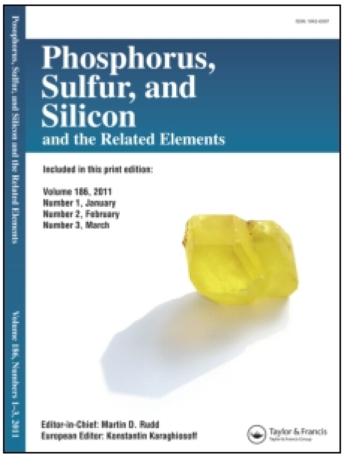

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CONJUGATE ADDITION OF A PHOSPHORUS YLIDE TO 3-CYANOCHROMONE

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CONJUGATE ADDITION OF A PHOSPHORUS YLIDE TO 3-CYANOCHROMONE

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Reaction of 3-cyanochromone with methylenetriphenylphosphorane yields the stabilised ylide (4) by way of a conjugate addition and subsequent ring opening. Variable temperature ^1H NMR spectroscopy indicates that this ylide undergoes rapid conformational interconversion at ambient temperature. X-ray crystallography established that (4) exists as the (*E*) isomer in the solid state.

Keywords: 3-Cyanochromone; methylenetriphenylphosphorane; conjugate addition; X-ray crystallography; variable temperature ^1H NMR spectroscopy

INTRODUCTION

Conjugate additions to chromones (4*H*-[1]benzopyran-4-ones) by nitrogen nucleophiles *e.g.* hydrazines[1], hydroxylamine[1,2] and amidines[3], are well documented and follow an identical mechanistic pathway that results in the formation of *o*-hydroxyphenyl pyrazoles, isoxazoles and pyrimidines, respectively. The reaction of chromones with organo- magnesium or lithium reagents affords complex mixtures of products which result from 1,2- and 1,4-addition[4]. Greater regioselectivity has attended the addition of organocopper reagents to chromones, particularly those which possess

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an electron withdrawing group at C-3 *e.g.* formyl, acetyl, ester, nitrile and phenylsulfinyl, where exclusive conjugate addition is observed[5].

We have previously reported the addition of the reactive ylide methylene triphenylphosphorane ($Ph_3P{=}CH_2$) to some α-diketones and α-methylene ketones. In the former, regiospecific attack of the phosphorane at the more electrophilic carbonyl group gave α-methylene ketones exclusively. However, when excess phosphorane was used an α-ketol rearrangement ensued which gave a new stabilised phosphorane[6,7]. The addition of $Ph_3P{=}CH_2$ to the latter α-methylene ketones unexpectedly proceeded in an exclusive 1,4-fashion to afford γ-diphenylphosphinyl ketones. In view of this unusual conjugate addition of the reactive phosphorane, $Ph_3P{=}CH_2$, to α-methylene ketones we now report our preliminary findings on the addition of $Ph_3P{=}CH_2$ to 3-cyanochromone.

DISCUSSION

3-Cyanochromone (1) was obtained from 3-formylchromone in two steps by regioselective oximation and subsequent acetic anhydride promoted dehydration[8].

The nitrile function in (1) is much less susceptible to nucleophilic addition *c.f.* the aldehyde group. Thus, in marked contrast to the reaction of 3-formylchromone which reacts with a range of phosphorus stabilised carbanions at the aldehyde group[9], 3-cyanochromone (1) may be expected to react at either the carbonyl group or at C-2 (a conjugate addition). Conjugate addition of Wittig reagents (alkylidenetriphenylphosphoranes) to α,β-unsaturated ketones are not particulary common, but have been observed when attack at the carbonyl function is sterically hindered[10]. Addition of (1) to a cold stirred THF solution of methylenetriphenylphosphorane, generated from *n*-butyllithium and methyltriphenylphosphonium bromide, gave an orange/brown precipitate. After dilution of the reaction mixture with water the precipitate was collected by vacuum filtration and washed with water then ethanol and finally with a little diethyl ether. Recrystallisation from CH_2Cl_2/MeOH gave a pure compound as bright yellow cubes.

The ^1H NMR spectrum of this compound in $CDCl_3$ at 24 °C was quite remarkable. Four signals were poorly resolved, three of which appeared as broad multiplets (δ 5.5, 6.8 and 7.9) and the remaining signal as a broad singlet at δ 8.3 (Figure 1a). With the exception of a low field, D_2O exchangeable signal at δ 12.8, all of the remaining signals appeared as multiplets in the range δ 6.9–7.8. No improvements in the resolution of the ^1H NMR spectrum were observed when C_5D_5N was employed as the solvent.

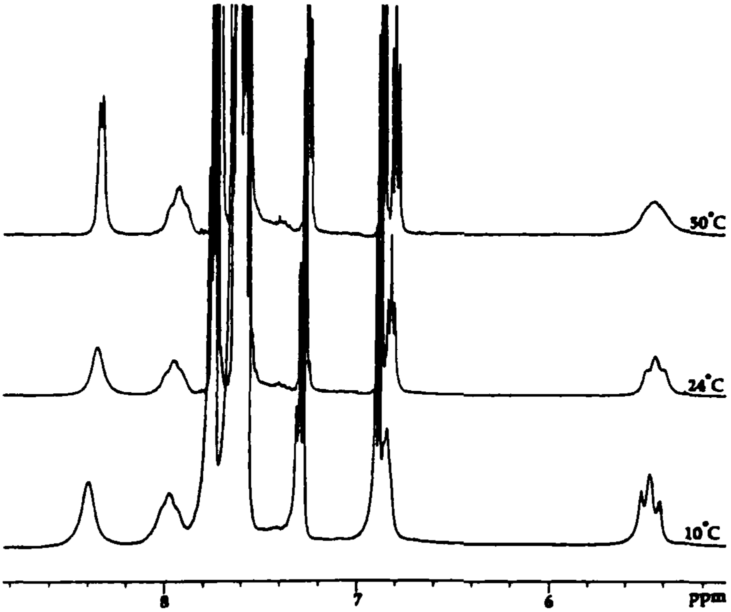


FIGURE 1A Variable Temperature (50–10 °C) ^1H NMR Spectra of the Ylide (4)

The ^1H NMR spectrum was then recorded at various temperature intervals over the range 50 – -50 °C in $CDCl_3$ (Figure 1a, b). Marked improvement in the resolution of the broadened signals was observed at −50 °C.

The signals at δ 5.5 and δ 7.9 appeared as well resolved double doublets with $J = 21.6$ and 16.2 Hz and $J = 19.8$ and 16.2 Hz, respectively. The signals at δ 6.8 and at δ 8.3 now appeared as a triplet and as a dd respectively, the latter exhibiting typical *o*- and *m*- coupling constants for an aromatic ring proton. The magnitude of the coupling constants for the dd at δ 5.5 suggests coupling to a phosphorus atom $^2J_{P\text{-}H} = 21.6$ Hz, which is in

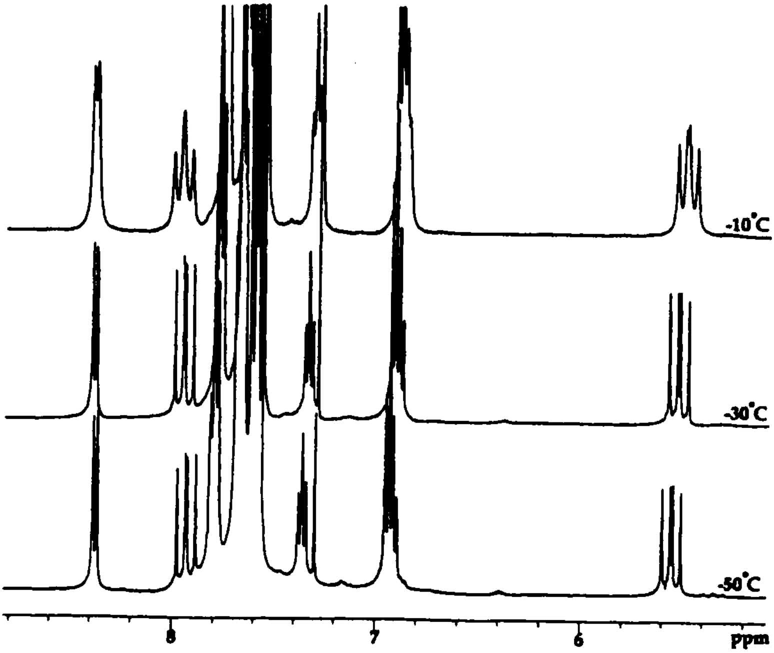
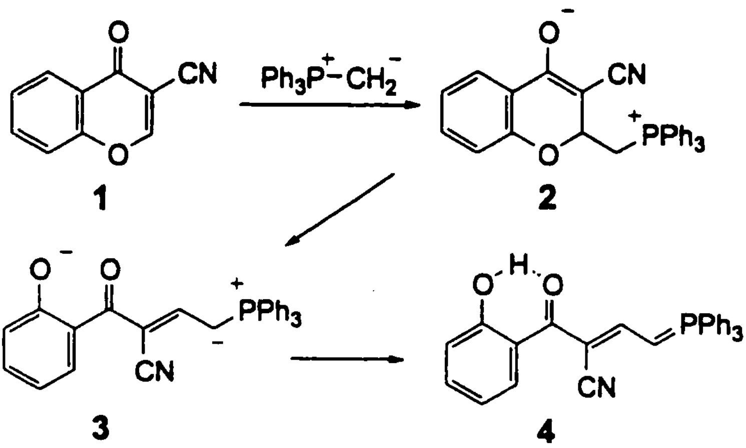


FIGURE 1B Variable Temperature (-10 – -50 °C) ^{1}H NMR Spectra of the Ylide (4)

accord with literature values[7,11,12] and to a *trans* disposed proton $^3J_{H\text{-}H} = 16.2$ Hz. The latter coupling is reflected in the dd at δ 7.9 which also exhibits coupling to a phosphorus atom, $^3J_{P\text{-}H} = 19.8$ Hz. This value compares favourably with other $^3J_{P\text{-}H}$ values when the proton and a phosphorus atom are in a *cis* arrangement[13].

In the ^{13}C NMR spectrum the signal for the C=O group appears at δ 161.5 and that for the nitrile group as a doublet ($^4J_{P\text{-}C} = 10.7$ Hz) at δ 156.1. The chemical shift of these signals compares favourably with those of (1) where the carbonyl and nitrile group carbons resonate at δ 162.5 and δ 156.2, respectively[14]. The ^{31}P NMR spectrum displayed a signal at δ 20.26, a chemical shift which is comparable with those of P atoms in other stabilised ylides[7,11,12,15]. From this spectroscopic data the following structure (4) can be proposed and its formation rationalised by the mechanism depicted in Scheme 1.

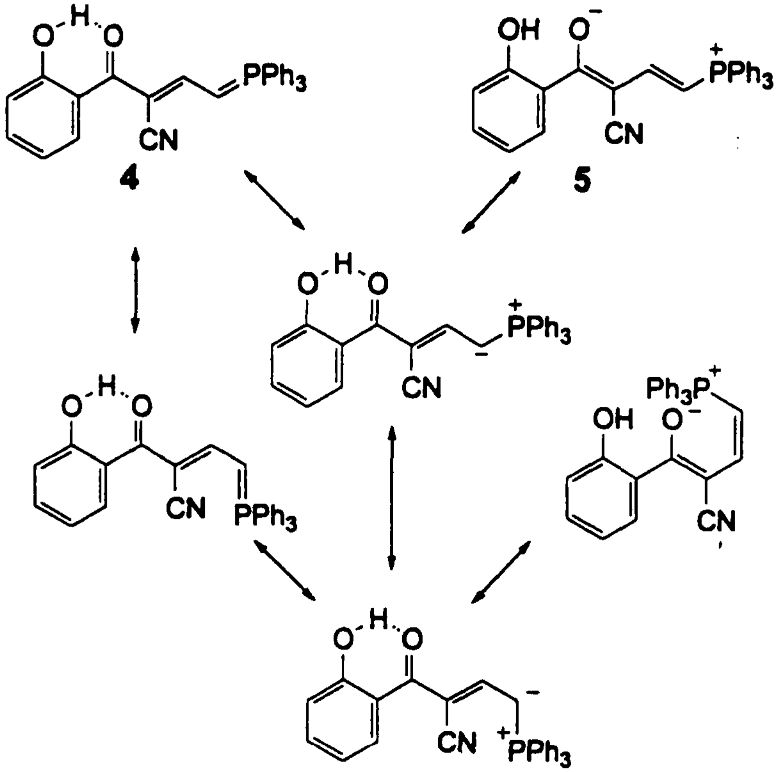


SCHEME 1

Conjugate addition of methylenetriphenylphosphorane to 3-cyanochromone (1) affords the betaine (2). The conjugate addition of heteronucleophiles to chromones frequently results in rupture of the pyranone ring[1,2,3]. A similar sequence operates for (2) to afford (3), which after proton transfer results in the new ylide (4). Cleavage of the chromone ring is stereospecific and gives the (*E*) isomer of (4), a consequence of an *anti* elimination of the enolate (2).

Clearly from its ^1H NMR spectrum (4) is undergoing conformational interconversion in solution. It is possible that (4) can interconvert between a variety of other valence isomers and rotamers (Scheme 2). The interconversion between *cis-* and *trans-* confomers of some δ-oxo ylides has been observed[13].

The absolute structure of the ylide (4) in the solid state was determined by X-ray crystallography (Figure 2)[16]. Bond lengths and angles obtained from X-ray crystallographic studies on "reactive" alkylidenetriphenylphosphoranes (Ph_3P=CR"R") have been collated[17] and indicate that the P-C ylide bond length in these compounds is *ca* 1.67 Å, very close to the theoretical P-C double bond distance of 1.667 Å, but appreciably different from the P-C single bond length of 1.872 Å[18]. Replacement of the phenyl groups with bulky alkyl groups results in a lengthening of the P-C ylide



SCHEME 2

bond[19]. The P=C bond length for ylides in which the P=C unit is conjugated to a C=O group *e.g.* $Ph_3P{=}CHC(O)R$[20a-g], is usually slightly longer, *ca.* 1.74 Å, than those of reactive ylides.

Data for the present ylide (4) (Table I) indicate a P(1) – C(1) bond length of 1.743 Å which is comparable with those values reported for stabilised ylides. In the four carbon unit C(1) – C(4) the greatest degree of double bond character is noted between C(1) – C(2) with bond length of 1.351 Å, much shorter than the theoretical C-C single bond length of 1.54 Å and comparing favourably with the C=C bond length of 1.34 Å. The bond lengths for C(2) – C(3) (1.413 Å) and C(3) – C(4) (1.425 Å) are somewhat longer and fall midway between the values for C-C and C=C bond lengths.

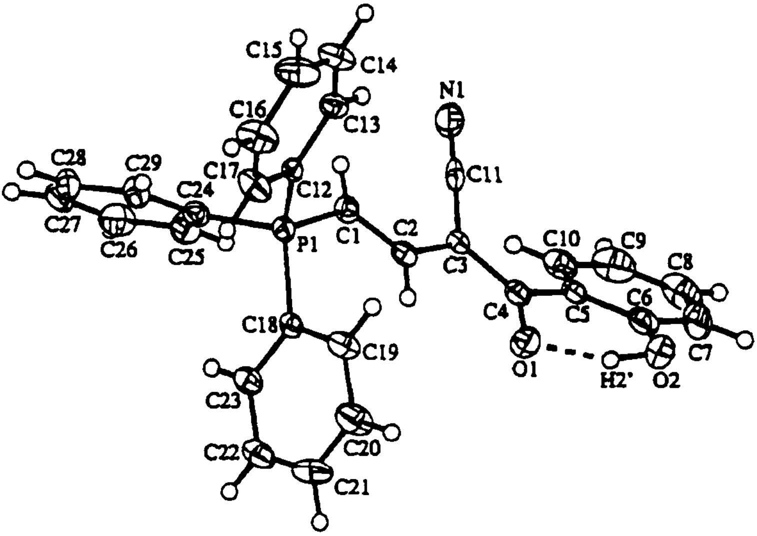


FIGURE 2 X-Ray Crystallographic Structure of the Ylide (4)

The O(1) – C(4) bond distance of 1.273 Å is longer than the typical C=O bond length of 1.22 Å but is shorter than the C-O single bond length of 1.43 Å[21]. This shortening of the C(3) – C(4) and lengthening of the O(1) – C(4) bonds is attributed to significant delocalisation of electron density over the C(1) – O(1) unit, thus providing an enolate type structure. Evidence for such delocalisation has been provided by alkylation experiments on β-oxophosphoranes where the major products resulted from *O*-alkylation[12,22].

Extensive delocalisation in (4) is consistent with the observed additional data, where the absorption band for the C=O stretch appears at 1614, cm^{-1} compared with 1661 cm^{-1}for the C=O stretch in 3-cyanochromone[8].

The three phenyl groups on the P atom are oriented in a propellor-like manner with respect to the P(1) – C(1) bond and the P-phenyl bond lengths are 1.806 Å for P(1) – C(12) and 1.804 Å for P(1) – C(18) with P(1) – C(24) somewhat shorter at 1.797 Å, the reason for this reduction in bond length being unclear. However, all are comparable with the P-C bond length of *ca.* 1.82 Å in triphenylphosphine[23]. The C-P-C bond angles are in the range 108 to 112° and indicate that the P atom has adopted a tetrahedral geometry.

TABLE I Selected Bond lengths (Å) and Angles (°) for the Ylide (4)

P(1)-C(1)	1.743(3)	C(6)-O(2)	1.366(4)
C(1)-C(2)	1.351(4)	C(3)-C(11)	1.437(5)
C(2)-C(3)	1.413(5)	C(11)-N(1)	1.150(4)
C(3)-C(4)	1.425(4)	P(1)-C(12)	1.806(3)
C(4)-C(5)	1.484(5)	P(1)-C(18)	1.804(3)
C(4)-O(1)	1.273(4)	P(1)-C(24)	1.797(4)
O(2)-H(2')	1.00(4)		
C(1)-P(1)-C(24)	108.2(2)	C(2)-C(3)-C(4)	119.1(3)
C(1)-P(1)-C(18)	110.1(2)	C(2)-C(3)-C(11)	117.1(3)
C(24)-P(1)-C(18)	109.4(2)	C(4)-C(3)-C(11)	123.3(3)
C(1)-P(1)-C(12)	111.9(2)	O(1)-C(4)-C(3)	120.0(3)
C(24)-P(1)-C(12)	108.9(2)	O(1)-C(4)-C(5)	116.9(3)
C(18)-P(1)-C(12)	108.3(2)	C(3)-C(4)-C(5)	123.0(3)
P(1)-C(1)-H(1)	117.94(11)	C(6)-C(5)-C(4)	119.2(3)
C(1)-C(2)-C(3)	128.4(3)	C(10)-C(5)-C(4)	122.1(3)
C(1)-C(2)-H(2)	115.8(2)	N(1)-C(11)-C(3)	176.0(4)
C(3)-C(2)-H(2)	115.8(2)		

Clearly from these data the structure proposed for the ylide (4) on the basis of NMR spectroscopy has to be revised for the compound in the solid state where structure (5) (Scheme 2) or a resonance hybrid between (4) and (5) is more representative.

CONCLUSION

Methylenetriphenylphosphorane initiates a Michael-induced ring cleavage of 3-cyanochromone *via* conjugate addition to C-2 affording a novel stabilised ylide. Cleavage of the chromone ring is stereospecific and gives the (*E*) isomer of (4), a consequence of an *anti* elimination of the enolate (2).

EXPERIMENTAL

Melting points were determined in capillary tubes and are uncorrected. Infrared spectra were recorded on a Mattson-Polaris Fourier Transform spectrophotometer. ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on a Jeol lambda series 400MHz instrument for solutions in $CDCl_3$; coupling constants are given in Hz.

Preparation of (E)-2-(2-hydroxybenzoyl)-4-(triphenylphosphoranylidene)but-2-enonitrile (4)

n-Butyllithium (2.5 M in hexanes, 12.3 mmol) was added dropwise *via* syringe over 5 min. to a cold (-10 °C) stirred suspension of methyltriphenylphosphonium bromide (12.3 mmol) in anhydrous THF (50 cm^3) under nitrogen. The resulting clear brown solution was allowed to warm to RT over 1h. 3-Cyanochromone (11.7 mmol) was added in a single portion to the Wittig reagent followed by anhydrous THF (10 cm^3) and the resulting precipitate was stirred for 1 h. The reaction mixture was diluted with water (50 cm^3) and the precipitate collected by vacuum filtration. The resulting orange / brown solid was washed with ethanol and then diethyl ether and then air dried. The crude material was washed with hot ethyl acetate / hexane (1:1) dried and then recrystallised from MeOH / CH_2Cl_2 to afford (4) as bright yellow cubes (37%), m.p. 190 – 210°C (decomp.), ν_{max}(Nujol) 2180(s), 1614(w), 1577(w), 1556(m), 1518(s), 1109(s), 854(s) cm^{-1}; δ_H (50°C) 5.53 (1H, bs, P=C$\underline{H}$-CH), 6.79 (1H, m, Ar-H), 6.86 (1H, m, Ar-H), 7.25 (1H, m, Ar-H), 7.55 – 7.75 (15H, m, Ar-H), 7.93 (1H, bs, P=CH-C$\underline{H}$), 8.33 (1H, bd, *J* 7.3, Ar-H), 12.81 (1H, bs, OH); δ_H (-50°C) 5.54 (1H, dd, *J* 21.6, 16.2, P=C$\underline{H}$-CH), 6.90 (2H, m, Ar-H), 7.30 (1H, m, Ar-H), 7.56 – 7.81 (15H, m, Ar-H), 7.92 (1H, dd, *J* 19.8, 16.2, P=CH-C$\underline{H}$), 8.36 (1H, dd, *J* 7.8, 1.2, Ar-H), 12.96 (1H, bs, OH); $\delta^{31}P$ (24 °C) 20.26; (Found: M^+, 447.1390; C, 77.6; H, 4.9; N, 3.2; P, 6.8. $C_{29}H_{22}NO_2P$ requires M^+, 447.1388; C, 77.8; H, 5.0; N, 3.1; P, 6.9%).

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[16] Crystal data: $C_{29}H_{22}NO_2P$, $M = 447.45$, monoclinic, $P2(1)/n$, a = 10.4822(11), b = 14.179(3), c = 15.830(2) Å, $\beta = 98.83(2)°$, V = 2324.9(6) Å^3, $Z = 4$, $D_x = 1.278$ Mgm^{-3}, $\lambda = 0.71069$ Å, $\mu = 0.145$ mm^{-1}, $F(000) = 936$, T = 150K. Data collection and treatment: yellow crystal, size 0.28 × 0.15 × 0.10 mm, θ range for data collection 1.94 to 24.91°, index ranges h −12 to 11, k −16 to 16, l −18 to 17, 11027 (3227 unique) reflections collected. Structure solution and refinement: full matrix least-squares refinement on F^2, goodness of fit = 0.779, R indices (all data) R1 = 0.0859, wR2 = 0.0948. Full crystallographic details have been deposited at the Cambridge Crystallographic Data Centre (reference CCDC 145327).

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