DOI: 10.1002/ejoc.200600432

Comparative Study of the Phospha- and Arsa-Wittig Reaction Using ^{1}H, ^{75}As and ^{17}O NMR Spectroscopy

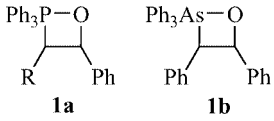
Christian Raeck[a] and Stefan Berger*[a]

Keywords: Oxaarsetanes / Stereoselectivity / Wittig reactions / NMR spectroscopy

The existence of oxaarsetanes during an arsa-Wittig reaction has been proved by ^{1}H and ^{17}O NMR spectroscopy. ^{75}As NMR spectra were obtained from the corresponding arsonium salts and arsane oxides. The dynamic ^{1}H NMR spectra of phospha- and arsaylides were compared.

Introduction

The Wittig reaction for the olefination of aldehyde and ketone functionalities using phosphorus ylides has a key position in organic chemistry.[1] Since the recognition of the potential of this reaction the mechanism has been widely discussed.[2] Oxaphosphetanes **1a** (Scheme 1) are the key intermediates of the reaction, as shown in 1973 by Vedejs and Snoble using low-temperature ^{31}P NMR spectroscopy.[3]

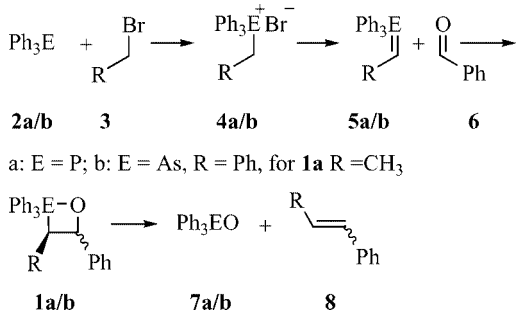


1a **1b**

Scheme 1.

Besides phosphorus, there are other elements that can be used in Wittig-type reactions and arsenic is one of the most common alternatives. The arsa-Wittig reaction is one of the most useful reactions in olefination chemistry because of its high stereoselectivity and mild reaction conditions.[4] The first publication to report on an arsa-Wittig reaction (1937) was by Heffe and it preceded indeed the original paper by Wittig by 16 years.[5] The first systematic investigation was performed in 1960 by Henry and Wittig.[6] Two possible reaction pathways of the arsa-Wittig reaction were observed.[6,7] One pathway proceeds via an oxaarsetane, like the phospha-Wittig reaction, with olefins being formed as products. The other pathway is supposed to proceed via a betaine as intermediate, like the reaction of sulfur-ylides with carbonyl functions leading to epoxides.[8,9] Until now no direct spectroscopic evidence for the intermediates of either pathway has been available.

From an NMR point of view, the phospha-Wittig reaction is ideal to study since all the reaction steps can be controlled. Starting with the ^{31}P NMR spectrum of the phosphane **2a**, its quaternisation to the phosphonium salt **4a** can be observed, followed by deprotonation to ylide **5a**. Finally, the ^{31}P NMR spectrum of oxaphosphetane **1a** and phosphane oxide **7a** as end-products can be easily observed (Scheme 2).



Scheme 2. Intermediates of the Wittig reaction.

The study of the arsa-Wittig reaction by ^{75}As NMR spectroscopy was anticipated to be more difficult as a result of the large quadrupolar moment of the ^{75}As nucleus and its relatively low resonance frequency. The quadrupole moment creates broad lines in the spectra of arsenic derivatives, especially for those that are not symmetrically substituted at the arsenic atom, and acoustic ringing prohibits the acquisition of good spectra. Indeed, ^{75}As NMR spectra have only been reported for cases in which the substituents are chemically very similar to each other and placed in a tetrahedral sphere around the arsenic atom.[10]

Herein we report our attempts to obtain ^{75}As NMR spectra of several components during an arsa-Wittig reaction and to provide spectroscopic proof of oxaarsetanes **1b** as the key intermediates of the reaction.

[a] Institut für Analytische Chemie, Fakultät für Chemie und Mineralogie, Universität Leipzig,
Linné-Strasse 3, 04103 Leipzig, Germany

Results and Discussion

In order to maintain the symmetry around the arsenic nucleus we chose triphenylarsane as the starting compound and quaternised it with benzyl bromide. In addition, ethylidenetriphenylarsorane is known to be very reactive and leads to epoxides via betaines as intermediates.[8,9] The particular arsa-Wittig reaction with benzylidenetriphenylarsorane was to be compared with the phospha-Wittig reaction involving the same substitution pattern. After preparing the ylides from their arsonium and phosphonium salts, respectively, benzaldehyde was added as the carbonyl compound in all experiments at room temperature. In agreement with the literature,[9,11] we observed the formation of stilbene **8** in both reactions, but with the expected differences in yields and stereochemistry, as given in Table 1. The reason for the high stereoselectivity of the arsa-Wittig reaction is the higher reactivity of the arsenic ylide relative to the phosphorus ylide.[9] This high stereoselectivity was also noticeable when the reaction temperature was lowered to –100 °C. The high reactivity of the arsenic ylide is responsible for the unchanged yield and stereoselectivity. In the case of the phosphorus ylide, the stereoselectivity changes with temperature.[11]

Table 1. Yields and stereochemical outcomes of Wittig reactions with benzaldehyde starting from either phosphonium salt **4a** or arsonium salt **4b**.

T [°C][a]	Ph_3PBnBr (**4a**)		$Ph_3AsBnBr$ (**4b**)	
	$(Z)/(E)$[b]	Yield [%][c]	$(Z)/(E)$[b]	Yield [%][c]
Room temp.	39:61	80	1:99	56
–100	60:40	81	1:99	61

[a] Addition of benzaldehyde. [b] $(Z)/(E)$ ratios were determined on the isolated product by NMR spectroscopy. [c] All yields were determined on isolated products.

Since the intermediates of the phospha-Wittig reaction were characterised by ^{31}P NMR spectroscopy, then ^{75}As NMR spectra should provide related characteristics of the intermediates of the arsa-Wittig reaction. All the anticipated intermediates of the arsa-Wittig reaction are shown in Scheme 2.

The arsenic species were investigated by ^{75}As NMR spectroscopy using a modified spin-echo pulse sequence with a reduced delay after the 180° pulse. Thus, the rising echo signal was also recorded enhancing the signal-to-noise ratio and in addition the acoustic ringing of the probe head was suppressed. Typical ^{75}As NMR spectra of benzyltriphenylarsonium bromide (**4b**) and triphenylarsane oxide (**7b**) are shown in Figure 1. The NMR chemical shift changes from 220 ppm for **4b** to 324 ppm in the case of **7b**. The linewidth (full width at half maximum) is nearly unchanged at about 5 kHz indicating similar electronic environments around the quadrupolar nucleus of the arsenic atom. Unfortunately, despite many attempts and modifications of the pulse sequences and spectrometer conditions, no other intermediates such as the arsenic ylide **5b** or the oxaarsetane **1b** gave reliable ^{75}As NMR spectra. Therefore, other NMR spectroscopic methods were used to obtain more information about these intermediates.

We first focussed on the ylides. Ylides can be characterised by two mesomeric resonance structures, the ylide and ylene structure (see Scheme 3). For benzylic ylides an additional resonance structure is possible. This mesomeric ylide structure stabilises the negative charge by delocalisation in the aromatic ring. By recording the ^1H NMR spectra of the aromatic protons at low temperatures it should be possible to observe slow rotation around the C_α–C_β bond of the benzylic group. The ^1H NMR spectra of the benzylic group of the arsorane **5b** and phosphorane **5a** are shown in Figure 2. At low temperatures the rotation around the C_α–C_β bond of the benzylic group is indeed slow on the NMR timescale. Therefore, NMR signals of all five protons can be recorded separately. At higher temperatures the rotation becomes faster resulting in an exchange of the 1-H and 5-H as well as the 2-H and 4-H atoms. This leads to broader signals and ultimately, after coalescence, only three sharp

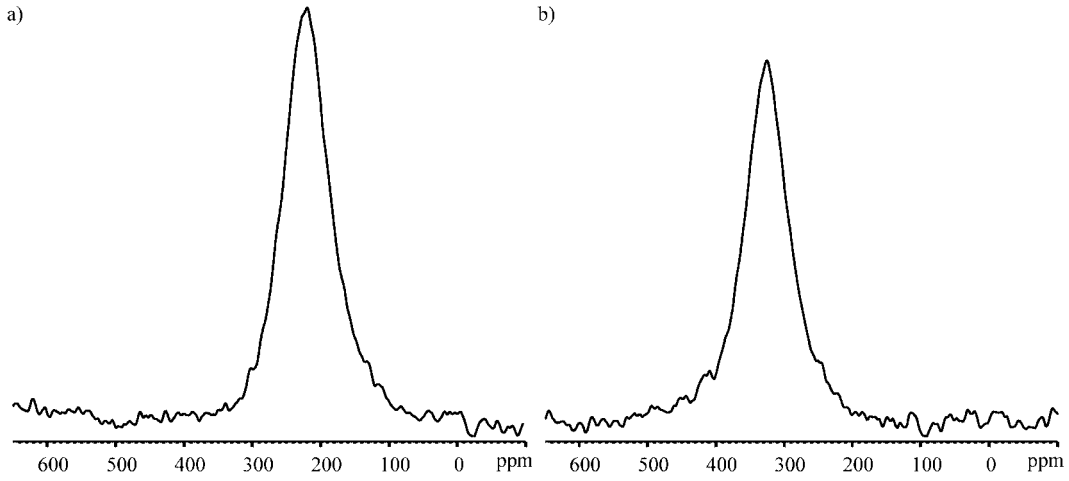
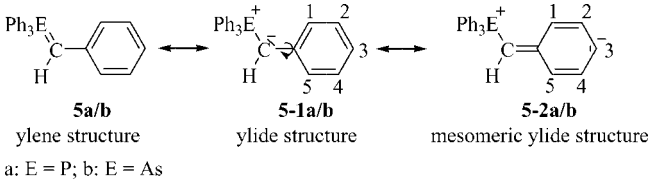


Figure 1. ^{75}As NMR spectra (0.05 M in CD_3OD) of a) benzyltriphenylarsonium bromide (**4b**) and b) triphenylarsane oxide (**7b**).

signals can be observed pertaining to the *ortho*, *meta* and *para* protons. Line-shape analysis provides thermodynamic data on the rotation barrier. For the arsorane $\Delta H^{\#}$ and $\Delta S^{\#}$ are 37.3 ± 1.5 kJ/mol and –10.9 ± 7.2 J/mol K yielding a $\Delta G^{\#(298)}$ value of 40.5 ± 3.7 kJ/mol. The phosphorane provides $\Delta H^{\#}$ and $\Delta S^{\#}$ values of 38.6 ± 2.1 kJ/mol and 13.3 ± 11.5 J/mol K yielding a $\Delta G^{\#(298)}$ value of 34.6 ± 5.5 kJ/mol.



Scheme 3. Mesomeric resonance structures of benzylic ylides.

Whereas we assume that the small values of $\Delta S^{\#}$ essentially mean a negligible activation entropy contribution, the $\Delta G^{\#}$ values indicate that for arsenic the contribution of the ylide versus the ylene structure is a bit more pronounced compared with phosphorus, in accordance with the literature.[12–14]

Having characterised the ylide **5b** only the oxaarsetane **1b** remained to be proven. A first indication of its existence was found in the ^{1}H NMR spectrum after addition of benzaldehyde to the ylide solution at –40 °C. Two signals arise as doublets coupling with each other (Figure 3). These protons belong to the oxaarsetane ring. This is astonishing since the analogous oxaphosphetane is not stable even at very low temperatures. When the temperature was raised stepwise to 30 °C these signals slowly disappeared with a concomitant increase in signals from stilbene. This corresponds to a slow reaction at room temperature.

These proton signals are not strict proof of an oxaarsetane because it is also conceivable that a betaine having two protons in the neighbourhood will give a similar spectrum. But the chemical shifts do indicate a four-membered ring. See for comparison ref.[15]. The coupling constant of 8.6 Hz do not allow the ring and betaine structures to be distinguished. Therefore, the benzaldehyde was labelled with ^{17}O. Since the benzylic oxaphosphetane is not stable we switched for comparison to the oxaphosphetane generated from ethylidenetriphenylphosphorane and benzaldehyde which has been proven to be stable at low temperatures by ^{31}P NMR spectroscopy.[16,17] Replacing methyl by phenyl in the γ position with respect to the oxygen atom in the four-membered ring was not expected to lead to a significant difference in the ^{17}O chemical shift. The ^{17}O NMR spectrum from the reaction of ethylidenetriphenylphosphorane and [^{17}O]benzaldehyde at –40 °C is displayed in part a of Figure 4. The signal at δ = 22 ppm belongs to the oxaphosphetane. The small signal next to the oxaphosphetane stems from the triphenylphosphane oxide generated during the addition of benzaldehyde to the ylide solution outside the NMR spectrometer. After raising the temperature to 25 °C the oxaphosphetane signal was consumed and the triphenylphosphane oxide signal dominated (Figure 4, b). Repetition of the experiment with benzylidenetriphenylarsorane (**5b**) provided the spectrum shown in Figure 4 (c). At –40 °C again a signal at around 22 ppm indicates the existence of the oxaarsetane **1b**. This was verified by raising the temperature as the signal disappeared and the oxide signal at δ = 50 ppm increased.

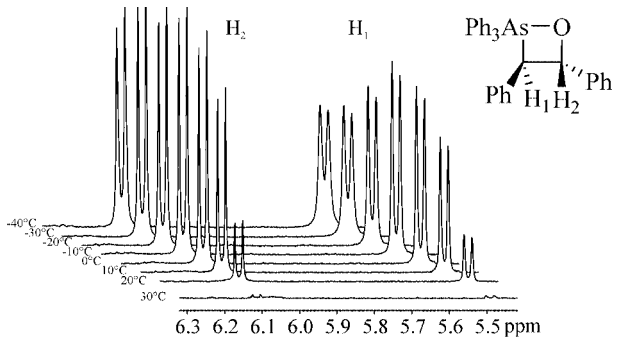


Figure 3. ^{1}H NMR spectra of the oxaarsetane **1b** (0.2 M in [D$_8$]-THF).

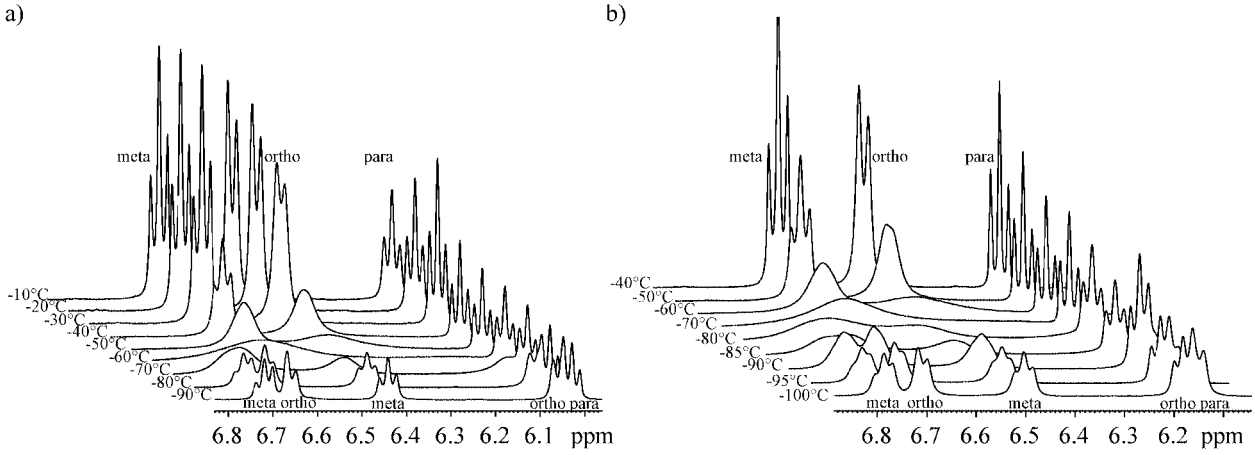


Figure 2. Dynamic ^{1}H NMR experiments (0.2 M in [D$_8$]THF) for a) benzylidenetriphenylarsorane (**5b**) and b) benzylidenetriphenylphosphorane (**5a**).

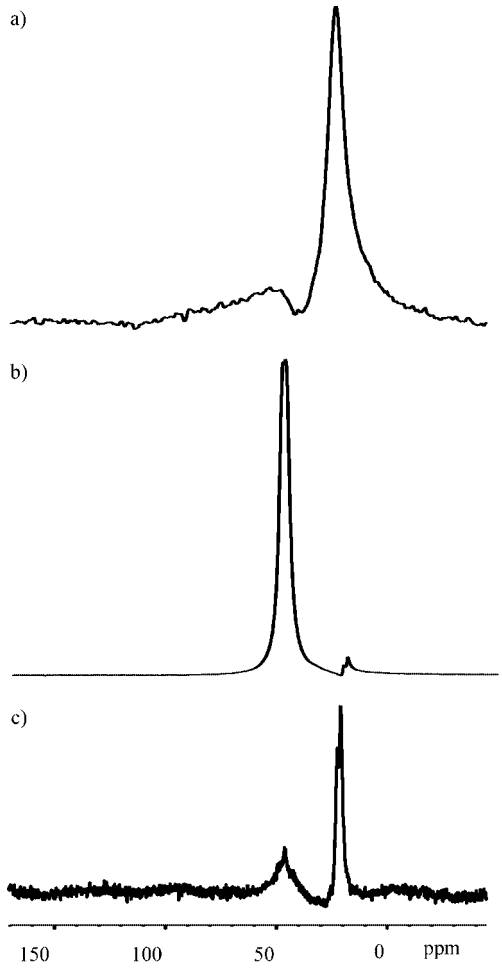


Figure 4. ^{17}O NMR spectra of a) the oxaphosphetane of ethylidenetriphenylphosphorane at –40 °C, b) triphenylphosphane oxide (**7a**) at 25 °C and c) oxaarsetane **1b** at –40 °C.

Conclusions

In summary we have shown by various NMR methods that oxaarsetanes exist and the reaction mechanism of the arsa-Wittig reaction is identical to that of the phospha-Wittig reaction.

Experimental Section

All compounds were prepared according to literature procedures.[17,18] All reactions were carried out with careful exclusion of moisture and air. The THF used was dried with sodium/benzophenone and freshly distilled prior to use. The benzaldehyde was also distilled. All routine NMR spectra were recorded with a Bruker DRX 400 spectrometer in $CDCl_3$, with TMS as an internal shift reference. ^{75}As NMR spectra were also recorded with a Bruker DRX 400 spectrometer and referenced to the Ξ scale. The ^{17}O NMR spectra were recorded with a Bruker DRX 600 spectrometer with $[D_8]$THF as solvent, shifts being referenced to the Ξ scale. The IR spectrum was recorded with a Thermo Nicolet Avatar 360 FT-IR E.S.P. spectrometer. Spectra simulations were performed by using SpinWorks 2.4.[19]

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Received: May 17, 2006
Published Online: August 24, 2006

