maxima (neat) 3.20 (w), 3.38 (vs), 6.0 (vs), 6.10 (vs), 7.06 (vs), 8.30 (m), 8.60 (vs), 9.16 (m), 11.11 (m), and 13.62 (s) μ.

Anal. Calcd. for $C_8H_{13}N$ (V and VI): C, 78.05; N, 11.38. Found (V): C, 77.27; N, 10.72. Found (VI): C, 78.42; N, 11.17.

erythro-**3-Ethylamino-4-hydroxy-1,5-hexadiene (IIa).**—The *erythro*-amino alcohol IIa was obtained by dissolving II in 1.5 times its volume of pentane. This solution was cooled in a −50° bath until crystallization occurred. Without agitation, the temperature was brought to 0°. Filtration and recrystallization from pentane yielded the *erythro*-amino alcohol IIa as a white solid, m.p. 45–45.5°.

The proton spectrum of IIa, in CCl_4, showed N-ethyl multiplets centered at τ 8.93 and 7.43, a complex vinyl multiplet between 3.90 and 5.13, and O- and N-methinyl multiplets centered at 5.91 and 7.0, respectively. The position of the hydroxy and amino proton signals coincided with the N-methinyl resonance. The signal intensities were in accord with theory.

threo-**3-Ethylamino-4-hydroxy-1,5-hexadiene (IIb).**—The filtrates from IIa isolation were combined, repeatedly cooled, and filtered until crystallization failed to occur upon cooling. In this manner the *threo* isomer IIb, with a configurational purity of 90% (by n.m.r.[16]), was obtained as a colorless oil.

The n.m.r. spectrum of the *threo*-amino alcohol gave N-ethyl signals centered at τ 8.93 and 7.45, a vinyl multiplet between 3.86 and 5.11, and O- and N-methinyl signals at 5.91 and 7.10, respectively. The relative signal intensities agreed with expectations. Hydroxyl and –NH signals appeared as a broad singlet at τ 6.22.

erythro-**3-Ethylamino-4-hydroxy-1,5-hexadiene Hydrochloride (IIIa).**—Dry hydrogen chloride was bubbled into an ethereal solution of IIa until precipitation ceased. Filtration and recrystallization from isopropyl alcohol gave IIIa, m.p. 119–120°.

threo-**3-Ethylamino-4-hydroxy-1,5-hexadiene Hydrochloride (IIIb).**—In a similar manner IIb yielded, after recrystallization from toluene, IIIb, m.p. 99–101°.

erythro-**3-Ethylamino-4-hydroxy-1,5-hexadiene Sulfate Ester (IVa).**—By the procedure previously described IIIa was converted to IVa quantitatively. Washing the crude reaction mixture with isopropyl alcohol gave IVa as a white solid, m.p. 176–178° dec.

threo-**3-Ethylamino-4-hydroxy-1,5-hexadiene Sulfate Ester (IVb).**—In a like manner IVb was obtained from IIIb. IVb recrystallized from isopropyl alcohol as a white solid, m.p. 205–207° dec.

Ring Closure of IVa.—The sulfate ester IVa (5 g., 26.6 mmoles) dissolved in 20 ml. of water was added dropwise to 18 g. (226 mmoles) of a hot 50% NaOH solution. Steam distillation during the addition resulted in the isolation of 0.95 g. (34.1% yield) of a pale yellow oil. Gas chromatographic analysis of this oil showed the presence of *trans*-N-ethyl-2,3-divinylaziridine, free of the azepine VI.

If the temperature of ring closure was ambient and the time of reaction was 24 hr., ring closure gave a 50.2% yield of V.

Ring Closure of IVb.—Cyclization of IVb was carried out in the manner described for the ring closure of IVa. At either steam-distillation temperatures or at ambient temperatures for 18 hr. a 54% yield of a pale yellow oil was obtained. The composition of this oil was 89% N-ethyl-4,5-dihydroazepine and 11% *trans*-N-ethyl-2,3-divinylaziridine according to gas chromatographic and n.m.r. analysis.

Cyclopentene-1-carboxaldehyde-N-ethylimine (VII).—N-ethyl-4,5-dihydroazepine was heated at 100° for 1 hr. in the presence of a trace of moisture. Gas chromatographic analysis showed the presence of a new product VII.

The proton spectrum of VII disclosed a slightly broad singlet at τ 2.0 (—N=CH—), a vinyl multiplet at 3.97, a N-methylene quadruplet centered at 6.60, an allylic multiplet centered at 7.55, a ring methylene pentuplet centered at 8.05, and methyl resonance at 8.83.

Reaction of VII with 2,4-dinitrophenylhydrazine reagent yields the corresponding hydrazone, m.p. 205–207°. No depression occurred when the hydrazone of VII was mixed with the 2,4-dinitrophenylhydrazone of cyclopentene-1-carboxaldehyde.[18]

(18) H. J. Shine and R. H. Snyder, *J. Am. Chem. Soc.*, **80**, 3064 (1958).

Phosphonic Acids and Esters. VIII. Facile Hydrolytic Cleavage of Carbon–Phosphorus Bonds in Pyrrylphosphonates and Phosphine Oxides[1,2]

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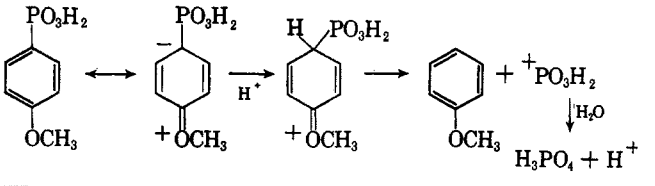
In contrast to the generally observed stability of the carbon–phosphorus bond of dialkyl arylphosphonates toward basic reagents, diethyl 2-pyrrylphosphonate undergoes a facile cleavage with the formation of pyrrole and 2-ethylpyrrole when treated with aqueous sodium hydroxide. Similar treatment of tri(2-pyrryl)phosphine oxide results in cleavage with the formation of pyrrole. The failure of the 1-methyl analogs to undergo cleavage under comparable conditions indicates that these degradations proceed by abstraction of the 1-proton of the pyrryl derivative, conversion of the resulting anion by protonation or alkylation to a pyrrolenine derivative, and collapse of the pyrrolenine to the observed products. The phosphonopyrroles polymerized in the presence of aqueous acid; evidence for the occurrence of electrophilic dephosphonations under these conditions was obtained.

In the great majority of arylphosphonic acids and their derivatives, the carbon–phosphorus bond is quite stable under hydrolytic conditions, resisting the action of both concentrated base and acid for extended periods of time.[4] However, in phosphonate structures which possess electron-donor groups (amino, dimethylamino, hydroxy, and methoxy) in *ortho* or *para* positions, this bond is cleaved readily by a variety of electrophilic reagents.[4] Lesfauries[5] has shown that *p*-anisylphosphonic acid is cleaved to anisole and phosphoric acid by the action of both hydrobromic and sulfuric acids and has postulated the following cleavage mechanism. In



(1) Part VII: M. Gordon, V. A. Notaro, and C. E. Griffin, *J. Am. Chem. Soc.*, **86**, 1898 (1964). A preliminary account of these results was given before the Symposium on Mechanisms of Reactions of Organophosphorus Compounds, 140th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1961.

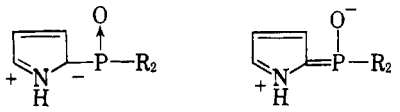
(2) This study was supported in part by a research grant (CY-5338) from the National Cancer Institute, Public Health Service.

(3) (a) Taken in part from the M.S. Thesis of R. P. P., University of Pittsburgh, 1961; (b) National Science Foundation Undergraduate Research Participant, 1961–1962.

(4) For a summary of pertinent references, see L. D. Freedman and G. O. Doak, *Chem. Rev.*, **57**, 479 (1957).

(5) P. Lesfauries, Dissertation, University of Paris, 1950, cited in ref. 4; M. P. Viout and P. Rumpf, *Compt. rend.*, **239**, 1291 (1954).

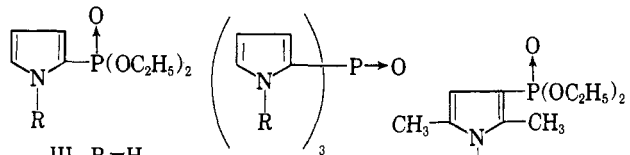
a study of the absorption spectra of pyrrylphosphine oxides,[6] the donor properties of the pyrryl ring system were shown to result in significant contributions of canonical structures such as I and II (R = 2-pyrryl). Since similar electron delocalizations should exist in the 2-pyrrylphosphonates (I and II, R = alkoxyl), electrophilic cleavage of the carbon–phosphorus bond in these



I II

compounds and the pyrrylphosphine oxides might be anticipated, assuming the validity of the mechanistic postulations of Lesfauries.[5] Additionally, the 2-pyrrylphosphonates represent simple vinylogs of the *o*- and *p*-aminophenylphosphonic acids which have been shown to undergo electrophilic cleavage.[4] In order to test this hypothesis, a study of the chemical behavior of a number of 2-phosphonopyrrole systems was undertaken.

The compounds chosen for study were the diethyl 2-pyrrylphosphonates (III and IV), the previously prepared 2-pyrrylphosphine oxides (V and VI),[6] and, for comparison, diethyl 3-(2,5-dimethylpyrryl)phosphonate (VII). The reverse addition technique of Burger and Dawson[4,7] (addition of pyrrylmagnesium bromide to



III, R=H
IV, R=CH$_3$

V, R=H
VI, R=CH$_3$

VII

diethyl chlorophosphate) was used successfully in the preparation of III. The 1-methyl analog IV was similarly prepared by the addition of 1-methylpyrryllithium to diethyl chlorophosphate; brief reaction times (1 hr.) were necessary, since longer reaction times led to the formation of VI as the sole product.[6] The attempted formation of VII by both direct and reverse addition of 2,5-dimethylpyrrylmagnesium bromide[8] to diethyl chlorophosphate gave 2,5-dimethyl-3-ethylpyrrole (VIII) as the sole isolable product. Although alkylations of Grignard reagents by dialkyl chlorophosphates have not been reported previously, Gilman and Gai[9] have shown that sterically hindered Grignard reagents are alkylated by trialkyl phosphates and the direct methylation of pyrrylmagnesium bromide by trimethyl phosphate has been demonstrated recently.[10] The infrared spectra of both III and IV showed absorptions characteristic of 2-substituted pyrroles[11] and arylphosphonates.[12] The absence of N-phosphorylation in the formation of III was established by the presence of N–H absorption (3436 cm.$^{-1}$)[11] in the infrared and by proton magnetic resonance (p.m.r.) studies. The p.m.r. spectrum of III in $CDCl_3$ showed multiplets at τ = 2.76, 3.24, and 3.71 p.p.m. (relative intensities 0.95:1.00:2.05) due to the N-, 5-, and 3,4-protons. The presence of any significant amount of N-isomer would have been readily detected by changes in relative intensities. IV showed multiplets at τ = 3.26 (5-H) and 3.96 (3,4-H) and a singlet at 6.23 p.p.m. (N-CH_3).[13] Ester proton absorptions were observed at τ = 8.75 (CH_3) and 6.05 p.p.m. (CH_2) for both III and IV.

Attempted cleavage of III with refluxing aqueous hydrochloric acid of varying concentrations (1–50%) led to formation of a resinous material in near-quantitative yield, reflecting the well-known sensitivity of pyrrole derivatives to protic acids.[14] The phosphorus analysis of the resin was significantly less than theory for a simple polymer of III, indicating the possible occurrence of carbon–phosphorus bond cleavage. Similar results were obtained on attempted acidic cleavage of V; phosphorus and nitrogen analyses for the resin again indicated the possible occurrence of cleavage. Attempted reactions of III and V with aqueous hydrochloric acid at room temperature also gave a resin; aqueous acetic and trifluoroacetic acids gave either resin or recovered starting materials, depending on reaction conditions. No direct evidence for carbon–phosphorus bond cleavage was obtained in any of these experiments.

Because of the failure of attempted acidic cleavages, bromination of III was examined. Dephosphonation of arylphosphonates by attack of molecular bromine[4] and the displacement of carboxyl and acetyl groups by bromine in pyrrole derivatives have been previously observed.[14] The reaction of bromine with III in both ethanol and acetic acid led to the formation of a solid product; the infrared spectrum of this product was transparent in the regions characteristic of phosphoryl (1220–1270 cm.$^{-1}$) and POC_2H_5 (1150–1180 and 1010–1050 cm.$^{-1}$) groupings,[12] indicating that the diethylphosphono group had probably been displaced by bromine. Attempted purification of this product by column chromatography indicated it to be a complex mixture. None of the fractions isolated showed the infrared characteristics of the expected cleavage product, tetrabromopyrrole; the majority of the fractions isolated showed strong carbonyl bands at 1720–1728 cm.$^{-1}$ indicative of either aliphatic aldehyde or ketone functions. Thus brominative dephosphonation was accompanied by ring opening. Since the sequence of dephosphonation and ring opening could not be established, no further bromination studies were attempted.

Attempted basic hydrolysis (refluxing 10% aqueous sodium hydroxide) of III led to completely unanticipated results, *i.e.*, quantitative dephosphonation with the formation of pyrrole (70%) and 2-ethylpyrrole (IX, 28%). Previous studies[4] have shown that the carbon–phosphorus bond of arylphosphonates is quite stable to the action of base, and basic conditions are routinely employed for the hydrolysis of dialkyl arylphosphates

(6) C. E. Griffin and R. A. Polsky, *J. Org. Chem.*, **26**, 4772 (1961); C. E. Griffin, R. P. Peller, K. R. Martin, and J. A. Peters, *ibid.*, **30**, 97 (1965).

(7) A. Burger and N. D. Dawson, *ibid.*, **16**, 1250 (1951).

(8) G. Plancher and B. Tanzi, *Atti. accad. naz. Lincei, Mem., Classe sci. fis., mat. e nat., Sez. II*, [5] **23**, 412 (1914); H. Booth, A. W. Johnson, E. Markham, and R. Price, *J. Chem. Soc.*, 1587 (1959).

(9) H. Gilman and B. J. Gai, *J. Am. Chem. Soc.*, **82**, 6326 (1960).

(10) C. E. Griffin and R. Obrycki, *J. Org. Chem.*, **29**, 3090 (1964).

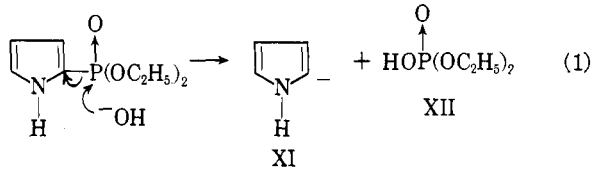
(11) A. R. Katritzky, *Quart. Rev.* (London), **13**, 353 (1959); A. R. Katritzky and A. P. Ambler, "Physical Methods in Heterocyclic Chemistry," Vol. II, A. R. K., Ed., Academic Press, New York, N. Y., 1963, p. 161.

(12) L. C. Thomas and R. A. Chittenden, *Spectrochim. Acta*, **20**, 467, 489 (1964).

(13) The p.m.r. spectra of V and VI serve as models: V, τ = 2.83 (N-H), 3.18 (5-H), and 3.67 (3,4-H) p.p.m.; VI, τ = 3.20 (5-H), 4.0 (3,4-H), and 6.17 p.p.m. (N-CH_3).

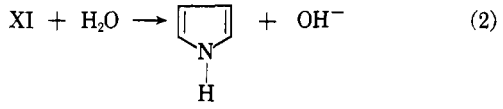
(14) A. H. Corwin in "Heterocyclic Compounds," Vol. I, R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1950, p. 277ff.

to the corresponding monoesters.[15] The only phosphonate structures which undergo ready carbon–phosphorus bond cleavages under basic conditions are structures possessing an electron-attracting group in close proximity to the phosphono group, notably the dialkyl acylphosphonates,[4] and 2-chloroalkyl-[16] and *p*-nitrobenzylphosphonic (X) acids.[17] Since the pyrryl ring is a strong electron donor, the cleavage observed in the case of III is unique among hydrolytic dephosphonations. Swan[17] has proposed an SN2 displacement of *p*-nitrotoluide anion by attack of hydroxide ion at phosphorus as the mechanism of cleavage of X[18]; similar displacements on phosphorus have been postulated for the cleavage of 2-chloroalkylphosphonic acids[16] and for the conversion of trischloromethylphosphine to methyl bisalkoxymethylphosphine oxides.[19] An analogous mechanism (A, eq. 1 and 2) would provide a rationale for the formation of pyrrole in the hydrolysis of III.



(1)

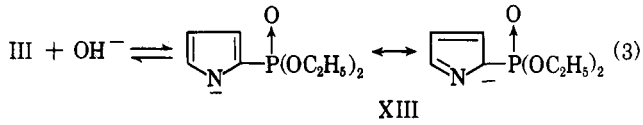
XI XII



(2)

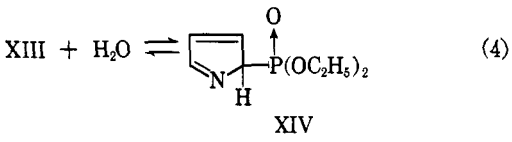
2-Ethylpyrrole could be formed by alkylation of XI by either III or XII. However, two objections can be raised to such a mechanism. III is cleaved significantly more readily than X,[17] a result contrary to expectation on the basis of the above mechanism. It would be expected that the ease of cleavage would reflect the stability of the leaving group and *p*-nitrotoluide anion should be much more stable than XI because of extensive electron delocalization. Secondly, in relatively dilute aqueous solution, protonation of XI by water is much more likely than alkylation of XI by either III or XII; the relatively high yields of IX would not be expected on the basis of this mechanism.

An alternative mechanism (B, eq. 3–6) was considered to be more consistent with the observed results. Conversion of III to its anion XIII in at least modest equilibrium concentrations would be anticipated since Treibs and Kolm have shown that pyrroles bearing electron-attracting substituents (formyl, acetyl, and carbethoxy) are readily converted to their N-sodio derivatives by sodium ethoxide in ether.[20] Protonation of XIII at the 2-position would yield the pyrrolenine XIV which could either undergo proton abstraction to regenerate XIII or collapse with carbon–phosphorus bond cleavage to give the aromatic anion XV, and XVI. Reaction of water with XV and XVI would generate pyrrole and XII. The role postulated for hydroxide ion is solely the generation of the anion XIII, which then



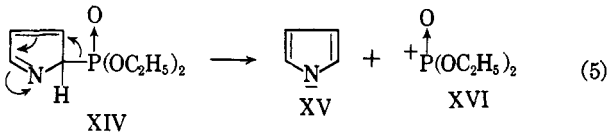
(3)

XIII



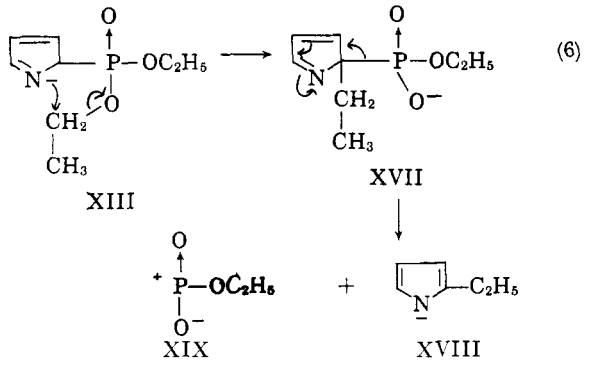
(4)

XIV



(5)

XIV XV XVI



(6)

XIII XVII XIX XVIII

undergoes carbon–phosphorus bond cleavage (eq. 4 and 5) by the typical electrophilic process postulated by Lesfauries.[5] Formation of 2-ethylpyrrole could result from an alternative mode of collapse of XIII. Attack of the negative charge at the 2-position of XIII on an O-ethyl group would lead to the pyrrolenine XVII, which could undergo scission to form XVIII and XIX. Protonation of XVIII and hydration of XIX would lead to IX and monoethyl phosphate. A number of examples of the ability of tetracovalent phosphorus esters to alkylate anions,[9,10] and oxygen and nitrogen nucleophiles[21,22] have been reported. A process similar to that of eq. 3 and 6 has been demonstrated by Szmuszkovicz[22] who showed that alkaline hydrolysis of diethyl γ-(3-indolyl)-γ-ketopropylphosphonate (XX) led to the formation of a monobasic acid, ethyl γ-[3-(1-ethylindolyl)]-γ-ketopropylphosphonate, as the major product. Conversion of XX to its N-anion by base followed by alkylation of the anion by the dialkyl phosphonate was postulated as the course of the reaction.

Formation of significant amounts of IX in the hydrolysis of III is deemed more likely by the steps outlined in mechanism B than in mechanism A. The pertinent step (eq. 6) involves a four-centered transition state with a geometry similar to that of the Wittig reaction[23] and should be of higher probability than an intermolecular alkylation of XI by III (mechanism A). The intramolecular alkylation of XIII to form XVII would be expected to compete favorably with intermolecular protonation of XIII by solvent.[24] The yield of IX was shown to be independent of the concentration of III in

(15) R. Rabinowitz, *J. Am. Chem. Soc.*, **82**, 4564 (1960).

(16) J. A. Maynard and J. M. Swan, *Australian J. Chem.*, **16**, 596 (1963).

(17) A. Meisters and J. M. Swan, *ibid.*, **16**, 725 (1963).

(18) For a general discussion of SN2 displacements at phosphorus, see R. F. Hudson, "Advances in Inorganic Chemistry and Radiochemistry," Vol. 5, H. J. Emeleus and A. G. Sharpe, Ed., Academic Press, New York, N. Y., 1963, p. 347.

(19) M. I. Kabachnik and E. N. Tsvetkov, *Dokl. Akad. Nauk SSSR*, **143**, 592 (1962).

(20) A. Treibs and H. G. Kolm, *Ann.*, **606**, 166 (1957).

(21) F. R. Atherton, *Quart. Rev.* (London), **3**, 151 (1949); T. L. Fletcher, M. E. Taylor, and A. W. Dahl, *J. Org. Chem.*, **20**, 1021 (1955); F. W. Hoffman and H. D. Weiss, *J. Am. Chem. Soc.*, **79**, 4759 (1957).

(22) J. Szmuszkovicz, *ibid.*, **80**, 3782 (1958).

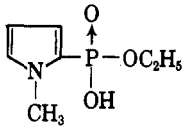
(23) S. Trippett, *Quart. Rev.* (London), **17**, 406 (1963).

(24) Although XIV and XVII are postulated as discrete species in eq. 4 and 6, the two carbon–phosphorus bond cleavage processes for XIII leading to pyrrole and IX may be synchronous.

solution, indicating an intermolecular ethylation of XIII by III to be unlikely. The pyrrolenines XIV and XVII may also undergo cleavage by attack of hydroxide ion on phosphorus. Thus, displacement of pyrryl anion XV from XIV would yield diethyl phosphate (XII) directly. The experimental evidence allows no choice between the possible modes of cleavage of the pyrrolenines.

A choice between mechanisms A and B is dependent upon the demonstration of the necessity of the 1-proton of III for cleavage, *i.e.*, the proton abstraction step of eq. 3. The ease of proton abstraction was demonstrated by the complete exchange of the 1-proton under conditions comparable to those of the cleavage reaction. On treatment with 10% NaOD in D_2O at 37° for 8 hr., the p.m.r. signal for the 1-proton of III (τ = 2.76 p.p.m.) disappeared; no other changes in the spectrum other than those anticipated from loss of spin–spin coupling with the 1-proton were observed indicating that negligible cleavage occurred under these conditions.

Convincing evidence in support of mechanism B was provided by the behavior of IV with base. Treatment of IV with refluxing 10% aqueous sodium hydroxide gave the monoester XXI, the normal product of the



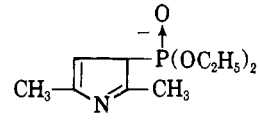
XXI

basic treatment of dialkyl arylphosphonates,[15] in 67% yield. The expected cleavage products, 1-methyl- and 1-methyl-2-ethylpyrroles, were not detected; a 27% recovery of IV was obtained, giving a mass balance of >94% for the reaction. The failure of IV to undergo carbon–phosphorus bond cleavage established mechanism B as the operative mechanism for the hydrolytic cleavage of III. If mechanism A were operative, comparable amounts of cleavage in III and IV would be expected since there should be little difference in the stabilities of the pyrryl and 1-methylpyrryl anions.

Further evidence for base-catalyzed carbon–phosphorus bond cleavages in the phosphonopyrroles was provided by the behavior of the oxides V and VI. Treatment of V with refluxing 10% aqueous sodium hydroxide gave pyrrole as the sole isolable product. The yield of pyrrole was, after correction for recovered V, 87% based on the stoichiometry 3V → 3 pyrrole + H_3PO_4. The high yield of pyrrole indicates that the products resulting from cleavage of one and two pyrryl–phosphorus bonds [bis(2-pyrryl)phosphinic and 2-pyrrylphosphonic acids] undergo hydrolytic cleavage readily. The results obtained with the 1-methyl analog VI again support the operation of mechanism B and rule against attack of hydroxide ion at phosphorus. Treatment of VI with aqueous base under the reaction conditions used in the cleavage of V led to recovery of VI (96%); no 1-methylpyrrole could be detected in the reaction mixture.

As in the case of III, the basic cleavage of V is remarkably facile. Cleavage of carbon–phosphorus bonds in phosphine oxides by the action of base have been observed in a number of cases,[25] but the degradation normally requires much more drastic conditions than those cited above. Thus, Horner has shown that fusion with sodium hydroxide at 200–300° is required for the cleavage of methyldiphenylphosphine oxide to benzene and methylphenylphosphinic acid.[26]

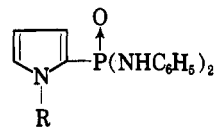
In view of the results obtained in the hydrolysis of III, the formation of 2,5-dimethyl-3-ethylpyrrole (VIII) in the reaction of 2,5-dimethylpyrrylmagnesium bromide (XXII) with diethyl chlorophosphate (XXIII) can be rationalized. Because of the ease of displacement of chlorine from phosphorus by nucleophiles,[18] it is unlikely that XXIII functions as an alkylating agent directly. However, the expected product VII from the reaction of XXII and XXIII could undergo exchange with XXII to give its anion (organomagnesium reagent); one of the canonical structures (XXIV) of this anion could undergo an intramolecular ethylation and



XXIV

cleavage in analogy to III (eq. 6) to give VIII. The greater acidity of the 1-proton of VII (*vs.* 2,5-dimethylpyrrole) should provide a driving force for exchange with XXII. Evidence for the exchange of pyrrylmagnesium halides with pyrroles has been obtained by a number of investigators.[8,10] Such a process would be facilitated by the reduction in steric repulsions in the conversion of VII to VIII. In order to provide evidence for this interpretation, the reaction of III with pyrrylmagnesium bromide was examined. After a 48-hr. reflux period, 2-ethylpyrrole was isolated in 12% yield, indicating the process VII → XXIV → VIII to be feasible.

Two further phosphonopyrroles (XXV and XXVI) were prepared as part of this study; the reaction of N,N′-diphenylphosphorodiamidic chloride (XXVII) with the appropriate pyrrylmagnesium reagent was employed for synthesis. Attempted acidic hydrolyses of



XXV, R=H
XXVI, R=CH_3

each led to results similar to those obtained with III and IV. Basic hydrolyses led to complex mixtures which could not be purified; elemental analyses, neutralization equivalents, and p.m.r. spectra indicated these products to be mixtures of mono- and diamidates.

Although the ultraviolet spectra of the phosphine oxides V and VI provide evidence for d_π–p_π interactions between the pyrryl π-system and the phosphono group,[6] no such interaction is evident from the spectra of the pyrrylphosphonates examined in this study. III and IV (λ_{max} 211–218 mμ) show the typical absorption of an unperturbed pyrrole ring (pyrrole λ_{max} 211 mμ).[6] The absorption curves of XXV–XXVII are essentially identical (λ_{max} 228–232 and 273–276 mμ) and quite similar to that of acetanilide[27] (λ_{max} 242 and 280 mμ)

(25) K. D. Berlin and G. B. Butler, *Chem. Rev.*, **60**, 243 (1960).

(26) L. Horner, H. Hoffman, and H. G. Wippel, *Chem. Ber.*, **91**, 61 (1958).

(27) H. E. Ungnade, *J. Am. Chem. Soc.*, **76**, 5133 (1954).

indicating that the only operative delocalizations in XXV–XXVII involve interactions of the lone pair of electrons on nitrogen with the phosphono group. These results bear out the much greater importance of dp_π interactions between nonbonding electrons of electronegative atoms with phosphonyl groups than the comparable bonding with π-systems.[6,18]

Experimental[28]

Diethyl 2-Pyrrylphosphonate (III).—A solution of 0.6 mole of 2-pyrrylmagnesium bromide in 500 ml. of anhydrous ether was prepared according to standard procedures.[10,29] The Grignard solution was added dropwise over a period of 5 hr. to a gently refluxing and stirred solution of diethyl chlorophosphate (102.3 g., 0.6 mole) in 500 ml. of anhydrous ether. The solution was cooled to room temperature and poured over a mixture of ice and 200 ml. of 50% hydrochloric acid. The ethereal layer was separated immediately and the aqueous layer was extracted with ether. The combined ethereal layers were washed with 5% aqueous sodium bicarbonate, dried over magnesium sulfate, and reduced in volume at room temperature to give a brown oil. The oil was distilled to yield 5.7 g. (14.2% recovery) of pyrrole, b.p. 48–60° (52 mm.), and 37.0 g. (30.6%) of a colorless oil (III), b.p. 117–119° (14 mm.).[30]

Anal. Calcd. for $C_8H_{14}NO_3P$: C, 47.29; H, 6.95; N, 6.90. Found: C, 47.09, 47.17; H, 7.10, 7.15; N, 7.02, 6.99.

In subsequent preparations, III boiled at 77° (0.6 mm.), 82–85° (2.0 mm.), and 136° (23 mm.). A tarry pot residue (19.0 g.) remained after the distillation cited above. III absorbed in the infrared at 3436 w, 2445 w, 1590 m, 1462 s, 1391 s, 1370 s, 1294 s, 1267 s, 1160 s, 982 s, and 869 m ($CHCl_3$ solution) and 1242 w, 1217 m, 1206 m, 1052 s, 1022 s, and 935 m cm.$^{-1}$ (CCl_4 solution). The ultraviolet spectrum of III showed maxima at 211 and 297 mμ (ϵ 6540 and 44.6) and a minimum at 267 mμ (ϵ 7.7).

Diethyl 2-(1-Methylpyrryl)phosphonate (IV).—A solution of 0.25 mole of N-methylpyrryllithium in 100 ml. of absolute ether was prepared according to the method of Shirley, *et al.*[31]; an 18-hr. reflux period was used for metalation of N-methylpyrrole by *n*-butyllithium. The lithium reagent slurry was transferred under nitrogen to a dropping funnel and added over a period of 2 hr. to a solution of 51.6 g. of diethyl chlorophosphate (0.3 mole) in 50 ml. of absolute ether. The reaction mixture was maintained at ice-bath temperatures throughout the period of addition. The addition was slightly exothermic and gave a brown solution; after the addition was completed, the reaction mixture was refluxed for 1 hr. and hydrolyzed with a saturated solution of ammonium chloride. The ethereal layer was separated, and the aqueous layer was washed with ether; the combined ethereal layers were washed with water, dried over magnesium sulfate, and concentrated to give a dark oil. Distillation gave 3.2 g. (16.0% recovery) of 1-methylpyrrole and 13.4 g. (30.8%) of IV, b.p. 122.5–126° (3.0 mm.).[30]

Anal. Calcd. for $C_9H_{16}NO_3P$: C, 49.76; H, 7.43; N, 6.45. Found: C, 49.59, 49.81; H, 7.45, 7.61; N, 6.34, 6.32.

IV absorbed in the infrared at 1590 m, 1460 s, 1391 s, 1368 s, 1294 s, 1260 s, 1166 s, 1050 s, 1020 s, 982 s, 933 m, and 870 m cm.$^{-1}$ (liquid film). The ultraviolet spectrum of IV showed a maximum at 218 mμ (ϵ 6400).

Longer reflux periods (3–20 hr.) led to the formation of VI (5–28%) under otherwise identical reaction conditions.[6] In one reaction (3-hr. reflux), triethylphosphate (40%) was isolated, indicating cleavage of the solvent by the aryllithium reagent.

Attempted Preparation of Diethyl 3-(2,5-Dimethylpyrryl)phosphonate (VII).—A solution of 19.0 g. (0.2 mole) of 2,5-dimethylpyrrole[32] in 150 ml. of absolute ether was added gradually with cooling (ice bath) to a solution of 0.2 mole of ethylmagnesium bromide in 150 ml. of absolute ether. The reaction mixture was refluxed for 2 hr. A solution of 34.1 g. (0.2 mole) of diethyl chlorophosphate in 300 ml. of absolute ether was added dropwise with constant stirring to the refluxed Grignard solution. After addition was completed (1.5 hr.), the reaction mixture was refluxed for 1.5 hr. and poured over ice. The ethereal layer was separated, and the aqueous layer was extracted with ether. The combined ether extracts were dried over magnesium sulfate and reduced in volume to give 15 ml. of a brown oil. The oil was distilled to yield two fractions, b.p. 46–60° (2.0 mm.), 5.0 g., and b.p. 60–73° (2.4 mm.), 4.0 g. The infrared spectra of both fractions were essentially identical. The fractions were combined and redistilled to give 7.1 g. (28.8%) of **2,5-dimethyl-3-ethylpyrrole** (VIII),[30] b.p. 53° (1.5 mm.), lit. b.p. 112° (42 mm.)[33] and 93–94° (21 mm.).[34]

Anal. Calcd. for $C_8H_{13}N$: C, 77.99; H, 10.63; N, 11.37. Found: C, 77.91; H, 10.92; N, 11.15.

VIII absorbed in the infrared at 3448 s, 3356 s, 2398 w, 1709 w, 1605 w, 1449 s, 1399 s, 1374 s, 1295 s, 1149 s, and 998 w ($CHCl_3$ solution); 1238–1256 s (unresolved doublet), 1053 s, and 784 s cm.$^{-1}$ (liquid film). The p.m.r. spectrum of VIII as a neat liquid showed absorptions at τ = 8.95 (triplet, CH_2—CH_3), 8.02 and 7.97 (singlets, ring CH_3), 7.52 (quartet, CH_2—CH_3) and 4.45 p.p.m. (multiplet, 4-H). Similar results were obtained by addition of the Grignard solution to the chlorophosphate solution; VIII was obtained in 15–26% yield.

Hydrolyses of Diethyl 2-Pyrrylphosphonate (III). A. Acidic Hydrolysis.—A mixture of 10.2 g. of III (0.048 mole) and 200 ml. of 50% aqueous hydrochloric acid was refluxed for 8 hr. A dark brown tarry material (9.8 g.) formed and was removed by filtration. This material was washed successively with alcohol, acetone, and ether and dried at 100° (1.0 mm.), 8.4-g. recovery.

Anal. Calcd. for $(C_8H_{14}NO_3P)_x$: P, 15.25. Found: P, 14.87, 14.72.

No characterizable material was isolated by ether extraction of the aqueous solution. Similar results were obtained on hydrolysis with 1–10% aqueous hydrochloric acid at reflux and at room temperature and with refluxing 50% aqueous acetic acid for reaction periods of 5–48 hr. Attempted cleavages with 50% aqueous acetic and trifluoroacetic acids at room temperature (10–24 hr.) gave small amounts of tar (10–35%) and recovered starting material.

B. Basic Hydrolysis.—A mixture of 12.0 g. of III (0.059 mole) and 100 ml. of 10% aqueous sodium hydroxide was refluxed for 44 hr. The reaction mixture was extracted with ether and the ethereal extracts were dried over magnesium sulfate and concentrated to give 15 ml. of a yellow oil. Fractional distillation of the oil gave 2.5 g. (70%) of pyrrole, b.p. 64–65° (66 mm.), and 1.3 g. (28%) of **2-ethylpyrrole**[30] **(IX)**, b.p. 62° (15 mm.), $n^{25}D$ 1.4985, lit. b.p. 59–60° (15 mm.),[35] $n^{23}D$ 1.4960.[36]

Anal. Calcd. for C_6H_9N: C, 75.74; H, 9.53; N, 14.73. Found: C, 75.68; H, 9.35; N, 14.81.

IX absorbed in the infrared at 3344 s, 3077 w, 2907 s, 1698 w, 1567 m, 1531 w, 1458 m, 1420 m, 1347 w, 1285 m, 1138 w, 1115 m, 1094 m, 1074 m, 1046 s, 1014 s, 929 m, 882 m, and 867 w cm.$^{-1}$ (liquid film). The p.m.r. spectrum of IX as a neat liquid showed absorptions at τ = 8.88 (triplet, CH_3), 7.55 (quartet, CH_2), 4.34 (doublet, 3-H), 3.99, and and 3.62 p.p.m. (multiplets, 4,5-H).

Acidification of the basic aqueous solution and extraction with chloroform led to the isolation of a trace amount of crystalline material which could not be identified or characterized. Similar yields of IX (26.5–29%) and pyrrole (68–71%) were obtained using 200 ml. of 10% aqueous base and 0.06 mole of III and using 50% aqueous ethanol as solvent.

Basic Hydrolysis of Diethyl 2-(1-Methylpyrryl)phosphonate (IV).—A mixture of 10.6 g. of IV (0.049 mole) and 150 ml. of 10% aqueous sodium hydroxide was refluxed for 23 hr. to give a homogeneous solution. The reaction mixture was cooled to room temperature and extracted with ether. The etheral extracts were dried over magnesium sulfate and distilled to give 2.9 g. of IV

(28) All reactions were carried out under a dry nitrogen atmosphere; starting pyrroles were distilled prior to use and stored under nitrogen. Infrared spectra were determined on Perkin-Elmer Model 21 and Beckman IR-8 spectrophotometers as dilute solutions in 0.1-mm. cells or as liquid films between sodium chloride plates. Ultraviolet spectra were determined with a Cary Model 14 spectrophotometer as dilute solutions (10^{-4}–10^{-5} molar) in 95% ethanol. P.m.r. spectra were determined with a Varian Associates A-60 spectrometer (probe temperature 37°) using tetramethylsilane as an internal standard. All melting points are uncorrected. Microanalyses were performed by Galbraith Microanalytical Laboratories.

(29) P. S. Skell and G. P. Bean, *J. Am. Chem. Soc.*, **84**, 4655 (1962).

(30) Compounds III, IV, VIII, and IX underwent air oxidation slowly, but were stable under a nitrogen atmosphere at 0–25°.

(31) D. A. Shirley, B. H. Gross, and P. A. Roussel, *J. Org. Chem.*, **20**, 225 (1955).

(32) D. M. Young and C. F. H. Allen, *Org. Syn.*, **16**, 25 (1936).

(33) K. Hess, F. Wissing, and A. Suchier, *Ber.*, **48**, 1878 (1915).

(34) L. Knorr and K. Hess, *ibid.*, **44**, 2763 (1911).

(35) K. Hess and F. Wissing, *ibid.*, **47**, 1416 (1914).

(36) W. Herz and C. F. Courtney, *J. Am. Chem. Soc.*, **76**, 576 (1954).

(27.3% recovery). No free pyrroles were detected in the ethereal extracts by gas–liquid chromatography.[37] The aqueous solution was acidified with 5% hydrochloric acid and concentrated at 10° under reduced pressure to precipitate a colorless solid which was recrystallized from ethanol–benzene to give **ethyl 2-(1-methylpyrryl)phosphonate (XXI)**, m.p. 131–32°, 6.2 g. (66.7%).

Anal. Calcd. for $C_7H_{12}NO_3P$: C, 44.44; H, 6.40; P, 16.38; neut. equiv., 189.2. Found: C, 44.38; H, 6.51; P, 16.20, 16.26; neut. equiv., 188.5, 188.3.

XXI was somewhat unstable in solution, giving a brown tar on heating in either water or ethanol.

Hydrolyses of Tri-2-pyrrylphosphine Oxide (V). A. Acidic Hydrolysis.—A solution of 1.2 g. of V (0.0049 mole), 150 ml. of 50% aqueous hydrochloric acid, and 20 ml. of 95% ethanol was refluxed for 10 hr. On cooling to room temperature, a dark brown resin separated. The resin was washed with acetone and ether and dried at 110° (1 mm.) to give 1.03 g. of material.

Anal. Calcd. for $(C_{12}H_{12}N_3OP)_x$: N, 17.13, P, 12.63. Found: N, 17.32, 17.41; P, 12.27, 12.38.

Similar results were obtained in the attempted hydrolyses of V using the conditions employed in the hydrolysis of III.

B. Basic Hydrolysis.—A mixture of 0.9 g. of V (0.0037 mole) and 70 ml. of 10% aqueous sodium hydroxide was refluxed for 24 hr. The solution was cooled to room temperature and extracted with ether. The ethereal extracts were dried over magnesium sulfate and reduced in volume to give a brown oil. The oil was dissolved in 95% ethanol and water was added to precipitate V, 0.08 g. (8.9% recovery). The aqueous ethanol solution was extracted repeatedly with ether and the ethereal extracts were dried over magnesium sulfate and distilled to give 0.6 g. (0.0089 mole) of pyrrole. No further materials were isolated or detected.[37]

Bromination of Diethyl 2-Pyrrylphosphonate (III).—A solution of bromine (32.0 g., 0.2 mole) dissolved in 30 ml. of 95% ethanol was added dropwise over a period of 1 hr. to a stirred solution of 9.4 g. of III (0.04 mole) in 100 ml. of 95% ethanol. The solution was stirred for 1 hr. and diluted with 500 ml. of water. The aqueous suspension was extracted with ether and the ethereal extracts were concentrated under reduced pressure to give a brown oil which solidified on treatment with aqueous ethanol. The solid was chromatographed on a neutral alumina column (1 × 70 cm.) by elution with benzene and methanol. None of the fractions showed infrared absorptions characteristic of an authentic sample of tetrabromopyrrole.[38] A number of fractions eluted with methanol showed carbonyl bands at 1720–1728 cm.$^{-1}$.

Reaction of Diethyl 2-Pyrrylphosphonate (III) with Pyrrylmagnesium Bromide.—A solution of 0.10 mole of pyrrylmagnesium bromide in 150 ml. of absolute ether was added at 0° to a solution of 20.3 g. (0.10 mole) of III in 100 ml. of absolute ether. The reaction mixture was refluxed for 48 hr. and hydrolyzed with ice-cold deoxygenated water.[10] The aqueous layer was extracted with ether the combined ethereal extracts were dried over magnesium sulfate and concentrated under reduced pressure to give a yellow oil. Distillation gave 6.57 g. of pyrrole (98% recovery), b.p. 64–65° (66 mm.), 1.14 g. (12%) of 2-ethylpyrrole,[37] b.p. 60–61° (15 mm.), and 17.1 g. (84% recovery) of III, b.p. 82–85° (2.0 mm.).

N,N′-Diphenylphosphorodiamidic Chloride (XXVII).—This compound was prepared according to the procedure of Cook, *et al.*,[39] The material was recrystallized from 95% ethanol, m.p. 161–162°, lit.[39] m.p. 167°. The ultraviolet absorption spectrum of XXVII showed maxima at 232 and 273 mμ (ε 29,000 and 2090), shoulders at 268 and 282 mμ (ε 1875 and 1710), and minima at 212 and 253 mμ (ε 11,500 and 1095).

N,N′-Diphenyl-2-pyrrylphosphonodiamidate (XXV).—Powdered XXVII (20.0 g., 0.075 mole) was added in portions to a solution of 0.215 mole of pyrrylmagnesium bromide in 125 ml. of absolute ether. The reaction mixture was refluxed for 2 hr., cooled, and poured over a mixture of ice and 100 ml. of 50% hydrochloric acid. The ether layer was separated and washed with 10% aqueous sodium hydroxide and with water. Repeated cooling of the ether solution to 0° led to the precipitation of a colorless solid (3.1 g., 14%), m.p. 217–228°. Recrystallization from 95% ethanol gave XXV, m.p. 240–241°.

Anal. Calcd. for $C_{16}H_{16}N_3OP$: C, 64.64; H, 5.43. Found: C, 64.49, 64.58; H, 5.54, 5.50.

XXV absorbed in the infrared at 3226 w, 1610 w, 1508 m, 1416 m, 1287–1299 w (unresolved doublet), 1215 s, 1202 s, 1068 m, 1045 w, 995 m, 928 w, 755 m, 743 m, 733 s, and 688 m cm.$^{-1}$ (Nujol mull). The ultraviolet spectrum of XXV showed maxima at 228 and 273 mμ (ε 33,000 and 1860), shoulders at 268 and 280 mμ (ε 1630 and 1390), and minima at 213 and 252 mμ (ε 24,100 and 723).

N,N′-Diphenyl-2-(1-methylpyrryl)phosphonodiamidate (XXVI)—A solution of 5.8 g. of 1-methylpyrrole (0.072 mole) in 50 ml. of absolute ether was added gradually at room temperature to a solution of 0.072 mole of ethylmagnesium bromide in 100 ml. of absolute ether. After addition was completed, the reaction mixture was refluxed for 1.5 hr. and powdered XXVII (8.2 g., 0.034 mole) was added in portions. The reaction mixture was refluxed for 2 hr. and poured over a mixture of ice and 100 ml. of 50% hydrochloric acid. The ethereal layer was separated and washed with 10% aqueous sodium hydroxide and with water. The ether layer was dried over magnesium sulfate and cooled to 0°; after 1 week, 0.5 g. (4.7%) of XXVI precipitated. XXVI was recrystallized from aqueous ethanol, m.p. 220–221°.

Anal. Calcd. for $C_{17}H_{18}N_3OP$: C, 65.58; H, 5.83; P, 9.94. Found: C, 65.41; H, 6.09; P, 10.19.

XXVI absorbed in the infrared at 3600 m, 1600 m, 1490 m, 1400 w, 1280 m, 1230–1210 s (unresolved doublet), 1170 w, 1025 w, 995 s, 960 m, 935 m, 900 w, 745 s, and 680 s cm.$^{-1}$ (Nujol mull). The ultraviolet spectrum of XXVI showed maxima at 232 and 276 mμ (ε 18,350 and 1553), shoulders at 270 and 283 mμ (ε 1420 and 1190), and minima at 215 and 258 mμ (ε 11,600 and 963).

XXVI could also be prepared in comparable yield by the reaction of XXVII and N-methylpyrryllithium in ether.

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(37) The estimation and identification of a number of simple pyrroles was carried out by comparison of the gas–liquid chromatographic behavior of unknowns with the behavior of authentic samples. The columns employed and experimental procedures have been described previously.[10]

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