12, 63988-93-2; 13, 63988-94-3; sodium 5-methyl-2-thiophenesulfonate, 63988-95-4; 2-methyl-5-thiophenesulfonyl, 55854-45-0; mesitylene, 108-67-8; 2-hydroxy-3,5-dichlorobenzyl chloride, 6333-33-1; 2,4-dichlorophenol, 120-83-2; formaldehyde, 50-00-0; 3,5-dimethylbenzyl bromide, 27129-86-8; amyl bromide, 110-53-2; 2-bromopentane, 107-81-3; 2-thiophenesulfonyl chloride, 16629-19-9; thiophene, 110-02-1; chlorosulfonic acid, 7790-94-5.

Notes and References

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Proaporphine–Aporphine Dimers and a Bisaporphine Derived from the Tumor-Inhibitory Alkaloid Thalicarpine[1a]

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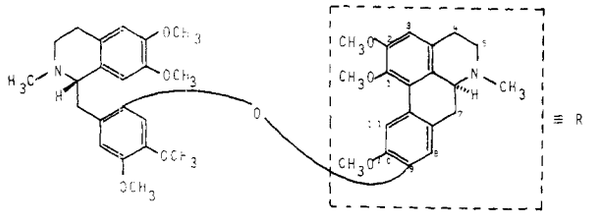
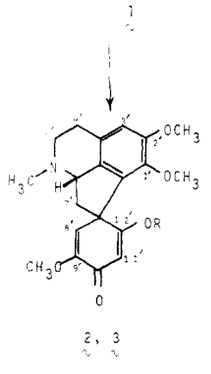
Oxidation of the tumor inhibitory alkaloid thalicarpine (1), a benzylisoquinoline–aporphine dimer, with VOF_3 in TFA gave a mixture of diastereoisomeric dienones **2** and **3**, a new type of proaporphine–aporphine alkaloid. The major isomer **2** was converted to the epimeric dienols **6a** and **6b** which, upon treatment with BF_3–Et_2O in CH_2Cl_2, gave another new type of alkaloid, bisaporphine **8**. Preliminary testing results indicate that bisaporphine **8** is active in vitro against cells derived from the human carcinoma of the nasopharynx (KB).

The alkaloid thalicarpine,[2] which has the aporphine–benzylisoquinoline structure **1**,[3] exhibits a significant inhibitory activity against the Walker 256 intramuscular carcinosarcoma in rats over a wide dosage range.[4]

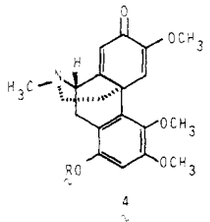
In order to gain some insight into the structure–tumor inhibitory activity relationship in this alkaloid series, we have undertaken studies directed toward structural modifications of thalicarpine. We report herewith the conversion of thalicarpine (**1**) to a new type of alkaloid, proaporphine–aporphine dimers **2** and **3**, and thence to another new type of alkaloid, bisaporphine **8**. Both **2** and **8** serve as models for types of alkaloids which have not been isolated from natural sources to date.





2, **3**

Recently, a number of nonphenol oxidative coupling reactions which yield spirodienone intermediates and products have been reported.[5-10] Thus, morphinandienones (e.g., **4**) have been recognized as the primary products of chemical[5,6] as well as electrooxidative coupling of nonphenolic tetrahydrobenzylisoquinoline precursors. On the other hand, chemical[6] and electrochemical[9] oxidative coupling of tetramethoxylated bibenzyls gave dihydrophenanthrone derivatives via five-membered ring spirodienone intermediates, similar to the proerythrinadienone-type systems (e.g., **5**). Oxidation



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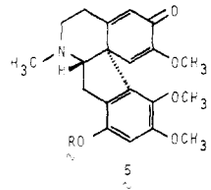

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of nonphenolic phenethyltetrahydroisoquinolines using vanadium oxytrifluoride (VOF_3) in trifluoroacetic acid (TFA) to homoaporphines via homoproerythrinadienone intermediates[10] was also reported.

Thalicarpine (**1**), a nonphenolic alkaloid, was thus subjected to chemical as well as anodic oxidative coupling reactions to elaborate the benzyltetrahydroisoquinoline part of the molecule. The oxidation of thalicarpine (**1**) was best performed by treating 0.4 mmol of the alkaloid in CH_2Cl_2, TFA,[11] and FSO_3H with 2.5 molar equiv of VOF_3 in TFA and ethyl acetate at −10 °C for 10 min. The product was a mixture of dienones **2** and **3**, diastereomers at the spiro ring junction. The two isomers were separated by preparative thin layer chroma-

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Table I. NMR Resonances of Dienones and Dienols [a]

		2	3	6a	6b	7a	7b
N-Methyl	N-6	2.44	2.43	2.42	2.42	2.44	2.40
	N-6′	2.58	2.49	2.57	2.55	2.48	2.49
Methoxyl	C-1	3.68	3.65	3.61	3.59	3.64	3.64
	C-2[b]	*3.84*	*3.85*	*3.88*	*3.82*	*3.78*	*3.82*
	C-10	*3.88*	*3.89*	*3.94*	*3.88*	*3.85*	*3.88*
	C-1′[b]	3.71	3.71	3.73	3.74	3.73	3.73
	C-2′[b]	3.74	3.75	3.85	3.79	3.78	3.75
	C-9′	3.59	3.65	3.58	3.59	3.61	3.59
Aromatic	C-3[c]	6.67	6.68	6.62	6.60	6.63	6.60
	C-8	6.94	6.80	6.88	6.95	6.76	6.82
	C-11	8.09	8.14	8.10	8.08	8.08	8.09
	C-3′[c]	6.63	6.64	6.62	6.60	6.63	6.60
Olefinic	C-8′	5.63	5.59	4.91	4.96	4.83[d]	4.84[d]
	C-11′	5.81	5.46	5.02[d]	4.88[d]	4.72	4.70

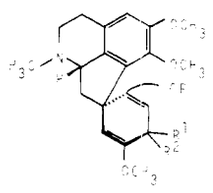
[a] Values are given in δ units relative to tetramethylsilane as internal standard. All spectra were recorded in $CDCl_3$. [b] The values are interchangeable for these methoxyl signals. [c] The values are interchangeable for these aromatic protons. [d] Doublet (J = 4–5 Hz).

tography (PTLC) and isolated in crystalline form in 72% and 5% yield, respectively. In contrast to VOF_3–(TFA–TFAA) oxidation, anodic oxidation of thalicarpine (**1**) in TFA–TFAA using tetraethylammonium tetrafluoroborate as supporting electrolyte gave the dienones **2** and **3** in yields of 40 and 5%, respectively.

The infrared spectra of both isomers showed typical dienone absorptions at 1655, 1635, and 1605 cm^{-1}. The UV spectra of both **2** and **3** exhibited λ_{max}(EtOH) 232 (sh), 258, 263, 275, and 304 nm. The mass spectra showed a molecular ion peak at *m/e* 680 for both isomers and a base peak at *m/e* 324 (R^+) for the major isomer (**2**) and 340 (OR^+ or $M^+ - OR$) for the minor isomer (**3**). The NMR signals (Table I) were assigned by comparison to those of similar systems.[12-14]

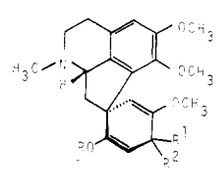
The possibility of a morphinandienone-type (**4**) or a proerythrinadienone-type (**5**) structure for the oxidation products was excluded by the formation of a mixture of diastereoisomeric dienones and further modifications of the dienones and further modifications of the dienones as described below.

Dienones **2** and **3** were subjected to the acid-catalyzed dienone–phenol rearrangement under a variety of conditions (i.e., concentrated HCl in glacial acetic acid, BF_3–Et_2O in CH_2Cl_2, TFA) but unchanged starting material was recovered in each case. In contrast, the epimeric dienols, represented as **6a** and **6b**,[15] obtained by sodium borohydride reduction of the major dienone **2** in 75 and 15% yield, underwent smooth dienol–benzene rearrangement upon treatment with boron trifluoride etherate in CH_2Cl_2 at 0 °C for 10 min. Thus, dienol



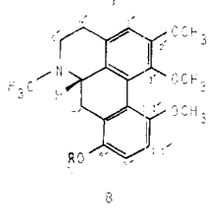
6a, R¹=OH; R²=H

b, R¹=H; R²=OH



7a, R¹=OH; R²=H

b, R¹=H; R²=OH



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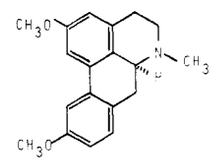
6a was converted to a bisaporphine (**8**) in 80% yield as the dihydrobromide salt. The structure of bisaporphine **8** was confirmed by sodium in liquid ammonia cleavage[16] of the bisaporphine. The nonphenolic product was indistinguishable in terms of melting point, TLC, UV, NMR, mass spectra, and specific rotation from an authentic sample of L(+)-2,10-dimethoxyaporphine (**9**) derived from sodium in liquid ammonia cleavage of thalicarpine.[17] From the physical data obtained, the phenolic product could have been either **10a** or **10b.** However, inspection of the NMR spectrum of the acetate **10c,** prepared by treatment of the phenolic product with acetic



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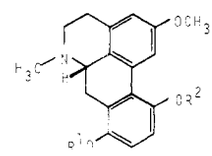

10a, R¹=H; R²=OH

b, R¹=CH₃; R²=H

c, R¹=COCH₃; R²=CH₃

anhydride–pyridine, revealed that there was no change in the chemical shift of the C-1 proton at δ 7.75 (1 H, d, $J_{1,3}$ = 2.4 Hz). This suggested that the structure of the phenolic product was **10a.** Had the structure been **10b,** the C-1 H signal should have been shifted farther downfield. Further support for the structure of the phenolic product came from the study of the effect of alkali on the NMR spectrum of the phenolic product (**10a**) in Me_2SO-d_6, which showed a signal at δ 5.59 (2 H, s) for the C-9 and C-10 protons. Upon addition of a drop of alkali (sodium hydroxide in CD_3OD), the signal at δ 5.59 was shifted to δ 5.32 and appeared as an AB quartet ($J_{9,10}$ = 6 Hz, $\Delta\nu_{AB}$ = 8 Hz), whereas there was no change in the chemical shift of the C-1 proton, again confirming the structure of the phenolic product as **10a.**

In contrast to the acid-catalyzed rearrangement of the dienols **6a** and **6b** to bisaporphine **8,** the dienols, represented as **7a** and **7b,** obtained by borohydride reduction of the minor dienone **3,** gave only cleavage products upon treatment with boron trifluoride etherate in CH_2Cl_2. Further investigation of these cleavage products was not pursued.

The bisaporphine (**8**) is active (ED_{50} = 1.85 μg/mL) in vitro against cells derived from the human carcinoma of the nasopharynx (KB) and is now undergoing preliminary testing under the auspices of the National Cancer Institute.

Experimental Section

Melting points were determined on a Mettler FP2 melting point apparatus and are uncorrected. Ultraviolet spectra were determined

on a Beckman DK-2A recording spectrophotometer. NMR spectra were recorded on a JEOL PFT-100P pulse Fourier transform NMR spectrometer, using tetramethylsilane as internal standard. Infrared spectra were determined on a Perkin-Elmer 337 recording spectrophotometer. Mass spectra were obtained on Hitachi Perkin-Elmer RMU-6E and Atlas MS-902 spectrometers. Thin-layer chromatography was carried out on commercially prepared TLC plates (E. M. Reagents). Preparative TLC was carried out with silica gel (F-254 2 × 200 × 200, or 0.5 × 200 × 200, or 0.25 × 200 × 200 mm) plates. Visualization of the alkaloids was performed by spraying the entire analytical plate, or the edges of the preparative plate, with an aqueous solution of iodoplatinic acid reagent (1.0 g in 250 mL of water containing 15 g of potassium iodide) and/or ultraviolet light. Microanalyses were carried out by Atlantic Microlab, Inc., Atlanta, Ga. Column chromatography was carried out on Silica Gel 60 (70–230 mesh ASTM) obtained from E. M. Reagents. Anhydrous sodium sulfate was used as the drying agent, exclusively.

Proaporphine–Aporphine Dimers (2 and 3). (A) By Chemical Oxidation. A solution of 280 mg (0.4 mmol) of thalicarpine in 2 mL of dichloromethane and 1 mL of TFA–TFAA (20:1 by weight) was cooled to −10 °C (ice–salt bath). Following the addition of 0.1 mL of fluorosulfonic acid, a solution of 240 mg (1.9 mmol) of vanadium oxytrifluoride in 1 mL of ethyl acetate and 2 mL of TFA–TFAA (20:1 by weight) was added and the resulting dark brown solution was stirred for 10 min. The reaction was quenched with 15 mL of 10% aqueous citric acid solution, made alkaline with 58% ammonium hydroxide, and extracted with dichloromethane. The dichloromethane solution was washed with saturated brine, dried over anhydrous sodium sulfate, and evaporated to leave 305 mg of a yellow foam, which was applied to nine 0.5-mm preparative silica gel plates and eluted with 10% methanol in chloroform. Two bands with R_f 0.55 and 0.35 were obtained. The higher R_f band after extraction with 20% methanol in chloroform and crystallization from methanol–ether–hexane (1:10:1) gave 204 mg (72%) of the proaporphine–aporphine dimer **2** as dirty white crystals: mp 178.5–180 °C; UV λ_{max}(EtOH) (log ϵ) 232 (sh, 4.63), 258 (4.39), 263 (4.40), 275 (4.32), 304 (4.18) nm; IR ($CHCl_3$) 2790, 2815, 1650, 1633, 1603 cm^{-1}; mass spectrum *m/e* 680 (M^+), 679, 678, 665, 637, 622, 340, and 324; $[\alpha]^{29}_D$ −17° (0.32, $CHCl_3$).

Anal. Calcd for $C_{40}H_{44}O_8N_2 \cdot CH_3OH$: C, 69.08; H, 6.78; N, 3.92. Found: C, 68.80; H, 6.78; N, 3.92.

The lower R_f band after extraction with 20% methanol in chloroform and crystallization from methanol–ether–hexane (1:10:1) gave 13 mg (5%) of the proaporphine–aporphine dimer **3** as dirty white crystals: mp 175.5–177.3 °C; UV λ_{max}(EtOH) (log ϵ) 232 (sh 4.67), 258 (4.42), 263 (4.41), 275 (4.30), 304 (4.2) nm; IR ($CHCl_3$) 2793, 2818, 1658, 1635, 1605 cm^{-1}; mass spectrum *m/e* 680 (M^+), 679, 678, 665, 637, 622, 340, and 324; $[\alpha]_D$ +61.2° (0.32, $CHCl_3$).

Anal. Calcd for $C_{40}H_{44}O_8N_2 \cdot CH_3OH$: C, 69.08; H, 6.78; N, 3.92. Found: C, 69.07; H, 6.91; N, 3.94.

(B) By Anodic Oxidation. The oxidation was conducted in a three-compartment cell (which separated the anode, cathode, and reference electrode solutions by glass frits) in conjunction with a Princeton Applied Research Model 376 potentiostat. The anode was a platinum mesh and a stainless steel spatula served as the cathode. The anode compartment had an approximate 120 mL volume in which the solution was agitated by means of a magnetic stir bar. A 0.1 N $AgNO_3$ solution in acetonitrile in contact with an Ag wire served as the reference.

Thalicarpine (208 mg; 0.3 mmol) was added to the anode compartment containing 120 mL of a mixture of TFA–TFAA (20:1 by weight). Tetraethylammonium tetrafluoroborate (3.0 g) was added as a background electrolyte to the anode and 1.0 g to the cathode compartments. The electrolysis was carried out at a constant potential of 1.4 V at room temperature. The initial current was 35 mA; it dropped as the reaction proceeded. The electrolysis was stopped when the current attained a constant minimum value (3 mA after 70 min). The anolyte was evaporated under reduced pressure and the residue was taken up in water and made alkaline with 58% NH_4OH. The organic material was extracted with chloroform. The chloroform solution was dried and evaporated to give a dark brown gum which was quickly passed through a short column of silica gel using 2% methanol in chloroform. The product obtained was purified by preparative layer chromatography as described in section A to give 82 mg (40%) of **2** and 11 mg (5%) of **3**.

Sodium Borohydride Reduction of Dienones 2 and 3. To a stirred solution of 200 mg (0.29 mmol) of **2** in 5 mL of ethanol was added 100 mg of sodium borohydride portionwise over 10 min under cooling, and the reaction mixture was allowed to stir for 5 h at room temperature. After removal of the solvent, the residue was suspended in water and extracted with dichloromethane. The dichloromethane extract was washed with saturated brine, dried over anhydrous sodium sulfate, and evaporated to give 210 mg of a colorless glass which was applied to five 0.5-mm preparative silica gel plates and eluted with 10% methanol in chloroform. Two bands with R_f 0.6 and 0.35 were obtained. The higher R_f band after extraction with 20% methanol in chloroform and crystallization from ether gave 140 mg (70%) of the dienol **6a** as slightly yellow crystals: mp 171–173 °C; UV λ_{max}(EtOH) (log ϵ) 268 (sh, 4.20), 278 (4.30), 302 (4.15), 312 (sh, 4.03); IR ($CHCl_3$) 3475, 2780, 2820, 1600, 1658 cm^{-1}; mass spectrum *m/e* 682 (M^+, very weak), 664 ($M^+ - 18$, base peak).

Anal. Calcd for $C_{40}H_{46}O_8N_2$: C, 70.36; H, 6.80; N, 4.10. Found: C, 70.31; H, 6.84; N, 4.10.

The lower R_f band after extraction with 20% methanol in chloroform and crystallization from ether gave 30 mg (15%) of the dienol **6b** as slightly yellow crystals: mp 185–187 °C; UV λ_{max}(EtOH) (log ϵ) 268 (sh, 4.22), 278 (4.32), 302 (4.17), 312 (sh, 4.05) nm; IR ($CHCl_3$) 3480, 2780, 2825, 1600, 1658 cm^{-1}.

Anal. Calcd for $C_{20}H_{46}N_2O_8 \cdot {}^3/_4H_2O$: C, 69.06; H, 6.87; N, 4.02. Found: C, 69.06; H, 7.08; N, 4.01.

Similarly, dienone **3** (100 mg) was reduced to give **7a:** 63 mg (62%); mp 139–142 °C; UV λ_{max}(EtOH) 268, 278, 302, 314 (sh) nm; IR ($CHCl_3$) 3470, 1655, 1601 cm^{-1}; mass spectrum *m/e* 682 (M^+), 664 ($M^+ - 18$, base peak), and **7b:** 15 mg (15%); mp 193.5–194 °C; UV λ_{max}(EtOH) 268, 278, 304, 319 nm; IR ($CHCl_3$) 3975, 1650, 1605 cm^{-1}; mass spectrum *m/e* 682 (M^+), 664 ($M^+ - 18$, base peak).

Bisaporphine (8). A solution of 100 mg (0.15 mmol) of dienol **6a** in 4 mL of dichloromethane was cooled to 0 °C and treated with 0.1 mL of boron trifluoride etherate, drop by drop, with stirring and the resulting yellow solution was stirred for an additional 10 min. The reaction mixture was diluted with water, made alkaline with 58% ammonium hydroxide, and extracted with dichloromethane. The dichloromethane extract was washed with saturated brine, dried, and evaporated to leave a yellow glass which was applied to three 0.5-mm preparative silica gel plates and eluted with 10% methanol in chloroform. The major band was collected and extracted with 20% methanol in chloroform. Evaporation of the solvent and crystallization of the residue as the hydrobromide salt from methanol–ether gave 96 mg (80%) of bisaporphine **8** as an amorphous powder: mp 216–218 °C; UV λ_{max}(EtOH) (log ϵ) 278 (4.51), 304 (4.47) nm; NMR ($CDCl_3$) δ 8.17 (s, 1 H, C-11 H), 7.11–6.86 (AB quartet, C-9′ and C-10′ H, J_{AB} = 9 Hz), 6.66, 6.59, and 6.47 (each s, 3H, Ar H), 3.95, 3.89, 3.58, 3.87 (each s, 12 H, OCH_3), 3.70 (s, 6 H, OCH_3), 2.46 and 2.36 (each s, 6 H, NCH_3); mass spectrum *m/e* 664 (M^+), 649 ($M^+ - CH_3$), 633 ($M^+ - OCH_3$).

Anal. Calcd for $C_{40}H_{44}O_7N_2 \cdot 2HBr \cdot 2H_2O$: C, 55.69; H, 5.84; N, 3.25. Found: C, 55.71; H, 5.68; N, 3.33.

By following the above procedure, dienol **6b** was also converted to the bisaporphine **8** in 74% yield. However, similar treatment of dienols **7a** and **7b** yielded only a mixture of cleavage products. Further investigation of these products was not pursued.

Sodium–Liquid Ammonia Cleavage of Bisaporphine 8. A solution of 80 mg of **8** in 5 mL of dry THF was added dropwise to a stirred solution of 0.08 g of sodium metal in 60 mL of ammonia at −75 °C under a nitrogen atmosphere. A blue color persisted for 2 h, at which time the mixture was allowed to stand overnight. The residue was treated with 5% hydrochloric acid to pH 7.5 and extracted with dichloromethane. The dichloromethane solution was washed with saturated brine, dried, and evaporated to leave a brown residue which was applied to four 0.25-mm preparative silica gel plates and eluted with 10% methanol in chloroform. Two major alkaloid bands with R_f 0.4 and 0.15 were obtained.

L(+)-2,10-Dimethoxyaporphine (9). The high R_f band was isolated to yield 10 mg of **9** as a light yellow oil which was crystallized from methanol as the hydriodide salt to give 5 mg of product: mp 237–239 °C; mmp; UV λ_{max}(EtOH) (log ϵ) 266 (4.10), 272 (4.12), 298 (3.68), 310 (3.75), and 318 (3.76); mass spectrum *m/e* 295 (M^+), 294, 280, 274, 251, and 97; NMR ($CDCl_3$) δ 7.23 (d, 1 H, C-1 H, $J_{1,3}$ = 2.4 Hz), 7.16 (d, 1 H, C-8 H, $J_{8,9}$ = 8.0 Hz), 7.10 (d, 1 H, C-11 H, $J_{9,11}$ = 2.5 Hz), 6.85, 6.83, 6.77, and 6.61 (d, 1 H, C-3 H, $J_{3,1}$ = 2.4 Hz), 3.85 and 3.84 (each s, 6 H, OCH_3), 2.55 (s, 3 H, NCH_3); infrared spectrum in chloroform, as well as $[\alpha]^{24}_D$ = 111.8°, were identical with those of an authentic sample obtained by sodium–liquid ammonia cleavage of thalicarpine.

8-Hydroxy-2,11-dimethoxyaporphine (10a). The low R_f band was isolated to yield 10 mg of **10a** as a slightly yellow oil: $[\alpha]^{24}_D$ +133° (*c* 0.70, chloroform); mass spectrum *m/e* 311 (M^+); UV λ_{max}(EtOH) 266, 276, 300, 310, and 318 nm; NMR ($CDCl_3$) δ 7.75 (d, 1 H, C-1 H, $J_{1,3}$ = 2.7 Hz), 6.65 (s, 2 H, C-9 and C-10 H), 6.58 (d, 1 H, C-3 H, $J_{3,1}$ = 2.7 Hz), 5.44 (6s, 1 H, OH), 3.80 and 3.77 (each s, 6 H, OCH_3), 2.58 (s, 3 H, NCH_3).

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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(15) Inspection of molecular models suggested that the transition state for the formation of the ring junction represented by **6a** and **6b** might be of lower energy than for the formation of that represented by **7a** and **7b** due to the steric interaction between the C-6′ proton and the aporphine ring in **7a** and **7b**. Consequently, the major dienone (**2**) is thought to have a spiro ring junction as represented in **6a** and **6b**, and the minor dienone (**3**) as represented in **7a** and **7b**.
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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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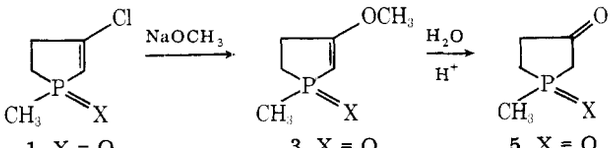
Enamines are formed in high yield by the displacement of chlorine from 1-methyl-3-chloro-2-phospholene sulfides with pyrrolidine, piperidine, morpholine, and cyclohexylamine. Alkylation fails to occur at C-2, the β carbon of the enamine system, but does occur readily on sulfur, making available a family 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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