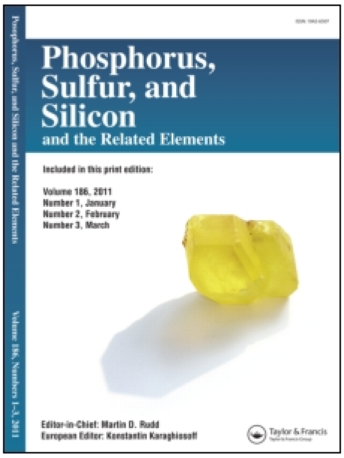

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THE REACTION OF WADSWORTH-EMMONS-HORNER† REAGENTS WITH *o*- AND *p*-QUINONEIMINES

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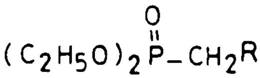
Wittig-Horner reagents (**1a–c**) react with *o*-quinone diimine (**2a**) to give the respective phosphonate adducts (**3a–c**) and the alkylated product **4**. The reaction of *p*-quinone diimine (**2b**) with the same reagents yield adducts **5**, **6** and **7**, respectively. Structural reasoning for the new compounds was based on compatible analytical and spectral data. The mechanism that accounts for formation of adducts **3** is illustrated in Scheme 2.

Key words: Wittig-Horner reagents; N,N′-3,5-cyclohexadiene-1,2-diylidenebis (benzamide); and N,N′-2,5-cyclohexadiene-1,4-diylidenebis (benzamide).

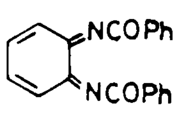
INTRODUCTION

The Wittig and Wittig-Horner reactions are both versatile synthetic methods, but the latter has the advantage of requiring less expensive starting materials and simpler product separations.[1–3] In previous publications[4,5] we examined the action of Wittig-Horner reagents (**1**) on *o*- and *p*-quinones. The present work is an extension of the behaviour of *o*- and *p*-quinone diimines **2** towards the same reagents (**1**).

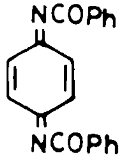


$$(C_2H_5O)_2\overset{\overset{O}{\parallel}}{P}-CH_2R$$

1a, R = $COOC_2H_5$
b, R = $COOCH_3$
c, R = CN



2a



2b

RESULTS AND DISCUSSION

We have found that the reaction of N,N′-3,5-cyclohexadiene-1,2-diylidenebis (benzamide) **2a** with two mol equivalents of Wittig-Horner reagents (**1a–c**), in the presence of alcoholic sodium ethoxide solution, proceeds at room temperature to give chromatographically pure adducts formulated as **3** and **4**, respectively. The trans configuration of compounds **3** is more common than the cis forms due to steric hindrance.

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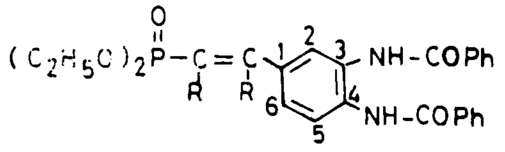
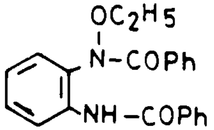
†Also named as Wittig-Horner reagents.

‡To whom correspondence should be addressed.





3a, R = $COOC_2H_5$
b, R = $COOCH_3$
c, R = CN

4

Scheme 1

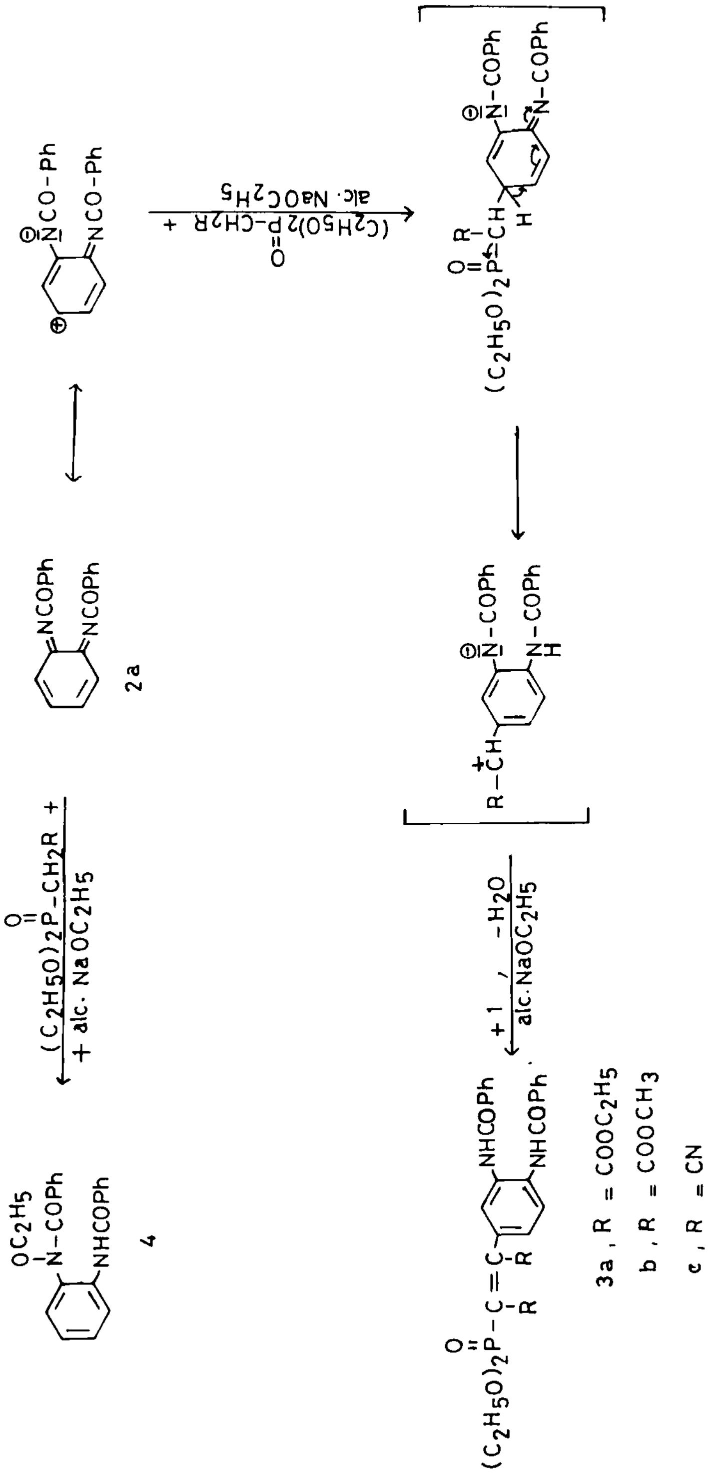
Structure **3** was indicated by the following evidence: (a) Correct elementary analyses and molecular weight determination (MS) were obtained for all the products. (b) Adducts **3** possess the phosphonate structure since they exhibit a positive shift in their ^{31}P NMR spectra (vs. 85% H_3PO_4) and absorb in the region characteristic for this class of compounds.[6–8] The IR spectra of these adducts (in KBr), revealed the presence of two strong-NH absorption bands around 3300 and 3160 cm^{-1}. Moreover, the IR spectra of adduct **3** showed strong absorption bands around 1230 cm^{-1} (P=O, bonded)[9] and around 1050 cm^{-1} (P—O—C_2H_5). The ^1H NMR spectrum (200 MHz) of compound **3a**, for example, disclosed the presence of signals at δ = 1.05 (3H, CH_3-ethoxy, t), 1.15 (3H, CH_3-ethoxy, t), 4.15 (2H, CH_2-ethoxy, q), 4.25 (2H, CH_2-ethoxy, q) corresponding to the two ester groups. The two ethoxy groups attached to the phosphorus atom appeared as a triplet centered at 1.25 (6H, CH_3, t) and a quintet centered at 3.95 (4H, CH_2, q). The ^1H NMR spectrum of compound **3a** showed a doublet centered at 7.15 ppm with $J_{H\text{-}2,H6}$ = 2.3 Hz ascribed to the C-2 proton (Scheme 1). This value is in agreement with the value expected for aromatic protons in the meta position.[10] The two ortho methine protons at C-5 and C-6 appeared as a pair of doublets at δ = 7.91 and 7.86 ppm with coupling constant values of $J_{H\text{-}5,H6}$ = 7.3 Hz and $J_{H\text{-}6,H2}$ = 2.3 Hz which are identical with those values cited for the aromatic protons in ortho, and meta position[10,11] (Scheme 1). The exchangeable (D_2O) protons (NH) appeared as two singlets at 9.8 and 9.85 ppm.

The other compound isolated was established to be the alkylated[12] product **4** from its analysis, IR, ^1H NMR and mass spectroscopic data (cf. Experimental). The alkylation was also observed in the reaction of Wittig-Horner reagents with pyrroles.[12]

Worth mentioning is that when quinoneimine **2a** was allowed to react with one equivalent of the carbanion reagents **1**, adducts **3** were isolated in low yield together with (o-phenylenedibenzamide). A possible explanation for the course of the reaction of Wittig-Horner reagents **1** with N,N′-3,5-cyclohexadiene-1,2-diylidenebis (benzamide) (**2a**) is shown in Scheme 2.

Quinone diimines **2a** react with two moles of the Wittig-Horner reagents to give the stable phosphonate derivatives **3a–c** (possibly via 1:4 addition) and the alkylated[12] product **4**.

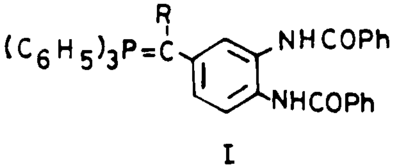
Although *o*-quinone diimines have been reported[13] to react with one equivalent of Wittig reagents to yield the corresponding alkyl 3,4-bis(benzoylamino-α-triphenylphosphoranylidene) α-benzeneacetate derivatives **I**, a different behaviour is



3a, R = $COOC_2H_5$
b, R = $COOCH_3$
c, R = CN

Scheme 2

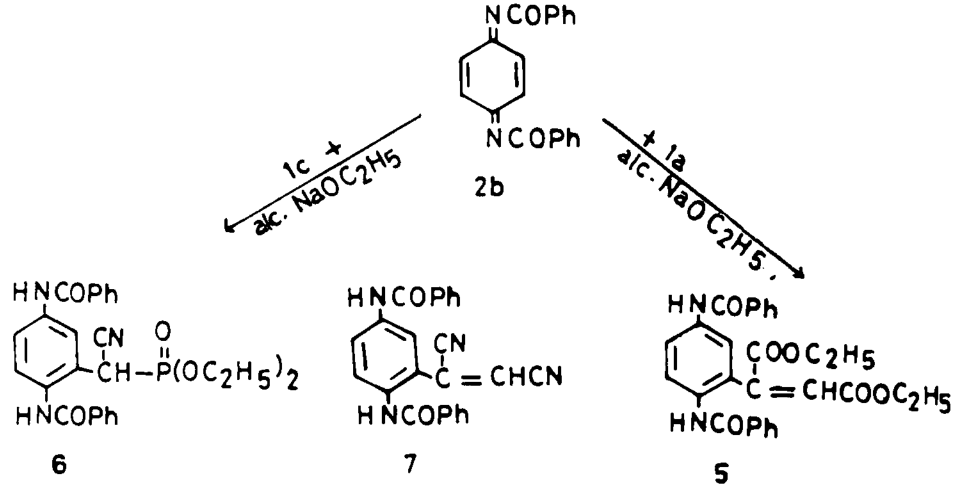
observed in the reaction of the same quinoneimine **2a** with Wittig-Horner reagents **1**.



I

The reaction of N,N′-2,5-cyclohexadiene-1,4-diylidenebis (benzamide) (**2b**) with Wittig-Horner reagents 1 was also investigated. When *p*-benzoquinone diimine **2b** was treated with one equivalent of triethylphosphonoacetate (**1a**) in the presence of alcoholic sodium ethoxide solution for 6 hr, adduct **5** and *p*-benzoquinone diimine **2b** were isolated. Carrying out the reaction using two moles of the phosphonate anion **1a** instead of one mole led to the formation of adduct **5** in good yields. The structure of the new compound **5** is assignable from its analysis, IR, ^{1}H NMR and mass spectral data (cf. Experimental).

When **2b** was allowed to react with one equivalent of diethyl (cyanomethyl) phosphonate **1c**, in the presence of alcoholic sodium ethoxide solution, adduct **6** was isolated in 75% yield. When *p*-quinone diimine **2b** was allowed to react with two molar equivalents of **1c**, adducts **6** (50%) and **7** (30%) were isolated (Scheme 3). Structure elucidation of adduct **6** was based on the following evidence. (a) Correct elemental analysis and molecular weight determination by (MS). (b) Its IR spectrum, in KBr, exhibits strong absorption bands at 3328 (NH), 3274 (NH), 1230 cm^{-1} (P=O, bonded) and at 1047 (P—O—C_2H_5), (c) Compound **6** exhibits $\delta = +19.95$ in its ^{31}P NMR spectrum which clearly indicates a phosphonate structure. (d). The ^{1}H NMR spectrum of compound 6 exhibits signals at $\delta = 1.25$ (6H, $P(OCH_2CH_3)_2$, t), 3.9 (4H, P—$(OCH_2CH_3)_2$, m), 9.4 (1H, NH, s), 9.9 (1H, NH,



Scheme 3

s). The spectrum also revealed a complex pattern due to the aromatic protons (13H, m) in the region 7.08–8.01 ppm.

The mass spectrum of compound **6** yielded a prominent ion peak at m/e 491 which is in accord with structure **6**. The identity of the other isolated product 7 is assignable from elemental analysis, IR, ^{1}H NMR and mass spectral data (cf. Experimental).

The significance of these findings is not only the discovery of a new reaction of Wittig-Horner reagents, but also the establishment of a novel method for the synthesis of new phosphonate products. It is noteworthy that quinoneimines **2a** and **2b** behave towards Wittig-Horner reagents in a manner different from that already reported by us with Wittig reagents.[13,14]

EXPERIMENTAL

All melting points are uncorrected. Triethylphosphonoacetate, methyl diethylphosphonoacetate and diethyl (cyanomethyl) phosphonate were prepared by means of the Michaelis-Arbuzov reaction.[15,16] The IR spectra were measured in KBr with a Perkin Elmer infracord Spectrophotometer Model 157, Grating. The ^{1}H NMR spectra were run on a Varian Spectrophotometer at 200 MHz, using TMS as an internal reference. The ^{31}P NMR spectra were recorded in $CDCl_3$ (vs. H_3PO_4 as external standard) with a JNM-PS-100 Fa Spectrometer. ^{13}C NMR spectra were taken in $CDCl_3$, on a Varian Spectrometer at 200 MHz. The mass spectra were run at 70 eV with Kratos MS equipment and/or a Varian MAT 311 A Spectrometer.

Reaction of triethylphosphonoacetate (**1a**) *with o-benzoquinone diimine* (**2a**). A solution of 2 moles of sodium ethoxide in absolute ethanol was treated with an equimolar amount of the phosphonate (**1a**) (0.44 g; 0.002 mol), after 5 min 1 mol of *o*-quinone diimine (**2a**)[17] (0.31 g; 0.001 mol) was added and the resulting reaction mixture was stirred at room temperature for 4 hr. The reaction mixture was extracted with ethyl acetate, and the extracts were evaporated in a vacuum. The residual materials were applied to a silica gel column using acetone/petroleum ether (60:40, v:v) as eluent to give (**3a**) as colorless crystals m.p 206–208°C, yield (60%).

$C_{32}H_{35}N_2O_9P$ (622.55). Anal. Calcd., C, 61.74; H, 5.66; N, 4.50; P, 4.98; Found, C, 61.67; H, 5.69; N, 4.48; P, 4.93%.
Mol wt (MS) = 622 (M^+, 12%).
^{13}C NMR: δ 136.14 (d, J_{CP} = 94 Hz, ($-C{=}\underline{C}-P<$), 135.19 (d, $^{2}J_{CP}$ = 24 Hz, ($\underline{C}{=}C-P<$), 168.7, 168.4 (two s, $NH\underline{CO}Ph$), 174.5, 175.1 (two s, C=O, esters), 65.9 (d, $P-(O\underline{C}H_2CH_5)_2$), 15.58 (s, $P-(OCH_2\underline{C}H_3)_2$), 65.09, 64.39, (two s, $COO\underline{C}H_2CH_3$), 17.87, 17.99 (two s, $COOCH_2\underline{C}H_3$).
^{31}P NMR: δ = +19.95.

Compound (**4**): eluent chloroform/petroleum-ether (60:40, v:v), yield (10%), as colorless crystals m.p 284–285°C.
$C_{22}H_{20}N_2O_3$ (360.411). Anal Calcd., C, 73.32; H, 5.60; N, 7.77; Found, C, 73.30; H, 5.58; N, 7.74%.
Mol wt (MS) = 360 (M^+, 25%).
IR: 3160 cm^{-1} (NH), 1753 cm^{-1} (C=O, ester), 1650 cm^{-1} (C=O, amide) and at 1602 cm^{-1} (C=C, aromatic).
^{1}H NMR: δ 1.4 (t, $O-CH_2CH_3$), 4.1 (q, $O-CH_2CH_3$) and at 10.1 (s, 1H, NH).

Reaction of methyl diethylphosphonoacetate (**1b**) *with o-benzoquinone diimine* (**2a**). A solution of 2 moles of sodium ethoxide in absolute ethanol was treated with an equimolar amount of the phosphonate (**1b**), (0.42 g; 0.002 mol) after 5 min 1 mole of *o*-quinone diimine (**2a**) (0.31 g; 0.001 mol) was added and the resulting reaction mixture was stirred at room temperature for 6 hr. The reaction mixture was extracted with diethyl ether, and the extracts were evaporated under reduced pressure. The residue was subjected to silica gel column chromatography using ethyl acetate/petroleum ether 80:20, (v:v) as eluent to give compound (**3b**) as colorless crystals mp. 196–198°C, yield (65%).

$C_{30}H_{31}N_2O_9P$ (594.55). Anal Calcd., C, 60.61; H, 5.26; N, 4.71; P, 5.21; Found, C, 60.60; H, 5.21; N, 4.70; P, 5.39%.
Mol wt (MS) = 594 (M^+, 95%).

IR: 3466, 3160 cm^{-1} (NH), 1733 cm^{-1} (C=O, ester), 1652 cm^{-1} (C=O, amide), 1230 cm^{-1} (P=O), 1049 cm^{-1} (P—O—C_2H_5), at 1600 cm^{-1} (C=C, aromatic).
^{1}H NMR: δ 1.2 ppm [t, 6H, P=O $(OCH_2CH_3)_2$], 4.1 [m, 4H, P=O $(OCH_2CH_3)_2$], 3.4, 3.7 (s, 6H, 2$COOCH_3$), 9.6, 9.75 (NH, two sharp singlets, exchangeable with D_2O) and 7.1–8.0 ppm (13H, aromatic, m).

Compound **4** was also isolated and identified (m.p., mixed m.p.)

Similarly, diethyl(cyanomethyl)phosphonate (**1c**) (0.35; 0.002 mol) reacted with *o*-quinone diimine (**2a**) (0.31 g; 0.001 mol) to give compound (**3c**) eluent: acetone, petroleum ether 70:30, (v:v), yield (70%), m.p. 168–170 C.

$C_{28}H_{25}N_4O_5P$ (528.5). Anal Calcd., C, 63.63; H, 4.76; N, 10.6; P, 5.86; Found, C, 63.60; H, 4.73; N, 10.58; P, 5.82%.
Mol wt (MS) (528) (79%).
IR: 3454, 3300 cm^{-1} (NH, amide), 1753 cm^{-1} (C=O, ester), 1650 cm^{-1} (C=O, amide), 1230 cm^{-1} (P=O), 1049 cm^{-1} (P—OC_2H_5) and at 1602 (C=C, aromatic).
^{1}H NMR: δ 1.2, 1.3 ppm (two t, 6H, P=O(O—CH_2—$CH_3)_2$), 4.25 (m, 4H, P=O(O—$CH_2CH_3)_2$), 9.9, 10.1 ppm. (NH, two sharp singlets, exchangeable with D_2O) and at 7.35–8.1 ppm (multiplet, aromatic protons).
^{31}P NMR δ = +14.18 ppm.

Compound **4** was also isolated and identified (m.p., mixed m.p.).

Reaction of triethylphosphonoacetate (**1a**) *with p-benzoquinone diimine* (**2b**). A solution of 2 moles of sodium ethoxide in absolute ethanol was treated with an equimolar amount of the phosphonate (**2b**) after 5 min 1 mole of the quinone diimine (**2b**)[18] (0.31 g; 0.001 mol) was added and the resulting reaction mixture was stirred at room temperature for 6 hr. The reaction mixture was extracted with ethyl acetate, and the extract was evaporated under reduced pressure. The residual material was purified by silica gel column chromatography using ethyl acetate/petroleum ether (60:40, v:v) as eluent to give (**5**) as colorless crystals m.p 182–183°C, yield (75%).

$C_{28}H_{26}N_2O_6$ (486.52). Anal Calcd., C, 69.12; H, 5.39; N, 5.76; Found, C, 69.10; H, 5.35; N, 5.70%.
Mol wt (MS) = 486 (50%).
IR: 3310, 3280 cm^{-1} (NH); 1753 cm^{-1} (C=O, ester), 1650 cm^{-1} (C=O, amide) and 1602 cm^{-1} (C=C, aromatic).
^{1}H NMR δ 1.15 (t, 3H, $COOCH_2CH_3$), 1.3 (t, 3H, $COOCH_2CH_3$), 4.1 (q, 2H, $COOCH_2CH_3$), 4.3 (q, 2H, $COOCH_2CH_3$), 6.3 (s, 1H, =CH), 9.4 (s, 1H, NH), 9.7 (s, 1H, NH) and at 7.4–8.15 (m, 13H, aromatic).
Similarly, diethyl(cyanomethyl)phosphonate (**1c**) (0.35 g; 0.002 mol) reacted with *p*-quinone diimine (**2b**) (0.31 g; 0.00 1 mol) to give compound (**6**) eluent ethyl acetate/petroleum ether, 95:5, (v:v) yield (50%) m.p. 190–192°C.
$C_{26}H_{26}N_3O_5P$ (491.481). Anal Calcd., C, 63.54; H, 5.33; N, 8.55; P, 6.30; Found, C, 63.50; H, 5.31; N, 8.52; P, 6.28%.
Mol wt (MS) = 491 (90%).

Compound (**7**), eluent:ethyl acetate/petroleum ether (85:15 v:v), yield (30%), m.p 183–185°C.

$C_{24}H_{16}N_4O_2$ (392.418). Anal Calcd., C, 73.46; H, 4.11; N, 14.28; Found, C, 73.46; H, 4.2; N, 14.26%.
Mol wt (MS) = 392. (15%).
IR: 3310, 3280 cm^{-1} (NH), 1650 cm^{-1} (C=O, amide) and 1602 cm^{-1} (C=C, aromatic).
^{1}H NMR: δ 6.23 (s, 1H, =CH), 9.4 (s, 1H, NH), 9.7 (s, 1H, NH) and 7.4–8.15 (m, 13H, aromatic).

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