Organophosphorus Intermediates. Part VI.[1] Base-catalysed Reaction of Methyl Phosphinate with Tetraphenylcyclopentadienone

By **Christopher J. R. Fookes** and **Michael J. Gallagher,*** School of Chemistry, University of New South Wales, P.O. Box 1, Kensington, New South Wales, Australia 2033

Tetraphenylcyclopentadienone is rapidly reduced by methyl phosphinate in the presence of base, the major products being 2,3,4,5-tetraphenylcyclopent-3-enone (3) and dimethyl phosphonate, formed together with small amounts of *trans*- and *cis*-2,3,4,5-tetraphenylcyclopent-2-enone and 4- and 5-hydroxy-2,3,4,5-tetraphenylcyclopent-2-enones, (5) and (6). A mechanism involving decomposition of the monoanion of methyl phosphinate to hydride ion and methyl phosphenite is suggested to account for the products formed. No compounds with carbon–phosphorus bonds were detected.

TETRAPHENYLCYCLOPENTADIENONE (tetracyclone) reacts with P^{III} [1-6] and P^{IV} [7-11] nucleophiles to give a remarkable variety of products which, depending on conditions and reagent, arise by bond formation between phosphorus and the carbonyl oxygen atom or any of the ring carbon atoms. We now describe the reaction of methyl phosphinate with the ketone in the presence of triethylamine which gives rise to no detectable products containing carbon–phosphorus bonds.

This study arose from an examination of the alkylation of the readily accessible [12] methyl phosphinate as a potential route to new organophosphorus heterocycles. In the presence of base this ester adds easily to Michael acceptors [1,13] but attempted reactions with alkyl halides invariably afforded poor yields of the corresponding phosphonate [reaction (i)]. Full details of these

$$MeO{\cdot}P(:O)H_2 + RX \xrightarrow{Base} (MeO)_2P(:O)R \quad (i)$$

reactions will be reported elsewhere, but a possible mechanism considered was a hydride ion transfer from the monoanion of the ester to a molecule of the neutral ester [reaction (ii)]. We have previously invoked such a hydride ion transfer to account for the reducing properties of pyridinium phenylphosphinate and other P^{IV} nucleophiles towards tetracyclone.[7]

$$MeO{\cdot}P(:O)H_2 \longrightarrow MeO{\cdot}\bar{P}(:O)H \xrightarrow{MeO{\cdot}P(:O)H_2} (MeO)_2P(:O)H \xleftarrow{MeOH} MeO{\cdot}P{:}O + O{:}PH_3 + MeO^- \quad (ii)$$

Since tetracyclone is easily reduced to the stable, crystalline *trans*-2,3,4,5-tetraphenylcyclopent-2-enone, methyl phosphinate was treated with base in the presence of the ketone in order to intercept the hydride-ion-transfer step. The purple colour of the ketone was discharged and work-up after brief heating afforded the expected monoenone (2) in 70—90% yield. Examination of the mother liquors confirmed that the bulk (76%) of the phosphorus was then present as the phosphonate (1).

In order to determine whether the monoenone (2) was formed directly or *via* an unstable addition product of methyl phosphinate and the monoenone the reaction was carried out without heating and the product chromatographed over silica gel. Under these conditions the major component was the 3-enone (3), recognisable by its i.r. carbonyl band at 1 755 cm^{-1} and the absence of αβ-unsaturated carbonyl absorption in the u.v. spectrum. The ^1H n.m.r. spectrum of the crude 3-enone (3) showed a single sharp peak at δ 4.88 together with a much smaller peak (<5%) at slightly higher field (δ 4.72). We therefore tentatively assign to the major component *cis*-stereochemistry, since the aliphatic protons of the *trans*-isomer should each be shielded by the 'opposite' phenyl group. Accompanying this compound were lesser amounts of an αβ-unsaturated cyclopentenone identified from the coupling constant of the non-aromatic protons (*J* 7.5 Hz) as *cis*-2,3,4,5-tetraphenylcyclopent-2-enone (4).[14] Small quantities of the *trans*-isomer (2) were also obtained.

The minor products of the reaction are of great interest, though present in small amounts and requiring careful chromatography for their isolation. The hydroxycyclopentenone (5) was readily identified by its spectroscopic properties; the position of the hydroxy-group was confirmed by comparison with an authentic sample prepared by base-catalysed condensation of benzil with dibenzyl ketone.[15] The literature preparation gives a mixture of stereoisomers which may be separated by chromatography. Stereochemistry is readily assigned since the solitary aliphatic ring proton in the *trans*-diphenyl isomer will resonate at higher field as a consequence of shielding by the phenyl group on the adjacent carbon atom [*cf.* (4) and (2)].[2] The preparation

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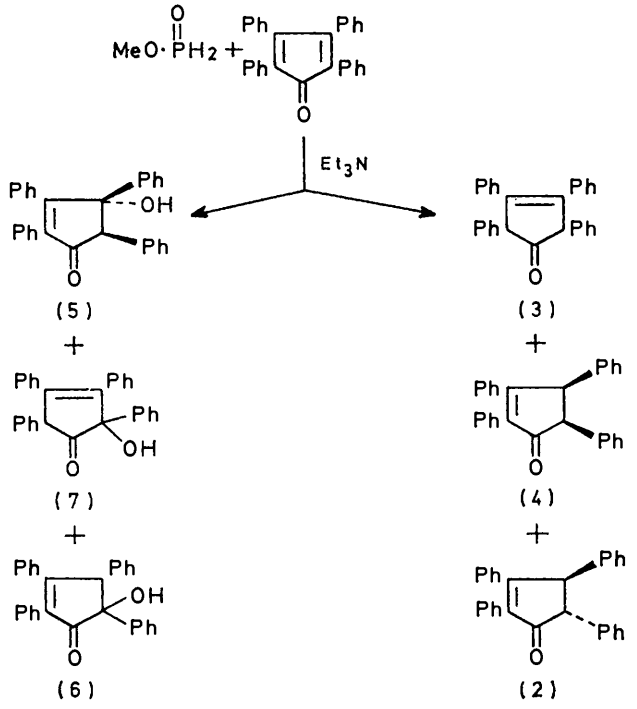
of (5) is a modification of the preparation of tetracyclone itself, which is indeed formed in considerable amounts. However, (5) is not a contaminant of the starting dienone used in the reduction reactions.

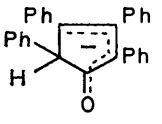
The hydroxy-enone (6) was only isolated in very small amount (<1%) and was difficult to separate from a more abundant contaminant to which structure (7) is assigned largely on the basis of its i.r. carbonyl absorption (1 755 cm^{-1}). The structure of (6) is confirmed by its spectroscopic properties, which are similar to those of (5).

Examination of the reaction mixture immediately after the colour of the dienone was discharged revealed that the 3-enone (3), and the hydroxy-enones (5)—(7) were already present, whereas the enones (2) and (4)

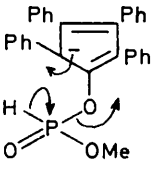


SCHEME 1

and the *trans*-diphenyl isomer of the hydroxy-enone (5) only appeared later, or when the solution was warmed. Treatment of dilute solutions of (5) (*cis* or *trans*) with triethylamine in chloroform–methanol resulted in slow (24 h) equilibration to give a *ca.* 50 : 50 mixture. Under similar conditions the ketones (2)—(4) showed clearly the sequence (3) ⟶ (4) ⟶ (2). After 24 h complete conversion of (3) and (4) into (2) was achieved, and under no circumstances was either (3) or (4) detected in basic solutions of (2). However, quenching of the enolate of (2) formed under aprotic conditions affords good yields of (4).[14] We conclude therefore that the unconjugated enone (3) is the kinetically preferred protonation product of the enolate (8) which arises either by direct hydride transfer from methyl phosphinate monoanion or by ready decomposition of an intermediate such as (9). We cannot exclude the intermediacy of the anion of an enol phosphonate such as (9) and enol phosphonates as a class appear to be unknown. However, enol phosphates are the major products of the reaction of dimethyl



(8)



(9)

phosphonate with tetracyclone under similar conditions [7] and though ring methylation occurs when trimethyl phosphite is the nucleophile it does so with formation of a good leaving group. Thus there seems no reason why the hypothetical intermediate (9) should decompose so readily and we prefer hydride ion transfer from the anion of methyl phosphinate.

Addition of a phosphorus nucleophile α to the carbonyl carbon atom has previously been attributed to steric factors.[7,10] It seems unlikely that the attacking species in this instance is sufficiently bulky to support this contention. What seems more probable is that the kinetically preferred site of nucleophilic attack is the α-position but that, unless the incoming group is bulky, rearrangement to the thermodynamically more stable γ-substituted αβ-unsaturated species is rapid and irreversible. Such an interpretation is not at variance with previous experimental results on the attack of phosphorus(IV) nucleophiles on tetracyclone.[7-11] Miller and his co-workers have observed that when the incoming group is the bulky diphenylphosphinoyl rearrangement occurs without migration of the substituent.[10] Also the preferred site of attack on 2-methyl-3,4,5-triphenylcyclopentadienone is the methyl-bearing carbon atom.[8,10] It seems likely that the thermodynamic preference of the substituent for the position β to the carbonyl is dictated by the bulk of the groups on the other ring carbon atoms. Further, though most reductions of tetracyclone afford the *trans*-monoenone (2) as the major product,[16] such reactions are usually carried out under relatively forcing and/or basic conditions, and it may be that the enone (3) is the normal product of a hydride-ion-transfer reaction to tetracyclone but is never seen because of its rearrangement to give, ultimately, the thermodynamically most stable isomer (2).

The formation of the hydroxy-enones (5) and (6) is more difficult to account for. Neither can be detected as an impurity in the tetracyclone and neither is formed when methyl phosphinate is omitted from the reaction mixture or is replaced by water. The same products are obtained when the reaction is carried out with exclusion of light. We suggest that they may arise by 1,2- and 1,4-cycloaddition to the olefinic system of tetracyclone by methyl phosphenite, which is postulated as arising in the hydride-ion-transfer step (Scheme 2).

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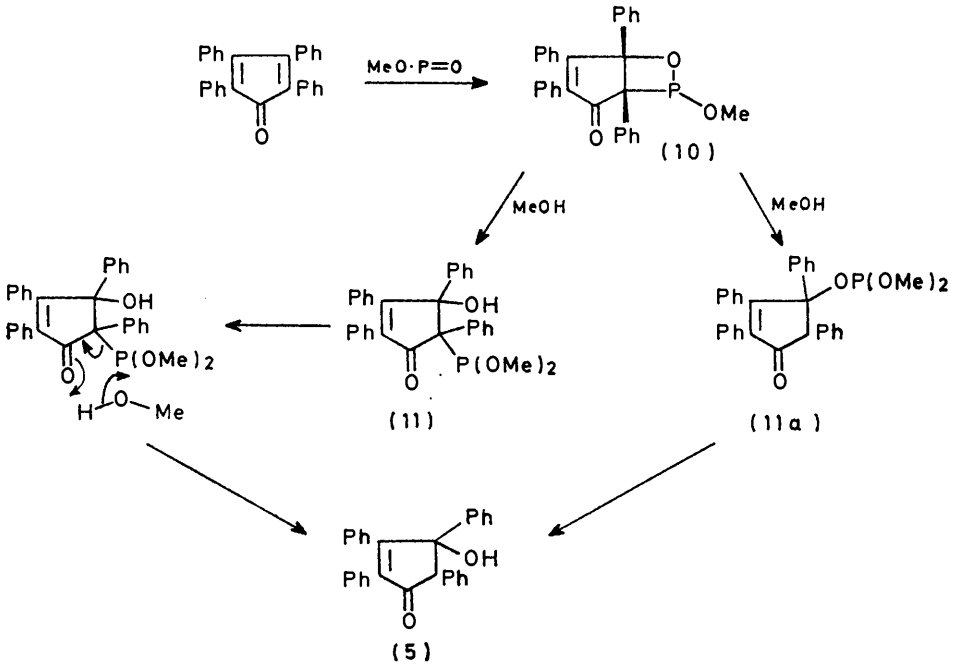
The resulting oxaphosphetan is a phosphonite and as such is able to undergo a rapid exchange reaction with methanol (formed in the preparation of methyl phosphinate) to give the ring-opened β-oxo-phosphonite (11). This reaction should be facilitated by strain in the bicyclic intermediate (10). Conversion of this intermediate, a β-oxo-phosphonite, into the hydroxy-enone (5) could occur *via* a cyclic transition state, as shown (however, the chemistry of such compounds is unknown).

Mass Spectra of Hydroxycyclopentenones.—The mass spectra of all pure compounds obtained in this study were recorded. The only novelties observed were in those of the hydroxy-compounds *cis*- and *trans*-(5) and (6). In these spectra the parent ion was the base peak and a major fragmentation was the loss of OH and not water. Benzylic and/or tertiary alcohols usually show only very weak parent ions and the base peak corresponds to loss of water from the parent ion. Presumably



SCHEME 2

Alternatively, these steps could be reversed producing first (11a) which subsequently exchanges to give (5). The unconjugated enone (7) would be expected to rearrange to the conjugated isomer (6) under the basic conditions of the reaction.

An alternative possibility is that the enolate originally formed by hydrogen-ion-transfer to tetracyclone undergoes autoxidation affording hydroperoxides which are subsequently reduced by methyl phosphinate to the hydroxy-compounds. We consider this very unlikely on two counts. First, the reactions are carried out under nitrogen, and secondly, the equilibrations of the enones (2)—(4) with base in methanol–chloroform were carried out without precautions to exclude oxygen for a lengthy period (48 h) during which time no new substances were formed in amounts that could be detected by t.l.c.

We also examined briefly the use of benzaldehyde rather than tetracyclone as a hydride ion acceptor. However, the only product isolated was methyl bis-(α-hydroxybenzyl)phosphinate, in low (25%) yield. Whether hydride ion transfer or simple addition to the carbonyl carbon atom occurs will clearly be a function of the structure of the carbonyl compound.

in *cis*- and *trans*-(5) the ion resulting from loss of neutral OH will be strongly stabilised in comparison with the radical ion of tetracyclone, which would be obtained by loss of water. In the case of (6), however, the generation of a positive charge adjacent to a carbonyl group would be expected to destabilise the species resulting from loss of OH, but this does not occur.

EXPERIMENTAL

Reactions were carried out under nitrogen unless otherwise noted. Tetracyclone was commercial material containing no impurities detectable by t.l.c. Methyl phosphinate was prepared by Fitch's method [12] and used immediately. ^{31}P N.m.r. spectroscopy showed a purity of 90%; no phosphonate impurity was detected. Unless otherwise specified chromatography was carried out on short, wide (5 cm) columns of t.l.c. silica gel; petroleum refers to the fraction of b.p. 60—80°. Known compounds marked with an asterisk were identified by comparison with authentic materials. Spectroscopic details were as previously described.

Reductions of Tetracyclone.—(a) *With heating.* A solution of the ketone (0.974 g) in dry benzene (30 ml) containing triethylamine (0.5 g) was gently warmed and titrated with a solution of methyl phosphinate (*ca.* 0.135M) in dry benzene.

Complete decolourisation required 23.5 ml (*ca.* 1.25 mol equiv.) of ester. When set aside (4 h) the solution slowly developed a pink colour. The mixture was evaporated, the residue was taken up in benzene (50 ml), and the solution was evaporated. Chromatography of the final residue on silica gel (35 g) afforded, after traces of tetracyclone and small intermediate fractions, *trans*-2,3,4,5-tetraphenylcyclopent-2-enone * (2) (eluant 1 : 1 benzene–petroleum) (0.6 g, 62% after recrystallisation). About 100 mg remained in the mother liquor. Further elution of the column ($CHCl_3$) afforded a number of fractions containing mixtures which were combined and recrystallised (EtOH) to give *r*-4-hydroxy-2,3,4,*t*-5-tetraphenylcyclopent-2-enone * (5) (55 mg). The mother liquors were evaporated to dryness and rechromatographed (benzene as eluant) affording (5) (38 mg) and its stereoisomer (29 mg). On a larger scale (10 g of ketone), the chromatography could be omitted and the enone (2) obtained by crystallisation in yields as high as 95%.

In a separate experiment (2 g of tetracyclone) a weighed amount of toluene was added to a sample of the concentrated reaction mixture; the solution was diluted with $CDCl_3$ and the ^1H n.m.r. spectrum measured. The yield of dimethyl phosphonate was readily obtained by comparison of the MeOP and ArMe signals.

In the cold. The reaction was repeated with tetracyclone (1.0 g) and performing all operations at room temperature or below. Chromatography (35 g of silica; elution with benzene–light petroleum) afforded a viscous oil (*ca.* 850 mg) shown by t.l.c. to be a mixture of two compounds, the major one of which slowly crystallised and was 2,3,4,5-*tetraphenylcyclopent*-3-*enone* (3); m.p. 126—128°, $\nu_{max.}$ 1 755 cm^{-1} (C=O) (Found: C, 90.15; H, 5.7%; *M*, 386. $C_{29}H_{22}O$ requires C, 90.1; H, 5.7%; *M*, 386). It could be recrystallised by dissolving in methanol at room temperature and chilling, but heating slowly converted it into a mixture of the *cis*- and *trans*-2-enones. On exposure to air it slowly developed a pink colour. The mother liquors when evaporated and triturated with methanol afforded largely *cis*-tetraphenylcyclopent-2-enone (4), m.p. 126—129°; $\nu_{max.}$ 1 705 cm^{-1} (C=O); ^1H n.m.r. ABq δ_A 4.90, δ_B 4.44 (J_{AB} 7.5 Hz), δ 7.17 (m, ArH) [lit.,[14] m.p. 127—128°; $\nu_{max.}$ 1 700 cm^{-1}; δ_A 4.45, δ_B 4.90 (J_{AB} 7.5 Hz)]. Small amounts of the *trans*-isomer * were also isolated. The ^1H n.m.r. spectrum of the original crude oil showed it to be a mixture of the 3-enone (3) and the 2-enone (4) in the ratio 9 : 1.

Further elution of the column (PhH–$CHCl_3$ 4 : 1) yielded several fractions containing mixtures which were combined and recrystallised (EtOH) giving the hydroxy-enone * (5) (35 mg). The mother liquors were rechromatographed (5 g of silica); elution with benzene yielded 5-*hydroxy*-2,3,4,5-*tetraphenylcyclopent*-2-*enone* (6) (5 mg) as yellow crystals, m.p. 195—210° (from aqueous ethanol); $\nu_{max.}$ 3 480 (OH) and 1 697 cm^{-1} (C=O). (Found: M^+, 402.1617. $C_{29}H_{22}O_2$ requires *M*, 402.1618).

The cold reaction was repeated on twice the above scale and chromatography was carried out as rapidly as possible. The results were substantially the same except that the isolated yield of pure 3-enone (3) was higher and that of the conjugated enones (2) and (4) was lower. The crystalline fraction containing the 5-hydroxy-ketone (6) proved to be an inseparable mixture (t.l.c.) most probably of the conjugated (6) and unconjugated (7) ketones: the i.r. spectrum showed two carbonyl bands (1 755 and 1 698 cm^{-1}) in addition to hydroxy-absorption (3 480 cm^{-1}) but was in other respects similar to that of the hydroxy-enone (6).

The Isomeric 4-*Hydroxy*-2,3,4,5-*tetraphenylcyclopent*-2-*enones*.—The literature method [15] was followed, with dibenzyl ketone (1 g), benzil (1 g), and aqueous potassium hydroxide (33%; 2 ml). The crude product was chromatographed (30 g of silica; elution with benzene) giving tetracyclone * and starting materials, followed by r-4-*hydroxy*-2,3,4,t-5-*tetraphenylcyclopent*-2-*enone* (5) (190 mg), m.p. 204—205° (from ethanol) (Found: C, 86.6; H, 5.5%; *M*, 402. $C_{29}H_{22}O$ requires C, 86.5; H, 5.5%; *M*, 402); $\nu_{max.}$ 3 455 (OH) and 1 685 cm^{-1} (C=O); δ 4.63 (1 H, s, PhC*H*), 6.56 (1 H, s, OH), and 7.10 (2 OH, m, ArH) and r-4-*hydroxy*-2,3,4,c-5-*tetraphenylcyclopent*-2-*enone* (560 mg), m.p. 100—120° (from ethyl acetate–petroleum) or 95—105° (from ethanol); solvent of crystallisation could only be removed by prolonged drying under vacuum, giving material of m.p. 125.5—126.5° (Found: C, 86.5; H, 5.5%; *M*, 402); $\nu_{max.}$ 3 460 (OH) and 1 686 cm^{-1} (C=O); δ 4.27 (1 H, s, ArC*H*), 6.10 (1 H, s, OH), and 7.25 (20 H, m, ArH).

Reaction with Benzaldehyde.—Methyl phosphinate (0.01 mol) was added to a solution of benzaldehyde (2.2 g, 0.02 mol) in dry benzene (50 ml) containing triethylamine (*ca.* 1 ml). The mixture was boiled (10 min), evaporated to dryness, and chromatographed (35 g of silica). Benzene eluted benzaldehyde and small amounts of unidentified products. The residue crystallised on the column and was removed with chloroform. Recrystallisation (benzene–methanol) afforded *methyl bis*-(α-*hydroxybenzyl*)*phosphinate* (0.67 g, 26%), m.p. 164—165.5° (Found: C, 61.8; H, 5.8. $C_{15}H_{17}O_4$ requires C, 61.6; H, 5.9%). Despite the sharp m.p. the ^1H n.m.r. spectrum clearly showed the presence of the two diastereoisomers in the *ratio ca.* 60 : 40. In [$^2H_6$]dimethyl sulphoxide as solvent the two hydroxy-protons appeared as a doublet of quartets (δ 6.23 and 6.33; $^3J_{HCOH}$ 7; $^3J_{PCOH}$ 16.5 Hz) and the benzylic protons as an apparent triplet resulting from the fortuitous overlap of two doublets (δ 5.21 and 5.33; $^3J_{HCOH}$ 7; $^2J_{PCH}$ 0.5 Hz). These assignments were confirmed by exchange with D_2O. The low value of $^2J_{PCH}$ is not unusual.[17] Curiously, only a sharp doublet was observed for the $POCH_3$ group (δ 2.99; $^3J_{POCH}$ 9.5 Hz).

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