Polystyrenes with chiral phosphoramide substituents as Lewis base catalysts for asymmetric addition of allyltrichlorosilane: enhancement of catalytic performance by polymer effect†

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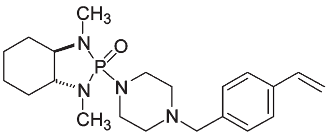
In the asymmetric addition of allyltrichlorosilane to benzaldehyde, polystyrenes with chiral phosphoramide substituents as Lewis base catalysts showed up to 2.4 times better catalytic activity and 1.4 times higher enantioselectivity than the corresponding low-molecular-weight analogues.

Asymmetric reactions using organocatalysts have attracted growing attention,[1] due to a wide variety of catalyst designing, the metal-free conditions, and the avoidance of the use of expensive transition metals. Chiral Lewis base-promoted asymmetric additions of allylic trichlorosilanes and trichlorosilyl enol ethers to aldehydes are among the most studied organocatalytic asymmetric reactions.[2] In these reactions, the ternary complex of allylic trichlorosilane (or trichlorosilyl enol ether), aldehyde, and chiral Lewis base, through a closed transition assembly, realises not only high asymmetric induction but also a high degree of diastereoselectivity.

Chiral phosphoramides are the first and the most studied Lewis base promoters for the asymmetric allylation of aromatic and unsaturated aldehydes,[2b,3] and catalytic asymmetric allylation using various chiral Lewis bases has been widely investigated.[4] For the asymmetric allylation with allyltrichlorosilanes catalysed by chiral phosphoramides, Denmark *et al.* revealed that there are two transition states where one or two phosphoramides coordinate to a hypervalent silicon atom. The reaction *via* the transition state coordinated with two phosphoramides is found to show higher reactivity and stereoselectivity than the reaction through the one-phosphoramide pathway. Therefore, the catalytic activity and the enantioselectivity of the reaction were decreased when a catalytic amount of the phosphoramide was used.[3a,3c–e]

Thus, a polymeric catalyst having chiral phosphoramides as side chains is expected to show better reactivity and selectivity than the corresponding low-molecular-weight catalyst, since local concentration of the phosphoramide units around a polymer chain remains high regardless of the amount of the polyphosphoramide, and this "polymer effect" makes coordination of plural phosphoramides to the silicon atom predominant even if a catalytic amount of polyphosphoramide is used. In this study, we report the synthesis of polystyrenes having chiral phosphoramides as ring substituents and their use as asymmetric catalysts for the allylation of benzaldehyde with allyltrichlorosilane. To our best knowledge, there are no examples on the synthesis of polymers having chiral phosphoramides and on the asymmetric allylation or aldol reaction catalysed by polymer-supported chiral Lewis bases.[5–7]

Starting from (1*R*,2*R*)-*N,N′*-dimethyl-1,2-cyclohexanediamine,[8] chiral phosphoramide monomer **1**, having a piperazine linkage between a styrene unit and a phosphoramide group, was prepared. Monomer **2**, in which chiral phosphoramide was directly connected to a styrene unit, was also synthesised from the same starting material.



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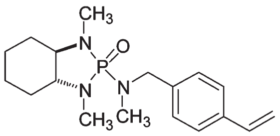
$[\alpha]_D^{20}$ = -65.5 (c = 1.0, CHCl$_3$)



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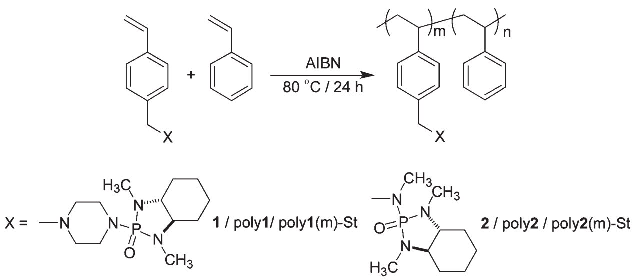
$[\alpha]_D^{20}$ = -62.7 (c = 1.0, CHCl$_3$)

The results of radical homo- and copolymerisations of the chiral monomers and the properties of the obtained polymers are exhibited in Table 1.†[9] The homopolymers (poly**1** and poly**2**) were obtained in good yields (entries 1, 4). Little changes in specific

Table 1 Radical homo- and copolymerisations of the chiral phosphoramide monomers



Entry	Monomer(s) (feed ratio)	Polymer[a]	Yield (%)	η_{sp}/c[b]	$[\alpha]_D^{20}$[c]
1	**1**	Poly**1**	84	0.173	−62.5
2	**1**, styrene (75:25)	Poly**1**(75)–St	76	0.092	−50.1
3	**1**, styrene (50:50)	Poly**1**(47)–St	68	0.150	−47.5
4	**2**	Poly**2**	72	0.082	−61.2
5	**2**, styrene (75:25)	Poly**2**(71)–St	73	0.087	−45.2
6	**2**, styrene (50:50)	Poly**2**(37)–St	57	0.084	−38.7
7	**2**, styrene (25:75)	Poly**2**(23)–St	72	0.070	−35.8

[a] The value in parentheses indicates the ratio of phosphoramide unit determined from ^{1}H–NMR spectrum. [b] 0.5 g dL^{-1} in chlorobenzene at 30 °C. [c] c = 1.0 g dL^{-1}, CHCl$_3$.

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† Electronic supplementary information (ESI) available: experimental details for the synthesis of the monomers, polymerisation, and asymmetric allylation. See http://www.rsc.org/suppdata/cc/b4/b417311b/
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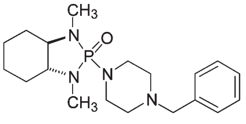
rotation were observed between the monomers and the corresponding homopolymers, and this implies that these polymers do not have higher-order structures. The copolymers between the chiral phosphoramide monomers and styrene with various ratios [poly**1**(m)–St, poly**2**(m)–St: m indicates the ratio of phosphoramide unit determined from the ^{1}H–NMR spectrum] were also successfully prepared (entries 2–3, 5–7). The molecular weights of the polymers were evaluated by reduced viscosity because these polymers did not show any peak in GPC measurements. For comparison of catalytic activity and stereoselectivity, chiral phosphoramides **3–5** were prepared as the low-molecular-weight analogues of the polymeric phosphoramides.[8,10]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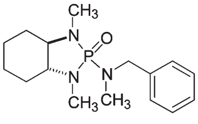
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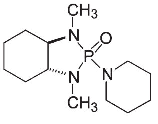
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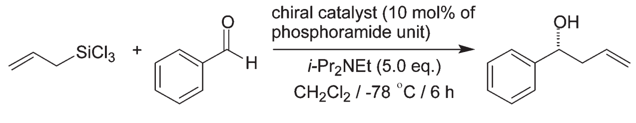
The polystyrenes having chiral phosphoramides as the ring substituents, as well as the low-molecular-weight analogues, were used as the Lewis base catalysts for the asymmetric addition of allyltrichlorosilane to benzaldehyde. The amount of catalyst used in the allylations is calculated based on phosphoramide unit and, therefore, the mole of phosphoramide groups in the reaction system catalysed by the polyphosphoramides is the same as in that catalysed by the low-molecular-weight analogues. Ethyldiisopropylamine was added to assist reaction turnover.[3c,4b] Table 2 summarises the results of the asymmetric allylation. The reactions catalysed by the polymeric phosphoramides were found to show better yield and higher enantiomeric excess (ee) compared to those with the corresponding low-molecular-weight analogues (entries 1 *vs.* 8, 4 *vs.* 9). Especially, poly**2**, which does not have piperazine linkage, exhibited remarkable improvement in both the yield (84%) and the stereoselectivity (63% ee) (entry 4). These values are 2.4 times better and 1.4 times higher, respectively, than those with the corresponding low-molecular-weight analogue (entry 9). The yield and the ee attained by the use of poly**2** as the catalyst were better than those obtained by phosphoramide **5**, the most effective unidentate phosphoramide catalyst reported by Denmark *et al.*[3a] (entry 10). These results strongly suggest that coordination of two (or more) phosphoramides to a hypervalent silicon atom by the polymer effect enhances the reactivity and promotes the asymmetric induction. Denmark *et al.* reported that the bis-phosphoramide catalysts having two phosphoramide units connected with a five-methylene tether showed the best performances due to appropriate chelation of the phosphoramides to the silicon atom, and the bis-phosphoramides with shorter or longer methylene tethers had poorer activity and selectivity than the corresponding unidentate phosphoramides.[3c–e] In contrast, the polymeric phosphoramide catalysts used in this study exhibited higher performance both in the activity and the selectivity than the unidentate ones although the tethers between phosphoramide groups in the polymeric catalysts were much longer than five carbons. Thus, the principal reason for the high activity and selectivity of the polymeric catalysts would be the favourable multiple coordination of the phosphoramide units induced by the polymer effect. Utilisation of multidentate polymer ligands can be regarded as a new strategy for the design of efficient chiral Lewis base catalysts.

Table 2 Asymmetric allylation with the polymeric chiral phosphoramides and the low-molecular-weight analogues



Entry[a]	Catalyst	Silane (eq.)[b]	Yield (%)[c]	ee (%)[d]
1	Poly**1**	1.2	62	51
2	Poly**1**(75)–St	1.2	50	49
3	Poly**1**(47)–St	1.2	43	49
4	Poly**2**	1.2	84	63
5[e]	Poly**2**	10	28	56
6	Poly**2**(71)–St	1.2	82	62
7	Poly**2**(37)–St	1.2	84	62
8	**3**	1.2	43	40
9	**4**	1.2	35	45
10	**5**	1.2	36 (40[e,f])	60 (53[e,f])

[a] Unless specified, the reactions were carried out with 5.0 eq. of *i*-Pr$_2$NEt. [b] Aldehyde: 1.0 eq. [c] Isolated yield. [d] Determined by chiral HPLC (CHIRALCEL® OD-H, 2-propanol–hexane = 1:20). [e] Without *i*-Pr$_2$NEt. [f] The value with the reaction for 24 hours reported by Denmark *et al.* (reference 3a).

The effect of the number of phosphoramide units in a polymer chain was also examined by using the copolymers having various ratios of phosphoramide units. In the case of poly**1**–Sts, the yields of the product decreased as the number of phosphoramides in a polymer chain decreased while the enantiomeric excesses almost remained unchanged (entries 1–3). These results suggest that the amine structure derived from piperazine in the phosphoramide unit, as well as ethyldiisopropylamine, may work as accelerator of reaction turnover. On the other hand, no change was observed in both the enantioselectivity and the yield when a series of poly**2**–Sts was used as the chiral Lewis base catalysts (entries 4, 6, 7). This indicates that 37% of chiral phosphoramide units in a polymer chain is sufficient for multiple coordination. In the absence of ethyldiisopropylamine, a large decrease in the yield of the homoallylic alcohol was observed in spite of the use of a large excess of allyltrichlorosilane (entry 5).

In summary, we have developed polymeric catalysts having chiral phosphoramide structures as the ring substituents of polystyrene for the Lewis base-catalysed asymmetric addition of allyltrichlorosilane to benzaldehyde. The polymeric catalysts showed higher catalytic activity and enantioselectivity than the corresponding low-molecular-weight analogues. The polymer effect makes the coordination of two (or more) chiral phosphoramides to the silicon atom favourable, and this would improve the enantiomeric ratios and the yields of the reactions. Thus, the introduction of chiral Lewis bases onto polymeric supports would become a novel candidate for design of efficient asymmetric Lewis base catalysts. The polymer-catalysed asymmetric allylation reported here is a unique system where the introduction of chiral catalysts onto a polymer chain increases the activity and the stereoselectivity of the catalysts. Investigations into understanding the complexation between the hypervalent silicon atom and the polymeric catalysts by using model compounds,[3e] recycling of the polymeric catalysts and preparing more efficient catalysts are currently in progress in our laboratory.

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