1,2-Dibromoethylsulfur Pentafluoride.—Bromine reacted very slowly with $SF_5CH{=}CH_2$ at room temperature. The addition of bromine was effected readily by exposing a mixture of 20.8 g. (0.135 mole) of $SF_5CH{=}CH_2$[1] and 21.6 g. (0.135 mole) of Br_2 to a 275-w. G. E. sun lamp (about 12 in. away) for 37 min. during which time the reflux temperature rose from 42 to 85°. Distillation gave 34.6 g. (82%) of $SF_5CHBrCH_2Br$, a yellowish liquid, b.p. 50–52° at 20 mm., $n^{25}D$ 1.4433.

Anal. Calcd. for $C_2H_3Br_2F_5S$: Br, 50.9; F, 30.2; S, 10.2. Found: Br, 50.8; F, 29.4; S, 10.1.

2,2-Bis(acetoxy)ethylsulfur Pentafluoride.—To a mixture of 3.53 g. (0.0207 mole) of SF_5CH_2CHO[6] and 11.0 g. (0.108 mole) of acetic anhydride was added 1 drop of concentrated sulfuric acid whereupon the temperature rose to about 40°. Distillation of the mixture after standing for 4 hr. gave 5.5 g. (98%) of $SF_5CH_2CH(O_2CCH_3)_2$, b.p. 49° at 0.15 mm., $n^{25}D$ 1.3793.

Anal. Calcd. for $C_6H_9F_5O_4S$: C, 26.5; H, 3.31; S, 11.8. Found: C, 26.9; H, 3.38; S, 11.8.

1-Bromovinylsulfur Pentafluoride.—A mixture of 119 g. (0.38 mole) of $SF_5CHBrCH_2Br$, 58 g. of powdered K_2CO_3 (0.42 mole), and 200 ml. of acetone was stirred for 75 min. during which time the temperature rose to 33°. Gas chromatographic analysis of the reaction mixture indicated that virtually all of the starting material had reacted after 75 min. Distillation through a precision still gave 71 g. of $SF_5CBr{=}CH_2$, b.p. 86°, $n^{25}D$ 1.3814.

Anal. Calcd. for $C_2H_2BrF_5S$: Br, 34.3; F, 40.8; S, 13.8. Found: Br, 34.4; F, 39.9; S, 13.6.

The fluorine and proton resonance spectra (see Table I) of this compound were consistent with the proposed structure.

1,1,2-Tribromoethylsulfur Pentafluoride.—A mixture of 50 g. (0.21 mole) of $SF_5CBr{=}CH_2$ and 34 g. (0.21 mole) of bromine was prepared at room temperature. An exothermic reaction occurred almost immediately, and cooling was applied to lower the temperature to about 5°. The mixture was gradually warmed from 5 to 25° over a period of 1.5 hr., allowed to stand at room temperature overnight, and then irradiated for 2 hr. with a 275-watt G. E. sun lamp located about 12 in. from the flask. Distillation of the product through a Vigreux column gave 74 g. (88%) of $SF_5CBr_2CH_2Br$, b.p. 42° at 0.5 mm., $n^{27}D$ 1.4973.

Anal. Calcd. for $C_2H_2Br_3F_5S$: Br, 61.03; F, 24.19; S, 8.16. Found: Br, 60.46; F, 24.33; S, 7.98.

Both the infrared spectrum and n.m.r. spectra were consistent with this structure.

Silver Salt of Ethynylsulfur Pentafluoride.—To a mixture of 1.7 g. of $AgNO_3$, 3.5 ml. of water, 2.5 ml. of CH_3OH, and 2.2 ml. of concentrated NH_4OH contained in a flask equipped with a magnetic stirrer and a Dry Ice-cooled condenser was added by distillation 0.7 g. of $SF_5C{\equiv}CH$. A white precipitate formed immediately. The solid was removed by filtration and washed with water. There was obtained 1.1 g. of product after air drying for 2 hr.; it decomposed rapidly when heated to 60°. The infrared spectrum showed strong absorption at 4.85 ($C{\equiv}C$), at 10–11 (S-F), and at 2.9 and 6.0 μ owing to water. When this product was dried in a desiccator over P_2O_5, it decomposed.

F^{19} n.m.r. showed absorptions in acetone at −8485, −8460, and −8440 c.p.s. from 1,2-difluoro-1,1,2,2-tetrachloroethane (external) which indicated SF_5.

Attempts to obtain good elemental analyses were thwarted by the decomposition of the silver salt on drying. A sample dried in high vacuum at room temperature for 1 hr. gave 35.0% Ag (calcd., 41.5%). A sample air dried for 1 week gave 33.7% Ag and 14.7% F (calcd., 36.7%).

Acknowledgment.—We wish to thank Messrs. C. B. Matthews, H. Foster, R. J. Berndt, and C. G. Wortz and Miss N. E. Schlichter for help in obtaining and interpreting spectral and dipole moment data. We are indebted to Dr. C. W. Tullock for uncovering the first lead to a synthesis of $SF_5C{\equiv}CH$.

The Pyridinolysis of Diaryl Methyl Phosphates

D. WENDELL OSBORNE

Edgar C. Britton Research Laboratory, The Dow Chemical Company, Midland, Michigan

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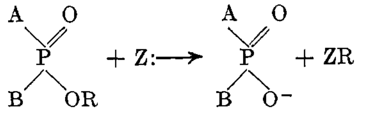
Di(*para*-substituted phenyl) methyl phosphates (I) containing NO_2, CN, Br, Cl, H, and $OCH_2C_6H_5$ groups have been synthesized and their reaction with pyridine to form N-methylpyridinium di(*para*-substituted phenyl) phosphates studied. The reaction is facilitated by electron-withdrawing groups and has a Hammett ρ-value of +1.10. It is characterized by a small activation energy and log *PZ* of about 10.2 kcal./mole and 4.7, respectively. The n.m.r. chemical shifts of the methyl groups of I also generally increase with the electron-attracting ability of the substituent.

Aliphatic esters of phosphoric acid react with many nucleophilic reagents including amines,[1] phenols,[2] thiourea,[3] and mercaptide ions[4] by displacement on carbon to form alkylated products (reaction 1). Although these alkylation reactions are well known, very little has been reported about the effect of the substituents attached to phosphorus on them. Qualitatively, it has been observed that the rate of reaction increases with the electron-attracting ability of the substituents.[5-8] For example, dimethyl phosphoramidates react with triethylamine faster than do methyl phosphorodiamidates,[5] and the relative rates of reaction of $(CH_3O)_2P(O)Y$ with tertiary amines fall in the order $Y = H > SCH_3 > OCH_3 > CH_3$.[7] There is, however, a scarcity of quantitative data and the studies are greatly complicated by uncertainty in assigning relative steric and electronic properties to substituents attached directly to phosphorus.



(1)

In order to obtain quantitative information about the effect of substituents on the reactivity of phosphate esters as alkylating agents, the reaction of a series of di(*para*-substituted phenyl) methyl phosphates, I, with pyridine has been studied. Since the substituents in this series cannot interact directly with the phosphorus atom and steric effects are essentially constant, the relative rates of reaction should be a reflection of only the electronic effect of the substituents. This system also doubles the electronic effect, which was expected to be

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[1] J. H. Billman, A. Radike, and B. W. Mundy, *J. Am. Chem. Soc.*, **64**, 2977 (1942).

[2] C. R. Noller and G. R. Dutton, *ibid.*, **55**, 424 (1933).

[3] J. B. Parker and T. D. Smith, *J. Chem. Soc.*, 442 (1961).

[4] R. G. Harvey and E. V. Jensen, *J. Org. Chem.*, **28**, 470 (1963).

[5] J. Cheymol, P. Chabrier, M. Selin, and T. N. Thanh, *Compt. rend.*, **259**, 1240 (1963).

[6] P. Chabrier, N. T. Thuong, C. Clergue, and E. Larrant, *ibid.*, **257**, 2846 (1963).

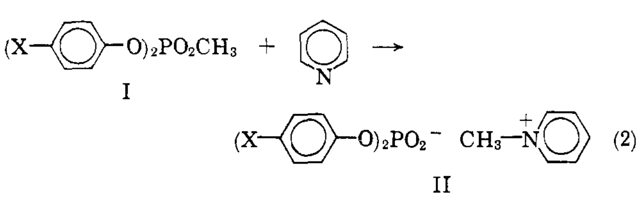
[7] P. Chabrier, N. T. Thuong, and C. Clergue, *ibid.*, **257**, 697 (1963).

[8] C. Stolzer and A. Simon, *Ber.*, **96**, 453 (1963).

small, and eliminates possible side reactions by having only one alkyl group.

The demonstration that many insecticidal phosphorus esters, including O,O-dimethyl O-2,4,5-trichlorophenyl phosphorothioate,[9] O,O-dimethyl O-*p*-nitrophenyl phosphorothioate,[10] and O,O-dimethyl S-(N-methylcarbamoylmethyl) phosphorodithioate[11] are converted to nontoxic monodemethylated derivatives in mammals suggests that a better understanding of this type of reaction could be important in the study of the toxicology and persistence of these compounds.

Kinetics.—Di(*para*-substituted phenyl) methyl phosphates (I, X = NO_2, CN, Br, Cl, H, and $OCH_2C_6H_5$) were found to react quantitatively with pyridine by displacement on carbon to form N-methylpyridinium di(*para*-substituted phenyl) phosphates, II (reaction 2).


I

II

(2)

The product salts, which are hygroscopic and difficult to handle, were converted to the corresponding dicyclohexylammonium di(*para*-substituted phenyl) phosphates, III, for isolation and identification (Table I).

Table I

Dicyclohexylammonium Di(*para*-substituted phenyl) Phosphates

Substituent	M.p., °C.	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N
NO_2	191–192	55.3	6.19	8.07	55.4	6.11	8.14
CN	166.5–168	64.9	6.70	8.73	65.0	6.43	8.16
Br	167–168	48.9	5.48	2.33	49.1	5.16	2.33
Cl	159.5–161	57.6	6.44	2.80	57.7	6.27	3.03
H	188–189.5	66.9	7.94	3.25	67.3	8.02	3.21
$OCH_2C_6H_5$	169–169.5	71.0	7.21	2.18	70.8	7.26	2.19
H, NO_2	197–198.5	60.5	6.98	5.88	60.7	6.96	5.76

The salt II (X = H) was, however, isolated in one case. The presence of the N-methylpyridinium ion in each of the products was confirmed by the observation of a singlet n.m.r. absorption at about −4.55 p.p.m. (from TMS), which can be attributed to its methyl protons. The exact chemical shift varied slightly depending on the anion present. The straightforward, quantitative nature of the reaction was demonstrated by the lack of extraneous absorptions in the n.m.r. spectra of the reaction mixtures and by the observation that the sum of the concentrations of I and II remained constant throughout the reactions with the final concentration of II equal to the initial concentration of I (*vide infra*).

Kinetic studies were made at 30° in excess pyridine as solvent. The reactions were followed by observation of the decrease with time of the integrated intensity of the methyl proton n.m.r. absorptions of I relative to the constant absorption of the methyl protons of toluene, which was added as a standard. The increase in the N-methylpyridinium ion methyl proton absorption with time was also determined in this manner. The data from a typical run are given in Table II. Plots of log [I] against time were found to be linear over several half-lives and to have correlation coefficients of 0.941 to 0.999 indicating the reactions are pseudo first order under these conditions. The derived rate constants, which were calculated by the least-squares method, are given in Table III. Duplicate runs gave rate constants which agreed within two standard errors. The combined concentration of I and II was found to be unchanged throughout each of the reactions with standard deviations of 1.2 to 3.7%. This compares reasonably well with the expected 2% error in integration,[12] and confirms the validity of the analytical method. The concentration of phosphate ester was not precisely the same for each of the compounds or for the duplicate runs. The nitro derivative, in particular, was run at a lower concentration owing to its lack of solubility. The rate constant for I (X = H), however, was found to be unchanged at concentrations between about 0.38 and 0.69 *M* which covers the range involved; thus, as expected for first-order reactions, this should not introduce a serious error.

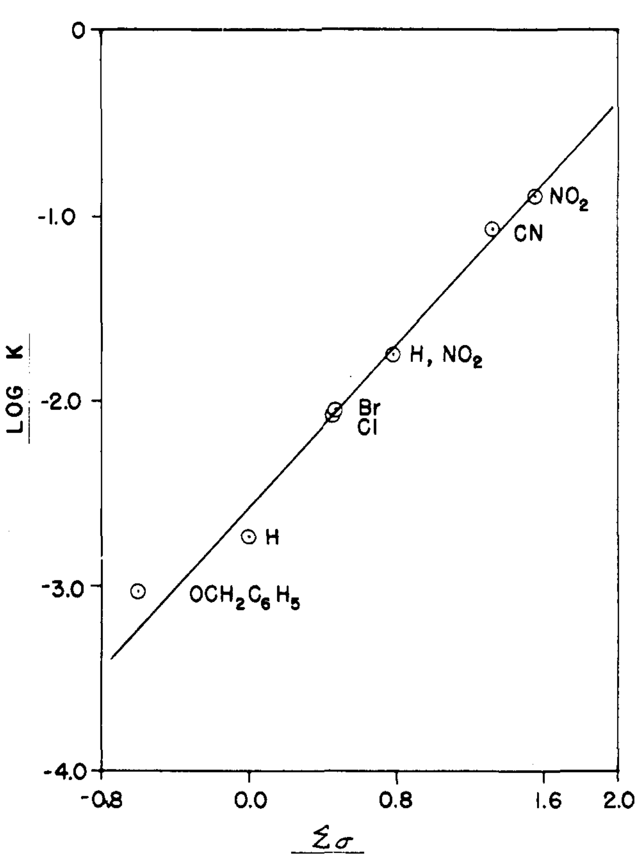


Fig. 1.—Hammett plot for pyridinolysis of di(*para*-substituted phenyl) methyl phosphates.

Analysis of the rate constants by means of the Hammett equation (Fig. 1) yields ρ +1.10 (standard error = 0.04, correlation coefficient = 0.995, σ = 0 ordinate intercept = −2.574). This indicates the reaction is facilitated quite markedly by electron-attracting groups in view of the eight atoms separating the substituents from the reaction center. The influence is similar to ρ 1.3 found for the hydrolysis of substituted phenyl diethyl phosphates at pH 9.5, which involves displace-

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[9] F. W. Plapp and J. E. Casida, *J. Agr. Food Chem.*, **6**, 662 (1958).

[10] W. C. Danterman, J. E. Casida, J. B. Knaak, and T. Kowalczyk, *ibid.*, **7**, 188 (1959).

[11] F. W. Plapp and J. E. Casida, *J. Econ. Entomol.*, **51**, 800 (1958).

[12] Model A-60 Analytical N.m.r. Spectrometer System Instruction Manual, Varian Associates, Palo Alto, Calif., 1962.

TABLE II

PYRIDINOLYSIS OF DI-*p*-BROMOPHENYL METHYL PHOSPHATE

Time, min.	Ester-toluene[a]	$C_5H_5NCH_3^+$-toluene[a]	(Ester + $C_5H_5NCH_3^+$)-toluene[a]	δ, p.p.m.	
				Ester CH_3	$C_5H_5NCH_3^+$
0	1.248[b]	0.000[b]	1.248[b]	...	...
6	1.152	0.054	1.206	−3.92	...
38	0.928	0.318	1.246	−3.94	−4.60
67	0.730	0.512	1.242	−3.96	−4.61
102	0.505	0.693	1.198	−3.95	−4.62
147	0.340	0.895	1.235	−3.96	−4.63
198	0.215	1.003	1.218	−3.96	−4.64
278	0.113	1.160	1.273	−3.97	−4.63

[a] Ratio of concentrations; toluene concentration is constant. [b] Concentration of solution prepared.

TABLE III

RATES OF PYRIDINOLYSIS AND N.M.R. PARAMETERS OF DI(*para*-SUBSTITUTED PHENYL) METHYL PHOSPHATES

Substituents	$k \times 10^3$ min.$^{-1}$ [a]	S.E. $\times 10^3$ [a]	Av. concn. of I + II[b,c]	δ of CH_3, p.p.m. $CDCl_3$[d,e]	Δδ (H-X), p.p.m.		J (H to P), c.p.s. $CDCl_3$[g]	$^1/_2\Sigma\sigma$[h]
					$CDCl_3$[e,f]	C_5H_5N[e,f]		
NO_2	129	5	0.69 (0.01)	−4.038	0.080	0.17	11.95	0.778
CN	86.0	2.1	1.14 (0.02)	−4.007	0.049	0.12	11.8	0.660
NO_2, H	17.7	0.4	1.28 (0.03)	−3.997	0.039	0.09	11.7	0.389
Br	8.97	0.17	1.23 (0.03)	−3.957	−0.007	0.03	11.7	0.232
Cl	8.28	0.13	1.35 (0.02)	−3.951	−0.001	0.04	11.8	0.227
H	1.88	0.03	1.33 (0.03)	−3.958	...	...	11.6	0.000
$OCH_2C_6H_5$	0.953	0.026	1.10 (0.02)	−3.920	−0.038	0.01	11.6	−0.0251[i]

[a] At 30 ± 2° in excess pyridine as solvent; average of two or more runs. [b] Typical run using arbitrary but internally consistent molar units; standard deviation in parenthesis. [c] I and II as defined in the text. [d] Side-band technique used for measurements; probable error, 0.003 p.p.m. [e] Extrapolated to infinite dilution. [f] Δδ (H–X) is the difference in chemical shift between the methyl protons of I, X = H, and I, X = other than H. [g] Probable error, ±0.1 c.p.s. [h] σ-Values from *para*-substituted benzoic acid acidity [D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, **23**, 420 (1958)]. [i] Calculated from the rate of hydrolysis of ethyl *p*-benzyloxybenzoate [B. Jones and J. Robinson, *J. Chem. Soc.*, 3845 (1955)].

ment on phosphorus.[13] A larger value of 1.90 was obtained at pH 7.6.[14] It is also similar to the ρ of about 1 estimated for the reaction of substituted methyl benzoates with triethylamine.[15]

The efficient transmission of electronic charge through the phosphate group observed is in good agreement with the molecular orbital model of phosphates proposed by Cruickshank.[16] The two pentacentric π-bond molecular orbitals employed in this theoretically derived structure involve empty d-orbitals of phosphorus and the unshared p-electrons of each of the neighboring oxygen atoms and have electron distributions which are highly dependent upon the availability of electrons at each of the oxygen atoms.[16,17] Consequently, electronic effects, such as those due to X in I, should be efficiently transmitted through phosphate groups by deformation of π-orbitals. This model also demands that each of the two substituents of I influence the electronic structure independently. The rate of pyridinolysis of methyl *p*-nitrophenyl phenyl phosphate (Table III) which falls within one standard error of the 1.91×10^{-2} min.$^{-1}$ value calculated from the Hammett plot obtained utilizing only the symmetrically substituted phosphates, I, gives evidence that this is the case.

The Arrhenius thermodynamic parameters of the reaction of diphenyl methyl phosphate (I, X = H) were calculated from the rate constants at 30° (1.88×10^{-3} min.$^{-1}$), 40° (4.41×10^{-3} min.$^{-1}$), 60° (7.11×10^{-3} min.$^{-1}$), and 80° (2.79×10^{-2} min.$^{-1}$). The low energy of activation of 10.2 ± 1.9 kcal./mole and small frequency factor (log *PZ*) of 4.7 ± 1.3 obtained reflect the similarity of reaction 2 with the Menschutkin reaction of methyl iodide with pyridine. Values of 13.2 to 14.9 kcal./mole and 4.3 to 7.6 have been established for the methyl iodide reaction in nonpolar solvents.[18] This suggests that a highly ordered but energetically favorable transition state including at least one molecule of pyridine is involved in the reaction. The uncertainty in the values, which can be attributed partially to the relatively poor temperature control, precludes a more detailed interpretation.

N.m.r. Chemical Shifts.—The n.m.r. chemical shifts and coupling constants (P to H) of the methyl group of I were also found to correlate qualitatively with the Hammett σ-constants of X, both generally increasing with increasing σ-values (Table III). In deuteriochloroform solvent ranges of δ = 0.118 p.p.m. and *J* = 0.35 c.p.s. were observed. Similar effects were observed in pyridine. Thus, the substituents of I affect the electron density of the distant methyl group in the ground state as well as in the transition state for the reaction with nucleophilic reagents. The correlations were not, however, good enough to allow a reliable prediction of reaction rates from n.m.r. data. Solvent–phosphate interactions, such as hydrogen bonding,[19] undoubtedly account for some of the deviation in chemical shifts.[20] The chemical shifts given are extrapolations to infinite dilution. These observations are in general agreement with the reported qualitative correlation between Taft's σ*-constants and the chemical

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[13] R. L. Metcalf and T. R. Fukuto, *J. Agr. Food Chem.*, **4**, 930 (1956).

[14] W. N. Aldrich and A. N. Davidson, *Biochem. J.*, **51**, 62 (1952).

[15] L. P. Hammett and H. L. Pflueger, *J. Am. Chem. Soc.*, **35**, 4079 (1933).

[16] D. W. J. Cruickshank, *J. Chem. Soc.*, 5486 (1961).

[17] H. H. Jaffe, *J. Phys. Chem.*, **58**, 185 (1954).

[18] N. J. T. Pickles and C. N. Hinshelwood, *J. Chem. Soc.*, 1353 (1936).

[19] L. F. Audrieth and A. D. F. Toy, *J. Am. Chem. Soc.*, **64**, 1553 (1942).

[20] G. Martin and A. Besnard, *Compt. rend.*, **257**, 2463 (1963).

TABLE IV

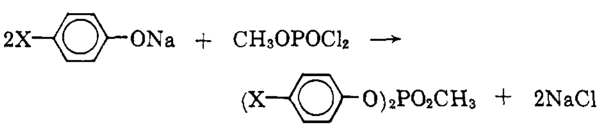
DI(*para*-SUBSTITUTED PHENYL) METHYL PHOSPHATES

Substituents	Yield, %	B.p. (μ) or m.p., °C.	$n^{25}D$	Calcd., % C	Calcd., % H	Calcd., % P	Found, % C	Found, % H	Found, % P
NO_2	14	140–141[a]							
CN	29		1.5600	57.3	3.53	9.86	57.2	3.66	9.44
Br	38	115–120 (0.3)	1.5775	37.0	2.63	7.33	37.0	2.69	6.92
Cl	53	100–102 (0.3)	1.5510	46.9	3.33	9.31	46.7	3.20	9.56
H	48	77–81 (0.3)[b]	1.5356[b]						
$OCH_2C_6H_5$	24	53–54.5		68.1	5.28	6.50	65.5	5.28	6.48
H, NO_2	26	120–122 (0.2)	1.5585	50.5	3.91	4.53[c]	50.2	3.83	4.45[c]

[a] J. A. A. Ketelaar and G. R. Gersmann [*J. Am. Chem. Soc.*, **72**, 5777 (1950)] gives m.p. 141–142.5°. [b] Lit.[23] b.p. 125° (0.03 mm.), $n^{25}D$ 1.5337. [c] % N.

shift and coupling constant of the methyl protons in the system $(A)(B)P(O)OCH_3$ [where A and B are F, Cl, $CO_2C_2H_5$, SCH_3, OH, OCH_3, $N(CH_3)_2$, and CH_3].[21]

Synthesis of Phosphates.—The di(*para*-substituted phenyl) methyl phosphates (I, X = NO_2, CN, Br, Cl, and $OCH_2C_6H_5$) were prepared by the reaction of methyl phosphorodichloridate with sodium *para*-substituted phenoxides (reaction 3). The reactions, which


(3)

were carried out at ambient temperatures in inert solvents, were complete in 3 hr. The yields obtained were low, 14–53%, but no attempt was made to find the optimum conditions. A similar synthesis of I (X = CO_2CH_3) has been reported.[22] The sodium phenoxides required were prepared with either sodium methylate or sodium hydride. The yields and properties of these compounds are given in Table IV.

Diphenyl methyl phosphate[23] was prepared by the reaction of diphenyl phosphorochloridate with methanol and triethylamine. The rapid, exothermic reaction gave a 48% yield of the product. Methyl *p*-nitrophenyl phenyl phosphate was synthesized from phenyl phosphorodichloridate by consecutive reactions with *p*-nitrophenol and methanol, both using triethylamine as the acid acceptor. The over-all yield was 26%. These compounds are also summarized in Table IV.

The liquid phosphates, except I (X = CN), were purified by repeated low-pressure distillations until vapor phase chromatographic analysis indicated <1% of impurities were present. The cyano compound, however, was unstable to heat and was purified by elution chromatography on silica gel.

Experimental

Kinetics.—A 0.615 *M* solution of toluene in pyridine was prepared from freshly distilled reagents and used in all the reactions. Approximately 0.6 *M* solutions of substrate in this were prepared by weighing 0.40-mmole portions of I into n.m.r. sample tubes and at the initial time adding 0.50 ml. of solvent. The samples were placed in a water bath at 30.00 ± 0.02°. Periodically the samples were transferred to a Varian A-60 n.m.r. spectrometer at 30 ± 2°[24] and the spectrum was scanned in the −6- to −2-p.p.m. (from TMS) region and integrated two or more times. The solutions involving I (X = NO_2 and CN) and I (X = H) at higher temperatures were kept in the spectrometer throughout the run because of their rapid rates of reaction. The integrated absorptions of the methyl groups of I, II, and toluene were recorded along with the chemical shifts of I and II. An example is given in Table II. The rates were calculated from plots of ln [I]/[toluene] *vs.* time, the slopes and standard errors of which were determined by the least-squares method. The average values of ([I] + [II])/[toluene] and their standard deviations were also computed (Table III).

Isolation of Products.—The reaction mixtures were allowed to evaporate to dryness and the residues were dissolved in aqueous ethanol. The resulting solutions were acidified with 0.1 *N* hydrochloric acid and then treated with enough dicyclohexylamine to make them basic. After dilution of the mixtures with water the precipitates were filtered and washed with water and hexane to obtain the dicyclohexylammonium salts. These can be recrystallized from mixtures of ethyl acetate and ethanol. The physical constants and analytical data are given in Table I.

Isolation of N-methylpyridinium diphenyl phosphate was accomplished by extraction of the reaction mixture with several small portions of hexane and recrystallization of the remaining solid from a chloroform–carbon tetrachloride mixture. A small amount of white solid containing some water of hydration, determined by infrared analysis, was obtained, m.p. 63–64°.

Anal. Calcd. for $C_{18}H_{18}NO_4P$: N, 4.08. Found: N, 3.75.

Synthesis of Di-*p*-chlorophenyl Methyl Phosphate.—A solution of 25.7 g. (0.20 mole) of *p*-chlorophenol and 50 ml. of 4 *N* sodium methoxide in methanol in 200 ml. of benzene was distilled to remove the methanol. After 150 ml. of solvent was removed it was replaced with 150 ml. of benzene. This was repeated twice (total distillate 450 ml.). The resulting mixture was cooled to 6° with an ice bath and methyl phosphorodichloridate was added dropwise over a 20-min. period at 6–12°. The mixture was allowed to warm to room temperature and stir overnight. It was then filtered, the precipitate was washed with benzene, and the combined benzene filtrates were washed twice with water. The resulting solution was evaporated to dryness and distilled twice through a 1-ft. Claisen head still at 0.2 μ. The colorless oil which distilled at 100–102° (17.80 g., 53.4% theory), was 99.9% pure by vapor phase chromatography. Compounds I (X = Br, NO_2, CN, and $OCH_2C_6H_5$) were prepared similarly. The yields, physical properties, and analytical data are given in Table IV.

Synthesis of Diphenyl Methyl Phosphate.—To a solution of 53.7 g. (0.20 mole) of diphenyl phosphorochloridate in 300 ml. of benzene was added a mixture of 9.6 g. (0.30 mole) of methanol and 20.2 g. (0.20 mole) triethylamine. The addition was made over a 15-min. period. The temperature rose to a maximum of 44° and triethylammonium chloride precipitated immediately. The mixture was stirred for 2 hr. and filtered, and the salt was washed with benzene. The filtrate and washed with water, evaporated to dryness, and distilled twice through a 1-ft. Claisen head still at about 0.3 μ. The 25.6 g. (48.4% theory) of colorless oil obtained at 72–81° was 99.5% pure by vapor phase chromatography (Table IV).

Synthesis of Methyl Phenyl *p*-Nitrophenyl Phosphate.—Phenyl phosphorodichloridate, 52.75 g. (0.25 mole), and *p*-nitrophenol, 34.8 g. (0.25 mole), were dissolved in 200 ml. of carbon tetrachloride and triethylamine, 25.2 g. (0.25 mole), added dropwise over a 25-min. period. A white precipitate began to form immediately and the temperature rose to a maximum of 57.5°. The mixture was stirred for 2 hr. It was filtered and the salt

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[21] G. Mavel and G. Martin, *J. chim. phys.*, **59**, 762 (1962).

[22] J. Mather and A. A. B. Brown, British Patent 912,287 (Dec. 5, 1962).

[23] F. Cramer, K. Paweljik, and F. W. Lichtenthaler, *Ber.*, **91**, 1555 (1958).

[24] The precision of the temperature control of the spectrometer is ±2°: Variable Temperature System for A-60 Analytical Spectrometers Instruction Manual, Varian Associates, Palo Alto, Calif., 1963.

was washed with more solvent. The combined filtrates were treated with a mixture of methanol, 9.20 g. (0.29 mole), and triethylamine, 25.2 g. (0.25 mole). The addition required 10 min. and the temperature rose to a maximum of 69°. The mixture was stirred for 2 hr. and filtered, and the solids were washed with more solvent. Evaporation of the carbon tetrachloride left a dark oil which was distilled three times at about 0.2 μ to obtain a pale yellow oil, 20.2 g. (26.2% theory). This was 99% pure by vapor phase chromatography. Its physical constants and analyses are given in Table IV.

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Some Reactions and Properties of 2-Phenyl-3,3-dimethyl-3,4,5,6-tetrahydropyrazine

CALVIN L. STEVENS, K. GRANT TAYLOR,[1] AND MORTON E. MUNK

Department of Chemistry, Wayne State University, Detroit, Michigan

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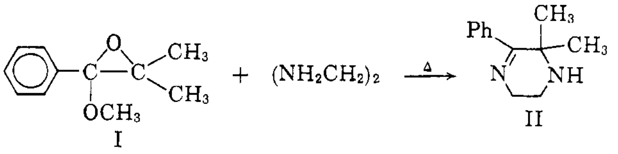
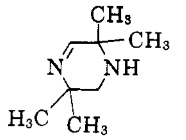
The reaction of epoxy ether I with ethylenediamine produced the 3,4,5,6-tetrahydropyrazine II in high yield. The reduction and hydrolysis reactions of II were studied. Also, the use of the >C=N function of II as a blocking group in the synthesis of unsymmetrically N-substituted piperazines was briefly investigated.

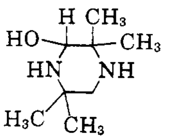
When epoxy ether I was refluxed with ethylenediamine in toluene, 2-phenyl-3,3-dimethyl-3,4,5,6-tetrahydropyrazine (II) was isolated in 91% yield. Relatively little is reported concerning the chemistry of this type of tetrahydropyrazine with only two authors reporting chemical characterization in the literature. Aston[2] and co-workers prepared three tetrahydropyrazines *via* the Grignard reaction on 1,2,2,5,5-pentamethyldihydropyrazinium iodide (1). More recently Plante[3] and co-workers isolated tetrahydropyrazine III from the Raney nickel dehydrogenation of 5-amino-2,2,5-trimethyl-3-azahexan-1-ol and characterized it as the monohydrate dihydrochloride salt, formulated as IV.



 (1)

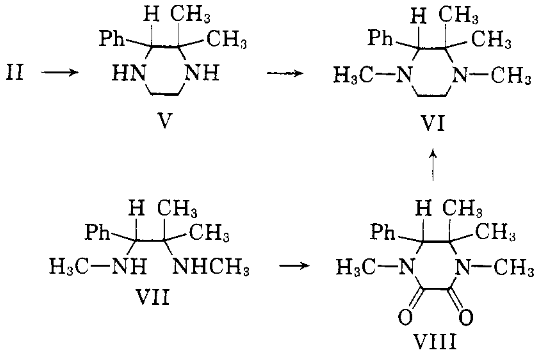


III

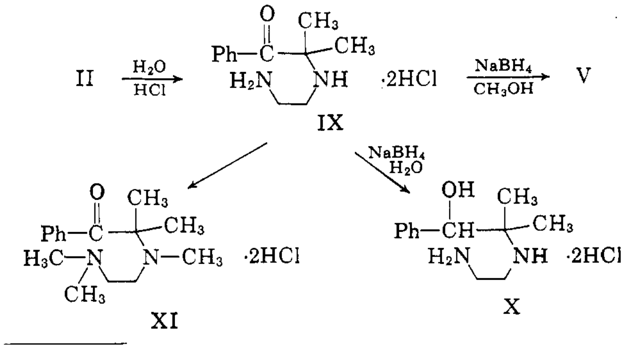


IV

The structural assignment of II was supported by its infrared spectrum which indicated NH absorption at 3.08 and a strong C=N band at 6.13 μ and confirmed by the following sequence of reactions. Sodium borohydride reduction of II afforded piperazine V in high yield. The tetramethylpiperazine VI was then prepared from V by the Clarke–Eschweiler procedure.[4] Piperazine VI was then synthesized by an alternate route. Diamine VII[5] was converted with oxalyl chloride[6] to oxamide VIII which in turn was reduced with lithium aluminum hydride to VI, identical with that prepared *via* tetrahydropyrazine II.



The cyclic imine II provided an interesting example for a hydrolysis study. An ultraviolet spectrum of II in ethanol showed only end absorption; however, in 5 *N* hydrochloric acid a maximum developed at 254 mμ (ϵ 6500). These values were close to those reported for α-amino ketones[7] and suggested the existence in solution of 2-(2-aminoethylamino)-2-methylpropiophenone dihydrochloride (IX). Indeed, when an aqueous hydrochloric acid solution of II was evaporated to dryness, the amino ketone dihydrochloride IX was isolated in high yield. That the structure of IX was as shown and



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(1) Abstracted from a portion of the Ph.D. Thesis of K. G. Taylor, Wayne State University, 1963.

(2) J. G. Aston, D. Ailman, C. Scheuermann, and J. Koch, *J. Am. Chem. Soc.*, **56**, 1163 (1934).

(3) L. T. Plante, W. Lloyd, C. Shilling, and L. Clapp, *J. Org. Chem.* **21**, 82 (1956).

(4) Piperazines V and VI were conveniently isolated as their hydrochloride salts.

(5) Prepared by reduction of the corresponding α-aminoimine, made in turn from the epoxy ether I *via* the α-amino ketone: *cf.* ref. 7.

(6) The procedure of B. Ambrecht, L. Rice, C. Grogan, and E. Reid, [*J. Am. Chem. Soc.*, **75**, 4829 (1953)] was used.

(7) C. L. Stevens and C. H. Chang, *J. Org. Chem.*, **27**, 4392 (1962).