Reactions of Stabilised Phosphorus Ylide with Nitrilium Trifluoromethanesulphonate Salts

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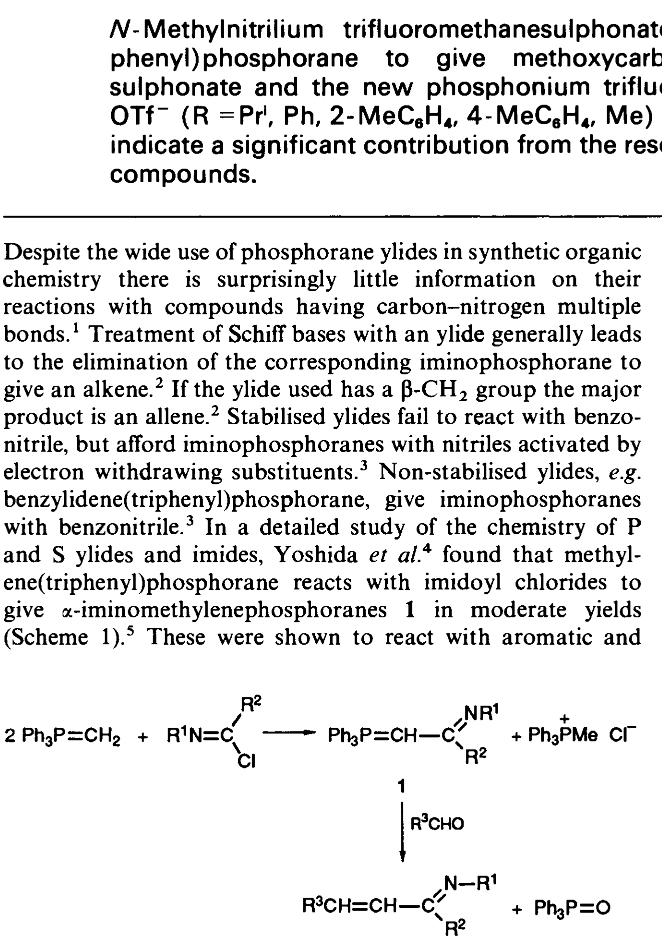
N-Methylnitrilium trifluoromethanesulphonates react readily with methoxycarbonylmethylene(triphenyl)phosphorane to give methoxycarbonylmethyl(triphenyl)phosphonium trifluoromethanesulphonate and the new phosphonium trifluoromethanesulphonates $[Ph_3PC(CO_2Me)=CRNHMe]^+OTf^-$ (R = Pr^i, Ph, 2-MeC_6H_4, 4-MeC_6H_4, Me) in moderate yields. ^{31}P and ^{13}C NMR spectroscopic data indicate a significant contribution from the resonance form $[Ph_3PC(CO_2Me)-CR=NHMe]^+OTf^-$ in the compounds.

Despite the wide use of phosphorane ylides in synthetic organic chemistry there is surprisingly little information on their reactions with compounds having carbon–nitrogen multiple bonds.[1] Treatment of Schiff bases with an ylide generally leads to the elimination of the corresponding iminophosphorane to give an alkene.[2] If the ylide used has a β-CH_2 group the major product is an allene.[2] Stabilised ylides fail to react with benzonitrile, but afford iminophosphoranes with nitriles activated by electron withdrawing substituents.[3] Non-stabilised ylides, *e.g.* benzylidene(triphenyl)phosphorane, give iminophosphoranes with benzonitrile.[3] In a detailed study of the chemistry of P and S ylides and imides, Yoshida *et al.*[4] found that methylene(triphenyl)phosphorane reacts with imidoyl chlorides to give α-iminomethylenephosphoranes **1** in moderate yields (Scheme 1).[5] These were shown to react with aromatic and aliphatic aldehydes to give αβ-unsaturated imines **2**. Bestmann has described the synthesis of enaminophosphonium chlorides, $[Ph_3PCR=CHNMe_2]^+Cl^-$, together with the alkyltriphenylphosphonium chloride $[Ph_3PCH_2R]^+Cl^-$, from reactions between alkylidenetriphenylphosphorane with either chloromethylene(dimethyl)ammonium chloride[6] or more recently, with tetramethylformamidinium chloride.[7]



Scheme 1

Our interest in nitrilium salt chemistry[8–10] suggested the possibility that the reactions of phosphorus ylides with nitrilium trifluoromethanesulphonates might prove to be a useful method for the synthesis of enaminophosphonium salts which are unattainable by the methods of either Yoshida or Bestmann. Other methods are available for the synthesis of enaminophosphonium salts,[11] but none of these, with the possible exception of that of Schweizer,[12,13] can claim to be of general applicability. We now describe our investigation of the reactions of the stabilised ylide, $Ph_3P=CHCO_2Me$, with some *N*-methylnitrilium trifluoromethanesulphonates.

Results and Discussion

N-Methylnitrilium trifluoromethanesulphonate salts, which are easily prepared by the reaction of an aliphatic or aromatic nitrile with methyl trifluoromethanesulphonate,[8] are only soluble in polar solvents such as nitromethane, dichloromethane and acetonitrile. Ether solvents, particularly tetrahydrofuran, undergo electrophilic ring opening in the presence of the nitrilium salts and have to be avoided. An initial experiment was carried out by dropwise addition of a solution of methoxycarbonylmethylenephosphorane (1 equiv.) in dry nitromethane to 1 equiv. of *N*-methylisobutyronitrilium trifluoromethanesulphonate in the same solvent at room temperature to give $[MeO_2CCH_2PPh_3]^+OTf^-$ (52%) and compound **3a** (43%), as a white, crystalline solid. All subsequent experiments were carried out using dry dichloromethane as a solvent for both the nitrilium salts and the phosphorane to give the new enaminophosphonium trifluoromethanesulphonates **3b–e**.

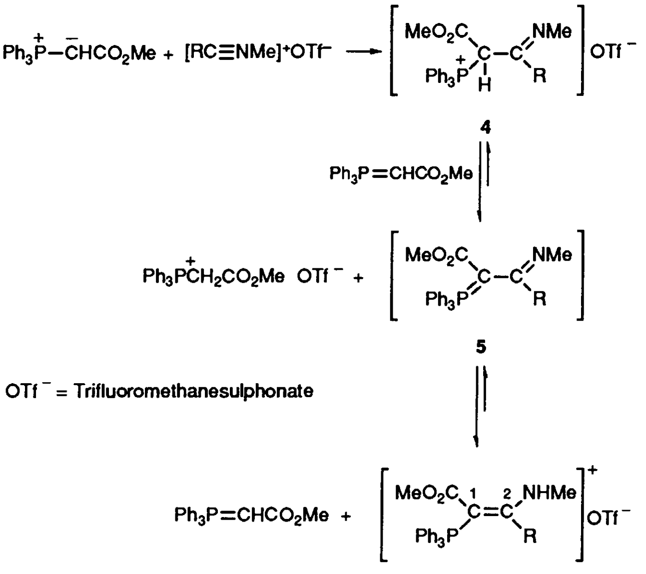
The isolated yields of these enaminophosphonium salts ranged from 31 to 64% and reaction was always accompanied by appreciable formation of the phosphonium salt $[Ph_3PCH_2CO_2Me]^+OTf^-$. In all the reactions investigated, variable amounts of intractable oils are also formed, most particularly when the nitrilium salt has an aliphatic or benzylic R group having acidic α-hydrogens. There is some evidence[14] to suggest that, in part, these oils may arise by deprotonation of the nitrilium salt to give vinylidenamine intermediates $[R^1R^2C=C=NMe]$. The formation of the phosphonium salt $[Ph_3PCH_2CO_2Me]^+OTf^-$ can be explained by a transylidation reaction of the initially formed product **4** to give the iminophosphorane **5** according to Scheme 2. In all cases the major isolated product was the enaminophosphonium salt **3** rather than the α-iminophosphonium salt **4**. The isomerisation of **4** to **3** probably occurs *via* the intermediate **5**, since precipitation of up to 50% yield of the phosphonium salt, $[Ph_3PCH_2CO_2Me]^+X^-$ is seen immediately on mixing the homogeneous solutions of the ylide and the nitrilium salts—implying a transylidation reaction. There could be an equilibrium reaction between **5** and the phosphonium salt $[Ph_3PCH_2CO_2Me]^+OTf^-$ although **5** will be a much weaker base than the phosphorane $[Ph_3P=CHCO_2Me]$. Alternatively **5** could become protonated during work up.

The compounds **3a–e** showed an N–H stretching vibration in the range 3225–3396 cm^{-1} in the IR spectrum, and a strong band at 1580–1610 cm^{-1} for ν(C=C) or ν(C=N) in addition to the carbonyl vibration of the ester group. The ^1H NMR spectra all showed a doublet (*J* 5 Hz) in the range δ 2.72–3.20 for the NHMe group and a broad N–H proton at δ 10–11. In the ^{13}C NMR spectra (Table 1), the chemical shifts and P–C coupling constants of the C-1 atom indicate predominant sp^2 hybridisation of this carbon atom. Schweizer[12] has shown that for enamino phosphonium salts J_{P-P} is large (77–132 Hz). The ^{13}C

Table 1 ^{31}P and ^{13}C NMR spectroscopic data for the compounds **3**

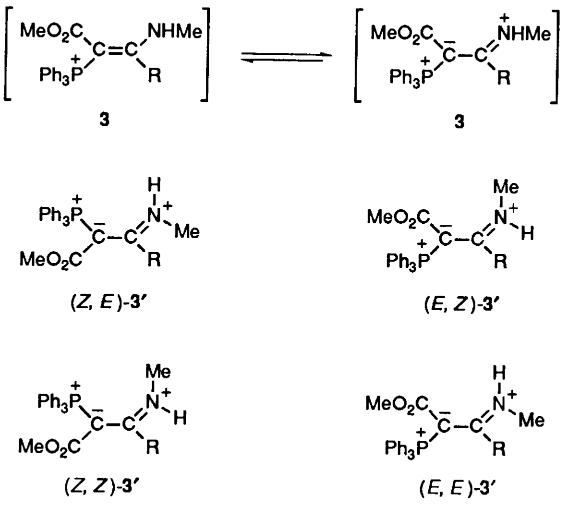
R	δ_P(ppm) (ratio[a])	δ_C(ppm) (J_{P-C}/Hz)						
		C-1	C-2	CO_2Me	$CO_2\mathit{Me}$	NMe	*ipso*-C	Other bands
Me_2CH[b]	+16.3 (24) +17.6 (1.3)	Not seen	168.0 (10.0)	173.0 (17.0)	50.6	34.6	123.1 (92.9)	(*c*)
C_6H_5	+17.6 (2) +17.4 (24)	70.4 (122.2)	168.3 (9.3)	174.6 (17.1)	51.1	32.6	122.4 (93.7)	(*d*)
$2\text{-}MeC_6H_4$	+18.07	70.5 (124.0)	168.3 (11.0)	173.8 (18.0)	50.9	31.3	122.5 (94)	(*e*)
$4\text{-}MeC_6H_4$	+20.3	70.5 (124.1)	168.3 (11.0)	174.6 (17.0)	51.0	32.4	122.5 (94.0)	(*f*)
Me	+19.14	68.2 (122.2)	168.1 (9.7)	173.1 (16.2)	50.6	31.3	122.6 (91.6)	(*g*)

[a] Ratio of major–minor isomers. [b] This spectrum was of poor quality and the band for C-1 could not be observed—it may be masked by the $CDCl_3$ absorptions. [c] 132.8 (*ortho*-C (10), 129.7 (*meta*-C) (12.7), 133.5 (*para*-C), 18.4 (Me_2CH) and 39.6 ($Me_2C\mathit{H}$) (2.0). [d] 132.8 (*ortho*-C) (9.9), 129.3 (*meta*-C) (13.1), 135.1 (*para*-C) (3.1), 127.5, 133.1, 130.5 and 133.7. [e] 132.8 (*ortho*-C) (9.5), 129.1 (*meta*-C) (13.0), 134.0 (*para*-C) and 19.0 ($\mathit{Me}C_6H_4$). [f] 132.8 (*ortho*-C) (13.0), 129.0 (*meta*-C) (13.0), 132.8 (*para*-C), 21.2 ($\mathit{Me}C_6H_4$), 127.5, 127.9, 128.1, 130.5, 133.6 and 140.9. [g] 133.0 (*ortho*-C) (9.8), 129.8 (*meta*-C) (13.3), 133.7 (*para*-C) (3.3) and 20.5 (C-*Me*) (3.7).



a; R = $CHMe_2$; 43%
b; R = C_6H_5; 31%
c; R = $2\text{-}MeC_6H_4$; 60%
d; R = $4\text{-}MeC_6H_4$; 64%
e; R = Me 40%

Scheme 2



chemical shift of C-1 falls in the range of δ 68–71, while that of C-2 is between δ 168.0–168.3. This suggests that there is considerable electron delocalisation and these compounds are best described as a resonance hybrid of the structures **3** and **3′**.

A similar conclusion has been reached by Bestmann[7] for the compounds $[Ph_3\overset{+}{P}CR{=}CHNMe_2]Cl^-$ (where R = H, Me, Et, Pr, PrS, Ph or CO_2Me). This implies that in compounds **3a–e** there will be hindered rotation about both the C=C and C–N bonds leading to the possibility of the four isomers shown. It will be noted from Table 1 that the ^{31}P NMR spectrum of compounds **3a** and **3b** show evidence for a trace of another product. Spectroscopy did not allow a distinction between the four possibilities and a single crystal X-ray study on compound **3a** was therefore carried out. The results, which are reported elsewhere,[15] clearly show that the major isomer has the *E,Z*-configuration. The C(1)–C(2) bond length is 1.44 Å and the C(2)–N bond length is 1.30 Å which is in keeping with the resonance hybrid structure proposed from the spectroscopic data and it is assumed that in all the compounds **3a–e** the *E,Z*-configuration is the major or only isomer isolated. It is not possible to identify the minor isomer present in the samples of **3a** and **b**.

The compounds of type **3** react readily with a base to generate the corresponding ylide **5**, but, not surprisingly, this doubly stabilised ylide does not react with aldehydes at room temperature over several hours.

Experimental

Methyl trifluoromethanesulphonate was freshly prepared by reaction of trifluoromethanesulphonic acid with dimethyl sulphate[8] and was distilled immediately before use. The *N*-methylnitrilium salts were prepared by addition of the nitrile (1 equiv.) to methyl trifluoromethanesulphonate (1 equiv.) under argon as described previously.[8] Methoxycarbonyl(triphenyl)-phosphorane was a commercial sample (Lancaster Synthesis) used without further purification. Dichloromethane and nitromethane were purified and dried by established procedures.[16] IR spectra were recorded on a Perkin-Elmer model PE 298; ^{1}H and ^{19}F NMR spectra on a Perkin-Elmer R32 spectrometer at 220 MHz (^{1}H) and 84.6 MHz (^{19}F), while ^{31}P and ^{13}C NMR spectra were recorded on a WP 80 spectrometer operating at 32.44 and 20 MHz, respectively. All *J* values are in Hz. Unless otherwise stated all reactions were carried out under dry argon atmosphere.

Reactions of Methoxycarbonylmethylene (triphenyl) phosphorane with Nitrilium Trifluoromethanesulphonate Salts.—(*a*) N-*Methylisobutyronitrilium trifluoromethanesulphonate.* A solution of the phosphorane (4.1 g, 12.36 mmol) in dry nitromethane (20 cm^3) was added dropwise during 10 min to a solution of the nitrilium salt (2.88 g, 12.36 mmol) in nitromethane (10 cm^3) at room temperature resulting in a colour change from pale yellow to orange. The mixture was stirred for 6 h at room temperature before removal of the solvent under reduced pressure to give an orange oil. This was washed with ethyl acetate (3 × 100 cm^3) to give methoxycarbonylmethyl(triphenyl)phosphonium trifluoromethanesulphonate (3.13 g, 6.46 mmol, 52%) as a white solid, m.p. 134–135 °C. After filtration the filtrate was allowed to evaporate slowly to give white crystals of 2-*isopropyl*-1-*methoxycarbonyl*-2-*methylaminovinyl*(*triphenyl*)*phosphonium trifluoromethanesulphonate* **3a** (3.0 g, 5.2 mmol, 43%), m.p. 49–52 °C (Found: C, 57.3; H, 5.2; N, 2.5. $C_{27}H_{29}F_3NO_5PS$ requires C, 57.1; H, 5.1; N, 2.5%) ν_{max}(Nujol)/cm^{-1} 3225m (N–H), 1650s (C=O) and 1610s (C=N); δ_H(CDCl$_3$; TMS int. ref.) 0.75 (d, 6 H, *J* 7, 2 × Me), 2.0 (septet, 1 H, C*H*Me$_2$), 3.20 (d, 6 H, N-Me *J* 5 and OMe overlapping), 7.4–7.8 (m, 15 H, C_6H_5) and 10.95 (br s, 1 H, NH); δ_F(CDCl$_3$; TFA ext. ref.) −0.99.

(*b*) N-*Methylbenzonitrilium trifluoromethanesulphonate.* The phosphorane (5.78 g, 17.3 mmol) in dry dichloromethane (25 cm^3) was added dropwise to the nitrilium salt (4.64 g, 17.3 mmol) in the same solvent and the mixture was stirred at room temperature for 3 h before removal of the solvent to give an orange oil. This was washed with ethyl acetate (5 × 50 cm^3) to give methoxycarbonylmethyl(triphenyl)phosphonium trifluoromethanesulphonate (3.5 g, 7.2 mmol, 42%) which was filtered off; slow evaporation of the filtrate during 15 h gave 1-*methoxycarbonyl*-2-*methylamino*-2-*phenylvinyl*(*triphenyl*)*phosphonium trifluoromethanesulphonate* **3b** (3.20 g, 5.32 mmol, 31%), which was recrystallised from dichloromethane by dropwise addition of diethyl ether to give white crystals, m.p. 180–186 °C (Found: C, 59.0; H, 4.2; N, 2.46. $C_{30}H_{27}F_3NO_5PS$ requires C, 59.9; H, 4.49; N, 2.32%). ν_{max}(Nujol)/cm^{-1} 3210s (N–H), 1675vs (C=O) and 1590 (C=N); δ_H(CDCl$_3$; TMS int. ref.) 2.74 (d, 3 H, *J* 5, N-Me), 3.12 (s, 3 H, OMe), 6.85 (d, 2 H, *J* 8, *ortho* H), 6.99 (t, 2 H, *J* 8, *meta* H), 7.20 (t, 1 H, *J* 8, *para* H), 7.4–7.7 (m, 15 H, Ph$_3$P) and 10.9 (br s, 1 H, NH); δ_F(CDCl$_3$; TFA ext. ref.) −0.66.

(*c*) N,2-*Dimethylbenzonitrilium trifluoromethanesulphonate.* A mixture of the phosphorane (3.56 g, 10.6 mmol) and the nitrilium salt (3.0 g, 10.6 mmol) in dichloromethane (20 cm^3) was stirred at room temperature for 24 h. Removal of the solvent and treatment of the residual red oil with ethyl acetate (50 cm^3) gave methoxycarbonylmethyl(triphenyl)phosphonium trifluoromethanesulphonate (1.55 g, 3.2 mmol, 30%) which was filtered off. Evaporation of the filtrate gave an oil which was dissolved in the minimum amount of dichloromethane and then slowly diluted with diethyl ether to give white crystals of 1-*methoxycarbonyl*-2-*methylamino*-2-o-*tolylvinyl*(*triphenyl*)-*phosphonium trifluoromethanesulphonate* **3c** (3.9 g, 6.3 mmol, 60%), m.p. 202–205 °C (Found: C, 60.2; H, 4.8; N, 2.3. $C_{31}H_{29}F_3NO_5PS$ requires C, 60.5; H, 4.7; N, 2.3%) ν_{max}(Nujol)/cm^{-1} 3300m (N–H), 1600s (C=O) and 1580s (C=N); δ_H(CDCl$_3$; TMS int. ref.) 1.85 (s, H, Me), 2.62 (d, 3 H, *J* 5, N-Me), 3.15 (s, 3 H, OMe), 6.65 (d, 1 H, *J* 8, 6.88–7.15 (m, 4 H), 7.3–7.7 (m, 15 H, PPh$_3$) and 10.9 (br s, 1 H, NH); δ_F(CDCl$_3$; TFA ext. ref.) −0.44.

(*d*) N,4-*Dimethylbenzonitrilium trifluoromethanesulphonate.* The phosphorane (3.56 g, 10.6 mmol) and nitrilium salt (3.2 g, 11.0 mmol) in dichloromethane (25 cm^3) at room temperature during 24 h gave, after removal of the solvent and washing with ethyl acetate, methoxycarbonylmethyl(triphenyl)phosphonium trifluoromethanesulphonate (1.6 g, 3.3 mmol, 31%) which was filtered off. The residual oil after evaporation of the filtrate was recrystallised from dichloromethane by addition of diethyl ether to give white crystals of 1-*methoxycarbonyl*-2-*methylamino*-2-p-*tolylvinyl*(*triphenyl*)*phosphonium trifluoromethanesulphonate* **3d** (4.2, 6.8 mmol, 64%), m.p. 110–114 °C; ν_{max}(Nujol)/cm^{-1} 3220m (N–H), 1665s (C=O) and 1580s (C=N); δ_H(CDCl$_3$; TMS int. ref.) 2.32 (s, 3 H, Me), 2.8 (d, 3 H, *J* 5, N-Me), 3.10 (s, 3 H, OMe), 6.80 (s, 4 H, aromatic), 7.4–7.8 (m, 15 H, PPh$_3$) and 10.9 (br s, 1 H, NH); δ_F(CDCl$_3$; TFA ext. ref.) −0.64.

(*e*) N-*Methylacetonitrilium trifluoromethanesulphonate.* Evaporation of the solvent from the reaction between the phosphorane (4.3 g, 12.9 mmol) and the nitrilium salt (2.6 g, 12.9 mmol) in dry dichloromethane (25 cm^3) at room temperature during 3 h gave an orange oil. Treatment of this with ethyl acetate gave methoxycarbonylmethyl(triphenyl)phosphonium trifluoromethanesulphonate (3.5 g, 7.23 mmol, 56%). After filtration the filtrate was allowed to evaporate slowly to give 1-*methoxycarbonyl*-2-*methyl*-2-*methylamino*(*vinyl*)*triphenylphosphonium trifluoromethanesulphonate* **3e** (2.8 g, 5.19 mmol, 40%) as a white solid, m.p. 40–45 °C (Found: C, 54.9; H, 4.1; N, 2.1. $C_{25}H_{25}F_3NO_5PS$ requires C, 55.6; H, 4.74; N, 2.65%); ν_{max}(Nujol)/cm^{-1} 3225m (N–H), 1660vs (C=O) and 1590vs (C=N); δ_H(CDCl$_3$; TMS int. ref.) 1.65 (s, 3 H, Me), 3.10 (s, 3 H, OMe), 3.15 (d, 3 H, *J* N-Me), 7.68–7.9 (m, 15 H, PPh$_3$) and 10.85 (br s, 1 H, NH); δ_F(CDCl$_3$; TFA ext. ref.) −0.8 p.p.m.

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