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ORGANOPHOSPHORUS COMPOUNDS—XVI

THE REACTION OF PHOSPHITE ESTERS WITH VICINAL TRIKETONE MONOHYDRATES

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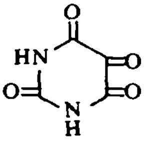
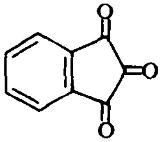
Abstract—Trialkyl phosphites react with the monohydrates of 1,2,3-indantrione (ninhydrin) (VII) and 1,3-diphenylpropanetrione (VIII) to give the corresponding phosphate derivatives XIa–c and XVIIIa–c. The same compounds are obtained upon reacting VII and/or VIII with the proper dialkyl hydrogen phosphite. The trialkyl phosphites cause the quantitative reduction of perinaphthindantrione (IX) and/or its monohydrate (X) producing dihydroxy-peri-naphthindenone (XXI). On the other hand, dialkyl hydrogen phosphites add to IX (or X), yielding compounds XXIIa–c.

Structural reasonings based on UV, IR and NMR spectral data are presented.

THE ACTION of trialkyl phosphites on some polycarbonyl compounds, namely, alloxan (I),[1] 1,2,3-indantrione (II)[2] and 1,3-diphenylpropanetrione (III),[3] has been reported.


I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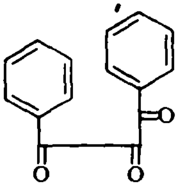
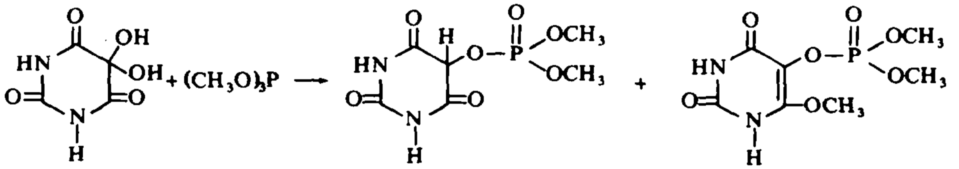
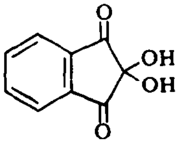

III

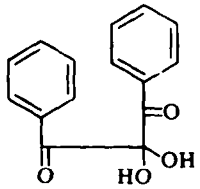
The structures of the products isolated from these reactions varied a great deal, depending on the nature of the carbonyl compound. Very little is known, however, about the behaviour of the corresponding monohydrates towards the same phosphite reagents. Ramirez *et al.*[1] found that alloxan monohydrate (IV) reacts with trimethyl phosphite to give 5-hydroxybarbituric acid 5-dimethyl phosphate (V) and the uracil phosphate VI. The latter compound represented the main reaction product when anhydrous alloxan (I) was used.


IV V VI

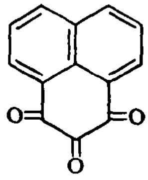
The object of the present investigation is to gain knowledge about the behaviour of the monohydrates of 1,2,3-indantrione (ninhydrin) (VII) and of 1,3-diphenylpropanetrione (VIII) towards the action of alkyl phosphites. The study is extended to



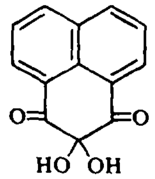
VII



VIII



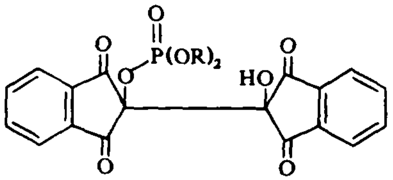
IX



X

include the reaction of peri-naphthindantrione (IX) and its hydrated form (X) with the same reagents. No work on these compounds from the present standpoint has hitherto been described.

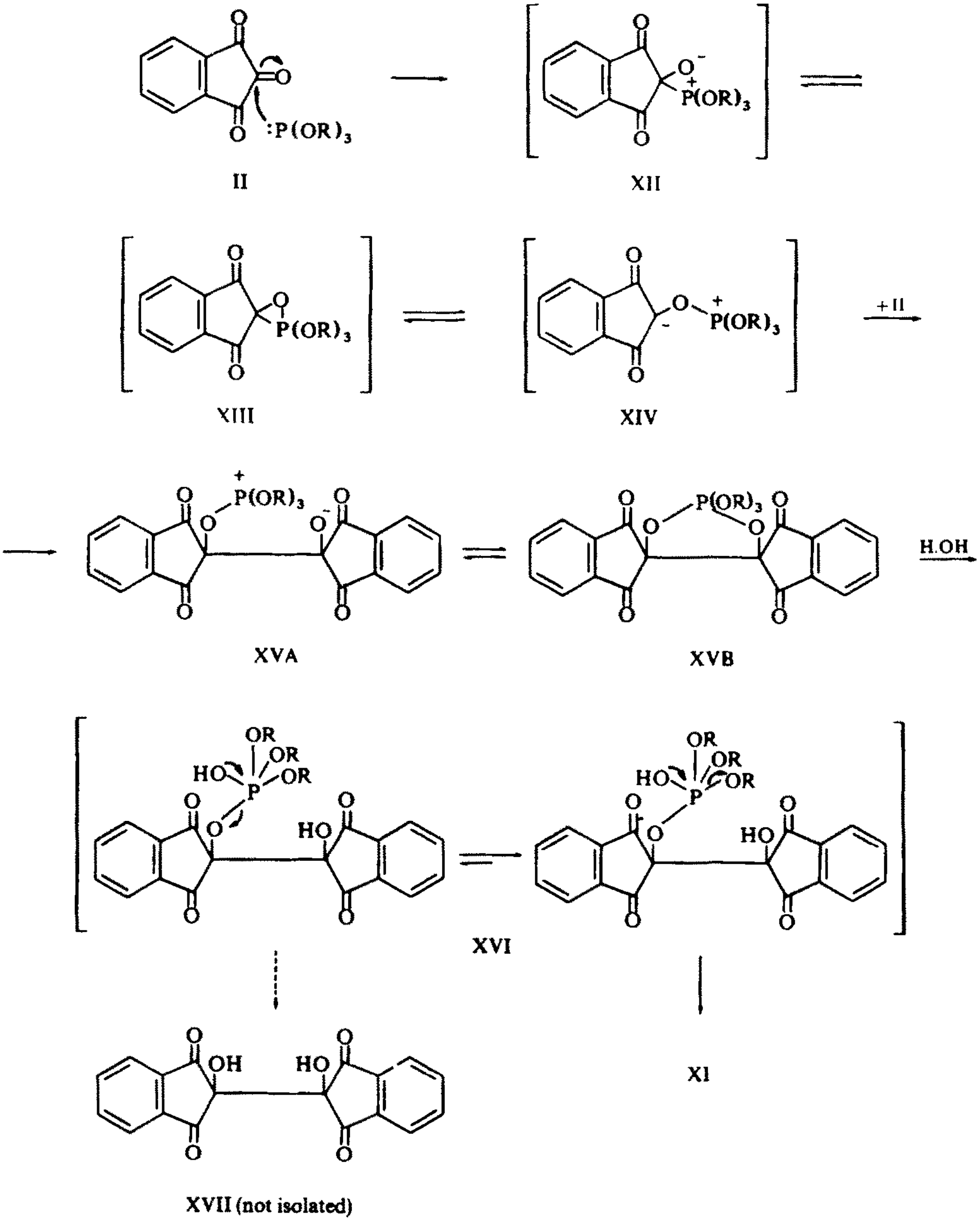
Reaction of ninhydrin with alkyl phosphites. Ninhydrin (VII) reacted with trimethyl-, triethyl-, and triisopropyl phosphites, in boiling methylene chloride, to give the phosphate derivatives XIa-c, respectively. The latter compounds were identical (mixed m.p. and comparative IR spectra) with those prepared by the action of the corresponding dialkyl hydrogen phosphites on 1,2,3-indantrione (II).[4]



XIa: R = Me
b: R = Et
c: R = i − Pr

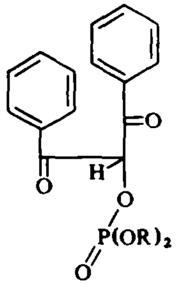
A mechanism for the formation of compounds XI from VII is presented in Scheme I. This involves the initial dehydration of VII to give 1,2,3-indantrione (II).[5] In this respect, the action of the phosphite reagent resembles that proposed for the primary electrochemical process encountered in the reduction of VII.[6] Attack by phosphorus on the middle carbonyl carbon of II yields the phosphonium species XII. Rearrangement of XII, via a cyclic 3-membered ring-intermediate (XIII) gives the activated form XIV, being favoured by $p_\pi - d_\pi$ interactions.[7a] Structure XIV reacts further with a second molecule of II to form the dipolar structure XVA, existing probably in equilibrium with saturated 5-membered cyclic oxyphosphorane XVB. The addition of elements of water to XV produces a transient intermediate (XVI) with pentacovalent phosphorus.[8–10] This collapses to give the observed products (XI). The alternate hydrolysis path to hydrindantin (XVII; not isolated) is thus avoided. Supporting this

SCHEME 1

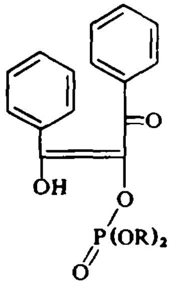


idea is the fact that XIa, taken as an example, was obtained in a good yield when the 2:1 adduct (XV, R = Me) was kept in long contact with water.

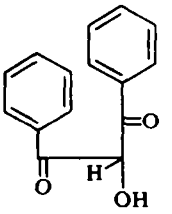
Reaction of 1,3-diphenylpropanetrione monohydrate with alkyl phosphites. The trione hydrate (VIII) reacted with trimethyl-, triethyl-, and triisopropyl phosphites at 25°, in methylene chloride, to form 1:1 adducts assigned structure XVIIIA. The other tautomeric form XVIIIB should not be overlooked, since these adducts respond positively to the ferric chloride reaction, giving a red colour, and dissolve freely in 10% aqueous alkali. The formation of XVIII was accompanied by *ca* 20% of the colourless crystalline 2-hydroxy-1,3-diphenylpropanedione (XIX).[11] Adducts XVIII regenerated the anhydrous propanetrione (III) and the respective dialkyl hydrogen phosphite, when subjected to pyrolysis. Boiling XVIII with 10% HCl gave one and the same compound, namely, 2-hydroxy-1,3-diphenylpropanedione (XIX). On the other hand, treatment of XVIII with aqueous alkali yielded benzoic acid. Further, compound XVIIIa, for example, proved identical (comparative IR and NMR spectra) with that obtained by the action of dimethyl hydrogen phosphite on the triketone III (Experimental). The same compound (XVIIIa) was obtained when the pentaoxyphosphorane XX[3] was subjected to mild hydrolysis with water (*cf* Scheme II).



XVIIIA



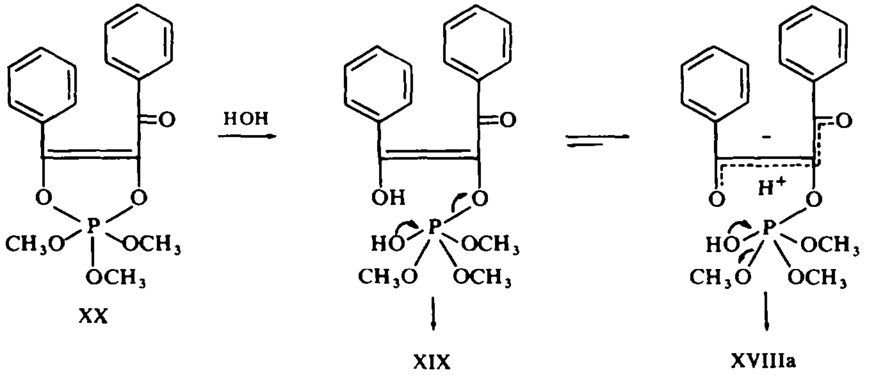
XVIIIB



XIX

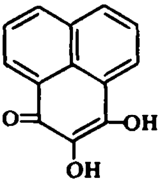
a: R = Me
b: R = Et
c: R = i − Pr

SCHEME II

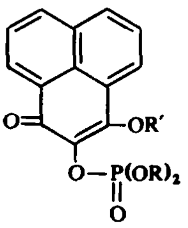


The IR spectrum of XVIIIa (liquid film) showed bands at 1710 and 1690 cm^{-1} (C═O group), 1600 cm^{-1} (C═C, aromatic), 1260 cm^{-1} ($\geqslant$P═O) and at 1050 cm^{-1} (P—O—CH_3).[12] The H^1 NMR spectrum of XVIIIa had one 6H doublet (J_{HP} = 11·5 c/s at τ 6·2, due to the two OMe groups. The aromatic protons gave multiplets at τ 1·99 ($4H^1$) and τ 2·44 ($6H^1$). The spectrum revealed also the presence of an acidic proton as a singlet at τ −2·6 (probably OH proton).

Reaction of peri-naphthindantrione and its monohydrate with alkyl phosphites. When peri-naphthindantrione (IX) reacted with the trialkyl phosphite at 10°, in methylene chloride, a red crystalline dihydroxy-peri-naphthindenone (XXI),[13] was isolated almost quantitatively. The same was true with peri-naphthindantrione monohydrate (X).



XXI

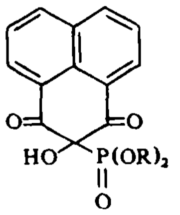


XXIIa: R = Me: R′ = H
b: R = Et; R′ = H
c: R = iPr: R′ = H
d: R = R′ = Me

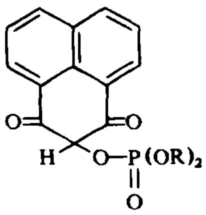
The action of dialkyl hydrogen phosphites on peri-naphthindantrione (IX) and its monohydrate X, was also investigated. Dimethyl-, diethyl-, and diisopropyl hydrogen phosphites reacted with IX (or X) to give mainly the 1:1 adducts XXIIa–c, respectively. The enediol phosphate structure XXII was based on the following evidence: (i) The UV absorption spectrum of XXIIc, in ethanol, resembled that of dihydroxy-peri-naphthindenone (XXI). Both compounds showed their principal absorptions around the 240 mμ and 340 mμ regions. A hypsochromic shift of 7 mμ was shown, however, in the spectrum of XXIIc, in the longer wave absorption. The spectrum of peri-napthindantrione monohydrate (X) showed maxima at 228 mμ and 320 mμ, respectively. (ii) The IR spectrum of XXIIc, in KBr, showed a weak and broad absorption band around 3340 cm^{-1} (OH group). Bands at 1640 cm^{-1} (C═O), 1590 and 1550 cm^{-1} (C═C, aromatic), 1260 cm^{-1} ($\geqslant$P═O) and at 1020 cm^{-1} (P—O—C_3H_7—i)[12] appeared also in the spectrum. (iii) The H^1 NMR spectrum of XXIIc revealed the presence of 12 protons as two doublets at τ 8·95 and τ 9·05 both with J = 2·5 c/s, resulting from the two isopropyloxyl groups. A multiplet was visible for the two methine protons at *ca* τ 5·45 which may result from the overlap of two multiplets; one from proton–proton coupling and the other from proton-phosphorus coupling, assuming the J_{CH-CH} and J_{CH-P} constants are close in value.[14] All the aromatic protons appeared in the region τ 1·5–2·5 and the integral was defined as 6 protons. (iv) Treatment of XXIIa–c with 10% HCl affected their hydrolysis to dihydroxy-peri-naphthindenone (XXI) in a quantirative yield. Meanwhile, naphthoic acid was mainly produced when these compounds were treated with 10% Na OHaq

Moreover, treatment of adduct XXIIa with ethereal diazomethane, afforded the corresponding monomethyl ether (XXIId). The identity of XXIId was further verified from correct combustion values, IR and H^1 NMR spectral data (Experimental). This adds further evidence to the enediol phosphate structure XXII.

Although the above results exclude the alternate α-hydroxyphosphonate structure XXIII for the trione-dialkyl hydrogen phosphite adducts, still there is a possibility for its initial formation. This undergoes rearrangement to the more stable phosphate structure XXIV which tautomerizes to the enediol compounds (XXIIa–c).



XXIII



XXIV

R = Alkyl

The results of the present investigation allow certain interesting conclusions to be drawn. While alloxan (I) and its monohydrate (IV) react with trialkyl phosphites mostly as a *p*-quinone,[1] a different behaviour is noted with the vicinal triketone derivatives of the present study. Thus, trialkyl phosphites react with II and III on one hand, and with VII and VIII, on the other, to yield the corresponding phosphoranes XV and XX, and the phosphates XI and XVIII. The same phosphite reagents, however, cause the reduction of IX and X. This disparity in behaviour towards the trialkyl phosphite reagents is in accord with that noted in other reactions, e.g., the Strecker's degradation.[15, 16] Apparently, the high redox potential of IX (or X)[17] together with the strong reducing character of the tertiary phosphite reagents[7b, 18], would facilitate the further reduction of any pentaoxyphosphorane that chances to form. In support of this idea is the fact that the less powerful nucleophile (reducing) dialkyl hydrogen phosphites[19] produce with IX and X, the stable phosphates XXII. In this respect, IX (X) behaves in a manner similar to II (VII) and III (VIII).

EXPERIMENTAL

All m.ps are uncorrected. CH_2Cl_2 was freshly distilled over P_2O_5. The ether (peroxide-free) and benzene (thiophene-free) used, were dried (Na). Trialkyl phosphites were purified by treatment with Na followed by fractional distillation, and dialkyl hydrogen phosphites were freshly distilled.

The UV measurements were made using a Carl-Zeiss PMQ II Spectrophotometer in absolute spectroscopic ethanol. The IR spectra were recorded with a Carl-Zeiss Infracord Spectrophotometer Model "UR 10" and the NMR spectra were performed on a Varian A 60 Spectrometer in $CDCl_3$ solution, using TMS as an internal standard.

Action of trialkyl phosphites on ninhydrin (VII). A mixture of ninhydrin[20] (0·7 g; 0·004 mole) and trimethyl phosphite[21a] (1·3 g; 0·01 mole) in CH_2Cl_2 (30 ml), was refluxed for 12 hr. After cooling, the pt was (0·77 g; 90%), dried and recrystallized from acetone–EtOH (1:2) to give XIa as colourless crystals, m.p. 245–247°, either alone or upon admixture with an authentic sample.[4]

Similarly, XIb (85%) and XIc (90%) were obtained upon reacting VII with triethyl,[21b] and triisopropyl phosphite[21b], respectively. Compounds XIb and XIc were identified by comparison of their m.ps with authentic specimens.[4]

Following the same procedure using 0·01 mole of dimethyl,[22a] diethyl,[22b] or diisopropyl hydrogen phosphites[22b] with ninydrin (0·004 mole), gave rise to XIa–c (yield *ca* 90 %), as proved by m.p. and mixed m.p. determinations with corresponding authentic samples.[4]

Action of water on XV (R = Me). Compound XV (R = Me)[2] (0·5 g) was treated with water (30 ml) and left at room temp for 24 hr. The insoluble material was collected (*ca* 0·4 g; 80 %), and recrystallized from acetone–EtOH (1:2) to give colourless crystals of XIa (m.p. and mixed m.p.)[4]

Action of trialkyl phosphites on 1,3-*diphenylpropanetrione monohydrate* (*VIII*). To a soln of VIII[23] (1 g; 0·004 mole) in CH_2Cl_2 (30 ml), was added trimethyl phosphite (0·6 g; 0·005 mole) and the mixture kept at 25° for 6 hr. After cooling to 10°, the product was filtered off, recrystallized from light petroleum (b.p. 80–100°) to give XIX as colourless crystals (*ca* 0·1 g; 20 %), m.p. 110° either alone or upon admixture with an authentic material.[11]

The filtrate was freed from all the volatile materials at 60° (bath temp) under reduced pressure (5 mm/Hg) and the oily residue underwent decomposition on further high vacuum distillation (200°, 0·5 mm/Hg). Thus, purification was achieved by dissolving in dry chloroform and repeatedly (3 times) running the soln through a column (3 cm × 30 cm) charged with 20 g alumina (Aluminium oxyd Woelm, Alkalifrei, annährend neutral, Akt. Stufe 1, M. Woelm-Eschwege). After removing the solvent, *in vacuo*, XVIIIa was collected (0·5 g; 75 %), as a pale yellow liquid, n_D^{25} 1·4800. (Found: C, 58·55; H, 5·85· P, 9·00. Calc. for $C_{17}H_{17}O_6P$: C, 58·62; H, 4·92; P, 8·89 %).

Similarly, XVIIIb and XVIIIc were obtained upon reacting triethyl-, and triisopropyl phosphites, respectively, with VIII and removal of XIX (*ca* 20 %) that formed in each reaction.

Compound XVIIIb (70 %) was obtained as a pale yellow liquid, n_D^{25} 1·4704. (Found: C, 60·91; H, 5·30; P, 8·12. Calc. for $C_{19}H_{21}O_6P$: C, 60·64; H, 5·62; P, 8·23 %).

Phosphate XVIIIc (n_D^{25} 1·3951) was isolated in a 65 % yield as a yellow liquid. (Found: 62·59; H, 6·03; P, 7·58. Calc. for $C_{21}H_{25}O_6P$: C, 62·37; H, 6·23; P, 7·65 %).

Action of dialkyl hydrogen phosphites on VIII. A mixture of VIII (1 g; 0·004 mole) and dimethyl hydrogen phosphite (11 g; 0·1 mole) was heated at 50° for 6 hr. After cooling to 10°, the substance that deposited was collected (*ca* 0·1 g; 20 %) recrystallized from light petroleum (b.p. 80–100°) and proved to be XIX.[11]

Excess phosphite was removed from the filtrate at 60° under reduced pressure (5 mm/Hg). The oily residue was dissolved in chloroform and purified by column chromatography (Al_2O_3) as before. After removal of the solvent, *in vacuo*, the remaining liquid (n_D^{25} 1·4800; 80 %) proved to be XVIIIa (comparative IR and NMR spectra).

Similarly, XVIIIb (75 %) and XVIIIc (75 %) were obtained and identified, upon reacting diethyl-, and diisopropyl hydrogen phosphites, respectively, with VIII and isolation of compound XIX (*ca* 20 %) that formed in each reaction.

In parallel experiments performed by allowing III[23] to react with the above dialkyl hydrogen phosphites, at ambient temp for 24 hr, identical products were isolated and the yields were approximately the same.

Action of water on the pentaoxyphosphorane XX. A mixture of XX[3] (3·6 g) and water (30 ml) was kept at room temp for 12 hr. After decanting the aqueous phase, the remaining oily material was dissolved in cold EtOH (10 ml) then left in the refrigerator. The substance that deposited was filtered off (0·36 g; 30 %), dried, recrystallised from light petroleum (b.p. 80–100°) and proved to be XIX.[11]

The filtrate was freed from EtOH, *in vacuo*, and the oily residue was dissolved in chloroform, purified over alumina, *vide supra*, (1·2 g; 70 %) and proved to be XVIIIa (comparative IR and NMR spectra).

Degradation experiments with phosphates XVIII

(a) *Pyrolysis*. Compound XVIIIa, taken as an example, (1 g) was heated under reduced pressure (0·5 mm/Hg) in an apparatus equipped for fractional distillation. The drops collected at 40° gave the violet colour reaction described for dimethyl hydrogen phosphite.[24] The fraction at 170° (*ca* 0·6 g; 85 %) proved to be III (m.p. and mixed m.p.).[23]

(b) *Acid hydrolysis*. Compound XVIIIa (0·7 g) was heated with 10 % HCl (15 ml) on a steam-bath for 1 hr. After cooling, the oily layer was dissolved in EtOH (10 ml) and kept at 5° for 24 hr. The product was collected and recrystallized from light petroleum (b.p. 80–100°) to give colourless crystals (0·45 g; 95 %) of 2 XIX.[11]

(c) *Alkali hydrolysis*. A mixture of XVIIIa (0·7g) and 10 % NaOH aq (20 ml) was refluxed for 2 hr. After cooling, the soln was acidified with 15 % HCl. The ppt was (*ca* 0·45 g; 90 %) crystallized from water to give colourless plates of benzoic acid (m.p. and mixed m.p.).

Action of trialkyl phosphites on peri-naphthindantrione (IX). A soln of the trialkyl phosphite (0·05 mole) was added dropwise to a suspension of IX[13] (0·005 mole) in 30 ml CH_2Cl_2 (or benzene) at 10° and the mixture kept at room temp for 1 hr. The red crystaline product (yield 95 %), recrystallized from toluene and proved to be XXI (m.p. and mixed m.p.).[13]

Compound XXI was also obtained in almost quantitative yield when the trialkyl phosphite reacted with X under the same experimental conditions.

Reaction of dialkyl hydrogen phosphites with IX (*or* X). To a suspension of IX (or X) (0·5 g) in CH_2Cl_2 (20 ml) was added dimethyl hydrogen phosphite (1 g) at 10° and the mixture kept at room temp for 24 hr. After evaporating the solvent, *in vacuo*, the residue was recrystallized from benzene light petroleum (b.p. 40–60°) to give XXIIa (0·65 g; 85 %) as golden yellow crystals, m.p. 184–186° (dec). (Found: C, 56·56; H, 4·04; P. 9·97. Calc. for $C_{15}H_{13}O_6P$: C, 56·25; H, 4·09; P, 9·67 %).

In a similar manner, XXIIb and XXIIc were obtained by the action of diethyl-, and diisopropyl hydrogen phosphite, respectively, on IX (or X).

Compound XXIIb (75 %) was recrystallized from CH_2Cl_2-light petroleum (b.p. 40–60°) as yellow crystals, m.p. 172–174° (dec). (Found: C, 58·82; H, 4·87; P, 9·14. Calc. for $C_{17}H_{17}O_6P$: C, 58·62; H, 4·92; P, 8·89%).

The yellow crystals of XXIIc were obtained from CH_2Cl_2-light petroleum (b.p. 40–60°; yield 80 %), m.p. 150–152 (dec). (Found: C, 60·43; H, 5·88; P, 8·38. Calc. for $C_{19}H_{21}O_6P$: C, 60·63; H, 5·62; P, 8·23 %). Ethanol max, 236 mμ (ε = 3200) and 339 mμ (ε = 900).

Action of diazomethane on XXIIa. A mixture of XXIIa (0·5 g) and ether (10 ml) was treated with an ethereal diazomethane soln (from 3 g nitrosomethylurea) then kept at 5° for 6 hr. After removal of ether, the residue was recrystallized from benzene–light petroleum (b.p. 40–60°) to give XXIId (90 %) as yellow crystals, m.p. 122–124° (dec). (Found: C, 57·62; H, 4·43: P. 9·56. Calc. for $C_{16}H_{15}O_6P$: C, 57·52; H. 4·50; P, 9·26 %). The IR spectrum (KBr) had bands at 1650 cm^{-1} (C═O), 1290 cm (—P═O) and at 1050 cm^{-1} (P—O—CH_3).[12] The H^1 NMR spectrum had a 6H^1 doublet centered at τ 5·95 with J_{HP} = 12c/s (for the two OMe groups on phosphorus), a 3H^1 singlet at τ 5·7 (due to the OMe group on the vinyl carbon) and a 6H^1 multiplet centered at τ 1·9 (for the aromatic protons).

Acid hydrolysis of compounds XXIIa–c. A mixture of XXIIa, taken as an example, (0·2 g) and 15 % HCl (15 ml), was heated on a steam bath for 1 hr. The red product was filtered off (*ca* 0·08 g; 90 %), recrystallized from toluene and proved to be XXI.[13]

Alkali hydrolysis of compounds XXIIa–c. A mixture of XXIIa (0·2 g) and 10 % Na OH aq (10 ml) was boiled for 1 hr. The yellow deposit after acidification with 15 % HCl, was collected (80 %), crystallized from EtOH and proved to be naphthoic acid (m.p. and mixed m.p.).

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