

## Probing Hydrogen-bonding Patterns in Cocrystals of Amides and Triarylphosphine Oxides Using High-resolution Solid-state $^{31}\text{P}$ NMR Spectroscopy

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The isotropic  $^{31}\text{P}$  chemical shift for hydrogen-bonded cocrystals formed between aryl sulfonamides and triarylphosphine oxides shows a linear correlation with the number of hydrogen-bonds,  $\text{N-H}\cdots\text{O-P}$ , formed by each triarylphosphine oxide fragment; this result can now be applied as a means of deriving information on the hydrogen-bonding patterns in related cocrystals of unknown structure.

Although the principles underlying hydrogen-bond formation are reasonably well understood, and simple rules have been developed<sup>1-3</sup> and applied<sup>4</sup> to the systematic description of hydrogen-bonding patterns in some systems, the determination of the hydrogen-bonding pattern in specific cases still generally requires full structure determination from X-ray or neutron diffraction data. Many hydrogen-bonded solids, however, are not amenable (for example, on account of their microcrystallinity) to direct structure-elucidation *via* diffraction-based techniques, and alternative approaches for determination of their hydrogen-bonding arrangements are required. In an attempt to circumvent the necessity of relying upon diffraction-based techniques, we have explored a method for counting the number of hydrogen bonds in cocrystals containing triarylphosphine oxides,  $\text{Ar}_3\text{PO}$ , by use of high-resolution solid-state  $^{31}\text{P}$  NMR spectroscopy. Specifically, the  $^{31}\text{P}$  NMR spectra presented here were recorded using the standard  $^{31}\text{P}$  CP-MAS method, which combines the  $^{31}\text{P}$ - $^1\text{H}$  cross polarization (CP) and magic-angle sample-spinning (MAS) techniques together with high-power  $^1\text{H}$  decoupling. A related, but much more narrowly specific, application of high-resolution solid-state NMR spectroscopy for studying structural trends has been the correlation of  $^{29}\text{Si}$  chemical shifts with Si-O-Al bond angles in sodalites.<sup>5</sup>

Triarylphosphine oxides form hydrogen-bonded cocrystals with a wide range of molecules containing hydrogen-bond

donor groups; in these materials, the  $\text{Ar}_3\text{PO}$  molecules can form one,<sup>3,6-11</sup> two,<sup>3,12,13</sup> or three<sup>14</sup> hydrogen bonds. We report here that there is a linear correlation between the isotropic  $^{31}\text{P}$  chemical shift and the number of hydrogen bonds per  $\text{Ar}_3\text{PO}$  molecule in cocrystals formed with N-H proton donors.

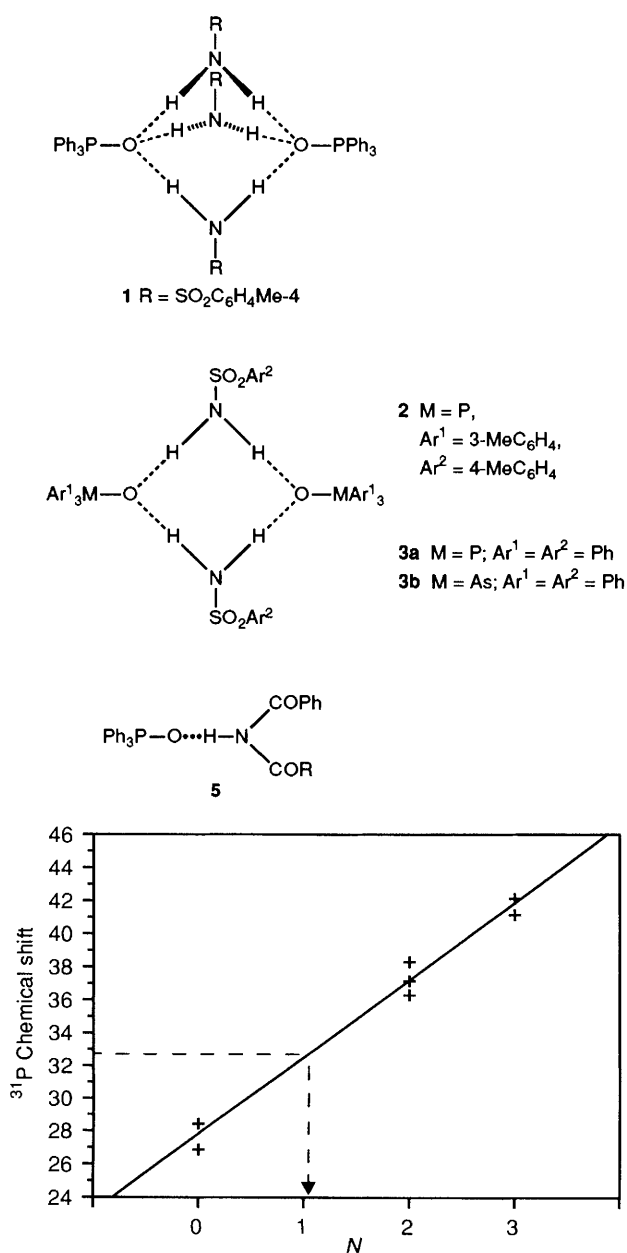
For polycrystalline triphenylphosphine oxide (TPPO) (Aldrich) two isotropic  $^{31}\text{P}$  resonances of roughly equal intensities were observed<sup>†</sup> at  $\delta$  26.7 and 28.4. TPPO is known to be polyphasic existing in both monoclinic and orthorhombic forms;<sup>15</sup> after recrystallisation of the commercial material from toluene, which yields the monoclinic form,<sup>15</sup> a single resonance at  $\delta$  26.8 was observed, while after recrystallisation from petroleum, which yields the orthorhombic form,<sup>16</sup> the  $^{31}\text{P}$  CP-MAS spectrum showed an intense resonance at  $\delta$  28.5,

<sup>†</sup> High-resolution solid-state  $^{31}\text{P}$  NMR spectra were recorded at 202.458 MHz, using the CP-MAS ( $^{31}\text{P}$ - $^1\text{H}$  cross polarization/magic-angle sample spinning/high-power  $^1\text{H}$  decoupling) technique, on a Bruker MSL500 spectrometer. Typical conditions were:  $^1\text{H}$  90° pulse length = 5  $\mu\text{s}$ ; CP contact time = 3 ms; total recycle delay = 30 or 60 s. For all samples, at least two spectra were recorded using different magic-angle spinning speeds (typically between *ca.* 6 and *ca.* 8 kHz) to allow isotropic peaks and spinning sidebands to be assigned unambiguously. All chemical shifts are given relative to the  $^{31}\text{P}$  resonance in 85%  $\text{H}_3\text{PO}_4$  as external standard.

**Table 1** Isotropic  $^{31}\text{P}$  chemical shifts for cocrystals of  $\text{Ar}_3\text{PO}$  with amides and for the two crystal phases of  $\text{Ph}_3\text{PO}$ 

		Number of hydrogen bonds ( $N$ ) per $\text{Ar}_3\text{PO}$ molecule	Isotropic $^{31}\text{P}$ chemical shift ( $\delta$ )
$(\text{Ph}_3\text{PO})_2(\text{H}_2\text{NSO}_2\text{C}_6\text{H}_4\text{Me}-4)$	<b>1</b>	3	42.2
$[(3\text{-MeC}_6\text{H}_4)_3\text{PO}](\text{H}_2\text{NSO}_2\text{C}_6\text{H}_4\text{Me}-4)$	<b>2</b>	2	41.1
$(\text{Ph}_3\text{PO})(\text{H}_2\text{NSO}_2\text{Ph})$	<b>3a</b> · 0.5 acetone	2	38.3
	<b>3a</b> · 0.5 ethanol	2	36.2
$(\text{Ph}_3\text{PO})[\text{HN}(\text{COMe})\text{Ph}]$	<b>4</b>	— <sup>a</sup>	37.2
$\text{Ph}_3\text{PO}$ , orthorhombic		0	32.7
$\text{Ph}_3\text{PO}$ , monoclinic		0	28.5
		0	26.8

<sup>a</sup> Unknown, see discussion in text, and Fig. 1.



**Fig. 1** Graph showing the linear correlation between isotropic  $^{31}\text{P}$  chemical shift ( $\delta$ ) and the number ( $N$ ) of  $\text{N}-\text{H}\cdots\text{O}-\text{P}$  hydrogen bonds per  $\text{Ar}_3\text{PO}$  molecule. Experimental data points for cocrystals of *known structure* are denoted +. The best-fit straight line through these data points is shown, and is defined by the equation:  $\delta = 27.7 + 4.7 N$ . Using this relationship, the number of hydrogen bonds per  $\text{Ph}_3\text{PO}$  molecule in **4** (for which  $\delta = 32.7$ ) is confidently predicted to be  $N = 1$  (as shown by the dotted lines).

with a minor resonance at  $\delta$  26.8. We thus assign the  $\delta$  26.8 and 28.5 resonances to the monoclinic and orthorhombic phases respectively. The only significant structural differences between these two phases of TPPO are in the phenyl ring conformations and in the molecular packing arrangement; nevertheless these are sufficient to produce the observed difference in chemical shifts.

Polycrystalline samples of the cocrystals of  $\text{Ph}_3\text{PO}$  and  $(3\text{-MeC}_6\text{H}_4)_3\text{PO}$  with sulfonamides, and with  $\text{PhNHCOMe}$  gave the isotropic  $^{31}\text{P}$  chemical shifts listed in Table 1. With the exception of **1**, which gave two closely separated resonances of approximately equal intensity, freshly prepared samples of all systems gave a single resonance.† For **1**, a single-crystal X-ray diffraction study<sup>14</sup> has shown that there are two similar but non-identical  $\text{Ph}_3\text{PO}$  fragments in the supramolecular aggregate which has 3-fold rotational symmetry; hence two  $^{31}\text{P}$  resonances of similar chemical shift, as observed, are expected. Single-crystal X-ray diffraction studies<sup>12</sup> have shown that there is only one  $^{31}\text{P}$  environment in the structure of **2**, as the supramolecular aggregate in this system is centrosymmetric. The related system **3a** crystallises from acetone as a solvate containing one molecule of acetone per aggregate; this cocrystal is isomorphous and isostructural with the corresponding solvate of **3b** ( $\text{Ph}_3\text{AsO})(\text{H}_2\text{NSO}_2\text{Ph})$ , the crystal structure of which does *not* contain any close contacts between the hydrogen-bonded aggregates and the solvent of crystallisation.<sup>12</sup> The small difference in isotropic  $^{31}\text{P}$  chemical shift observed for the isomorphous solvates of **3a** with acetone and ethanol represents the effects of the different solvent molecules lying in the cavities between the aggregates.

The correlation between the isotropic  $^{31}\text{P}$  chemical shift and the number of hydrogen bonds formed per  $\text{Ar}_3\text{PO}$  molecule is shown in Fig. 1; the clear discrimination shown between the different numbers of hydrogen-bond donors should enable this correlation to be utilised in a predictive manner for a wide range of hydrogen-bonded  $\text{Ar}_3\text{PO}$  cocrystals (provided, of course, that the samples are monophasic). Thus, as shown in Fig. 1, we predict that in cocrystals of **4**, the structure of which has not yet been determined because single crystals of appropriate quality for single-crystal X-ray diffraction studies have not been obtained, there is one hydrogen bond per  $\text{Ph}_3\text{PO}$  unit. Members of the closely related series of adducts **5**,  $(\text{Ph}_3\text{PO})[\text{HN}(\text{COPh})(\text{COR})]$  ( $\text{R} = \text{Me}, \text{Et}, \text{Ph}$ )<sup>3</sup> all contain only one hydrogen bond per  $\text{Ph}_3\text{PO}$  molecule and it is difficult to envisage any other plausible pattern in **4**.

† Polycrystalline samples of **1**, stored at room temperature for  $>3$  yr, also showed a low-intensity resonance at  $\delta$  10.5; in  $\text{CD}_2\text{Cl}_2$  solution these samples showed  $\delta$  29.0 (lit.<sup>14</sup> for  $\text{Ph}_3\text{PO}$  in  $\text{CD}_2\text{Cl}_2$ ,  $\delta$  29.2) and  $\delta$  14.9 (lit.<sup>14</sup> for  $\text{Ph}_3\text{P}=\text{NSO}_2\text{C}_6\text{H}_4\text{Me}-4$  in  $\text{CD}_2\text{Cl}_2$ ,  $\delta$  14.7). Similarly stored polycrystalline samples of **3a** also showed a resonance at  $\delta$  11.1; in  $\text{CD}_2\text{Cl}_2$  solution, these samples had  $\delta$  28.5 and 15.1. These observations result from a spontaneous, but slow, solid-state dehydration reaction, converting  $\text{Ph}_3\text{PO}$  and  $\text{H}_2\text{NSO}_2\text{Ar}$  to the phosphinimines  $\text{Ph}_3\text{PNSO}_2\text{Ar}$ , ( $\text{Ar} = \text{Ph}$  or  $4\text{-MeC}_6\text{H}_4$ ).

The dominant factor in the correlation between the isotropic  $^{31}\text{P}$  chemical shift and the number of hydrogen bonds appears to be the expected deshielding of the  $^{31}\text{P}$  nucleus as the number of hydrogen bonds increases. Other environmental factors appear to have comparatively little effect. For example, the P–O distances are essentially the same in all the systems considered here, and are independent of the number of hydrogen bonds per P–O group: 1.494(2) and 1.491(2) Å respectively in the monoclinic and orthorhombic modifications of TPPO<sup>15</sup> itself (at 100 K), 1.490(3) and 1.494(3) Å in cocrystal **1**<sup>14</sup> and 1.494(2) Å in cocrystal **2**.<sup>12</sup>

This approach to the counting of hydrogen bonds will prove invaluable in the structural investigation of crystalline systems for which crystals of sufficient size and quality for single-crystal X-ray diffraction studies cannot be obtained, as well as for amorphous materials and for other systems such as ordered multilayers. For O–H hydrogen-bond donors, structural data on cocrystals with  $\text{Ar}_3\text{PO}$  are surprisingly sparse, and only examples containing a single hydrogen bond per  $\text{Ar}_3\text{PO}$  molecule are known so far.<sup>7–9</sup> Work is in progress to extend the present study from NH donors to OH and other classes of hydrogen-bond donors; this will allow (*inter alia*) a detailed rationalization to be established for the form of the linear relationship between  $\delta$  and  $N$  (see Fig. 1).

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