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Dimethyl Acetylenedicarboxylate and Phospholes: A Variety of Reaction Pathways

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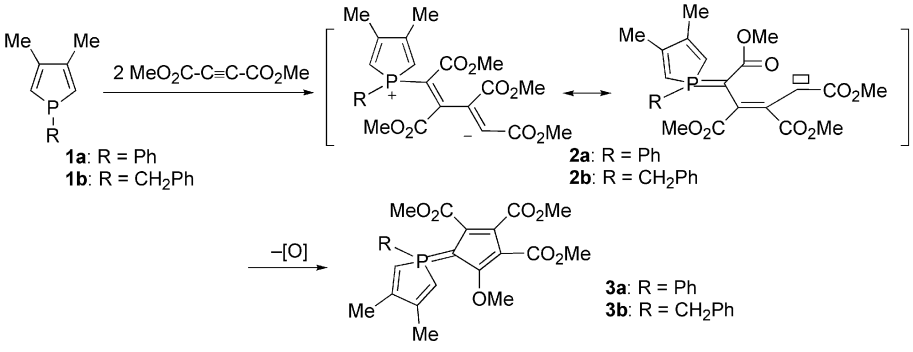
Correcting an earlier report, the reaction of 1-phenyl-3,4-dimethylphosphole (**1a**) with an excess amount of dimethyl acetylenedicarboxylate (DMAD) at room temperature affords the stable cyclopentadienylidenephosphorane **3a** resulting from unexpected deoxygenation of initially formed [phosphole + 2DMAD] adduct **2a** by the starting phosphole. The identity of **3a** was established by X-ray crystal structure analysis. DFT calculations on a model [1+2] adduct similar to **2a** shows a bent allenic structure and an ambident reactivity for the terminal carbon of the $(DMAD)_2$ chain. Cyclopentadienylidenephosphorane **3b** is also obtained with 1-benzylphosphole **1b**. With 1-stannylphosphole **1c**, a 1:3 adduct with a seven-membered ring (i.e., **5**) is obtained. It was also characterized by X-ray crystal structure analysis. Finally, with 1-benzyl-2-benzoylphosphole **1d**, the P lone pair has lost its nucleophilicity and a [4+2] cycloaddition takes place with the dienol tautomer of the unsaturated ketone to give phosphindole **6**, also characterized by X-ray.

Introduction

Since the pioneering work of Tebby on the reactions of triphenylphosphane with dimethyl acetylenedicarboxylate (DMAD),[1] the reactivity of tervalent phosphorus derivatives with DMAD has been consistently investigated and has yielded a lot of unpredictable results.[2] The phosphole case has been already studied in some depth by Hughes.[3] It appeared that these reactions yielded a variety of ylides, some having ring-expanded or ring-fused structures. Unfortunately, the assignments were made on the sole basis of spectroscopic data and could not be considered as definitively established. In view of our long-standing interest in phosphole chemistry, we decided some time ago, to reinvestigate the reactions of some phospholes with DMAD, trying whenever possible to establish the structures of the products by X-ray crystal structure analysis. We have published a first report[4] on the reaction of 1-phenyl-3,4-dimethylphosphole (**1a**) with DMAD with results at variance with those of Hughes. The 1:2 adduct thus produced seemed to have the structure of ylide **2a** on the basis of ^{13}C NMR spectroscopic data (Scheme 1). Unfortunately, we were unable to grow crystals of **2a**, and this formula remained tentative because the analogous adduct with triphenylphosphane is known to be highly unstable.[1] We describe herein additional results that supplement and correct our earlier data while underlying the broad variety of structures that can be obtained through this apparently simple chemistry. All of our structures have been definitively established by X-ray crystal structure analysis.



Scheme 1. The reaction of 1-phenyl- and 1-benzyl-3,4-dimethylphosphole with DMAD.

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Results and Discussion

After numerous unsuccessful attempts, we were finally able to grow crystals of the reaction product of **1a** with DMAD. The quality of the crystals was rather poor, so the structural parameters are only approximate, but the collected data establish beyond any doubt that the actual structure of the product is that of **3a**, as shown in Figure 1. The $(DMAD)_2$ substituent has cyclized to give a cyclopentadienylidenephosphorane. The peak at δ = 159.06 ppm in the ^{13}C NMR spectrum that was formerly assigned to a carbonyl carbon atom in fact corresponds to C9 [d, $^2J_{C,P}$ = 7.5 Hz, =*C*(OMe)-]. The structural parameters of the cyclopentadiene ring are closely similar to those of other cyclopentadienylidenephosphoranes.[5] The unexpected reaction that takes place is the deoxygenation of the methoxycarbonyl substituent on the α carbon of the $(DMAD)_2$ chain of initially formed [1:2] adduct **2a** (Scheme 1).The deoxygenation of **2a** is probably effected by the starting phosphole itself. The mechanism likely involves a bisylide ([2+2] adduct)[6] whose cyclization by intramolecular Wittig reaction is possible due to the flexibility of the poorly conjugated chain (see later). Indeed, when mixing the phosphole and the excess amount of DMAD in dichloromethane, two peaks appear in the ^{31}P NMR spectrum at δ = 19.6 and 40.7 ppm. The first one corresponds to **3a**, whereas the second one corresponds to the monomeric phosphole oxide[7] that slowly disappears by [4+2] dimerization (δ = 52.5 and 74.1 ppm, $J_{P,P}$ = 39.6 Hz).

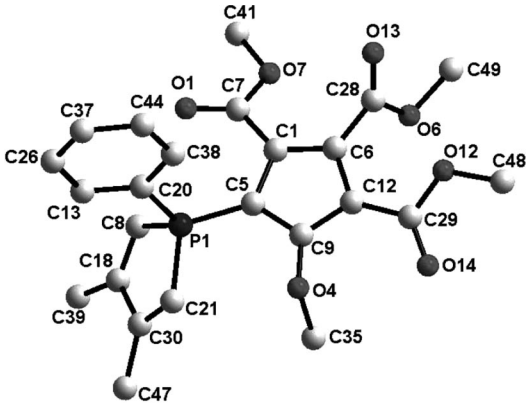
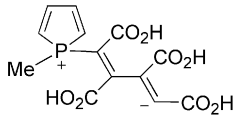


Figure 1. X-ray crystal structure of cyclopentadienylidenephosphorane **3a**. Main bond lengths [Å] and angles [°]: P1–C5 1.732(6), P1–C8 1.780(6), P1–C20 1.800(7), P1–C21 1.773(7), C5–C1 1.452(8), C1–C6 1.394(8), C6–C12 1.436(8), C12–C9 1.394(8), C9–C5 1.406(8); C8–P1–C21 92.7(3), C5–P1–C20 112.6(3), C1–C5–C9 105.8(5), P1–C5–C1 126.7(4), P1–C5–C9 127.4(4).

To better understand the chemistry of initially formed [1+2] adduct **2a**, we decided to perform a DFT study of model compound **4** at the B3LYP/6-311+G(d,p) level.[8] The computed structure is shown in Figure 2. The $(DMAD)_2$ substituent is highly distorted, and the two DMAD units are orthogonal (C14–C15–C16–C17 88.50°). As a result, the delocalization along the chain is weakened and a strong bond alternation is observed. The bond between the two units has essentially single-bond character (C15–C16 1.485 Å). The terminal carbon (C17) displays a structure similar to that of a disymmetrical bent allene:[9] C16–C17 1.312 Å, C17–C30 1.421 Å, C16–C17–C30 138.84°, C15–C16···C30–O32 88.3°. The planes of the two π systems are indeed orthogonal. The HOMO (Figure 3) is strongly localized at C17 and its shape resembles an in-plane lone pair. Surprisingly, the Mulliken charge is strongly negative at C16 (–1.56) and strongly positive at C17 (+0.83). Thus, we expect that C17 will display both nucleophilic and electrophilic reactivities. The resulting picture is more complex than what would be expected from the classical mesomeric representation of these [1+2] adducts.



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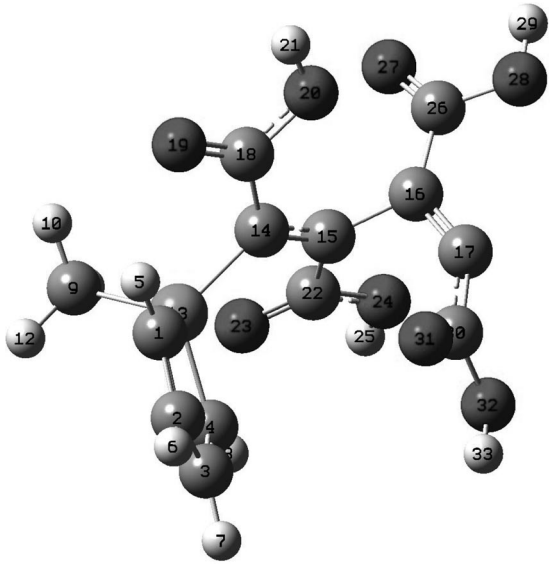


Figure 2. Computed structure of **4**: Main bond lengths [Å] and angles [°]: P–C14 1.802, C14–C15 1.390, C15–C16 1.485, C16–C17 1.312, C17–C30 1.421, C30–O31 1.224, C30–O32 1.370, P–C1 1.816, P–C4 1.812, P–C9 1.821, C1–C2 1.341, C2–C3 1.476, C3–C4 1.342; C1–P–C4 92.43, C9–P–C14 113.55, C13–C14–C15 124.24, C14–C15–C16 123.68, C15–C16–C17 105.89, C16–C17–C30 138.84, C17–C30–O31 124.57, C17–C30–O32 113.90; P–C14–C15–C16 151.43, C14–C15–C16–C17 88.50, C15–C16–C17–C30 11.68, C16–C17–C30–O31 74.28.

We then decided to investigate the influence of the phosphole P-substituent on the course of its reaction with DMAD. With 1-benzylphosphole **1b**, we obtained a product whose ^{13}C NMR spectrum is closely similar to that of **3a**, and hence its formula **3b**. Replacing **1a** by stannylphosphole **1c** yielded an entirely different result. A 1:3 adduct with a seven-membered ring **5** was produced (Scheme 2).

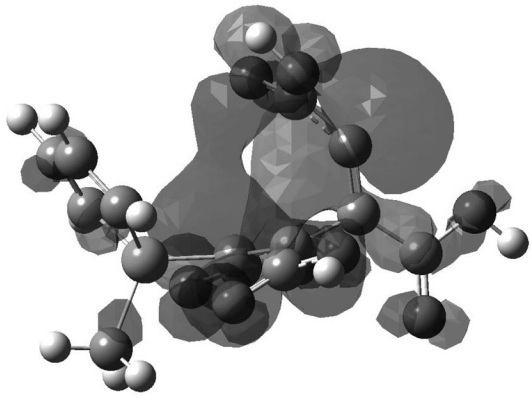
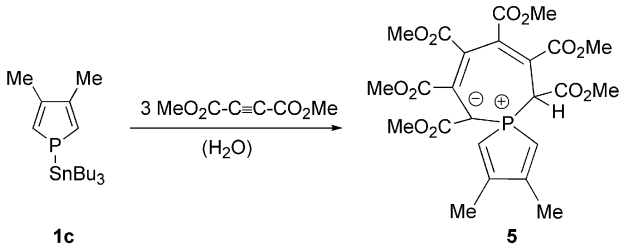
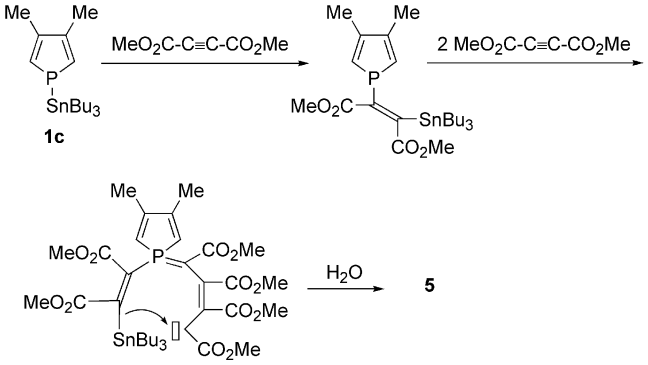


Figure 3. HOMO of adduct **4** as computed by DFT.



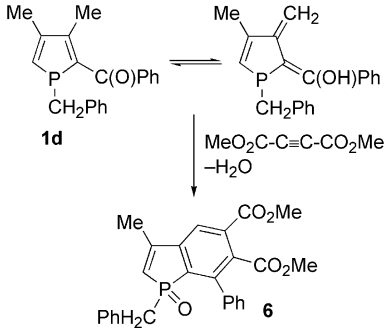
Scheme 2. Formation of a seven-membered ring from 1-stannylphosphole **1c**.

The structure of **5** was established by X-ray analysis (Figure 4). The representation fits the data of the structure with a long C16–C12 (1.443 Å), a short C7–C12 (1.386 Å), a long C4–C7 (1.446 Å), and a short C1–C4 bond (1.352 Å). All the carbon atoms of the seven-membered ring are planar, except C13. The two sides of the phosphole ring are sharply inequivalent due to the chirality of C13. This inequivalence is quite visible in the ^{1}H NMR spectrum of **5**, which shows two α-CH signals at δ = 5.70 and 6.48 ppm. The most logical mechanism for the formation of **5** is depicted in Scheme 3.



Scheme 3. Proposed mechanism for the formation of seven-membered ring **5**.

The first step involves insertion of DMAD into the reactive P–Sn bond, followed by the formation of a 1:2 adduct between the P lone pair and DMAD, as usual. Then, the nucleophilic carbon carrying tin attacks the electrophilic carbon at the end of the $(DMAD)_2$ chain, thus forming



Scheme 4. Formation of a phosphindole from a 2-acylphosphole.

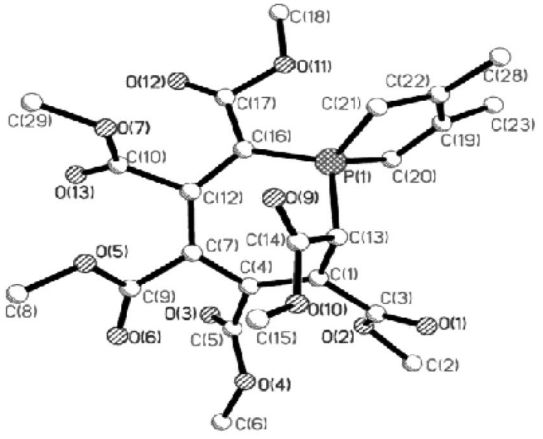


Figure 4. X-ray crystal structure of seven-membered ring **5**. Main bond lengths [Å] and angles [°]: P–C20 1.809(12), P–C21 1.796(10), C19–C20 1.292(17), C19–C22 1.505(17), C21–C22 1.383(15), P–C16 1.743(10), C12–C16 1.443(15), C12–C7 1.386(16), C4–C7 1.446(13), C1–C4 1.352(13), C1–C13 1.482(14), P–C13 1.812(10); C20–P–C21 95.0(5), C13–P–C16 108.4(5).

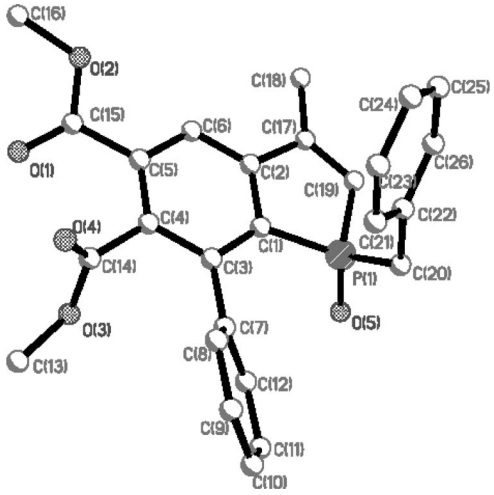


Figure 5. X-ray crystal structure of phosphindole **6**. Main bond lengths [Å] and angles [°]: P–O5 1.481(3), P–C1 1.823(3), P–C19 1.773(4), P–C20 1.798(4), C1–C2 1.399(5), C2–C17 1.495(4), C17–C19 1.338(5); C1–P–C19 92.14(17).

the seven-membered ring. It is interesting to note that this mechanism relies on the electrophilic nature of the terminal carbon of the $(DMAD)_2$ chain as predicted by our theoretical calculation on **4**.

We then investigated the reaction of DMAD with 1-benzyl-2-benzoyl-3,4-dimethylphosphole (**1d**).[10] The lone pair of **1d** has almost completely lost its nucleophilicity. As a result, DMAD does not react at phosphorus any more. The product of the reaction is phosphindole **6** (Scheme 4). The structure of **6** was established by X-ray crystal structure analysis (Figure 5). The product results from the reaction of DMAD with the dienol tautomer of the 2-acylphosphole.

Conclusions

As can be seen, the outcome of the reaction of DMAD with phospholes heavily depends on the nature of the phosphole substituents. Some of the products of this very diverse chemistry might have some synthetic interest.

Experimental Section

General Methods: All reactions were performed under nitrogen by using standard Schlenk techniques. Nuclear magnetic resonance spectra were obtained with a Bruker Avance 300 spectrometer operating at 300.13 MHz for ^{1}H, 75.45 MHz for ^{13}C, and 121.496 MHz for ^{31}P. Chemical shifts are expressed in ppm downfield from internal TMS (^{1}H and ^{13}C) and external 85% H_3PO_4 (^{31}P). All coupling constants (*J*) are reported in Hz. Mass spectra were recorded with an LC-MSD-Trap-XCT instrument by electrospray ionization (ESI).

Synthesis of 3b: 1-Phenyl-3,4-dimethylphosphole (0.4 mL, 2.12 mmol) in dry THF (10 mL) was allowed to react with an excess amount of lithium wire until P–Ph bond cleavage was complete. After the remaining amount of lithium was removed, the solution was treated with *tert*-butyl chloride (230 μL, 2.12 mmol) and heated to 60 °C for 1.5 h. Then, benzyl bromide (230 μL, 2.12 mmol) was added at –78 °C. After warming to room temperature, DMAD (730 μL, 6.00 mmol) was added. The crude organic product was purified by chromatography (silica gel; petroleum ether/ethyl acetate, 1:4). A green liquid was collected and, once concentrated, 125 mg of pure product was obtained (13% yield). ^{31}P NMR ($CDCl_3$): δ = 24.0 ppm. ^{1}H NMR ($CDCl_3$): δ = 2.04 (s, 6 H, Me), 3.33 (s, 3 H, OMe), 3.69 (d, $^2J_{H,P}$ = 16.2 Hz, 2 H, CH_2P), 3.73 (s, 3 H, OMe), 3.83 (s, 3 H, OMe), 3.91 (s, 3 H, OMe), 6.43 (d, $^2J_{H,P}$ = 27.9 Hz, 2 H, =CHP), 7.03–7.27 (m, 5 H, Ph) ppm. ^{13}C NMR ($CDCl_3$): δ = 17.74 (d, $^3J_{C,P}$ = 10.5 Hz, Me), 32.78 (d, $^1J_{C,P}$ = 51.7 Hz, CH_2P), 50.77 (s, OMe), 51.57 (s, OMe), 52.20 (s, OMe), 63.03 (s, OMe), 77.95 (d, $^1J_{C,P}$ = 93.8 Hz, C=P),107.05 (d, $J_{C,P}$ = 14.2 Hz, C=C), 108.42 (d, $J_{C,P}$ = 9.0 Hz, C=C), 116.25 (d, $^1J_{C,P}$ = 87.7 Hz, =CHP), 126.77 (d, $^2J_{C,P}$ = 12.0 Hz, Ph C *ipso*), 127.70 (d, $J_{C,P}$ = 3.7 Hz, Ph CH *para*), 128.54 (d, $J_{C,P}$ = 3.0 Hz, Ph CH), 129.85 (d, $J_{C,P}$ = 6.0 Hz, Ph CH), 130.23 (d, $J_{C,P}$ = 8.2 Hz, C=C), 157.67 [d, $^2J_{C,P}$ = 18.0 Hz, =C(Me)],158.43 [d, $^2J_{C,P}$ = 6.7 Hz, =C(OMe)], 163.77 (d, $J_{C,P}$ = 3.0 Hz, CO), 166.31 (s, CO), 169.90 (d, $J_{C,P}$ = 3.0 Hz, CO) ppm.

Synthesis of 5: 1-Phenyl-3,4-dimethylphosphole (0.4 mL, 2.12 mmol) in dry THF (10 mL) was allowed to react with an excess amount of lithium wire until P–Ph bond cleavage was complete. After the remaining amount of lithium was removed, the solution was treated with aluminum trichloride (95 mg, 0.7 mmol) at 0 °C for 30 min. Then, tri-*n*-butyltin chloride (575 μL, 2.12 mmol) was added at –78 °C. After warming to room temperature, DMAD (1040 μL, 8.50 mmol) was added. The crude organic product was purified by chromatography (silica gel; dichloromethane/ethyl acetate, 1:1). A yellow solid was collected and, once concentrated, 54 mg of a pure product was obtained (7% yield). ^{31}P NMR ($CDCl_3$): δ = 38.6 ppm. ^{1}H NMR ($CDCl_3$): δ = 2.12 (s, 3 H, Me), 2.14 (s, 3 H, Me), 3.55, 3.64, 3.72, 3.78, 3.79, 3.81 (6 s, 6 × 3 H, OMe), 4.23 (d, $^2J_{H,P}$ = 15.3 Hz, sp^3 CH-P), 5.70 (d, $^2J_{H,P}$ = 29.7 Hz, =CH-P), 6.48 (d, $^2J_{H,P}$ = 30.0 Hz, =CH-P) ppm. ^{13}C NMR ($CDCl_3$): δ = 17.43 (d, $^3J_{C,P}$ = 18.5 Hz, Me), 17.96 (d, $^3J_{C,P}$ = 19.0 Hz, Me), 42.40 (d, $^1J_{C,P}$ = 57.4 Hz, sp^3 CH-P), 51.40, 51.81, 52.41, 52.66, 53.03, 53.7058.23 (d, $^1J_{C,P}$ = 119.5 Hz, ylide C=P), 117.23 (d, $^1J_{C,P}$ = 96.1 Hz, =CH-P), 121.41 (d, $^1J_{C,P}$ = 76.6 Hz, =CH-P), 154.98 [d, $^2J_{C,P}$ = 22.8 Hz, =C(Me)], 158.92 [d, $^2J_{C,P}$ = 20.9 Hz, =C(Me)], 165.86–169.061 (C=O) ppm.

Synthesis of 6: 1-Phenyl-3,4-dimethylphosphole (0.4 mL, 2.12 mmol) in dry THF (10 mL) was allowed to react with an excess amount of lithium wire until P–Ph bond cleavage was complete. After the remaining amount of lithium was removed, the solution was treated with *tert*-butyl chloride (230 μL, 2.12 mmol) and heated to 60 °C for 1.5 h. Then, benzoyl chloride (248 μL, 2.12 mmol) was added at –78 °C. After warming to 0 °C, *t*BuOK was added (240 mg, 2.12 mmol). The resulting mixture was heated at 60 °C for 2 h. Then, benzyl bromide (230 μL, 2.12 mmol) was added at –78 °C. After warming to room temperature, DMAD (246 μL, 2.00 mmol) was added. After the reaction was complete, the crude organic product was purified by chromatography (silica gel; dichloromethane/ethyl acetate, 5:2). A colorless solid was collected and, once concentrated, 125 mg of pure product was obtained (13% yield). ^{31}P NMR ($CDCl_3$): δ = 46.3 ppm. ^{1}H NMR ($CDCl_3$): δ = 2.18 (br., 3 H, Me), 2.60–3.01 (m, 2 H, $PhCH_2$), 3.59 (s, 3 H, OMe), 3.93 (s, 3 H, OMe), 6.04 (d, $^2J_{H,P}$ = 25.2 Hz, 1 H, PCH=), 6.84–7.79 (m, 11 H, PhH) ppm. Selected ^{13}C NMR ($CDCl_3$): δ = 16.61 (d, $^3J_{C,P}$ = 15.8 Hz, Me), 35.51 (d, $^1J_{C,P}$ = 64.1 Hz, $PhCH_2$), 52.45, 52.97 (2s, OMe), 122.03 (d, $^1J_{C,P}$ = 111.7 Hz, PCH=), 165.45 (C=O), 168.21 (C=O) ppm.

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