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A new access to diazaphospholes *via* cycloaddition–cycloreversion reactions on triazaphospholes†

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A novel bis-CF_3-substituted diazaphosphole was synthesized selectively from hexafluoro-2-butyne and a 3*H*-1,2,3,4-triazaphosphole derivative. The [4+2] cycloaddition and subsequent cycloreversion reaction under elimination of pivaloyl nitrile affords the product in high yield. The heterocycle coordinates *via* the phosphorus atom to a $W(CO)_5$-fragment and shows stronger π-accepting properties than the triazaphosphole.

3,5-Disubstituted 3*H*-1,2,3,4-triazaphospholes (**B**) are the phosphorus congeners of the well-studied 1,2,3-triazoles (**A**), according to the isolobal relationship between a trivalent P-atom and a C–H fragment (Chart 1).

These λ^3, σ^2 phosphorus heterocycles have a conjugated π-system with a high degree of aromaticity.[1] They can easily be prepared regioselectively by a modular [3 + 2] cycloaddition reaction, starting from various aryl/alkyl-azides and phosphaalkynes.[2,3] Despite the fact that 3*H*-1,2,3,4-triazaphosphole derivatives have been synthesized independently by Carreé and Regitz already in 1984, the first reports on their coordination chemistry have not appeared in literature before 2010.[2,4] As ambidentate ligands the coordination of the heterocycle to a metal center might proceed either *via* the phosphorus atom or the nitrogen donors N^1 or N^2 (Chart 1, **C**). However, the η^1(P)-coordination mode has so far only been observed in a Pt(0)-complex.[4b]

Even less is known about the chemical reactivity of 3*H*-1,2,3,4-triazaphosphole derivatives. We could demonstrate that the cationic phosphorus analogues **D** of neutral mesoionic carbenes (1,2,3-triazolylidenes) can be obtained by quaternization of the N1 atom in **B** with Meerwein salts.[5] Moreover, we noticed that the introduction of electron-withdrawing *N*-sulfonyl groups at the N^3-atom changes the reactivity of the corresponding triazaphosphole considerably. In the presence of stoichiometric amounts of $AuCl{\cdot}S(CH_3)_2$, loss of N_2 and the formation of *cyclo*-1,3-diphospha(III)-2,4-diazane-Au(I) complexes of type **E** were observed.[6] Inspired by the fact that 6-membered azaphosphinines and 5-membered azaphospholes can undergo [4 + 2] cycloaddition reactions with various alkynes under subsequent nitrile elimination, we decided to investigate the reactivity of **B** towards alkynes in more detail with the aim to synthesize 2*H*-1,2,3-diazaphosphole derivatives (**G**) directly in one step (Chart 2).[7]

These heterocycles are otherwise only accessible by multistep synthetic procedures.[8] In fact, similar reactions with RC≡P elimination from oxadiphospholes and selenadiphospholes *via* a concerted mechanism have been reported.[9] Moreover, an imino-substituted diazaphosphole biradicaloid showed facile isonitrile cycloaddition, but no subsequent cycloreversion.[10]

The 3,5-disubstituted triazaphosphole **1** was prepared according to literature procedures from PhN_3 and ^{t}Bu-C≡P.[2a] Triazaphosphole **3** does not react with dimethyl

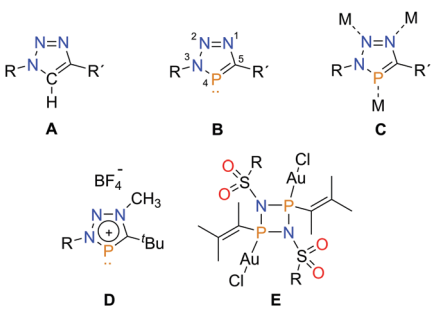

Chart 1 Triazole **A**, triazaphosphole **B** and possible coordination modes **C**. Selected examples (**D** and **E**) for the reactivity of **B**.

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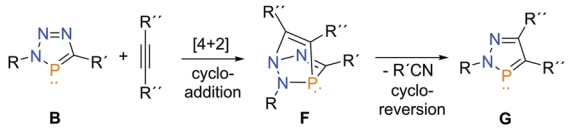
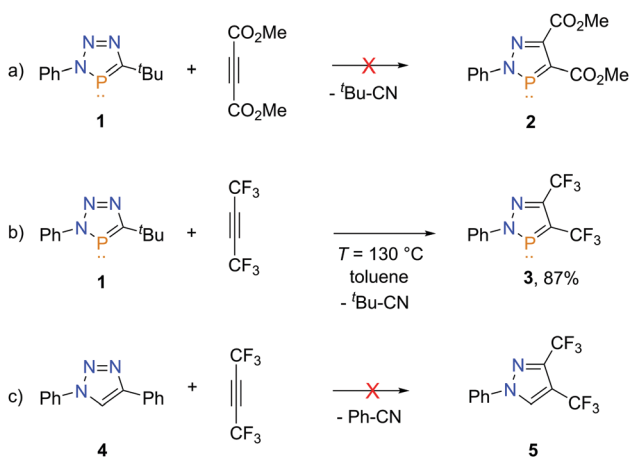


Chart 2 Attempted synthesis of **G**, starting from **B** and an alkyne.

acetylenedicarboxylate (DMAD) to diazaphosphole **2** (Scheme 1a). Using the stronger dienophile hexafluoro-2-butyne, however, elimination of ^{t}Bu–C≡N and, according to $^{31}P\{^{1}H\}$ NMR spectroscopy, quantitative formation of diazaphosphole **3** was observed (Scheme 1b). We could not detect the apparent intermediate **F** (Chart 2) during the course of the reaction. Interestingly, triazoles, such as **4**, did not react with $CF_3C{\equiv}CCF_3$ to the CF_3-substituted pyrazole **5**, although cycloaddition/cycloreversion reactions on 1,2,3-triazoles with DMAD have been reported in the literature (Scheme 1c).[11] This is particularly intriguing as 1-aryl-3,4-bis(trifluoromethyl)-substituted pyrazole motifs (**5**), are present in numerous pharmacologically relevant and bioactive nitrogen heterocycles and have to be prepared *via* a multistep synthesis.[12] Our novel diazaphosphole **3** thus represents a phosphorus derivative of this compound class.

Diazaphosphole **3** was obtained as an off-white solid in 87% isolated yield and shows a signal at δ(ppm) = 234.4 (q, $^{3}J_{P-F}$ = 25.5 Hz) in the $^{31}P\{^{1}H\}$ NMR spectrum (starting material **1**: δ(ppm) = 174.3). For the CF_3-groups, resonances at δ(ppm) = −53.3 (dq, $^{3}J_{F-P}$ = 25.5, $^{5}J_{F-F}$ = 7.4 Hz) and δ(ppm) = −61.8 (qd, $^{5}J_{F-F}$ = 7.4 Hz, $^{4}J_{F-P}$ = 1.2 Hz) were observed in the $^{19}F\{^{1}H\}$ NMR spectrum. Single crystals of **3** suitable for X-ray diffraction were obtained by slow evaporation of a dichloromethane solution and the molecular structure of **3** in the crystal is depicted in Fig. 1 along with selected bond lengths and distances.

Fig. 1 represents the first crystallographically characterized CF_3-substituted diazaphosphole. From the X-ray data it is evident that the heterocycle is fully planar and that the P(1)–C(8) and N(1)–N(2) bond distances in **3** are very similar to the ones observed in the starting material **1**,[13] with P–C and C–C bond lengths characteristic for aromatic compounds. The significantly negative NICS(1) values (see Table S1 in the ESI†)



Scheme 1 Reactivity of **1** and **4** towards electron-withdrawing alkynes.

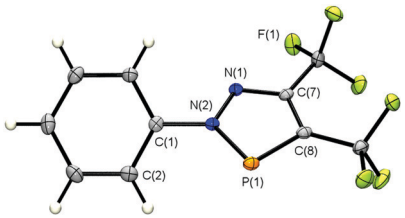


Fig. 1 Molecular structure of **3** in the crystal. Displacement ellipsoids are shown at the 50% probability level. Selected bond lengths (Å) and angles (°): P(1)–N(2): 1.693(2), P(1)–C(8): 1.712(2), C(8)–C(7): 1.406(3), C(7)–N(1): 1.323(3), N(1)–N(2): 1.349(2), N(2)–C(1): 1.436(3). N(1)–N(2)–C(1)–C(2): 145.9(2).

are in accordance with aromaticity. Apparently, exchanging pivaloyl nitrile by a perfluorobutyne-moiety does not cause a significant structural change within the heterocycle. The same holds for the inter-ring N(2)–C(1) distance. Also, the N(2)–P(1)–C(8) and P(1)–N(2)–N(1) angles as well as the torsion angle N(1)–N(2)–C(1)–C(2) in **3** are very similar compared to the data found for triazaphosphole **1**.

In order to understand the reaction mechanism, ωB97X-D/6-311 + G** DFT calculations (see ESI†) were performed after validating the optimized geometries with the X-ray data of **3** (see Table S2, ESI†). This level of theory was used successfully for cycloaddtion reactions before.[14]

The concerted cycloaddition–cycloreversion process (Fig. 2, Chart 2 and ESI†) is in full agreement with all experimental observations. The cycloaddition step **B**→**F** (Chart 2) is nearly thermoneutral, while the ^{t}BuC≡N eliminating cycloreversion (forming **G**) is highly exergonic. Accordingly (see Hammond principle), the rate determining step of the overall reaction is **TS1**, that allows the formation of **3** (27.3 kcal mol^{-1} activation Gibbs free energy) but not of **2** and **5** (barriers 31.9 kcal mol^{-1},

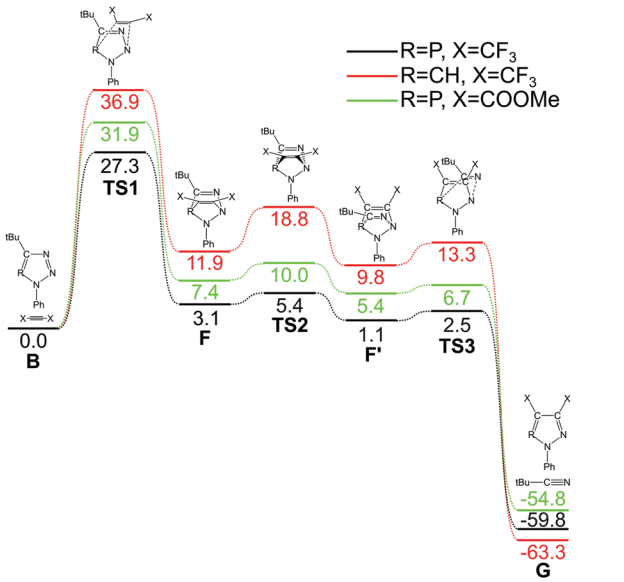


Fig. 2 ωB97X-D/6-311 + G**(PCM = toluene) Gibbs free energy (T = 130 °C) profiles for the reactions in Scheme 1. Relative energies (in kcal mol^{-1}) are compared to the initial van der Waals complex of the reactants.

36.9 kcal mol^{-1}, respectively). It is noteworthy that IRC calculations reveal, that the Ph substituent at the nitrogen atom should be in endo position with respect to the approaching/leaving group for any [4 + 2] cycloaddition step. The interconversion **F**→**F′** is needed prior to the retro cycloaddition step, by flattening the pyramidal nitrogen atom *via* a small barrier. The fact that no intermediate **F/F′** could be detected is in accordance with the very small barrier for the cycloreversion step.

A comparison of the Kohn–Sham orbitals of the parent CF_3-substituted diazaphosphole, the parent 2*H*-1,2,3-diazaphosphole and the parent 3*H*-1,2,3,4-triazaphosphole (Fig. S1, ESI†) shows, that in all three heterocycles, the π-type LUMO has a large coefficient at the phosphorus atom, indicating good π-acceptor properties when coordinated *via* the phosphorus atom to a metal center. While the orbital energies of the unsubstituted diazaphosphole are generally destabilized with respect to the triazaphosphole (Fig. S1, ESI†), in accordance with the observed ionization energies,[1] CF_3-substitution acts strongly stabilizing (Fig. S1, ESI†). Altogether, **3** should be a stronger π-acceptor than **1**. In all three compounds, the lone pair at the phosphorus atom (mixed with the nitrogen in-plane lone-pair) is represented by the HOMO−2 (CF_3-diazaphosphole: E = −11.24 eV; 3*H*-1,2,3,4-triazaphosphole: E = −10.92 eV; 2*H*-1,2,3-diazaphosphole: E = −10.21 eV). Consequently, triazaphospholes and diazaphospholes are expected to be rather weak σ-donors, as anticipated for low-coordinate phosphorus compounds. The π-donor properties of triazaphospholes and diazaphospholes are evident from the HOMOs, each having a large π-coefficient at the phosphorus atom, as it is known for other electron-rich phosphorus heterocycles.[15] Again, due to the energetically higher HOMO, triazaphosphole **1** should show stronger π-donor properties than the CF_3-substituted diazaphosphole **3**.

The interplay between the above described effects makes the coordination behavior of compound **3** highly interesting, also with respect to triazaphospholes. As a matter of fact, the coordination chemistry of 2*H*-1,2,3-diazaphospholes is largely unknown and only a few examples can be found in the literature. Chart 3 shows the possible coordination modes for this class of compounds. Analogous to triazaphospholes, diazaphospholes are ambidentate ligands and can coordinate to a metal center either *via* the phosphorus lone pair (**H**) or the nitrogen donor (**I**). This has been demonstrated in a few cases by van Koten, Schmidpeter and co-workers by using suitable Pt(II) and Pd(II) complexes as metal precursor.[16] The simultaneous coordination of a diazaphosphole to two metal fragments (**J**) has so far not been observed. Only recently, Erben and co-workers have investigated the synthesis and coordination chemistry of Si-bridged, chelating diazaphospholes.[17]

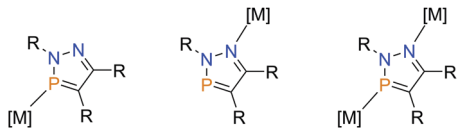
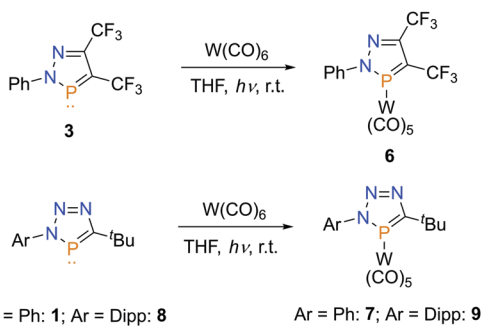


Chart 3 Possible coordination modes (**H–J**) of diazaphospholes.

We decided to focus on the synthesis of a tungsten carbonyl complex of **3**, as it can provide valuable information on the electronic ligand properties *via* IR spectroscopy. Moreover, ^{31}P NMR spectroscopy would immediately reveal, whether the coordination of the ligand to the $W(CO)_5$ fragment occurs *via* the phosphorus or the nitrogen donor. **3** was reacted with one equivalent of $W(CO)_6$ in THF at room temperature and under UV irradiation (Scheme 2). After only a short time, the formation of a single new resonance at δ(ppm) = 217.3 was observed in the $^{31}P\{^1H\}$ NMR spectrum, which corresponds to a coordination shift of $\Delta\delta$(ppm) = 17.1 compared to the starting material.[18] The selective reaction towards product **6** was complete within 68h. Interestingly, the signal of the product at δ(ppm) = 217.3 shows tungsten satellites with a coupling constant of $^1J_{W-P}$ = 326.5 Hz (Fig. S9, ESI†). This indicates that coordination of the ligand to the metal center occurs *via* the phosphorus atom, in agreement with the calculated 10.6 kcal mol^{-1} preference of the coordination at phosphorus over nitrogen. For comparison reasons, we also reacted triazaphospholes **1** and **8** (Ar = 2,5-diisopropylphenyl, Dipp) with $W(CO)_6$ in THF at room temperature and under irradiation with UV light. The course of the reaction was again followed by means of NMR spectroscopy, which revealed a selective and quantitative formation of a new species within 5d. The new compounds (**7**, **9**) show a signal at δ(ppm) = 136.1, respectively δ(ppm) = 160.6 in the $^{31}P\{^1H\}$ NMR spectrum ($\Delta\delta$(ppm) = 38.2, 39.7). Much to our surprise, these signals also show tungsten satellites ($^1J_{P-W}$ = 262.1 Hz; 285.6 Hz), which verifies that also **1** and **8** coordinate *via* the phosphorus atom to the metal center. This is particularly interesting taking into account that a coordination *via* N^1 or N^2 (Chart 1) has so far been observed for the majority of triazaphosphole-based complexes.[4,19] The calculated 0.6 kcal mol^{-1} energy difference between the two complexation modes of **1** indicates that subtle steric effects determine the complexation site in triazaphospholes.

A comparison of the IR spectra of **6**, **7** and **9** further shows, that the wavenumbers of the CO stretching frequencies are shifted to higher values in **6** compared to the ones found for **7** and **9** (Table 1). This is in line with the expected lower net-donor properties of **3** compared to **1** and **8**.

Thus, the CF_3-substituted diazaphosphole **3** is a stronger π-accepting ligand than triazaphospholes **1** and **8**, if coordination to the metal center proceeds *via* the phosphorus donor.



Scheme 2 Synthesis of W(0)-complexes **6** and **7**.

Table 1 Experimental wavenumbers [in cm^{-1}] for the CO stretching modes. These data were also supported by DFT calculations (see Table S3 in the ESI)

	$\tilde{\nu}_{(CO)}$ [cm^{-1}]			
6	2089	2017	2002	1934
7	2077	2023	1980	1885
9	2081	2000	1954	1934

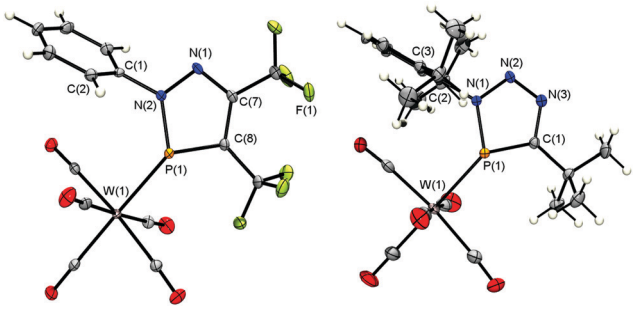


Fig. 3 Molecular structures of **6** (left) and **9** (right) in the crystal. Displacement ellipsoids are shown at the 50% probability level. Selected bond lengths (Å) and angles (°): **6**: P(1)–N(2): 1.677(2), P(1)–C(8): 1.707(2), C(8)–C(7): 1.413(3), C(7)–N(1), N(1)–N(2): 1.361(3), P(1)–W(1): 2.3890(6), N(2)–C(1): 1.441(3). N(1)–N(2)–C(1)–C(2): 64.1(3). **7**: Only one independent molecule is shown. P(1)–N(2): 1.675(2), P(1)–C(1): 1.712(2), C(1)–N(3): 1.357(3), N(3)–N(2): 1.303(2), N(2)–N(1): 1.358(2), N(1)–C(2): 1.446(2), C(1)–C(14): 1.521(3), P(1)–W(1): 2.4512(5). N(1)–P(1)–C(1): 88.67(9), N(2)–N(1)–C(2)–C(3): 86.3(2).

Finally, single crystals of **6** and **9**, suitable for X-ray diffraction, could be obtained by slow evaporation of the solvent of a saturated solution of **6** and **9** in *n*-pentane. Fig. 3 shows the molecular structures of **6** and **9** in the crystal, along with selected bond lengths and angles. The W(0) complexes **6** and **9** show a slightly distorted octahedral coordination geometry and unequivocally confirm that the heterocycles coordinates *via* the phosphorus atom to the $W(CO)_5$ fragment. Compared to the solid state structure of the free ligand **3** (Fig. 1), the P(1)–C(8) and P(1)–N(2) bonds in **6** are slightly shortened upon coordination of the ligand to the metal center (1.707(2) Å and 1.677(2) Å in **6** *vs.* 1.712(2) Å and 1.693(2) Å in **3**). For steric reasons, the aryl rings in **6** and **9** are rotated out of the heterocyclic plane (see also Fig. 1).

We could demonstrate for the first time that a 3*H*-1,2,3,4-triazaphosphole derivative undergoes a selective [4 + 2] cycloaddition with hexafluoro-2-butyne with subsequent elimination of pivaloyl nitrile to afford a bis-CF_3-substituted diazaphosphole in high yield. According to the isolobal relationship between a trivalent phosphorus atom and a C–H fragment, this heterocycle represents a phosphorus congener of a bis-CF_3-substituted pyrazole, which finds applications as a bioactive nitrogen heterocycle. The novel diazaphosphole forms an $(L)W(CO)_5$-complex, in which the ligand coordinates *via* the phosphorus atom to the metal center. In combination with DFT-calculations, the experimental results show that the bis-CF_3-substituted diazaphosphole is a stronger π-acceptor than the corresponding triazaphosphole, which was used as a starting material. Our results demonstrate that bis-CF_3-substituted diazaphospholes are accessible in a facile manner. Their use as novel π-accepting ligands in coordination chemistry and homogeneous catalysis as well as the investigation of their potential bioactive properties is currently explored.

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Conflicts of interest

There are no conflicts to declare.

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