Bis(phosphino)carbodiimide: A Bis(1,3)-dipole

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Bis[bis(diisopropylamino)phosphino]carbodiimide (**1**) reacts with 1 equiv of dimethyl acetylenedicarboxylate affording the [3 + 2] cycloadduct **2** in 92% yield, showing that a phosphinocarbodiimide acts as a 1,3-dipole. Addition of a second equivalent of alkyne to **2** gives rise to the formal [2 + 7] cycloadduct **5** in 85% yield. Migration of a carbomethoxy group is observed on thermolysis of **5** at 80 °C, leading to a new bicyclo[4.3.0] derivative **7** in 90% yield. The X-ray diffraction study of derivatives **5** and **7** is presented. The mechanisms rationalizing the formation of **2**, **5**, and **7** are discussed.

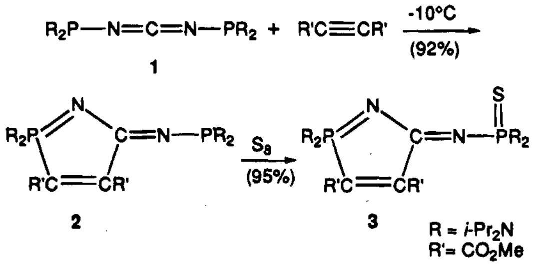
Introduction

Few reactions rival the cycloaddition processes in the number of bonds that undergo transformation during the reaction, giving products considerably more complex than the reactants.[1] In this field, carbodiimides appeared to be particulary versatile dipolarophiles, since they can be involved in [2 + 2], [2 + 3], and [2 + 4] cycloaddition reactions.[2] Their synthetic potential can even be enhanced by the presence of substituents which can be involved in the annelation process.[2,3] It has recently been shown that the classical reactivity of an organic function can be dramatically modified by the presence of a σ^3,λ^3-phosphorus substituent. For examples, phosphino-substituted nitrilimines,[4] diazo derivatives,[5] and azides[6] behave as formal 1,4-dipoles, whereas *N*-phosphino imines react as 1,3 dipoles,[7] toward electron poor alkynes. In this paper, we report that a bis(phosphino)carbodiimide can behave as a 1,3-dipole, or even as a bis(1,3-dipole).

Results and Discussion

Bis[bis(diisopropylamino)phosphino]carbodiimide (**1**)[8] reacted with 1 equiv of dimethyl acetylenedicarboxylate at −10 °C in THF affording heterocycle **2** in 92% yield.

Scheme 1



The ^{31}P NMR spectrum consisted of two doublets of quintets at +59.99 (J_{PP} = 2.8 Hz, J_{PH} = 18.2 Hz) and +68.83 ppm (J_{PP} = 2.8 Hz, J_{PH} = 10.2 Hz); the values of the $^3J_{PH}$ coupling constants were typical of a σ^3- and σ^4-phosphorus atom,[9] respectively, indicating that one of the phosphorus atoms was involved in the reaction process. The five-membered ring structure was apparent in the ^{13}C NMR spectrum [δ 131.19 (J_{PC} = 86.8 and 5.0 Hz, PC), 158.72 (J_{PC} = 26.7 and 10.9 Hz, PC*C*), 162.56 (J_{PC} = 32.0 and 7.1 Hz, PNC)]. Lastly, addition of elemental sulfur led to compound **3** (95% yield), confirming our hypothesis (Scheme 1).

This formal [3 + 2] cycloaddition process is analogous to that described by Schmidpeter et al. with *N*-phosphino imines;[7] the formation of heterocycle **2** results from the nucleophilic addition of the phosphorus atom to the electron-poor alkyne followed by a 1,5-electrocyclization.

Since derivative **2** featured a remaining N-phosphino imine moiety, it was tempting to use it as starting material for a further [3 + 2] cycloaddition reaction. According to a ^{31}P NMR correlation spectrum, addition of 1 equiv of dimethyl acetylenedicarboxylate to compound **2** did not lead to the expected spiro compound **4**, but gave rise to two products **5′** and **5″** in a 1/1 ratio (δ ^{31}P +72.83, +22.34, J_{PP} = 14.0 Hz; +70.48, +23.09, J_{PP} = 14.0 Hz), in a total yield of 85%. The same mixture was also obtained in 93% yield by adding 2 equiv of alkyne to the carbodiimide **1**. All attempts to separate these two products by fractional crystallization or column chromatography failed. Mass spectroscopy and elemental analysis confirmed that both adducts **5′** and **5″** formally arose from the addition of 1 equiv of alkyne to **2** and thus were isomers. A ^{13}C{^{31}P} NMR study showed

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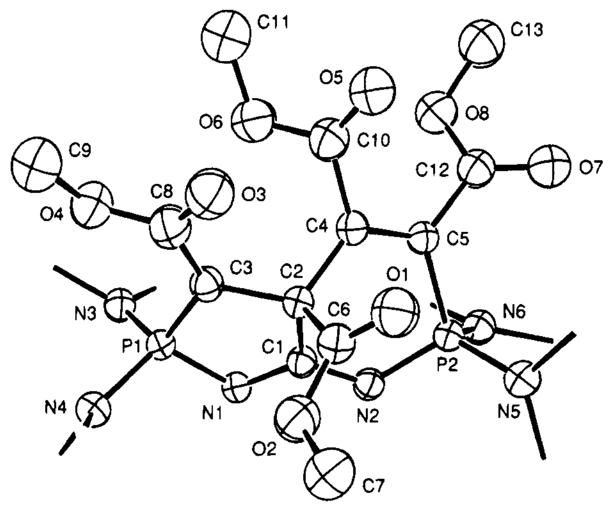


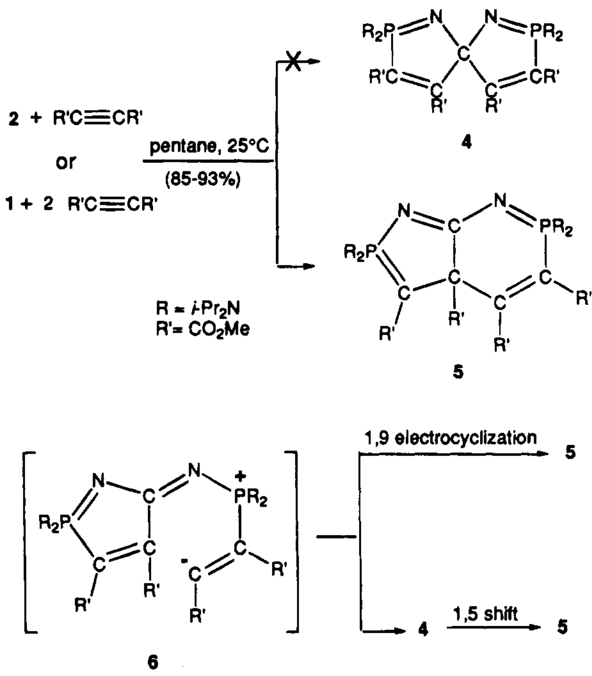
Figure 1. ORTEP drawing of **5**. Hydrogen atoms and isopropyl groups are omitted for clarity.

that both isomers had a very similar structure, and of special interest, two types of carbon directly bonded to the phosphorus atoms [δ 53.51 (J_{PC} = 125.9 Hz), 54.20 (J_{PC} = 126.3 Hz) and 125.91 (J_{PC} = 108.7 Hz), 127.46 (J_{PC} = 107.8 Hz)], indicating that the σ^3-phosphorus atom of **2** was involved in the reaction process. However, the exact structure of the products could only be established thanks to an X-ray diffraction study. Single crystals were grown from a petroleum ether/ether solution, the thermal ellipsoid plot of the molecule is shown in Figure 1.[10] It is important to note that the melting points of several single crystals were identical (93 °C, dec), and that the ^{31}P NMR spectrum of a pentane solution of these crystals was identical to that of the crude mixture, demonstrating that in solution **5′** and **5″** were in equilibrium, and crystallized as **5**.

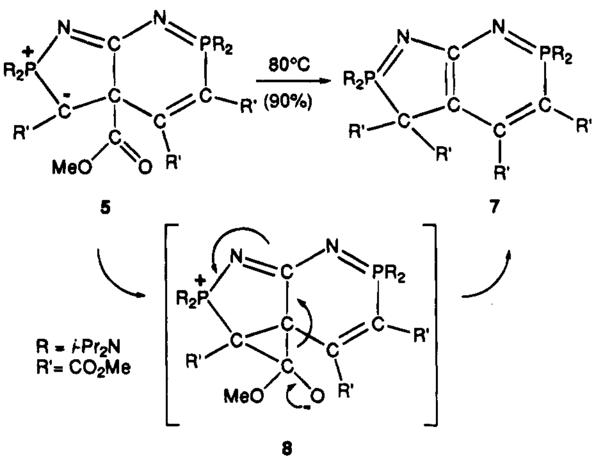
Compound **5** is a fused [4.3.0]heterocycle featuring a phosphorus-ylide function in the five-membered ring [P1−C3: 1.719(3) Å], and an azaphospha-ylide moiety in the six-membered ring [P2−N2: 1.588(3) Å]. The five-membered ring is almost planar [maximum deviation C1: 0.033(3) Å], while the six-membered ring has a boat conformation. Since the spectroscopic data for **5′** and **5″** in solution fit nicely with the structure observed for **5** in the solid state, it is quite likely that **5′** and **5″** are conformers.

The reaction of **2** with dimethyl acetylenedicarboxylate probably involves the nucleophilic attack of the σ^3-phosphorus atom to the electron-poor alkyne leading to the zwitterionic intermediate **6**. At a first glance, compound **5** results from a direct 1,9-electrocyclization. However, it is well established that formal [7 + 2] cycloaddition reactions involve the primary formation of spiro derivatives of type **4**, which undergo subsequent ring expansion reactions via a 1,5 sigmatropic shift.[1a,11] Therefore, assuming that compound **4** is an intermediate (although not detected by low temperature NMR experiments), and since bicyclo derivative **5** can be obtained directly by addition of 2 equiv of alkyne to **1**, the bis(phosphino)carbodiimide **1** formally acts as a bis(1,3-dipole).

Scheme 2



Scheme 3



Interestingly, a further rearrangement occurred on heating derivative **5** in toluene for a few minutes at 80 °C, giving **7** in 90% yield (Scheme 3). Mass spectroscopy and elemental analysis revealed that no fragmentation reaction occurred, but, surprisingly, a NMR study showed that two of the four carbomethoxy groups became equivalent [^1H NMR: δ 3.52, 3 H; 3.60, 3 H; 3.67, 6 H; ^{13}C NMR: 49.90, 51.19, 52.43 (s, CH_3O), 167.30 (d, J_{PC} = 4.0 Hz, $C(CO)_2$), 167.68 (dd, J_{PC} = 34.0 and 8.1 Hz, CCO), 170.06 (d, J_{PC} = 18.4 Hz, CCO)]. The structure of **7** was clearly established by an X-ray diffraction study.[10] The thermal ellipsoid plot of the molecule is shown in Figure 2. The six-membered ring is nearly planar [maximum deviation P2: 0.042(7) Å], with the bond lengths having values that lie halfway between single and double bonds indicating some degree of delocalization.

A reasonable mechanism for the formation of the fused [4.3.0]heterocycle **7** involves the intramolecular nucleophilic attack of the carbonyl group bonded to the bridge-

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[10] The author has deposited atomic coordinates for the structure of **5** and **7** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

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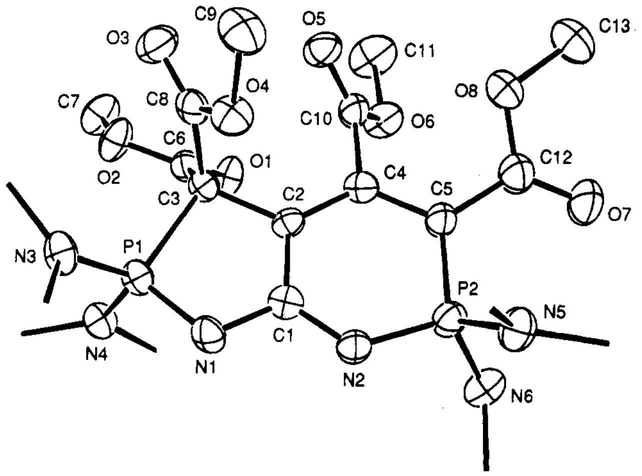

Figure 2. ORTEP drawing of **7**. Hydrogen atoms and isopropyl groups are omitted for clarity.

head carbon by the ylidic carbon atom, leading to the cyclopropanic intermediate **8**. Then, the cascade formation of the O1—C6, C1—C2 ,and N1—P1 double bonds gives **7** (Scheme 3).

The use of heteroelements to transform (1,*n*)-dipoles into (1,*n* + 1)-dipoles as well as the study of other bisdipoles are under active investigation.

Experimental Section

All experiments were performed in an atmosphere of dry argon. Melting points are uncorrected.

Heterocycle 2: A THF solution (10 mL) of dimethyl acetylenedicarboxylate (0.86 mL; 7.00 mmol) was added dropwise at −10 °C to a THF solution (15 mL) of bis[bis(diisopropylamino)phosphino]carbodiimide (**1**)[8] (3.5 g; 6.97 mmol). The solution was allowed to warm to room temperature and the solvent removed under vacuum. The residue was washed three times with pentane (3 × 10 mL) at −30 °C, and **2** was obtained as a viscous red oil (4.13 g; 92%); ^{1}H NMR (CDCl$_3$) δ 1.04 (d, J_{HH} = 6.8 Hz, 12 H), 1.22 (d, J_{HH} = 6.8 Hz, 12 H), 1.38 (d, J_{HH} = 6.2 Hz, 12 H), 1.42 (d, J_{HH} = 6.2 Hz, 12 H), 3.35 (s, 3 H), 3.60 (m, 4 H), 3.67 (s, 3 H), 3.87 (d sept, J_{PH} = 10.2 Hz, J_{HH} = 6.8 Hz, 4 H); ^{13}C NMR (CDCl$_3$) δ 23.24 (d, J_{PC} = 1.9 Hz), 23.79 (d, J_{PC} = 2.2 Hz), 25.06 (d, J_{PC} = 9.4 Hz), 25.36 (d, J_{PC} = 6.2 Hz), 46.06 (d, J_{PC} = 12.8 Hz), 47.93 (d, J_{PC} = 8.6 Hz), 52.12 (s), 52.19 (s), 131.19 (dd, J_{PC} = 86.8 and 5.0 Hz), 158.72 (dd, J_{PC} = 26.7 and 10.9 Hz), 162.56 (dd, J_{PC} = 32.0 and 7.1 Hz), 163.60 (dd, J_{PC} = 10.1 and 2.1 Hz), 166.17 (d, J_{PC} = 29.0 Hz); ^{31}P NMR{^{1}H} (CDCl$_3$) +59.99 (d, J_{PP} = 2.8 Hz), +68.83 (d, J_{PP} = 2.8 Hz).

Heterocycle 3: Elemental sulfur (0.21 g; 6.50 mmol) was added at room temperature to a THF solution (20 mL) of 2 (4.13 g; 6.41 mmol). The solution was stirred for 1 h at room temperature and the solvent removed under vacuum. The residue was washed three times with pentane (3 × 10 mL), and **3** was obtained as an orange solid (4.12 g; 95%): mp 179–181 °C; ^{1}H NMR (CDCl$_3$) δ 1.09 (d, J_{HH} = 6.8 Hz, 12 H), 1.11 (d, J_{HH} = 6.8 Hz, 12 H), 1.21 (d, J_{HH} = 6.8 Hz, 12 H), 1.25 (d, J_{HH} = 6.8 Hz, 12 H), 3.65 (m, 8 H), 3.68 (s, 3 H), 3.72 (s, 3 H); $_{13}$C NMR (CDCl$_3$) δ 22.27 (d, J_{PC} = 1.6 Hz), 23.56 (d, J_{PC} = 2.0 Hz), 22.80 (d, J_{PC} = 2.2 Hz), 23.50 (d, J_{PC} = 1.8 Hz), 45.36 (d, J_{PC} = 6.5 Hz), 47.49 (d, J_{PC} = 5.4 Hz), 52.05 (s), 52.28 (s), 132.90 (dd, J_{PC} = 86.8 and 3.1 Hz), 160.77 (dd, J_{PC} = 11.3 and 4.4 Hz), 161.58 (dd, J_{PC} = 34.0 and 27.7 Hz), 163.60 (dd, J_{PC} = 10.1 and 2.7 Hz), 166.17 (d, J_{PC} = 29.8 Hz); ^{31}P NMR{^{1}H} (CDCl$_3$) +60.08 (d, J_{PP} = 0.9 Hz), +60.59 (d, J_{PP} = 0.9 Hz); IR (THF, ν(cm^{-1})): 1748, 1724 (CO); CIMS (*m*/*z*) 677 (M$^+$ + 1). Anal. Calcd for $C_{31}H_{62}N_6O_4P_2S$: C, 55.05; H, 9.17; N, 12.43. Found: C, 55.12; H, 9.24 ; N, 12.50.

Bicyclo [4.3.0] Derivative 5: A pentane solution (10 mL) of dimethyl acetylenedicarboxylate (0.64 mL; 5.18 mmol) was added dropwise, at room temperature, to a pentane solution (15 mL) of derivative 2 (3.33 g; 5.18 mmol). The solution was stirred 30 min at room temperature and filtered and the solvent removed under vacuum. After recrystallization at room temperature from a petroleum ether/ether solution, **5** was obtained as orange crystals (1.73 g; 85%): mp 93 °C dec; ^{13}C NMR (CDCl$_3$) δ 23–25 (m), 46–48 (m), 51.22, 51.96, 52.09, 52.14, 52.28, 52.43, 52.46, 52.56 (s), 53.51 (d, J_{PC} = 125.9 Hz), 54.20 (d, J_{PC} = 126.3 H), 65.15 (dd, J_{PC} = 36.8 and 14.0 Hz), 65.50 (dd, J_{PC} = 36.8 and 13.9 Hz), 125.91 (d, J_{PC} = 108.7 Hz), 127.46 (d, J_{PC} = 107.8 Hz), 160.27 (dd, J_{PC} = 9.2 and 9.1 Hz), 160.52 (dd, J_{PC} = 9.2 and 9.1 Hz), 164.86 (d, J_{PC} = 9.1 Hz), 164.92 (d, J_{PC} = 8.0 Hz), 165.43 (d, J_{PC} = 9.1 Hz), 165.48 (d, J_{PC} = 19.2 Hz), 165.65 (d, J_{PC} = 14.1 Hz), 166.18 (d, J_{PC} = 14.1 Hz), 169.66 (dd, J_{PC} = 4.5 and 2.2 Hz), 170.48 (dd, J_{PC} = 5.0 and 2.1 Hz), 171.96 (dd, J_{PC} = 21.1 and 8.0 Hz), 172.66 (dd, J_{PC} = 21.1 and 8.0 Hz); ^{31}P NMR{^{1}H} +22.34 (d, J_{PP} = 14.0 Hz), +23.09 (d, J_{PP} = 14.0 Hz), +70.48 (d, J_{PP} = 14.0 Hz), +72.83 (d, J_{PP} = 14.0 Hz); IR (THF, ν(cm^{-1})) 1733.5 (CO); CIMS (*m*/*z*): 787 (M$^+$ + 1). Anal. Calcd for $C_{37}H_{68}N_6O_8P_2$: C, 56.51; H, 8.71; N, 10.69. Found: C, 56.47; H, 8.74 ; N, 10.62.

Bicyclo [4.3.0] Derivative 7: A toluene solution (15 mL) of 5 (2.0 g; 2.54 mmol) was heated at 80 °C for 20 min. The solution was allowed to cool to room temperature and the solvent removed under vacuum. After recrystallization at room temperature from a THF/pentane solution, **7** was obtained as yellow crystals (1.80 g; 90%): mp 232 °C; ^{1}H NMR (CDCl$_3$): δ 1.12 (d, J_{HH} = 6.8 Hz, 12 H), 1.22 (d, J_{HH} = 6.8 Hz, 12 H), 1.25 (d, J_{HH} = 10.4 Hz, 12 H), 1.28 (d, J_{HH} = 7.3 Hz, 12 H), 3.52 (s, 3 H), 3.60 (s, 3 H), 3.67 (s, 6 H), 3.75 (m, 8 H); ^{13}C NMR (CDCl$_3$) δ 22.86 (d, J_{PC} = 3.4 Hz), 23.12 (d, J_{PC} = 2.3 Hz), 24.30 (s), 45.29 (d, J_{PC} = 6.3 Hz), 48.33 (d, J_{PC} = 5.0 Hz), 49.90 (s), 51.19 (s), 52.43 (s), 68.46 (d, J_{PC} = 47.3 Hz), 72.88 (d, J_{PC} = 135.7 Hz), 104.25 (dd, J_{PC} = 12.1 and 12.1 Hz), 144.37 (dd, J_{PC} = 14.1 and 13.1 Hz), 167.30 (d, J_{PC} = 4.0 Hz), 167.68 (d, J_{PC} = 34.0 and 8.1 Hz), 170.06 (d, J_{PC} = 18.4 Hz), 171.73 (dd, J_{PC} = 18.6 and 8.8 Hz); ^{31}P NMR{^{1}H} (CDCl$_3$) +36.30 (d, J_{PP} = 6.8 Hz), +66.03 (d, J_{PP} = 6.8 Hz); IR (THF, ν(cm^{-1})) 1742 (CO); CIMS (*m*/*z*) 787 (M$^+$ + 1). Anal. Calcd for $C_{37}H_{68}N_6O_8P_2$: C, 56.51; H, 8.71; N, 10.69. Found: C, 56.42; H, 8.76 ; N, 10.59.

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