

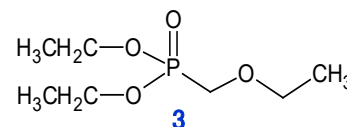
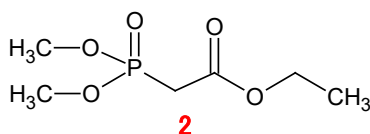
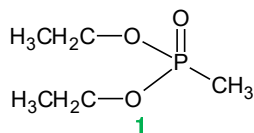
## Analyzes of alkyl phosphonate mixtures

Product used : Nuclear Magnetic Resonance (NMR)

In nuclear magnetic resonance (NMR) analyzes of phosphorus-containing compounds,  $^1\text{H}$  and  $^{13}\text{C}$  signals near phosphorus are affected by heteronuclear spin couplings. Given the natural abundance of  $^{31}\text{P}$  at 100%, these splittings are easily visible, reducing sensitivity and increasing complexity. Additionally, some of these compounds are unstable in solvents, leading to the formation of decomposition products, which further complicates the interpretation of  $^1\text{H}$  and  $^{13}\text{C}$  spectra. On the other hand, when analyzing phosphorus-containing samples,  $^{31}\text{P}$  NMR information can be invaluable for structural analysis. To illustrate this, we will provide some examples below. In the measurements detailed in this application note, we utilized the ROYAL Probe™ P+ [1], capable of  $^1\text{H}$ ,  $^{31}\text{P}$ , and X triple-resonance measurements. We employed a three-channel 600 MHz NMR spectrometer, the JNM-ECZL600G, featuring one high-frequency (HF) and two low-frequency (LF) channels.

### Sample information

Alkyl phosphonates known as Horner-Emmons reagents are used in the olefination reaction. These include diethyl methylphosphonate **1**, ethyl dimethyl phosphonoacetate **2**, and diethyl (ethoxymethyl) phosphonate **3**. They were mixed and dissolved in  $\text{CDCl}_3$  to create a sample containing 4.8 vol% of each compound.



### $^{13}\text{C}$ NMR spectrum

A conventional  $^{13}\text{C}$  spectrum of the sample recorded with  $^1\text{H}$  decoupling is depicted in Fig. 1. Upon examining the expansions of this spectrum in Fig. 2, an experienced chemist may observe that several signals appear doubled, indicating splitting caused by  $^{13}\text{C}$ - $^{31}\text{P}$  coupling. However, identifying such signal doublings may prove challenging in the case of unknown samples or very complex mixtures with numerous carbon signals. To illustrate the efficacy of triple-resonance experiments, a  $^{13}\text{C}$  spectrum recorded with simultaneous  $^1\text{H}$  and  $^{31}\text{P}$  decoupling is presented in Fig. 2c) and Fig. 2d). A straightforward comparison between the double-resonance and triple-resonance spectra allows for the unequivocal identification of carbon signals split by one-bond  $^{13}\text{C}$ - $^{31}\text{P}$  couplings, which can exceed 100 Hz in alkyl phosphonates. The signals observed at 10.85 ppm ( $J_{\text{CP}} = 144 \text{ Hz}$ )<sup>1</sup>, 33.13 ppm ( $J_{\text{CP}} = 135 \text{ Hz}$ )<sup>2</sup>, and 64.35 ppm ( $J_{\text{CP}} = 167 \text{ Hz}$ )<sup>3</sup> can thus be attributed to the carbon atoms directly bound to phosphorus, with the one-bond coupling constants provided in parentheses. Smaller splittings are indicative of 2-bond and 3-bond interactions. Table 1 summarizes the  $^{13}\text{C}$  chemical shifts and  $^{13}\text{C}$ - $^{31}\text{P}$  coupling constants.

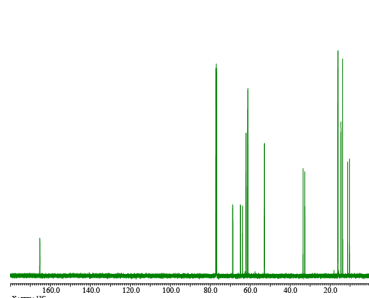


Fig. 1:  $^{13}\text{C}$  NMR spectrum

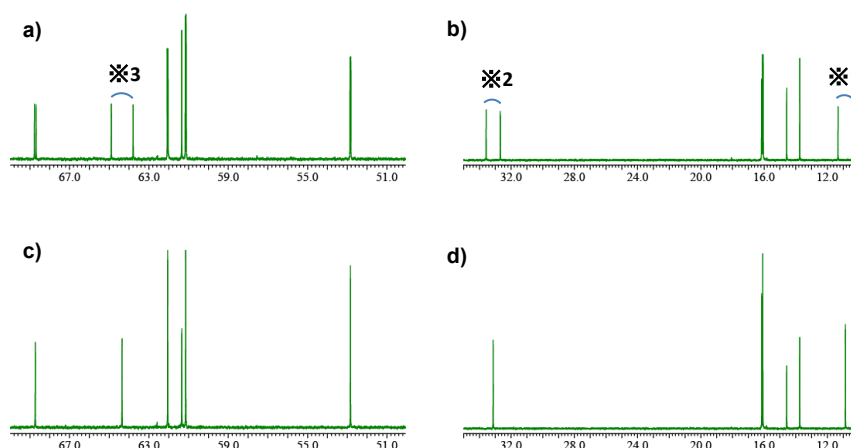


Fig. 2: Expanded regions of  
a)  $^{13}\text{C}\{^1\text{H}\}$  and b)  $^{13}\text{C}\{^1\text{H}\}\{^{31}\text{P}\}$  spectra in the range of 50-70 ppm,  
c)  $^{13}\text{C}\{^1\text{H}\}$  and d)  $^{13}\text{C}\{^1\text{H}\}\{^{31}\text{P}\}$  spectra in the range of 10-35 ppm

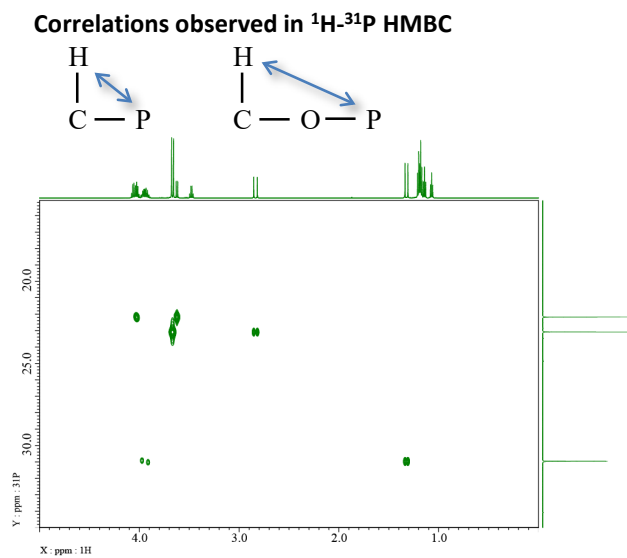
Table 1:  $^{13}\text{C}$  chemical shifts and coupling constants

No.	$^{13}\text{C}$ /ppm	J /Hz
1	10.85	$^1J_{\text{CP}}=144$
2	13.75	-
3	14.57	-
4	16.08	$^nJ_{\text{CP}}=7$
5	16.15	$^nJ_{\text{CP}}=6$
6	33.13	$^1J_{\text{CP}}=135$
7	52.84	$^nJ_{\text{CP}}=6$

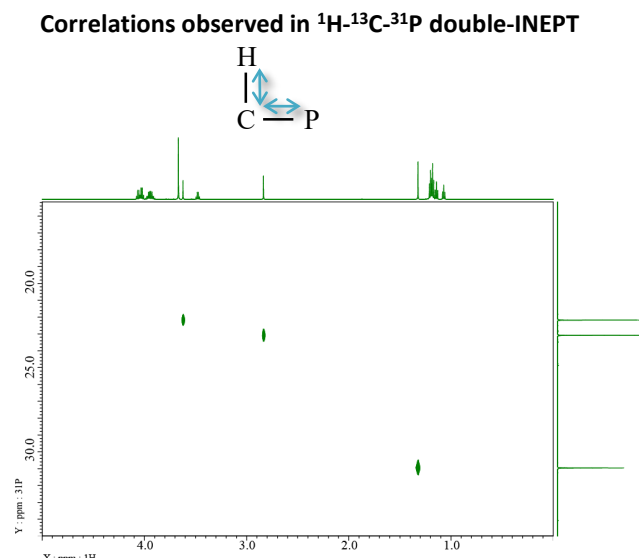
No.	$^{13}\text{C}$ /ppm	J /Hz
8	61.14	$^nJ_{\text{CP}}=6$
9	61.35	-
10	62.05	$^nJ_{\text{CP}}=7$
11	64.35	$^1J_{\text{CP}}=167$
12	68.73	$^nJ_{\text{CP}}=12$
13	165.29	$^nJ_{\text{CP}}=6$

## Difficulty in interpretation of $^1\text{H}$ - $^{31}\text{P}$ HMBC and use of double-INEPT H-C-P experiment

Fig. 3 shows the  $^1\text{H}$ - $^{31}\text{P}$  HMBC spectrum.  $^1\text{H}$ - $^{31}\text{P}$  coupling via 2- and 3-bonds are observed, but it is difficult to distinguish each from this spectrum. On the other hands, by measuring the  $^1\text{H}$ - $^{13}\text{C}$ - $^{31}\text{P}$  double-INEPT as shows Fig. 4, only the 2-bonded  $^1\text{H}$ - $^{31}\text{P}$  can be selectively extracted [2]. Then we can distinguish between 2- and 3-bonds by comparing them. the  $^1J_{\text{CH}}$  and  $^1J_{\text{CP}}$  couplings are used to obtain correlations in double-INEPT, since  $^1J_{\text{CP}}$  of alkyl phosphonates have a large coupling constant as mentioned above, it is possible to extract only the H-C-P coupling by setting the parameters according to that.



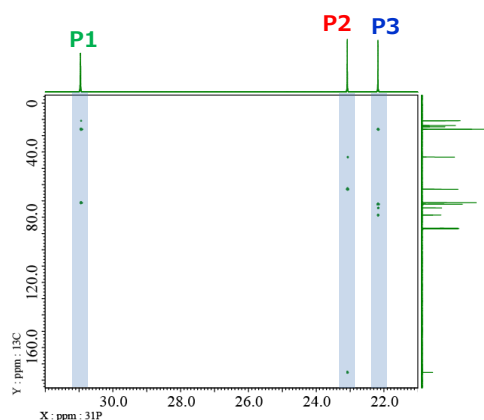
**Fig. 3:**  $^1\text{H}$ - $^{31}\text{P}$  HMBC spectrum  
Longrange\_j : 8 Hz



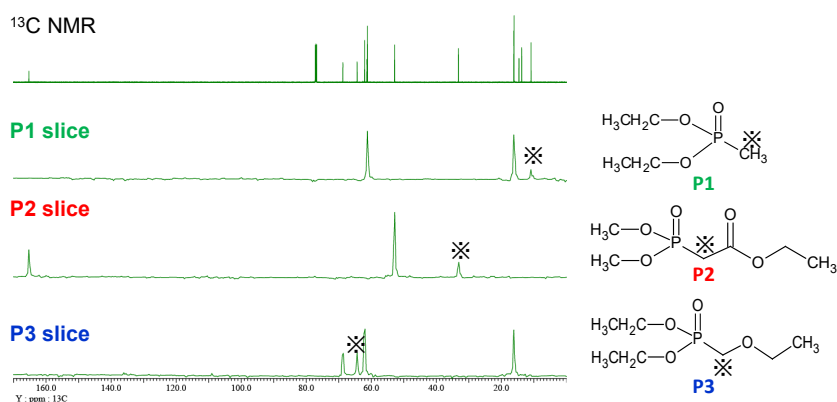
**Fig. 4:**  $^1\text{H}$ - $^{13}\text{C}$ - $^{31}\text{P}$  double-INEPT spectrum  
j\_ch : 140 Hz, j\_cp : 145 Hz

## Assignment of each $^{31}\text{P}$ - $^{13}\text{C}$ coupling partners

$^{31}\text{P}$ - $^{13}\text{C}$  correlations can also provide significant insights into the structural analysis of phosphorus-containing compounds. Correctly chosen and optimized  $^{31}\text{P}$ - $^{13}\text{C}$  correlation experiments enable the identification of  $^{13}\text{C}$  coupling partners for each  $^{31}\text{P}$  nucleus. Fig. 5 illustrates a  $^{31}\text{P}$ - $^{13}\text{C}$  LR-HSQC (Long-Range Heteronuclear Single-Quantum Coherence) spectrum. The pulse program employed was a standard HSQC, with parameters optimized for long-range  $^{13}\text{C}$ - $^{31}\text{P}$  couplings, thereby capturing correlations from weak couplings as well. In Fig. 6, we compare the  $^{13}\text{C}$  NMR spectrum with three slices extracted from the  $^{31}\text{P}$ - $^{13}\text{C}$  LR-HSQC spectrum for each phosphorus atom. This facilitates the assignment of  $^{13}\text{C}$  signals to individual phosphonates. Additionally, Fig. 6 demonstrates that  $^{31}\text{P}$ - $^{13}\text{C}$  LR-HSQC enables the detection of carbon atoms up to three bonds away from each phosphorus atom.



**Fig. 5:**  $^{31}\text{P}$ - $^{13}\text{C}$  LR-HSQC  $\{^1\text{H}\}\{^{13}\text{C}\}$  spectrum  
J\_constant : 10 Hz



**Fig. 6:** Comparison of  $^{13}\text{C}$  spectrum and slices extracted from  $^{31}\text{P}$ - $^{13}\text{C}$  LR-HSQC  $\{^1\text{H}\}\{^{13}\text{C}\}$  spectrum  
\* one-bond correlation

**Reference** : [1] JEOL Application note NM220010  
: [2] *Tetrahedron Letters* 48 (2007) 7586–7590

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