Experimental Section

Starting Materials. (-)-(*S*)-*O*-Menthyl *p*-toluenesulfinate was prepared by the method of Phillips;[12] mp 106–107 °C; $[\alpha]_{589}$ -195° (*c* 1.97, acetone) (lit.[13] mp 108–109 °C; $[\alpha]_{589}$ -210°[18]). (-)-(*S*)-*O*-Menthyl *n*-butanesulfinate was prepared according to Mislow et al.;[8] $[\alpha]_{589}$ -49.3° (*c* 1.75, acetone) (lit.[8] $[\alpha]_D$ -50°). (-)-(*S*)-*O*-Menthyl methanesulfinate was prepared according to the procedure described by Andersen;[6] $[\alpha]_{589}$ -60.2° (*c* 1.35, acetone) (lit. $[\alpha]_D$ -99 ± 1° (*c* 2.04, acetone)).

The Grignard reagents used in this work were prepared as usual in ether solution. Then, ether was removed in vacuo at room temperature, and benzene was added (100 mL for each 0.03 mol of R^2MgX) to the residue.

Synthesis of Chiral Sulfoxides 2. General Procedure. A solution of *O*-menthyl sulfinate 1 (1 equiv) in benzene (30 mL/10 mmol of 1) was added dropwise to a benzene solution of Grignard reagent (2 equiv) at room temperature. After completion of the addition, the reaction mixture was stirred for 0.5 h at room temperature. Then, the reaction mixture was treated with aqueous ammonium chloride solution, saturated with sodium chloride, and extracted with chloroform. The combined organic layers were washed with 5% sodium carbonate solution and water and dried over magnesium sulfate. Evaporation of the solvents yielded an oil which was purified by chromatography on silica gel with hexane, hexane–ether, and chloroform as eluents. The yields and optical rotations of sulfoxides 2 obtained in this way are collected in Table I.

Registry No. (-)-(*S*)-1 (R^1 = *p*-toluene), 1517-82-4; (-)-(*S*)-1 (R^1 = Bu), 81769-14-4; (-)-(*S*)-1 (R^1 = Me), 81769-15-5; (+)-2 (R^1 = *p*-toluene;R^2 = Me), 1519-39-7; (+)-2 (R^1 = *p*-toluene; R^2 = Et), 1519-40-0; (+)-2 (R^1 = *p*-toulene; R^2 = I-Pr), 1517-74-4; (+)-2 (R^1 = *p*-toluene; R^2 = Bu), 20288-49-7; (+)-2 (R^1 = *p*-toulene; R^2 = Ph), 16491-20-6; (-)-2 (R^1 = Me; R^2 = Pr), 37177-70-1; (+)-2 (R^1 = Bu; R^2 = Me), 763-95-1.

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Synthesis and Stereochemistry of 1,5-Diazatricyclo[4.4.0.0^{3,5}]decane

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The bicyclo[3.1.0]hexane moiety has been the subject of many spectroscopic investigations due to the peculiar cyclopropane effect exerted in polycyclic compounds.[1] We report the conformational analysis of the unknown, 1,5-diazatricyclo[4.4.0.0^{3,5}]decane (**8**) obtained by cyclization of a mixture of the 2-(4-hydroxybutyl)-1,3-diazabicyclo-[3.1.0]hexane epimers **5** and **6** which are new compounds in this series.[2]

Synthesis

The aminolysis of 2-(dimethylamino)tetrahydropyran (**1**) with 2-(aminomethyl)aziridine (**2**) affords a good yield of a mixture of the isomeric compounds **5** and **6** (Scheme I) in a 65:35 ratio (by integration of NMR signals). All attempts (TLC, GLC, HPLC) to separate **5** and **6** failed. The diastereoselectivity observed in this reaction arises from the difference in the reactivity of the two intermediates **3** and **4** (in their preferred *E* configuration): compound **5** is expected to result from the less hindered attack of the aziridine on the imino carbon. Similar imino alcohol participation in those aminolyses was previously noted.[3]

Treatment of the mixture of **5** and **6** with triphenylphosphine–carbon tetrachloride in a basic medium (triethylamine) gives only one liquid compound, **8**, in 21% yield, plus polymeric material. The mechanism of the reaction of triphenylphosphine–carbon tetrahalide with alcohols and β-amino alcohols has been described,[4] and a Walden inversion has been observed in the ring closure of ephedrine.[5] In the transition state of an S_N2 pathway, entering and leaving groups are opposite (180° position); distortion of bond angles and distances favors alternative reactions. With an axial N-3 lone pair, ring closure of **5** would require severe steric interactions; with an equatorial N-3 lone pair, orbital overlapping (N-3 lone pair and C–O σ bond) is noneffective (deviation from the ideal transition state) so that competitive intermolecular reaction is favored. The tricyclic compound is expected to result from the cyclization of **6** which can take place without steric hindrance and with the required trajectory if the N-3 lone pair is equatorial (this equatorial position is preferred as indicated below). Similar ring closure of two isomeric 2-(4-hydroxybutyl)-4-methyltetrahydro-1,3-thiazoles has been reported;[6,7] in that case the formation of two compounds had been observed. Then stereocontrol appears in the cyclization of the mixture of **5** and **6**, due to the presence of the aziridinyl ring.

Conformational Analysis

The structures of the two epimers **5** and **6** were established by NMR spectroscopy. The chemical shifts of C-1′ and C-6 of the major isomer appear upfield relative to those of the minor one: this normal γ effect[8] indicates in **5** a cis relationship of the aziridino methylene and the 2-substituent. The H-6 signals have been assigned according to the ethylenimine rule[9] ($J_{erythro} > J_{threo}$); the H-6 trans to the N-1 lone pair is more shielded than the cis H-6, in agreement with literature data.[10] The two epimers display similar vicinal coupling constants ^3J(H-4,H-5), and so the 1,3-diazabicyclo[3.1.0]hexane moiety would adopt the same conformation in both cases. The low value (ca. 0.5 Hz) observed for ^3J(H-4$_{endo}$,H-5) indicates that the relevant dihedral angle is in the range of the minimum of the Karplus curve (ca. 80° is measured on Dreiding stereomodels): these data suggest a "boatlike" form for the

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Scheme I

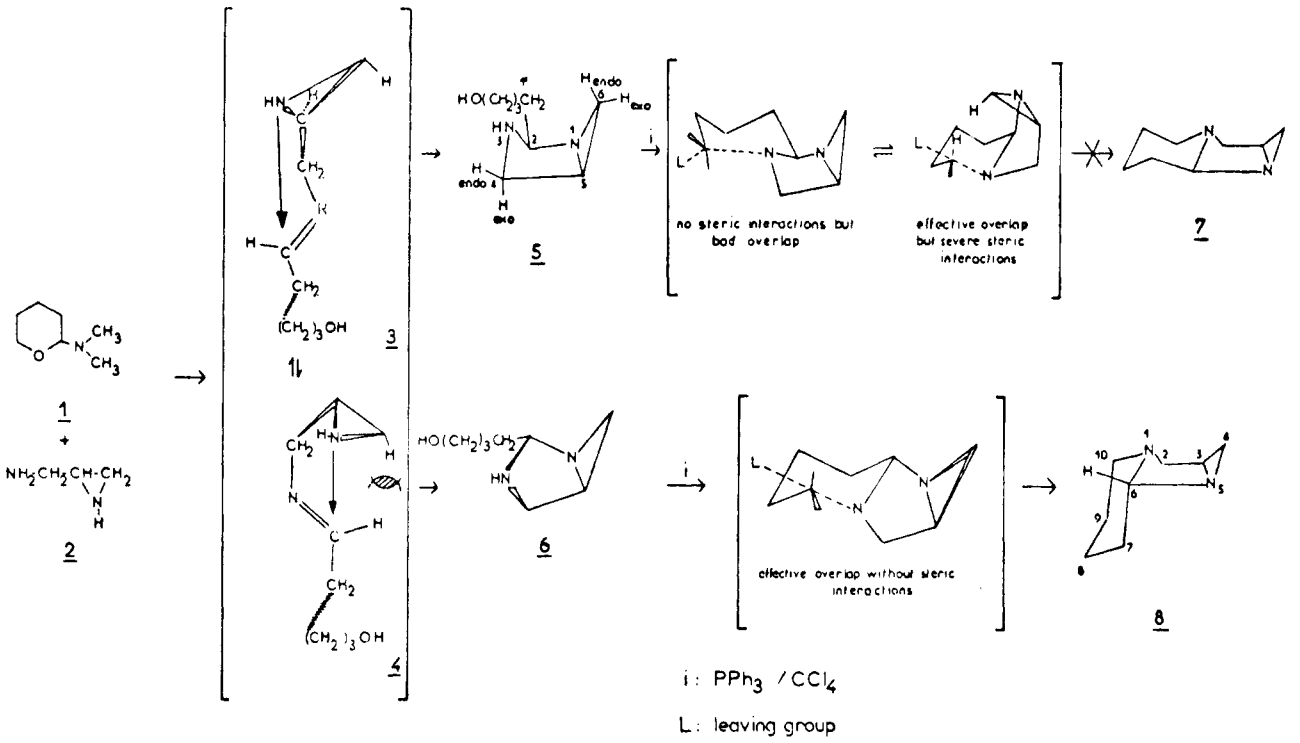

Table I. ^{13}C NMR Data[a]

	C-2	C-4	C-5	C-6	C-1′	C-4′
5	78.9 (152)	46.8 (140)	37.5 (180)	19.8 (163)	31.6 (125)	61.5 (139)
6	80.3 (148)	45.0	37.8	25.5	35.4	61.5
	C-6	C-2	C-3	C-4	C-7	C-10
8	81.3 (139)	52.2 (136)	34.0 (180)	22.4 (167 and 172)	28.2 (125)	49.8 (133)

[a] Chemical shifts in parts per million downfield from Me_4Si (δ). ^1J(C,H) values (in hertz) are in parentheses. Compounds 5 and 6 were analyzed in $CDCl_3$ and 8 in the pure liquid state.

Table II. ^1H NMR Data[a]

	H-6			H-4			
	exo	endo	H-5	δ(endo)	^2J	δ(exo)	H-2
5	1.45 (4.9)	1.21 (3.3)	2.40	3.20 (0.5)	12.3	2.99 (2.3)	3.89 (5.5)
6	1.65	1.13 (3.3)	2.43	3.16 (0.5)	12.3	2.99 (2.3)	3.81

	H-4			H-2			
	exo	endo	H-3	δ(endo)	^2J	δ(exo)	H-6[c]
8[b]	1.31 (5.2)	1.99 (3.0)	2.29	3.13 ($\leq$0.5)	8.6	2.40 (3.4)	2.81

[a] Chemical shifts are in parts per million downfield from Me_4Si. Coupling constants are given in hertz (^3J in parentheses). Compounds were analyzed in $CDCl_3$ at 80.131 MHz for 5 and 6 and at 200.057 or 350.00 MHz for 8. [b] Other data: 1.18 (H-7 ax, J_{ae} = 3.4, $^2J = J_{aa}$ = 12.5), 1.27 (H-8 ax, J_{ae} = 3.5, $^2J = J_{aa}$ = 12.6), 1.39 (H-9 ax, J_{ae} = 4.2, $^2J = J_{aa}$ = 12.4), 1.53 (H-9 eq), 1.82 (H-8 eq), 1.93 (H-7 eq), 2.06 (H-10 ax, J_{ae} = 3.0, $^2J = J_{aa}$ = 11.2), 2.99 (H-10 eq). The signals were assigned by selective decouplings and with the homonuclear correlated two-dimensional spectrum. Weaker couplings (ca. 0.5 Hz) appear between H-4_{endo} and H-4_{exo} (^2J) and between H-4_{endo} and H-2_{exo} (^4J). [c] J_{aa} = 9.9 Hz and J_{ae} = 2.2 Hz.

compounds 5 and 6 as for the bicyclo[3.1.0]hexane itself.[1a-c] ^{13}C chemical shift differences between the carbons of the aziridine ring are of same magnitude in epimer 6 and in compound 8. No shielding effect appears for C-4 as expected for the unobtained cis epimer of 8. Therefore, the trans configuration is assigned to the tricyclic compound. The largest values of the one-bond (C,H) coupling constant (C-3 and C-4 in 8 and as C-5 and C-6 in 6) are in agreement with the literature data for aziridinyl systems.[11] Ring closure lowers the ^1J(C,H) of the aminal carbon (ca. 10 Hz) as observed in thiazolidine system.[7] In the ^1H NMR spectrum of 8, H-6 appears as a doublet of doublets with values of 9.9 and 2.2 Hz for ^3J: this indicates that H-6 is axial in the piperidine ring (J_{aa} and J_{ae}, respectively) and so confirms the cis junction of the six-membered ring. Other ^1H NMR data suggest a boat form of the diazabicyclohexane moiety of 8: the endo H-2 appears at 3.13 ppm as a doublet resulting from the splitting by the exo H-2 (so ^3J(H-2_{endo},H-3) $\leq$ 0.5 Hz); a chair conformation of the bicyclohexanic part would increase the couplings between H-2 and H-3.

Comparison between 6 and 8 leads to the following observations. (i) Ring closure gives rise to a deshielding of

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the endo proton of the aziridino methylene. The lone-pair anisotropy of N-3 (in **6**) or N-1 (in **8**) would account for this chemical shift difference, so H-3 is expected to have a preferred axiallike orientation in the bicyclic compound **6**. This position would result from the repulsive nonbonded interaction between the aziridine "π-electron" system and the N-3 lone pair. (ii) The N-1 lone pair in **8** has an upfield shifting effect on the antiperiplanar exo H-2[12] and an increasing effect on the algebraic value of the H-2 geminal coupling[13] with respect to the corresponding protons of **6**.

EI (or CI) spectra confirm the structure of compounds **5**, **6**, and **8**. These products exhibit a molecular ion (or protonated ion), and the base peak is the 1-aza-3-azonia-bicyclo[3.1.0]hex-2-ene cation (**9**) for **5** and **6** and the tetrahydropyridinium cation (**10**) for **8**.

Experimental Section

All melting and boiling points are uncorrected. Basic nitrogen analyses were performed by titration, controlled by potentiometry, with a solution of perchloric acid in acetic acid. Infrared spectra were obtained from a Perkin-Elmer 21 or Beckman 4210 spectrometer. ^{1}H NMR spectra were recorded on a Cameca 350, Varian XL 200, or Bruker WP 80 instrument. The natural-abundance ^{13}C NMR spectra were obtained by Fourier transformation carried out on a Bruker WP 80 spectrometer operating at 20.15 MHz and using a 2–2.5-kHz spectral width, 8K memory points, and a flip angle of 30°. Mass spectrometry was performed on a Ribermag R 10-10 quadrupole spectrometer equipped with a Sydar 121 data system. GLC analyses were carried out on a Girdel 30 instrument equipped with a 60-m glass capillary column coated with Carbowax 20M or with a 2-m glass column packed with 3% OV-17 (or 2.75% Carbowax 4000M and 0.75% potassium hydroxide) on Chromosorb W HP (100–120 mesh).

2-(4-Hydroxybutyl)-1,3-diazabicyclo[3.1.0]hexanes 5 and 6. A mixture of 2-(dimethylamino)tetrahydropyran[14] (12.9 g, 0.1 mol) and 2-(aminomethyl)aziridine[15] (7.6 g, 0.106 mol) was stirred at room temperature for 48 h and then heated at 65 °C under reduced pressure for 8 h to yield a mixture of the amines **5** and **6**: 13.1 g (84%); bp 128 °C (0.4 mm); n^{21}_D 1.5050; IR (neat) 3280 (OH), 3055 and 3030 (aziridine) cm^{-1}; EI mass spectrum, m/z (relative intensity) 83 (**9**, 100), 155 (M − 1), 156 (M$^{+\cdot}$); CI (isobutane) mass spectrum, m/z (relative intensity) 157 (M + 1, 100), 197 (M + 41), 213 (M + 57). Anal. Calcd for $C_8H_{16}N_2O$: N, 17.95. Found: N, 17.78.

1,5-Diazatricyclo[4.4.0.0^{3,5}]decane (8). A mixture of the amines **5** and **6** (6 g 0.038 mol) was treated with triphenylphosphine (13.6 g, 0.052 mol), carbon tetrachloride (9.4 g, 0.061 mol), and triethylamine (4 g, 0.039 mol) in 35 mL of acetonitrile as previously described[6] for 2-(4-hydroxybutyl)tetrahydro-1,3-thiazole to yield **8**: 1.10 g (21%); bp 62 °C (7 mm); n^{18}_D 1.4990; IR (neat) 3060, 3025, 2985 cm^{-1}; EI mass spectrum, m/z (relative intensity) 84 (**10**, 100), 138 (M$^{+\cdot}$); CI (isobutane) mass spectrum, m/z (relative intensity) 139 (M + 1, 100). Anal. Calcd for $C_8H_{14}N_2$ N, 20.27. Found: N, 20.16. Dipicrate, mp 138 °C. Anal. Calcd for $C_{20}H_{20}N_8O_{14}$: basic N, 4.70. Found: basic N, 4.65.

Acknowledgment is made to Dr. R. Richarz and Varian AG (NMR Applications Laboratory, Zug, Zwitzerland) for recording the homonuclear correlated two-dimensional ^{1}H NMR spectrum of the tricyclic compound.

Registry No. **1**, 37019-50-4; **2**, 55099-23-5; **5**, 82165-82-0; **6**, 82165-83-1; **8**, 82165-84-2.

Supplementary Material Available: Homonuclear correlated two-dimensional ^{1}H spectrum of compound **8** (1 page). Ordering information is given on any current masthead page.

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Bicyclic Dioxaphosphoranes. 2. Spectral Properties Indicative of a Karplus Relationship in Phosphoranes

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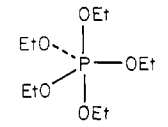
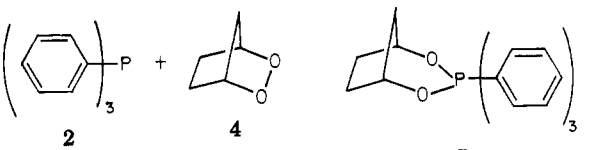
In 1964 Denney reported the first reaction of a trivalent phosphorus compound, triethyl phosphite, with a dialkyl peroxide, diethyl peroxide.[1] The product of that reaction was a stable phosphorane, pentaethoxyphosphorane (**1**).



1

Since that initial report the reactions of trivalent phosphorus with several acyclic[2] and cyclic peroxides[3] have been reported. The reaction of triphenylphosphine (**2**) with tetramethyldioxetane (**3**) has been extensively investigated from a mechanistic point of view;[5] however, it is remarkable how very little is known about the effect of structure on the mechanism of insertion of phosphorus into the oxygen–oxygen bond.

We have recently reported[6] that **2** reacts with the prostaglandin endoperoxide model,[7] 2,3-dioxabicyclo-[2.2.1]heptane (**4**) to produce a stable phosphorane **5**. (eq 1). We have suggested that this reaction is a concerted



2 **4** **5** (1)

insertion of phosphorus into the oxygen–oxygen bond. Evidence was also presented which suggested that phosphorane **5** hydrolyzed in nonpolar media by an outersphere mechanism (attack at carbon) rather than by the established innersphere mechanisms[8] (attack at phosphorus). The interest in this ring system[9] has prompted us to report the synthesis of three more phosphoranes, kinetic data for their formation, and their interesting spectral properties.

The addition of methyl diphenylphosphinite, dimethyl phenylphosphonite, and trimethyl phosphite to **4** dissolved

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