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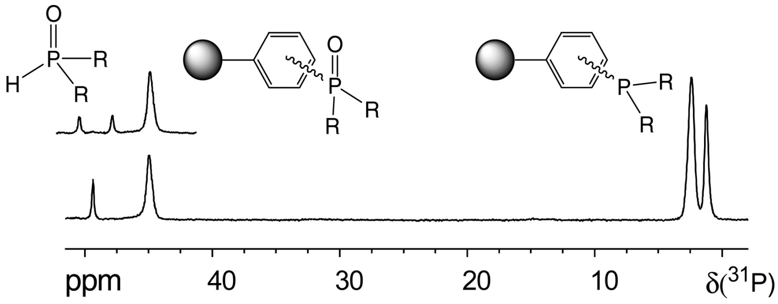

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Quantitative Determination of Loadings and Oxidation Products of Polystyrene-Bound Phosphines Using ^{31}P MAS NMR

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The use of ^{31}P magic angle spinning (MAS) NMR for the quantitative determination of resin loadings and the building up of oxidation products was investigated. Loadings of polystyrene-bound phosphines were evaluated via addition of triphenyl phosphate as reference compound. Results for a series of phosphines are consistent with those obtained from well-established analytical methods. The compounds were also investigated with ^{13}C MAS NMR, and the individual oxidation stabilities were monitored under oxygen atmosphere.

Introduction

In the field of phosphine-mediated organic chemistry, the use of polymer-bound phosphines has successfully been adapted to the conversion of alcohols to alkyl chlorides[1] and, in Wittig[2−4] or Mitsunobu[5−7] reactions, to facilitate the separation of the products from phosphine oxides at the end of the reaction. Diphenylphosphino polystyrene resins have also been employed to generate polymer-bound iridium,[8,9] nickel,[10] rhodium,[11−13] and ruthenium[14] catalysts for use in hydrogenation,[8,9,11] alkene dimerization,[10] and hydroformylation[12−14] reactions. Diphenylphosphinomethyl polystyrene resins have been used to complex palladium[15−18] and rhodium[11] for use as reusable catalysts in Suzuki[15] and hydrogenation[8,9,15] reactions, respectively.

The loading of the resins may be determined by elemental phosphorus analysis or by elemental bromine analysis after derivatization of the phosphines to the corresponding benzylbromides. To circumvent these principally undesired "destructive" and material- and time-consuming steps, analytical developments are directed to the on-resin analysis of the solid-supported compounds, both at intermediate stages and of the final product. Recent examples of these efforts involve ^{31}P NMR spectroscopy.[19] Although gel-phase NMR spectroscopy in combination with magic angle spinning (MAS) has advanced to the point that liquidlike spectra can be obtained for most resin-bound molecules,[20] this method is not often used for the quantification of resin loadings. Examples of ^{19}F gel-phase NMR in conjunction with a polymeric support or reagents bearing ^{19}F [21−24] or fluorobenzene as an internal standard[25] have been published, and ^{13}C MAS NMR[26] has been investigated for the quantitative analysis of a set of modified polystyrene (PS) resins used as starting materials for solid-phase organic synthesis. In the present study, a series of diphenylphosphino and dialkylphosphino polystyrene resins were studied with ^{31}P MAS NMR. In addition to the reproducible quantification of phosphine loadings, valuable information on the building up of phosphine oxides "on-resin" and the stability of these compounds under different atmospheric conditions could be obtained at the same time.

Results and Discussion

The ^{31}P chemical shifts of triaryl and trialkyl phosphines and their oxides cover the range from +60 to −60 ppm, with the oxides shifted to higher frequencies. Since the early days of NMR spectroscopy, this nucleus has been frequently investigated, and ^{31}P data have been compiled, for example, in ref 27. For the quantitative investigation of polymer-bound phosphines, we chose the reference compound triphenyl phosphate for three reasons: (a) the ^{31}P chemical shift of −18.0 ppm does not normally interfere with the signals of interest; (b) $O{=}P(OPh)_3$ is a solid, and therefore, exactly known amounts are readily available; and (c) the stability against oxidation and different chemicals is high enough to circumvent degradation processes during NMR measurements.

A necessary condition to obtain quantifiable ^{31}P NMR spectra is knowledge of the T_1 relaxation behavior of the individual components, because quantitative spectra require a recycle delay between individual pulses of $>5T_1$ of the slowest-relaxing nucleus. In chloroform solutions containing triphenylphosphine, triphenylphosphine oxide, and triphenyl phosphate, a longest T_1 value of 4.0 s was obtained for the latter. After the addition of 0.1 M chromium(III) acetylacetonate ($Cr(acac)_3$) as relaxation reagent, T_1 of triphenyl phosphate decreased to 800 ms; thus, a recycle delay of 4 s is sufficient for quantification purposes and was chosen whenever $Cr(acac)_3$ as relaxation reagent was present.

The accuracy of quantitative determinations of phosphines and phosphine oxides by ^{31}P NMR in solution has been shown to be better than 3%.[28] To reevaluate the reproduc-

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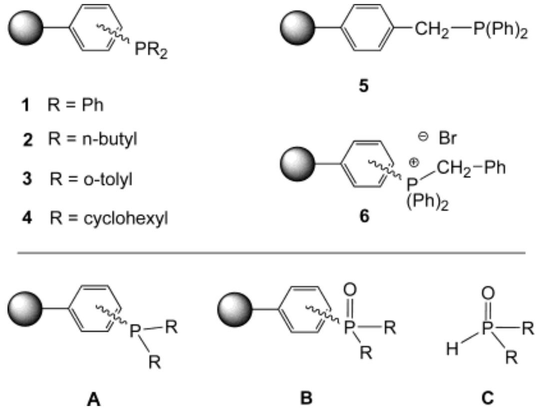

Figure 1. Structure formula of the investigated resin-bound phosphines **1**−**6** and general structures of the parent compounds (**A**) and their oxidation products (**B** and **C**).

ibility and accuracy of quantitative determinations by ^{31}P NMR, a test mixture containing exact amounts of triphenylphosphine and triphenyl phosphate was investigated (for sample composition, see the Experimental Section). The ^{31}P NMR spectra were recorded using either a solution-state broadband probe with 5-mm sample tubes or a solid-state CP/MAS probe equipped with 4-mm zirconia rotors. ^{31}P NMR resonances were observed at −18.0 ppm for $O{=}P(OPh)_3$, at −5.8 ppm for PPh_3, and at 29.4 ppm for $O{=}PPh_3$, the oxidation product of PPh_3. Integration yielded the relative sample composition straightforwardly. Whereas the relative amount of triphenyl phosphate was determined correctly (43.6 ± 0.4 mol %), we found, indeed, that the weighed amount of 56.4 mol % for PPh_3 was composed of 55.4 ± 0.4 mol % of the expected compound and 1.0 ± 0.1 mol % of its oxidized form, $O{=}PPh_3$. No differences were observed between the two probes. Vigorous shaking of a pure sample of PPh_3 in $CDCl_3$ under atmospheric conditions for several minutes led to an increase of the $O{=}PPh_3$ content to 2.5 mol %, demonstrating the sensitivity of phosphines under oxygen atmosphere.

A set of five different batches of chloroform-swollen triphenylphosphine polystyrene resins (**1a**−**e**) and five variably substituted phosphines (**2**−**6**) were investigated by ^{31}P-{^{1}H} MAS NMR spectroscopy. The structures of the resin-bound compounds are shown in Figure 1, and detailed information on their origins is given in the Experimental Section.

The resin-bound phosphines (m_{resin}) and the reference compound $O{=}P(OPh)_3$ (m_{ref}) were weighed directly into the zirconia rotors, and the loading, l_i, was determined according to eq 1,

$$l_i = 1000\,\frac{m_{\text{ref}}}{\text{MG}_{\text{ref}}}\,\frac{n_{\text{P(ref)}}}{I_{\text{ref}}}\,\frac{I_i}{m_{\text{resin}}}\quad[\text{mmol/g}] \tag{1}$$

where MG_{ref} is the molecular weight of triphenyl phosphate, and the number of atoms, $n_{\text{P(ref)}}$, contributing to its ^{31}P signal intensity is 1. The relative intensities of the reference signal I_{ref} as well as I_i of the polymer-bound component were determined from the ^{31}P{^{1}H} MAS NMR spectra.

For the signals of polymer-bound triphenylphosphine and triphenylphosphine oxide of **1a**, the addition of 0.1 M $Cr(acac)_3$ to the chloroform solvent reduced the T_1 relaxation times to 110−150 ms and again to 800 ms for $O{=}P(OPh)_3$. The stability of every resin-bound phosphine against the relaxation reagent has been monitored by determination of the molecular composition with and without addition of the Cr^{3+} salt.

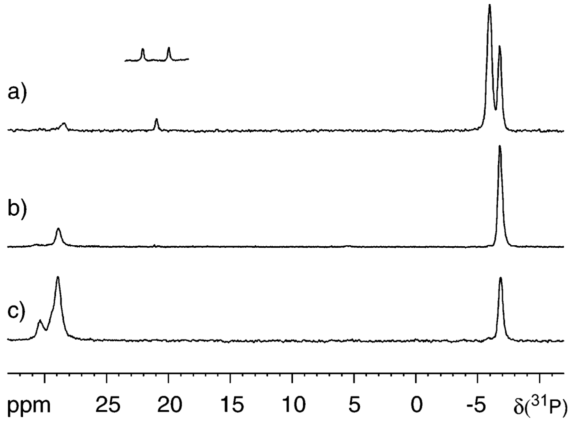

Figure 2. ^{31}P{^{1}H} MAS NMR spectra (161.97 MHz, 2000 Hz MAS rate) of $PS{-}PPh_2$ resins swollen in $CDCl_3$: (a) **1a**, the insert shows the spectrum without ^{1}H decoupling; (b) **1c**; and (c) **1d**.

In Figure 2, the ^{31}P{^{1}H} NMR spectra of three different batches of **1** are shown. The signals in the low-frequency region of the spectra originate from the expected compound with the substructure **A** (Figure 1). The ^{31}P NMR signal of **1a** is split into two resonance lines, with an intensity ratio of 2/1 (Figure 1a); the same signal splitting was observed for **1b** (spectrum not shown). The resin **1c** has been synthesized by polymerization of styrene using the comonomer 4-bromostyrene. Thus, its single ^{31}P NMR resonance at −6.7 ppm (Figure 2b) may be unambiguously attributed to a diphenylphosphino moiety attached in para position to the polystyrene resin, whereas the higher frequency signal at −5.9 ppm of **1a** (Figure 2a) may be assigned to the meta isomer. All ^{31}P chemical shifts were internally referenced relative to the signal of triphenyl phosphate at −18.0 ppm. Only small deviations of ±0.1 ppm were found for the reevaluated chemical shifts of different samples. The data of the main product (substructure **A**, Figure 1) is summarized in Table 1. The ^{31}P NMR signals of the oxidation products (substructure **B**) appear at 29 ppm. For **1d**, a sample that had been stored under normal atmosphere over years, an additional signal was observed at 31 ppm (not assigned).

The sharp signal at 21.0 ppm visible in the ^{31}P NMR spectrum of **1a** shows a splitting into a doublet with $^1J(^1H,^{31}P) = 481$ Hz in spectra recorded without proton decoupling during acquisition (insert of Figure 2a). It was shown by filtration and washing of swollen beads that this component was not attached chemically to the resin. The structure of $O{=}PPh_2H$ (structure **C**, Figure 1) was established unequivocally by 2D ^{1}H,^{13}C correlation experiments (HSQC[29] and HMBC[30]; for ^{1}H, ^{13}C, and ^{31}P chemical shifts, see the Experimental Section). The relative amount of $O{=}PPh_2H$ in a tightly closed solid-state sample rotor of **1a** increased from 3.4 to 5.6 mol % over several days. We also tried to determine the relative composition of **1a** (beads swollen in an excess of chloroform) by gel-phase ^{31}P NMR using a solution-state broadband probe. The relative amounts of the

Table 1. Composition (mol %) and Loading of PS-Supported Triphenylphosphines Determined by $^{31}P\{^1H\}$ NMR (± SD) with δ (^{31}P) Chemical Shifts and Line Widths of *p*/*m*-**A**[a]

	p/*m*-**A**			**B**		**C**	
compd (no. measurements)	rel amt	δ (^{31}P) *p*/*m*, ppm $\Delta\nu_{1/2}$ *p*/*m*, Hz	loading, mmol/g	rel amt	loading, mmol/g	rel amt	loading,[b] mmol/g
1a	89.2	−6.7/−5.9	1.112	5.9	0.074	4.9	0.062
(5)	(±2.2)	44/60	(±0.066)	(±1.2)	(±0.016)	(±1.1)	(±0.014)
1b	90.8	−6.7/−5.9	1.472	9.1	0.147	0.1	0.002
(2)	(±0.4)	47/65	(±0.036)	(±0.3)	(±0.009)	(±0.4)	(±0.001)
1c	76.3	−6.7[c]	0.660	23.7	0.205		
(2)	(±0.1)	56	(±0.063)	(±0.1)	(±0.019)		
1d	29.8	−6.7[c]	0.367	70.2	0.862		
(3)	(±2.4)	59	(±0.028)	(±2.4)	(±0.034)		
1e	91.6	−7.1[c]	1.764	2.1	0.043	6.3[d]	0.104
(4)	(±0.8)	93	(±0.035)	(±0.2)	(±0.003)	(±1.0)	(±0.014)

[a] For substructures **A**−**C**, see Figure 1. [b] The components with substructure **C** are not resin-bound. [c] Only the para-substituted isomer was observed. [d] The signal at −14.7 ppm of a resin-bound component was not assigned.

resin-bound **A** and **B** could still be determined adequately (**A**/**B** = 93.8/6.2). In a solid-state rotor, the sample volume equals the coil volume, and therefore, the signal intensity of the whole sample is detected. In the sample tubes used for gel-phase NMR, the beads floated at the top of the liquid, leaving a zone with clear solution at the bottom, both regions partly outside the NMR detection zone. The soluble byproduct **C** and the reference triphenyl phosphate were distributed over the whole area. Therefore, the concentration of **C** with respect to **A** and **B** as well as the loadings of **A** and **B** could not be determined using the solution-state probe.

The ^{31}P line widths were evaluated by simultaneously fitting the three free parameters' chemical shift, line width, and signal intensity using Lorentzian shapes for all signals according to the protocol by Massiot.[31] For the reference compound O=P(OPh)$_3$, line widths of 21−24 Hz were determined. For **1e** ($\Delta\nu_{1/2}$ = 93 Hz, spectrum not shown), a sensibly enhanced value has been found, as compared to the other PS−PPh$_2$ resins ($\Delta\nu_{1/2} \approx$ 44−65 Hz, Table 1), owing to the more rigid structure of **1e** (2% cross-linking of **1e**, as compared to 1% for all other resins). For **1a** and **1b**, the line widths of the diphenylphosphino moieties attached in meta position to the polystyrene backbone show slightly enhanced values when compared to *p*-**A** (Table 1). The reason for this observation may be a decrease of mobility caused by hindered rotation around the aryl-polystyrene bonding of *m*-**A**, as compared to *p*-**A** (Figure 1). The relative sample compositions and the loadings of **1a**−**1e** are given in Table 1. The integration of the ^{31}P resonances of **1e** from 30 to −20 ppm, including a broad background signal (0 to −20 ppm) and the not assigned signal at −14.7 ppm, yielded a loading of 2.85 mmol/g phosphorus (manufacturer value as determined by P elemental analysis: 3.08 mmol/g). The remaining loading data determined by ^{31}P NMR will be compared and discussed with the results from P or Br elemental analysis later in the text.

The ^{31}P NMR spectra of alkyl and aryl substituted phosphines **2**−**6** (Figure 1) bound to PS resins are shown in Figure 3. At −18.0 ppm the signal of the reference compound O=P(OPh)$_3$ is observable in the spectrum of **6** (Figure 3e). For clarity, all other spectra are shown for samples without addition of triphenyl phosphate. For compounds **2**, **3**, and **4**, the signal pattern with a splitting of the phosphine resonances in the low-frequency region is observable with an intensity ratio of 2/1. As shown for **1**, this signal pattern may be explained by the ^{31}P NMR resonances of the meta-substituted PS moieties at higher, and the para-substituted components at lower, frequencies.

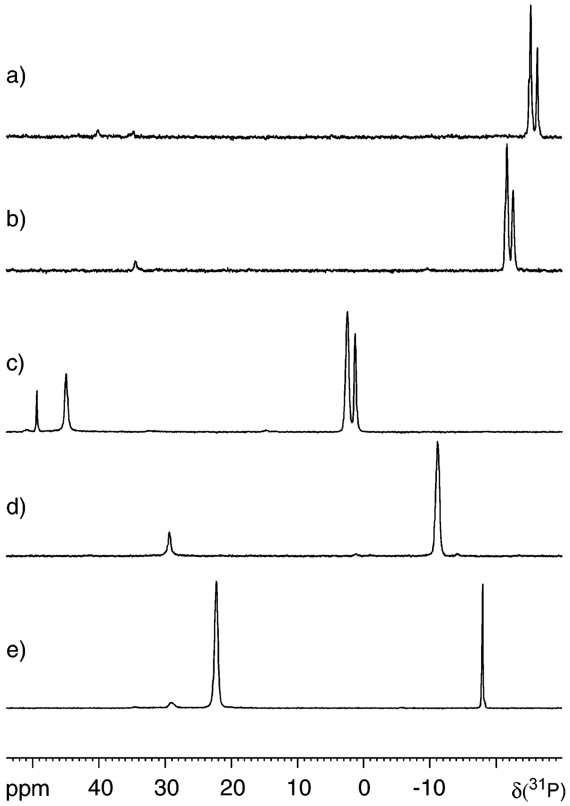

Figure 3. $^{31}P\{^1H\}$ MAS NMR spectra (161.97 MHz, 2000 Hz MAS rate) of PS-supported phosphines: (a) **2**, PS−P(*n*-butyl)$_2$; (b) **3**, PS−P(*o*-tolyl)$_2$; (c) **4**, PS−P(cyclohexyl)$_2$; (d) **5a**, PS−CH$_2$−PPh$_2$; and (e) **6**, PS−(benz)PPh$_2^+$Br$^-$, the signal at −18.0 ppm stems from O=P(OPh)$_3$.

The relative composition of most compounds showed the expected phosphines (substructure **A**) as the major component (~90% purity, Table 2). However, resin **4** bearing cyclohexyl substituents (71%) and resins **5a** (82%) and **5b** (46%, spectrum not shown in Figure 3) with phosphinomethyl ligands showed appreciably reduced purity and consequently decreased activity of these resins used for chemical syntheses. It was noticed that for resins of type **5**,

Table 2. ^{1}J (^{1}H,^{31}P), δ^{31}P, Line Widths $\Delta\nu_{1/2}$, Compositions, and Loadings Determined by ^{31}P NMR of PS-Supported Phosphines **2**−**6**

compd; ^{1}J (^{1}H,^{31}P), Hz	substructure	δ ^{31}P, ppm	$\Delta\nu_{1/2}$, Hz	composition,[a] mol %	loading,[b] mmol/g
2	*p*/*m*-**A**	−26.2/−25.2	31/50	91.6	0.373
J = 444	**C**	34.9	33	5.1	0.025
	B	40.2	80	3.3	0.011
3	*p*/*m*-**A**	−22.6/−21.6	43/59	88.0	0.713
J = 475	**C**	17.3	22	1.2	0.009
	B	34.5	64	4.6	0.032
	n.a.[d]	≈100		6.2	0.071
4	*p*/*m*-**A**	1.2/2.4	45/74	71.3	0.868
	B	45.0	74	20.7	0.244
J = 431	**C**	49.4	27	5.2	0.058
	n.a.[d]	51/58		2.8	0.036
5a[c]	n.a.[d]	−14.2		1.3	0.023
	p-**A**	−11.2	109	82.2	1.348
	B	29.3	85	16.5	0.288
5b	n.a.[d]	−14.2		0.8	0.012
	p-**A**	−11.2	109	46.0	0.677
	B	29.3	83	53.2	0.783
6	*p*-**A**	22.2	94	94.3	1.066
	B	29.0	160	5.7	0.069

[a] Mean value of four different samples. [b] Mean value of two different samples. Components with substructure **C** are not resin-bound. [c] Traces of O═PPh$_2$H (**C**) with ^{1}J (^{1}H,^{31}P) = 475 Hz were detected. [d] Signals not assigned.

there was a marked tendency to oxidation, depending on the reaction and workup conditions. Much lower amounts of phosphine oxides were produced when the temperature was kept low and the methanol washes were carried out quickly. The total loading of **5b** (1.47 mmol/g) is on the same order as the value of 1.66 mmol/g obtained for **5a**, because the resins were prepared according to the same procedure.

The presence of products with the structural formulas **C** (Figure 1), released by oxidation reaction, was indicated by the coupling constants ^{1}J (^{1}H, ^{31}P) in the range of 430−480 Hz observed in the ^{31}P NMR spectra of **2** − **4** recorded without ^{1}H decoupling (Table 2). Amounts of up to 6 mol % of unknown components were detected for **3**−**5**. The loading of 1.07 mmol/g determined for **6** corresponds to a value of 1.31 mmol/g for its parent compound **1b**, because **6** was prepared by reaction of **1b** with benzylbromide. This agrees with the data found for **1b** (1.47 mmol/g) of the main component (*p*/*m*-**A**) in the series of polystyrene supported triphenylphosphines (Table 1). As found for **1a** and **1b**, smaller line widths were found without exceptions for components with substructures *p*-**A**, as compared to *m*-**A**. The observed line widths of 22−33 Hz for the released products **C** are on the same order as the signals of O═P(OPh)$_3$ (21−24 Hz).

The loadings of polystyrene-supported resins are normally determined by phosphorus or by bromine elemental analysis after coupling of the phosphines to the corresponding benzylbromides. In Table 3, the values obtained by these methods are compared to the loadings determined by the ^{31}P MAS NMR method. The total loadings shown in Tables 1 and 2 were considered (substructures **A**−**C**, including the not-assigned signals), because the phosphorus elemental analysis does not differentiate between chemically distinguishable species. The data were cross-checked using the ^{13}C MAS NMR method developed earlier[26] (Experimental Section). For each of the compounds **2**−**6** individually, unambiguously assignable carbon resonances were determined, which do not overlap with signals from the polystyrene framework (^{13}C chemical shifts and number of carbon atoms contributing to the signals are given in Table 3). Their signal intensities were weighed against the signals of the reference compound tetrakis(trimethylsilyl)silane or the solvent and the loadings obtained according to the method A, which was chosen preferentially, since for **3**, **5a**, and **6**, substantial signal overlapping of the phosphine ligands with the ^{13}C NMR resonances of the polystyrene framework was observed, making the application of method B difficult.[26]

Table 3. Loading of Polystyrene-Bound Phosphines from ^{13}C{^{1}H}[a] and from ^{31}P{^{1}H} MAS NMR with Standard Deviations and from Phosphorus or Bromine Elemental Analysis[b]

	elemental analysis					
compd	P	Br	loading (^{31}P),[c] mmol/g	loading (^{13}C),[d] mmol/g	δ ^{13}C, ppm	no. carbons
1a	1.5	1.2	1.25 ± 0.07			
2	0.68	0.50	0.41 ± 0.02	0.66	13.3	2C
3	0.80		0.83 ± 0.05	0.75	20.6	2C
4	1.43		1.21 ± 0.04	1.40	21−35	12C
5a	1.8	1.1	1.66 ± 0.07	1.30	138.0	2C
6			1.14 ± 0.04	1.23	30.3	1C

[a] δ ^{13}C and no. of carbon atoms used for determination according to ref.26. [b] Br analysis after coupling with benzylbromide. [c] Total amounts given in Tables 1 and 2. The standard deviations of 2−4 independently measured samples are considered. [d] Single measurements with estimated standard deviations of ± 6%. [26]

Standard deviations in the range of 3.3−6.0% were obtained for the loadings determined by ^{31}P MAS NMR (median at 4.6%, Table 3). For the ^{13}C NMR method, deviations of 3.3−11.4% with a median at 6.3% were observed. [26] Since in the current contribution, only single ^{13}C MAS NMR experiments were performed, individual standard deviations of 6% were assumed. For **1a**, the loading of 1.25 mmol/g determined by ^{31}P NMR is situated between the 1.5 mmol/g determined by elemental analysis of phos-

Table 4. Composition and Loading of Polystyrene-Bound Phosphines Exposed to Oxidation for 68 h[a] Monitored by $^{31}P\{^1H\}$ MAS NMR

compd	*p*/*m*-**A**, mol %	**B**, mol %	n.a.,[d] mol **%**	**C**[b]	loading after oxidation, mmol/g	loading before oxidation,[c] mmol/g
1a	81.6	18.4		+++	1.18	1.19
1b	80.5	19.5		+++	1.54	1.62
1c	61.7	38.3		+	0.69	0.87
1d	12.0	88.0		−	1.21	1.23
1e	85.9	14.1		−	2.06	1.91
2	48.2	35.9	15.9	+++	0.34	0.38
3	82.1	12.6	5.3	+	0.67	0.82
4	35.3	61.1	3.6	+++	0.86	1.15
5a	22.2	77.3	0.5	+++	1.32	1.66
6	94.4	5.6		−	0.98	1.14

[a] 7 bar O_2, ambient temperature, swollen in $CDCl_3$. [b] Elimination products (substructure **C**) found in the filtered solution (+++, clearly detectable by ^{31}P NMR; +, minor amounts; −, not detectable). [c] Loading of polystyrene-bound compounds (substructure **C** excluded) from Tables 1 and 2. [d] n.a. Signals not assigned.

phorus and 1.2 mmol/g from elemental analysis of bromine after coupling with benzylbromide. The value of 1.11 mmol/g obtained for the main component (see Table 1) corresponds well with the data of the bromine elemental analysis, since exclusively the component with substructure **A** is able to react with benzylbromide. The evaluation of ^{13}C NMR data for **1a** was not possible because of the overlapping of the carbon signals in the aromatic region with the resonances of the polystyrene backbone as well as unclear signal assignments. Whereas the loading of 0.68 mmol/g from phosphorus elemental analysis of **2** is in excellent agreement with the value of 0.66 mmol/g from the ^{13}C NMR method, it remains unclear why the ^{31}P NMR data showed a 40% reduced value of 0.41 mmol/g. However, the loading of 0.50 mmol/g, determined by bromine analysis after chemical conversion to the benzylbromide, showed a trend in the same direction as the ^{31}P NMR data. For resins **3**, **4**, and **6**, the results from elemental analysis and from ^{13}C and ^{31}P NMR are consistent within the accuracy of the measurements (within two standard deviations, 95% confidence level). On the other hand, larger variations were observed for **5a**. The results determined by the ^{31}P NMR method and the phosphorus elemental analysis (1.66 and 1.8 mmol/g, respectively) are of the same order. The loading of 1.35 mmol/g (determined for the component with substructure **A**, Table 2) is comparable to the data obtained by ^{13}C NMR. Nevertheless, they exceed the value of 1.1 mmol/g from bromine elemental analysis (+20%). This might be explained by incomplete conversion of **5a** to the corresponding benzylbromide.

The oxidation stability of the resins was investigated under oxygen atmosphere (7 bar O_2, ambient temperature, and beads swollen in chloroform). In Figure 4, the typical behavior of conversion from substructure **A** to **B** is monitored for **4**. The relative amount of the main component (71.3%, Table 2) decreased to 60.4 and 35.3% after 2 and 68 h, respectively, under oxygen atmosphere. At 16 and 32 ppm, new signals of yet not identified byproducts appeared. The insert at high frequency (Figure 4a) shows the ^{31}P NMR spectrum without proton decoupling, monitoring the presence of the cleavable oxidation product **C** with ^1J (^1H, ^{31}P) = 431 Hz.

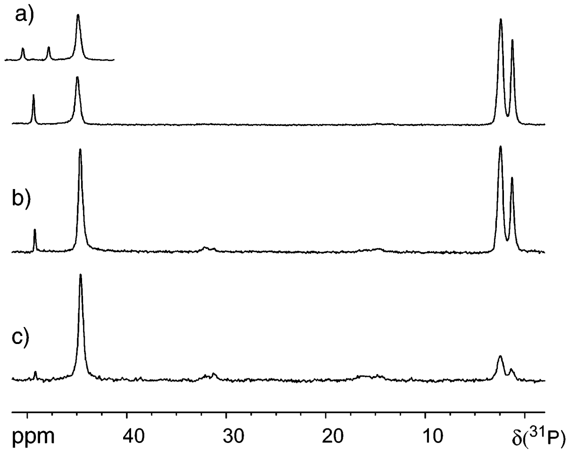

Figure 4. Oxidation progress of PS−P(cyclohexyl)$_2$ (**4**) monitored by $^{31}P\{^1H\}$ MAS NMR after (a) 0 h, (b) 2 h, and (c) 68 h, respectively, with (b) and (c) subjected to a 7-bar O_2 atmosphere. The insert of (a) shows the spectral region without ^1H decoupling.

The soluble products, which did arise upon oxidative cleavage, were isolated from the solid support by washing the resin with chloroform-*d*, followed by partial evaporation of the solvent. ^1H and ^{31}P NMR spectra could be obtained of these isolated fractions; however, the rather low concentrations of these components and impurities observable in the ^1H solution state NMR spectra prevented their complete assignment by 2D ^1H,^{13}C correlation experiments. Whereas **1c** and **3** showed only minor amounts of the released phosphine oxides (substructure **C**), the resins **1d**, **1e**, and **6** showed no soluble, phosphorus-containing products at all (Table 4).

Additionally, the relative sample composition and loading of the polystyrene-bound phosphines after exposure for 68 h to a 7-bar oxygen atmosphere is summarized in Table 4. Before sample preparation, the oxidized resins were washed with chloroform and methanol and dried under high vacuum until constant weight was obtained. Except for **1d**, the relative sample compositions of the resins bearing aromatic substituents only (**1a**−**1e** and **3**) show low conversions from the phosphines (substructure **A**) to the corresponding phosphine oxides (substructure **B**). Thus, their handling in chemical syntheses may be rather uncritical. The same is true for **6**, in which the composition remained virtually the same. However, the resins with alkyl substituents (**2**, **4**, and **5**) showed increased oxygen sensitivity and lost their activities rapidly. The relative concentrations of the resin-bound, not-assigned byproducts of resins **3**, **4**, and **5a** remained stable (compare Tables 2 and 4), whereas for **2**, new ^{31}P NMR signals were observed at 22.0 and 32.0 ppm during the oxidation process with relative amounts of totally 16% (Table 4). The tendency to decreased loading values after the oxidation process can be explained by the release of cleavable components.

Conclusions

The stability and composition of resins can have significant effects on the reproducibility and yield of solid-phase phosphine-mediated reactions. These properties vary considerably within and between batches of commercially available beads, and quantifiable analytical methods to study them are required. The ^{31}P MAS NMR method presented allows fast and simultaneous determination of loading and composition by integration of NMR intensities of selected resin resonances and signals of an internal reference compound. The application of the method shows several advantages compared to the ^{13}C NMR work published recently.[26] Within 10 min, the ^{31}P NMR spectra show reasonable signal/noise ratios (^{13}C: 2−3 h) with ∼10 w/w % of the compound needed, and minor components (≈ 1%) are also detectable. The larger dispersion of chemical shifts in ^{31}P NMR allows the differentiation between similar substructures (e.g., phosphines from phosphine oxides or even para from meta phosphine-substituted aromatics), which could not be distinguished by ^{13}C MAS NMR.

Considerable amounts of resin-bound phosphine oxides and cleavable products were detected in the investigated samples. The results obtained by elemental analysis of phosphorus include these byproducts and do not normally agree with the potential reactivity of the resins expected for syntheses. The chemical conversion of solid-phase bound phosphines to the corresponding benzylbromides with subsequent bromine elemental analysis reflects the reactivity of the beads much better. However, this additional step is time-consuming, and the completeness and selectivity of reaction must be well established.

The stability of the swollen resins to oxidation was investigated under oxygen atmosphere. It was observed that the activity of phosphines bearing aromatic substituents remained reasonably high, whereas alkyl-substituted phosphines showed fast deactivation of the reactive sites.

Experimental Section

Chemicals and Polystyrene-Supported Phosphines. Chloroform-*d* (99.8 atom % D) was purchased from Dr. Glaser AG, CH-Basel, tetrakis(trimethylsilyl)silane (purum, >97%, art. 87642, lot 46539/1), triphenylphosphine (99.8%, art. 93090, lot 407575/1), triphenylphosphine oxide (99.7%, art. 93100, lot 405798/1), and chromium(III)acetylacetonate ($Cr(acac)_3$, pract., 97%)) were from Fluka-Chemie AG, CH-Buchs. The reference compound triphenyl phosphate (99.9%, art. 2,4128-8, lot PU07025DR) and the high-loaded, polymer-supported triphenylphosphine (art. 36,645-5 (**1e**)) were purchased form Aldrich, CH-Buchs. The following polystyrene-supported phosphines from Calbiochem-Novabiochem, CH-Läufelfingen, were investigated in detail: four batches of triphenylphosphine polystyrene (**1**) (art. 01-64-0308, lots A25793 (**1a**), CR-304 (**1b**), CR-309 (**1c**), and HWS-363.2 highly oxidized (**1d**)), di-*n*-butylphenyl phosphine polystyrene (**2**) (art. 01-64-0402, lot A24928), di-*o*-tolylphenyl phosphine polystyrene (**3**) (art. 01-64-0395, lot A24515), dicyclohexylphenyl phosphine polystyrene (**4**) (art. 01-64-0394, lot A24516), diphenyl phosphinomethyl polystyrene (art. 01-64-0351, lots A25625 (**5a**) and A26108 (**5b**)), and benzyl triphenyl phosphonium bromide polystyrene (**6**) (lot CR-310, derivative of **1b**).

NMR Experiments. The ^{31}P MAS NMR spectra were recorded on a Bruker ASX-400 MHz NMR spectrometer at ambient temperature using a 4-mm CP/MAS broadband probe. The resins were weighed directly into the zirconia rotors (12−30 mg, depending on the swelling capacity). The internal reference triphenyl phosphate was weighed to the resin as chloroform solution (110−140 mg) doped with 0.1 M chromium(III) acetylacetonate as relaxation reagent; the parameter m_{ref} (see eq 1) was calculated as $m_{\text{solution}}m_{\text{O=P(OPh)}_3}/(m_{\text{O=P(OPh)}_3} + m_{\text{chloroform}})$. The ^{31}P NMR spectra were acquired in the inverse gated mode at 161.98 MHz with a 4.0-μs 90° pulse length, a sweep width of 47 kHz, a proton decoupling field of 25 kHz (SPINAL-64 decoupling[32]), and a MAS rotation rate of typically 2000 Hz. For a reasonable signal-to-noise ratio for the minor components, typically 128 transients were recorded (8k data points) applying relaxation delays of 4 s (16 transients and 60-s delays were used for samples without Cr^{3+}relaxation reagent). The FIDs were zero-filled to 16 k data points and treated with 5-Hz line-broadening before Fourier transformation, and the relative signal intensities were determined using the Bruker integration routine. The baselines of the integrals were corrected manually, and the integral values were determined relative to the signal of the reference compound triphenyl phosphate. The ^{31}P chemical shifts are given in parts per million (ppm) relative to the signal of $O{=}P(OPh)_3$ at −18.0 ppm as internal standard. The line widths were evaluated using the line-shape-fitting program dmfit developed by Massiot et al. (program available at no charge at http://crmht-europe.cnrs-orleans.fr/dmfit/default.htm).[31] Good convergence was reached for every spectrum using appropriate numbers of signals with Lorentzian shapes by simultaneously fitting the three free parameters, chemical shift, line width, and signal intensity. The ^{31}P T_1 spin lattice relaxation times were determined with the inversion recovery experiment;[33] the results are given as the mean of an area and intensity fit of 16 ascending delays (500 μs, 20 s). The solution-state ^{1}H NMR spectra were recorded on a broad-band probe applying 90° pulse widths of 11.2 μs, and for the ^{31}P spectra, 45° pulse widths of 4.0 μs with relaxation delays of 4 s were used with ^{1}H WALTZ[34] decoupling (decoupling field of 2.3 kHz). To investigate the accuracy of the ^{31}P concentration determinations, a test solution containing 113.5 mg of PPh_3 and 109.3 mg of $O{=}P(OPh)_3$ dissolved in 4.00 g of $CDCl_3$ was prepared.

The ^{13}C NMR solid-state spectra of the phosphines were recorded on a 7-mm CP/MAS probe at 100.61 MHz with a MAS rate of 2000 Hz. The samples were prepared directly in the zirconia rotors by weighing known amounts of the resins (20−70 mg, depending on the swelling capacity), the internal reference tetrakis(trimethylsilyl)silane (6−12 mg), and the solvent chloroform-*d* (≈360 to 400 mg) doped with 0.1 M chromium(III) acetylacetonate. ^{13}C single-pulse spectra were acquired in the inverse gated mode at 100.61 MHz with 4.8-μs 90° pulse lengths and a proton decoupling field of 30.5 kHz (SPINAL-64 decoupling sequence[32]). The spectra were processed according to the experimental setup as described in ref 26.

The structure of diphenylphosphine oxide (O═)PPh$_2$H was characterized using ^{1}H,^{13}C 2D correlation experiments on a 5-mm broadband inverse probe with *z*-gradient (100% gradient strength of 10 G cm^{-1}) and 90° pulse lengths of 8.2 (^{1}H) and 10.5 μs (^{13}C). The gradient selected 2D ^{1}H,^{13}C chemical shift correlated spectra were recorded in chloroform solution (HSQC[29] and HMBC;[30] spectral data available from the author). The following chemical shifts have been assigned: δ ^{1}H (CDCl$_3$, 400.13 MHz): 8.08 (1H, d, *J*(H,P) = 481 Hz), 7.58 (2H, *p*-H), 7.51 (4H, *m*-H), 7.33 (4H, *o*-H). δ ^{13}C (100.61 MHz): 133.2 (d, *p*-C), 132.7 (s, *ipso*-C), 131.4 (*d*, *o*-C), 129.5 (d, *m*-C). δ ^{31}P (161.98 MHz): 21.0. The ^{1}H and ^{31}P NMR spectra correspond to the data given in the literature. δ ^{1}H (C$_6$D$_6$, 80 MHz): 7.74 (1H, d, *J*(H,P) = 476 Hz), 7.45 (4H, *o*-H), 6.95 (8H, *p*- and *m*-H). δ ^{31}P (121 MHz): 18.6.[28]

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