

Solvent Effect and NMR Behaviour in a Chiral Amidophosphine Mediated Reaction of Organocuprate with Chalcone

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A dramatic reversal in the direction of enantiofacial differentiation has been observed in a chiral phosphine mediated reaction of organocuprate with chalcone providing *S*- and *R*-products in diethyl ether and tetrahydrofuran (THF), respectively, and correlated with the pattern of coordination.

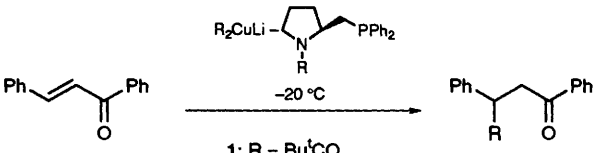
It is desirable to accumulate information on structure-enantioselectivity relationships for the design of chiral ligand-mediated enantioselective reactions of organocuprates.¹ From our studies toward a chiral noncovalently bound ligand-mediated enantioselective reaction of organocuprate,² we found a reversal in enantiofacial differentiation which was solvent dependent. Such a reversal has been described in recent asymmetric additions of organocuprate but without any structural information^{1,3} and would provide a good chance to study the structure of a chiral ligand-organocuprate complex. We describe here a correlation between enantiofacial differentiation and coordination pattern of the chiral amidophosphine-cuprate complex.

As summarized in Table 1, entries 1–5, a similar level of enantiofacial differentiation in the reaction of lithium dimethylcuprate-1 with chalcone was observed in diethyl ether, toluene and dimethylsulfide producing the *S*-product in 84–78% enantiomeric excess (e.e.). However, in tetrahydrofuran (THF) and dimethoxyethane (DME), a dramatic reversal of the direction in enantiofacial differentiation was observed to give the *R*-product in 50–30% e.e. This reversal of direction of differentiation was also observed in the reaction of lithium divinylcuprate with chalcone (entries 6 and 7). It is also surprising to find that a similar phenomenon was

observed in the reactions controlled by 2 and 3, giving *S*- and *R*-products in 71–66% e.e. in diethyl ether and THF, respectively (entries 8–11). Thus, the solvent-dependent reversal of the direction of enantiofacial differentiation is general in the reaction of the cuprates by the control of the chiral noncovalently bound ligands 1–3.

As has been described previously,² NMR analysis of 1 in a mixture of toluene-diethyl ether revealed that a large and metal-selective change in chemical shift was observed at the carbonyl carbon of 1 upon addition of lithium perchlorate, and at the carbons adjacent to phosphorus upon addition of copper bromide. However, as shown in Table 2, addition of lithium perchlorate to 1 in THF caused no significant change in the chemical shifts at the carbons, implying the existence of competitive coordination of THF with the lithium cation. As expected, addition of copper bromide induced large changes in the chemical shifts at the carbons [C-(3,4)] adjacent to phosphorus.†

† In a mixture of toluene-diethyl ether, quite large chemical shift changes for the 1-Me₂CuLi complex were observed at C(1)–C(4). In THF, significant but small changes in chemical shifts were observed at C(3) and C(4).

Table 1 Enantioselective addition of organocuprate^a


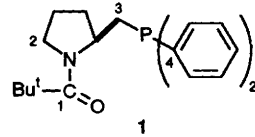
1; R = Bu^tCO
2; R = (Me₂N)₂PO
3; R = Me₂NCO

Entry	R ₂ CuLi	Phos- phine	Solvent	t/h	E.e. (%)	Product	
						R/S	Yield (%)
1	Me	1	Et ₂ O	1	84	S	79
2	Me	1	Toluene	1	78	S	87
3	Me	1	Me ₂ S	1	79	S	63
4	Me	1	THF	4	50	R	72
5	Me	1	DME	4	30	R	34
6	CH ₂ =CH	1	Et ₂ O	1	73	R	67
7	CH ₂ =CH	1	THF	4	24	S	25
8	Me	2	Et ₂ O	1	71	S	88
9	Me	2	THF	4	66	R	72
10	Me	3	Et ₂ O	1	67	S	88
11	Me	3	THF	4	68	R	72

^a To a mixture of RLi (3 equiv.), CuI (1.5 equiv.), and 1-3 (1.5 equiv.) in a solvent was added chalcone at -20°C. The mixture was worked-up as usual.³ E.e. and absolute configuration were determined by HPLC analysis using a chiral column and by optical rotation. Solvents other than diethyl ether contain 10% v/v diethyl ether derived from a low halide MeLi in diethyl ether.

The correlation between enantiofacial differentiation and NMR behaviour implies that, in THF, amidophosphine **1** behaves as a monodentate ligand and that phosphorus can still coordinate with copper but leaves the carbonyl oxygen free from coordination with lithium. On the other hand, in diethyl ether, **1** behaves as a bidentate ligand.² This situation would result in a structure change of the 1-cuprate complexes and subsequent reversal of the direction of enantiofacial differentiation.

Further studies toward development of more effective ligands are in progress.

Table 2 ¹³C NMR chemical shift changes (δ) of **1** in THF^a


	Initial chemical shift	+LiClO ₄ Δδ ^b	+CuBr· SMe ₂ Δδ ^b	+LiClO ₄ +CuBr· SMe ₂ Δδ ^b
C-1	175.7	+0.3 (+2.6)	+0.3 (+0.3)	+0.5
C-2	48.7	+0.1 (+1.0)	-0.2 (-0.2)	-0.2
C-3	33.7	-0.1 (-0.8)	-1.7 (-1.7)	-1.8
C-4	138.8	0 (-0.7)	-6.0 (-6.1)	-5.7
	141.3	0 (-1.1)	-4.9 (-4.6)	-4.9

^a Concentration was 0.07 mol dm⁻³ in [²H₈]THF. Values are referenced relative to the methylene carbon of [²H₈]THF as δ 25.3 for ¹³C. ^b Numbers in parentheses are chemical shift changes in diethyl ether-toluene solvent.

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