups in the corresponding oxides. The chemical shifts of methyl groups cis to the methoxy group (CH_3 axial in **3a** and CH_3 equatorial in **3b**) are downfield in relation to the signals of these methyl groups on the oxides **7a** and **7b**. This is due to the change of the substituent at phosphorus from oxygen to methoxy. In addition, the difference between the chemical shifts of the geminal methyl groups is less pronounced in the trans isomer **3b** than in the cis isomer **3a**, as it is observed for **7b** and **7a**, respectively. Finally, the ^{31}P NMR signals for each isomer appear at +67.27 ppm for **3a** and +69.97 ppm for **3b**.

The nucleophilic displacement reactions in aqueous sodium hydroxide carried out on salts **3a** and **3b** led, to our surprise, to the formation of phosphine oxides **7a** and **7b**, respectively, with complete retention of configuration at phosphorus (Scheme 5) for both. The stereochemistry observed in our study could be easily corroborated by direct comparison of the ^{1}H and ^{31}P NMR spectra of the isolated phosphine oxides of the substitution products with those of the phosphine oxides previously used as precursors for the synthesis of **3a** and **3b** since they are exactly the same compounds. The stereochemical behavior observed in our study dramatically contrasts the stereochemical behavior reported by Marsi in six-membered rings with phosphorus as the only heteroatom where the base-induced displacement of a methoxy group proceeds with complete inversion of configuration at phosphorus.

To explain the observed stereochemistry in these reactions, the reduced ring strain in six-membered rings with phosphorus as the only heteroatom as compared with phosphetanes and phospholanes must be taken into account since this allows the bonds directly attached to phosphorus in the six-membered ring to occupy equatorial−equatorial or equatorial−apical positions in the trigonal bipyramid phosphorane intermediates involved in these type of reactions. The pathway toward inversion reported for **1b** and **1d** was explained by an $S_N2(P)$ mechanism involving a phosphorane in which the six-membered ring can be placed in an equatorial−equatorial position as an intermediate. However, in **3a** and **3b**, this arrangement presumably could be less favorable, and a phosphorane with the six-membered ring in equatorial-apical positions can be suggested in order to alleviate the ring strain caused by the presence of the oxygen in the ring and a geminal methyl group at C(2).

On the basis of the latter and on the different mechanisms that have been proposed in the literature for the nucleophilic substitution at phosphorus in cyclic compounds, the mechanism involving Berry pseudorotations[19] of phosphoranes is the one that best explains our results. The pathway toward retention of configuration, taking **3a** as an example (Scheme 6), involves an apical attack of the OH species to produce phosphorane **8**. A pseudorotation toward phosphorane **9** places the OCH_3 leaving group in an apical position, and the base-induced elimination of this group in phosphorane **9** leads to oxide **7a** with retention of configuration. This condition of apical attack and apical departure is well supported by the extended principle of microscopic reversibility, which establishes that apical bonds are longer and weaker.[20] In addition, according to the scale of relative apicophi-

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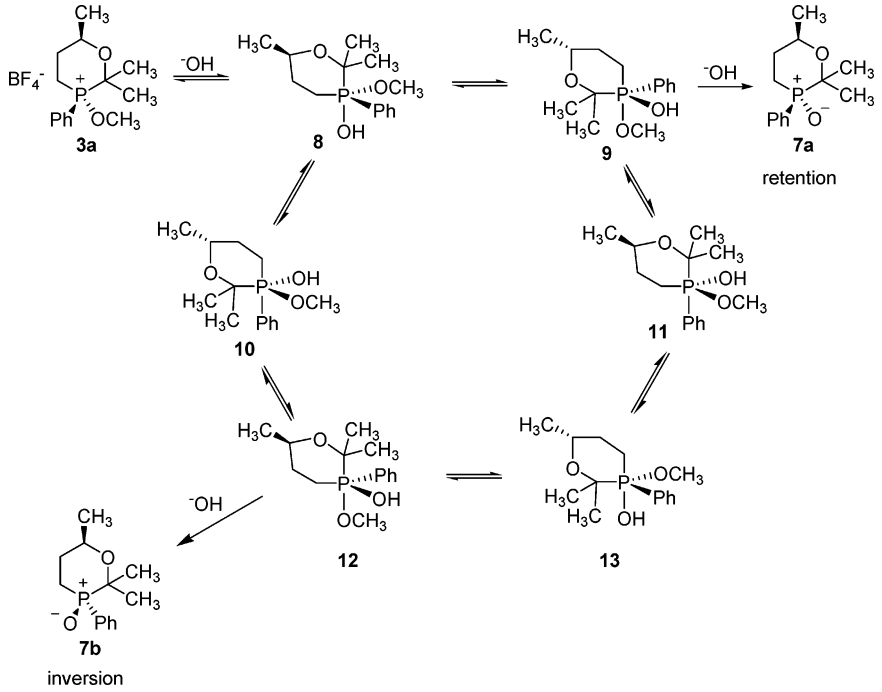
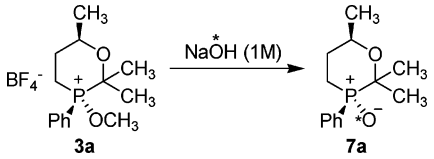
SCHEME 6



SCHEME 7



licities proposed by Trippett,[21] the methoxy group has a strong preference to occupy an apical position since it is the ligand bound to phosphorus with the highest relative value.

As can be seen in Scheme 6, the two possible pathways toward inversion of configuration require some additional and unfavored pseudorotations. For example, conversion of phosphoranes **8** to **10** or **9** to **11** would place the two electronegative substituents (OH and OCH_3) in equatorial positions and the bulky phenyl group in an apical position (phosphoranes **10** and **11**); subsequent pseudorotations from **10** to **12** or from phosphoranes **11** and **13** to **12** would be again required to place the methoxy group in an apical position prior to its elimination.

Evidence for a mechanism in which nucleophilic attack by the OH^- species occurs at phosphorus was obtained when the reaction of **3a** was carried out with NaOH enriched with ^{17}O (Scheme 7). The ^{17}O NMR of the product obtained in this reaction shows two signals, one at +19.04 ppm corresponding to the ^{17}O-enriched oxygen at phosphorus of significantly higher intensity than the other one at +29.781 ppm corresponding to the ring oxygen (^{17}O natural abundance), supporting the mechanism shown in Scheme 6. This is in agreement with previous results reported for **1b** and **1d** where no significant attack on the methoxy carbon was observed.[5] In addition, the high-resolution mass spectra shows that the labeled ^{17}O was incorporated in the resulting product.

Conclusion

We have accomplished the synthesis of some 1,3-oxaphosphorinanium compounds, a new kind of heterocyclic organophosphorus compounds not previously reported in the literature. The relative configuration of these compounds was established on the basis of an X-ray diffraction study of oxide **7a**. The base-induced cleavage of compounds **3a** and **3b** yields oxides **7a** and **7b** with complete retention of configuration at phosphorus, stereochemical behavior not reported in the literature before for these kind of compounds. We propose a mechanism in which apical attack of the nucleophile gives phosphorane **8**; a pseudorotation of **8** to **9** and apical departure of the leaving group from the latter phoshorane represent a possible pathway to explain the observed stereochemistry. In summary, the presence of oxygen on the six-membered ring dramatically changes the stereochemical course of these reactions, from complete inversion (**1b** and **1d**) to complete retention of configuration at phosphorus (**3a** and **3b**). In addition, we have gained synthetic access to these kinds of systems for future conformational studies that we have planned.

Experimental Section

Synthesis of 3-Hydroxybutylphenylphosphine[22] **6.** To 18.32 g (0.17mol) of phenylphosphine **4** dissolved in 60 mL of anhydrous THF was added dropwise with stirring 66.7 mL of 2.5 M *n*-butyllithium in hexanes. The reaction was kept at 0 °C under a nitrogen atmosphere during the addition until a yellowish precipitate was formed. The reaction mixture was cooled to −78 °C, and an equimolar amount of 2-methyloxetane **5** (12.0 g) was added dropwise with stirring. After the addition, the reaction mixture was allowed to come to room temperature and then refluxed for 2 h. The reaction mixture was cooled with an ice bath, and water was added dropwise until the organic layer became colorless. The organic layer was removed,

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and the aqueous layer was extracted with diethyl ether (2 × 150 mL). The organic layers and extracts were combined and filtered in vacuo, and the solvents were distilled off. Distillation in vacuo yielded 16.53 g (54%) of the desired product as a colorless liquid, bp 119−120 °C (1 mm), and 3.47 g (11%) of the minor isomer, 3-hydroxy-1-methyl-propylphenylphosphine, as a colorless liquid, bp 110−115 °C (1 mm). **Major Product, 6:** ^{31}P NMR ($CDCl_3$) δ −49.605, −49.849; ^{1}H NMR ($CDCl_3$) δ 1.130 (d, J = 6.2 Hz, 1.5H), δ 1.134 (d, J = 6.4 Hz, 1.5H), δ 1.58 (m, 2H), δ 1.7 (m, 2H), δ 3.3 (s, 1H), δ 3.57 (m, 1H), δ 7.27 (m, 3H), δ 7.53 (m, 2H), δ 7.42 (d, J = 466 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 23.36 (s), δ 23.42 (s), δ 26.4 (d, J = 16.3), δ 27.7 (d, J = 16.7), δ 31.1 (d, J = 5.35), δ 31.2 (d, J = 4.4), δ 67.3 (d, J = 11.4), δ 67.6 (d, J = 11.0), δ 129.1 (d, J = 12.6), δ 130.1 (d, J = 11.0), δ 132.5 (s), δ 132.73 (d, J = 3.05). Anal. Calcd for $C_{10}H_{15}OP$: C, 65.92; H, 8.30. Found: C, 65.70; H, 8.50. **Minor Product:** ^{31}P NMR ($CDCl_3$) δ −50.782; ^{1}H NMR ($CDCl_3$) δ 0.86 (d, J = 6.2, 1.5H), δ 0.89 (d, J = 6.6, 1.5H), δ 1.89 (m, 3H), δ 4.05 (t, J = 6.0, 2H), δ 7.41 (m, 3H), δ 7.7 (m, 2H), δ 7.5 (d, J = 464, 1H).

Synthesis of 3-Oxo-3-phenyl-2,2,6-trimethyl-1,3-oxaphosphorinane 7. 3-Hydroxybutylphenylphosphine **6** (4 g, 0.022 mol), dissolved in 60 mL of benzene, was mixed with 32.15 mL (0.438 mol) of anhydrous reagent-grade acetone, and then 0.189 g (1.097 mmol) of dried *p*-toluenesulfonic acid[23] was added. The reaction mixture was refluxed at 100 °C for 37 h using a Dean−Stark trap. At this point, an additional portion (21.7 mL, 0.3 mol) of acetone was added, and the reaction mixture was kept at reflux for an additional period of 47 h. After removal of the solvent, oxidation of the crude product was carried out by dissolving the material in 30 mL of benzene and adding, at 0 °C, 4.32 mL (0.02 mol) of 5.0 M *tert*-butylhydroperoxide in decane.[24] After the addition was completed, the reaction was allowed to come to room temperature and was stirred overnight at this temperature. The solvent was evaporated in vacuo and the crude product purified by flash column (silica gel, dichloromethane/2-propanol 95/5) to give 0.69 g (13%) of a colorless liquid corresponding to the mixture of diastereomeric oxides of **7**.

Separation of *cis*- and *trans*-3-Oxo-3-phenyl-2,2,6-trimethyl-1,3-oxaphosphorinanes 7a and 7b. The mixture of phosphorinane oxides **7a** and **7b** obtained in the previous step (0.5 g), was separated by chromatographic column (silica gel 230−400, acetone), affording 0.23 and 0.22 g of the isomerically pure *cis*- and *trans*-oxides, respectively.

3-Oxo-*r*-3-phenyl-2,2,*c*-6-trimethyl-1,3-oxaphosphorinane 7a. ^{31}P NMR ($CDCl_3$) δ +27.967; ^{1}H NMR ($CDCl_3$) δ 1.26 (d, J = 13.6 Hz, 3H), δ 1.29 (d, J = 6 Hz, 3H), δ 1.70 (d, J = 11.6 Hz, 3H), δ 2.12 (m, 4H), δ 4.1 (ddq, J = 2 Hz, J = 11.1 Hz, J = 6 Hz, 1H), δ 7.51 (m, 2H), δ 7.57 (m, 1H), δ 8.11 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 20.7 (d, J = 7.6), δ 22.4 (s), δ 24.7 (s), δ 29.5 (d, J = 79.31), δ 32.9 (d, J = 6.13), δ 67.4 (d, J = 6.13), δ 74.6 (d, J = 79.31), δ 128.5 (d, J = 10.76), δ 130.3 (s), δ 131.93 (s), δ 132.38 (d, J = 7.6); white solid, mp 102−104 °C. Anal. Calcd for $C_{13}H_{19}O_2P$: C, 65.53; H, 8.04. Found: C, 65.57; H, 7.82.

3-Oxo-*r*-3-phenyl-2,2,*t*-6-trimethyl-1,3-oxaphosphorinane 7b: ^{31}P NMR ($CDCl_3$) δ +28.266; ^{1}H NMR ($CDCl_3$) δ 1.28 (d, J = 6 Hz, 3H), δ 1.27 (d, J = 13.6 Hz, 3H), δ 1.38 (d, J = 12 Hz, 3H), δ 2.22 (m, 4H), δ 4.0 (ddq, J = 2 Hz, J = 11 Hz, J = 6 Hz, 1H), δ 7.48 (m, 2H), δ 7.55 (m, 1H), δ 7.78 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 20.7 (d, J = 5.4), δ 22.2 (s), δ 23.7 (s), δ 28.9 (d, J = 6.13), δ 29.9 (d, J = 70.2), δ 68.1 (d, J = 4.62), δ 74.9 (d, J = 76.30), δ 128.7 (d, J = 12.16), δ 130.5 (s), δ 131.5 (d, J = 9.15), δ 132.2 (d, J = 3.11); white solid, mp 112−115 °C. Anal. Calcd for $C_{13}H_{19}O_2P$: C, 65.53; H, 8.04. Found: C, 65.63; H, 7.93.

Synthesis of *cis*- and *trans*-3-Methoxy-3-phenyl-2,2,6-trimethyl-1,3-oxaphosphorinanium Tetrafluoroborate 3. For the preparation of the trans isomer **3b**, 0.05 g (0.21 mmol) of the *trans*-phosphine oxide **7b** was dissolved in 25 mL of dry methylene chloride. This solution was added to a suspension of 0.04 g (0.27 mmol) of trimethyloxonium tetrafluoroborate in dry methylene chloride, and the resulting mixture was stirred at room temperature for 6 h. The solution was evaporated to dryness in vacuo to give 0.06 g (78% yield) of the trans isomer **3b**: yellow oil, ^{31}P NMR ($CDCl_3$) δ +69.97; ^{1}H NMR ($CDCl_3$) δ 1.24 (d, J = 6.2, 3H), δ 1.24 (d, J = 14.2, 3H), δ 1.5 (d, J = 13.4, 3H), δ 2.94 (m, 4H), δ 4.1 (d, J = 11.4 Hz, 3H), δ 4.28 (m, 1H), δ 7.69 (m, 5H). Anal. Calcd for $C_{14}H_{22}BF_4O_2P$: C, 49.44; H, 6.52. Found: C, 49.58; H, 6.26. The cis isomer **3a**, was prepared in a similar manner from **7a** (cis oxide); evaporation of the solvent afforded 0.05 g (71% yield) of cis isomer **3a**: yellow oil, ^{31}P NMR ($CDCl_3$) δ +67.27; ^{1}H NMR ($CDCl_3$) δ 1.18 (d, J = 7.0, 3H), δ 1.37 (d, J = 16.2, 3H), δ 1.9 (d, J = 14, 3H), δ 3.13 (m, 4H), δ 4.1 (d, J = 11.0 Hz, 3H), δ 4.26 (m, 1H), δ 7.88 (m, 5H). Anal. Calcd for $C_{14}H_{22}BF_4O_2P$: C, 49.44; H, 6.52. Found: C, 49.52; H, 6.37.

Base Cleavage Reaction of 3-Methoxy-*r*-3-phenyl-2,2,*t*-6-trimethyl-1,3-oxaphosphorinanium Tetrafluoroborate 3b. To the *trans*-tetrafluoroborate salt **3b** (0.055 g, 0.162 mmol) was added 1 M sodium hydroxide (0.35 mL) at room temperature with stirring, continuing for 1 h at room temperature, and then heated under reflux for 2 h. The cooled reaction mixture was extracted with methylene chloride (5 × 25 mL). The combined extracts were dried with anhydrous sodium sulfate, and the solvent was distilled off to give 0.035 g (91% yield) of *trans*-oxide **7b** previously characterized.

Base Cleavage Reaction of 3-Methoxy-*r*-3-phenyl-2,2,*c*-6-trimethyl-1,3-oxaphosphorinanium Tetrafluoroborate 3a. The same procedure was followed as for the trans isomer with similar results.

Base Cleavage Reaction of 3-Methoxy-*r*-3-phenyl-2,2,*c*-6-trimethyl-1,3-oxaphosphorinanium Tetrafluoroborate 3a with ^{17}O-Enriched NaOH. To the *cis*-tetrafluoroborate salt **3a** (0.05 g, 0. mmol) prepared as described above was added 0.35 mL of a 1 M $NaO^{17}H$ solution ($NaO^{17}H$ was prepared by adding 0.0078 g of Na° to 0.0065 g of 35% ^{17}O, H_2O^{17}) at room temperature with stirring, continuing for 1 h at room temperature, and then heated under reflux for 2 h. The cooled reaction mixture was extracted with methylene chloride (5 × 25 mL). The combined extracts were dried with anhydrous sodium sulfate, and the solvent was distilled off to give 0.031 g (89% yield) of the ^{17}O-enriched *cis*-oxide **7a**. HRMS (EI): calcd for $C_{13}H_{19}O_2P$, 238.2625; found, 239.1201.

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Supporting Information Available: General information for compounds **3a**,**b**, **6**, and **7a**,**b** and crystallographic data for compound **7a** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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