8-O-Acetyl-2,11-dimethoxyaporphine (10c). A mixture of 4 mg of **10a**, 0.1 mL of pyridine, and 0.5 mL of acetic anhydride was allowed to stand overnight. Workup and purification by preparative layer chromatography using 10% methanol in chloroform afforded 4 mg of a yellow oil: IR ($CHCl_3$) 1770, 2790; UV λ_{max}(EtOH) 266, 272, 298, 310, and 318 nm; mass spectrum *m/e* 353 (M^+), 352, 338, 322, 310; NMR ($CDCl_3$) δ 7.75 (d, 1 H, C-1 H, $J_{1,3}$ = 2.4 Hz), 7.04, 6.95, 6.93, 6.84 (AB quartet, 2 H, C-10 and C-11 H, J = 9 Hz, $\Delta\nu_{AB}$ = 6 Hz), 6.62 (d, 1 H, C-3 H, J = 2.4 Hz), 3.88 and 3.82 (each s, 6 H, OCH_3), 2.60 (s, 3 H, NCH_3), 2.35 (s, 3 H, CH_3CO).

Registry No.—**1**, 5373-42-2; **2**, 64056-78-6; **3**, 64129-87-9; **6a**, 64129-86-8; **6b**, 64129-85-7; **7a**, 64056-79-7; **7b**, 64129-78-8; **8**, 64056-80-0; **9**, 64056-81-1; **10a**, 64056-82-2; **10c**, 64056-62-8.

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Synthesis and Carbon-13 Nuclear Magnetic Resonance Spectral Properties of Two New Enamine Systems: 3-Amino-2-phospholene Sulfides and Their *S*-Methyl Salts[1]

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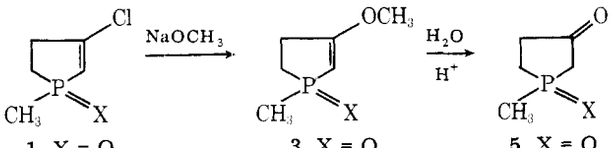
Enamines are formed in high yield by the displacement of chlorine from 1-methyl-3-chloro-2-phospholene sulfides with pyrrolidine, piperidine, morpholine, and cyclohexylamine. Alkylation fails to occur at C-2, the β carbon of the enamine system, but does occur readily on sulfur, making available a family of enamine derivatives bearing alkylthiophosphonio groups. These compounds have remarkably high field (δ 62–66) ^{13}C NMR signals for C-2 and are characterized also by a barrier to rotation about C–N that is greater even than that found in related enamino ketones. This barrier leads to separate ^{13}C signals for the α and for the β carbons of the amine moiety in the pyrrolidine derivative (coalescence temperature about 97 °C; $\Delta G^{\ddagger}$ about 18.7 kcal/mol). These effects are attributable to a substantial degree of sharing of the negative charge on C-2 of the iminium ion form with d orbitals of phosphorus; resonance forms expressing this delocalization resemble those of the ylide system. Acid hydrolysis of the methylthiophospholenium structure leads to ring opening, producing methyl methyl(3-oxobutyl)phosphinothiolate; basic hydrolysis effects only the displacement of the methylthio group, giving the corresponding phospholene oxide.

In previous work with the phospholene system, we have shown that a halogen atom separated by a double bond from a phosphoryl[2] (**1**) or thiophosphoryl[3] (**2**) group is activated



1, X = O
2, X = S
3, X = O
4, X = S
5, X = O
6, X = S

toward nucleophilic displacement by methoxide ion, and we have used the resulting enol ethers **3** and **4** to advantage in synthesizing keto derivatives **5** and **6**. We have now found that primary and secondary amines are also sufficiently nucleophilic to effect the halogen displacement, and we have obtained stable enamines in good yield by this process. The 3-chloro-2-phospholene sulfide system (as in **2**) is especially useful in this reaction since the starting material can be obtained in good purity, free of the isomeric 3-phospholene compound, by reacting the chloroprene–methylphosphonous dichloride cycloadduct with hydrogen sulfide.[3] The synthesis, properties, and spectra of this new family of thiophosphoryl enamines are the basis for the research discussed in this paper.

Synthesis and Structure of 3-Amino-2-phospholene Sulfides. The enamines **7–10** were prepared in 72–82% yield by refluxing a mixture of the amine and 1-methyl-3-chloro-2-phospholene sulfide (**2**). The products were nonhygroscopic solids, easily recrystallized from common solvents. Their enamine character came out clearly in their proton NMR spectra; acting in opposition to the deshielding effect of thiophosphoryl on the 2-position (cf.[3] δ 6.15 for **2**), shielding by electron release from nitrogen shifted the signal for the proton at this position to the range δ 4.1–4.5. The usual strong coupling (24 Hz) with ^{31}P was present. The proton NMR data

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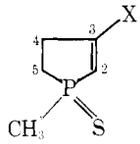
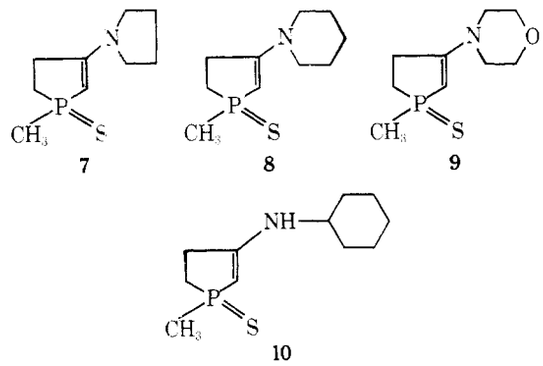
Table I. ^{13}C NMR Spectral Data for 3-X-2-Phospholene Sulfides[a]

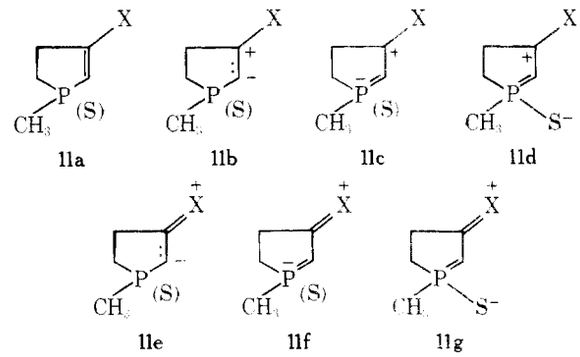


Registry no.	X	C-2	C-3	C-4[b]	C-5	PCH_3	C-1′	C-2′	C-3′	C-4′
				A. Enamines[c]						
64010-83-9	N (7)[e]	81.4(100)	159.1(47)	30.3(3)	30.7(53)	26.1(56)	48.1	25.2		
64010-84-0	N (8)[e]	85.1(101)	161.7(34)	30.1(2)	30.3(53)	*f*	48.1	25.4	24.0	
64010-85-1	O N (9)[e]	87.3(98)	161.6(34)	29.6(2)	30.1(53)	25.6(56)	47.1	66.3		
64010-86-2	NH (10)[e]	82.4(99)	158.7(35)	31.5	30.4(53)	25.7(56)	53.4	32.6	24.9	25.7
				B. Other Derivatives[g]						
	Cl (2)[d]	123.4(75)	150.0(40)	36.8	31.9(55)	23.7(50)				
	CH_3O (4)[d]	91.2(92)	171.6(40)	30.4	29.9(60)	25.0(50)				
	H (11)[d]	127.9(75)	147.3(20)	31.6(13)	30.3(45)	22.8(50)				

[a] Chemical shifts in $CDCl_3$ downfield from Me_4Si. Values in parentheses are coupling constants to ^{31}P, in Hz. [b] Unless otherwise noted, no coupling to ^{31}P was observed under conditions used. [c] Carbons of the amino fragment are numbered N-(C-1′)-(C-2′)-(C-3′)-(C-4′) [d] Taken on a Bruker HFX-10 spectrometer. [e] Taken on a JEOL FX-60 spectrometer with digital resolution to two decimals. [f] Overlapped with C-2′ signal. [g] Reported in ref 3.



7 8 9 10



11a 11b 11c 11d 11e 11f 11g

rule out the possibility that any substantial amount of imine tautomer is present in the cyclohexylamine derivative **10.**

Carbon-13 NMR Spectra of the Enamines. The ^{13}C NMR spectra were fully consistent with the assigned structures and are valuable additions to the compilation of ^{13}C data for the 2-phospholene sulfide system (data for **2, 4,** and the unsubstituted parent **11, X = H,** have been reported[3]). Data for the entire family are given in Table I to facilitate discussion of trends in the series. These trends are best examined in terms of the possible interaction of the π electrons with the thiophosphoryl group. The matter of conjugative interaction of π electrons with phosphorus functions remains unsettled.[4] Certainly there are cases which speak in favor of some degree of interaction, and indeed the activation of 3-chloro in 2-phospholene oxides and sulfides is among them. Two very recent studies on vinyl phosphonium salts, one on ^{13}C NMR effects,[5] the other on electrochemical properties,[6] speak especially strongly for a substantial degree of conjugative interaction in these charged species.

In the parent 2-phospholene sulfide (**11, X = H**), considerable polarization of the double bond is evident from the large difference in chemical shifts of C-2 (δ 127.9) and C-3 (δ 147.3). The structure of the parent may then be expressed as a resonance hybrid of forms **11a, 11b,** and **11c,** assuming in the latter form that some electron density developing on C-2 is shared with d orbitals of phosphorus. Increased electron density on sulfur is also a possibility as is expressed by **11d.** With electron releasing groups at the 3-position, as in the enol ether and enamines, significant contributions are also made by forms **11e–11g.**

Relative to the parent, very large upfield shifts occur at C-2 in the enamines **7–10** (δ 81–87) and the enol ether **4** (δ 91.2). This is quite the expected situation, as it has been seen in carbocyclic enamines[7] and enol ethers.[8] The shift is clearly the result of the large contribution to the hybrid of forms **11e–11f.** The coupling of ^{31}P with C-2 is also of interest; it is largest (99–101 Hz) in the enamines, having progressed from 75 Hz in the parent and 3-chloro derivative (**2**) through 92 Hz for the enol ether **4.** This one-bond coupling is thus directly related to the electron releasing ability of the 3-substituent. This effect has been observed in another family of vinylphosphorus compounds where the unit $XC{=}CP^+(C_6H_5)_3$ is present;[9] $^1J_{PC}$ is larger when X is an amino group than an alkoxy or alkyl group. These authors relate the effect to the sharing of the electron density at C-2 with the phosphorus d orbitals (as seen in **11f**), and not just to buildup of electron density on C-2, which in fact should cause a decrease in one-bond coupling.

In the enamines, the chemical shift of C-3 is brought to lower field (δ 159–162) from that in the parent, due to the electron-attracting effect of nitrogen and possibly to the β effect of the carbons attached to nitrogen. Another unusual coupling effect occurs at C-3; the magnitude of the two-bond coupling to ^{31}P is greatly increased on replacement of H by an atom of high electronegativity. In the parent, $^2J_{PC}$ is 20 Hz; for the enamines, values are in the range 34–47 Hz, as they are also for the 3-chloro and 3-methoxy derivatives. We have also

Table II. ^{13}C NMR Spectral Data for Methiodides of 3-Amino-2-phospholene Sulfides[a]

3-Amino	C-2	C-3	C-4[b]	C-4	PCH_3	C-1′	C-2′	C-3′	C-4′	SCH_3
N (12)′	62.3(107)	166.5(42)	30.6	22.3(55)	16.8(59)	48.23,49.34	23.72,24.77			12.2[d]
N (13)′	64.1(108)	148.3(42)	31.4	22.5(48)	17.3(60)	49.8[f]	25.23,25.91	23.7		12.7(3)
O N (14)′	66.5(107)	147.6(42)	31.4	22.2(48)	17.0(59)	48.3	66.1			12.8(3)
—NH (15)′	61.5(108)	148.6(42)	30.5	22.7(49)	17.1(60)	55.0	31.7	24.9	25.3	12.4(3)

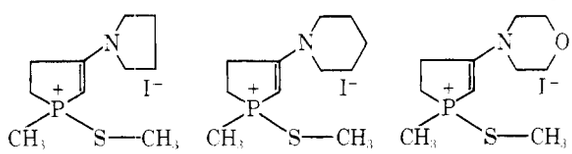
[a] Chemical shifts in $CDCl_3$ downfield from Me_4Si. Values in parentheses are coupling constants to ^{31}P, in Hz. [b] Coupling to ^{31}P is small (0–3 Hz) and not readily observed. [c] Taken on a Bruker HFX-10 spectrometer. [d] No coupling to ^{31}P observed. [e] Taken on a JEOL FX-60 spectrometer with digital resolution to two decimals. [f] Signal is distinctly broadened.

observed this effect among a similar series of 2-phospholene oxides.[10]

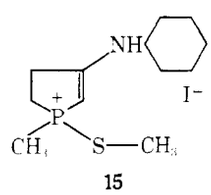
Chemical shifts for C-4 and C-5 in the enamines were readily distinguishable by their substantially different coupling to ^{31}P (nil and 53 Hz, respectively). The P-methyl signal is at slightly lower field in the enamines (δ 26) and in the enol ether **4** (δ 25) than in the 3-chloro derivative (δ 23.7) and the parent **11**, X = H (δ 22.8), but this relation is not seen for C-5 in the series even though its attachment is also to the thiophosphoryl group. A similar slight deshielding at C-1 of P-phenyl groups was seen in β-alkoxy and β-amino vinyltriphenylphosphonium salts relative to the β-methyl derivative.[9]

Carbon shifts in the amine fragment of **7–10** resembled those reported for comparable carbocyclic enamines,[7] and are not influenced by the presence of the thiophosphoryl group.

Formation and ^{13}C NMR Spectra of Methylthiophosphonium Salts. While simple enamines are readily alkylated on the β-carbon with alkyl halides, enamines bearing carbonyl or phosphoryl[2] groups on this carbon do not participate in this reaction and are usually recovered in unchanged form after product workup. Enamines with β-thiocarbonyl groups undergo alkylation on sulfur.[11] We have found that the thiophosphoryl enamines also fail to undergo C-alkylation, but they do react readily at sulfur to form isolatable quasi-phosphonium salts. S-Alkylation is a known property of phosphine sulfides,[12] but the reaction with methyl iodide occurs particularly easily with the enamines. This is consistent with the concept of sulfur assisting in the sharing of electron density, as expressed by resonance form **11g**. From enamines **7**, **8**, **9**, and **10** were obtained salts **12**, **13**, **14**, and **15**, respectively. Each is a crystallizable solid, showing good stability at room temperature if protected from water and light.



12 **13** **14**



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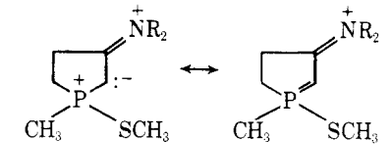
That methyl has indeed attacked on sulfur is readily apparent from spectral properties. In their ^1H NMR spectra, the salts still have a signal for an olefinic proton in the well-upfield enamine position (for **12**, overlapped by CH_2 signals), and a new methyl signal having the chemical shift and coupling to ^{31}P expected for the P^+SCH_3 function is present.

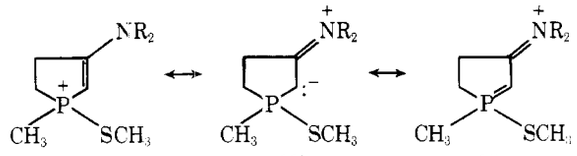


The ^{13}C NMR spectra of the salts show effects which are clear indicators of even greater electron release from nitrogen than is seen in the original enamine sulfides. All of the salts have their C-2 signals at remarkably high field (δ 62–66), having experienced upfield shifts of 20–22 ppm from the sulfides. This upfield shift is far beyond that to be expected simply from the conversion to positive phosphorus; this effect is observable at C-5 and is of the magnitude 7–8 ppm. A pronounced downfield shift occurs at C-3, which can be viewed as a consequence of greater positive character developing on nitrogen, or of increased polarization of the π-system by positive phosphorus. The most striking effect, however, is the development of a substantial barrier to rotation about the C–N bond. The barrier is revealed especially by the pyrrolidine derivative **12**, which shows separate signals for the α-carbons, as well as the β-carbons, of the amine fragment. In $CDCl_3$, the α-carbon signals are separated by 25.1 Hz, the β-carbons by 23.8 Hz. Proof that the signal splitting came from a rotational effect, and not from an extraordinary long-range coupling to ^{31}P or from the chirality of phosphorus, was obtained by observing the ^{13}C spectrum at elevated temperatures. Each of the two sets of signals exhibited coalescence phenomena, and both were reduced to sharp singlets above 100 °C. On cooling, the original doubling reappeared. No other spectral changes occurred in the heating–cooling cycle. The magnitude of the barrier to rotation can be calculated approximately from these observations. Using the α-carbon signals, which are in a clear region of the spectrum, we determined the coalescence temperature (T_c) to be 97 °C in $(CD_3)_2SO$; in this solvent, peak separation ($\Delta\nu$) was 30 Hz at 30 °C. From conventional equations,[13] $\Delta G^{\ddagger}$ was found to be 18.7 kcal/mol. The value is subject to refinement, especially if determined by full line shape analysis, but it is of use in giving an indication of the considerable magnitude of the barrier to rotation resulting from interaction with the phosphorus moiety. A β-carbonyl group also increases the barrier in enamines, but not to this extent; barriers for 4-dimethylamino-3-buten-2-one[14] and related compounds[15] are in the 13–14 kcal/mol range, with some enhancement (about 2 kcal/mol) when oxygen is replaced by sulfur.[16] There appears to be no prior record of the observation at room temperature of different ^{13}C NMR signals for the α-carbons on nitrogen, although separate $N–CH_3$ signals have been seen at low temperatures in β-acyl enamines.[17] The amine carbons of 1-pyrrolidinocyclohexen-3-one do not show nonequivalence at room temperature.[7]

The piperidino derivative **13** also showed manifestations of restricted rotation (distinct broadening of the α-carbon

signal at probe temperature; splitting of the β-carbon signal by 10 Hz) but to a smaller extent than seen for the pyrrolidino compound. No indications of restricted rotation were present in the spectrum of the morpholino compound **14**. The rotational barriers thus provide a sequence of relative electron releasing power of the amines: pyrrolidino > piperidino > morpholino. This is the same series proposed by others[7] in a ^{13}C NMR study of 1-amino-cyclohexen-3-ones, where the chemical shifts of the carbonyl carbon were used as a measure of relative electron release.

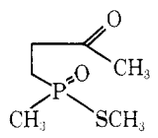
It is therefore concluded that the methylthiophosphonio enamines must have extensive electron delocalization which includes involvement of the phosphorus atom. This delocalization is expressed through resonance forms **16a–16c**. Forms



16a **16b** **16c**

16b and **16c** are seen to be those which describe ylides, an analogy drawn also by others for the similarly delocalized triphenylphosphonio enamines.[9]

Another unique property was observed in the hydrolytic behavior of the salts; on stirring at room temperature with aqueous HCl, salt **12** underwent ring opening as well as loss of the nitrogen fragment to produce the novel thiophosphinate **17**. The structure of this unexpected product, a distillable



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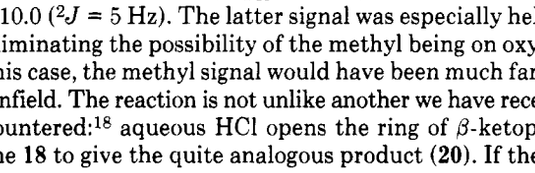
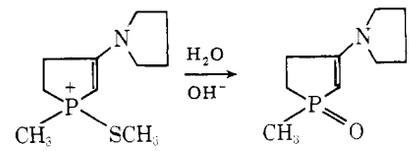
liquid, was clearly established by spectral examination. The keto group was evident from the infrared absorption at 1700 cm^{-1} and ^{13}C NMR signal at δ 205 ($^3J_{PC}$ = 15 Hz). Methyl on carbonyl was indicated by the ^1H NMR singlet at δ 2.24 and ^{13}C NMR singlet at δ 29.7, and methyl on sulfur by the doublet in the ^1H NMR at δ 2.35 ($^3J_{PH}$ = 11 Hz) and in the ^{13}C NMR at δ 10.0 (^2J = 5 Hz). The latter signal was especially helpful in eliminating the possibility of the methyl being on oxygen; in this case, the methyl signal would have been much farther downfield. The reaction is not unlike another we have recently encountered:[18] aqueous HCl opens the ring of β-ketophosphine **18** to give the quite analogous product (**20**). If the hydrolysis of the enamino salts is viewed as proceeding with initial attack at the enamine function, the product would be a ketone having a formal resemblance to salt **19**.



18 **19** **20**

With aqueous base, the hydrolysis takes an entirely different pathway. As has been reported for methiodides of tertiary phosphine sulfides,[12] nucleophilic attack results in displacement of the methylthio group with formation of the tertiary phosphine oxide retaining the cyclic structure (**21**). Structure **21** was confirmed by synthesis of the same compound from the 3-chloro-2-phospholene oxide (**1**) with pyrrolidine. Enamines in the 2-phospholene oxide series have previously been prepared from the 3-keto derivative and the secondary amine;[2] this process provides a product containing



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some of the 3-phospholene oxide isomer, however, and the chloride displacement process, which is reported here for the first time, is clearly preferable in giving an isomer-free product.

^{31}P NMR Spectra of the Enamines. The chemical shifts for the four thiophosphoryl enamines **7–10** all fall in the narrow range of +57.8 to +60.1 ppm (downfield relative to 85% H_3PO_4), which also includes values for the 3-chloro (+58.5) and 3-methoxy (+58.7) derivatives. The range is markedly upfield from the parent (**11**, X = H, +65.5). Were it not for the 3-chloro value, it might be possible to attribute this upfield shift to increased occupation of the phosphorus d orbitals (form **11e**), an effect known to cause shielding of ^{31}P.[5] But since there is evidence from both ^{13}C and ^1H NMR spectra for C-2 to suggest that the contribution of forms **11d** and **11e** must be quite small for the chloro compound, the degree of d-orbital occupation cannot be the only factor causing the upfield ^{31}P NMR shift, although it may have greater importance for the enamines and enol ether. It may be significant in this context that the ^{31}P shifts of the enamines, although quite similar, do show a trend of increased shielding with greater electron releasing ability of the amine (pyrrolidino, +57.8; piperidino, +58.1; morpholino, +58.7).

Alkylation on sulfur causes a downfield shift in the enamine. While the range of values is again small, the same trend of increased shielding with amine electron-releasing ability is present (pyrrolidino, +69.8; piperidino, +70.96; morpholino, +72.2).

Experimental Section

General. Proton noise-decoupled ^{13}C NMR spectra were obtained at 22.62 MHz on a Bruker HFX-10 spectrometer, or at 15.0 MHz with a JEOL FX-60 spectrometer, both using the Fourier transform technique. Samples were run in $CDCl_3$ solution with internal Me_4Si. Proton-decoupled ^{31}P NMR spectra were obtained with the Bruker instrument at 36.43 MHz and are referenced to external 85% H_3PO_4. ^1H NMR spectra were obtained on a JEOL MH-100 spectrometer using $CDCl_3$ as solvent with internal TMS. The sign convention used is the same for all nuclei (+ if downfield from the reference, − if upfield). Melting points are corrected. Elemental analyses were performed by MHW Laboratories, Garden City, Mich.

1-Methyl-3-pyrrolidino-2-phospholene 1-Sulfide (7). To a stirred, nitrogen-blanketed solution of 28.3 g (0.17 mol) of 1-methyl-3-chloro-2-phospholene-1-sulfide[3] in 175 mL of dry benzene was added dropwise a solution of 24.1 g (0.34 mol) of pyrrolidine in 50 mL of dry benzene. The mixture was refluxed for 46 h. It was then cooled and the precipitated pyrrolidine hydrochloride was removed by filtration. The filtrate was washed with water (2 × 20 mL); the organic layer was dried (Na_2SO_4) and most of the solvent was then removed on a rotary evaporator. The residual liquid was triturated with petroleum ether and yielded 28 g (82%) of solid enamine (**7**). This was recrystallized from a mixture of benzene and hexane: mp 71–72 °C; ^1H NMR ($CDCl_3$) δ 1.8–2 (m, NCH_2CH_2), 2.12–3.04 (m, PCH_2CH_2), 1.9 (d, $^2J_{PH}$ = 12 Hz, PCH_3), 3.16–3.44 (m, CH_2NCH_2), 4.12 ppm (d, $^2J_{PH}$ = 24 Hz, PCH = C); ^{31}P NMR ($CDCl_3$) δ +57.8; IR (Nujol) 1550 cm^{-1} (C=C); ^{13}C NMR (Table I).

Anal. Calcd for $C_9H_{16}NPS$: C, 53.73; H, 7.96; N, 6.96; P, 15.42; S, 15.92. Found: C, 53.65; H, 8.05; N, 6.75; P, 15.63; S, 16.15.

1-Methyl-3-piperidino-2-phospholene 1-Sulfide (8). A mixture of 3.5 g (0.021 mol) of 1-methyl-3-chloro-2-phospholene 1-sulfide and 8.9 g (0.05 mol) of freshly distilled piperidine was refluxed under nitrogen for 10 h. The excess amine was stripped off on a rotary evaporator; remaining traces were removed by high-vacuum evacuation. The residue was taken up in hot benzene and the amine salt was removed by filtration. Solvent was stripped from the filtrate and the residual oil was triturated with petroleum ether to give 4.5 g (75%) of

solid **8**. An analytical sample was purified by sublimation; mp 59–60 °C; ^{1}H NMR ($CDCl_3$); δ 1.56 (broad singlet, $-(CH_2)_3-$), 1.86 (d, $^2J_{PH}$ = 13 Hz, PCH_3), 2.1–3.0 (m, PCH_2CH_2), 3.16 (broad singlet, CH_2NCH_2) and 4.36 ppm (d, $^2J_{PH}$ = 24 Hz, PCH=C); ^{31}P NMR ($CDCl_3$) +58.1; IR (Nujol) 1550 cm^{-1} (C=C); ^{13}C NMR (Table I).

Anal. Calcd for $C_{10}H_{18}NPS$: C, 55.81; H, 8.37; N, 6.51; P, 14.42; S, 14.80. Found: C, 55.98; H, 8.50; N, 6.51; P, 14.65; S, 14.77.

1-Methyl-3-morpholino-2-phospholene 1-Sulfide (9). A mixture of 6 g (0.036 mol) of 1-methyl-3-chloro-2-phospholene 1-sulfide and 15.6 g (0.18 mol) of morpholine was refluxed under nitrogen for 10 h. The mixture was worked up as for **8**, yielding 5.6 g (72%) of desired product (**9**): mp 183–184 °C. A second crop (1.0 g) was obtained from the mother liquor. The total yield was 6.6 g (85%): ^{1}H NMR ($CHCl_3$) δ 1.91 (d, $^2J_{PH}$ = 14 Hz, PCH_3), 2.0–3.0 (m, PCH_2CH_2), 3.04–3.24 (m, CH_2NCH_2), 3.64–3.8 (m, CH_2OCH_2), 4.47 ppm (d, $^2J_{PH}$ = 24 Hz, PCH=C); δ ^{31}P NMR ($CDCl_3$) +58.7; IR (Nujol) 1550 cm^{-1} (C=C); ^{13}C NMR (Table I).

Anal. Calcd for $C_9H_{16}NOPS$: C, 49.77; H, 7.37; N, 6.45; P, 14.28; S, 14.74. Found: C, 49.81; H, 7.33; N, 6.34; P, 14.44; S, 14.62.

1-Methyl-3-cyclohexylamino-2-phospholene 1-Sulfide (10). A mixture of 5.4 g (0.03 mol) of 1-methyl-3-chloro-2-phospholene 1-sulfide and 25 mL of freshly distilled cyclohexylamine was refluxed with stirring under nitrogen for 12 h. The product (5.3 g, 72%) was isolated by the procedure used for **8**: mp 114–115 °; ^{1}H NMR ($CDCl_3$) δ 1.24–2.0 (m, $-(CH_2)_5-$), 1.86 (d, $^2J_{PH}$ = 13 Hz, PCH_3), 2.12–2.88 and 3.08 (m, overlapping PCH_2CH_2 and cyclohexyl H), 3.5 (broad singlet, NH, disappeared in D_2O), 4.28 ppm (d, $^2J_{PH}$ = 24 Hz, PCH=C); ^{31}P NMR ($CDCl_3$) +60.1; IR (Nujol) 1581 (C=C), 3150 cm^{-1} (NH); ^{13}C NMR (Table I).

Anal. Calcd for $C_{11}H_{20}NPS$: C, 57.64; H, 8.73; N, 6.11; P, 13.54; S, 13.97. Found: C, 57.86; H, 8.59; N, 6.17; P, 13.71; S, 14.15.

1-Methyl-1-methylthio-3-pyrrolidino-2-phospholenium Iodide (12). A solution of 1 g (0.005 mol) of phosphine sulfide **7** was stirred at room temperature under nitrogen for 24 h in 6 mL of benzene containing 0.7 g (0.005 mol) of methyl iodide. A white precipitate appeared within a few minutes of stirring. The product (1.7 g, 100%) was recrystallized from hot chloroform by adding benzene: mp 125–126 °C; ^{1}H NMR ($CDCl_3$) δ 2.04 (m, 4 H), 2.31 (d, $^2J_{PH}$ = 14 Hz, PCH_3 or SCH_3), 2.41 (d, $^2J_{PH}$ = 15 Hz, PCH_3 or $PSCH_3$), 2.6–3.92 ppm (m, 9 H, CH_2 and =CH); ^{31}P NMR ($CDCl_3$) +69.8; IR (Nujol) 1565 cm^{-1} (C=C); ^{13}C NMR (Table II).

Anal. Calcd for $C_{10}H_{16}INPS$: C, 35.01; H, 5.54; N, 4.08; P, 9.03; S, 9.33. Found: C, 34.83; H, 5.79; N, 3.89; P, 9.21; S, 9.25.

1-Methyl-1-methylthio-3-piperidino-2-phospholenium Iodide (13). A solution of 1.80 g (0.0084 mol) of phospholene sulfide **8** in 120 mL of dry benzene and 1.20 g (0.0085 mol) of methyl iodide was stirred under nitrogen at room temperature for 10 h. The precipitate was filtered off and washed with warm benzene: yield 1.8 g (60%); mp 119–120.5 °C after recrystallization from a hot chloroform solution on addition of benzene: ^{1}H NMR ($CDCl_3$) δ 1.73 (m, 6 H, $NCH_2CH_2CH_2$), 2.40 and 2.45 (both d, J_{PH} = 13 Hz, PCH_3 and SCH_3, unassigned), 3.00 (m, PCH_2CH_2), 3.30 (m, PCH_2), 3.50 (m, 4 H, NCH_2), 4.10 (d, $^2J_{PH}$ = 24 Hz, PCH=C); IR (Nujol) 1562 cm^{-1} (C=C); ^{31}P NMR δ +71.0 ($CDCl_3$); ^{13}C NMR (Table II).

Anal. Calcd for $C_{11}H_{21}INPS$: C, 37.00; H, 5.88; N, 3.92; P, 8.67. Found: C, 37.10; H, 5.82; N, 3.74; P, 8.87.

1-Methyl-1-methylthio-3-morpholino-2-phospholenium Iodide (14). A solution of 1 g (0.005 mol) of phosphine sulfide **9** in 60 mL of hot benzene was refluxed gently with 0.7 g (0.005 mol) of methyl iodide for 2 h under nitrogen. Within a few minutes a precipitate began to form. The product (1.1 g, 62%) was recrystallized from a mixture of chloroform and benzene: mp 160–161 °C; ^{1}H NMR ($CDCl_3$) δ 2.44 (d, $^2J_{PH}$ = 15 Hz, PCH_3 or SCH_3), 2.47 (d, $^2J_{PH}$ = 14 Hz, PCH_3 or SCH_3), 2.64–3.7 (m, overlapping PCH_2CH_2 and CH_2NCH_2), 3.76–4.0 (m, CH_2OCH_2), 4.31 ppm (d, $^2J_{PH}$ = 22 Hz, PCH=C); ^{31}P NMR ($CDCl_3$) +72.2; IR (Nujol) 1556 cm^{-1} (C=C); ^{13}C NMR (Table II).

Anal. Calcd for $C_{10}H_{19}INOPS$: C, 33.42; H, 5.29; N, 3.89; P, 8.63; S, 8.91. Found: C, 33.60; H, 5.47, N, 3.82; P, 8.77; S, 8.84.

1-Methyl-1-methylthio-3-cyclohexylamino-2-phospholenium Iodide (15). A solution of 0.4 g (0.0017 mol) of phosphine sulfide **10** in 25 mL of benzene was treated with 0.53 g (0.0017 mol) of methyl iodide. The mixture was stirred at room temperature for 15 h, following which the precipitated salt was recovered by filtration (0.4 g, 63%). Recrystallization by adding benzene to a hot chloroform solution gave **15**, mp 140.5–142 °C; ^{1}H NMR ($CDCl_3$) δ 1.26–1.98 (CH_2 groups of cyclohexyl), 2.32 (d, J_{PH} = 14 Hz, PCH_3 or SCH_3), 2.35 (d, J_{PH} = 15 Hz, PCH_3 or SCH_3), 2.6–3.6 (CH_2 groups of phospholene sulfide), 3.28 (CH of cyclohexyl), 3.85 (d, $^2J_{PH}$ = 27 Hz, PCH=C); ^{31}P NMR ($CDCl_3$) +69.6; ^{13}C NMR (Table II).

Anal. Calcd for $C_{12}H_{23}INPS$: C, 38.84; H, 6.20; P, 8.35; N, 3.71. Found: C, 38.80; H, 6.28; P, 8.27; N, 3.53.

Methyl Methyl(3-oxobutyl)phosphinothiolate (17). A solution of 2 g (0.0058 mol) of phospholenium salt **12** in 5 mL of dichloromethane was stirred at room temperature under nitrogen for 2 h with 1 mL of 3 N HCl. The aqueous layer was separated, neutralized, and extracted with chloroform (3 × 5 mL). The combined extracts were washed with saturated sodium bicarbonate and sodium chloride solutions, dried over sodium sulfate, and freed of solvent on the rotary evaporator. The reside (0.45 g, 43%) was purified by Kugelrohr distillation: ^{1}H NMR ($CDCl_3$) δ 1.81 (d, $^2J_{PH}$ = 14 Hz, PCH_3), 2.24 (s, $COCH_3$), 2.35 (d, $^3J_{PH}$ = 11 Hz, $PSCH_3$), 2.14–2.45 and 2.73–3.04 ppm (both m, CH_2CH_2); ^{31}P NMR ($CDCl_3$) +58.7; IR (Nujol) 1700 cm^{-1} (C=O); ^{13}C NMR ($CDCl_3$) δ 9.95 (d, $^2J_{PC}$ = 5 Hz, SCH_3), 19.24 (d, $^1J_{PC}$ = 70 Hz, PCH_3), 27.43 (d, $^1J_{PC}$ = 65 Hz, PCH_2), 29.65 (s, CCH_3), 35.84 (d, $^2J_{PC}$ = 5 Hz, CH_2C=O), 203.31 (d, $^3J_{PC}$ = 15 Hz, C=O).

Anal. Calcd for $C_6H_{13}O_2PS$: C, 40.00; H, 7.22; P, 17.22; S, 17.77. Found: C, 39.94; H, 6.98; P, 16.91; S, 17.51.

1-Methyl-3-pyrrolidino-2-phospholene Oxide (21). A mixture of the phospholenium salt **12** (1.6 g, 0.0046 mol) in 5 mL of dichloromethane and 1 mL of 3 N sodium hydroxide was refluxed under nitrogen for 1 h. The aqueous layer was separated and extracted with dichloromethane (3 × 5 mL). The combined dichloromethane solutions were washed with saturated sodium chloride, dried over sodium sulfate, and then stripped of the solvent on a rotary evaporator. The yield of oily product was 0.6 g (70%): ^{1}H NMR ($CDCl_3$) δ 1.65 (d, $^2J_{PH}$ = 13 Hz, PCH_3), 1.8–2.16 (m, 4 H, NCH_2CH_2), 2.36–2.96 (m, 4 H, PCH_2CH_2), 3.04–3.42 (m, 4 H, CH_2N), 4.16 (d, $^2J_{PH}$ = 20 Hz, PCH=C); IR (neat) 1565 (C=C), 1100 cm^{-1} (P=O). A sample was purified by Kugelrohr distillation for analysis.

Anal. Calcd for $C_9H_{16}NOP$: C, 58.38; H, 8.65; N, 7.57; P, 16.75. Found: C, 58.25 H, 8.56; N, 7.65; P, 16.57.

The same compound was formed by 16 h of refluxing of a mixture of 1 g (0.0067 mol) of 1-methyl-3-chloro-2- and 3-phospholene oxide[2] in 50 mL of benzene with 0.95 g (0.0134 mol) of pyrrolidine. The salt that precipitated was filtered off. The product obtained by evaporation of the solvent had ^{1}H NMR and IR spectra identical with those for the product from the basic hydrolysis of **12**.

Variable Temperature ^{13}C NMR Measurement. A sample of enamino salt **12** was dissolved in Me_2SO-d_6 and the chemical shifts were recorded relative to external Me_4Si in $CDCl_3$. The spectrum was recorded at probe temperature (about 30 °C) and the peak separation of the carbons α to nitrogen (30 Hz) was taken as the slow exchange limit. Coalescence occured at about 97 °C; due to the relatively small peak separation of the very sharp individual lines, it was difficult to make an accurate measurement of T_c by this method. The rate constant (k_c) for the process was determined from the expression $k_c = \pi\Delta\nu/\sqrt{2}$; with $\Delta\nu$ = 30 Hz, k_c is 66.6. The free energy of activation ($\Delta G_c^{\ddagger}$) was then determined from the expression $\Delta G_c^{\ddagger} = 2.3RT_c(10.32 + \log T_c/k_c)$; with T_c = 370 K, $\Delta G_c^{\ddagger}$ is 18.7 kcal/mol.

Registry No.—1, 22356-35-0; **2**, 58311-81-2; **12** charged, 64010-87-3; **12** uncharged, 64010-88-4; **13** charged, 64010-89-5; **13** uncharged, 64010-90-8; **14** charged, 64010-91-9; **14** uncharged, 64010-92-0; **15** charged, 64010-93-1; **15** uncharged, 64010094-2; **17**, 64010-95-3; **21**, 64010-96-4; pyrrolidine, 123-75-1; piperidine, 110-89-4; morpholine, 110-91-8; cyclohexylamine, 108-91-8; methyl iodide, 74-88-4.

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Synthesis of Some *B*-Nor-6,8-secoestranes and *B*,19-Dinor-6,8-secopregnanes

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Dehydrogenation of dehydroepiandrosterone (**1a**) and pregnenolone (**1b**) with DDQ, followed by dienone–phenol rearrangement and then hydrolysis and methylation, gave 3-methoxy-1-methylestra-1,3,5(10),6-tetraen-17-one (**3e**) and 3-methoxy-1-methyl-19-norpregna-1,3,5(10),6-tetraen-20-one (**3f**). The 6,7-olefinic moiety of **3e** and **3f** was cleaved with osmium tetroxide–sodium periodate to yield dialdehyde products **4a** and **4b**. Individual rotational isomers of the dialdehydes were seen in their ^{1}H NMR spectra. Decarbonylation of dialdehydes **4a** and **4b** to *B*-nor-6,8-secoestratriene **5a** and *B*,19-dinorpregnatriene **5b**, respectively, was accomplished with tris(triphenylphosphine)chlororhodium. The *B*-nor-6,8-secosteroids **5a** and **5b** were used as intermediates to prepare variously 17-substituted compounds **5c–e** and 4-en-3-one compounds **6a** and **6b**.

Since there are no reports in the literature of the preparation of either *B*-nor-6,8-secoestranes or *B*,19-dinor-6,8-secopregnanes, we undertook the synthesis of steroids with this feature. A brief degradative route (Scheme I) from naturally occurring steroids was chosen for investigation since this would provide final products with the natural stereochemical configuration.

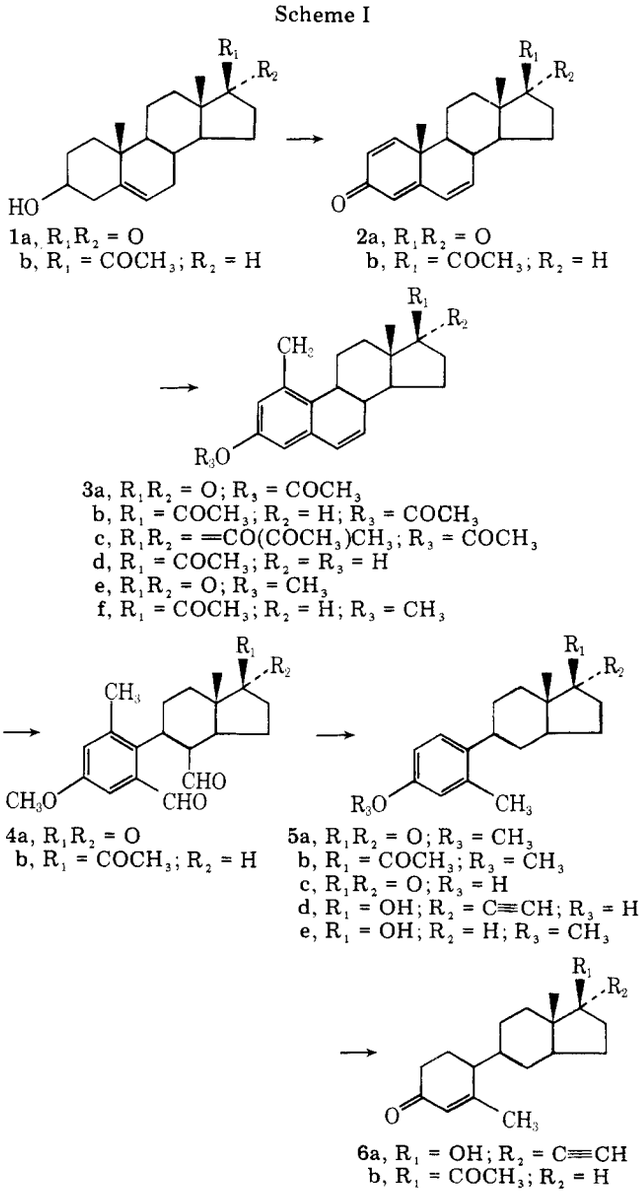
Dehydroepiandrosterone (**1a**) and pregnenolone (**1b**) were dehydrogenated with dichlorodicyanoquinone (DDQ) in refluxing dioxane to the corresponding trienes **2a** and **2b**.[1] On dienone–phenol rearrangement in acetic anhydride with toluenesulfonic acid catalyst, triene **2a** was converted to tetraene **3a**,[2] while triene **2b** was converted to a mixture of tetraene **3b** and diacetate **3c** with **3c** the major product.

The need for additional quantities of **3b** prompted a study of the hydrolysis of diacetate **3c** to determine if the 17-acetyl functionality with the normal β configuration and free of any 17α isomer contamination could be regenerated from the $\Delta^{17,20}$ enol acetate. Precedent existed for the conversion since Rubin and Blossey[3] have shown that pregnanes with the abnormal 17α configuration can be equilibrated to a mixture (85:15) of 17β and 17α isomers. The ^{1}H NMR spectrum of the crude phenol **3d**, obtained from basic hydrolysis of diacetate **3c**, had C-18 methyl absorptions at δ 0.52 and 0.87 ppm, clearly indicating the presence of both 17β- and 17α-acetyl moieties. Phenol **3d** was chromatographed and both early and late fractions gave identical ^{1}H NMR spectra; none of the 17α isomer could be found. Hydrolysis of monoacetate **3b** gave phenol **3d** whose melting point and ^{1}H NMR spectrum were identical with those of the phenol obtained from diacetate **3c**.

Hydrolysis of diacetate **3c** with methanolic sodium hydroxide followed by methylation with dimethyl sulfate also gave only the 17β isomer of *O*-methyl ether **3f**. This was confirmed by hydrolysis and methylation of monoacetate **3b**. In subsequent preparations, the mixture of acetates **3b** and **3c**, after filtration through a short column of alumina to remove polar impurities, was hydrolyzed, methylated, and purified. None of the 17α isomer could be detected in the *O*-methyl ether product **3f**.

Attempts to transform the 6,7-olefinic moieties of compounds **3e** and **3f** into dialdehyde functionalities employing sodium periodate and a catalytic amount of osmium tetroxide

Scheme I



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