by the reaction of phosgene with the 5-benzyl ester[11] of L-glutamic acid in tetrahydrofuran according to the procedure of Blout and co-workers.[8] After one recrystallization from ethyl acetate–hexane, the colorless solid melted at 91–93°.

4-(4-Diazo-3-oxobutyl)-2,5-oxazolidinedione, L-Form (IX).—A solution of 2.6 g. (0.01 mole) of the benzyl ester from above was hydrogenated in 70 ml. of anhydrous ethyl acetate over 0.6 g. of 10% Pd–C catalyst at 30 lb. hydrogen pressure for one hour. The catalyst was removed by filtration using Filter-Cel. The filtrate was evaporated *in vacuo* to yield a colorless crystalline solid that weighed 1.65 g. and was presumed to be X. This solid was treated immediately with 15 ml. of thionyl chloride. After 15 minutes of gentle warming (*ca.* 40°), a clear yellow solution resulted. The solution was evaporated *in vacuo*. The resulting yellow oil was redissolved in 20 ml. of dry tetrahydrofuran and the solution was added dropwise with stirring to an ice-cold tetrahydrofuran solution of diazomethane (prepared from 7 g. of nitrosomethylurea). The mixture was allowed to warm to room temperature, and after filtering, it was evaporated *in vacuo*. The orange-yellow gum appeared to be decomposing with the evolution of gas.

6-Diazo-5-oxo-L-norleucine (VIII).—Approximately 1 g. of the crude anhydride IX from above was treated with 15 ml. of water, and normal sodium hydroxide was added to a *p*H of 9. After 30 minutes, the *p*H was adjusted to 6.5 with hydrochloric acid and the solution was frozen and lyophilized to yield 1.2 g. of crude 6-diazo-5-oxo-L-norleucine, $E^{1\%}_{1\,\text{cm}}$ 347 at $\lambda^{\text{H}_2\text{O}}_{\text{max}}$ 275 mμ. The yellow solid was chromatographed on activated carbon as described previously. The amino acid was recrystallized from water–ethanol, yield 48 mg., m.p. 142–150° dec., $E^{1\%}_{1\,\text{cm}}$ 640 at $\lambda^{\text{H}_2\text{O}}_{\text{max}}$ 275 mμ. This product was identical with the 6-diazo-5-oxo-L-norleucine previously described according to the assay on the growth inhibition of *E. coli*.[3b]

DETROIT 32, MICH.

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[11] W. E. Hanby, S. G. Waley and J. Watson, *J. Chem. Soc.*, 3239 (1950).

[CONTRIBUTION FROM THE CHEMICAL CORPS, CHEMICAL RESEARCH DIVISION, CHEMICAL WARFARE LABORATORIES]

Organic Phosphorus Compounds. III.[1] O,O'-Dialkyl Alkylphosphonothioates and O-Alkyl Alkylphosphonochloridothioates

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The lower members of the series of O,O'-dialkyl methyl- and ethylphosphonothioates were prepared from the appropriate alkylphosphonothioic dichlorides and the sodium alkoxides by the method of Razumov and co-workers.[3] Several O-alkyl methyl- and ethylphosphonochloridothioates were prepared from the corresponding alkylphosphonothioic dichlorides and also by a one-batch procedure in which the appropriate alkylphosphonous dichloride in an inert reaction medium was converted successively with one mole equivalent each of an alcohol and an organic base to the corresponding alkyl alkylphosphonochloridite and further by the addition of sulfur to the desired chloridothioate without isolation of the intermediate.

The recent resolution of O-ethyl ethylphosphonothioic acid, $C_2H_5P(O)(OC_2H_5)SH$ or $C_2H_5P(S)(OC_2H_5)OH$, into its optically active isomers[4] made a practical method for the preparation of O-alkyl methyl- and ethylphosphonothioic acids desirable. Dialkyl esters of the type $RP(S)(OR')_2$ (I) and O-alkyl alkylphosphonochloridothioate of the type $RP(S)(OR')Cl$ (II) in which R represents a methyl or ethyl group and R' is an alkyl group seemed to be suitable starting materials for the preparation of the desired O-alkyl alkylphosphonothioic acids, $RP(O)(OR')SH$ or $RP(S)(OR')OH$ (III). Several representatives of the series of the esters I have been prepared previously by Russian investigators according to the following methods: (1) addition of sulfur to the corresponding dialkyl alkylphosphonites[3,5]; (2) reaction of the appropriate alkylphosphonothioic dichloride, $RP(S)Cl_2$ (IV), with sodium alkoxide[3] or with the appropriate alcohol and a base[3,5]; (3) treatment of O,O'-dialkyl sodium phosphothioite, $(R'O)_2P(S)Na$, with an alkyl halide[6]; and (4) reaction of dialkyl alkylanilidophosphonates with carbon disulfide.[7] However, chloridothioates of type II apparently have not been prepared before.

Since the esters I and the chloridothioates II can be converted readily by treatment with one mole equivalent of alcoholic alkali hydroxide to the alkali salts of the corresponding thioic acids III,[8] the preparation of the lower members of both series of derivatives I and II from methyl- and ethylphosphonous dichloride was investigated for the purpose of working out reliable preparative methods which would make these valuable intermediates readily accessible.

According to the methods reported for the esters I, their preparation from the phosphonous dichlorides can be accomplished by two different methods in two steps each. Conversion of the phosphonous dichloride with sulfur to the corresponding IV followed by treatment of the IV with an alcohol in the presence of a suitable hydrogen chloride acceptor[3,5] results in the formation of the desired I. The same products also are obtained when the phosphonous dichloride is first treated with the alcohol and base and the resulting dialkyl alkylphosphonite then treated with one mole equivalent of sulfur.

The addition of sulfur to methyl- and ethylphosphonous dichloride proceeds readily in excellent yields by the method of McIvor, McCarthy and Grant[9] according to which the calculated amount

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[1] Paper II of this series, F. W. Hoffmann and T. R. Moore, THIS JOURNAL, **80**, 1150 (1958).

[2] To whom requests for reprints should be addressed.

[3] A. I. Razumov, O. A. Mukhacheva and Sim-Do-Khen, *Izvest. Akad. Nauk S.S.S.R., Otdel Khim. Nauk*, 894 (1952); *C. A.*, **47**, 10466*c* (1953).

[4] H. Aaron, T. M. Shryne and J. Miller, THIS JOURNAL, **80**, 107 (1958).

[5] B. A. Arbuzov and N. J. Rispolozhenskii, *Izvest. Akad. Nauk S.S.S.R., Otdel Khim. Nauk*, 854 (1952) (*C. A.*, **47**, 9903*f* (1953)).

[6] M. I. Kabachnik and T. A. Mastryukova, *ibid.*, 163 (1953) (*C. A.*, **48**, 3243*e* (1954)); 193 (1956) (*C.A.*, **50**, 13727*g* (1956)).

[7] M. I. Kabachnik and V. A. Gilyarov, *Doklady Akad. Nauk S.S.S.R.*, **96**, 991 (1954); (*C. A.*, **49**, 8842*a* (1955)).

[8] A paper on the preparation of the III by this method is in preparation.

[9] The authors wish to express their gratitude to Drs. McIvor, McCarthy and Grant of the Defence Research Chemical Laboratories,

TABLE I

PHYSICAL AND ANALYTICAL DATA OF O,O′-DIALKYL ALKYLPHOSPHONOTHIOATES, $RP(S)(OR')_2$

R′	Yield, %	B.p. °C.	B.p. Mm.	n^{25}_D	d^{25}_4	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Phosphorus, % Calcd.	Phosphorus, % Found	Sulfur, % Calcd.	Sulfur, % Found
R = CH_3													
CH_3[e]	78[a]	40	4.0	1.4740	....	25.71	25.7	6.47	6.6	22.10	22.66	22.88	22.89
	69[b]	43	4.3	1.4744	1.1377		..		..		...		...
C_2H_5	76	46	2.3	1.4619	1.0503	35.70	35.2	7.79	7.9	18.41	18.60	19.07	19.3
	79[c]	36	1.2	1.4622	....		35.7		7.8		18.42		19.27
n-C_3H_7	74.5	39	0.18	1.4608	1.0092	42.84	42.7	8.73	8.7	15.78	16.10	16.34	16.55
i-C_3H_7	54	42	1.0	1.4512	0.9885		42.8		8.8		15.69		16.21
n-C_4H_9	85.5	51	0.090	1.4605	0.9817	48.19	48.1	9.44	9.4	13.81	14.23	14.30	14.30
n-C_5H_{11}	55A[b,d]	74	.050	1.4618	0.9636	52.35	52.1	9.99	9.9	12.27	12.58	12.71	12.87
	90	74	.080	1.4622	....		..		..		...		...
R = C_2H_5													
CH_3	69[a]	40	2.2	1.4722	1.1017	31.16	31.1	7.19	7.2	20.09	20.29	20.80	21.18
C_2H_5[f]	75[d]	42	1	1.4620	1.0297	39.55	39.5	8.30	8.3	17.00	16.99	17.60	17.60
	69	62	4	1.4622	....		39.9		8.1		17.15		17.52
n-C_3H_7[g]	83	42	0.13	1.4609	0.9958	45.70	45.6	9.11	9.0	14.73	15.00	15.25	15.47
i-C_3H_7	67	48	0.5	1.4521	0.9782		45.5		9.1		14.84		15.34
n-C_4H_9[h]	86	58	0.09	1.4617	0.9758	50.39	50.3	9.73	9.8	13.00	13.23	13.45	13.84
n-C_5H_{11}	78	77–79	.05	1.4646	0.9690	54.11	53.5	10.22	10.1	11.63	11.92	12.04	12.35
	89[d]	80–82	.11	1.4642	....		..		..		...		...
	67[c]	75–77	.05	1.4645	....		..		..		...		...

[a] Commercial sodium methoxide was used instead of a solution of metallic sodium in the appropriate alcohol as in most other runs. [b] Triethylamine was used as a hydrogen chloride acceptor in this run which employed anhydrous benzene as a reaction medium. [c] This run was performed in the usual manner except that only one g.-atom of sodium was used for each mole of IV. [d] Described in detail in the Experimental part. [e] Reported[6] b.p. 76.5–78° (13 mm.), n^{20}_D 1.4610, d^{20}_4 1.0553. [f] Reported[5] b.p. 80.5–81.0° (10 mm.), n^{20}_D 1.4558, d^{20}_4 1.0356. [g] Reported[5] b. 69–70° (1.5 mm.), n^{20}_D 1.4622, d^{20}_4 1.005. [h] Reported[6] b.p. 79.5–83°, n^{20}_D 1.4553, d^{20}_4 0.9775; reported[10] b.p. 97–98° (2 mm.), n^{20}_D 1.4510, d^{20}_4 0.9768.

of sulfur flowers is added in small portions to a stirred suspension of approximately 0.06 mole % of powdered anhydrous aluminum chloride in the alkylphosphonous dichloride while maintaining the reaction mixture at a temperature of 35–50° by external cooling. If the aluminum chloride is added, even in considerably larger amounts, to the stirred mixture of the dichloride and sulfur, the addition reaction proceeds very sluggishly and requires prolonged reflux periods for completion.

The addition of the appropriate IV to a solution of two equivalents of sodium in an excess of an aliphatic alcohol in the second step of method A gave yields of the corresponding I ranging between 70 and 90%, based on the IV. The use of an organic base (triethylamine, pyridine, diethylaniline, etc.) as a hydrogen chloride acceptor in this step proved to be less satisfactory because of the somewhat lower yields of the desired esters and the necessity of employing relatively large volumes of an inert solvent to keep the reaction mixture fluid. The physical and analytical data of the I are listed in Table I.

While O,O′-diethyl methylphosphonothioate and the O,O′-diethyl, di-n-propyl and di-n-butyl esters of ethylphosphonothioic acid have been reported previously,[5,6,10] none of the chloridothioates II derived from methyl- and ethylphosphonothioic acid seems to be known. The II were found to be readily accessible in moderate yields by treatment of the appropriate alkylphosphonothioic dichloride IV in an inert hydrocarbon medium with a mixture of one mole equivalent each of an alcohol and triethylamine (method A). In all runs performed in this manner, small amounts of the corresponding dialkyl esters I and unreacted IV also were obtained making the isolation of pure chloridothioates difficult. The crude yields of II were, in general, lower than the yields of the purified I from the same IV. The use of a solution of one equivalent of sodium in the appropriate alcohol instead of alcohol and triethylamine resulted unexpectedly in the exclusive formation of the diesters I. An alternate method (method B) for the preparation of the II consists in a one-batch conversion of the alkylphosphonous dichloride with one mole equivalent of an alcohol and an organic base to the alkyl alkylphosphonochloridite and further, without isolation of the intermediate, by addition of sulfur to the desired II. Although the yields of the II were usually in this procedure lower than in method A, the one-batch synthesis of the II offers considerable savings in time. While the II are useful intermediates for a large variety of sulfur-containing organic phosphorous compounds, the O,O′-dialkyl alkylphosphonothioates I offer a number of advantages as starting materials for the preparation of the alkyl alkylphosphonothioic acids III.

Table II lists the physical and analytical data for a number of O-alkyl methyl- and ethylphosphonochloridothioates prepared by methods A and B.

Repeated attempts to prepare O-methyl methylphosphonochloridothioate by method A resulted in the exclusive formation of high boiling pyro derivatives which were not investigated further. Some of the unreacted methylphosphonothioic dichloride also was recovered in all of these runs.

Ottawa, Canada, for the permission to use this information in the present paper.

(10) A. N. Pudovik and K. A. Kovyrzina, *Zhur. Obshchei Khim.*, **24**, 307 (1954); *C.A.*, **49**, 4498e (1955).

TABLE II

PHYSICAL AND ANALYTICAL DATA OF O-ALKYL ALKYLPHOSPHONOCHLORIDOTHIOATES, RP(S)(OR′)Cl

R′	Method	Yield,[a] %	B.p. °C.	B.p. Mm.	$n^{25}D$	d^{25}_4	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Phosphorus, % Calcd.	Phosphorus, % Found	Sulfur, % Calcd.	Sulfur, % Found	Chlorine, % Calcd.	Chlorine, % Found
							R = CH_3									
C_2H_5	A	76(35)	41	4.0	1.4950	1.1834	22.72	22.8	5.08	5.2	19.55	19.89	20.20	20.07	22.36	22.28
	B[b]	53	47	5.0	1.4930	....		22.7		5.2		19.52		20.27		21.73
n-C_3H_7	A	76(47)	45	0.5	1.4888	1.1481	27.82	27.9	5.84	5.8	17.95	18.15	18.54	18.52	20.58	20.93
	B	48	47	.8	1.4885	1.1461		..		..		17.85		18.54		20.12
i-C_3H_7	A	42.5(32.5)	41	.8	1.4821	1.1335		28.2		5.8		18.26		18.80		20.62
	B[b]	(25)	45–46	2.0	1.4822	1.1322		27.9		6.0		18.33		18.87		20.50
n-C_4H_9	A	65(37)	41	0.4	1.4861	1.1130	32.17	32.3	6.48	6.5		16.60	16.89	17.18	19.10	19.22
	B	47	48	1.3	1.4852	....		..		..		...		17.18		19.12
n-C_5H_{11}	A	74(49)	49	0.25	1.4840	1.0892	35.91	36.2	7.03	7.2	15.43	15.64	15.98	16.08	17.66	17.70
	B	32	58	1.0	1.4826	1.0857		36.3		7.1		15.57		16.20		18.19
							R = C_2H_5									
C_2H_5	A	71(20.5)	45	2.3	1.4911	1.1513	27.82	27.8	5.84	5.8	17.95	18.13	18.54	18.69	20.58	20.89
	B	58	60	5.0	1.4902	....		..		..		18.16		18.74		20.84
n-C_3H_7	A	66(45)	54	1.5	1.4874	1.1195	32.17	32.4	6.48	6.4	16.60	17.11	17.18	17.32	19.00	19.10
n-C_4H_9	A	68(38)	46	0.2	1.4849	1.0965	35.91	36.2	7.03	7.1	15.44	15.45	15.98	16.04	17.67	18.10
n-C_5H_{11}	A	61(50)	54	0.23	1.4845	1.0717	39.16	39.2	7.51	7.5	14.43	14.26	14.94	15.04	16.52	16.65

[a] Crude, once-distilled material which was still contaminated with IV and II; the figures in parentheses indicate the yields of pure product obtained by careful fractionation. [b] See Experimental part for details on this run.

Experimental

Preparation of Methylphosphonothioic Dichloride.[9]—To a stirred suspension of 32 g. (0.24 mole) of powdered, anhydrous aluminum chloride in 467 g. (4 moles) of methylphosphonous dichloride,[11] b.p. 81–82°, was added at room temperature 128 g. (4 g.-atoms) of sulfur flowers in small portions. A slow stream of nitrogen was passed through the apparatus during the entire operation. After the addition of the first portion of sulfur, the temperature of the reaction mixture began to rise slowly to about 40° while the aluminum chloride went into solution. The pot temperature was maintained during the further addition of the sulfur between 35 and 45° by occasionally immersing the reaction flask in a cooling bath. When a Dry Ice–acetone-bath was used, the addition of the sulfur could be carried out readily within a period of 10–15 minutes. After the addition was complete, the yellowish-brown, clear reaction mixture was allowed to stand overnight and was then distilled to give 545.5 g. (91.8%) of methylphosphonothioic dichloride, b.p. 44–45° (9 mm.), $n^{25}D$ 1.5485, d^{25}_4 1.4178.

Anal. Calcd. for CH_3Cl_2PS: C, 8.08; H, 2.02; P, 20.81; S, 21.50; Cl, 47.59. Found: C, 8.0; H, 2.1; P, 21.46; Cl, 47.67.

Preparation of Ethylphosphonothioic Dichloride.—Crude ethylphosphonous dichloride,[5] b.p. 108–115° (905 g., 6.9 moles), was converted in exactly the same manner as described for the methyl homolog with 55 g. (0.41 mole) of aluminum chloride and 231 g. (7.2 moles) of sulfur flowers in 83.3% yield to ethylphosphonothioic dichloride, b.p. 49° (6.9 mm.) [lit.[12] b.p. 78–81° (50 mm.)]. The small amount of excess sulfur used in this run was removed by filtration before distillation.

Anal. Calcd. for $C_2H_5Cl_2PS$: C, 14.72; H, 3.07; P, 19.02; S, 19.64; Cl, 43.52. Found: C, 14.8; H, 3.2; P, 19.16; S, 19.93; Cl, 43.43.

Preparation of O,O′-Dialkyl Alkylphosphonothioates (I).—Metallic sodium (1 or 2 g.-atoms) was added in small pieces gradually to a large excess of the appropriate anhydrous alcohol (500–1000 ml. per g.-atom of sodium). To the resulting sodium alkoxide solution was added with mechanical stirring 0.5 or 1.0 mole, respectively, of the alkylphosphonothioic dichloride in a dropwise fashion at such a rate that the temperature of the reaction mixture was maintained without external heating at approximately 30 to 40° below the boiling point of the alcohol. The reaction mixture was then stirred for an additional period of at least 4 hr. The precipitated, finely divided sodium chloride could be removed in a number of different ways without affecting the yield of the desired I noticeably. Filtration of the reaction mixture permitted the most rapid processing; however, when the sodium chloride was not retained completely by the filter, addition of a few ml. of water usually caused sufficient coagulation of the precipitate to allow its removal by filtration. In runs with the higher, water-immiscible alcohols, the sodium chloride was removed satisfactorily by washing with water. Alcoholic reaction mixtures which had been treated with water were dried with anhydrous sodium sulfate or with Drierite before removal of the excess alcohol by distillation. The liquid residue of the crude reaction product finally was fractionated to yield the I.

The general method is illustrated by the following two specific examples describing the preparation of O,O′-diethyl ethylphosphonothioate (V) and O,O′-di-*n*-pentyl ethylphosphonothioate (VI).

Ethylphosphonothioic dichloride (163 g., 1 mole) was added dropwise over a period of 0.5 hr. to a stirred solution of 46.0 g. of metallic sodium in 1000 ml. of absolute ethanol. During the addition period, the reaction mixture was maintained in the temperature range of 45 to 55° by cooling with an ice-bath. Stirring was then continued for an additional hour. After standing at room temperature overnight, the precipitated salt was removed by suction filtration. The filtrate was concentrated under reduced pressure to remove the excess ethanol and the residual crude product was distilled to yield 136.3 g. (75%) of V, b.p. 41–43° (1 mm.), $n^{25}D$ 1.4623–1.4619.

Dry 1-pentanol (2000 ml.) was heated to about 80° and 46 g. of metallic sodium was added in small pieces to the hot alcohol at such a rate as to maintain the reaction temperature below 100°. The resulting sodium alkoxide solution was allowed to cool to 65° and ethylphosphonothioic dichloride (163 g., 1 mole) was added dropwise to the stirred solution over a period of about 1 hr. while maintaining the reaction mixture at 65–75° by cooling with a water-bath. The mixture was stirred for an additional period of 2 hr. and then treated with 400 ml. of water to dissolve the precipitated sodium chloride. The organic layer was separated from the aqueous salt layer and the excess pentanol removed under reduced pressure. The residue of crude, oily product yielded on distillation *in vacuo* 208.5 g. (89%) of VI, b.p. 80–82° (0.06 mm.), $n^{25}D$ 1.4641–1.4642.

The preparation of O,O′-di-*n*-pentyl methylphosphonothioate (VII) employing triethylamine as a hydrogen chloride acceptor exemplifies this variation of the general method.

To a mixture of 176.3 g. (2 moles) of 1-pentanol and 202.0 g. (2 moles) of triethylamine in 400 ml. of dry benzene was added dropwise with stirring 149 g. (1 mole) of methylphosphonothioic dichloride over a period of about 1 hr. During the addition period, the mixture was cooled occasionally with an ice-bath to maintain a reaction temperature of 35–45°. After standing overnight at room temperature, the precipitated amine hydrochloride was removed by suction filtration and washed on the filter with 200 ml. of benzene. The filter cake was then dissolved in water and the small, upper, organic layer combined with the filtrate and washing. The combined benzene solutions were dried with Drierite and

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[11] The methylphosphonous dichloride was prepared by the reduction of the complex $[CH_3PCl_3][AlCl_4]$ in acetonitrile with aluminum following a method described by Shell Development Co., Emeryville, Calif., Final Report, Chemical Corps Contract No. DA-18-108-CML-721 (1950).

[12] W. L. Jensen, U. S. Patent 2,662,917 (1953).

distilled under reduced pressure to yield 139.5 g. (55.3%) of VII, b.p. 73–75° (0.05 mm.), $n^{25}\mathrm{D}$ 1.4618, d^{25}_{4} 0.9636. The same compound was obtained in 90% yield when sodium in pentanol was employed as a hydrogen chloride acceptor.

Preparation of O-Alkyl Alkylphosphonochloridothioates (II). Method A.—To a stirred solution of methyl- or ethylphosphonothioic dichloride in dry benzene (250–400 ml./mole) was added dropwise a mixture of one equivalent each of triethylamine and the appropriate alcohol. The resulting reaction mixture was stirred for periods of 2–4 hr. or overnight to assure complete reaction and was then filtered by suction to remove the precipitated triethylamine hydrochloride. The filter cake was washed with several small portions of dry benzene and the washings were combined with the original filtrate. After removal of the benzene under reduced pressure, the residual liquid product was fractionated to give the corresponding II as colorless, mobile liquids. The temperature of the reaction mixture was maintained in most runs between 35 and 45° during the addition and subsequent agitation period. A few comparative runs, however, carried out at the reflux temperature of the reaction mixture seem to indicate that the reaction temperature is without a marked effect on the yield of the II.

Because of the resistance of the II toward hydrolysis at room temperature, the amine hydrochloride could also be removed by dissolving in water and washing the benzene solution of the product with several portions of cold water. The washed solution was dried with Drierite and worked up in the usual manner. The crude yields of once-distilled II were, in general, in the range of 65 to 80%. This material, however, always was contaminated by several per cent. of unreacted phosphonothioic dichloride and dialkyl ester I. Removal of the contaminants by repeated fractionation resulted in a considerable loss of product.

Method B.—In this method, a mixture of methyl- or ethylphosphonous dichloride and an inert solvent (400–600 ml./mole), such as dry benzene or ligroin (b.p. 60–90°) was stirred while a slow stream of oxygen-free dry nitrogen was passed through the liquid phase during the entire run. To the stirred solution was added with cooling at an internal temperature of 10–20° a mixture of one mole equivalent each of triethylamine or diethylaniline and a suitable dry alcohol. The resulting slurry of amine hydrochloride was stirred for an additional period of 1–2 hours allowing the temperature of the reaction mixture to rise slowly to room temperature. The vigorously stirred reaction mixture containing the alkyl methyl- or ethylphosphonochloridite, respectively, was treated with the calculated amount of sulfur flowers in several portions at such a rate as to maintain a reaction temperature of 25–35°. After completion of the addition, distilled water (150–200 ml./mole phosphonous dichloride used) was added and the mixture stirred until the amine hydrochloride had passed into solution. The contents of the reaction flask was filtered by suction to remove the unreacted sulfur. The organic phase of the filtrate was washed with 1–1.5 *N* hydrochloric acid in order to remove any unreacted amine. After drying over Drierite or anhydrous magnesium sulfate, the solvent was removed from the solution under reduced pressure. The residual, crude, liquid product was purified by distillation *in vacuo* to yield the desired II. The general method B for the preparation of the II is illustrated by the following directions for the conversion of methylphosphonous dichloride to O-ethyl methylphosphonochloridothioate (VIII).

To a solution of 1170 g. (10 moles) of methylphosphonous dichloride in 4 l. of dry benzene was added with stirring over a period of 45 min. a mixture of 460 g. (10 moles) of absolute ethanol and 1012 g. (10 moles) of triethylamine. After completion of the addition, the mixture was stirred for an additional period of about 1 hr., then treated with stirring with 320 g. (10 g.-atoms) of sulfur flowers in several portions during 15 minutes. The resulting slurry of triethylamine hydrochloride and some unreacted sulfur was stirred for a period of 3 hr. By adding 2000 ml. of water to the stirred mixture, the amine hydrochloride was brought into solution. The remaining unreacted sulfur which collected mainly at the interphase between the two liquid phases was removed by suction filtration. The upper, organic layer of the filtrate was separated, washed once with 1 l. of 1 *N* hydrochloric acid and once with 1 l. of water and dried over anhydrous magnesium sulfate. After removal of the benzene from the filtered solution under reduced pressure, the crude liquid residue was distilled to yield 837 g. (53%) of VIII, $n^{25}\mathrm{D}$ 1.4930–1.4915.

In the preparation of O-isopropyl methylphosphonochloridothioate (IX) a modification of method B was applied which attempted to utilize advantageously the vast difference in the rates of the uncatalyzed sulfur addition to methylphosphonous dichloride and to the intermediate isopropyl methylphosphonochloridite, $CH_3P[OCH(CH_3)_2]Cl$. In this run, 1170 g. (10 moles) of methylphosphonous dichloride was placed into a reaction flask previously flushed with dry nitrogen. The dichloride was then diluted with 5 l. of ligroin (b.p. 60–90°), and 320 g. of sulfur flowers added to the solution. The resulting sulfur suspension was cooled with stirring to $-5°$ and approximately 90% of a mixture of 600 g. (10 moles) of dry isopropyl alcohol and 1012 g. (10 moles) of triethylamine was added at $-5 \pm 3°$ with vigorous stirring and cooling with a Dry Ice–acetone-bath. During the addition of the remaining 10% of the alcohol–amine mixture, the temperature in the reaction flask was allowed to rise without further external cooling to 45° and stirred for several hours until the temperature had dropped to room temperature. The precipitated triethylamine hydrochloride was removed by stirring the suspension with 3.5 l. of distilled water until solution had occurred. The layers were separated and the organic layer was filtered to remove 80.8 g. of unreacted sulfur. Removal of the solvent from the filtered organic layer under reduced pressure left a liquid residue which yielded upon repeated fractionation 345 g. (25%) of IX, b.p. 45–46° (2.0 mm.), $n^{25}\mathrm{D}$ 1.4817–1.4826; the $n^{25}\mathrm{D}$ value of an analytical middle-cut was 1.4822.

Although the yield of pure IX in this modification of method B was only 25%, calculated on the basis of methylphosphonous dichloride employed, it is only slightly lower than the over-all yield of refractionated IX (30%) obtained in the two steps of method A from the same starting material.

O-Isopropyl ethylphosphonochloridothioate (X) could not be obtained by method A in spite of several attempts under carefully controlled conditions. However, a small yield of this compound finally was obtained when a dilute solution of metallic sodium in dry isopropyl alcohol was added dropwise with stirring to 100% excess of ethylphosphonothioic dichloride in dry benzene at such a rate as to maintain a reaction temperature of 25–35° without external cooling. The precipitated sodium chloride was removed by suction filtration. After removal of the solvent and excess isopropyl alcohol, the residual mixture of unchanged thioic dichloride and product was fractionated to yield 12.5% of X, b.p. 60° (3.5 mm.), $n^{25}\mathrm{D}$ 1.4795–1.4775.

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