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A direct approach to selective sulfonation of triarylphosphines

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Abstract—A practical and convenient synthesis of mono-, di- and a trisulfonated phosphines from triphenylphosphine analogs, (2,4-dimethylphenyl)$_{3-n}$-(phenyl)$_n$-phosphine and (4-methoxyphenyl)$_{3-n}$-(phenyl)$_n$-phosphine ($n=0$–2), is described, respectively. This represents an easy way to prepare water-soluble phosphines with complete selectivity, and with essentially no phosphine oxide formation.

Aqueous-organic two-phase catalysis is one of the most dynamically developing areas of molecular catalysis, since it provides a simple solution to the problem of product isolation and catalyst recovery. The catalyst-complex, modified by water-soluble ligands, can be separated from the hydrophobic products by the separation of the aqueous and the organic phases. The significance of this environmentally benign concept is demonstrated by an increasing number of industrial applications,[1] however, it has obvious drawbacks. Meeting the double requirements of good catalytic activity and quantitative catalyst recovery is not always simple. Primarily, depending on the water-solubility of the substrate, besides the basic concept,[2] several modified techniques[3] can be adopted too. Thus, a need for applicable ligands with a wide range of water-solubility has arisen.

Sulfonated arylphosphines are used most frequently as modifying ligands in aqueous and aqueous-organic two-phase catalysis. In general, these phosphines are obtained by the direct sulfonation of the aromatic rings.[4] Selective sulfonation, controlling the number of entering SO_3 units, would be a direct way to control the hydrophilic character of the ligand.

Much effort has been devoted to the selective preparation of triphenylphosphine derivatives with different degrees of sulfonation. Most of these attempts have focused on the sulfonation medium, reaction conditions and work-up procedure.

Two reasons must be emphasized to explain why the syntheses of sulfonated triphenylphosphine-derivatives are fairly challenging. (i) The phenyl rings are directly attached to the phosphorus. Due to the deactivating effect of the protonated phosphorus atom, the sulfonation requires an aggressive sulfonating medium (fuming sulfuric acid), and relatively long reaction time. As a consequence, oxidation is a common side-reaction, particularly in the preparation of trisulfonated triphenylphosphine (TPPTS).[4b,4e] (ii) Differences between the activation energies for the sulfonation of the non-, mono- and disulfonated species are quite small. Accordingly, controlling the sulfonation degree is difficult and recognized as another major obstacle.

Due to the intensive academic and industrial interest of this area, several new methods have been developed recently. Herrmann and his co-workers have introduced the use of superacidic medium (a mixture of anhydrous sulfuric acid and orthoboric acid) for sulfonation of phosphines.[4g] Although this sulfonation method needs a slightly more complex work-up procedure than the conventional one, owing to the complete protonation of the phosphorus and the lack of free SO_3, oxidation can be mostly avoided.

A new method has been elaborated by Joó for the preparation of monosulfonated triphenylphosphine (TPPMS).[4i] The procedure is referred to by the authors as *incomplete monosulfonation*, which expresses very

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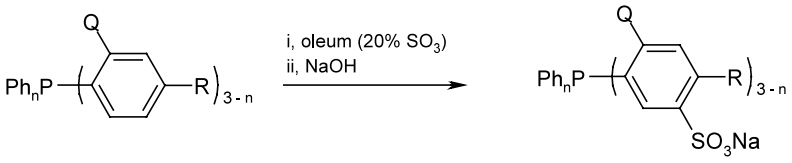
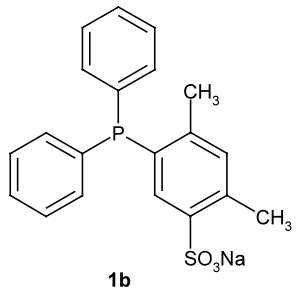
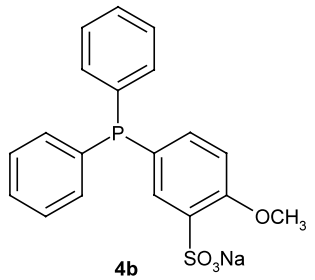


1a - 6a **1b - 6b**

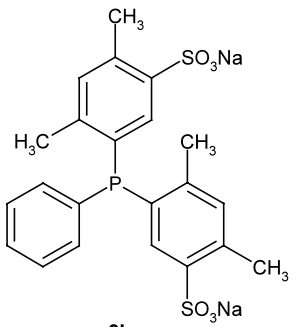
n = 0, 1, 2
Q = R = CH$_3$ or Q = H, R = OCH$_3$



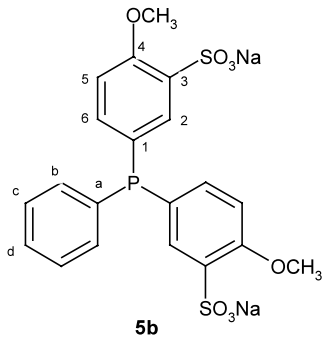
1b



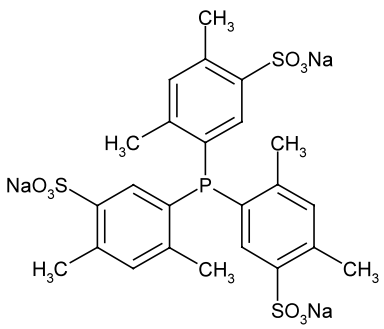
4b



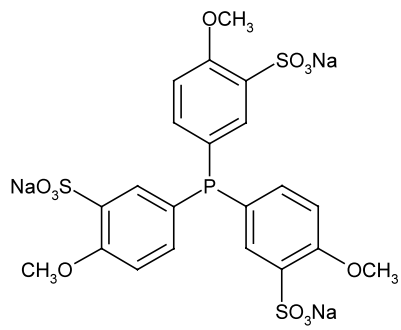
2b



5b



3b



6b

Scheme 1. Synthesis of novel sulfonated phosphines (**1b**–**6b**).

Table 1. New sulfonated phosphines **1b**–**6b** produced via Scheme 1[a]

Phosphine	Reaction time (h)	Isolated yield[b] (%)	Oxide content (%)	^{31}P NMR[c] (ppm)
1b	0.9	93	1	−10.9 (−12.2)
2b	2.5	85	4	−22.9 (−20.8)
3b	3	75	0	−27.0 (−30.0)
4b	1	>98	0	−2.7 (−6.6)
5b	2.5	95	1.5	−6.6 (−8.2)
6b	3	90	1	−7.6 (−9.5)

[a] Reaction conditions: 1 g (2.89–3.45 mmol) of each phosphine was dissolved in 2.5 ml of fuming sulfuric acid (20% free SO_3) at −5 to −8°C, and the mixture stirred at room temperature for the given reaction time.
[b] Yields are not optimized.
[c] Chemical shifts for the parent Ar_3P in parentheses.

well the point of the concept. In order to avoid oversulfonation, the reaction needs to be interrupted at moderate conversions. Although the yield is rather low (29% after recrystallization), the monosulfonated phosphine can be obtained with high purity, and the unreacted triphenylphosphine can be collected and reused. Another attractive feature of the method is that it eliminates the need for organic solvents in the course of the reaction.

Most recently, Williams and his co-workers have published a method for selective preparation of disulfonated triphenylphosphine (TPPDS).[4o] This method, based on the careful control of the reaction conditions and work-up procedure, provides TPPDS·$2H_2O$ in a yield of 60%.

Herein, we wish to report a completely new approach for selective and essentially oxide-free sulfonation of aryl phosphines. Our rapid access to water-soluble phosphines with different sulfonation degrees is based on the increased activity of certain phenyl rings of the parent phosphine. If the substituents of the phenyl rings are sufficiently activating, relatively mild conditions and short reaction times can be used, the substitution is selective, and the side reaction leading to the oxidized phosphines is avoided.

In order to demonstrate the idea, a number of methyl- and methoxy-substituted triphenylphosphine derivatives have been prepared and subjected to the simplest sulfonation procedure. The activating groups have been introduced into the *ortho*- and *para*-positions of the phenyl rings so that their directing effect would be in accordance with the directing effect of the phosphorus protonated in the acidic sulfonating medium (Scheme 1).

The phosphines **1a**–**6a** were prepared by the classical Grignard method.[5] Sulfonation of the phosphines was carried out in oleum (20% SO_3 content). In each case 1 g of a phosphine was sulfonated in 2.5 ml of oleum. The chosen ratio provides a slight excess of free SO_3 even in the preparation of the trisulfonated species. Decreasing the amount or concentration of the fuming sulfuric acid has not been attempted, when di- or monosulfonated phosphines have been prepared. Thus, we have demonstrated that the activating groups themselves assure the desired selectivity. In each case the sulfonation is complete in 1–3 hours. After neutralization of the acidic medium and removal of the water, the product is separated from the sodium sulfate by extraction with dry or wet methanol. Each of the sulfonated phosphines **1b**–**6b** was obtained with total selectivity, high yield and low degree of oxidation (Table 1).[6] It is worth noting that by introducing substituents into the *ortho*-positions of the phenyl-rings, the steric factors could also be influenced, which might be important in several catalytic reactions.

In summary, we have delineated a new approach to selective sulfonation of triarylphosphines. Introducing activating groups into the appropriate positions of certain phenyl-rings, the corresponding sulfonated phosphine can be obtained selectively. The readily available starting materials, simplicity of the sulfonation procedure, the short reaction times, high yields, total selectivities and low degree of oxidation of the products make this strategy attractive. The preparation of larger quantities of triaryl phosphines of this type will allow us to investigate the steric and electronic effects of the activating groups on catalytic activity. The results of this study will be presented in due course.

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6. A typical procedure: preparation and characterization of **5b**. The finely ground phosphine (1 g, 3.1 mmol) was added in small portions to the fuming sulfuric acid (2.5 mL containing 20% of free SO_3) at −8 to −5°C external temperature (ice/salt bath). Addition of the total amount of the phosphine took about 1 h. Having added the phosphine, the ice/salt bath was removed and the resulting mixture was stirred at room temperature for 2.5 h. The mixture was chilled again using an ice/salt bath, and crushed ice (approximately 10 g) was added over 30 min in order to stop the reaction. During the procedure the argon atmosphere was changed several times above the solution. The calculated amount of NaOH (3.8 g, 94.9 mmol) dissolved in deoxygenated water (30 mL) was added over 40 min to neutralize the solution. Fine adjustment of the pH to 7 was carried out using a digital pH meter. The water was removed in vacuum. The solid white residue was extracted with a mixture of methanol and water (40 mL/2 mL), then the remaining Na_2SO_4 was washed with methanol (40 mL) again. The methanol was evaporated in vacuum and the phosphine was dissolved in water. Removal of the water in vacuum yielded the methanol-free phosphine as a white shiny powder (1.65 g, 95%). $^{31}P\{^1H\}$ NMR (D_2O): δ −6.6 ppm (s); ^1H NMR (D_2O) δ 3.74 (s, 6H, OCH_3), 6.74 (d, $^3J_{HH}=8.5$ Hz, 2H, H*5*), 7.05–7.1 (mp, 4H, H*6* and H*b*), 7.19 (pseudo t, 2H, H*c*), 7.23 (t, $^3J_{HH}=7.5$ Hz, 1H, H*d*), 7.67 ppm (dd, $^3J_{PH}=7.5$ Hz, $^4J_{HH}$ 2.0 Hz, 2H, H*2*); $^{13}C\{^1H\}$ NMR (D_2O) δ 56.35 (s, OCH_3), 113.48 (d, $^3J_{PC}=7.3$ Hz, C*5*), 127.15 (d, $^3J_{PC}=7.2$ Hz, C*3*), 129.38 (d, $^3J_{PC}=7.6$ Hz, C*c*), 129.83 (s, *Cd*), 130.87 (d, $^1J_{PC}=7.3$ Hz, C*1*), 133.53 (d, $^2J_{PC}=19.5$ Hz, C*b*), 133.62 (d, $^2J_{PC}=22.7$ Hz, C*2*), 136.43 (d, $^1J_{PC}$ 7.3=Hz, C*a*), 138.96 (d, $^2J_{PC}=20.9$ Hz, C*6*), 157.67 ppm (s, C*4*). $^1H\{^{31}P\}$, ^1H–^1H COSY and ^1H–^{13}C COSY NMR spectra were in accordance with the structure and the interpretation of common NMR data above. MS (ESI^-, m/z): 503.2 $[M–Na^+]^-$, 481.0 $[M–2Na^+{+}H^+]^-$, 240.1 $[M–2Na^+]^{2-}$. Elemental analysis calcd for **5b**·$2H_2O$: P, 5.52%; S, 11.38%; Na, 8.18%. Found (ICP): P, 5.53%; S, 11.50%; Na, 8.21%; P:S:Na = 1:2.02:2.00.