Nucleophilic Reactivity of Organophosphorus Compounds. Part II.[1] The Reactions of Phosphorus Acids with Keten *OO*-, *ON*-, *OS*-, and *SS*-Acetals, Orthoesters, and Ketenimines

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The reactions of phosphoric, phosphonic, phosphomonothioic, and phosphodithioic acids with the title substrates are reported. Many of these reactions are of synthetic utility in the alkylation of phosphorus acids. The preparation of a keten acetal and an orthoester from (+)- or (−)-octan-2-ol are reported and their reactions with all three types of phosphorus acid proceed predominantly (88—100%) with inversion. The results are interpreted in terms of an ion-pair mechanism for the alkylation step of the reaction.

PART I [1] reported the reactions of phosphoric, phosphonic, and phosphonomonothioic acids with methylketen diethyl acetal (1) all of which gave good yields of ethyl propionate and the ethyl esters of the respective phosphorus acids. This facile alkylation has now been extended to include phosphoro- and phosphono-dithioic acids but more significantly a wide range of substrates has been explored with a view to establishing the reactivity and synthetic utility of each reagent for the esterification of phosphorus acids. The substrates investigated include keten *OO*-, *ON*-, *OS*-, and *SS*-acetals, orthoesters, and ketenimines.

A detailed mechanistic interpretation of the keten *OO*-acetal reaction will appear in Part III, but the preparation of an optically active keten acetal and its reactions with all three types of phosphorus acid are reported. The results (88—100% inversion, dependent upon the acid used) which are almost identical with those obtained using an optically active orthoester, serve to illuminate the mechanism of the second step of the reaction.

RESULTS AND DISCUSSION

Keten OO-*Acetals*.—The reactions described by equation (1) were generally carried out in benzene or a dialkyl ether by the dropwise addition of a solution of the phosphorus acid to a stirred solution of the keten acetal thermostatted at the required temperature. The phosphorus products and isolated yields of each reaction are given in Table 1. In each case an equivalent quantity of the carboxylic ester was isolated and identified by comparison with an authentic sample. Thus

$$XCH{:}C(OR)_2 + {>}P(Y)ZH \longrightarrow XCH_2CO_2R + \begin{matrix} {>}P(Y)ZR \\ + \\ {>}P(Z)YR \end{matrix} \quad (1)$$

R = Me or Et Y, Z = O or S

the generality of the reaction for the alkylation of phosphorus acids is established. The identities of the isolated phosphorus esters were verified by i.r. spectra (by comparison with the spectra of authentic samples, where available) and by ^{1}H n.m.r. data.

The reactions using phosphoric and phosphonic acids were characterised by relatively low yields of phosphorus esters. Using (1), ethanol was detected by g.l.c. and a by-product which accounted for *ca.* 32% of the starting keten acetal, was isolated by distillation. The i.r. spectrum indicated an αβ-unsaturated ester, ν 1730 cm^{-1}, and the n.m.r. spectrum was consistent with structure (6), presumably formed by acid-catalysed dimerisation of (1) [2] followed by dealkylation and the loss of ethanol [equation (2)]. A small amount

$$2\ \underset{(1)}{MeCH{:}C(OEt)_2} + (EtO)_2P(O)OH \longrightarrow \left[EtC(OEt)_2 \cdot MeCH \cdot \overset{+}{C}(OEt)_2 \quad \bar{O}_2P(OEt)_2 \right] \longrightarrow \underset{(6)}{EtC(OEt){:}CMeCO_2Et} + (EtO)_3PO + EtOH \quad (2)$$

(<10%) of the dimerisation product was also detected with some monothioic acids but the dithioic acids gave no by-products and yields of the phosphorus esters were correspondingly higher.

For the phosphoro- and phosphono-thioic acids there exists the possibility of forming thiono- or thiolo-esters [equation (3)]. It was reported originally that the

$$XCH{:}C(OR)_2 + {>}P(O)SH \longrightarrow \underset{\text{thioloester}}{{>}P(O)SR} \text{ or } \underset{\text{thionoester}}{{>}P(S)OR} + XCH_2CO_2R \quad (3)$$

exclusive product using a phosphonothioic acid was the phosphonothiolate [1] and g.l.c. (Pye–Argon chromatograph) appeared to confirm this. However, when reaction mixtures were analysed using a Perkin-Elmer F11 fitted with a flame-ionisation detector, quantities of thionoester varying from 1 to 5% of the theoretical yield of phosphorus ester were detected. Control experiments established that the phosphorus esters were not interconvertible under the reaction conditions and hence the small fraction of thionoester is a feature of the alkylation and represents *O*- *vs.* *S*-attack by the ambident phosphorus anion on the intermediate carboxonium ion. The effect on the thiono–thiolo ratio (P=S : P=O) of varying the temperature of the reaction, is shown in Table 2 from which it may be seen that the reactions to thiolo- or thiono-ester have similar

[1] Part I, C. D. Hall, *J. Chem. Soc.* (*B*), 1968, 708.
[2] S. M. McElvain, *Chem. Rev.*, 1949, **49**, 453.

TABLE 1

Reaction of keten acetals with organophosphorus acids in benzene at 25 °C

Substrate $XCH{:}C(OR)_2$	Acid	Phosphorus product	B.p. [°C (mmHg)]	Lit. b.p. [°C (mmHg)]	n_D^{20} found (lit.)	Yield (%)	^{1}H N.m.r. spectra [δ (p.p.m. from Me_4Si); J/Hz] of phosphorus esters in $CDCl_3$ (or CCl_4) ** δ	Assignment	J
$CH_3CH{:}C(OEt)_2$ (1)	$(EtO)_2P(O)OH$	$(EtO)_3PO$	107 (18)	98 (10) *a*	1·4048 (1·4055)	48			
$CH_3CH{:}C(OEt)_2$ (1)	$(EtO)_2P(O)SH$	$(EtO)_2P(O)SEt$ *	118 (13)	110 (11) *b*	1·4573 (1·4572)	78			
$CH_3CH{:}C(OEt)_2$ (1)	$(Pr^nO)_2P(O)SH$	$(Pr^nO)_2P(O)SEt$	146—148 (17)	†	1·4568	78	4·0 (4H, sex) 2·8 (2H, sex) 1·65—0·8 (13H, m)	$CH_3CH_2CH_2OP$ CH_3CH_2SP $CH_3CH_2CH_2CH_2OP$ + CH_3CH_2SP	^2J_P 8·0; ^1J_H 7·0 ^2J_P 15; ^1J_H 7·5
$CH_3CH{:}C(OEt)_2$ (1)	EtOMeP(O)SH	EtOMeP(O)SEt	96 (12)	96 (10) *c*	1·4719 (1·4730)	75			
$CH_3CH{:}C(OEt)_2$ (1)	$(EtO)_2P(S)SH$	$(EtO)_2P(S)SEt$	124—128 (17)	74—77 (10) *a*	1·5034 (1·5033)	86			
$CH_3CH{:}C(OEt)_2$ (1)	(EtO)EtP(O)OH	(EtO)EtP(O)OEt	141—144 (130)	91 (10) *d*	1·4156 (1·4163)	80			
$CH_3CH{:}C(OEt)_2$ (1)	(PriO)MeP(O)OH	(PriO)MeP(O)OEt	107—109 (40)	90—92 (20) *f*		70			
$CH_3CH{:}C(OEt)_2$ (1)	(EtO)EtP(O)SH	(EtO)EtP(O)SEt	52—54 (0·2)	103—104 (12) *g*	1·4731 (1·4732)	72			
$CH_3CH{:}C(OEt)_2$ (1)	$(Pr^nO)MeP(O)SH$	$(Pr^nO)MeP(O)SEt$	63—63·5 (0·6)	109—110 (12) *c*	1·4718 (1·4718)	72			
$CH_2{:}C(O\text{-}1\text{-methylheptyl})_2$	$(EtO)_2P(O)OH$	$(EtO)_2P(O)OCHMe[CH_2]_5Me$	71—73 (0·01)		1·4232	47	4·40br (1H, o) 3·97(4H,quin) 1·7—0·7 (22H, m)	P-OC*H* P-OCH_2CH_3 P-OCHCH_3 + P-OCHC_6H_{13}	$^1J_H \approx {}^2J_P \approx 6·5$ $^2J_P \approx {}^1J_H \approx 7·6$
$CH_2{:}C(O\text{-}1\text{-methylheptyl})_2$	$(EtO)_2P(O)SH$	$(EtO)_2P(O)SCHMe[CH_2]_5Me$	89—92 (0·02)		1·4591	29	4·04 (4H, quin) 3·31br (1H, o) 1·78—0·7 (22H, m)	P-OCH_2CH_3 P-SC*H* POCH_2CH_3 + PSCHCH_3 + PSCHC_6H_{13}	$^3J_P \approx {}^1J_H = 7·4$ $^1J_H \approx {}^2J_P = 7·2$
		$(EtO)_2P(S)OCHMe[CH_2]_5Me$	88—92 (0·01)		1·4517	37			
$CH_2{:}C(O\text{-}1\text{-methylheptyl})_2$	$(EtO)_2P(S)SH$	$(EtO)_2P(S)SCHMe[CH_2]_5Me$	92·5—94·5 (0·02)	74—76 (0·02) *h*	1·4913 (1·4918)	84			
$PhCH{:}C(OMe)_2$ (2)	EtOMeP(O)SH	EtOMeP(O)SMe	99—100 (13)	‡	1·4775	72			
$EtO_2CCH{:}C(OEt)_2$ (3) ¶	EtOEtP(O)OH	EtOEtP(O)OEt	90—91 (10)	91 (10)	1·4156 (1·4163)	75			
$EtO_2CCH{:}C(OEt)_2$ (3) ¶	EtOMeP(O)SH	EtOMeP(O)SEt	96 (12)	96 (10) *c*	1·4722 (1·4730)	73			
$CNCH{:}C(OMe)_2$ (4)	EtOEtP(O)OH	EtOEtP(O)OMe	70 (8)	78—79 (13) *e*	1·4180 (1·4220)	64			
$CNCH{:}C(OMe)_2$ (4)	EtOMeP(O)SH	EtOMeP(O)SMe	100 (14)	‡	1·4768	73	4·1 (2H, m) 2·25 (3H, d) 1·65 (3H, d) 1·30 (3H, t)	CH_3CH_2OP ‖ CH_3SP CH_3P CH_3CH_2OP	 ^2J_P 12·8 ^1J_P 15·5 ^1J_H 7·2
p-$NO_2C_6H_4CH{:}C(OEt)_2$ § (5)	$(EtO)_2P(O)SH$	$(EtO)_2P(O)SEt$	126 (20)	110 (11) *b*	1·4562 (1·4572)	80			

* Trace $(EtO)_2P(S)OEt$ detected by t.l.c. † Found: C, 43·1; H, 8·5. $C_8H_{19}O_3PS$ requires C, 42·5; H, 8·4%. ‡ Found: C, 31·3; H, 7·2; P, 19·5; S, 20·5. $C_4H_{11}O_2PS$ requires C, 31·2; H, 7·2; P, 20·1; S, 20·8%. § In Bun_2O solvent; ratio thiono : thiolo 0·01 : 1·00. ¶ Mixed at ambient temperature, then heated under reflux for 2 h. ‖ Denotes non-equivalence. ** br = Broad, not well resolved; d = doublet; t = triplet; quin = quintet; sex = sextet; o = octet; m = multiplet.

a I. M. Heilbron, 'Dictionary of Organic Compounds,' Eyre and Spottiswoode, London, 1965, p. 2729. *b* H. I. Jacobson, R. G. Harvey, and E. V. Jensen, *J. Amer. Chem. Soc.*, 1955, **77**, 6064. *c* K. A. Petrov, M. K. Bliznyuk, and I. Yu Mansurov, *Zhur. obshchei Khim.*, 1961, **31**, 176. *d* B. C. Saunders, G. J. Stacey, F. Wild, and I. G. E. Wilding, *J. Chem. Soc.*, 1948, 699. *e* J. Michalski, M. Mikolajczyk, and A. Tatajczak, *Chem. and Ind.*, 1962, 819. *f* R. F. Hudson and L. Keay, *J. Chem. Soc.*, 1960, 1859. *g* J. Michalski and J. Wieczorkowski, *Roczniki Chem.*, 1959, **33**, 105. *h* G. R. Norman, W. M. Le Suer and T. W. Mastin, *J. Amer. Chem. Soc.*, 1952, **74**, 161.

activation energies [$\delta E_a = E_a(P{=}S) - E_a(P{=}O) = 2$—$3$ kcal mol^{-1}].

TABLE 2

The reactions of phosphoro- and phosphono-thioic acids with (1) in benzene at various temperatures

Acid	Reaction temp. (°C)	P=S : P=O *
$(EtO)_2P(O)SH$	25	0·044
$(EtO)_2P(O)SH$	35	0·054
$(EtO)_2P(O)SH$	80	0·059
(EtO)MeP(O)SH	25	0·039
(EtO)MeP(O)SH	35	0·044
(EtO)MeP(O)SH	80	0·100

* By g.l.c. (F11) using a 6 ft fluorosilicone oil (QF1) column at 100°.

Keten ON-*Acetals*.[3,4]—The reactions of 1-ethoxyvinyldimethylamine (7) with phosphono- and phosphoro-thioic acids were investigated with a view to establishing the effect of nitrogen conjugated with the incipient carbonium ion, on the thiono–thiolo ratio of the phosphorus ester products [equation (4)]. The results with *O*-ethyl hydrogen methylphosphonothioate and *OO*-diethyl hydrogen phosphorothioate at various

$$(EtO)RP(O)SH + CH_2{:}C(OEt)NMe_2 \longrightarrow \underset{(7)}{} \qquad (4)$$

$$(EtO)RP(O)SEt + (EtO)RP(S)OEt + CH_3CONMe_2$$

$$R = EtO \text{ or } Me$$

temperatures in benzene, toluene, and dioxan are shown in Table 3. The thiono–thiolo ratio was higher than with (1) as substrate but the *difference* in activation energy for formation of thiono- *vs.* thiolo-ester, δE_a, remained about the same at $3·0 \pm 0·2$ in benzene and $3·4 \pm 0·2$ kcal mol^{-1}, in toluene. The results reveal a lower degree of discrimination in the alkylation step for the more resonance stabilised alkoxycarboimmonium ion intermediate. The better solvating power of dioxan (*vs.* hydrocarbon solvents) would also stabilise the immonium intermediate and this too, results in a higher degree of *O*-alkylation (18 *vs.* 10% in benzene)

[3] H. Meerwein, W. Florian, M. Schon, and G. Stopp, *Annalen*, 1961, **641**, 1.

[4] H. Bredereck, F. Effenberger, and H. P. Beyerlin, *Chem. Ber.*, 1964, **97**, 3076.

but a similar change of ester ratio over the temperature range examined. Therefore, in comparing the reactions of (7) and (1) with phosphomonothioic acids, there appears to be an entropy factor working in favour

TABLE 3

Reactions of (7) with phosphomonothioic acids at various temperatures

Solvent	Temp. (°C)	P=S : P=O *
Acid: (EtO)MeP(O)SH		
Benzene	9·5	0·092
Benzene	25	0·099
Benzene	35·5	0·115
Benzene	47·2	0·165
Benzene	80	0·238
Toluene	70	0·150
Toluene	80	0·172
Toluene	90	0·182
Toluene	100	0·210
Toluene	110	0·240
Dioxan	21	0·177
Dioxan	101	0·295
Acid: $(EtO)_2P(O)SH$		
Benzene	25	0·070 †
	80	0·127

* By g.l.c. (Griffin, D6, g.d.b. detector) using a 6 ft Carbowax 20 M column at 100°. † By g.l.c. (F11) using a 6 ft Carbowax 20M/TPA column at 160°.

of attack by oxygen on the intermediate from (7) although *S*-alkylation remains the energetically preferred pathway.

Keten OS-*Acetals*.[5,6]—The reactions of 1-ethoxy-1-ethylthioethylene (8) with diethyl hydrogen phosphate, *OO*-diethyl hydrogen phosphorothioate, and *OO*-diethyl hydrogen phosphorodithioate were investigated using benzene as solvent and a 1 : 1 molar ratio of (8) to acid.

With diethyl hydrogen phosphate at ambient temperature, (8) [5] reacted to give unidentified products but the acid remained and no phosphorus ester was detected in the reaction mixture. The n.m.r. data suggested dimerisation of (8) catalysed by the phosphorus acid. By adding the acid to a solution of (8) in benzene under reflux, a 25% yield of triethyl phosphate was isolated (*ca.* 50% in reaction mixture by g.l.c.) together with a mixture of ethyl thioloacetate (9), ethyl thionoacetate (10), and unidentified high boiling material [ratio (9) : (10) = 82 : 18 by g.l.c.]. The reaction with *OO*-diethyl hydrogen phosphorothioate in benzene however, proceeded at ambient temperature with evolution of heat. A g.l.c. analysis of the reaction mixture showed a thiolo- : thiono-ratio of phosphorus esters of 99 : 1 but a ratio (9) : (10) of 85 : 15. A 44% yield of triethyl phosphorothiolate was isolated from the reaction mixture [equation (5)]. *OO*-Diethyl hydrogen phosphorodithioate reacted with (8) at ambient temperature again with evolution of heat and a 78% yield of *OOS*-triethyl phosphorodithioate was isolated; the ratio of (9) : (10) was 90 : 10 (by g.l.c.).

$$(EtO)_2P(O)SH + CH_2{:}C(OEt)SEt \longrightarrow (EtO)_2P(O)SEt + CH_3CO{\cdot}SEt + CH_3CS{\cdot}OEt \quad (5)$$
(8) (9) (10)

$$(EtO)_2P(S)SH + (8) \longrightarrow (EtO)_2P(S)SEt + (9) + (10) \quad (6)$$

Keten SS-*Acetals*.[5-7]—With 1,1-diethylthioethylene (11), the reactions were also carried out in benzene with a 1 : 1 molar ratio of (11) and each of the phosphorus acids used with (8). Neither phosphorus or carboxylic esters were detected as products of any of these reactions. In fact with diethyl hydrogen phosphate there was apparently no reaction even after heating under reflux for 6 h. Close inspection of the n.m.r. spectrum of the reaction mixture however, revealed a small singlet at δ 1·83 (0·5H) which is assigned to protonated (11) in equilibrium with starting material [equation (7)]. The addition of *OO*-diethyl hydrogen phosphorothioate or *OO*-diethyl hydrogen phosphorodithioate to a solution of (11) in benzene both caused

$$(EtO)_2P(O)OH + CH_2{:}C(SEt)_2 \rightleftharpoons CH_3\overset{+}{C}(SEt)_2\bar{O}_2P(OEt)_2 \quad (7)$$

liberation of heat with the formation of a dark red solution. No phosphorus or carboxylic esters were formed but in both cases the n.m.r. spectrum revealed a broad singlet at δ 1·84 (1·25H in the case of the monothioic acid and 2·7H in the case of the dithioic acid). Obviously, the equilibria to an ion-pair (or addition product) are established to an extent dependent upon the strength of the acid. It would appear however, that the driving force derived from formation of a thiocarbonyl bond is not sufficient to promote alkylation of the acid anions.

Orthoesters.[8,9]—The reaction of orthocarboxylic esters with phosphorus acids is quite general and gives rise to alcohol, carboxylic ester, and phosphorus ester [equation (8)]. Using triethyl orthopropionate ($R^1 = R^2 = Et$) and a variety of phosphorus acids the products

$$R^1C(OR^2)_3 + R^3(R^4O)PXYH \longrightarrow R^1CO_2R^2 + R^3(R^4O)P(X)YR^2 + R^2OH \quad (8)$$

X, Y = O or S

were ethanol, ethyl propionate, and the corresponding ethyl ester of the phosphorus acid (Table 4). The latter were obtained in 70—90% yield and no product with an αβ-unsaturated ester structure was detected from any of these reactions. The products were identi-

[5] H. J. Alkema and J. F. Arens, *Rec. Trav. chim.*, 1960, **79**, 1257.

[6] Yu. A. Boiko, B. S. Kupiu, and A. A. Petrov, *Zhur. Org. Khim.*, 1966, **2**, 1923.

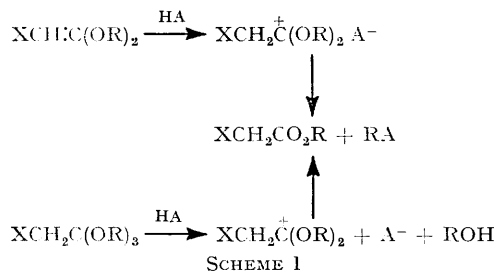
[7] H. C. Volgar and J. F. Arens, *Rec. Trav. chim.*, 1957, **76**, 847.

[8] R. H. De Wolfe, 'Organic Chemistry,' Academic Press, New York, vol. 14, 1970.

[9] E. H. Cordes, *Progr. Phys. Org. Chem.*, 1967, **4**, 1.

fied by i.r. and n.m.r. spectra and details of the latter appear in Table 1. Using monothioic acids the major product was the thiolate ester (*ca.* 97%) and the reaction with *OO*-diethyl hydrogen phosphorothioate at 25 and 80° in benzene showed a similar product ratio variation with temperature to that observed with (1).

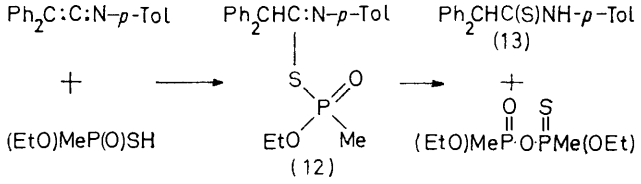
Hydrolysis of keten acetals proceeds *via* rate-determining protonation of the β-carbon atom [10] and the acid-catalysed hydrolysis of orthoesters is known to involve rate-determining ionisation of a protonated substrate to a carboxonium ion.[9] It seems likely, therefore, that this intermediate is common to the reaction of phosphorus acids with keten acetals and orthoesters (Scheme 1).



SCHEME 1

Triethyl orthothioformate and trimethyl orthothioacetate failed to react with any of the phosphorus acids after heating under reflux in dry benzene or ether for several hours. This is probably due to the lower basicity of sulphur and its failure to accommodate a proton prior to the rate-determining ionisation step coupled with weakness of the thiocarbonyl bond relative to carbonyl.

Diphenyl-N-p-*tolylketenimine*.[11]—The reaction of phosphoric acids with ketenimines is known to yield amide and pyrophosphate.[12] The rate-determining step was thought to be proton addition to carbon generating a carbonium ion which was stabilised by resonance with the imino-nitrogen atom. It was therefore of interest to examine the reaction of ketenimines with phosphomonothioic acids in order to establish the preference for sulphur or oxygen attack on the incipient carbonium ion. In the event of reaction with *O*-ethyl hydrogen methylphosphonothioate, the major products were diphenyl-*N*-*p*-tolylthioacetamide (13) and *OO'*-diethyl dimethylmonothionopyrophosphonate (14) presumably derived by attack of a second mole of acid on the addition product (12) which is a phosphorylating agent similar to the B2c type [13] [equation (9)]. Only a trace (<2%) of the amide expected from oxygen addition to the incipient carbonium ion was detected by t.l.c. The reaction is directly analogous to that observed with carbodi-imides [14] and serves to illustrate the fact that where addition intermediates are involved, the 'softer'



(9)

of the two nucleophiles (thiophosphoryl *vs.* phosphoryl anion) prefers to add to 'soft', resonance-stabilised carbonium ions.[15]

Keten Acetals and Orthoesters from (+)- *or* (−)-*Octan*-2-*ol*.—The original report [1] suggested the formation of an addition intermediate (15) from keten acetals or orthoesters with organophosphorus acids which subsequently suffered an intramolecular rearrangement *via* a six-membered, cyclic transition state to products (Scheme 2). The alternative mechanism involved formation of an ion-pair (16) and it was reasoned that if the group R was chiral and the keten acetal (or orthoester) was optically active, retention of configuration

TABLE 4

Reaction of triethyl orthopropionate with organophosphorus acids in benzene at 25 °C *

Acid	Phosphorus product	B.p. [°C (mmHg)]	Lit. b.p. [°C (mmHg)]	n_D^{20} found (lit.)	Yield (%)
$(EtO)_2P(O)OH$	$(EtO)_3PO$	*a*	*a*	*a*	68
$(EtO)EtP(O)OH$	$(EtO)_2EtP(O)$	*a*	*a*	*a*	87
$(EtO)_2P(O)SH$	$(EtO)_2P(O)SEt$	*a*	*a*	*a*	89
$(Pr^nO)_2P(O)SH$	$(Pr^nO)_2P(O)SEt$	*a*	*a*	*a*	85
$(EtO)MeP(O)SH$	$(EtO)MeP(O)SEt$	*a*	*a*	*a*	79
$(EtO)Pr^nP(O)SH$	$(EtO)Pr^nP(O)SEt$	118—124 (15)	85—86 (3) [b]	1·4682(1·4733)	68
$(EtO)_2P(S)SH$	$(EtO)_2P(S)SEt$	*a*	*a*	*a*	98
$(MeO)_2P(S)SH$	$(MeO)_2P(S)SEt$ ¶	97 (8)	†	1·5200	89
$(EtO)MeP(S)SH$	$(EtO)MeP(S)SEt$ §	110—112 (12)	‡	1·5250	83

* Reaction of trimethyl orthoacetate with *O*-ethyl dihydrogen methylphosphate in benzene gave a 90% yield of *O*-ethyl *S*-methyl methylphosphonothiolate, (EtO)MeP(O)SMe, b.p. 90—91° at 9 Torr, n_D^{20} 1·4785; see Table 1. † Found: C, 26·2; H, 6·05. $C_4H_{11}O_2PS_2$ requires C, 25·8; H, 5·95%. ‡ Found: C, 32·65; H, 7·4. $C_5H_{13}OPS_2$ requires C, 32·6; H, 7·1%. N.m.r. data [δ (p.p.m. from Me_4Si); *J*/Hz] in $CDCl_3$ (or CCl_4)]. § 4·10 (2H, m, CH_3CH_2OP), 2·95 (2H, o, CH_3CH_2SP, ^1J_H 7·5, ^2J_P 15·5), 2·05 (3H, d, CH_3P, ^1J_P 14·5), 1·33 (3H, t, CH_3CH_2OP), and 1·30 (3H, t, CH_3CH_2SP). ¶ 3·75 (6H, d, CH_3OP, ^2J_P 16·0), 2·80 (2H, sex, CH_3CH_2SP, ^1J_H 7·7; ^2J_P 17·0), and 1·30 (3H, t, CH_3CH_2SP).

[a] See Table 1. [b] M. I. Kabachnick and T. A. Mastryukova, *Bull. Akad. Sci. U.S.S.R.*, 1956, 193.

[10] V. Gold and D. C. A. Waterman, *J. Chem. Soc.* (*B*), 1968, 839.

[11] C. L. Stevens and G. H. Singhal, *J. Org. Chem.*, 1964, **29**, 34.

[12] R. J. Cremlyn, G. W. Kenner, A. R. Todd, *J. Chem. Soc.*, 1960, 4511.

[13] V. M. Clark, D. W. Hutchinson, A. J. Kirby, and S. G. Warren, *Angew. Chem. Internat. Edn.*, 1964, **3**, 678.

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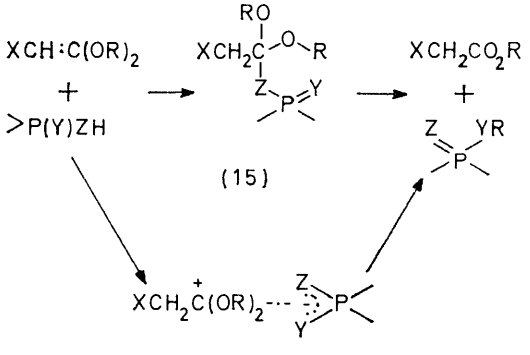
at R would signify intramolecular rearrangement of an addition intermediate whereas inversion would denote the ion-pair route. Optically active keten bis-1-methylheptyl acetal (X = H, R = 1-methylheptyl) and optically active tris-1-methylheptyl orthoformate were



SCHEME 2

prepared from (+)- or (−)-octan-2-ol and each was reacted in turn with diethyl hydrogen phosphate, *OO*-diethyl hydrogen phosphorothioate, and *OO*-diethyl hydrogen phosphorodithioate in diethyl ether or benzene as solvent. The resultant optically active diethyl 1-methylheptyl phosphorus esters were isolated and their rotations compared with the rotations of the same esters prepared from phosphorochloridates (17) or (18) and (+)-octan-2-ol (diethyl 1-methylheptyl phosphate and diethyl 1-methylheptyl phosphorothionate) and phosphorochloridates (17) or (18) with (+)-octan-2-thiol (*OO*-diethyl *S*-1-methylheptyl phosphorothiolate and *OO*-diethyl *S*-1-methylheptyl phosphorodithioate). The results are shown in Table 5

TABLE 5

Specific rotations, $[\alpha]_{436}^{25}$, of organophosphorus esters in Bu^n_2O; R = 1-methylheptyl

Ester	$[\alpha]_{436}^{25}$	Inversion (%)
$(EtO)_2P(O)OR$		
From $(EtO)_2P(O)Cl$ (17)—(+)-ROH	20·27	
From (+)-keten acetal	−17·96	88·2 ± 1·6
From (−)-orthoester	+17·87	88·5 ± 2·0
$(EtO)_2P(S)OR$		
From $(EtO)_2P(S)Cl$ (18)—(+)-ROH	+7·25	
From (+)-keten acetal	−7·13	98·1 ± 1·2
From (−)-orthoester *	+7·35	101·8 ± 1·2
$(EtO)_2P(O)SR$		
From $(EtO)_2P(O)Cl$ (17)—(+)-RSH	+6·59	
From (+)-keten acetal	−6·70	101·8 ± 3·0
From (−)-orthoester	+6·84	103·2 ± 1·0
$(EtO)_2P(S)SR$		
From $(EtO)_2P(S)Cl$ (18)—(+)-RSH	−21·78	
From (+)-keten acetal	+21·91	100·3 ± 2·4
From (−)-orthoester	−22·39	103·0 ± 0·3

* Calculated from rotation of thiolo–thiono mixture by subtraction.

and reveal between 88 and 100% inversion for all three types of acid with both classes of substrate. Only the dioxygen acids give any appreciable degree of racemisation (maximum 12%) or retention (maximum 6%) and in consequence the concept of an intramolecular rearrangement must be rejected. The latter requires frontside nucleophilic displacement on carbon by phosphoryl oxygen or sulphur and it seems likely that the barrier to such a process directs the reaction *via* the ion-pair route. In passing it should be noted that the optically active dithioate ester has a sign of rotation opposite to that expected from starting keten acetal or orthoester. It seems that the introduction of sulphur for oxygen through the series of phosphorus esters has a systematic effect in changing the sign of rotation. The phenomenon was confirmed by the observation that (+)-octan-2-thiol when reacted with *OO*-diethyl phosphorothiochloridate gave (−)-*OO*-diethyl *S*-1-methylheptyl phosphorodithioate.

The detailed mechanism of the overall reactions will be discussed in a subsequent paper but the above results serve to establish the general synthetic utility of keten acetals and orthoesters in the conversion of phosphorus acids to the corresponding esters. The conditions are mild and the products are often readily separated by fractional distillation. Orthoesters, which are available commercially, are the reagents of choice since the yields are high and by-product formation is minimal. Since the reaction does not involve bond cleavage at phosphorus, the alkylation of optically active phosphorus acids will be achieved with retention of configuration at phosphorus. In this connection, the suitability of the reactions for small scale work is an advantage.

EXPERIMENTAL

Analysis of mixtures by g.l.c. was carried out using either a Griffin D6 gas chromatograph fitted with a gas density balance detector and a digital integrator type 1E 165A (Gas Chromatography Ltd.) or a dual-column Perkin-Elmer F11 fitted with flame ionisation detectors and a Perkin-Elmer–Hitachi recorder with disc integrator. Columns were 2 m Carbowax 20M on Chromosorb or 2 m fluorosilicone oil (QF1) on Chromosorb.

I.r. spectra were recorded (as liquid films, solutions in CCl_4, or KBr discs) using Perkin-Elmer 237, 257, or 457 spectrometers. N.m.r. spectra were recorded (generally as solutions in $CDCl_3$ or CCl_4) using either Perkin-Elmer R10 or R12 60 MHz instruments; for high resolution spectra, Varian HA 100 or Bruker HFX 90 spectrometers were employed. Thanks are due to P.C.M.U. (Harwell) and Dr. D. Denney, Rutgers University, for 100 MHz spectra. Microanalyses were by Dr. F. B. Strauss, Oxford, and University College, London.

Preparation of Starting Materials.—The following keten acetals and orthoesters were all obtained by established literature preparations as indicated: methylketen diethyl acetal [16] (1); phenylketen dimethyl acetal [17] (2); ethoxycarbonylketen diethyl acetal [18] (3); cyanoketen dimethyl

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[17] S. M. McElvain and M. J. Curry, *J. Amer. Chem. Soc.*, 1948, **70**, 3781.

[18] S. A. Glickman and A. C. Cope, *J. Amer. Chem. Soc.*, 1945, **67**, 1017.

acetal[19] (4); 1-ethoxyvinyldimethylamine[20] (7); 1-ethoxy-1-ethylthioethylene;[5,6] 1,1-bisethylthioethylene;[5-7] triethyl orthothioformate;[21] trimethyl orthothioacetate.[22] Triethyl orthopropionate and trimethyl orthoacetate were commercial samples (Hopkin and Williams or B.D.H.) redistilled before use. Diphenyl-*N*-*p*-tolylketenimine was prepared by dehydration of diphenyl-*N*-*p*-tolylacetamide.[11]

The phosphorus acids were also prepared by established literature techniques.[23-25]

p-*Nitrophenylketen Diethyl Acetal.*—Ethanol (10·1 g, 0·22 mol) was added to a solution of *p*-nitrobenzyl cyanide (32·4 g, 0·20 mol) in ether–methylene chloride (1 : 1 v/v; 100 ml). Dry hydrogen chloride gas was passed through the ice-cold solution until 8·0 g (0·23 mol) had been absorbed. The solution was placed in the refrigerator for 3 days and the imidate hydrochloride which separated was filtered off, washed with ether, and dried under vacuum at 25° to give ethyl *p*-nitrobenzimidate hydrochloride (37·6 g, 77%) ν 1625 cm^{-1} ($C=\overset{+}{N}H_2$). The imidate hydrochloride (30·0 g, 0·123 mol) was shaken with dry ethanol (200 ml) for 2 h and left at ambient temperature for 10 days with occasional agitation. The remaining solid (mainly ammonium chloride) was filtered off and the ethanol distilled from the filtrate at 35° under vacuum. Dry ether was added to the yellow, residual liquid and the white precipitate which formed was filtered off and washed with ether. The combined filtrate and washings were washed with 10% sodium carbonate solution (2 × 50 ml), dried (K_2CO_3), filtered, and the ether was distilled on a rotary evaporator. The residual liquid was distilled under high vacuum (<0·1 mmHg) and when the bath temperature reached 130°, brisk evaporation of ethanol occurred and distillation of the residue gave an orange liquid which solidified to an orange solid. Redistillation gave an orange liquid (25·1 g, 86%), b.p. 139—144° at 0·15 mmHg, solidifying to an orange solid, m.p. 63—65°, which was recrystallised from ether–light petroleum (1 : 1 v/v) to give p-*nitrophenylketen diethyl acetal*, m.p. 67·5—69·5° (Found: C, 60·55; H, 6·4; N, 6·0. $C_{12}H_{15}NO_4$ requires C, 60·75; H, 6·35; N, 5·9%), ν 1625 cm^{-1} (C=C), δ ($CDCl_3$), 7·8 (4H, q), 4·6 (1H, s), 4·1 (4H, m), and 1·3 (6H, t), $\lambda_{max.}$ ($Bu^n{}_2O$) 370 nm (log ε 4·24).

(−)-*Tris*-1-*Methylheptyl Orthoformate.*—Triethyl orthoformate (15·56 g, 0·105 mol) and (−)-octan-2-ol (46·7 g, 0·359 mol),[26] $[\alpha]_D^{25}$ −8·77° (neat), were mixed in a 100 ml flask fitted with a 20 cm Vigreux column and distillation head and the flask was heated to 144° (oil-bath). After thermal equilibration, a few crystals of 2,6-dichlorobenzoic acid were introduced *via* the column and after a few seconds rapid distillation of ethanol occurred. The flask was then heated at 144° with stirring for 4 days and on raising the temperature to 200° a further quantity of ethanol distilled. Fractional distillation of the residue under vacuum gave (−)-tris-1-methylheptyl orthoformate (24·0 g, 87%), b.p. 138—143° at 0·014 mmHg, n_D^{20} 1·4378, α_D^{25} −19·774° (neat; *l* 1 dm) (lit.,[27] b.p. 202—203° at 1 mmHg, n_D^{20} 1·4365), δ (CCl_4), 5·14 (1H, s); *ca.* 3·75 (3H, m), and 1·7—0·7 (48H, m).

Keten Bis-1-*methylheptyl Acetal.*—Bromoacetaldehyde dimethyl acetal (Schuchardt; 67·6 g, 0·40 mol) and (+)-octan-2-ol (104·0 g, 0·80 mol),[26] $[\alpha]_D^{25}$ +9·05° (neat), were mixed in a 500 ml flask and a few crystals of 2,6-dichlorobenzoic acid were added. Distillation through a 30 cm Vigreux column at a bath temperature of 125 to 140° for a period of 48 h produced methanol (16·8 g, 0·525 mol, 66%). Distillation under vacuum gave three fractions,* the last of which was mainly (+)-bromoacetaldehyde bis-1-methylheptyl acetal (39·1 g, 27%), b.p. 110—123° at 0·01 mmHg. Redistillation gave the pure acetal, b.p. 108—108·5 at 0·01 mmHg, α_D^{25} +15·01° (neat; *l* 1 dm), δ (CCl_4) 4·67 (1H, t, $BrCH_2CH$); 3·65 [2H, m, $OCH(CH_3)C_6H_{13}$], 3·19 (2H, d, $BrCH_2$), and 1·7—0·7 (32H, m).

Potassium metal (9·12 g, 0·234 g atom) was added to t-butyl alcohol (200 ml; previously dried over calcium hydride) and the mixture was heated under reflux with stirring until the potassium metal dissolved. Some t-butyl alcohol (*ca.* 60 ml) was distilled off at atmospheric pressure until a faint precipitate of potassium t-butoxide appeared. The slurry was cooled to 40° when (+)-bromoacetaldehyde bis-1-methylheptyl acetal (65·7 g, 0·18 mol) was added over 5 min. with vigorous stirring. The dark coloured mixture was then heated under reflux for 10 h with stirring and allowed to stand at room temperature for a further 8 h. t-Butyl alcohol was distilled off at atmospheric pressure and finally at 13 mmHg (bath temperature 35°). The chocolate brown residue was fractionally distilled through a 20 cm Vigreux column to give (+)-*keten bis*-1-*methylheptyl acetal* (20·6 g, 40%), b.p. 117° at 0·04 mmHg, n_D^{20} 1·4388, α_D^{25} +13·208° (neat; *l* 1 dm), ν 1650 cm^{-1} (C=C), δ (CCl_4) 4·05 [2H, m, $OCH(CH_3)C_6H_{13}$], 3·08 (2H, s, $CH_2=C$), and 1·8—0·7 (32H, m) (Found: C, 75·0; H, 12·4. $C_{18}H_{36}O_2$ requires C, 76·05; H, 12·7%).

(+)-*Diethyl* 1-*Methylheptyl Phosphate.*—Sodium metal (1·13 g, 0·049 g atom) was heated under reflux with stirring with (+)-octan-2-ol {Fluka; $[\alpha]_D^{25}$ +9·51° (neat); 5·0 g, 0·0385 mol} and dry toluene (30 ml) until most of the sodium dissolved. A solution of *OO*-diethyl phosphorochloridate (6·65 g, 0·0385 mol) in dry toluene (20 ml) was added to the stirred, hot solution of the sodium alkoxide during 2 min when the solution became purple. After a further 5 h under reflux, the mixture was filtered through Hyflo and the solvent was removed from the filtrate and washings (toluene). Fractional distillation gave crude product (3·4 g), b.p. 73—86° at 0·018 mmHg which was refractionated to give the (+)-*phosphate* (1·56 g, 17%), b.p. 73—74° at 0·01 mmHg, n_D^{20} 1·4230, ν 1263 cm^{-1} (P=O), n.m.r., see Table 1 (Found: C, 53·65; H, 10·15; P, 11·55. $C_{12}H_{27}O_4P$ requires C, 54·15; H, 10·15; P, 11·65%). The material was free of impurity by g.l.c. (2 m; Carbowax 20M on chromosorb W, 80—100 mesh); see Table 5 for optical rotation.

(−)-OO-*Diethyl* O-1-*Methylheptyl Phosphorothionate.*—

* Recycling of the first two fractions [mainly(+)-octan-2-ol and (+)-bromoacetaldehyde methyl 1-methylheptyl acetal respectively] improved the overall yield of (+)-bromoacetaldehyde bis-1-methylheptyl acetal to 52%.

[19] S. M. McElvain and J. P. Schroeder, *J. Amer. Chem. Soc.*, 1949, **71**, 47.
[20] H. Bredereck, F. Effenberger, and H. P. Beyerlin, *Chem. Ber.*, 1964, **97**, 3076.
[21] A. Froling and J. F. Arens, *Rec. Trav. chim.*, 1962, **81**, 1009.
[22] L. C. Rinzema, J. Stoffelsma, and J. F. Arens, *Rec. Trav. chim.*, 1959, **79**, 354.
[23] G. M. Kosolapoff, 'Organophosphorus Compounds,' Wiley, London and New York, 1950.
[24] Houben-Weyl, 'Methoden der Organischen Chemie, Organische Phosphorverbindungen,' Georg Thieme Verlag, Stuttgart, 1963, Teil 1 and 2.
[25] S. Ohashi, *Topics Phosphorus Chem.*, 1964, **1**, 113.
[26] A. I. Vogel, 'Practical Organic Chemistry,' Longmans, London, 1966, p. 505.
[27] H. Hunter, *J. Chem. Soc.*, 1924, 1389.

The sodium salt of (−)-octan-2-ol {5·00 g, 0·0385 mol; $[\alpha]_D^{25}$ −8·77° (neat)} was prepared as described above and *OO*-diethyl phosphorothionochloridate (7·26 g, 0·0385 mol) in dry toluene (20 ml) was added dropwise to a stirred solution of the alkoxide under reflux during 2 min. After heating under reflux for 4·5 h, the suspension was left at room temperature overnight and the sodium chloride was filtered off through Hyflo. The filtrate and washings (toluene) were combined and solvent removed to give a pale yellow oil (9·22 g) which was fractionally distilled to give the (−)-*phosphorothionate* (4·26 g, 44%), b.p. 88—92° at 0·014 mmHg, n_D^{20} 1·4517, ν 820 cm^{-1} (P=S); [28] n.m.r., see Table 1 (Found: C, 50·45; H, 9·45; P, 11·3; S, 10·9. $C_{12}H_{27}O_3PS$ requires C, 51·05; H, 9·55; P, 11·0; S, 11·35%). The material was free of impurity by g.l.c.; see Table 5 for optical rotation.

(+)-OO-*Diethyl* S-1-*Methylheptyl Phosphorothiolate*.—Optically active octan-2-thiol was prepared by a modification of the route due to Kenyon.[29] To ice-cold toluene-*p*-sulphonyl chloride (38·1 g, 0·2 mol) in dry pyridine (60 ml) was added dropwise, with stirring, (−)-octan-2-ol {26·0 g, 0·2 mol; $[\alpha]_D^{25}$ −8·77° (neat)} in pyridine (60 ml). The solution was then stirred below 6° for 2 h and stored for a further 17 h at −6°. The mixture was then diluted with ether (500 ml) and washed with water (4 × 100 ml), ice-cold 1M-HCl (5 × 100 ml), 1M-sodium hydrogen carbonate (3 × 100 ml), and finally water (3 × 100 ml) before drying ($CaSO_4$), filtering, and evaporating the solvent to give the toluene-*p*-sulphonate (52·9 g, 93%) as a yellow oil, n_D^{20} 1·4893, α_D^{25} −6·825 (neat; *l* 1 dm).

The sulphonate (51·5 g, 0·183 mol) was then added dropwise, with stirring, over 5 min to potassium hydrogen sulphide [29] (1·87 mol) in ethanol (500 ml) under reflux. The mixture was heated under reflux for a further 5 min, then cooled rapidly to −5°, filtered, and the filtrate and washings [ether (6 × 200 ml)] were combined, washed with water (4 × 500 ml), dried ($CaSO_4$), filtered, and evaporated to give a pale yellow oil (24·3 g). Chromatography of the oil on Hopkin and Williams silica gel MFC (220 g; 0·65 m column) using light petroleum (b.p. 40—60°) as eluant gave an oil (20 g) which on fractional distillation gave (+)-octan-2-thiol (14·1 g, 53·3%), b.p. 73·5° at 13 mmHg, n_D^{20} 1·4493, $[\alpha]_D^{25}$ 28·36° (neat).

Sodium metal (0·89 g, 0·0385 g atom) was stirred and heated under reflux with (+)-octan-2-thiol (5·11 g, 0·035 mol) in toluene (40 ml). The mixture was cooled to 25° and *OO*-diethyl phosphorochloridate (6·04 g, 0·035 mol) in dry toluene (10 ml) was added over 2 min with stirring. After the exothermic reaction had subsided the mixture was heated under reflux for 3·5 h. The solvent was evaporated at 60° for 1·5 h and after the addition of ether (70 ml) the precipitate of sodium chloride was filtered through Hyflo and the solvent removed at 60° to give a pale yellow oil (18·76 g). Two fractional distillations gave the (+)-*phosphorothiolate* (1·13 g), b.p. 93—94° at 0·018 mmHg; n_D^{20} 1·4591, ν 1260 cm^{-1} (P=O), n.m.r., see Table 1 (Found: C, 52·05; H, 9·85; P, 10·95; S, 11·3. $C_{12}H_{27}O_3PS$ requires C, 51·05; H, 9·55; P, 11·0; S, 11·35%). The material was free of impurity by g.l.c.; see Table 5 for optical rotation.

Further product (1·8 g) was obtained by chromatography of the earlier fractions through Hopkin and Williams silica gel MFC (50 g) using light petroleum (b.p. 40—60°), then diethyl ether as eluant, followed by fractional distillation (total yield 41%).

OO-*Diethyl* S-1-*Methylheptyl Phosphorodithioate*.—The sodium salt of (+)-octan-2-thiol (5·11 g, 0·035 mol) was prepared as described above. *OO*-Diethyl phosphorothionochloridate (6·6 g, 0·035 mol) in toluene (10 ml) was added with stirring over 2 min and the mixture was heated under reflux with stirring for 3·5 h. The sodium chloride was removed as described previously and after evaporation of the solvent, fractional distillation of the residual oil gave the crude product (2·39 g), b.p. 96—98·5° at 0·016 mmHg. Chromatography of the crude material (2·3 g) on Hopkins and Williams silica gel MFC (46 g; 25 cm column) using light petroleum (b.p. 40—60°), then ether, as eluant gave an oil (2·24 g) which was fractionally distilled to give the phosphorodithioate (1·6 g), b.p. 92·5—94·5° at 0·017 mmHg, n_D^{20} 1·4913; ν 795 cm^{-1} (P=S); [28] for literature data, n.m.r. spectrum, and optical rotation see Tables 1 and 5; the material was free of impurity by g.l.c.

The same compound was prepared from *OO*-diethyl sodium phosphorodithioate and the (+)-toluene-*p*-sulphonate from (+)-octan-2-ol. The resultant ester had b.p. 105—107·5° at 0·1 mmHg, n_D^{20} 1·4914, $[\alpha]_D^{25}$ +9·80 ($Bu^n{}_2O$, *c* 5·492).

Reactions of Phosphorus Acids with Keten Acetals.—The experimental procedure for the reaction of keten dialkyl acetals with phosphorus acids was described previously.[1] Similar conditions (benzene or diethyl ether as solvents) and work-up procedures were used for the reactions of phosphorus acids with keten *ON*-, *OS*-, and *SS*-acetals. The reactions using optically active keten bis-1-methylheptyl acetal as substrate are described in detail below.

Reaction of (+)-*Acetal with Diethyl Hydrogen Phosphate*.—Diethyl hydrogen phosphate (3·1 g) in dry diethyl ether (20 ml) was added over 5 min to a stirred solution of the (+)-acetal (5·68 g, 0·02 mol) in ether (20 ml). The solution was heated under reflux for 2 h and then left at ambient temperature for 25 h before removing the excess of acid by stirring vigorously with a 5% solution of sodium hydrogen carbonate (20 ml) for 2 h. The ether phase was washed with water (2 × 10 ml) and then dried (Na_2SO_4). After filtration, the solvent was evaporated and the residual oil was fractionally distilled (×2) to give (−)-diethyl-1-methylheptyl phosphate (1·41 g, 47%), b.p. 68—72° at 0·007 mmHg, n_D^{20} 1·4232, i.r. and n.m.r. spectra identical with those of authentic samples; for optical rotation see Table 5.

Reaction of (+)-*Acetal with* OO-*Diethyl Hydrogen Phosphorodithioate*.—*OO*-Diethyl hydrogen phosphorodithioate (3·72 g, 0·02 mol) in dry ether (20 ml) was added with stirring to the acetal (5·68 g, 0·02 mol) in dry ether. After the initial exothermic reaction had subsided, the solution was heated under reflux for 2·5 h and then left at room temperature overnight before work-up as described above. Two fractional distillations of the crude product gave (+)-*OO*-diethyl *S*-1-methylheptyl phosphorothioate, b.p. 84° at 0·01 mmHg, n_D^{20} 1·4899, i.r. and n.m.r. spectra identical with those of authentic sample; for optical rotation see Table 5.

Reaction of (+)-*Acetal with* OO-*Diethyl Hydrogen Phosphorothioate*.—*OO*-Diethyl hydrogen phosphorothioate (1·38 g, 8 × 10^{-3} mol) in dry ether (15 ml) was added with stirring

[28] R. A. Chittenden and L. C. Thomas, *Spectrochim. Acta*, 1964, **20**, 1679.

[29] J. Kenyon, H. Phillips, and V. P. Pittman, *J. Chem. Soc.*, 1935, 1072.

to the acetal (2·30 g, 8×10^{-3} mol) in ether (10 ml). After heating under reflux for 2 h residual acid was removed by washing with aqueous sodium hydrogen carbonate and after drying, the solvent was evaporated to give an oil (3·01 g). Analysis by g.l.c. (Carbowax column) revealed a mixture of 1-methylheptyl acetate, *OO*-diethyl *O*-1-methylheptyl phosphorothionate, and the thiolo-isomer (ratio of latter two peaks 1 : 1·26). The oil was evaporated at 0·02 mmHg with the bath temperature rising 45°, the distillate (1·11 g; mainly the acetate) being collected, to leave a pale yellow oil (1·64 g), which was fractionally distilled to give a mixture of phosphorus esters (1·21 g), b.p. 92—115° at 0·08 mmHg. The esters were separated on eight 20 × 20 cm t.l.c. plates, coated with Merck $PF_{254+366}$ silica gel and eluting with light petroleum (b.p. 40—60°)–ether (9 : 1). The thiolo-ester remained at the origin and the thiono-ester had R_F 0·61. The esters gave i.r. and n.m.r. spectra identical with those of authentic samples. Crude yields (from t.l.c. plates) of the thiolo- and thiono-esters were 21 and 20% respectively.

Reactions of Orthoesters with Phosphorus Acids.—A representative reaction with *O*-ethyl hydrogen methylphosphonothioate is described. The phosphorothioate (2·0 g, 0·0143 mol) in benzene was added dropwise with stirring to triethyl orthopropionate (2·55 g, 0·0145 mol) in benzene (20 ml) and the mixture was heated under reflux for 1·5 h. G.l.c. analysis (QF1 column at 100°) revealed the presence of benzene, ethanol, ethyl propionate, *OS*-diethyl methylphosphonothiolate, and *OO*-diethyl methylphosphonothionate (ratio of latter two peaks 1·0 : 0·035). Low boiling material was distilled off at atmospheric pressure and the residue was fractionally distilled to give *OS*-diethyl methylphosphonothiolate (1·9 g, 79%), b.p. 95—97° at 10 mmHg, n_D^{20} 1·4725, ν 1225 cm^{-1} (P=O); n.m.r., see Table 1. Very similar conditions, with benzene, ether, or dioxan as solvent were used for all the phosphorus acids. With (—)-tris-1-methylheptyl orthoformate, benzene was used as the most convenient solvent. On reaction with *OO*-diethyl hydrogen phosphorothioate the crude mixture of phosphorus esters (66% yield) contained thiono- and thiolo-esters in the ratio 1 : 3·25, by g.l.c. Optical rotations of the pure phosphorus esters are detailed in Table 5.

*Reaction of Diphenyl-*N*-p-tolylketenimine with O-Ethyl Hydrogen Methylphosphonothioate.*—*O*-Ethyl hydrogen methylphosphonothioate (0·50 g, $3·6 \times 10^{-3}$ mol) in benzene (5 ml) was added dropwise, with stirring, to the imine (0·51 g, $1·8 \times 10^{-3}$ mol) in benzene (20 ml) and the mixture was heated under reflux for 2 h. The benzene was evaporated and ether (5 ml) was added followed by light petroleum (b.p. 40—60°) (10 ml). The solid which crystallised was filtered, washed with light petroleum (b.p. 40—60°) (3 × 5 ml) and recrystallised from toluene–hexane to give *diphenyl-*N*-p-tolylthioacetamide* (0·45 g, 90%), m.p. 183·5—184·5°, ν 3080 (N–H) and 1135 cm^{-1} (C=S) (Found: C, 79·65; H, 6·2; N, 4·3; S, 9·95. $C_{21}H_{19}NS$ requires C, 79·45; H, 6·05; N, 4·4; S, 10·1%).

The solvent was evaporated and distilled under vacuum to give *OO'*-diethyl dimethylmonothionopyrophosphonate (0·43 g, 95%), b.p. 88° at 0·05 mmHg, n_D^{20} 1·4730 (lit., b.p. 73—74° at $3·5 \times 10^{-4}$ mmHg, n_D^{20} 1·4679) ν 1260 cm^{-1} (P=O), δ ($CDCl_3$) 4·2 (4H, m, CH_3CH_2OP), 1·95 (3H, d, CH_3P=S), 1·65 (3H, d, CH_3P=O), and 1·3 (6H, t, CH_3CH_2OP).

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