

The Reactions of Wittig-Horner Reagents and Dialkyl phosphonate with 2-(phenylmethylene)-1,3-diphenylpropanedione

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Abstract: 2-(Phenylmethylene)- 1,3-diphenylpropanedione **1** reacts with Wittig- Horner reagent **6a** in the presence of sodium hydride as a base to give the novel phosphonate product **8a**. On the other hand, the cyclic phosphonate adduct **9a** was isolated from the reaction of **1** with Wittig- Horner reagent **6a** using alcoholic sodium alkoxide . The reaction of Wittig- Horner reagents **6b,c** with **1** afford the phosphonate derivatives **8b,c**. Moreover, dialkylphosphonate **7** reacts with **1** to give the dialkylphosphonate product **10**. Possible reaction mechanisms are considered and the structural assignments are based on analytical and spectroscopic evidence. The structure of the new dialkylphosphonate product **10** was confirmed by a single crystal X-ray determination.
Keywords : 2-(phenylmethylene)-1,3-diphenylpropanedione, Wittig-Horner Reagents, dialkylphosphonate, Phosphonate derivatives.

Introduction

Our previous work reported that 2-(phenylmethylene)-1,3-diphenylpropanedione (**1**) reacts with Wittig reagents **2** and trialkyl phosphonates **3** to give the corresponding phosphonate products **4a-c** and **5a-c**, respectively (Scheme 1)¹. In view of this and in continuation of our work in organophosphorus chemistry²⁻⁷, it was of considerable interest to investigate the behavior of 2-(phenylmethylene)- 1,3-diphenylpropanedione (**1**) towards Wittig- Horner reagents **6a-c** and dialkyl phosphonate **7** (Scheme 2). The purpose of this study was to determine the preferential site of attack by these reagents. A comparative study on the behavior of **2, 3, 6, and 7** toward 2-(phenylmethylene)- 1,3-diphenylpropanedione (**1**) is also reported.

Experimental

Melting points were determined in open glass capillaries using an Electrothermal IA 9100 series digital melting point apparatus (Electrothermal, Essex, U.K.) and IR spectra were measured in KBr pellets with a Perkin- Elmer infracord spectrophotometer model 157. The ¹H-NMR, ¹³C-NMR, and ³¹P-NMR spectra were recorded in CDCl₃ as a solvent on a Joel-500(125 MHz) spectrometer respectively, and the chemical shifts were recorded in values relative to TMS as internal reference. The mass spectra were recorded at 70 eV with a krotos MS equipment or Vario EI Instrument. The reported yields are of pure isolated materials obtained by column chromatography on silica gel 60(Merk).

Reaction of t-butyldiethylphosphonate (**6a**) with 2-(phenylmethylene) - 1,3-diphenyl- propanedione **1**

t-Butyldiethylphosphonate **6a** (0.22 g, 1 mmol) was dissolved in dry toluene (25 ml), and sodium hydride (0.024 g, 1 mmol) was added carefully with stirring. Then the starting material propanedione **1** (0.31g, 1mmol), was

added, and the mixture was refluxed for 6 h. After evaporation of the volatile material under reduced pressure, the residue was applied to silica gel column chromatography to give compound **8a**.

2-Diethyl(t-butylacetate)-2-benzyl-3-hydroxy-1,3-diphenylprop-2-en-1-one phosphonate (**8a**)

Eluent: petroleum ether-ethyl acetate (70/30, v/v). product **8a** was obtained as pale yellow crystals, yield 70%, m.p.190-191°C; IR (KBr): 3300,1770,1240,1050 cm^{-1} ; ^1H NMR : 1.32(s,9H,3CH₃), 1.19(m,6H,2CH₃), 2.90, 2.79[dd,1H,²J_{HP} = 21.4,J_{HH} = 16.5Hz, CH-P(O)], 3.01(s,OH),4.00,4.10 (2q,4H,2CH₂), 4.17(dd,1H,J_{HH}=14.5,³J_{HP}=7.56Hz), 7.54-7.39(m,10H,Ar),7.99-7.98(m,5H,Ar);¹³C NMR : 190.2,170.6,168.1,140.7,130.3, 134.6, 128.7,129.9,126.0,102.0,82.1,62.2,40.5,28.7,61.3,14.8; ³¹P NMR : 23.7 ppm; MS (EI): m/z 564; C₃₂H₃₇O₇P(564.61): calcd. C 68.07%, H 6.61%, P 5.49%; found C 68.21%, H 6.48%, P 5.60%.

When compound **8a** was boiled in alcoholic sodium ethoxide solution for a long time, it was recovered unchanged.

General method

A solution of sodium ethoxide (1mmol) in absolute ethanol (30 ml) was treated with an equimolar amount of Wittig-Horner reagent **6a-c** (1 mmol). Then propandione **1** (0.31 g, 1 mmol) was added, and the resulting mixture was refluxed for 2-6 h (TLC). Then it was poured on a small amount of water, extracted with ethyl acetate, and dried, the extracts were evaporated under reduced pressure. The residue was subjected to silica gel column chromatography to give compounds **9a** and **8b-c**, respectively.

Diethyl-5-benzoyl-2-oxo-4,6-diphenyl-3,4-dihydro-2H-pyran-3-yl phosphonate **9a**

Eluent: petroleum ether- acetone (85/15, v/v). product **9a** was obtained as pale yellow crystals, yield 65 %, m.p. 197-198 °C ; IR (KBr): 1770,1726,1230,1050 cm^{-1} ; ^1H NMR : 1.37(t,6H,2CH₃), 4.38(q,4H,2CH₂),2.61(dd, 1H,²J_{HP} = 16.8,CH-P), 4.21 (dd,1H,J_{HH} = 8.7,³J_{HP} = 10.5Hz, CH-CH),7.46-7.41(m,5H,Ar), 7.53-7.95 (m,5H,Ar), 8.10-8.03(m,5H,Ar); ¹³C NMR :189.4,166.7,168.1,150.5,134.4, 133.7, 132.7, 129.9, 126.0, 115.0, 61.3,14.7; MS(EI): m/z 490; C₂₈H₂₇O₆P(490.48): calcd.C 68.56, H 5.55%, P 6.31 % ; found C 68.40, H 5.65%, P 6.28%.

Diethyl-1,5-dicyano-3-(hydroxyl(phenyl)methylene)-2,4-diphenylpent-4-enyl phosphonate **8b**

Eluent: petroleum ether- ethyl acetate (80/20, v/v), product **8b** was obtained as white crystals, yield 75%, m.p.186-187°C; IR (KBr): 3400, 2260, 1230,1050 cm^{-1} , ^1H NMR : 1.31(t,6H,2CH₃),2.92 (dd,1H, CH-P,J_{HH} = 10.00,²J_{HP}= 15.8),4.17(q,4H,2CH₂), 4.31(dd, 1H, J_{HH} =6.85, ³J_{HP} =7.0Hz),6.3(s, 1H,CHCN),7.54-7.41(m,5H,Ar),7.96-7.95(m, 5H,Ar), 8.10 - 8.03(m,5H,Ar),13.59(s,1H, OH); MS(EI): m/z 512; C₃₀H₂₉N₂O₄P(512.10): calcd. C 70.30, H 5.70%, N 5.47%, P 6.04%; found C 70.10, H 5.56%, N 5.58%, P .6.28%.

Carring out the reaction using 2 moles of Wittig- Horner **6b** instead of 1 mole led to the formation of **8b** in good yield.

Diethyl-3-benzoyl-4-oxo-1,2,4,-triphenylbutyl-phosphonate **8c**

Eluent: petroleum ether- ethyl acetate (90/10, v/v), product **8c** was obtained as white crystals, yield 75%, m.p. 256-257 °C; IR (KBr): 1726,1230,1050 cm^{-1} ; ^1H NMR : 0.87 (t,6H,2CH₃), 2.53 (t,1H, Ph-CH, J_{HH} = 13.75), 2.47(dd, 1H, J_{HH} = 8.5,⁴J_{HP} = 4.5, Ph CO-CH),4.21 (q,2H,2CH₂), 7.54-7.41(m,5H,Ar), 7.96-7.95(m,5H,Ar),8.10-8.03(m,10H,Ar); ¹³C NMR :192.4, 133.2, 134.4, 133.7,132.7,129.9,29.9,128.2,127.1,126.8, 126.0,125.0; MS (EI) : m/z 540; C₃₃H₃₃O₅P(540.21): calcd. C 73.32, H 6.15%, P 5.73%; found C 73.20, H 6.30 %, P .6.65%.

Reaction of dimethylphosphite (**7**) with 2-(phenylmethylene)-1,3-diphenyl-propanedione

2-(Phenylmethylene)-1,3-diphenyl-propanedione **1** (0.31g,1mmol) was dissolved in dry toluene (25 ml),and dimethylphosphite (0.022 g, 2mmol) was added carefully with stirring. Then the mixture was refluxed for 4 h (TLC). The volatile material were evaporated under reduced pressure, and the residue was applied to silica gel column chromatography to give compound **10**.

Dimethyl-2-benzoyl-3-oxo-1,3-diphenylpropylphosphonate **10**

Eluent: petroleum ether- acetone (85/15, v/v), product **10** was obtained as colorless crystals, yield 65 %, m.p. 155-156°C; IR (KBr): 1690,1670,1242,1048 cm^{-1} ; ^1H NMR : 3.47[2d,6H,³J_{HP}=11.2 Hz, P(OCH₃)₂], 4.50(dd,1H, ²J_{HP}=23, J_{HH}=10.5 Hz, H-a), 6.45 (dd, 1H,³J_{HP}=11Hz,J_{HH}=10.5Hz, H-b),7.02-8.20(m,15H,Ar). MS(EI): m/z 422; C₂₄H₂₃O₅P (422.415): calcd. C 68.24%, H 5.48%, P 7.33%; found C 68.10, H 5.540, P 7.23%.

X-Ray Crystallographic Study⁸⁻¹²: A single crystal of **10** was grown by crystallization from cyclohexane. The crystal structure was solved and refined, using maXus (Nonius, Delft and Mac Science, Japan). MoK α ($\lambda=0.71073$ Å) and a graphite monochromator were used for data collection. A summary of the crystal analysis parameters is given in the Table 1. Details are contained in CCDC file No 857160 at Cambridge Crystallographic Center.

Table 1. X-ray crystallographic analysis of compound **10**

Compound 10			
Empirical formula	C ₂₄ H ₂₃ O ₅ P		
Formula weight	422.417		
Wavelength / Å	0.71073		
Crystal system/space group			
a / Å	9.9607 (5)	α / °	90.00
b / Å	13.8145 (7)	β / °	12.(18)x10 ¹
c / Å	18.2579(7)	γ / °	90.00 (2)
V / Å ³	2122.2(2)		
Z	4		
D _{calc} (g/cm ³)	0.001322		
Compound 10			
μ (mm ⁻¹)	0.16		
Color / Shape	Colorless/prismatic		
Temp (K)	298		
Theta rang for collection	2.910—27.485 °		
Independent reflections	5762		
Data/restraints/parameters	352		
Goodness of fit on F ²	0.036		
Final R indices [I>3 (I)]	R _{int} 0.034		
R indices (all data)	0.059		

Table II Selected Bond Lengths (Å) and Angles (°)

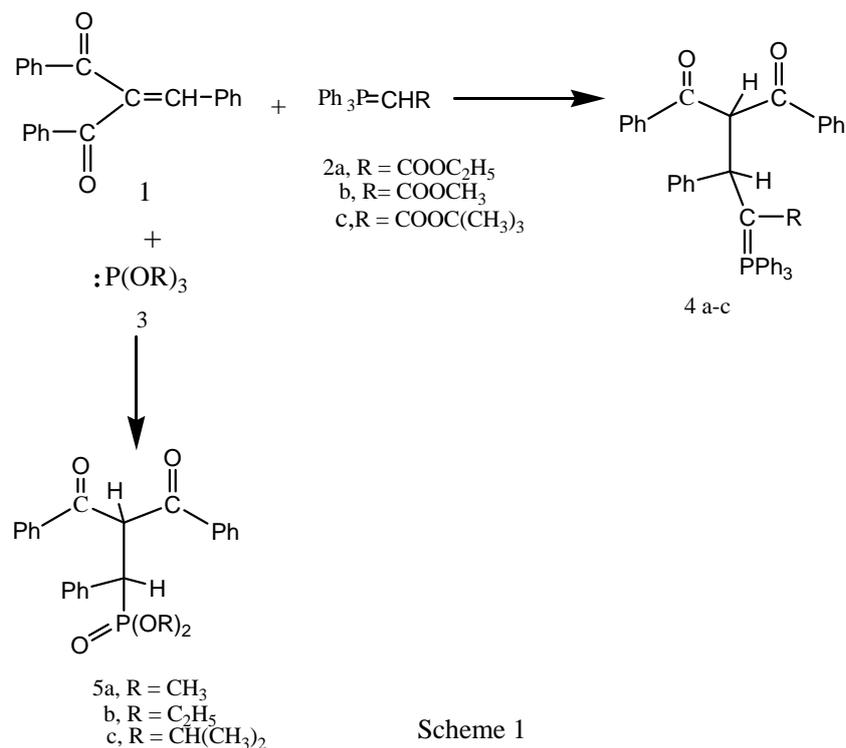
Compound 10					
O2- C10	1.220 (2)	P1- C8	1.803(2)	O4-C11	1.219 (2)
C7- C11	1.543(3)	P1- O3	1.462(15)	C7- C8	1.552(3)
O3-P1-C8	115.94 (9)	P1-O6-C26	119.0(2)	P1-O5-C30	122.0(15)
O6- P1-C8	103.04 (10)	O5-P1- O6	103.13 (8)	C11-O4-C12	32.84(12)
O3-P1-O6	115.28(9)	O3-P1-O5	113.64(9)	C9-O2-C10	32.84(12)

Results and Discussion

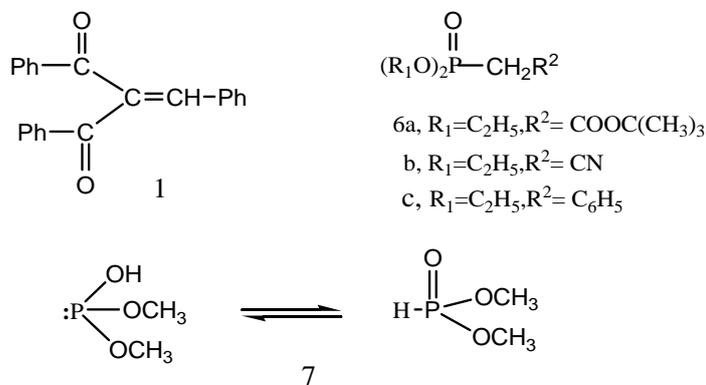
We have found that when 2-(phenylmethylene)- 1,3-diphenylpropanedione (**1**) was allowed to react with one equivalent of t-butyl diethylphosphonate (**6a**) in dry toluene in the presence of sodium hydride at reflux temperature for 6 h, product **8a** was isolated in 70% yield (Scheme 3). The structure elucidation of diethyl (t-butylacetate)-2-benzyl-3-hydroxy-1,3-diphenylprop-2-en-1-one phosphonate (**8a**) was established from its elemental analysis, IR, ¹H, ¹³C, ³¹P NMR and mass spectral data (cf. Experimental). The most important feature in the mass spectrum of **8a** is that the M⁺ was found at m/z=564. Moreover, a signal at $\delta = 23.7$ ppm was recorded in the ³¹P NMR of **8a** which fits with diethylphosphonoacetate.

On the other hand, the reaction of 2-(phenylmethylene)-1,3-diphenylpropanedione (**1**) with t-butyl diethylphosphonate (**6a**) was performed in alcoholic sodium ethoxide solution, two products formulated as **8a**

(15 %) and **9a** (60 %) were isolated (Scheme 3). Structure **9a** was established on the basis of its spectral data (elemental analysis, ^1H , ^{13}C , ^{31}P NMR, and MS, cf. Experimental) ¹³.

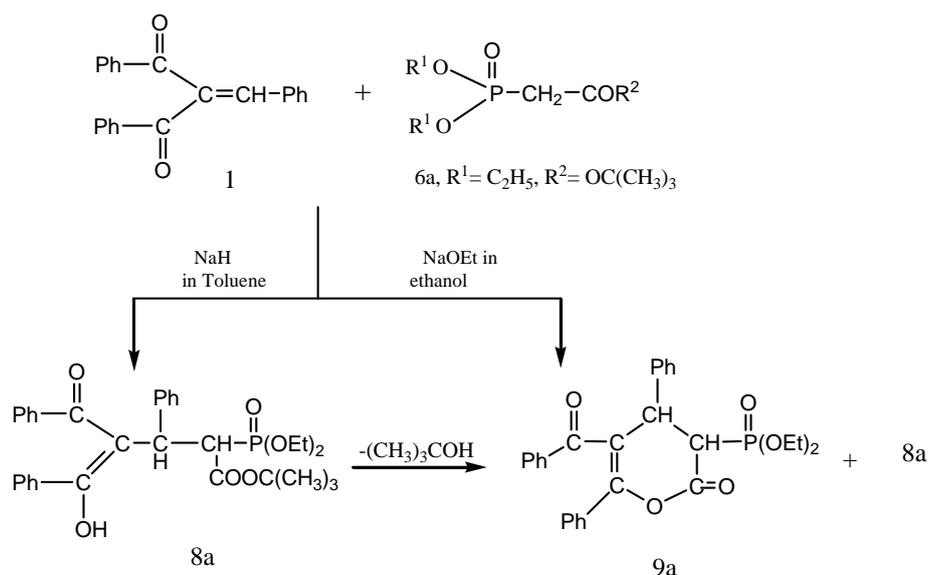


Scheme 1



Scheme 2

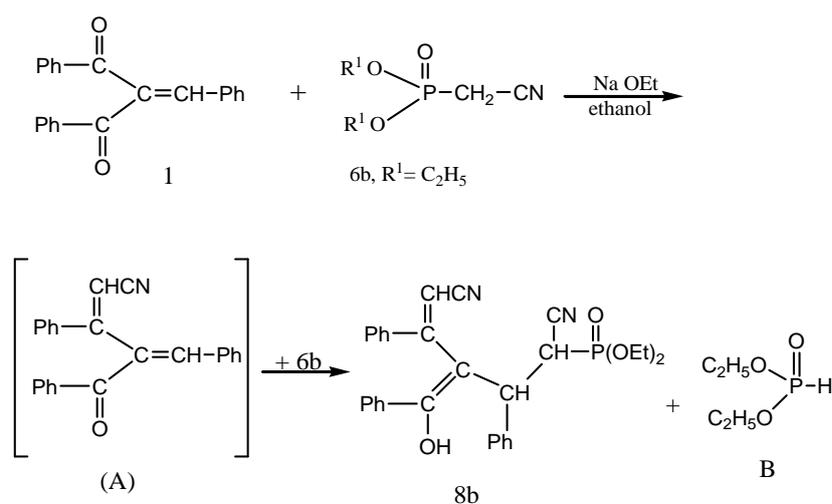
A possible explanation for the reaction course of **1** with Wittig-Horner reagent **6a** in the presence of NaH and/or NaOEt is shown in (Scheme 3). Initial attack of t-butyl-diethylphosphonoacetate (**6a**) on the most reaction center of **1** via intermolecular 1:4 addition gave the phosphonate product **8a**. Elimination of one molecule of alcohol from **8a** followed by intramolecular cyclization result in the formation of the cyclic phosphonate derivative **9a** (Scheme 3). Worthy to mention that when compound **8a** was boiled in alcoholic sodium ethoxide solution for a long time, it was recovered un-changed.



Scheme 3

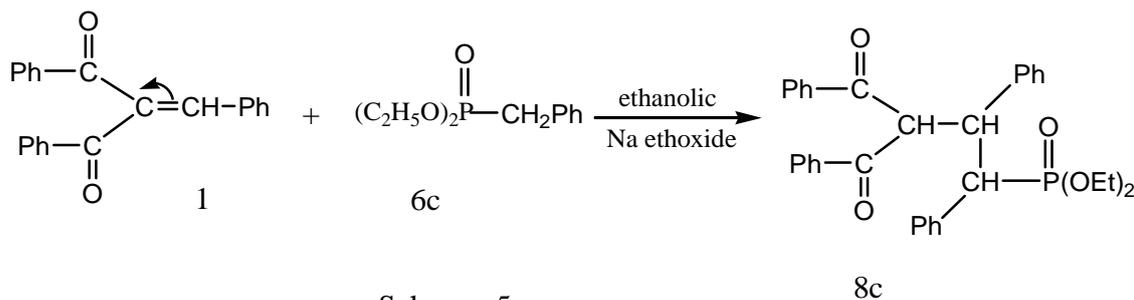
The reaction of **1** with diethyl(cyanomethyl)phosphonate **6b** was also investigated. When **1** was allowed to react with one mole equivalent of **6b** in the presence of alcoholic sodium ethoxide solution at reflux temperature for 4 h, adduct **8b** and unchanged of 2-(phenylmethylene)-1,3-diphenylpropanedione (**1**) were isolated.

Carrying out the reaction using 2 mole equivalents of Wittig- Horner reagent **6b** instead of 1 mole led to the formation of **8b** in a good yield (Scheme 4). Compound **8b** was chromatographically pure and shows a sharp melting point. The assigned enylphospho-nate structure **8b** is based on the correct elemental microanalysis, IR, 1H , ^{13}C , and mass spectral data (cf.Experimental). Compound **8b** can be obtained via carbonyl olefination by one mole of Wittig- Horner reagent **6b** to give the intermediate (A) followed by addition of another molecule of **6b** to afford diethyl-1,5-dicyano-3(hydroxyl(phenyl) methylene)-2,4- diphenylpent-4- enylphosphonate **8b** (Scheme 4). Under the influence of the base present in the reaction medium, elimination of diethyl phosphite was observed. The diethyl phosphite was detected in water layer by the development of a violet color on addition of 3,5 dinitrobenzoic acid¹⁴.



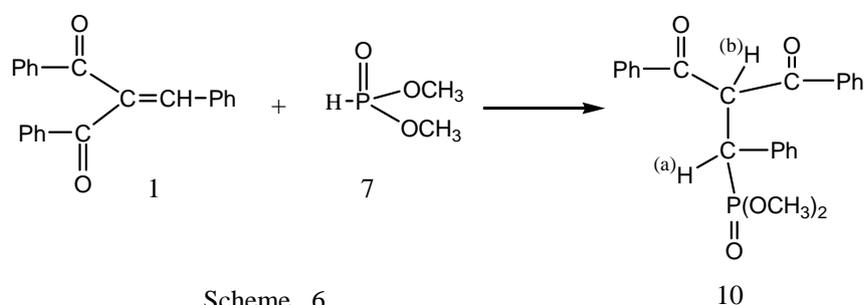
Scheme 4

Also, we have found that 2-(phenylmethylene)-1,3- diphenylpropanedione **1** reacts with one mole equivalent of benzyl-diethylphosphonoacetate **6c** in the presence of ethanolic sodium ethoxide solution under stirring at room temperature for 5 h to give product **8c** in 70 % yield (Scheme 5).



The structure assignments for compound **8c** is based upon elemental and spectroscopic data (IR, ^1H , ^{13}C , ^{31}P NMR and mass spectrum, cf. Experimental Section). A possible explanation for the course of the reaction of **1** with **6c** is shown in Scheme 5. Product **8c** is presumably formed through Michael addition of the Wittig-Horner reagent **6c** to the active methine carbon in compound **1** to afford the new phosphonate product **8c** (Scheme 5).

Furthermore, this study has been extended to include the reaction of **1** with dimethyl phosphonate **7** to establish whether it would behave in a similar manner. We have found that 2-(phenylmethylene)-1,3-diphenylpropanedione (**1**) reacted with dimethyl phosphonate **7** in the conventional manner to give the corresponding dimethylphosphonate product **10** (Scheme 6). Compound **10** is chromatographically pure and possesses a sharp melting point. Worth mentioning is that only one isomer of phosphonate **10** was isolated, which are assumed to have a trans configuration. The assigned trans configuration for this product is supported by ^1H NMR chemical shift and coupling constant of the two p-methine protons attached to the phosphorus atom¹⁵. Its ^1H NMR spectrum shows two signals at $\delta = 4.50$ (dd, $^2J_{\text{HP}} = 23.0$ Hz, $J_{\text{HH}} = 10.5$ Hz) and $\delta = 6.45$ (dd, $^3J_{\text{HP}} = 11$ Hz, $J_{\text{HH}} = 10.5$ Hz) corresponding to the exocyclic methine protons **a** and **b**, respectively. The observed difference in chemical shifts and the coupling constants indicate trans configuration rather than a cis configuration which would give rise to small coupling constants (6-7 Hz)¹⁵.



The assigned trans configuration of product **10** are established with certainty by X-ray analysis which confirm the suggested structure (cf. Fig 1).

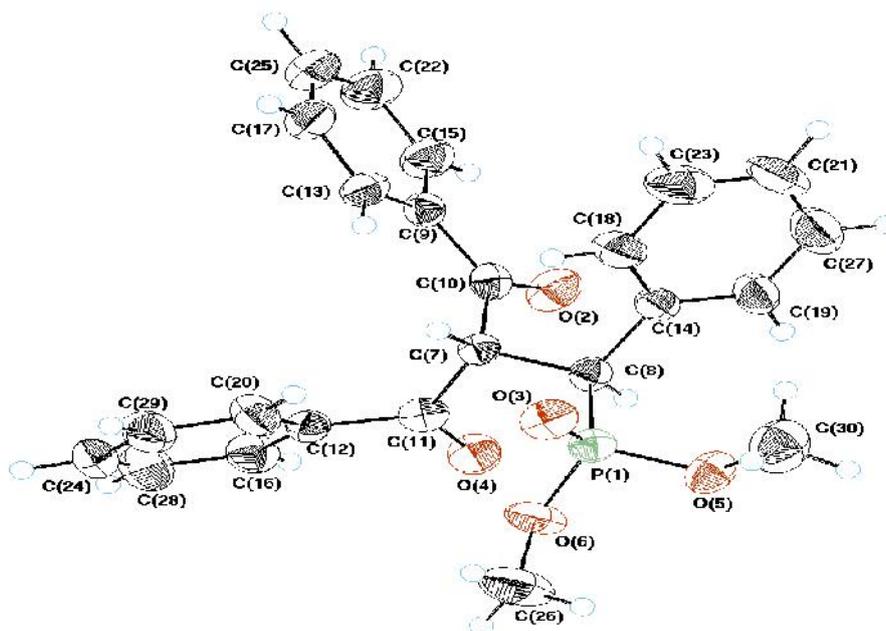


Fig 1 Molecular structure of **10** with aromatic numbering scheme; anisotropic displacement parameters are drawn at the 30% level and the hydrogen atoms are shown as spheres of arbitrary radii

Conclusion

From the results of the present investigation, it can be concluded that the reaction of 2-(phenylmethylene)-1,3-diphenylpropanedione **1** with Wittig-Horner reagents **6a,b** and **c** lead to different products, depending on the nature of the phosphorane reagent as well as the stability of the intermediates.

We have noted that the formation of the phosphonate products depend on the nature of the phosphonate anion, the base used, as well as on the reactivity of the intermediates. Significantly, the reactions of Wittig-Horner reagents with 2-(phenylmethylene)-1,3-diphenylpropanedione **1** are indicative of the broad reaction spectrum of which phosphonate anions are capable in addition to the usual olefin forming reaction.

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