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NMR Spectroscopic Observation of a Metal-Free Acetylide Anion

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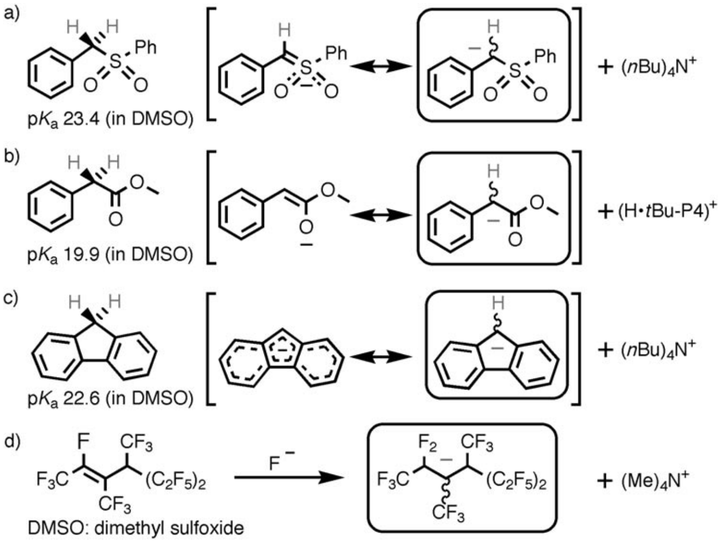
Abstract: A metal-free acetylide was observed by using NMR spectroscopy. Metal-free acetylides are closely related to reactive intermediates (carbanions) in solution; therefore, they have been regarded as unobservable species. However, we generated this highly reactive and unstable species through the deprotonation of phenylacetylene by using the strong nonmetallic phosphazene base *t*Bu-P4. In the presence of *t*Bu-P4, the *J* coupling between the ethynyl carbon and hydrogen nuclei ($^1J_{C,H}$) of phenylacetylene disappeared; this indicates the deprotonation of the alkyne terminal. Furthermore, a large low-field shift (approximately 90 ppm) of the alkyne carbon resonance was observed. We concluded that we have observed a metal-free carbanion with a formal charge on an sp-hybridized carbon atom for the first time.

Keywords: carbanions · density functional calculations · metal-free acetylide anions · phosphazenes · reactive intermediates

Introduction

The carbanion is a fundamental reactive species that is utilized in numerous organic reactions.[1] Generally, carbanions are generated from organometallics, such as Grignard reagents, organolithiums, metal acetylides, and so on.[1,2] These compounds can be regarded as carbanion equivalents, and have been characterized extensively.[1–3] However, as opposed to other reactive intermediates[4] (carbocations, free radicals, and carbenes), direct observation of intact or metal-free carbanions in solution is still rare. Although free carbanions have been characterized in the gas phase,[5] the instability of intact or metal-free carbanions in solution have hindered the development of methods for their observation. Moreover, their characterization is important for the understanding and control of reactions of carbanions in solution. To date, trials for the detection of metal-free carbanions in solution[6] are limited to those from carbonyl,[6d] sulfonyl,[6a–c] fluorenyl,[6e] and fluorocarbon[6f] compounds (Scheme 1). Important carbanions (reactive intermediates) such as metal-free acetylide anions (carbanions with a formal charge on an sp-hybridized carbon atom) have remained undetected, in spite of their frequent use in organic synthesis.[1]



Scheme 1. Known carbanion equivalents: a) sulfonylate, b) enolate, c) fluorenyl anion, d) anion from a fluorocarbon. *t*Bu-P4 is defined in Figure 1.

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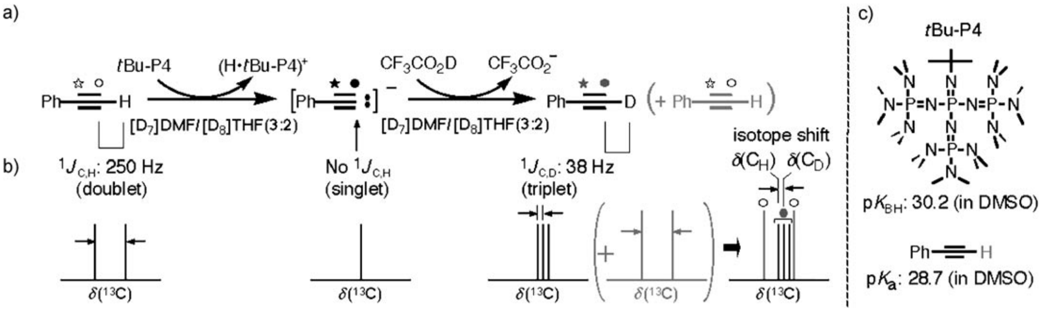


Figure 1. Generation of metal-free phenylacetylide anion in solution with the phosphazene base *t*Bu-P4. a) Course of the reaction. b) Putative spectral pattern of the alkyne terminal carbon resonance at each stage. c) Structures of *t*Bu-P4[9] and phenylacetylene with deprotonation site in gray.

Furthermore, the anionic centers of acetylide anions take a different hybridization state from those of metal-free anions such as enolates (carbanion equivalents of carbonyl compounds).[6] Therefore, we tried to generate the metal-free acetylide anion in solution.

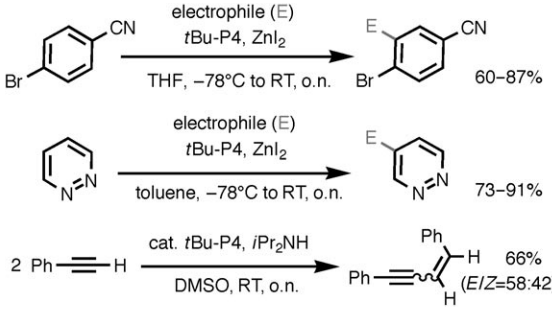
NMR spectroscopy is suitable for observing reactive intermediates, as it provides deep insight into the electronic structures of organic and inorganic compounds.[7] In particular, simultaneous monitoring of the resonances of several kinds of nuclei provides precise information about not only the electronic state, but also the solution equilibrium.[2,8] We previously reported the successful application of ^{15}N, ^{113}Cd, and ^{13}C NMR spectroscopy to the detection of metal–RNA interactions.[8] In the case of organometallics, Collum and co-workers revealed complexations and solution equilibria of organolithium compounds by using ^{6}Li, ^{13}C, and ^{15}N NMR spectroscopy.[2] Herein, we tried to detect the metal-free phenylacetylide anion by means of ^{13}C NMR spectroscopy.

Results and Discussion

We postulated that metal-free carbanions can be generated through deprotonation by an extraordinarily strong nonmetallic base. For this purpose, the phosphazene base *t*Bu-P4[9] is suitable, as it belongs to the strongest class of nonmetallic bases (Figure 1 a and c). In fact, *t*Bu-P4 promotes the deprotonative functionalization of aromatics and the formation of enynes from phenylacetylene (Scheme 2).[10] Furthermore, the pK_{BH} of *t*Bu-P4 (30.2 in DMSO[11]) is higher than the pK_a of the alkyne proton of phenylacetylene (28.7 in DMSO[12]) (Figure 1 c), which means that *t*Bu-P4 can deprotonate phenylacetylene. Therefore, by following the reaction scheme in Figure 1 a, we tried to generate metal-free phenylacetylide anion and record its NMR spectrum in the presence of *t*Bu-P4. To avoid undesired reactions of the acetylide anion, electrophiles were not added to the solutions.

Abstract in Japanese:

金属フリーのアセチリドアニオンが、^{13}C NMR スペクトルにより直接観測された。フェニルアセチレンのアセチレン末端プロトンを有機超強塩基である *t*-Bu-P4 塩基により引き抜くことによってアルキン末端にアニオンを発生させた。得られた金属フリーのアセチリドアニオンのアニオン中心（アセチレン末端炭素核）の化学シフト値は約 170 ppm という異常な低磁場の値を示した。量子化学計算でも低磁場シフトが妥当であるという結果が得られ、観測された分子種が金属フリーのアセチリドアニオンであることが示された。



Scheme 2. Deprotonative functionalization with *t*Bu-P4. o.n. = Overnight.

For the sake of clarity, we used ^{13}C-labeled phenylacetylene (mixture of Ph−C≡^{13}C−H (85 %) and Ph−^{13}C≡C−H (15 %); see Experimental Section for details). To highlight the presence or absence of the ethynyl proton of phenylacetylene, 1-dimensional (1D) ^{13}C NMR spectra (without ^{1}H decoupling) are useful for the following reasons. If a proton is present on the ethynyl carbon, its resonance will be split into two signals due to the one-bond C−H *J* coupling ($^{1}J_{C,H}$ ≈250 Hz; Ph−C≡*C*−*H*; Figure 1 b). On the contrary, if the ethynyl group is deprotonated, $^{1}J_{C,H}$ will disappear, and a single ethynyl carbon resonance will be observed (Figure 1 b). Furthermore, it is also interesting to monitor the chemical shifts, as a large chemical shift perturbation is expected for the anion center.

In Figure 2, 1D ^{13}C NMR spectra of phenylacetylene with and without *t*Bu-P4 are presented. In the absence of *t*Bu-P4, the alkyne terminal and internal carbon nuclei resonated at 80.7 and 84.3 ppm, respectively (Figure 2 a and b and Table 1). Surprisingly, in the presence of *t*Bu−P4, the resonance of the alkyne terminal carbon shifted to an extraordinarily low field at 168.7 ppm (Figure 2 c and d and Table 1). In general, alkyne carbon nuclei resonate between 65 and 95 ppm,[7b] and no alkyne carbon resonance at such a low

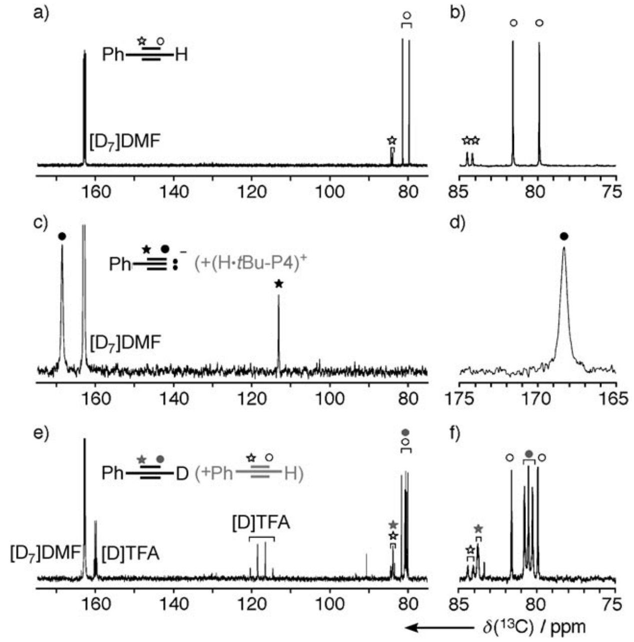


Figure 2. 1D ^{13}C NMR spectrum (without ^{1}H decoupling) for each condition. a) Spectrum of phenylacetylene alone (neutral conditions: ^{13}C-labeled phenylacetylene (25 mm) at −30 °C). b) Magnified view around the alkyne terminal carbon resonance in a). c) Spectrum of phenylacetylene with *t*Bu-P4 (basic conditions: ^{13}C-labeled phenylacetylene (25 mm) and *t*Bu-P4 (250 mm) at −30 °C). d) Magnified view around the alkyne terminal carbon resonance in c). e) Spectrum of phenylacetylene with *t*Bu-P4 and [D]TFA (acidic conditions: ^{13}C-labeled phenylacetylene (25 mm), *t*Bu-P4 (250 mm), and [D]TFA (500 mm) at −30 °C). f) Magnified view around the alkyne terminal carbon resonance in e). The alkyne terminal and internal carbon atoms and their resonances are labeled with circles and stars, respectively. Open symbols: normal phenylacetylene under neutral conditions; black symbols: phenylacetylene under basic conditions; gray symbols: deuterated phenylacetylene.

Table 1. Experimental and calculated chemical shifts of alkyne carbon nuclei.

Species	δ(Ct) [ppm][a]	δ(Ci) [ppm][b]	$^{1}J_{\mathrm{C,H}}$ [Hz]
Ph−C≡C−H (neutral)	80.7[c]	84.3[c]	252
Ph−C≡C−H + *t*Bu-P4 (basic)	168.7[d]	113.6[d]	
Ph−C≡C−H (calcd)[e]	81.9[f]	87.6[f]	247
Ph−C≡C^{-} (calcd)[g]	179.6[f]	115.8[f]	

[a] δ(Ct) = chemical shift of the alkyne terminal carbon (Ph−C≡*C*−H). [b] δ(Ci) = chemical shift of the alkyne internal carbon (Ph−*C*≡C−H). [c] Experimental chemical shift values from Figure 2 a and b. [d] Experimental chemical shift values from Figure 2 c and d. [e] Chemical shifts were calculated for a single phenylacetylene molecule (see Experimental Section). [f] Chemical shifts were calculated by using the GIAO method at the B3LYP/6-311++G(2d,p) level. [g] Chemical shifts were calculated for the ion pair Ph−C≡C^{-}·(H·*t*Bu-P4)$^{+}$ (see Experimental Section). Notably, the calculated $^{1}J_{\mathrm{C,H}}$ (Ph−C≡*C*−*H*) value was also in good agreement with experimental data. Further detailed considerations on the chemical shifts of this anionic species are described in the Supporting Information.

field has been reported. Furthermore, metal phenylacetylides resonate at different chemical shifts, at 100–150 ppm (see Supporting Information), which indicates that they are different compounds from the species observed here. Therefore, this extraordinary low-field shift of the resonance of the alkyne terminal carbon nucleus may indicate that we have observed novel phenomena and an unknown acetylide species. Interestingly, when deuterated trifluoroacetic acid ([D]TFA; 300 μmol) was added to the solution under basic conditions (Figure 2 c and d), neutral phenylacetylene was recovered almost quantitatively, and deuterium was introduced at the alkyne terminal (Ph−C≡C−*D*) in significant yield (the triplet resonances labeled with filled circles in Figure 2 e and f). Although protonated phenylacetylene (Ph−C≡C−*H*) was also derived (the doublet resonances labeled with empty circles in Figure 2 e and f), it would have been generated through back-donation of a proton from (H·*t*Bu-P4)$^{+}$ (see Supporting Information).

Next, we considered the *J* coupling. Under neutral (usual) conditions, one-bond C−H *J* coupling ($^{1}J_{\mathrm{C,H}} = 252$ Hz; Ph−C≡*C*−*H*) was observed as expected (Figure 2 a and b and Table 1). Under basic conditions, however, these couplings disappeared (Figure 2 c and d). As *J* coupling is generally known to arise from a covalent bond, the disappearance of $^{1}J_{\mathrm{C,H}}$ is direct evidence of the cleavage of the alkyne terminal C−H bond. It probably means that the solutes were transformed into phenylacetylide anions and phosphazenium cations. In any case, the disappearance of the *J* coupling is not explicable without the deprotonation of phenylacetylene. The data for the chemical shifts and coupling constants unambiguously indicate the generation of a novel acetylide species, most likely a metal-free acetylide anion in solution. Notably, the carbon resonance of Ph−C≡C−D was observed as a triplet due to *J* coupling with D ($I = 1$, $^{1}J_{\mathrm{C,D}} = 37.9$ Hz), which surely indicates that this resonance is that of the deuterated alkyne terminal carbon nucleus.

Theoretical chemical shifts from density functional theory (DFT) calculations with the gauge-independent atomic orbital (GIAO) method also support the generation of an acetylide anion. The calculated chemical shift for the alkyne terminal carbon of the phenylacetylide anion was 179.6 ppm, whereas that of the neutral phenylacetylene was 81.9 ppm (Table 1). Clearly, the observed chemical shift under basic conditions is much closer to the calculated value of the phenylacetylide anion (an ethynyl carbanion) than that of the neutral phenylacetylene (see Experimental Section). Interestingly, the alkyne terminal carbon resonated at increasingly lower field as the molar ratio [phenylacetylene]/[*t*Bu-P4] became smaller (Table 2). This means that the limiting

Table 2. Dependence of the chemical shifts of alkyne carbon nuclei on the molar ratio [phenylacetylene]/[*t*Bu-P4].

Species	δ(Ct) [ppm]	δ(Ci) [ppm]
Ph−C≡C−H (1.0 equiv) + *t*Bu-P4[a]	140.8	104.0
Ph−C≡C−H (0.1 equiv) + *t*Bu-P4[b]	168.7	113.6
Ph−C≡C−H (0.01 equiv) + *t*Bu-P4[c]	172.0	114.4

[a] Phenylacetylene (140 mm) and *t*Bu-P4 (140 mm) in [D$_8$]THF/[D$_7$]DMF (2:3) at −30 °C. [b] Phenylacetylene (25 mm) and *t*Bu-P4 (250 mm) in [D$_8$]THF/[D$_7$]DMF (2:3) at −30 °C. [c] Phenylacetylene (2.0 mm) and *t*Bu-P4 (200 mm) in [D$_8$]THF/[D$_7$]DMF (2:3) at −20 °C. In this experiment, ^{13}C-labeled phenylacetylene was used for higher sensitivity. Otherwise, the alkyne terminal resonances could not be observed below a molar ratio of 0.1 equivalents.

shift of the alkyne terminal resonance should be larger and closer to the calculated chemical shift. Accordingly, the chemical shifts observed under basic conditions are assigned to the metal-free acetylide anion (the ethynyl carbanion).

Conclusion

We have observed the metal-free phenylacetylide anion in solution, which is a first for carbanions with a formal charge on the sp-hybridized carbon atom.

Experimental Section

NMR Measurements

Phenylacetylene, *t*Bu-P4, and deuterated solvents were used as purchased (phenylacetylene: ISOTEC #604399, *t*Bu-P4 in hexane (1 M): Fluka #79421, $[\mathrm{D_8}]$THF: ISOTEC #184314, $[\mathrm{D_7}]$DMF (DMF = *N*,*N*-dimethylformamide): ISOTEC #189979, [D]TFA: Aldrich #30889-7). The current batch of phenylacetylene enriched in ^{13}C at C2 (the alkyne terminal carbon) (ISOTEC, Catalog #: 604399, Lot #: EQ0216-OOS, Sales #: 9060717) is a mixture of the alkyne labeled at the terminal carbon atom ($\mathrm{Ph{-}C{\equiv}{}^{13}C{-}H}$ 85 %) and the alkyne labeled at the internal carbon atom ($\mathrm{Ph{-}{}^{13}C{\equiv}C{-}H}$ 15 %).

The solutions for NMR measurements were prepared as follows. Hexane was evaporated from a solution of *t*Bu-P4 (150 µL, 150 µmol) in hexane in an NMR tube with a rubber septum under vacuum. Then, dry argon gas was introduced into the NMR tube. The resulting residue was dissolved in $[\mathrm{D_8}]$THF (200 µL). Then, phenylacetylene (15 µmol, 10 % *v*/*v* in $[\mathrm{D_7}]$DMF) was added to this solution at around −20 °C. Finally, $[\mathrm{D_7}]$DMF (300 µL) was added to the resulting solution at around −20 °C, and this basic solution was used for NMR measurements. Notably, even in the DMF/THF mixed solvent, the $\mathrm{p}K_{\mathrm{BH}}$ value of *t*Bu-P4 is thought to be higher than the $\mathrm{p}K_{\mathrm{a}}$ value of phenylacetylene, owing to the linear relationships of $\mathrm{p}K_{\mathrm{a}}$ values in different solvents.[13]

For deuteration of phenylacetylide anion, [D]TFA (300 µmol) was added to the above basic solution, and neutral phenylacetylene ($\mathrm{Ph{-}C{\equiv}C{-}D}$ and $\mathrm{Ph{-}C{\equiv}C{-}H}$) was recovered almost quantitatively. It was found that deuterium was introduced at the alkyne terminal ($\mathrm{Ph{-}C{\equiv}C{-}D}$) in significant yield (the triplet resonances labeled with filled circles in Figure 2 e and f). Chemical shifts of alkyne terminal carbon resonances were 80.6 ($\mathrm{Ph{-}C{\equiv}}C\mathrm{{-}D}$) and 80.8 ppm ($\mathrm{Ph{-}C{\equiv}}C\mathrm{{-}H}$). This chemical shift difference between deuterated and protonated nuclei is known as an isotope shift (Figure 1 b), which means that the derived species were identical except for the terminal hydrogen atoms (H or D). More importantly, the observed chemical shifts of the alkyne carbons under acidic conditions (Figure 2 e and f) were consistent with those of the original phenylacetylene (Figure 2 a and b); this is direct evidence that neutral phenylacetylene was regenerated.

NMR spectroscopic measurements were performed on a JEOL ECA600 spectrometer (600 MHz for ^{1}H, 151 MHz for ^{13}C). Typical 1D ^{13}C NMR spectra without ^{1}H decoupling were recorded with a spectral width of 47 169.811 Hz digitized into 65 536 complex points. For the neutral solution, 128 scans were averaged. This spectrum was processed with an exponential window function to give a line-broadening of 3 Hz. For the basic solution, 1024 scans were averaged. This spectrum was processed with an exponential window function to give a line-broadening of 10 Hz. Measurements under basic and neutral conditions were performed at −30 °C.

We gave each sample sufficient time for the solution to equilibrate before NMR spectral acquisition. Chemical shift referencing was performed by using the ^{13}C resonances of $[\mathrm{D_8}]$THF as internal references. We also performed indirect chemical shift referencing with the chemical shift referencing ratio ($\gamma(^{13}\mathrm{C})/\gamma(^{1}\mathrm{H})$)[14] and confirmed that both corrected chemical shift values were consistent with each other.

DFT Calculations

DFT calculations were carried out with Gaussian 03 on an Origin 3400 processor (Silicon Graphics Inc.).[15] Structural optimizations, vibrational analyses, and NMR shielding calculations were performed at the B3LYP/6–311++G(2d,p) level. Shielding values were calculated with the GIAO method.[16] The shielding values obtained were transformed into chemical shifts (δ_{target}) by using [Eq. (1)],[17] with the calculated shielding values of the target nuclei (σ_{target}) and tetramethylsilane (σ_{ref}).

$$\delta_{\mathrm{target}} = (\sigma_{\mathrm{ref}} - \sigma_{\mathrm{target}})/(1 - \sigma_{\mathrm{ref}}) \approx \sigma_{\mathrm{ref}} - \sigma_{\mathrm{target}} \qquad (1)$$

For the sake of clarity, chemical shifts of the acetylide anion ($\mathrm{Ph{-}C{\equiv}C^{-}}$) were calculated for the anion alone and for its complexes with THF, DMF, and phosphazenium cation, $(\mathrm{H{\cdot}}t\mathrm{Bu{\text{-}}P4})^{+}$. Among the above calculated models, the ion pair $\mathrm{Ph{-}C{\equiv}C^{-}}$ $(\mathrm{H{\cdot}}t\mathrm{Bu{\text{-}}P4})^{+}$ showed quite similar chemical shift values to the experimental (Table 1). Calculated chemical shift values are as follows (δ(Ct), δ(Ci)): $\mathrm{Ph{-}C{\equiv}C^{-}}$ alone: 214.8, 118.9 ppm; $\mathrm{Ph{-}C{\equiv}C^{-}{\cdot}THF}$: 204.0, 117.4 ppm; $\mathrm{Ph{-}C{\equiv}C^{-}{\cdot}(H{\cdot}}t\mathrm{Bu{\text{-}}P4)^{+}}$: 179.6, 115.8 ppm. For $\mathrm{Ph{-}C{\equiv}C^{-}{\cdot}DMF}$, chemical shifts were not calculated, as there was no converged structure or reasonable structure without imaginary frequencies for the calculated structures tested (B3LYP/6–31G(d) level).

Next, chemical shifts of neutral phenylacetylene ($\mathrm{Ph{-}C{\equiv}C{-}H}$) were calculated for phenylacetylene alone and for its complexes with THF and DMF. According to our calculations, all the complexes showed imaginary frequencies, which means that they are not stable. In contrast, the model of phenylacetylene alone did not show an imaginary frequency. Therefore, chemical shift values for phenylacetylene alone are listed in Table 1. Calculated chemical shift values are as follows (δ(Ct), δ(Ci)): $\mathrm{Ph{-}C{\equiv}C{-}H}$ alone: 81.9, 87.6 ppm. We also calculated the *J* coupling constant ($^{1}J_{\mathrm{C,H}}$: $\mathrm{Ph{-}C{\equiv}}C{-}H$) between the alkyne carbon and the alkyne hydrogen nuclei of neutral phenylacetylene. Interestingly, the calculated $^{1}J_{\mathrm{C,H}}$ value was in good agreement with the experimental. This indicates that the DFT calculations were performed correctly.

DFT calculations at the 6–311++G(2d,p) level were performed not only for small molecules but also for a very large molecular system of $\mathrm{Ph{-}C{\equiv}C^{-}{\cdot}(H{\cdot}}t\mathrm{Bu{\text{-}}P4)^{+}}$ ($M_{\mathrm{r}} = 735.47$). We emphasize that this level of DFT calculations of NMR chemical shifts (GIAO method) was the highest level for the $\mathrm{Ph{-}C{\equiv}C^{-}{\cdot}(H{\cdot}}t\mathrm{Bu{\text{-}}P4)^{+}}$ within the limits of both the software and hardware. Reviews on the theoretical chemistry of metal carbanions[3] and phosphazene bases[18] are present in the literature.

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