

oate (XI), m.p. 187–195°. Crystallization from methylene chloride-Skellysolve B mixture gave an analytical sample, m.p. 194–197°, $[\alpha]_D +147^\circ$; $\lambda_{\text{max}}^{\text{EtOH}}$ 238 m μ , a_M 23,100.

Anal. Calcd. for $C_{23}H_{32}O_4$: C, 74.16; H, 8.66. Found: C, 74.19; H, 8.74.

11 β ,21-Dihydroxy-11-methylpregna-4,17(20)-[cis]-dien-3-one (IVa). A mixture of 3.19 g. of methyl 11 β -hydroxy-11-oxopregna-4,17(20)-[cis]-dien-21-oate, 40 mg. of *p*-toluenesulfonic acid monohydrate, and 3 ml. of redistilled pyrrolidine in 75 ml. of benzene was heated under reflux, with a water take-off, for 1.5 hr. Then 65 ml. of benzene was removed by distillation and the remaining solvent was removed by distillation *in vacuo* below 45°. The crystalline residue of the 3-pyrrolidyl amine was dissolved in 40 ml. of benzene and added to a stirred suspension of 2.0 g. of lithium aluminum hydride in 100 ml. of ether. The mixture was stirred 1.5 hr., then 20 ml. of ethyl acetate was added slowly, followed by 20 ml. of water. The remaining ether was removed by distillation *in vacuo*, then 120 ml. of methanol was added and the mixture was stirred 20 min. at 45°. After addition of 30 ml. of 5% aqueous sodium hydroxide, stirring was continued 15 min. at 50°, then 8 ml. of glacial acetic acid was added and the methanol was removed *in vacuo*. A solution of 10 ml. of concentrated sulfuric acid in 200 ml. of water was added and the mixture was placed in the refrigerator overnight, giving 2.893 g. of IVa, m.p. 195–202°. Crystallization from methanol-water gave 2.258 g., m.p. 200–208°. A sample was crystallized from aqueous pyridine, aqueous acetic acid, and ethyl acetate, and melted at 205–211°.

The acetate (IVb), prepared as described above, had m.p. 112–115°, $[\alpha]_D +119^\circ$. The infrared spectra (Nujol mull) of samples of IVb prepared by the two routes were different, but chloroform solution spectra were identical, indicating that the samples were polymorphic. The same is true of the two samples of IVa having such different melting points.

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The Chemistry of the Aliphatic Esters of Phosphorodithioic Acids. IV. *O,O,S*-Trialkyl Phosphorodithioates by the Reaction of *O,O*-Dialkyl Hydrogen Phosphorodithioates with Their Salts¹

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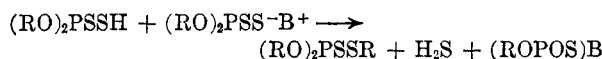
The preparation of trialkyl phosphates by the disproportionation of a mixture of a dialkyl hydrogen phosphate and its sodium salt at 300° has been reported.²

(1) For preceding article in this series, see W. E. Bacon and W. M. LeSuer, *J. Am. Chem. Soc.*, **76**, 670 (1954).

(2) G. M. Kosolapoff, "Organo-phosphorus Compounds," John Wiley & Sons, New York, 1950, p. 231.

In the presence of acid, the zinc salts of *O,O*-dialkyl phosphorodithioates have been reported to decompose into mixtures of olefins, hydrogen sulfide and meta-thiophosphate polymers at 130–180°.³

The present investigation has shown that the *O,O*-dialkyl hydrogen phosphorodithioates react with their amine salts to yield *O,O,S*-trialkyl phosphorodithioates. The reaction proceeds smoothly at temperatures above 70° in benzene and dioxane, and appears to be general for the alkyl esters. In agreement with the equation shown below, only one alkyl group was transferred from the alkylating moiety in the reactions studied, and H₂S was evolved simultaneously. The yields were in the range of 40–97% based on this equation.



The reaction rate was followed readily by titration of the unreacted acid in the reaction mixture. Table I shows the reaction rates, expressed as the time required for 50% reaction, for the reaction of *O,O*-diethyl hydrogen phosphorodithioate with its salts in refluxing benzene solution. The results indicated that the reaction rate increased with the increasing base strength of the unhindered amines; but the rates decreased with increasing substitution around the nitrogen atom of the amine.

TABLE I
REACTION RATES OF *O,O*-DIETHYL HYDROGEN PHOSPHORODITHIOATE WITH ITS AMINE SALTS

Salt	Hours required for 50% reaction
Triethylamine	1.8
Piperidine	2.4
Pyridine	3.8
α -Picoline	7.2
Aniline	7.8
2,6-Lutidine	11.6

The diaryl hydrogen phosphorodithioates do not undergo this reaction as shown by the fact that *O,O*-diphenyl hydrogen phosphorodithioate with its triethylamine salt gave no decrease in acidity after 5 hr. reflux in benzene.

Table II shows the reaction rates of several *O,O*-dialkyl hydrogen phosphorodithioates with their triethylamine salts in benzene solution, expressed as the time required for 50% reaction. In the group tested, the acids prepared from primary alcohols reacted faster than those prepared from secondary alcohols. Within each series the reaction rates decreased with increasing molecular weight.

(3) G. W. Kennerly, G. L. M. Christopher, and C. M. Judson, Abstracts of Papers, 122nd Annual Meeting, American Chemical Society, Atlantic City, N. J., Sept. 14–19, 1952, p. 31M.

TABLE II

REACTION RATES OF *O,O*-DIALKYL HYDROGEN PHOSPHORODITHIOATES WITH THEIR TRIETHYLAMINE SALTS

(RO) ₂ PSSH R =	Hours required for 50% reaction
Ethyl	1.8
<i>n</i> -Propyl	2.6
<i>n</i> -Butyl	2.6
<i>n</i> -Hexyl	3.4
2-Ethylhexyl	14.5
<i>i</i> -Propyl	15.2
<i>s</i> -Butyl	17.5
4-Methyl-2-pentyl	39.5

TABLE III

O,O,S-TRIALKYL PHOSPHORODITHIOATES (RO)₂PSSR

R	Amine	Mole Ratio ^a	Sol- vent	Time (hrs.)	Yield of Ester (%) ^b
C ₂ H ₅	C ₅ H ₅ N	1	A	38.5	58
C ₂ H ₅	C ₅ H ₅ N	2	B	4	91
C ₂ H ₅	C ₅ H ₅ N	5	A	21	84
C ₂ H ₅	C ₅ H ₅ N	5	B	8	63
C ₂ H ₅	(C ₂ H ₅) ₃ N	1	B	5	0
C ₂ H ₅	(C ₂ H ₅) ₃ N	2	B	6	41
C ₂ H ₅	(C ₂ H ₅) ₃ N	2.5	B	5	76
C ₂ H ₅	(C ₂ H ₅) ₃ N	5	A	21	84
C ₂ H ₅	(C ₂ H ₅) ₃ N	15	A	21	56
C ₂ H ₅	C ₅ H ₁₁ N	3	B	4	69
C ₂ H ₅	C ₅ H ₁₁ N	2	B	3	57
<i>n</i> -C ₃ H ₇	C ₅ H ₁₁ N	3	B	7	83
<i>i</i> -C ₃ H ₇	C ₅ H ₁₁ N	2	B	6	86
<i>i</i> -C ₃ H ₇	(C ₂ H ₅) ₃ N	3	B	9	69
<i>n</i> -C ₄ H ₉	(C ₂ H ₅) ₃ N	2	A	6	56
<i>s</i> -C ₄ H ₉	(C ₂ H ₅) ₃ N	2	A	17.5	59
<i>m</i> -C ₆ H ₁₃	(C ₂ H ₅) ₃ N	2	A	12.5	58
C ₆ H ₅	(C ₂ H ₅) ₃ N	2	A	5	0

Solvent A = benzene; Solvent B = dioxane. ^a Ratio of *O,O*-dialkyl hydrogen phosphorodithioate to amine. ^b Esters were identified by elemental analysis, and refractive index.

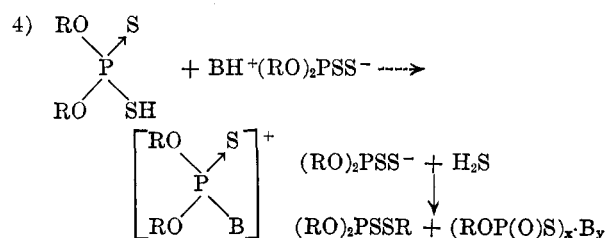
The amine appeared to act catalytically when the aminophosphonothionate complex was soluble in the solvent used for the reaction. This was shown by the reaction of 1 mole of triethylamine with 15 moles of *O,O*-diethyl hydrogen phosphorodithioate. In this reaction a 56% yield of distilled ester was obtained. When pyridine was used, the pyridine-ethyl phosphonothionate complex separated as a benzene-insoluble gum and the reaction stopped when all of the amine had been precipitated. The dialkyl hydrogen phosphorodithioates are strong

acids and are capable of removing the base from the amine-phosphonothionate initially formed, provided it does not escape by settling out.

A weak amine salt of the acid should also undergo the reaction, as some free acid would be present in the equilibrium mixture. Thus, the pyridine salt of *O,O*-diethyl hydrogen phosphorodithioate yielded 58% of the *O,O,S*-triethyl phosphorodithioate when refluxed in benzene. No reaction occurred when the triethylamine salt was refluxed in dioxane.

In general the amine-phosphonothionates were gummy impure materials—only the pyridine complex was obtained in a pure enough form to obtain satisfactory analyses.

The following sequence is suggested as a possible course for the reaction:



The electron shift which results when the ammonium ion approaches the phosphorus atom of the acid molecule culminates in the ejection of H₂S and the simultaneous formation of a carbonium ion which reacts with the *O,O*-dialkyl hydrogen phosphorodithioate ion. The rate determining step would be the approach of the ammonium ion to the phosphorus atom. This would explain the steric factors involved in the reaction rates discussed above.

EXPERIMENTAL

Reactions in benzene. The procedure followed for the reaction of the *O,O*-dialkyl hydrogen phosphorodithioates and their salts in benzene was in general as follows: The *O,O*-dialkyl hydrogen phosphorodithioate was dissolved in benzene and the amine was added slowly with stirring. The solution was heated at the reflux temperature for the period necessary to complete the reaction. Samples were removed at intervals and titrated in order that the course of the reaction might be followed. In some cases a gum-like layer separated from the solution, in which case the benzene layer was decanted from it. The benzene layer was washed successively with water, 5% hydrochloric acid solution, and water. It was dried over anhydrous sodium carbonate, the benzene was removed by distillation, and the residual ester was distilled through a 7-inch Vigreux column.

Reactions in dioxane were carried out in the same manner as above.

TABLE IV
ANALYSES OF *O,O,S*-TRIALKYLPHOSPHORODITHIOATES (RO)₂PSSR

R	B.P.	<i>n</i> _D ²⁵	Calculated		Found	
			P	S	P	S
<i>n</i> -C ₃ H ₇	87° at 0.3 mm.	1.4945	12.1	25.0	11.9	24.8
<i>i</i> -C ₃ H ₇	61.8° at 0.1 mm.	1.4851	12.1	25.0	12.1	25.6
<i>n</i> -C ₄ H ₉	96° at 0.06 mm.	1.4892	10.38	21.49	10.30	21.48
<i>s</i> -C ₄ H ₉	90° at 0.2 mm.	1.4862	10.38	21.49	10.50	21.50
<i>n</i> -C ₆ H ₁₃	Decd. ^a	1.4852	8.10	16.76	8.02	16.95

^a Sample was purified by extraction with 5% KOH, followed by two H₂O washes and dried to 100° at 0.1 mm.

O,O-Diethyl hydrogen phosphorodithioate and its amine salts. Pyridine Salt-Mole Ratio 1:1. Pyridine (19.0 g., 0.25 mole) and 95 g. (0.5 mole) of the acid-ester⁴ in 100 ml. of benzene were refluxed for 6 hr. This reaction yielded 52.2 g. (97%) of *O,O,S*-triethyl phosphorodithioate, b.p. 56–48° at 0.2 mm., n_D^{25} 1.5038.

Anal. Calcd. for $C_6H_{15}O_2S_2P$: P, 14.46; S, 29.93. Found: P, 14.60; S, 29.90.

The gum-like product that separated from the reaction mixture weighed 39 g. It dissolved in water with decom-

position and was soluble in ethyl acetate but insoluble in acetone, petroleum ether (30–60°) and benzene.

Anal. Calcd. for $EtOPOS.C_2H_5N$: P, 15.20; S, 15.75. Found: P, 15.28; S, 15.77.

The yields obtained with other amines, and with the various acid-amine ratios employed, are shown in Table III.

Typical analyses of the esters obtained are shown in Table IV.

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(4) T. W. Mastin, G. R. Norman, and E. A. Weilmuenster, *J. Am. Chem. Soc.*, **67**, 1662 (1945).

Pyridyloxazolidinediones and Related Compounds

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In extension of our work with the pyridylethylated oxazolidinediones^{1,2} and in view of recent interest in pyridyl hydantoins,³ we have investigated

(1) S. L. Shapiro, I. M. Rose, E. Roskin, and L. Freedman, *J. Am. Chem. Soc.*, **80**, 1648 (1958).

(2) S. L. Shapiro, I. M. Rose, E. Roskin, and L. Freedman, *J. Am. Chem. Soc.*, **81**, 386 (1959).

(3) C. Chu and P. C. Teague, *J. Org. Chem.*, **23**, 1578 (1958).

the preparation of pyridyl, picolyl, quinolyl, pyrimidyl, and imidazolylethyl oxazolidinediones of the type I. The compounds prepared have been described in Table I. In addition to the free bases, a number of methiodides of variants of I have been prepared.

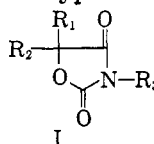
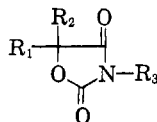


TABLE I. 3-PYRIDYL-OXAZOLIDINEDIONES AND RELATED COMPOUNDS



No.	$R_1^{a,b}$	M.P., ^c B.P. (Mm.), $R_1 = CH_3$, $R_2 = H$	R.S. ^d	Yield, ^e %	Formula	Analyses, % ^f					
						Carbon		Hydrogen		Nitrogen	
						Calcd.	Found	Calcd.	Found	Calcd.	Found
1 ^o	2-Py	134 (0.2)		62	$C_9H_8N_2O_3$	56.3	56.3	4.2	4.4	14.6	14.4
2 ^b	3-Py	119–120	A	33	$C_9H_8N_2O_3$	56.3	56.4	4.2	4.3	14.6	14.4
3	^b	164–166	B	65	$C_{10}H_{11}IN_2O_3$	36.0	35.6	3.2	3.5	8.4	8.1
4	3-CH ₃ -2-Py	126–130 (0.2)		45	$C_{10}H_{10}N_2O_3$	58.3	58.2	4.9	5.5	13.6	13.9
5 ^t	4-CH ₃ -2-Py	88–89	A	32	$C_{10}H_{10}N_2O_3$	58.3	57.8	4.9	4.8	13.6	13.6
6	6-CH ₃ -2-Py	95–96	A	28	$C_{10}H_{10}N_2O_3$	58.3	58.5	4.9	4.9	13.6	13.6
7 ^j	2-Pc	104–108 (0.02)		54	$C_{10}H_{10}N_2O_3$	58.3	57.8	4.9	5.1	13.6	13.2
8	^b	178–180	B	52	$C_{11}H_{13}IN_2O_3$	37.9	37.9	3.8	3.9	8.0	8.4
9	3-Pc	125–128 (0.12)		73	$C_{10}H_{10}N_2O_3$	58.3	58.5	4.9	5.2		
10	^b	151–153	B	88	$C_{11}H_{13}IN_2O_3$	37.9	38.3	3.8	3.9	8.0	8.3
11	4-Pc	112–113	A	58	$C_{10}H_{10}N_2O_3$	58.3	57.9	4.9	4.9		
12	^b	168–171	B	86	$C_{11}H_{13}IN_2O_3$	37.9	38.2	3.8	3.7	8.0	8.3
13 ^k	Im	152–154 (0.4)		46	$C_{10}H_{14}N_2O_2$	53.3	53.4	6.7	7.2		
		$R_1 = CH_3 = R_2$									
14	2-Py	118–119	A	76	$C_{10}H_{10}N_2O_3$	58.3	58.8	4.9	5.2	13.6	13.9
15	^b	163–164	B	10	$C_{10}H_{13}IN_2O_3$	37.9	38.3	3.8	3.7	8.0	7.7
16	3-Py	147–148	A	77	$C_{10}H_{10}N_2O_3$	58.3	58.1	4.9	4.7		
17	^b	201–202	B	84	$C_{11}H_{13}IN_2O_3$	37.9	38.2	3.8	3.8	8.0	8.2
18	4-Py	133–134	A	52	$C_{10}H_{10}N_2O_3$	58.3	58.3	4.9	5.0	13.6	13.9
19	^b	241–244	B	93	$C_{11}H_{13}IN_2O_3$	37.9	38.2	3.8	3.9	8.0	8.4
20	4-CH ₃ -2-Py	178–179	A	76	$C_{11}H_{12}N_2O_3$	60.0	60.1	5.5	5.3	12.7	12.7
21 ^t	2-Pc	59–60	C	44	$C_{11}H_{12}N_2O_3$	60.0	60.4	5.5	5.7	12.7	12.6
22	3-Pc	117–120 (0.05)		86	$C_{11}H_{12}N_2O_3$	60.0	60.8	5.5	5.7	12.7	12.3
23	4-Pc	94–95	A	64	$C_{11}H_{12}N_2O_3$	60.0	60.2	5.5	5.6	12.7	12.7
24	Qn	164–166	A	71	$C_{14}H_{12}N_2O_3$	65.6	65.7	4.7	4.9	10.9	10.7
25	^b	217–218	B	72	$C_{15}H_{15}IN_2O_3$	45.3	45.8	3.8	4.0	7.0	7.0
26	Pm	94–95	C	18	$C_{11}H_{13}N_3O_3$	56.2	56.2	5.6	5.3	17.9	17.8