A new route for the synthesis of amphiphilic and water-soluble ligands: mono- and di-tertiary phosphines having an alkylene sulfate chain

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Cyclic sulfates react with $LiPPh_2$ to form a series of new amphiphilic or water-soluble ligands: monotertiary phosphines with one or two alkylene sulfate chains and ditertiary phosphines with one or two hydrophilic tails attached to bridgehead carbon atom; the application of zwitterionic Rh^I complexes $(sulfatephos)_2Rh(cod)$ and (sulfatediphos)Rh(cod) in liquid biphasic catalysis has been demonstrated for the hydroformylation of styrene and oct-1-ene.

Much effort has been directed toward the synthesis of new catalytic species, with some recent focus on water-soluble catalysts.[1] Transition metal complexes can easily be rendered water-soluble by incorporating polar substituents,[2] *e.g.* SO_3Na, CO_2Na, OH, PMe_3^+, NMe_3^+, $PO(ONa)_2$ and polyethers. We reasoned that a new route to amphiphilic or water-soluble phosphine ligands would be of particular interest because (i) a wide range of starting compounds (*e.g.* diol, triol, tetraol) is available, (ii) the synthesis is simple and (iii) it might be possible to access a series of amphiphilic or water-soluble phosphines. To the best of our knowledge, only a very few examples of ligands with amphiphilic properties have been reported,[3] and the 'sulfated' phosphines reported here are the first examples of this kind.

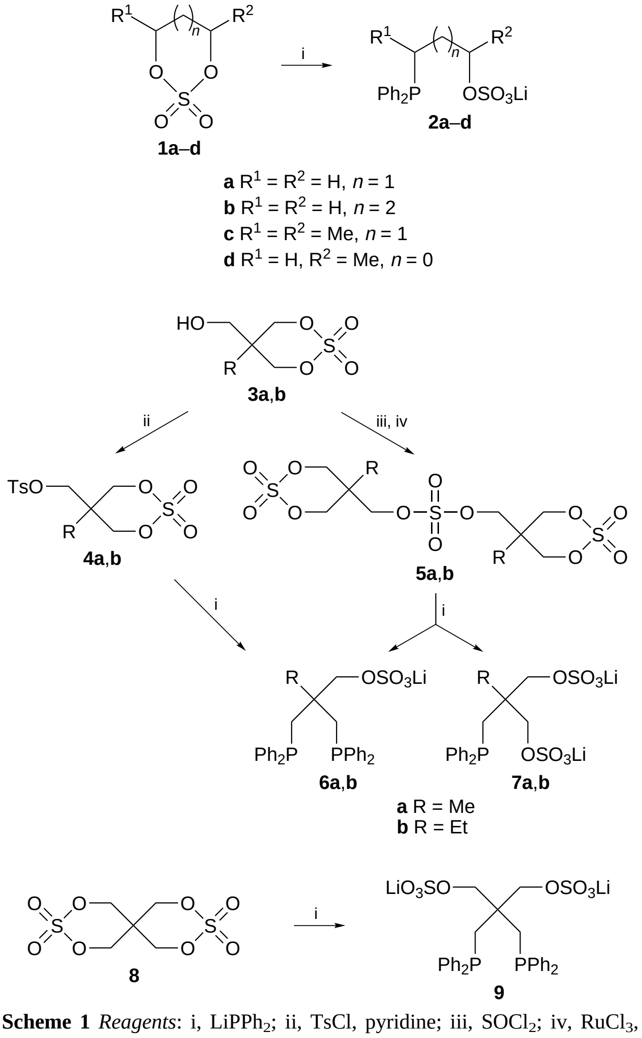
The mono- and bi-dentate phosphines were synthesized *via* the reaction of cyclic sulfates[4] with lithium diphenylphosphide. The water-solubility of these phosphines is provided by the sulfate group. Cyclic sulfates were obtained by a simple one-pot reaction from the corresponding diols, triols or tetraol following the procedure developed for 1,2-cyclic sulfates by Gao and Sharpless.[5] This involves the treatment of diols with $SOCl_2$ followed by ruthenium-catalysed oxidation.

The synthesis of the ligands is outlined in Scheme 1. A homologous series of monotertiary phosphines of the type $Ph_2PCH(R^1)(CH_2)_nCH(R^2)OSO_3Li$ (n = 1,2, R^1 = R^2 = H; n = 1, R^1 = R^2 = Me; n = 0, R^1 = H, R^2 = Me) has been prepared. Nucleophilic attack occurred with complete inversion at the stereogenic centre of the electrophilic cyclic sulfate (**1c**) and with complete regioselectivity (**1d**).

The new ligands are monotertiary phosphine ligands (sulfatephos) with one (**2**) or two alkylene sulfate chains (**7**) or ditertiary phosphine ligands (sulfate-dppp) with one (**6**) or two hydrophilic tails (**9**) attached to the bridgehead carbon atom. A general procedure for the conversion of cyclic sulfates to amphiphilic or water-soluble phosphines was developed (Table 1). Our approach combines the introduction of the PPh_2 moiety and the formation of the charged β-, γ- or ω-sulfate functionality. Note that the anionic nature of the sulfate moiety, which is still a leaving group, renders it kinetically less reactive than the cyclic sulfate. Although β-substituted ethyl sulfates are subjected to hydrolyse slowly in water[6] or rapidly by using a catalytic amount of sulfuric acid,[5] the lithium salts of the sulfates in Table 1 proved to be stable in neutral or slightly basic aqueous solution. For example, when an aqueous solution of **9** was heated at 80 °C for 1 h, no appreciable decomposition or hydrolysis was detected.

The double 'sulfation' of triols (**5**) or the 'sulfation' of triols followed by tosylation (**4**) suggests a variety of useful transformations of these forgotten electrophiles. From a synthetic point of view, noteworthy applications of our methodology are those involving the mixed acyclic-bicyclic sulfate esters **5**; they lead to ditertiary phosphines **6** with very poor water-solubility and water-soluble monotertiary phosphines **7** in one reaction. In addition, **6** can also be obtained from **4**.

Compound **9** forms a complex when reacted in a 2 : 1 ratio with $[Rh(COD)Cl]_2$ in MeOH or EtOAc–H_2O. ^{31}P NMR spectroscopic data of this complex are characteristic of a cationic complex [δ 13.9 (J_{RhP} 141 Hz) in CD_3OD or in D_2O)] and do not significantly differ from those derived from dppp.[7] The MS FAB^+ spectrum displays a $[M + Li]^+$ peak at 855 and the MS FAB^- spectrum displays a M^- peak at 848. A zwitterionic structure for the complex $[Rh(COD)((Ph_2PCH_2)_2C(CH_2OSO_3Li)(CH_2OSO_3))]$ is suggested in which one of the OSO_3^- groups of the ligand acts as the counterion for rhodium.



Scheme 1 *Reagents*: i, $LiPPh_2$; ii, TsCl, pyridine; iii, $SOCl_2$; iv, $RuCl_3$, $NaIO_4$

Table 1 Synthesis of cyclic sulfates, amphiphilic and water-soluble phosphines[a]

Cyclic sulfate			Phosphine			Phosphine oxide[c]
	Yield[b] (%)	Mp/°C		Yield[b] (%)	δ_P	δ_P
1a	91	59–60	**2a**	84	−16.1[d]	43.8[d]
1b	89	40–42	**2b**	81	−15.9[e]	44.2[d]
1c	62	31	**2c**	86	1.1[e]	48.1[d]
1d	83	oil	**2d**	86	−21.8[d]	38.4[d]
3a	77	oil				
3b	83	oil				
4b	50	74	**6b**	70	−26.2[e]	33.3[e]
5a	36	152–4	**6a**	55	−25.6[e]	32.9[e]
			7a	50	−28.6[d]	37.3[d]
5b	41	95–98	**6b**	79	−26.2[e]	33.3[e]
			7b	65	−28.4[d]	36.8[d]
8	17	279	**9**	73	−28.9[d]	35.4[d]

[a] Reactions were performed by the addition of sulfate to the solution of $LiPPh_2$ in THF at 0 to −5 °C. [b] Isolated but not optimized yields. [c] Phosphine oxide was obtained at room temperature by oxidation of the phospine with H_2O_2 in water or in a mixture of water and MeOH. [d] $^{31}P\{^1H\}$ NMR (D_2O). [e] $^{31}P\{^1H\}$ NMR ($CDCl_3$).

A preliminary investigation of the potential of **2c** and **9** in liquid biphasic catalysis has been carried out. Oct-1-ene is hydroformylated in a H_2O–PhMe or H_2O–oct-1-ene biphasic system in the presence of $[Rh(COD)Cl]_2$ associated with **2c** (35 bar of CO, 35 bar of H_2, 60 °C, 1 : 300 Rh to substrate ratio, 6 h, 100% conversion). In both cases, the reaction gives nonanal (54%), branched aldehydes (44%) [2-methyloctanal (38%) and 2-ethylheptanal (6%)] and isomerized octenes (2%). Most importantly, the catalytically active rhodiumcarbonyl–surfactant-phosphine complex is quantitatively recovered by simple extraction with water of the organic phase, which contains the product; the aqueous phase could be reused with a slight loss of catalytic activity. When styrene was hydroformylated in a H_2O–PhMe biphasic system, complete chemoselectivity for aldehydes and a high regioselectivity (up to 91%) for branched aldehydes were achieved in 3 h. Although the (1*R*,3*S*)-1-methyl-3-(diphenylphosphino)butyl lithium sulfate salt is chiral, no optical induction has been observed.

When the hydroformylation of styrene was performed with the highly water-soluble ligand **9**, complete chemoselectivity for aldehyde and an 81% regioselectivity for branched aldehydes was achieved. After reaction the organic phase was colourless, and the rhodium is located in the aqueous phase, which could be reused with a slight loss of catalytic activity. When the residue derived from the hydrocarbon layer was analysed by ^{31}P NMR spectroscopy, no appreciable amount of phosphorus was detected.

In conclusion we have introduced a new class of amphiphilic and water-soluble mono- and di-tertiary phosphines with considerable promise for the modification of liquid biphasic catalysis. The simplicity of the procedure and the rich achiral and chiral pool of diols, triols and tetraols should give synthetic chemists many ideas for the synthesis of achiral and even chiral water-soluble phosphines. With the homologous series of ligands, we are uniquely situated to vary the water-solubility imposed by the number of the sulfate groups and PPh_2 moieties without significantly varying the electronic nature of the metal centres in a corresponding series of complexes.

Financial support from the Hungarian National Science Foundation (OTKA-T016269) and the Ministry of Culture and Education (FKFP-0803/1997) is gratefully acknowledged. We are grateful to Mr Béla Édes for skillful assistance in the catalytic experiments.

Footnote and References

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Received in Cambridge, UK, 10th September 1997; 7/06602C