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Synthesis of New Sulfonium Ylides Bearing the Chiral Diazaphospholidine Group as Reagents for Asymmetric Cyclopropanation

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ABSTRACT: *Sulfonium ylides derived from chiral N,N'-substituted (benzyl, isopropyl, neopentyl) phosphonamides were prepared by reacting appropriate chiral diamidophosphites with potassium hydride and chloromethyl methyl sulfide, and then with methyl iodide in the presence $AgBF_4$ to give the corresponding sulfonium salts in high yields. One of them was analyzed by X-ray crystallography. The salts upon treatment with different bases (LithiumDiisopropylAmine, BuLi, K_2CO_3) were converted in situ into ylides, which were reacted with activated olefins to produce phosphonocyclopropanes as a mixture of two diastereoisomers with moderate-to-high diastereoselectivities.* © 2014 Wiley Periodicals, Inc. Heteroatom Chem. 25:690–697, 2014; View this article online at wileyonlinelibrary.com. DOI 10.1002/hc.21183

INTRODUCTION

Aminophosphonic acids (APs) are analogues of protein and nonprotein amino acids. They attracted a great interest of scientific community due to very wide spectrum of biological activities [1]. Since the planar carboxylic group in aminoacids is replaced by a tetrahedral phosphonic acids moiety, APs mimic the unstable tetrahedral transition state formed in enzymatic peptide bond cleavage and act as inhibitors of proteolytic enzymes. Moreover, they show antibacterial, anticancer, and antiviral properties as well as exhibit pesticidal, insecticidal, and herbicidal activities. The selected APs have found practical applications in medicine and agriculture.

As part of our program on the asymmetric synthesis of APs [2], we have also been engaged in the invention and development of methods for the synthesis of aminocyclopropanephosphonic acids, which are the so-called conformationally constrained APs [3]. It should be pointed out that the design and synthesis of conformationally constrained peptidomimetics has been an important strategy in modern drug discovery processes. Our endeavors resulted in the elaboration of new asymmetric synthesis of β-amino-γ-phenylcyclopropanephosphonic acid [4], cyclopropylphosphonate analogues of purine nucleotides [5], and 2-amino-6-phosphonobicyclo[3.0.1]hexane-2-carboxylic acid [6]. These constrained analogues of APs were obtained by a tandem Michael addition/ring closure reaction of achiral, properly

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Dedicated to Professor Renji Okazaki on the occasion of his 77th birthday.

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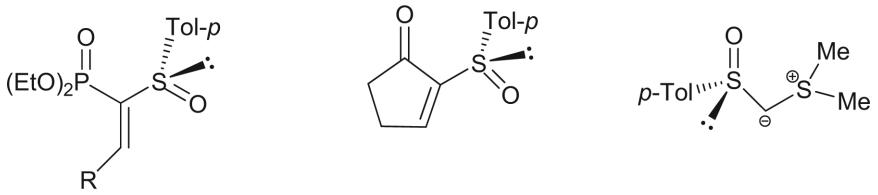
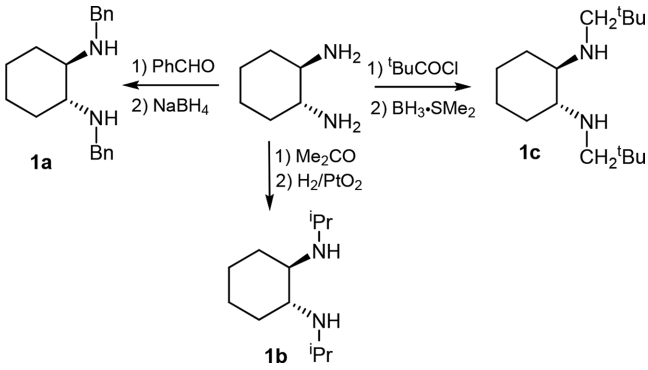


FIGURE 1 Chiral sulfinyl reagents used in cyclopropanation.

substituted sulfur ylides to chiral electron-deficient alkenes such as 1-(diethoxyphosphoryl)vinyl *p*-tolyl sulfoxide and 2-(*p*-tolylsulfinyl)cyclopent-2-enone (see Fig. 1).

Recently, Midura and colleagues have designed and synthesized a new type of a chiral sulfur ylide containing the sulfinyl group bonded to the ylidic carbon atom [7]. Using this ylide, she prepared in three steps (*R*)-[2,2–$^2H_2$]-1-aminocyclopropane-1-phosphonic acid in which the α-carbon atom is chiral due to isotopic substitution (CH_2 vs. CD_2) [8].

In this paper, we wish to describe the synthesis of new chiral sulfur ylides in which the ylidic carbon atom is bonded to the chiral diamidophosphonic group derived from *trans*-*N*,*N*'-disubstituted 1,2-diaminocyclohexane. This stereodirecting group with a cyclic diamino C_2-symmetric system at phosphorus was introduced to asymmetric synthesis by Hanessian et al. [9] and also used in the asymmetric synthesis of β-aminocyclopropanephosphonic acid [10]. Our initial results on asymmetric cyclopropanation of activated alkenes with these new sulfonium ylides are also reported herein.



SCHEME 1 Synthesis of *N*,*N*'-disubstituted *trans*-1,2-cyclohexanediamines **1a–c**.

RESULTS

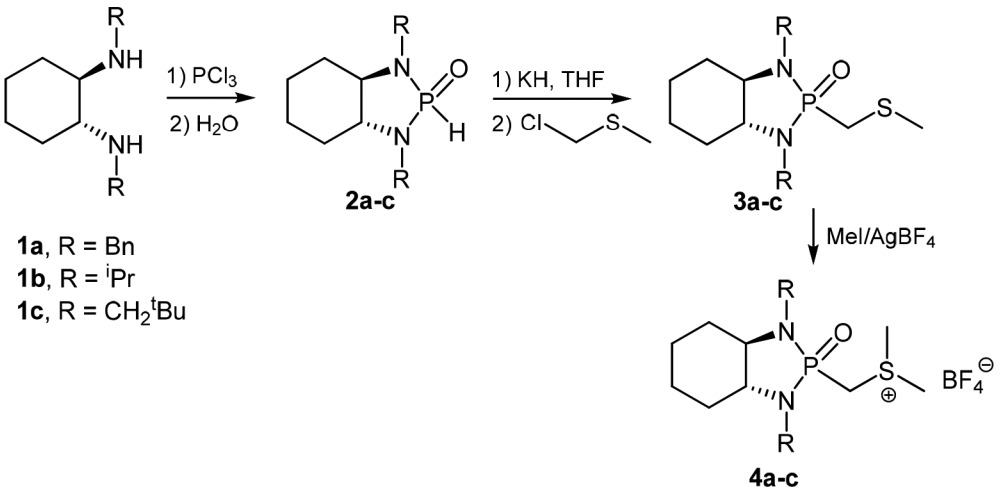
The enantiomerically pure *trans*-1,2-cyclohexanediamine [11] was converted into its *N*,*N*'-dibenzyl analogue **1a** through reductive amination with benzaldehyde [12]. The *N*,*N*'-diizopropyl-(1*R*,2*R*)-1,2-cyclohexanediamine **1b** was obtained by a reaction with acetone, followed by H_2/PtO_2 reduction in ethanol [13]. The *N*,*N*'-dineopentyl-*trans*-(1*R*,2*R*)-1,2-cyclohexanediamine **1c** was prepared from the corresponding *N*,*N*'-diacyl compound by reduction with $BH_3{\cdot}SMe_2$ in THF [14] (Scheme 1).

Condensation of the diamines **1a–c** with PCl_3 and Et_3N in a toluene solution followed by filtration of the resulting $Et_3N{\cdot}HCl$ gave the crude diamido chlorophosphites. The addition of 1 equiv of water and 1 equiv of NEt_3 to a toluene solution of the latter gave the corresponding diamido phosphites **2a–c** (Scheme 2) [15].

We have found that phosphonamides **2** react with potassium hydride and chloromethyl methyl sulfide at low temperature in THF to give optically active (methylsulfanyl)methylphosphonamides **3**. After chromatographic purification to remove unreacted chloromethyl methyl sulfide, phosphonamides **3a–c** were obtained as viscous oils in 64–76% overall yields. These new compounds were fully characterized by NMR, IR, MS, and elemental analysis or HRMS. The methylsulfanyl protons in the ^1H NMR spectra of **3** appeared as singlets at 2.12 and 2.13 ppm for **3a** and **3b**, respectively, and as a doublet with a small coupling constant $^4J_{P\text{-}H} = 1.5$ Hz for **3c**. The ^{31}P NMR spectra show singlets at 32.4–39.8 ppm in $CDCl_3$. The ^{13}C NMR spectra exhibit characteristic doublets at 31.2–33.0 ppm with a large coupling constant: 88.7 Hz for **3c**, 113.3 Hz for **3b**, and 131.2 Hz for **3a,** which are typical for the P–C–S methylene bridge.

The phosphonamides **3a–c** formed the corresponding sulfonium salts **4a–c** upon treatment with methyl iodide in the presence of $AgBF_4$ (Scheme 2). They were purified by column chromatography and characterized by NMR spectroscopy. The ^1H NMR spectra showed strong signals of the two methyl groups, which appear as singlets in the region of 2.78–3.18 ppm. In the ^{31}P NMR ($CDCl_3$) spectra, the salts **4** resonate at 24.2–31.1 ppm.

Single crystals of the salt **4a**, which were suitable for X-ray diffraction study, were obtained by slow diffusion of hexane into a saturated solution of **4a** in chloroform. The molecular structure of this compound is depicted in Fig. 2. Absolute



SCHEME 2 Synthesis of sulfonium salts **4a–c**.

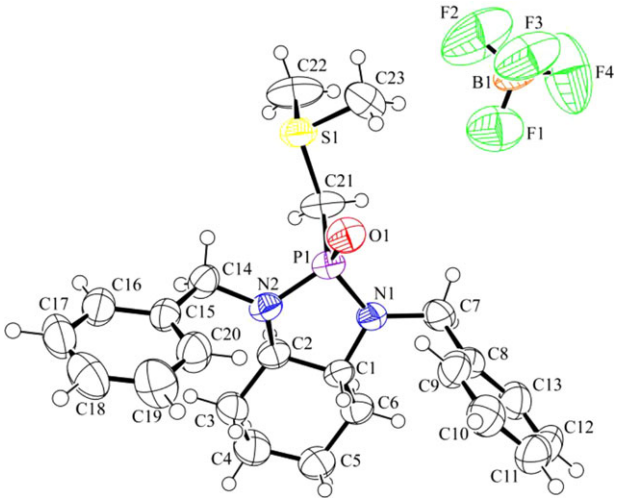


FIGURE 2 Molecular structure of solid **4a**. The thermal ellipsoids were drawn at the 50% probability level. Selected bond distances (Å) and angles (°): P(1)—N(1), 1.641(3); P(1)—N(2), 1.634(3); P(1)—C(21), 1.822(3); S(1)—C(21), 1.787(3); S(1)—C(22), 1.793(4); S(1)—C(23), 1.762(4); N(1)—C(1), 1.464(4); N(1)—C(7), 1.471(4); N(2)—C(2), 1.481(4); N(2)—C(14), 1.462(4); C(1)—C(2), 1.514(4); P(1)—O(1), 1.459(2); O(1)—P(1)—N(1), 121.6(1); O(1)—P(1)—N(2), 117.4(1); O(1)—P(1)—C(21), 107.4(1); N(2)—P(1)—N(1), 94.9(1); N(2)—P(1)—C(21), 109.8(2); O(1)—P(1)—N(1), 121.6(1).

configuration of the two carbon atoms was confirmed as R_{C1} and R_{C2}. The P–N distances are 1.641(3) and 1.634(3) and are slightly shorter than in the other phosphonamides [16–20, 22]. The valence angles of the sulfur atom are in the range of 101.3(2)–103.8(2) and are characteristic for the tetrahedral geometry. The sum of valence angles of nitrogen atoms are ΣN1 = 355.8(6)° and ΣN2 = 351.4(6)° instead of ΣN = 360° for planar groups, which proves the nonplanar configuration of nitrogen. Both nitrogen atoms are tilted out of the plane formed by the three neighboring atoms, about 0.181(3) and –0.259(3) Å. The phosphorus center adopts a slightly deformed tetrahedral geometry. The average value of the six valence angles around the phosphorus atom is 109.3°. Torsion angles are in the range of 94.9 (1)°–121.6 (1)°. The N2–P1–N1 torsion angle is the smallest, and the O–P–N angle is the largest. The same relationships exist in other phosphonamides [16–24]. The angle between the phenyl rings, C8–C13 and C15–C20, is 35.7(2)°. The cyclohexane ring C1–C6 adopts a chair conformation [16, 17, 19, 20, 24], C3 and C6 atoms are tilted with respect to the plane C1, C2, C4, C5 of –0.725(6) and 0.717(5) Å, respectively. The five-membered ring has an envelope conformation [17, 20]. The C2 atom is tilted from the plane 1 (P1, N1, N2, C1) of 0.593 Å, and the angle between the planes 1 and 2 (N2, C2, C1) is 39.5 (2)° [16]. The angle between the cyclohexane ring and five-membered ring is –5.07(9)° [23].

The C22 and C23 atoms of the methyl groups adopt a conformation *–ap* (ϕ = –176.9(3)°) and *+sc* (ϕ = 76.9(3)°) relative to the phosphorus atom P1. The atoms O1, N1, and N2 adopt a conformation *–sc* (ϕ = –31.1(3)°), *–ap* (ϕ = –161.6(2)°), and *+ac* (ϕ = 97.6(2)°), respectively, relative to the phosphorus atom P1 (Fig. 3).

The crystal structure of the compound **4a** is stabilized by weak hydrogen bonds (Fig. 4, Table 1).

The generation of sulfonium ylides was achieved by treatment of the sulfonium salts **4a–c** with butyllitium, lithium diisopropylamide in THF or K_2CO_3 in dichloromethane. Owing to their instability, the

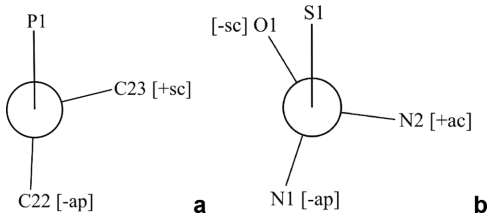


FIGURE 3 Newman projection along the C21—S1 bond (a) and C21—P1 bond (b) for compound **4a**.

resulting ylides **5a–c** are characterized only by the ^{31}P NMR. A significant downfield shift has been observed in the ^{31}P NMR spectra of the compounds **5a–c** (**5a** δ = 45.8 ppm; **5b** δ = 43.4 ppm; **5c** δ = 50.4 ppm) in comparison with the sulfonium salts **4a–c** (**4a** δ = 28.1 ppm; **4b** δ = 24.2 ppm; **4c** δ = 31.1 ppm).

The ylides **5a–c** were found to react with different activated symmetrical 1,1-disubstituted ethylenes [R^1 = P(O)$(OEt)_2$, SO_2Ph, COO^tBu], yielding a mixture of the two diastereoisomeric cyclopropanes **6**, **7**, and **8** in moderate-to-good yields and with diastereoselectivity in the range from 60:40 to 90:10 (Scheme 3, Table 2). The presence of two electron-withdrawing groups in ethylenes makes them much more reactive than those with one activating group such as, e.g., vinylphosphonate. We found that the reaction of ylides **5a–c** with vinylphosphonate does not lead to the corresponding cyclopropanes. A similar lack of reactivity of the ylides was observed with diethyl 2-(propan-2-ylidene)malonate. In this case, the decisive factor is probably the steric hindrance. Therefore, as shown in Table 2, preliminary results of the cyclopropanation reaction represent a compromise between the electron and steric factors having an influence on the reaction course. Moreover, an inspection of the results in Table 2 revealed that a little better stereoselection was obtained with smaller substituents such as Bn (entry 1, 7) and ^{i}Pr (Entry 2, 5), whereas slightly worse for larger substituents like neopentyl (entry 3, 6). Other aspects of the asymmetric cyclopropanation reaction briefly reported herein such as the effect of solvent and base on yield and diastereoselectivity, separation of diastereoisomers, and determination of their absolute configuration and hydrolysis of the chiral phosphonamido auxiliary are under current investigation.

TABLE 1 Hydrogen-Bond Parameters (Å, °) for **4a**

	D—*H*	*H*···*A*	*D*···*A*	*D*—*H*···*A*
C23—H23A···O1	0.96	2.46	3.116(5)	125.7
C20—H20···N2	0.93	2.56	2.889(4)	101.5
C22—H22A···F3^i	0.96	2.39	3.251(5)	148.5

Symmetry codes: (i) 2 – *x*, –1/2 + *y*, 1/2 – *z*.

CONCLUSIONS

In conclusion, we have presented the synthesis of a new type of sulfonium ylides containing a chiral stereodirecting phosphonoamido group derived from *N*,*N*'-disubstituted *trans*-diaminocyclohexane. The reaction of the sulfonium ylides prepared with activated olefins afforded cyclopropylamidophosphonates with moderate-to-high diastereoselectivities. Further studies on asymmetric cyclopropanation are continued.

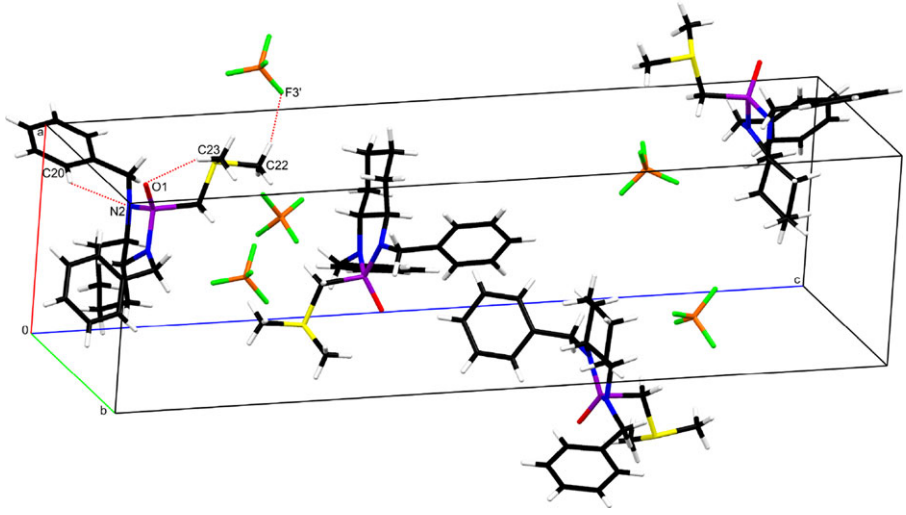
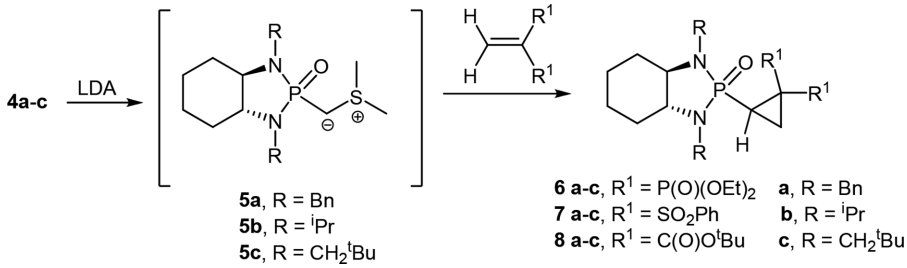


FIGURE 4 Unit-cell packing diagram for **4a**. Dashed line represents a hydrogen bond.



SCHEME 3 Synthesis of cyclopropanes **6–8**.

TABLE 2 Formation of Cyclopropanes **6–8** from Ylides **5**

Entry	*Compound*	*R*	*R¹*	*Ratio of Diastereoisomers*[a]	*Yield*[b] *(%)*
1	**6a**	Bn	$P(O)(OEt)_2$	85:15	63
2	**6b**	^{i}Pr	$P(O)(OEt)_2$	90:10	70
3	**6c**	$^{t}BuCH_2$	$P(O)(OEt)_2$	67:33[d]	66
4	**7a**	Bn	SO_2Ph	60:40[c]	60[c]
5	**7b**	^{i}Pr	SO_2Ph	90:10	52
6	**7c**	$^{t}BuCH_2$	SO_2Ph	64:36[d]	60
7	**8a**	Bn	$COO^{t}Bu$	80:20[c]	62[c]
8	**8b**	^{i}Pr	$COO^{t}Bu$	60:40	35
9	**8c**	$^{t}BuCH_2$	$COO^{t}Bu$	75:25[d]	38

[a]Determined from the ^{31}P NMR spectra of the crude product mixture.
[b]Yield of isolated product after chromatographic work-up.
[c]K_2CO_3 in CH_2Cl_2 was used as a base.
[d]BuLi in THF was used as a base.

EXPERIMENTAL

General

^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on a Bruker AC 200 spectrometer at 200.13, 50.32, and 81.02 MHz, respectively (using $CDCl_3$ as a solvent) unless otherwise noted. IR spectra were measured on an Ati Mattson Infinity FTIR 60 spectrometer. MS spectra (FAB and HRMS) were recorded on a Finnigan MAT 95 spectrometer. Optical rotation values were measured in a 100-mm cell on Perkin–Elmer 241 MC under Na lamp radiation. Column chromatography was conducted on a Merck silica gel (70–230 mesh). All solvents were dried by conventional methods and distilled before use. All commercially available products were purified by either distillation or crystallization and were bought from Aldrich. Tetraethyl ethenylidenebis(phosphonate) [25] and di-*tert*-butyl methylenemalonate [26] were obtained according to a known procedure.

General Procedure for Synthesis of Sulfides **3a–c**

To a suspension of 0.735 g (5.5 mmol) of KH (30% dispersion in mineral oil) in 10 mL of THF, a solution of 5 mmol of phosphorus acid diamide **2** was added in 20 mL of THF at –78°C. The resulting mixture was allowed to warm to room temperature and stirred for 1 h. The temperature was decreased to –78°C, and 0.483 g (5 mmol) of chloromethyl methyl sulfide in 5 mL of THF was added dropwise and stirred for 12 h at room temperature. The mixture was washed at 0°C with 5 mL of a saturated solution of NH_4Cl and extracted with CH_2Cl_2 (2×10 mL). After aqueous work-up, the organic layer was separated, dried ($MgSO_4$), and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using toluene/ethyl acetate (2/1 v/v) for elution to give viscous oil of sulfide **3**.

1,3-Bis(phenylmethyl)-2-[(methylthio)methyl] octahydro-2-oxide-(3aR,7aR)-1H, 1,3,2-benzodiazaphosphole ***3a***. Yellowish oil; 83% yield; $[\alpha]_D^{25} = -69$ ($CHCl_3$, 1.1). IR (film): ν = 2935, 2862, 1453, 1209, 1171, 1028, 738 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.70–7.05 (m, 10H), 4.62–4.25 (m, 2H), 4.20–3.82 (m, 2H), 3.14 (ddd, J = 2.8, 2.9, 11.8 Hz, 1H), 3.00–2.62 (m, 3H), 2.13 (s, 3H), 1.90–1.45 (m, 4H), 1.35–0.72 (m, 4H) ppm. ^{31}P NMR (81 MHz, $CDCl_3$): δ = 37.3 (s) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 139.8, 138.5, 128.4, 128.2, 127.4, 127.1, 126.9 (s), 65.2, 63.8 (d, J = 6.8 Hz), 47.6, 46.5 (s), 31.2 (d, J = 131.2 Hz), 29.5 (d, J = 6.1 Hz), 24.2 (s), 13.5 (d, J = 6.7 Hz) ppm. MS(FAB) 401 (M + H). HRMS (FAB) calcd. for $C_{22}H_{30}OPSN_2$ $[M + H]^+$ 401.1816; found 401.1820.

TABLE 3 Crystallographic Data for **4a**

Crystal data	
$C_{23}H_{32}N_2OPS{\cdot}BF_4$	$D_x = 1.308$ g·cm^{-3}
$M_r = 502.36$	Mo Kα radiation
Orthorhombic, $P2_12_12_1$	Cell parameters from 18,034 reflections
$a = 8.6160$ (2) Å	$\theta = 1.9$–$27.8°$
$b = 9.2538$ (2) Å	$\mu = 0.24$ mm^{-1}
$c = 31.9945$ (8) Å	$T = 296$ (2) K
$V = 2550.95$ (10) Å^3	Needle, colorless
$Z = 4$	0.35 × 0.15 × 0.10 mm
Data collection	
Kuma KM4 CCD area-detector diffractometr	3,707 reflections with $I > 2\sigma(I)$
ω scan	$R_{int} = 0.029$
Absorption correction: none	$\theta_{max} = 27.0°$
$T_{min} = 0.922$, $T_{max} = 0.977$	$h = -11 \rightarrow 10$
45,044 measured reflections	$k = -11 \rightarrow 11$
5,376 independent reflections	$l = -39 \rightarrow 39$
Refinement	
Refinement on F^2	Calculated weights $w = 1/[\sigma^2(F_o^2) + (0.0817P)^2]$, where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.043$	$(\Delta/\sigma)_{max} < 0.0001$
$wR(F^2) = 0.144$	$\Delta\rho_{max} = 0.32$ e Å^{-3}
$S = 1.12$	$\Delta\rho_{min} = -0.29$ e Å^{-3}
5,376 reflections	Extinction correction: none
300 parameters	Absolute structure/ Flack [23] parameter
H atoms constrained to parent site	Flack parameter: – 0.10 (10)

1,3-Bis(1-methylethyl)-2-[(methylthio)methyl] octahydro-2-oxide-(3aR,7aR)-1H, 1,3,2-benzodiazaphosphole ***3b***. Yellowish oil; 87% yield; $[\alpha]_D^{25} = -75$ ($CHCl_3$, 1). IR (film): $\nu = 2930$, 2871, 1440, 1209, 1015, 693 cm^{-1}.^{1}H NMR (200 MHz, $CDCl_3$): $\delta =$ 3.65–3.27 (m, 2H), 3.08–2.84 (m, 3H), 2.80–2.58 (m, 1H), 2.12 (s, 3H), 2.10–1.83 (m, 2H), 1.80–1.52 (m, 2H), 1.30 (d, $J = 6.8$ Hz, 6H), 1.28–1.17 (m, 4H), 1.15 (d, $J = 6.8$ Hz, 6H) ppm. ^{31}P NMR (81 MHz, $CDCl_3$): $\delta = 32.4$ (s) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): $\delta =$ 60.6 (d, $J = 7.5$ Hz), 59.6 (d, $J = 6.2$ Hz), 44.6 (d, $J =$ 2.5 Hz), 43.8 (d, $J = 5.5$ Hz), 33.0 (d, $J = 113.3$ Hz), 30.1 (d, $J = 7.5$ Hz), 29.7 (d, $J = 10.1$ Hz), 24.0 (s), 23.0 (d, $J = 3.0$ Hz), 21.8 (d, $J = 4.5$ Hz), 20.4, 20.0 (s), 17.6 (d, $J = 7.5$ Hz) ppm. MS(FAB) 305 (M + H). Anal. Calcd. for $C_{14}H_{29}N_2POS$ (304.46): C, 55.22; H, 9.62. Found: C, 55.18; H, 9.66.

1,3-Bis(2,2-dimethylpropyl)-2-[(methylthio) methyl]octahydro-2-oxide-(3aR,7aR)-1H, 1,3,2-benzodiazaphosphole ***3c***. Yellowish oil; 85% yield; $[\alpha]_D^{25} = -77$ ($CHCl_3$, 1). IR (film): $\nu = 2973$, 2870, 1458, 1220, 1106, 1043, 731, 705 cm^{-1}. ^{1}H NMR (200 MHz, C_6D_6): $\delta = 3.65$ (dd, $J = 16.7$, 16.7 Hz, 1H), 3.04 (d, $J = 13.7$ Hz, 2H), 2.92–2.80 (m, 2H), 2.65–2.30 (m, 2H), 2.12 (dd, $J = 14.6$, 14.6 Hz, 1H), 1.78 (d, $J = 1.5$ Hz, 3H), 1.75–1.58 (m, 2H), 1.55–1.28 (m, 2H), 1.07 (s, 9H), 1.02–0.83 (m, 4H), 0.99 (s, 9H) ppm. ^{31}P NMR (81 MHz, C_6D_6): $\delta =$ 39.8 (s) ppm. ^{13}C NMR (50 MHz, C_6D_6): $\delta = 67.1$ (d, $J = 5.7$ Hz), 66.2 (d, $J = 7.6$ Hz), 58.2 (s), 56.7 (d, $J =$ 2.5 Hz), 32.3 (d, $J = 20.5$ Hz), 32.0 (d, $J = 21.6$ Hz), 31.2 (d, $J = 88.7$ Hz), 29.3 (d, $J = 6.7$ Hz), 25.4 (s), 18.1 (d, $J = 9.0$ Hz) ppm. MS(FAB) 361 (M + H). Anal. Calcd. for $C_{18}H_{37}N_2POS$ (360.58): C, 59.95; H, 10.36. Found: C, 59.81; H, 10.34.

General Procedure for Synthesis of Sulfonium Salts **4a–c**

To a solution of sulfide **3** in methyl iodide, $AgBF_4$ at 0°C was added and the suspension was stirred at room temperature overnight. Volatiles were removed in vacuo, and acetone was added. The yellow precipitate that formed was collected by filtration on Celite, and a solution was concentrated to give a sulfonium salt **4** as a glassy white or yellowish solid. Colorless needle-shaped crystals suitable for X-ray crystallography were obtained by slow diffusion of hexane into a saturated solution of **4a** in chloroform.

{[1,3-Bis(phenylmethyl)octahydro-2-oxide-(3aR, 7aR)-1H-1,3,2-benzodiazaphosphol-2-yl]methyl}(dimethyl)sulfonium Tetrafluoroborate ***4a***. Colorless crystals; 87% yield; $[\alpha]_D^{25} = -35$ ($CHCl_3$, 1.2). IR

(film): ν = 3030, 2938, 2866, 1454, 1211, 1106, 1053, 1067, 739, 700 cm^{-1}.^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.70–7.05 (m, 10H), 4.50–3.95 (m, 3H), 3.80 (dd, J = 10.8, 10.9 Hz, 1H), 3.40 (dd, J = 12.1, 12.4 Hz, 1H), 3.06 (dd, J = 11.5, 11.5 Hz, 1H), 2.82 (s, 3H), 2.78 (s, 3H), 2.05–1.85 (m, 2H), 1.82–1.45 (m, 3H), 1.43–1.05 (m, 3H), 1.04–0.65 (m, 2H) ppm. ^{31}P NMR (81 MHz, $CDCl_3$): δ = 28.1 (s) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 138.8 (d, J = 5.0 Hz), 136.5, 128.9, 128.7, 128.3, 127.7, 127.5, 127.2 (s), 63.4 (d, J = 9.5 Hz), 62.5 (d, J = 7.0 Hz), 46.1 (s), 45.5 (d, J = 4.5 Hz), 38.8 (d, J = 104.8 Hz), 29.0 (d, J = 8.4 Hz), 28.5 (d, J = 9.0 Hz), 26.9, 24.7 (s) ppm. MS(FAB) 415 (M-BF_4). HRMS (FAB) calcd. for $C_{23}H_{32}OPSN_2$ $[M - BF_4]^+$ 415.1973; found 415.1989.

{[1,3-Bis(1-methylethyl)octahydro-2-oxide-(3aR, 7aR)-1H-1,3,2-benzodiazaphosphol-2-yl]methyl} (dimethyl)sulfonium Tetrafluoroborate ***4b***. Glassy white solid; 90% yield; $[\alpha]_D^{25}$ = –24 ($CHCl_3$, 1). IR (film): ν = 3028, 2944, 2870, 1208, 1064, 1071, 736 cm^{-1}.^{1}H NMR (200 MHz, $CDCl_3$): δ = 4.10–3.65 (m, 2H), 3.65–3.40 (m, 2H), 3.18 (s br, 6H), 3.08–2.75 (m, 2H), 2.34–1.97 (m, 2H), 1.97–1.65 (m, 2H), 1.60–1.08 (m, 4H), 1.35 (d, J = 5.9 Hz, 6H), 1.25 (d, J = 5.9 Hz, 6H) ppm. ^{31}P NMR (81 MHz, $CDCl_3$): δ = 24.2 (s) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 62.8 (d, J = 7.8 Hz), 58.9 (d, J = 6.0 Hz), 45.4 (d, J = 3.0 Hz), 43.0 (d, J = 4.0 Hz), 37.5 (d, J = 108.0 Hz), 30.6 (d, J = 7.0 Hz), 28.9 (d, J = 9.2 Hz), 24.8, 24.0, 22.6 (s), 22.0 (d, J = 4.0 Hz), 21.1, 20.9 (s), 20.5 (d, J = 6.5 Hz) ppm. MS (FAB) 319 (M – BF_4). Anal. Calcd. for $C_{15}H_{32}N_2POSBF_4$ (406.27): C, 44.34; H, 7.95. Found: C, 44.28; H, 7.92.

{[1,3-Bis(2,2-dimethylpropyl)octahydro-2-oxide-(3aR,7aR)-1H-1,3,2-benzodiazaphosphol-2-yl]methyl}(dimethyl)sulfonium Tetrafluoroborate ***4c***. Glassy yellowish solid; 95% yield; [α] = –22 ($CHCl_3$, 1). IR (film): ν = 3032, 2941, 2851, 1452, 1207, 1050, 1073, 732 cm^{-1}.^{1}H NMR (200 MHz, $CDCl_3$): δ = 4.15–3.95 (m, 1H), 3.80–3.56 (m, 1H), 3.15 (s, 6H), 3.05–2.23 (m, 4H), 1.92–1.71 (m, 2H), 1.58–1.10 (m, 4H), 1.10–0.90 (m, 4H), 0.96 (s, 9H), 0.93 (s, 9H) ppm. ^{31}P NMR (81 MHz, $CDCl_3$): δ = 31.1 (s) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 64.6 (d, J = 8.6 Hz), 64.0 (d, J = 11.0 Hz), 57.7 (s), 55.5 (d, J = 28.1 Hz), 54.4 (d, J = 33.6 Hz), 38.2 (d, J = 98.5 Hz), 32.9, 31.7, 30.9, 28.6, 28.3, 27.3, 27.1, 24.3, 22.9 (s) ppm. MS(FAB) 375 (M – BF_4). Anal. Calcd. for $C_{19}H_{40}N_2POSBF_4$ (462.46): C, 49.34; H, 8.74. Found: C, 49.29; H, 8.72.

X-Ray Crystallography

Crystal Data for {[1,3-bis(phenylmethyl)octahydro-2-oxide-(3aR,7aR)-1H-1,3,2-benzodiazaphosphol-2-yl]methyl}(dimethyl)sulfonium Tetrafluoroborate ***4a***. $C_{23}H_{32}N_2OPS{\cdot}BF_4$, colorless, needle 0.35 × 0.15 × 0.10 mm, orthorhombic, space group $P2_12_12_1$, a = 8.6160 (2), b = 9.2538 (2), c = 31.9945 (8) Å, V = 2550.95 (10) Å^3, M_r = 502.36, Z = 4, d_{calcd} = 1.308 g cm^{-3}, μ = 0.24 mm^{-1}, T = 296 (2) K, $F(000)$ = 1056 (see Table 3). *Data collection*: Kuma KM4 CCD area-detector diffractomer with graphite monochromatized Mo Kα radiation. Measured reflections 45,044 (θ_{max} 27.0°), 5376 independent (R_{int} 0.029). Structure solution: direct method, anisotropic refinement on F^2 for all non-H atoms, hydrogen atoms attached to C atoms were included using a riding model. The structure was refined over 3707 reflections with $I > 2\sigma(I)$ (300 refined parameters with 12.4 reflections on parameter). The correct absolute structure was proved by the Flack parameter [27] x = –0.10 (10). For all data, the final wR_2 was 0.144, R_1 = 0.043, S = 1.12, max. $\Delta\rho$ = 0.32 e Å^{-3}. Data processing was carried out with the Oxford Diffraction [28, 29]; structure solution SHELXS [30]; structure refinement SHELXL [31].

SUPPLEMENTARY MATERIAL

Full details (excluding the structure factors) for the structure reported in this paper have been deposited at the Cambridge Crystallographic Data Center, as supplementary publication no. CCDC 976694 and can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (e-mail: deposit@ccdc.cam.ac.uk).

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