Nucleophilic Reactivity of Organophosphorus Compounds. Part I. The Reaction of Phosphonic and Thiophosphonic Acids with Diethylmethylketen Ketal

By **C. D. Hall,** Department of Chemistry, King's College, Strand, London W.C.2

Diethylmethylketen ketal reacts with alkyl hydrogen alkylphosphonates or alkyl hydrogen alkylphosphonothionates in benzene solution to give ethyl propionate and alkyl ethyl alkylphosphonate or alkyl ethyl alkylphosphonothiolate in yields in excess of 90%. A mechanism is suggested involving the addition of the phosphonic or thiophosphonic acid to the double bond of the ketal *via* the nucleophilic oxygen atom of either acid, followed by rearrangement of the resultant intermediate through a six-membered cyclic transition state to give the products. Intermolecular hydrogen bonding between alkyl hydrogen alkylphosphonothionates and alkyl ethyl alkylphosphonothiolates is also reported and discussed.

CURRENT interest in the nucleophilic reactivity of organophosphorus compounds [1,2] and increasing knowledge on the mechanism of proton transfer to olefins [3,4] prompted an investigation of the reactions of phosphorus oxyacids and phosphorus thioacids with olefins. The substrate chosen initially was diethylmethylketen ketal since this compound is rapidly hydrolysed to ethyl propionate under acid-catalysed conditions. Alkyl hydrogen alkylphosphonates (I) react with *OO*-diethylmethylketen ketal (II) in anhydrous benzene to give the corresponding alkyl ethyl alkylphosphonate (III) and ethyl propionate (IV) in high yields (>90%). The products were

---

[1] R. F. Hudson, 'Structure and Mechanism in Organophosphorus Chemistry,' Academic Press, London and New York, 1965.

[2] R. F. Hudson, *Chimia* (*Switz.*), 1962, **16**, 173.

[3] V. Gold and M. A. Kessick, *Discuss. Faraday Soc.*, 1965, 39.

[4] V. Gold, *Chimia* (*Switz.*), 1965, **19**, 508.

$$\underset{(I)}{R^2O{\cdot}R^3P(O)OH} + \underset{(II)}{CH_3CH{=}C(OEt)_2} \longrightarrow \underset{(III)}{R^2O{\cdot}R^3P(O)OEt} + \underset{(IV)}{EtCO_2Et}$$

R^2 = Et, Pr^i
R^3 = Et, Me

separated by fractional distillation and the yield of ethyl propionate was estimated by g.l.c. and identified by i.r. spectroscopy. No ethanol was detected in the mixtures and the distillation residue was identified by i.r. as unchanged (I) and contained no detectable tetra-alkylpyrophosphonate as a product. The results are summarised in Table 1.

TABLE 1

The reaction of alkyl hydrogen alkylphosphonates (I) with diethylmethylketen ketal (II)

$R^3PO(OR^2)OH$	Molar ratio I : II	Products and yield [% based on (II)] From (II)	From (I)
R^2 = Et R^3 = Et (Ia)	1 : 1	(IV) 84%	(IIIa; $R^2 = R^3$ = Et) 80%, b.p. 141—144°/130 mm. Residue: (Ia) 27%
R^2 = Et R^3 = Et (Ia)	2 : 1	(IV) 68%	(IIIa; $R^2 = R^3$ = Et) 72%, b.p. 104·5—105·5°/30 mm. (Ia) 102%, b. p. 118—122°/1·3 mm.
R^2 = Pr^i R^3 = Me (Ib)	1 : 1	(IV) 70%	(IIIb; R^2 = Pr^i, R^3 = Me) 70%, b.p. 107—109°/40 mm. (Ib) 30%
R^2 = Pr^i R^3 = Me (Ib)	2 : 1	(IV) 66%	(IIIb) 83%, b.p. 99—100°/35 mm. (Ib) 110%, b.p. 87—88°/0·15 mm.

The ethyl propionate content of (II) (see Experimental Section) was allowed for in calculating the yields of (IV) from the reactions and a recorded yield of 75% of (IV) therefore represents a quantitative conversion of (II) into (IV). Table 1 shows that this conversion is in the region of 90—100% in all cases. Allowance was also made for the t-butyl propionate impurity in calculating the yields of (III) and a recorded yield of 75% of (III) represents a quantitative conversion of (I) into (III).

The reactions were repeated under the same conditions with alkyl hydrogen alkylphosphonothionates (V) in place of the oxygen acids. Again the reactions were exothermic and the products were exclusively (IV) and the corresponding alkyl ethyl alkylphosphonothiolate (VI). The results are summarised in Table 2.

$$\underset{(V)}{R^2O{\cdot}R^3P(S)OH} + \underset{(II)}{CH_3CH{=}C(OEt)_2} \longrightarrow R^2O{\cdot}R^3P(O)SEt + (IV)$$
$$(VI)$$

With allowance for the impurities in (II) the recorded yields of (IV) and (VI) (at 70—80%) represent a minimum of 90% conversion of (II) and (V) into (IV) and (VI) respectively.

A g.l.c. analysis of the low-boiling (benzene–ethyl propionate) fractions failed to detect ethanol or ethyl propiothionate as products and the absence of alkyl ethyl alkylphosphonothionates as products was proved by g.l.c. analysis of the mixtures before distillation.

Independent experiments showed that alkyl ethyl alkylphosphonothionates did not rearrange to the corresponding alkyl ethyl alkylphosphonothiolates in the presence of (*a*) alkyl hydrogen alkylphosphonothionates, (*b*) ethyl propionate, or (*c*) diethylmethylketen ketal under the solvent and temperature conditions of the observed reaction.

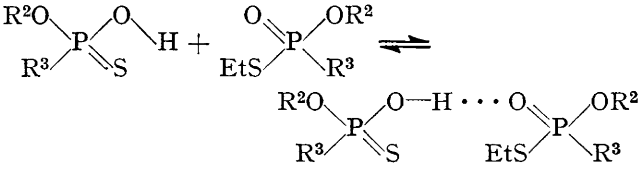
TABLE 2

The reaction of alkyl hydrogen alkylphosphonothionates with diethylmethylketen ketal

$R^3{\cdot}R^2OP(S)OH$ (V)	Molar ratio V : II	Products and yields [% based on (II)] From (II)	From (V)
R^2 = Et R^3 = Et (Va)	1 : 1	(IV) 78%	(VIa; $R^2 = R^3$ = Et) 75%,* b.p. 52—54°/0·2 mm. Residue: 1 : 1 molar mixture of (V) and (VI). (V) 7% recovery
R^2 = Pr^n R^3 = Me (Vb)	1 : 1	(IV) 78%	(VIb; R^2 = Pr^n, R^3 = Me) 72%,* b.p. 63—65·5°/0·6 mm. Residue: 1 : 1 molar mixture of (V) and (VI). (V) 18% recovery
R^2 = Et R^3 = Me (Vc)	1 : 1	(IV) 74%	(VIc; R^2 = Et, R^3 = Me) 70%,* b.p. 53·5—55·5°/0·22 mm. Residue: 1 : 1 molar mixture of (V) and (VI). (V) 14% recovery
R^2 = Et R^3 = Me	2 : 1	(IV) 80%	1 : 1 molar mixture of (V) and (VI) (R^2 = Et, R^3 = Me), b.p. 93—94·5°/0·6 mm. Residue: mainly (V). (VI) 83%

* The yields quoted include the quantity of (VI) not separated from (V) by distillation.

It was found that (VI; a, b, c) could not be separated from the equivalent molar quantity of (V; a, b, c) by fractional distillation. Mixtures of these compounds co-distilled in a 1 : 1 molar ratio. Control experiments showed that equimolar mixtures of (V) and (VI) had i.r. spectra identical with those of the highest-boiling fractions or residues from the reactions (see Table 2), which were not aggregate spectra of the components. The i.r. spectra of the mixtures were characterised by a strong band at *ca.* 1185 cm.$^{-1}$ [not present in (V) and (VI)] and by a broadening of the P–O–H stretching absorption of (V) (*ca.* 3000 cm.$^{-1}$). The latter indicates a change from the very weak P–OH • • • S intramolecular bonding in (V) to relatively strong P–OH • • • O intermolecular hydrogen bonding in the mixtures. The band at *ca.* 1185 cm.$^{-1}$ (see Table 3) in the mixtures is assigned to the P=O stretching vibration of (VI) (normally at *ca.* 1220 cm.$^{-1}$) [5] which displays a shift to longer wavelength



---

[5] L. C. Thomas and R. A. Chittenden, *Spectrochim. Acta*, 1964, **20**, 467.

owing to intermolecular bonding with (V). This agrees with the reported value[5] of 1175—1215 cm.$^{-1}$ for the P=O stretching vibration of compounds of type (I).

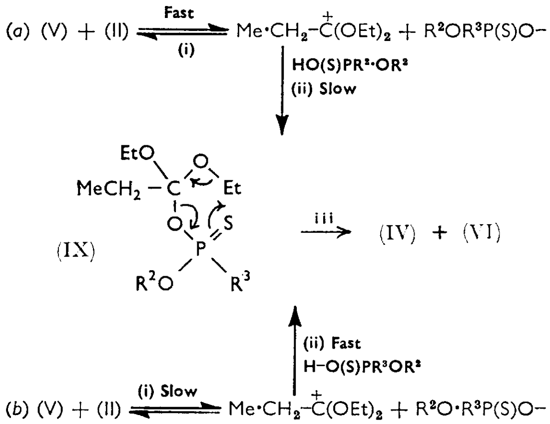
TABLE 3

Infrared data on 1 : 1 molar mixtures of (V) and (VI)

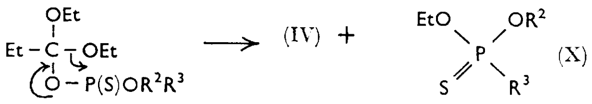
Compound	R^2	R^3	B. p.	ν(P=O) (cm.$^{-1}$)
$R^2O{\cdot}R^3P(O)SEt$	Et	Et	52—54°/0·2 mm.	1213
	Et	Me	53—55°/0·2 mm.	1220
	Pr^n	Me	63—65°/0·6 mm.	1222
$R^2OR^3P(O)SEt$	Et	Et	79—80°/0·2 mm.	1184
$R^2OR^3P(S)OH$	Et	Me	93—94°/0·6 mm.	1186
(1 : 1 molar)	Pr^n	Me	—	1188

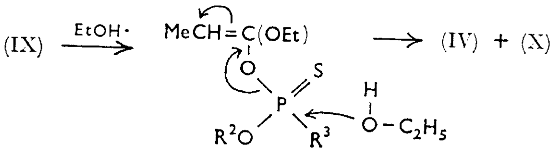
As expected there was no detectable interaction (i.r.) between (Va, c) and either diethylethylphosphonothionate (X; $R^2 = R^3 =$ Et) or diethylmethylphosphonothionate (X; $R^2 =$ Et, $R^3 =$ Me) since both intra- and inter-molecular hydrogen bonding would be with sulphur in these cases. Likewise (IIIa, b) did not co-distil or show any interaction with (Ia, b) since in these cases the intramolecular P–OH • • • O bonding in (Ia, b) would predominate.

A number of mechanisms are theoretically possible for the reactions described in Tables 1 and 2 but the observations with the thioacids leave only two reasonable mechanistic routes, (*a*) and (*b*).

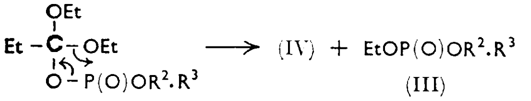


Step (iii) is common to both reaction paths and involves an intramolecular rearrangement of the intermediate (IX) through a six-membered cyclic transition state. An alternative mechanism involving a four-centre rearrangement of (IX) would yield the alkyl ethyl alkylphosphonothionate (X). It was shown that (X) did not rearrange to (VI) under the reaction conditions (such rearrangements are slow especially in non-polar media[6]). This eliminates the four-centre transition state and also the possibility of nucleophilic attack by sulphur followed by rearrangement of the resultant thiono-ester (X) to the thiolo-ester (VI). Further, it rules out the remote possibility of elimination of ethanol from (IX) followed by nucleophilic attack by ethanol to give (X).

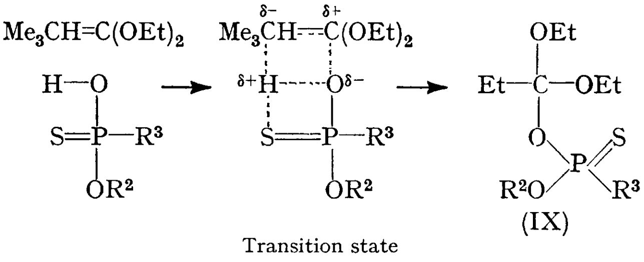




However, the four-membered transition state remains a possibility for the reaction of (II) with the oxygen acids.



Of the alternatives for the formation of (IX), path (*a*) seems unlikely since (I) and (V) would be virtually unionised in the benzene medium and the mechanism does not conform to that accepted for the addition of hydrogen halides to olefins in aprotic[7] and aqueous[8] medium. Route (*b*) involving rate-determining addition of a proton to the double bond of (II) appears more feasible and the free carbonium-ion intermediate (VIII) may be formed in this step. Intermediate (VIII) would be stabilised to a limited extent by conjugation with the ethoxy-groups but would probably still consistute a ' hard ' acid[9] and as such would be susceptible to attack by a ' hard ' base, *i.e.*, the oxygen atom in the thiophosphonate ambident nucleophile. It is possible, however, that the mechanism is a concerted process involving transfer of a proton from (V) (or I) to (II) through a four-membered transition state or an ion-pair, giving (IX) without the intervention of a free carbonium ion and followed by a fast rearrangement of (IX) to products.



Such a mechanism would circumvent the high energy of activation expected in forming a carbonium ion in the aprotic medium and has a precedent in the mechanism suggested for the acid-catalysed acylation of amines by dimethylketen.[10] The proton transfer from (V) to (II) may be assisted by weak intramolecular bonding with sulphur or by association with a second molecule of (V). In the case of the oxygen acids the proton must be regarded as equidistant between the two oxygen atoms

---

[6] T. R. Fukoto and R. L. Metcalfe, *J. Amer. Chem. Soc.*, 1954, **76**, 5103.

[7] E. S. Gould, ' Mechanism and Structure in Organic Chemistry,' Holt, Rinehart, and Winston, New York, 1960, p. 516.

[8] V. Gold and D. C. A. Waterman, *Chem. Comm.*, 1967, 40.

[9] R. G. Pearson, *Chem. Brit.*, 1966, 103.

[10] P. J. Lillford and D. P. N. Satchell, *J. Chem. Soc.*, 1967, 360.

and the question of ambident nucleophilicity does not arise.

Kinetic studies are in progress and definitive evidence for the detailed mechanism must await the result of this work and parallel studies with related substrates such as the keten *ON*- and keten *NN*-acetals, and substituted ketenimines, where mesomeric stabilisation of a carbonium-ion intermediate by conjugation with nitrogen may change the mode of attack by the ambident nucleophile. Nucleophilic attack by sulphur (>95%) has been observed with *N*-*p*-tolyldiphenylketenimine and mixed oxygen–sulphur attack (ratio dependent on the conditions) for keten *ON*-acetals.[11]

EXPERIMENTAL

Anhydrous (sodium-dried and distilled) AnalaR benzene was used as solvent.

Infrared spectra were obtained as liquid films with a Perkin-Elmer 137 Infracord and a Perkin-Elmer 257 spectrometer; n.m.r. spectra were recorded on a Perkin-Elmer R10, 60 Mc./sec. instrument with deuteriochloroform as solvent and tetramethylsilane as internal standard.

The benzene and ethyl propionate fractions were analysed by g.l.c. on a Perkin-Elmer Fraktometer fitted with a 6-m. silicone oil, DC200 column, operating at 90°. It was shown that these conditions would effectively separate ethanol, isopropyl alcohol, benzene, and ethyl propionate and the column was calibrated for quantitative use by injecting known weight-ratio mixtures of these compounds.

The g.l.c. analyses of the mixtures were on a 1 m. Carbowax column at 100° in a Pye Argon Chromatograph and these conditions provided a clean separation of dialkyl alkylphosphonothiolates from the thionate isomers.

OO-Diethylmethylketen ketal was prepared by the method of McElvain and Davie.[12]

Reaction of Alkyl hydrogen Alkylphosphonates (I) *with Diethylmethylketen ketal* (II).—A solution of (I) ($2\cdot5 \times 10^{-2}$ mole) in benzene (5 ml.) was added dropwise at room temperature with stirring to a solution of (II) (3·25 g., $2\cdot5 \times 10^{-2}$ mole) in benzene (20 ml.). When the initial exothermic reaction subsided the solution was heated under reflux for 2 hr. The mixture was transferred to a semimicro distillation unit fitted with a 10 cm. Vigreux column and was then fractionally distilled from an oil-bath first at atmospheric pressure to remove benzene (and some ethyl propionate), then at 200 mm. to remove the remaining ethyl propionate. The benzene and ethyl propionate fractions were weighed and analysed by g.l.c. The clear liquid residue was fractionally distilled at 30—120 mm. and the alkyl ethyl alkylphosphonate was collected, weighed, and identified by b.p.,[13] and i.r. and n.m.r. spectra, by comparison with the spectra of authentic materials. The residue in the distillation flask was subsequently distilled at *ca.* 0·2 mm., the distillate being weighed and identified as starting material (I) by b.p. and i.r. spectrum.

In the final experiment of Table 1, the g.l.c. analysis of the low-boiling (benzene) fractions revealed a small amount (<3%) of a material with an unexpectedly high retention (8·2 cm.). This was shown to be t-butyl propionate by comparison with the g.l.c. of an authentic sample under identical column conditions and this finding was confirmed by comparing the i.r. spectrum of the condensate from the g.l.c. column (peak, 8·2 cm.) with the i.r. spectrum of authentic t-butyl propionate.

A g.l.c. analysis revealed that (II) contained ethyl propionate (*ca.* 10%) and t-butyl propionate (*ca.* 16%). The t-butyl propionate in (II) accounted for the small amount of carbonyl impurity detected by i.r. spectroscopy in the dialkyl alkylphosphonates distilled from the reaction mixtures. The carbonyl impurity (*ca.* 10%) was separated from the phosphonate esters by chromatography on neutral alumina (Woelm, Grade II) with benzene, then chloroform, as eluent, or by careful distillation in a spinning-band column.

Reaction of Alkyl Hydrogen Alkylphosphonothionates (V) *with* (II).—(a) 1 : 1 *Molar ratio.* A solution of (V) ($2\cdot5 \times 10^{-2}$ mole) in benzene (5 ml.) was added dropwise at room temperature with stirring to a solution of (II) (3·25 g., $2\cdot5 \times 10^{-2}$ mole) in benzene (20 ml.). An exothermic reaction occurred during the addition and finally the solution was heated under reflux for 2 hr. The products were separated by fractional distillation and the benzene and ethyl propionate fractions were analysed by g.l.c. The phosphorus-containing components were distilled at 0·2—0·6 mm. and the *O*-alkyl *S*-ethyl alkylphosphonothiolate (VI) so obtained was identified by b.p. and i.r. and n.m.r. spectra by comparison with the b.p.[13] and spectra of authentic material. The highest-boiling fraction and the residue 1 : 1 molar mixtures of (V) and (VI).

(b) 2 : 1 *Molar ratio,* (V) : (II). A solution of ethyl hydrogen methylphosphonothionate (Vc) (7·0 g., 5×10^{-2} mole) in benzene (5 ml.) was added dropwise at room temperature with stirring to a solution of (II) (3·25 g., $2\cdot5 \times 10^{-2}$ mole) in benzene (20 ml.). After the addition the mixture was heated under reflux for 2 hr. and the product was fractionally distilled. A g.l.c. analysis of the low-boiling fractions showed the yield of ethyl propionate to be 2·0 g. [100% on (II)] and the colourless liquid residue was distilled to give 6·4 g. of a fraction of b.p. 93—94·5°/0·6 mm. [lit.,[13] b.p. 87—88°/7 mm. for *OS*-diethyl methylphosphonothiolate (VIc) and 34·5—35·5°/0·4 mm. for *OO*-diethyl methylphosphonothionate). The i.r. spectrum of the distillate showed ν 1180s and 3000 cm.$^{-1}$ (v-broad and s) and these bands were not present in the spectra of (Vc) or (VIc). An equimolar mixture of (Vc) and (VIc) distilled unchanged at 93—94°/0·6 mm. and the i.r. spectrum was identical to that of the distillate obtained from the reaction.

Similarly, equimolar mixtures of (i) ethyl hydrogen ethylphosphonothionate (Va) and *OS*-diethylethyl phosphonothiolate (VIa) and (ii) n-propyl hydrogen methylphosphonothionate (Vb) and *O*-n-propyl-*S*-ethyl methyl phosphonothiolate (VIb) had i.r. spectra which were not additive spectra of the two components but displayed bands at *ca.* 1180s and *ca.* 3000 cm.$^{-1}$ (v-broad and s); the mixtures could not be separated by distillation.

Equimolar mixtures of (i) ethyl hydrogen ethylphosphonothionate (Va) and *OO*-diethyl ethylphosphonothionate and (ii) ethyl hydrogen methylphosphonothionate (Vc) and *OO*-diethyl methylphosphonothionate had i.r. spectra which were simple aggregates of the spectra of the components and the mixtures were easily separated by fractional distillation.

[7/1634 *Received, December 13th,* 1967]

---

[11] P. G. LeGras and C. D. Hall, unpublished results.

[12] S. M. McElvain and W. R. Davie, *J. Amer. Chem. Soc.*, 1951, **73**, 1400.

[13] Houben-Weyl, ' Methoden der Organischen Chemie, Organische Phosphorverbindungen,' Teil 1, 1963, p. 338.