

Formation of phosphoranes from methyl maleanilates and related substrates with triphenylphosphine and their Wittig olefinations with aromatic aldehydes

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Abstract. An efficient method to obtain phosphoranes from triphenylphosphine (TPP) and maleic anhydride (MA), dialkyl maleates, N-aryl maleimides and methyl N-aryl maleanilates is reported. These stabilised phosphoranes react with aromatic aldehydes to yield *E*-olefins but fail to react with monoketones and 1,2-diketones. With the more reactive triketone, ninhydrin, the reaction is positive. The order of reactivity of these reagents in olefination appears to be imides = isomaleimides > maleanilates > dialkyl maleates > anhydrides.

Keywords. Wittig reactions; maleic acid derivatives; stabilised phosphoranes.

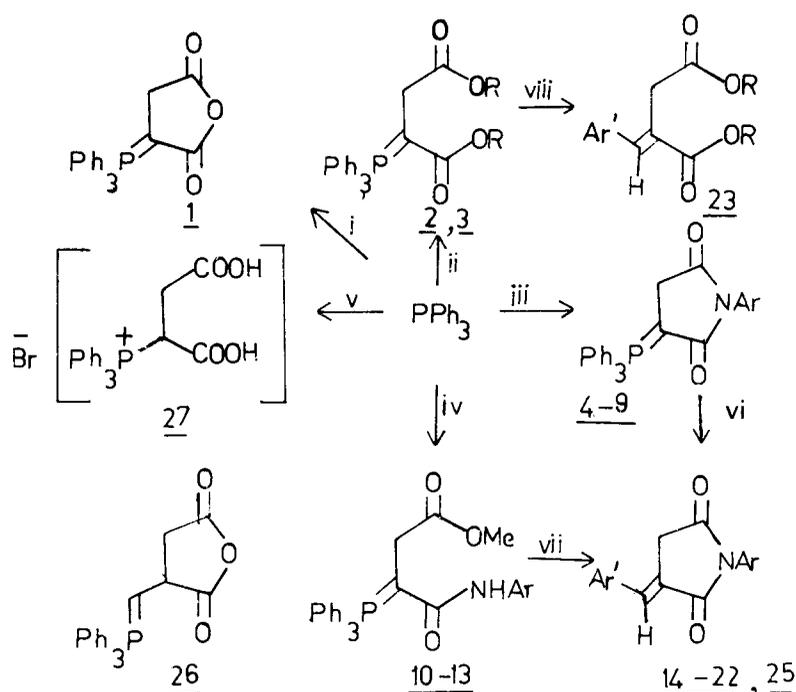
1. Introduction

The reactivity of maleic anhydride and its derivatives towards dinucleophiles such as *o*-aminophenol (Patel *et al* 1979), *o*-phenylenediamine (Patil *et al* 1990), thiourea (Wani *et al* 1990), *o*-aminothiophenol (Shaikh *et al* 1986) and anthranilic acid (Argade and Balasubramaniyan 1988) has been the subject of our earlier investigations on designing heterocycles. We noticed that nucleophilic additions of triphenylphosphine (TPP) to maleic anhydride (MA) and its derivatives have received only scanty attention so far. A limited number of stabilised phosphoranes from TPP and maleic anhydride, dialkyl maleates or fumarates, maleimides and isomaleimides are reported and are used either as routine Wittig reagents (Armstrong *et al* 1976; McMurry and Donovan 1977; Tong and Isoe 1983; Barrett *et al* 1986) or as α -carbanion sources (Cooke and Manning 1981). Their application in olefinations has not been studied in any detail. In this study, we report a detailed investigation of the formation of thirteen phosphoranes and of their Wittig reactions with several carbonyl derivatives.

2. Results and discussion

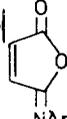
Triphenylphosphine (TPP) is reported to react smoothly with maleic anhydrides (MA), (to give 1), maleimides (to give 4) and isomaleimides (to give 4) (Hedaya and

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(i) MA, acetone, RT, 15 min

(ii) ROOCCH^{Z/E}=CHCOOR, HBr 48%, acetonitrile, reflux, 1 h

(iii) Maleimide or isomaleimide , acetone, RT, 15 min

(iv) MeOOCCH^{Z/E}=CHCONHAr, acetone, RT, overnight

(v) HOOCCH^{Z/E}=CHCOOH, HBr, acetonitrile, reflux, 15 min

(vi) Ar'CHO, AcOH, 60–70°, 15 min

(vii) Ar'CHO, AcOH:C₆H₆ (1:9) reflux, 4–5 h

(viii) Ar'CHO, AcOH:C₆H₆ (1:9), reflux, 20–22 h

Scheme 1.

Theodoropoulos 1968) and dialkyl maleates and fumarates (to give 2, 3) (Osuch *et al* 1964) to furnish the respective phosphoranes (scheme 1). However, the reported yields (46–66%) were only moderate in the case of MA and maleimides (Hedaya and Theodoropoulos 1968). We noticed that use of benzene or acetone as solvent dramatically improved the yield to 90–95%. We have established that methyl N-arylmaleanilates also afforded excellent yields of the new class of phosphoranes under these conditions. In these reactions, the orientation of the initial nucleophilic addition of TPP to C_β of the α,β-unsaturated carbonyl system (activation by –COOR > –CONHAr) agrees with our earlier observations on the addition of amines to maleanilates (Bhatia *et al* 1984). The IR spectra of these derivatives displayed bands at 1180ν(C=P), 1684ν(NHCO), 1708ν(CO₂ Me) and 3340 cm⁻¹ν(NH). The characteristic PMR absorptions for methylene hydrogens in methyl triphenylphosphoranylidene

Table 1. Physical and spectral data for the phosphoranones derived from maleic acid and derivatives with TPP (scheme 1, 4–13).

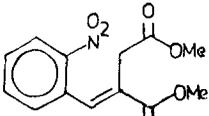
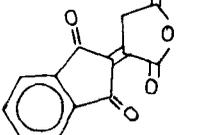
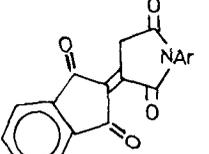
Compound no.*	Ar	m.p. (°C) (% yield)	IR (cm ⁻¹)	PMR (ppm)
<u>4</u>	C ₆ H ₅	177–178 (90)	1180, 1630 1700	3.5(<i>bs</i> , 2H), 7.5–8.0 (<i>m</i> , 20H)
<u>5</u>	2-H ₃ CC ₆ H ₄	192–193 (66)	1180, 1715	—
<u>6</u>	4-H ₃ CC ₆ H ₄	189–190 (80)	1160, 1645, 1715	—
<u>7</u>	2-O ₂ NC ₆ H ₄	204–205 (85)	1160, 1650 1710	—
<u>8</u>	4-O ₂ NC ₆ H ₄	161–162 (72)	1160, 1650 1720	—
<u>9</u>	2-H ₃ C, 5-O ₂ NC ₆ H ₃	191–192 (66)	1160, 1650 1720	2.18(<i>s</i> , 3H), 3.08(<i>bs</i> , 2H), 7.3–7.7(<i>m</i> , 18H)
<u>10</u>	C ₆ H ₅	184–185 (85)	1180, 1644 1712, 3468	—
<u>11</u>	2-H ₃ CC ₆ H ₄	164–165 (85)	1180, 1645 1720, 3200	—
<u>12</u>	4-H ₃ CC ₆ H ₄	189–190 (80)	1180, 1684 1708, 3340	2.43(<i>s</i> , 3H), 2.96(<i>s</i> , 3H) 3.36(<i>d</i> , 2H, <i>J</i> = 1.66 Hz), 7.16–7.86(<i>m</i> , 4H), 8.13 (<i>s</i> , 15H), 0.89(<i>s</i> , 1H, D ₂ O exch)
<u>13</u>	2-H ₃ C, 5-O ₂ NC ₆ H ₃	144–145 (63)	1180, 1640 1740, 3200	—

*4–9 were obtained from maleimides and the corresponding isomaleimides.

succinamate appeared as a doublet at δ 3.36 with $J = 1.66$ Hz (table 1, 12); the earlier values reported for these protons are δ 2.93 in dimethyl triphenylphosphoranylidene succinate (Osuch *et al* 1964) and δ 2.78 in the corresponding diethyl ester (Eyjolfsson 1970). We are inclined to correct the earlier values since a large number of related systems examined by us have consistently shown ¹H-NMR observations for the methylene hydrogens in the range δ 3.08–3.50.

The phosphoranones thus obtained (scheme 1, 1–13) were subjected to Wittig olefination with a series of aldehydes and ketones. The reactions failed with monoketones (acetophenone, benzophenone) and diketones (benzil, acetyl acetone, ethyl acetoacetate, benzoyl acetone). The only positive case was provided by the 1,2,3-triketone, ninhydrin (table 2, 2, 24, 25), where the enhanced carbonyl reactivity could make up for the sluggishness of the stabilised Wittig reagent. The reaction of 1 also failed with aliphatic and aromatic aldehydes. The phosphoranones 4, 6–8 derived from N-arylmaleimides underwent clean olefination (acetic acid, 60–70°, 15 min) with several aldehydes in consistently high yields (table 2, 14–22). Disappearance of the IR band at 1180 cm⁻¹ ν (C=P) with concomitant gain in intensity at 1600 cm⁻¹ ν (C=C) supports the olefinic structure of the products (Barrett *et al* 1986). A 2H-doublet at δ 3.6–3.9 (CH₂, $J = 1–3$ Hz) and a 1H-triplet (occasionally poorly resolved) at δ 7.9–9.1 (vinylic H, $J = 1–3$ Hz) confirm this assignment in all these cases. A study of the reported PMR values for such olefins (Nair and Adams 1961; Eyjolfsson 1970; Armstrong *et al* 1976;

Table 2. Physical and spectral data for the Wittig products (scheme 1, 14–25).

Compound no.*	Ar	Ar'	m.p. (°C) (% yield)	IR (cm ⁻¹)	PMR (ppm)
<u>14</u>	C ₆ H ₅	C ₆ H ₅	192–193 (85)	1700, 1645	3.75(<i>dd</i> , 2H), 7.1–7.5 (<i>m</i> , 10H), 7.8(<i>t</i> , 1H)
<u>15</u>	C ₆ H ₅	2-CH ₃ OC ₆ H ₄	159–160 (60)	1700, 1620	—
<u>16</u>	C ₆ H ₅	2-O ₂ NC ₆ H ₄	181–183 (90)	1714, 1668	3.53(<i>d</i> , 2H, <i>J</i> = 1.66 Hz), 7.4(<i>m</i> , 9H)
<u>17</u>	4-H ₃ CC ₆ H ₄	C ₆ H ₅	171–172 (73)	1712, 1600	2.33(<i>s</i> , 3H), 3.76(<i>d</i> , 2H, <i>J</i> = 1.66 Hz), 7.33(<i>s</i> , 5H), 7.46(<i>s</i> , 4H), 7.73(<i>m</i> , 1H)
<u>18</u>	4-H ₃ CC ₆ H ₄	2-CH ₃ OC ₆ H ₄	181–182 (60)	1700, 1620	2.37(<i>s</i> , 3H), 3.64(<i>d</i> , 2H, <i>J</i> = 1.66 Hz), 3.86(<i>s</i> , 3H), 6.8–6.93(<i>m</i> , 4H), 7.02–7.46 (<i>m</i> , 4H), 8.06(<i>t</i> , 1H)
<u>19</u>	4-H ₃ CC ₆ H ₄	2-O ₂ NC ₆ H ₄	192–193 (85)	1664, 1606	2.4(<i>s</i> , 3H), 3.58(<i>s</i> , 2H), 7.4 (<i>s</i> , 4H), 7.5–7.7(<i>m</i> , 7H), 8.1(<i>bs</i> , 1H)
<u>20</u>	2-O ₂ NC ₆ H ₄	C ₆ H ₅	170–171 (52)	1715, 1650	3.73(<i>d</i> , 2H, <i>J</i> = 3Hz), 7.4(<i>s</i> , 5H), 7.2–7.9(<i>m</i> , 4H), 8.1(<i>t</i> , 1H, <i>J</i> = 3Hz)
<u>21</u>	2-O ₂ NC ₆ H ₄	2-O ₂ NC ₆ H ₄	185–186 (65)	1710, 1690	3.2(<i>d</i> , 2H, <i>J</i> = 3Hz), 7.33–7.9 (<i>m</i> , 8H), 8.1(<i>t</i> , 1H, <i>J</i> = 3Hz)
<u>22</u>	4-O ₂ NC ₆ H ₄	C ₆ H ₅	206–208 (80)	1705, 1650	3.76(<i>d</i> , 2H, <i>J</i> = 3 Hz), 7.4(<i>s</i> , 5H), 7.55(<i>d</i> , 2H, <i>J</i> = 9 Hz), 7.65(<i>t</i> , 1H <i>J</i> = 3 Hz), 8.24(<i>d</i> , 2H, <i>J</i> = 9 Hz)
<u>23</u>			95 (66)	1726, 1652 1518	3.33(<i>s</i> , 2H), 3.73(<i>s</i> , 3H), 3.88 (<i>s</i> , 3H), 7.2–7.7(<i>m</i> , 4H), 8.16(<i>s</i> , 1H)
<u>24</u>			185–186 (65)	1730, 1602 1750	—
<u>25</u>			220–222 (70)	1720, 1600	—

* 14 was obtained using 4 or 10. 17, 18, 19 were obtained using 6 or 12. Yields of the olefins from either method were comparable.

Gosney and Rowley 1979; Tong and Isoe 1983; Barrett *et al* 1986; Awad *et al* 1989) reveals that vinylic protons in *E*-isomers appear in the range δ 6.60–8.10 while in *Z*-isomers, they appear upfield, around δ 5.52–6.0. Reactions of phosphoranes 4, 6–8

with aromatic aldehydes afforded samples 14–22 each of which manifested a vinylic proton absorption at δ 7.25–8.24 suggestive of their *E*-assignment. A more definitive method for stereochemical assignment in these cases appears desirable.

The phosphoranes 10/12 did not react with aromatic or aliphatic aldehydes under short reaction times. However, on prolonged reflux for 4–6 h in acetic acid–benzene (1:9), the reaction furnished products which turned out to be the arylidenesuccinimides, 14, 17–19. Presumably, the relatively sluggish ester phosphoranes cyclize to the more reactive imide phosphoranes prior to olefination.

The diester phosphoranes 2 (Osuch *et al* 1964) and 3 (Eyjolfsson 1970) were readily obtained from dialkyl maleates or fumarates and TPP (CH_3CN , HBr 48%, reflux, 1 h) in 70% yield. Unfortunately, they were inert even with aldehydes under a variety of Wittig conditions. However, the phosphorane 2 caused olefination of the more reactive 2-nitrobenzaldehyde on prolonged reflux to furnish dimethyl 2-nitrobenzylidene succinate, a well-characterised solid (table 2, 23); in a recent report, such derivatives were stated to be oils (Awad *et al* 1989). This is not surprising since purification of these compounds required repeated recrystallisations.

In our attempt to determine the structural requirement for successful formation of like phosphoranes, we experimented with several conjugated carbonyl systems. Substituted maleic anhydrides such as methyl maleic anhydride (MMA) and phenyl maleic anhydride failed to give similar phosphoranes. The reported reaction of MMA and TPP (Hedaya and Theodoropoulos 1968) could not be reproduced by us. Itaconic anhydride was expected to give the phosphorane 26 which on olefination would yield substituted succinic anhydride and thereon substituted itaconic anhydrides. However, this did not succeed. Even though maleimides afforded the corresponding phosphoranes in excellent yields, maleic hydrazide led to only negative results. Methyl hydrogen maleate or fumarate on similar treatment also failed to yield the expected phosphoranes. We notice from an earlier study (Hoffmann 1961) that in the case of olefinic substrates carrying a free COOH, the corresponding salts (27), were invariably obtained.

3. Experimental

The melting points reported are uncorrected. IR spectra were recorded on a Hitachi 270–30 (KBr pellet) or Perkin–Elmer R 37 (nujol mull) spectrophotometer (ν in cm^{-1}). PMR spectra were recorded in CDCl_3 on a Varian FT-80A using TMS as internal standard (chemical shifts in δ ppm). Elemental analyses observed were within the limits of accuracy ($\pm 0.3\%$).

3.1 Preparation

Details of preparation of maleanilic acids, maleimides, isomaleimides, methyl maleanilates and methyl fumaranilates are as described earlier (Wani *et al* 1991, and references cited therein).

3.2a *Reaction of TPP with MA, N-arylmaleimides, N-arylisomaleimides and methyl-N-arylmaleanilates.* General procedure: Equimolar (0.01 M) solutions of TPP in acetone (20 ml) and of MA, or N-arylmaleimide ($\text{Ar}=\text{C}_6\text{H}_5$, 2-Me C_6H_4 , 4-Me C_6H_4 , 2-O $_2\text{NC}_6\text{H}_4$, 4-O $_2\text{NC}_6\text{H}_4$, 2-Me-5-O $_2\text{NC}_6\text{H}_3$), or N-aryl isomaleimide (Ar = same as in maleimide) or methyl N-aryl maleanilate ($\text{Ar}=\text{C}_6\text{H}_5$, 2-Me C_6H_4 , 4-Me C_6H_4 ,

2-Me-5-O₂NC₆H₃) in acetone (10 ml) were stirred at room temperature for 15 minutes. With MA, the initial clear solution turned orange in colour, and then became turbid after 5 minutes. The products, which precipitated as amorphous, nearly colourless powders, were filtered, washed with acetone (2 × 5 ml) and recrystallised from the same solvent (table 1, 1, 4-9, 10-13). Identical phosphoranes were obtained from maleimides and the corresponding isomaleimides in the reaction (see text).

3.2b Reaction of TPP with dimethyl/diethyl maleates or fumarates: To a solution of TPP (0.01 M) in acetonitrile (20 ml) and the diester (0.01 m), equimolar amount of HBr (48%) aqueous solution was added and the mixture refluxed for 1 h. The reaction mixture was then poured onto crushed ice and the solid obtained was washed with ether. The clear aqueous solution of the phosphonium salt was treated with sodium hydroxide (20%, 20 ml). The precipitated ylid 2/3 was filtered, dried and recrystallised from benzene-acetone (80:20).

3.3 Reaction of 4, 6, 7 or 8 with aldehydes (for 14-22): General procedure

A mixture of phosphorane 4, 6, 7 or 8 (0.01 M) and the appropriate aldehyde (0.01 M) in acetic acid (5 ml) was warmed on a water bath maintained at 60–70° for 15 minutes. After cooling, the reaction mixture was diluted with methanol (10–15 ml) to cause complete separation of the product. The solid was then filtered, dried and recrystallised from 95% EtOH.

3.4 Reaction of 2 with 2-nitrobenzaldehyde

To a solution of 2 (0.01 M) in benzene-acetic acid (9:1, 10 ml), 2-nitrobenzaldehyde (0.01 m) was added and the mixture refluxed for 20–22 h. After cooling, a pasty product that separated from the dark red reaction mixture was solidified by repeatedly washing it with *n*-hexane. The solid was filtered and dried (table 2, 23).

3.5 Reaction of 10 & 12 with aldehydes: General procedure

An equimolar (0.01 M) mixture of ylid 10 or 12 and the appropriate aldehyde, taken in benzene-acetic acid (9:1, 10 ml), was refluxed for 4–6 h. The reaction mixture after cooling was diluted with methanol (10–15 ml). The solid that separated was filtered, washed with benzene and dried. The products obtained in each case were identical (m.p. mixed, tlc, IR, PMR) to those obtained by reacting 4 or 6 and the appropriate aldehyde (table 2, 14, 17, 18 and 19). Blank experiments of heating 10-13 in benzene established their conversion to 4-6 and 9, respectively.

4. Conclusions

In summary, we have demonstrated that (1) several stabilised phosphoranes can be readily obtained from TPP and maleic acid derivatives except when a free COOH is present; (2) their reactivity is, however, limited to satisfactory olefination of only aldehydes; (3) among them, the imide adducts are synthetically more useful; (4) the olefinic systems obtained have the *E*-geometry as is generally the case with other

stabilised phosphoranes; (5) the order of reactivity of the phosphoranes derived from the derivatives appear to be imides = isomaleimides > maleanilates > dialkyl maleates > anhydride, and (6) these reagents do not appear to offer a good alternative to the Stobbe synthesis for obtaining succinylidene systems.

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