diglyme for 1 hr. GLC analysis (SE-30) indicated a 95% yield of V. The product was isolated by distillation: bp 74° (5 mmHg) [lit. bp 121° (30 mmHg)];[23] NMR ($CDCl_3$) δ 1.6 (m, broad, 6, aliphatic), 3.6 (m, broad, 4, $-CH_2O$ and CH_2Cl), 3.9 (s, 1, OH).

Acknowledgment. We wish to thank the Research Corporation for support of this study.

Registry No.—I, 54844-22-3; II, 7031-03-0; III, 54844-23-4; IV, 10317-10-9; V, 5259-98-3; *p*-tolylthiol, 106-45-6; 5-hexen-2-one, 109-49-9; 1-hexen-5-ol, 626-94-8.

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Mechanisms and Stereochemistry of Displacement of Methoxide Ion by Hydroxide Ion from Phosphorus in Phospholanium and Phosphorinanium Salts

Kenneth L. Marsi

Department of Chemistry, California State University, Long Beach, Long Beach, California 90840

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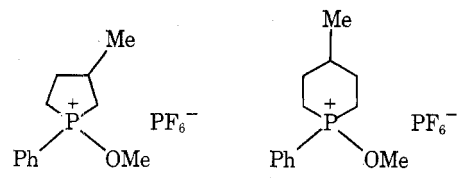
The synthesis of the cis and trans isomers of 1-methoxy-3-methyl-1-phenylphospholanium hexafluorophosphate is reported. Hydroxide displacement of methoxide from the trans isomer leads to 3-methyl-1-phenylphospholane 1-oxide with 51% retention and 49% inversion of configuration at phosphorus, while cleavage of the cis isomer gives the same product with 42% retention and 58% inversion. The cis and trans isomers of 4-methyl-1-phenylphosphorinane 1-oxide were also prepared and methylated with retention to yield the corresponding *cis*- and *trans*-1-methoxy-4-methyl-1-phenylphosphorinanium hexafluorophosphates. Alkaline cleavage of the cis and trans phosphorinanium salts leads to complete inversion of configuration as a result of nucleophilic attack at phosphorus. ^{18}O-Labeling experiments reveal that, under reaction conditions employed, nucleophilic attack at methoxy carbon occurs to the extent of 11% in the phospholanium salts and 9% in the phosphorinanium salts. The stereochemistry of nucleophilic displacement at phosphorus in both systems can be rationalized in terms of stereoelectronic vs. ring strain effects in phosphorane intermediates.

As part of a continuing study of the effect of ring size on the mechanism and stereochemistry of displacement of leaving groups from phosphorus in heterocyclic phosphonium salts,[1] we wish to report results of hydroxide ion displacement of methoxide ion from *cis*- and *trans*-1-methoxy-3-methyl-1-phenylphospholanium (**1**) and *cis*- and *trans*-1-methoxy-4-methyl-1-phenylphosphorinanium (**2**) hexafluorophosphates.



1 2

Synthesis of and Assignment of Stereochemistry to Alkoxyphosphonium Salts. These compounds were prepared by alkylation of the stereoisomerically pure phosphine oxides[1d,f] with trimethyloxonium hexafluorophosphate (eq 1). As expected, alkylation occurred with retention of configuration at phosphorus as shown previously for the phosphetane oxide system.[2] It was also possible to alkylate the oxides by use of methyl fluorosulfonate ("Magic Methyl"). ^1H NMR analysis of methoxyphosphonium fluorosulfonates formed also indicated stereospecific alkylation. However, because the fluorosulfonate salts were difficult to obtain in a pure crystalline form for the purpose of elemental analysis, trimethyloxonium hexafluorophosphate was used and found to be superior in this respect. Characteristics of these compounds are listed in Table I.

$$R_3P{=}O + (CH_3)_3O^+\ PF_6^- \longrightarrow R_3P^+OCH_3\ PF_6^- + (CH_3)_2O \quad (1)$$

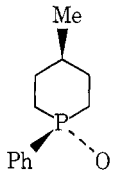
The cis and trans stereochemistry for isomers of **1** was established indirectly by an X-ray crystal structure determination.[3] The stereostructure of the isomers of **2** was assigned by ^1H NMR analysis of the oxides (**3**) from which they were derived, together with corroborating physical properties of the oxides. With respect to cyclohexane, the conformational preferences for methyl and phenyl[4] are such that for the 1,4-trans arrangement of these two groups

Table I
Methoxyphospholanium (1) and Methoxyphosphorinanium (2) Hexafluorophosphates[a]

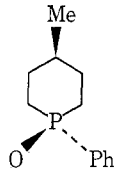
		NMR Data[c]			
		CCH_3		OCH_3	
Salt	Mp,[b] °C	δ	J_{HCCH}, Hz	δ	J_{POCH}, Hz
trans-1	50–50.5	1.22	5.2	3.80	12.0
cis-1	50–53	1.25	4.5	3.82	12.0
trans-2	122–128[d]	0.96	5.2	3.72	11.6
cis-2	118–119.5	1.37	3.0	3.59	11.4

[a] Prepared from the corresponding pure oxides by treatment with trimethyloxonium hexafluorophosphate. [b] Melting points were taken for the crude material without recrystallization but after thorough washing with ether. [c] Spectra were determined at 60 MHz in chloroform-*d* with a JEOL C-60H spectrometer. Chemical shifts are measured from Me_4Si. [d] Prior to washing with ether.

in **3b** the predominant, if not exclusive, conformer would be expected to be (e)-methyl-(e)-phenyl. At ambient tem-



3a



3b

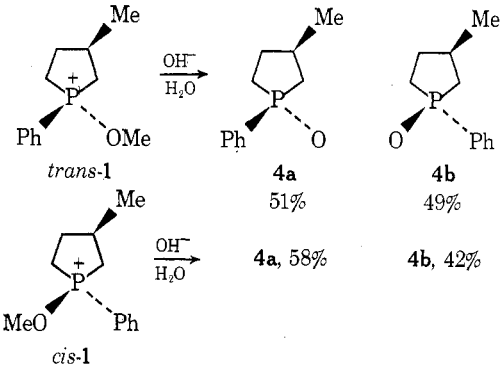
δ (CH_3), ppm	Doublet 0.89 (J = 6.0 Hz)	Unresolved doublet, 0.99 (J = 1.0 Hz)
Mp, °C	60–61	148–149
R_f (acetone, silica gel G)	0.11	0.26

perature, for example, *trans*-1-methyl-4-phenylcyclohexane is detectable only in the ee conformation. The coupling constant for $HCCH_3$ for the trans isomer is 3.5 Hz and the methyl doublet is poorly resolved.[5] *cis*-1-Methyl-4-phenylcyclohexane, on the other hand, has been determined to exist predominantly (>90%) in the (a)-methyl-(e)-phenyl conformation and the well-resolved methyl doublet displays a coupling constant of 6.9 Hz.[5] In general, protons on axial methyl groups are known to show larger coupling constants with vicinal tertiary ring protons,[5,6] and equatorial methyl protons not only exhibit smaller coupling constants with tertiary protons[5,6] but are also characteristically structureless or poorly resolved.[5,7] On this basis the lower melting isomer is assigned the structure **3a** with methyl and phenyl in axial and equatorial positions, respectively, in the predominant isomer in solution (CH_2Cl_2). The higher melting isomer is assigned the structure **3b** with both phenyl and methyl occupying equatorial positions, probably exclusively.[8] Moreover, a cis 1,4-methyl–oxygen arrangement (**3b**) might be expected to result in deshielding[9] of the methyl group, while a shielding effect on the methyl substituent might be anticipated from a cis methyl–phenyl configuration (**3a**). In this respect also the chemical shifts for **3a** and **3b** are consistent with configurational assignments.

Physical properties give additional support to the assignment of stereochemistry. It is well known that equatorially oriented polar substituents usually result in higher retention times than do polar axial groups in chromatographic separations of epimers.[5,10] Thus **3b** would be predicted to have a higher R_f number than **3a** which could be more strongly adsorbed through the conformer containing an equatorial phosphoryl oxygen. Melting point data, although not always reliable, also tend to support the assigned structure.[11]

Results

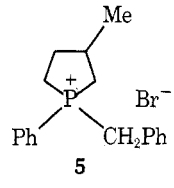
Results for the aqueous hydroxide cleavage of the phospholanium isomers are given in eq 2 and 3.[12] Only one enantiomer of each salt is shown, although racemic mixtures were used in this study.



trans-1 **4a** 51% **4b** 49% (2)

cis-1 **4a**, 58% **4b**, 42% (3)

As seen from Table I, the chemical shifts of the *C*-methyl and *O*-methyl groups for *trans*-**1** and *cis*-**1** are virtually identical at 60 MHz. The oxides also have nearly identical shifts.[1f] Thus the oxide mixtures could neither be analyzed directly by NMR nor stereospecifically reconverted to 1 for analysis. Also decoupled ^{31}P NMR (40.5 MHz) signals for the isomeric oxides cannot be distinguished from each other in mixtures. Therefore, the oxide mixture was stereospecifically reduced to the corresponding phosphines (complete retention)[1f] which were quaternized with benzyl bromide (complete retention)[13] to yield a mixture of the diastereomeric benzylphosphonium salts (**5**).



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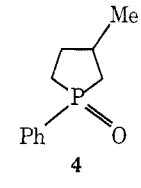
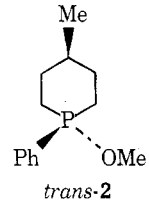


4

These mixtures in D_2O were analyzed by ^1H NMR at 220 MHz and the separated benzyl doublets integrated to give the compositions shown in eq 2 and 3.

The two phosphorinanium salts (*trans*-**2** and *cis*-**2**), when decomposed by aqueous alkali under the same conditions as the phospholanium salts, behaved identically; i.e., within experimental error by ^1H NMR detection at the concentrations used, both experienced complete *inversion* of configuration at phosphorus as exemplified in Scheme I.

Scheme I



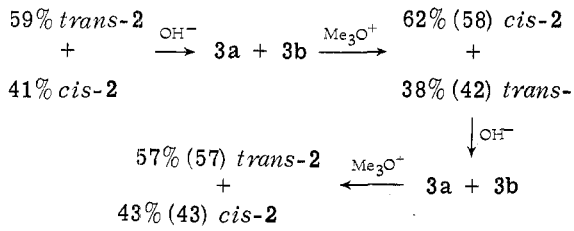
trans-**2** $\xrightarrow[H_2O]{OH^-}$ **3b** (cis oxide) 100% + **3a** (trans oxide) 0%

cis-**2** $\xrightarrow[H_2O]{OH^-}$ 0% 100%

Analyses of the oxides were accomplished by stereospecific reconversion to the methoxyphosphonium salts **2** with trimethyloxonium hexafluorophosphate and integration of the separated *O*-methyl doublets recorded at 60 MHz (cf. Table I). These results were checked by completion of a

stereochemical cycle for a mixture of oxides as shown in Scheme II.

Scheme II

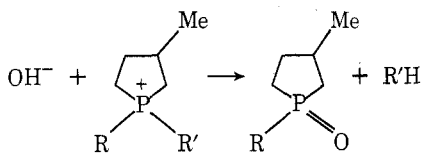


The *calculated* percent composition of **2** [assuming a 9% ^{1}H NMR detection limit for retention upon hydroxide cleavage (vide infra)], after steps 2 and 4 in Scheme II, is shown in parentheses in the scheme.

In order to determine whether any retention of configuration occurred below ^{1}H NMR detection level and, if so, to explain such retention of configuration in the cleavage of **1** and **2**, oxides **3** and **4** were enriched in ^{18}O by treatment of the respective oxides with $^{18}OH_2$ acidified with hydrogen chloride.[14] The oxides enriched in ^{18}O were methylated with trimethyloxonium hexafluorophosphate and the labeled salts cleaved with hydroxide as before. Examination of the oxides showed, after correction for natural abundance, 11.3 ± 0.5% retention of label for the base cleavage of **1** and 8.7 ± 0.5% for that of **2**.

Discussion

Cleavage of the Methoxyphospholanium Salts (1). Previous investigations into the stereochemistry of displacement of leaving groups in system **6** by hydroxide are summarized in eq 4. When the nucleophile is butoxide in



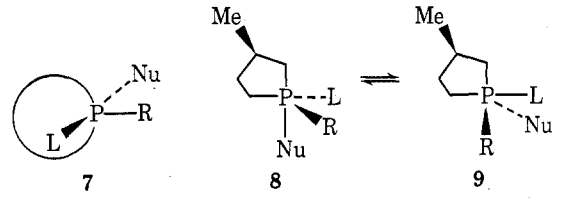
(4)

6

R = Ph; R′ = CH_2Ph; retention of configuration at phosphorus[1c,f]

R = Me; R′ = Ph; stereomutation at phosphorus[1f]

the cleavage of the 1-methyl-1-benzyl analog of **6**, predominant retention of configuration is observed,[1b] while displacement of trichlorosiloxide as leaving group by trichlorosilyl anion as nucleophile (in the reduction of **4a** by Si_2Cl_6) leads ultimately to predominant inversion of configuration.[1c] These stereochemical results have been rationalized in terms of the competition between stereoelectronic and ring strain effects involving proposed phosphorane intermediates.[15] Briefly stated, it is held that electronegative substituents have a preference for apical positions in trigonal bipyramidal phosphoranes. However, the reaction pathway involving such an intermediate may be modified in cases when two of the ligands at phosphorus are part of a four-, five-, or in some cases a six-membered ring, because of ring strain introduced by ee disposition of ring bonds (**7**). Thus only leaving groups of comparatively high electronegativity, where relief of "stereoelectronic strain" exceeds relief of "ring strain", are permitted to occupy an apical position. This then accounts for predominant inversion of configuration at phosphorus in the reduction of **4a** by Si_2Cl_6 where the leaving group is $OSiCl_3^-$. In cases of poor leaving groups (low electronegativity), as exemplified by benzyl, ring strain dictates stereochemistry of the initially



7 **8** **9**

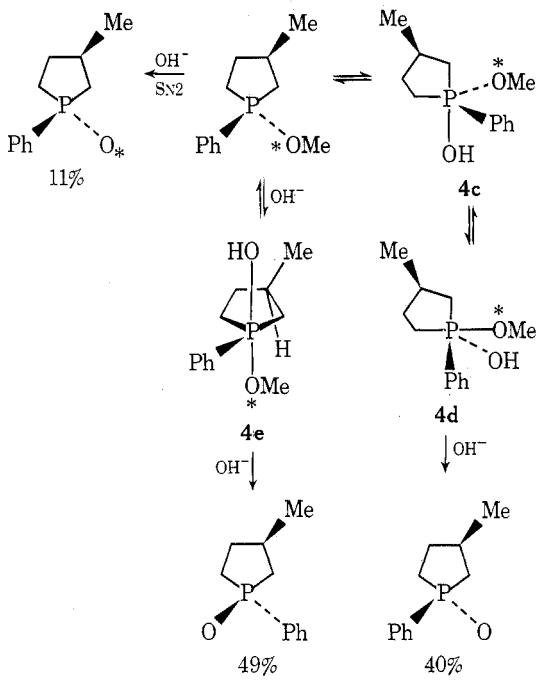
formed phosphorane as shown by structure **8** where L is benzyl and R is phenyl or methyl. Loss of benzyl may occur apically from **9** after one pseudo-rotation with no net change of configuration at phosphorus. Such is observed for aqueous alkaline cleavage of **8** (L = CH_2Ph; R = Ph or Me; Nu = OH).[1a-c,f] For a leaving group such as phenyl, which is even poorer than benzyl as demonstrated by competitive cleavage experiments,[16] the energy barriers to pseudo-rotation among phosphoranes leading to stereomutation at phosphorus, after attachment of hydroxide ion to phosphorus, is lower than the energy barrier preceding product formation. This has been observed for **8** where L = Ph, R = Me, and Nu = OH,[1f] and where a thermodynamic mixture of diastereomeric phosphine oxides has been found to be formed from the equilibrating mixture of phosphoranes.

In this work we have observed a still different type of behavior for the cleavage of a phospholanium salt as exemplified by the hydroxide decomposition of **1**. Experimental results suggest that three different reactions are occurring simultaneously in the conversion of the isomers of **1** to a mixture of the corresponding oxides. Stereoelectronic strain and ring strain are evidently of comparable magnitude where methoxide ion is a leaving group. Thus intermediates **7** and **8** (L = OMe; R = Ph; Nu = OH) are *both* viable.

The product compositions shown in eq 2 and 3 are not reasonably accounted for by complete stereochemical equilibrium through pseudo-rotation of phosphorane intermediates. Even though the cleavage results are similar for *trans*-**1** and *cis*-**1** they are nevertheless detectably different and reproducibly so. Thus pseudo-rotation, if it occurs, can only be competitive with product formation. However, competitive pseudo-rotation would not be consistent with the observation that loss of benzyl, a poorer leaving group than methoxy, from **6** by hydroxide cleavage occurs with complete retention of configuration at phosphorus.[1a-d] If the theory of stereoelectronic strain were to apply to the case of methoxyphospholanium salts one would predict with some assurance that methoxy would fall somewhere between benzyl and trichlorosiloxy in its apicophilicity relative to the intermediate phosphorane formed. This prediction is evidently borne out by our findings.

Coexistent with the duality of mechanism accompanying attack at phosphorus by hydroxide is the occurrence of nucleophilic attack at methoxy carbon as revealed by the retention of some ^{18}O label. Although a diastereomeric mixture of methoxyphospholanium salts was used because of stereomutation accompanying incorporation of label into the oxide starting material, it is reasonable to assume that nucleophilic attack at carbon should be relatively uninfluenced by the stereochemistry at the ring methyl because of its remoteness from the site of reaction. Therefore, *trans*-**1** is apparently decomposed by aqueous sodium hydroxide in the manner displayed in Scheme III for molecules of the labeled compound. Isomer *cis*-**1** similarly yields 58% inverted product, 31% retained product by attack of hydroxide at phosphorus, and 11% retained product by attack of hydroxide at carbon. It is tempting to explain the reduced amount of inversion at phosphorus for *trans*-**1** as compared to *cis*-**1** by steric interference of the ring methyl to attack by hydroxide from that side of the ring.

Scheme III

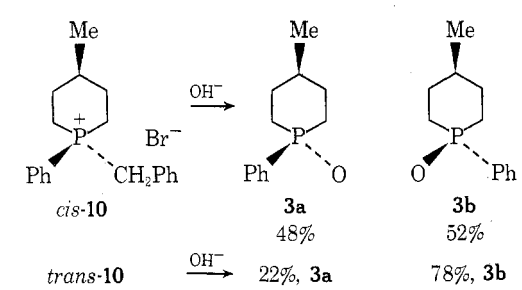


Although Scheme III shows attack opposite the 1,2 ring bond by hydroxide, attack opposite the 1,5 ring bond is also possible and would also yield product of retained configuration. These two attack routes are not strictly equivalent sterically but are expected to be very nearly so based upon models. Assuming both routes of attack to be identical, it is possible to calculate the following relative reaction rates for the three cleavage processes.

	Relative rates	
	trans-1	*cis*-1
Attack at C	1.0	1.0
Attack opposite a ring bond (retention)	1.8	1.4
Attack at P (inversion)	4.5	5.3

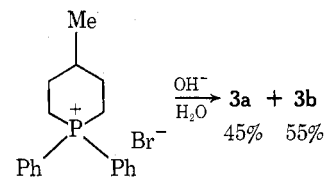
It is seen that the kinetically favored process for both compounds is inversion, with *cis*-1 more reactive in this respect than *trans*-1.

Cleavage of the Methoxyphosphorinanium Salts (2). In a previous communication[1d] we reported trans and cis isomers of **10** to undergo base cleavage with the results indicated. This evidence was interpreted[1e] as illustrating a



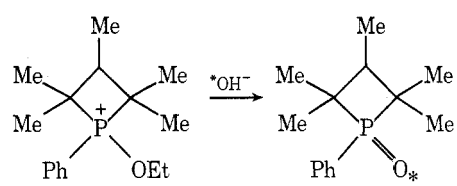
dual mechanism involving attack at phosphorus in a manner similar to that portrayed in Scheme III for methoxyphospholanium salts. That **3a** and **3b** do not result from a common intermediate is attested to by the fact that *cis*-**10** and *trans*-**10** give *different* ratios of the same products. Analogous results have been reported for a bicyclic phosphorinanium salt.[17]

It now appears that the findings shown in Scheme I are entirely consistent with hydroxide attack at phosphorus with *exclusive* inversion, the small amount of retention observed occurring *only* by SN2 attack by hydroxyl at carbon. The NMR analysis indicated a maximum limit of 9% retention for both isomers and the mass spectral determination of ^{18}O in the labeled salt and the oxide resulting from cleavage of the salt showed 8.7% retention of label. The greater apicophilicity of methoxide as compared to benzyl permits the former to occupy an apical position (relief of stereoelectronic strain) in the phosphorane of lowest energy. The stereoelectronic effect completely offsets any ring strain effect in this instance because of the increased ring size, whereas in the example of the cleavage of **10**, stereoelectronic and ring strain effects are comparable. It should be parenthetically stated that the high stereospecificity of this reaction allows convenient access to **3a**. Oxides **3a** and **3b** are obtained as a mixture by base cleavage of **11**. Pure



3b is readily obtained in good yield from this mixture by recrystallization from CCl_4. Preparation of the methoxy salt of **3b** followed by cleavage and recrystallization, then, can afford pure **3a**.

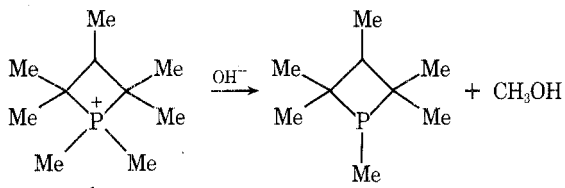
Comparison of Behavior of Phosphonium Salts of Different Ring Size. Mislow et al. have reported that hydroxide displacement of ethoxy from the cis and trans isomers of **12** takes place without any measurable accompanying attack at ethoxy carbon to give **13**.[18] However, the



error limits given for ^{18}O analysis of the hydroxide solution and the products are such that a maximum of 7.6% attack at carbon could have occurred without detection. Hydroxide attack at the *P*-methyl carbon of **14**[19] to yield **15** in 1.8% yield has also been reported. The extent of displacement at the ethoxy methylene carbon in **12**, if it occurs, is less than for **1** and **2**. The diminished (or possible absence of) attack at carbon in this case is most likely due to a combination of effects: the lowered activation energy for attack at phosphorus in the four-membered ring system as compared to the five- or six-membered systems and the lower reactivity of ethyl *vs.* methyl in SN2 reaction at carbon. The former effect is reflected in reaction rates determined by Cremer et al.,[20a] who have shown that, for base cleavage of selected benzyl salts, the phosphetanium salt reacts on the order of 10^4 times as fast as the phospholanium and 10^6 times faster than the phosphorinanium salt. The latter effect is seen, for example, in the average 30-fold greater reactivity of methyl as compared to ethyl in SN2 reactions.[20b] It might also be noted that C–O cleavage has been observed in dialkoxyphosphonium salts.[21]

In the progression stereomutation, retention, inversion, it is found that for ring systems studied which contain alkoxy substituents, retention occurs for hydroxide attack at phosphorus in the four-membered ring.[18] Both retention and inversion are observed with the five-membered ring, and inversion takes place with the six-membered ring. The

six-membered ring behaves essentially as an acyclic monoalkoxyphosphonium salt, since Mislow et al. have reported complete inversion of configuration at carbon by hydroxide cleavage of ethoxymethyl-β-naphthylphenylphosphonium nitrate.[2] Hexachlorodisilane reduction of **4a** has been reported to occur with *predominant* inversion of configuration, the lack of complete stereospecificity being attributed to $SiCl_4$-induced stereomutation at phosphorus or the operation of a dual mechanism.[1c] Our reported observation of the existence of a dual mechanism for P–O cleavage in **1** now makes plausible the dual mechanism explanation for the *small* amount of retention witnessed in the reduction of **4a**, since $OSiCl_3$ would be expected to be more apicophilic than methoxy.



14 15

Experimental Section[22]

Preparation of the Cis and Trans Isomers of 3-Methyl-1-methoxy-1-phenylphospholanium Hexafluorophosphate (1). For the preparation of the trans isomer of **1**, 2.98 g (15.3 mmol) of the phosphine oxide[1f] **4a** was dissolved in 25 ml of dry methylene chloride. This solution was added to a suspension of 3.51 g (17 mmol) of trimethyloxonium hexafluorophosphate in dry methylene chloride and the resulting mixture was stirred at room temperature overnight. Traces of insoluble residue were removed by centrifugation and the solution was evaporated to dryness in vacuo. The glassy residue crystallized upon standing and the resulting crystals were triturated with 150 ml of anhydrous ether in 10-ml portions. The crystals were then dissolved in dry methylene chloride and anhydrous ether was added until an oil separated. The oil was triturated twice with anhydrous ether, and upon drying in vacuo the oil crystallized to give 1.60 g of *trans*-**1**: mp 50–52.5°; cf. Table I for NMR data.

Anal. Calcd for $C_{12}H_{18}F_6P_2O$: C, 40.69; H, 5.12. Found: C, 40.95; H, 5.40.

The cis isomer of **1** was similarly prepared from **4b**:[1f] mp 50–53°; mixture melting point with the trans isomer of **1** gave 29–44°; cf. Table I for NMR data for *cis*-**1**.

Anal. Calcd for $C_{12}H_{18}F_6P_2O$: C, 40.69; H, 5.12. Found: C, 40.80; H, 5.39.

***cis*-4-Methyl-1-phenylphosphorinane 1-Oxide (3b).** 4-Methyl-1,1-diphenylphosphorinanium bromide[23] (**11**, 10 g, 28.6 mmol) was added to 50 ml of 5 *M* sodium hydroxide and the mixture was refluxed for 8 hr. The resulting reaction mixture was extracted twice with 20-ml portions of chloroform, and the separated aqueous layer was saturated with sodium chloride and again extracted three times with 20-ml portions of chloroform. The extracts were combined, the chloroform was distilled, and the residue was sublimed to give 5.90 g of a hygroscopic mixture of *trans*- and *cis*-4-methyl-1-phenylphosphorinane 1-oxide, mp 90.5–112°.

Anal. Calcd for $C_{12}H_{17}OP$: C, 69.21; H, 8.23. Found: C, 69.32; H, 8.21.

Chromatographic separation of this mixture on silica gel G with acetone and spot development with iodine vapors gave two spots of R_f 0.11 (**3a**) and 0.26 (**3b**). Elution of the spots and uv analysis of aqueous solutions at 218 nm (ϵ 8840 for both isomers) showed the cleavage mixture to be 45% **3a** and 55% **3b**.

Four recrystallizations of the cleavage mixture from 1:1 hexane–carbon tetrachloride furnished crystals: mp 147.8–148.9°; NMR (CH_2Cl_2, Me_4Si) δ 0.99 (unresolved d, 3, J = 1.0 Hz, CCH_3).

Anal. Calcd for $C_{12}H_{17}OP$; C, 69.21; H, 8.23. Found: C, 69.39; H, 8.40.

***trans*-4-Methyl-1-phenylphosphorinane 1-Oxide (3a).** A portion of the cleavage mixture was separated on Brinkmann precoated silica gel 60 F-254 preparative TLC plates with acetone. The component of R_f 0.11 was removed by chloroform extraction of the silica gel and, after evaporation of the chloroform, the residue was then distilled. The distillate of bp 146° (0.1 mm) crystallized to a hygroscopic solid upon standing: mp 60–61°; NMR (CH_2Cl_2, Me_4Si) δ 0.89 (d, 3, J = 6.0 Hz, CCH_3).

Anal. Calcd for $C_{12}H_{17}OP \cdot \frac{1}{4}H_2O$: C, 67.74; H, 8.29. Found: C, 67.93; H, 8.51.

***cis*-1-Methoxy-4-methyl-1-phenylphosphorinanium Hexafluorophosphate (2).** The same procedure was followed as for the preparation of the methoxyphospholanium salts; cf. Table I for physical properties.

Anal. Calcd for $C_{13}H_{20}F_6OP_2$: C, 42.39; H, 5.47. Found: C, 42.65; H, 5.64.

Cleavage of *trans*-1-Methoxy-3-methyl-1-phenylphospholanium Hexafluorophosphate (1). The hexafluorophosphate salt (*trans*-**1**, 1.07 g) was added to 34 ml of 0.50 *N* sodium hydroxide at room temperature with stirring, whereupon the solid dissolved. The solution was then slowly heated to reflux. The cooled reaction mixture was extracted five times with 25-ml portions of methylene chloride, the solvent was distilled from the combined extracts and the residue was distilled to give a 97% yield of 3-methyl-1-phenylphospholane 1-oxide: bp 125° (0.1 mm) (Kugelrohr) [lit. bp of trans oxide, 115–125° (0.05 mm); cis oxide, 120° (0.01 mm)].[1f] The ^{1}HNMR spectrum (60 MHz) indicated a mixture of oxides.

In order to analyze the oxide mixture it was reduced in 81% yield with phenylsilane (retention)[24] and the resulting phosphine mixture was quaternized with benzyl bromide (retention)[13] to give a mixture of the benzyl salts in 98% yield (mp 154–165°) the composition of which was determined by integration of the benzyl protons at 220 MHz: NMR (D_2O, DSS) δ 1.20 (overlapping d, CCH_3), 4.10 (overlapping d, J = 15 Hz, CH_2Ph). Integration gave 49% *trans*-**5** salt, δ 4.11 (d, J = 15 Hz, CH_2Ph), and 51% *cis*-**5** salt, δ 4.09 (d, J = 15 Hz, CH_2Ph).

Cleavage of *cis*-3-Methyl-1-methoxy-1-phenylphospholanium Hexafluorophosphate (1). The same procedure was followed as for the trans isomer with similar results except that the mixture of benzyl salts melted at 145.5–155.0° and the NMR analysis gave 42% *trans*-**5** and 58% *cis*-**5**.

Cleavage of *trans*-1-Methoxy-4-methyl-1-phenylphosphorinanium Hexafluorophosphate (2). The same procedure was followed as for *trans*-**1** above. A yield of 83% of the oxide was obtained which was methylated as described for **4a** above. The mixture was analyzed by integration of the methoxy protons (cf. Table I). The cleavage of the cis isomer and analysis of the product were similarly carried out. The reactions and analyses shown in the stereochemical cycle in Scheme II were similarly conducted. At concentrations used, it was determined that the presence of a maximum of about 9% of the minor isomer was needed before detection and integration of the methoxy peaks could be achieved.

^{18}O Labeling of 3-Methyl-1-phenylphospholane 1-Oxide. A mixture of 1.00 g of **4a**[1f] and 5 ml of unnormalized 10 atom % ^{18}O water was acidified to ca. pH 1 with hydrogen chloride and the resulting mixture was refluxed for 72 hr at 100°. Most of the water was then distilled off and the remainder was removed by azeotropic distillation with benzene. After evaporation of the benzene, the residue was distilled to yield 0.97 g of the oxide, bp 115° (3 mm) (Kugelrohr). The methoxy salt **1** was prepared and cleaved as described previously. ^{18}O content: methoxy salt, 0.452 ± 0.001 atom %; oxide **4** resulting from cleavage, 0.232 ± 0.001 atom %.

^{18}O Labeling of 4-Methyl-1-phenylphosphorinane 1-Oxide. This was accomplished by treatment of **3b** in the same fashion as above to give the oxide of bp 145° (0.08 mm) (Kugelrohr). The methoxy salt **2** was prepared and cleaved as previously described. ^{18}O content: methoxy salt, 0.422 ± 0.001 atom %; oxide resulting from cleavage, 0.223 ± 0.001 atom %.

***trans*- and *cis*-1-Benzyl-4-methyl-1-phenylphosphorinanium Bromides (10).** Phosphine oxide **3b** was reduced with phenylsilane to the corresponding *trans*-4-methyl-1-phenylphosphorinane, bp 76° (0.15mm) (Kugelrohr), and the phosphine was quaternized with benzyl bromide to give an overall yield of 86.5% of *trans*-1-benzyl-4-methyl-1-phenylphosphorinanium bromide (**10**), mp 196° (EtOH–EtOAc).

Anal. Calcd for $C_{19}H_{24}BrP$: C, 62.81; H, 6.66. Found: C, 63.09; H, 6.40.

cis-1-Benzyl-4-methyl-1-phenylphosphorinanium bromide (**10**) was prepared from phosphine oxide **3a** by the procedure described immediately above, mp 161–163° (not sharp). This salt was found to be hygroscopic.

Anal. Calcd for $C_{19}H_{24}BrP \cdot \frac{3}{4}H_2O$: C, 60.56; H, 6.82. Found: C, 60.52; H, 6.92.

Cleavage of *trans*- and *cis*-1-Benzyl-4-methyl-1-phenylphosphorinanium Bromides (10). *trans*-**10** (0.50 g) was dissolved

in 4.5 ml of 1.00 *N* NaOH and the resulting mixture was refluxed for 9 hr. The cooled reaction mixture was extracted with two 5-ml portions of chloroform, and the aqueous layer was saturated with sodium chloride and then extracted with two 5-ml portions of chloroform. The chloroform were evaporated and the residue was sublimed at 0.25 mm to yield 97.5% of a mixture of oxides (**3**), mp 73–133°.

Anal. Calcd for $C_{12}H_{17}OP$: C, 69.21; H, 8.23. Found: C, 69.47; H, 8.20.

This mixture was analyzed by TLC as described above for the cleavage products of 4-methyl-1,1-diphenylphosphorinanium bromide (**11**) and gave 78% **3b** and 22% **3a**.

The cis isomer of **10** was similarly cleaved to give a hygroscopic mixture of oxides.

Anal. Calcd for $C_{12}H_{17}OP \cdot \frac{1}{4}H_2O$: C, 67.74; H, 8.29. Found: C, 67.93; H, 8.39.

The analysis of this mixture gave 52% **3b** and 48% **3a**.

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Registry No.—*cis*-**1**, 55043-89-5; *trans*-**1**, 55043-91-9; *cis*-**2**, 55043-93-1; *trans*-**2**, 55043-95-3; **3a**, 55043-96-4; **3b**, 55043-97-5; **4a**, 55043-98-6; **4b**, 55043-99-7; *cis*-**5**, 54932-29-5; *trans*-**5**, 55044-00-3; *cis*-**10**, 55044-01-4; *trans*-**10**, 55044-02-5; **11**, 55044-03-6; trimethyloxonium hexafluorophosphate, 12116-05-1.

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Concerning the Mechanism of the Characteristic Ring D Fragmentation of Steroids[1]

D. C. Mammato and George A. Eadon*

Department of Chemistry, State University of New York at Albany, Albany, New York 12222

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The electron impact induced fragmentations of $\Delta^{13(18)}$-13,17-seco-5α-*D*-homoandrostene (VI) and $\Delta^{13(14)}$-13,17-seco-5α-*D*-homoandrostene (VII) were investigated. Both compounds and appropriate deuterium-labeled analogs fragmented in accord with the existing mechanistic proposal for the characteristic ring D fragmentation of steroids. First field-free region metastable intensities were consistent with structural identity among the *m/e* 217 ions from 5α-pregnane and the *D*-seco steroids, and among the *m/e* 218 ions from the same sources; widely divergent metastable intensities were observed from known isomeric ions. Evidence was obtained for significant interconversion of the molecular ions of VI and VII. The results of these experiments lend powerful support to the previously proposed ring D fragmentation mechanisms.

The most conspicuous peaks in the mass spectra of steroid hydrocarbons such as pregnane (I) or cholestane (II) appear at *m/e* 217 and 218, corresponding to the elimination of ring D and the side chain at C-17.[2] Since these fragmentations persist even in highly functionalized steroids, and since they are of obvious diagnostic importance (they define the molecular weight of the side chain at C-17), a number of investigators have attempted to determine the mechanisms by which these peaks arise. Initially, this was an area of some controversy.[3-5] The elegant and extensive deuterium-labeling experiments of Djerassi[2] provided data which permitted formulation of a plausible mechanism for the genesis of these ubiquitous peaks (Scheme I).

Initial charge localization in the C-13–C-17 bond (I → a) was postulated, since it results in the formation of a stable tertiary carbonium ion and a secondary (R = alkyl) or primary (R = H) radical site, and relieves the strain inherent in the trans hydrindan ring system. Deuterium-labeling experiments demonstrated that the genesis of the *m/e* 217 ion (c) involved transfer of the C-14 hydrogen atom to the eliminated moiety; such a process appears plausible, since it generates an ionized double bond between C-13 and