

Scheme 2.

Table 1. The alkylation of the imines **8A** and **8Ba** with 4-nitrobenzyl bromide

Run	Imine	Reaction conditions ^a			Amino ester 10a Isolated yield / %
		Base (6.0 eq.)	Additive (0.2 eq.)	Time / min.	
1	8Aa	LiOH	—	90	N.R.
2	8Aa	NaOH	—	90	N.R.
3	8Aa	KOH	—	90	N.R.
4	8Aa	NaOH	BzIN ⁺ Et ₃ Cl ⁻	15	64 ^b
5	8Aa	KOH	18-crown-6	15	58 ^b
6	8Ba	LiOH	—	20	66 ^b
7	8Ba	NaOH	—	90	56 ^b
8	8Ba	KOH	—	90	trace

^aAll runs were carried out at room temperature. ^bPLP model compounds **3A**, **B** were recovered in 73-80% yields.

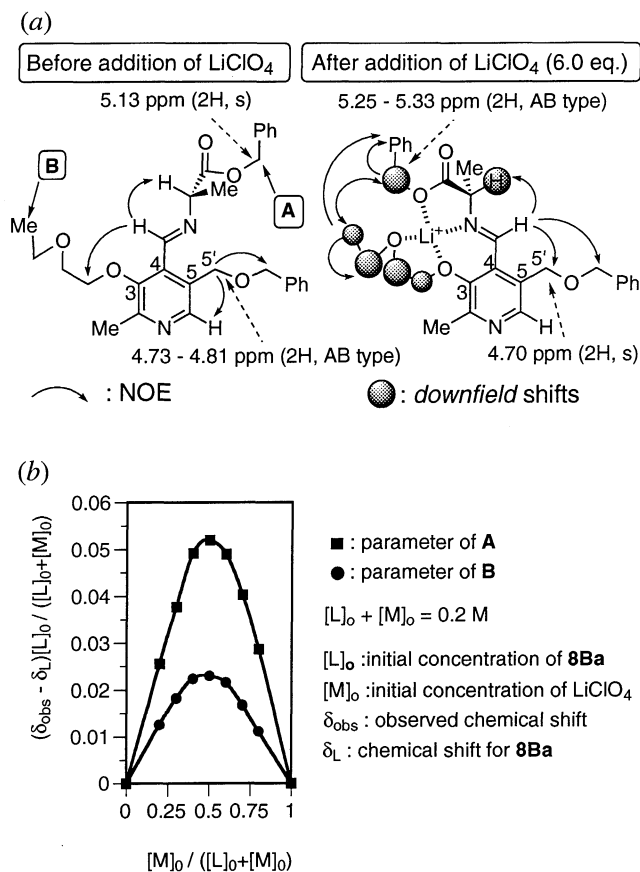
Table 2. The alkylation of the imines **8Ba** and **8Bb**

Run	Imine	Reaction conditions ^a		Amino ester	
		R ³ X	Time / min.	Product	Isolated yield ^b / %
1	8Ba	allyl bromide	15	10b	70
2	8Ba	propargyl bromide	15	10c	84
3	8Ba	benzyl bromide	30	10d	56
4	8Ba	ethyl bromoacetate	60	10e	58
5	8Bb	methyl iodide	30	10d	54

^aAll runs were carried out at room temperature. ^bPLP model compound **3B** was recovered in 77-87% yields.

yields (Runs 4, 5). On the other hand, in the case of the ethoxyethoxy analog **8Ba**, α -alkylation took place smoothly without any PTC (Runs 6, 7). The alkylation proceeded most readily with LiOH. Sodium hydroxide was shown to be less effective for the alkylation and the alkylation with KOH hardly occurred (Run 8). Alkylations of **8Ba** or **8Bb** with various alkylating agents and LiOH also gave the alkylated products **10b-e** in moderate yields (Table 2). The same product **10d** was obtainable both by benzylation of **8Ba** and by methylation of **8Bb** (Runs 3, 5). These results indicate that the ethoxyethoxy imino esters **8B** have a strong Li⁺-ionophore activity, probably owing to a chelate model **11** which structurally resembles to a Li⁺-12-crown-4 complex.

In order to make the ionophore activity of **8B** clear, we evaluated the interaction between Li⁺ and the imine **8Ba** by means of the ¹H-NMR spectra in CD₃CN (Figure 1). By the addition of LiClO₄, the signals for protons on C-3 side-chain and the imino ester moiety moved to *downfield*. Changing of the splitting patterns of some these signals were also recognized [Figure 1-(a)]. These observations could be explained in terms of the Li⁺-induced conformational change as illustrated in Figure 1-(a). Nuclear Overhauser effect (NOE) experiments [Figure 1-(a)] and the shift experiments by a continuous addition of LiClO₄ (a continuous variation method)⁶ [Figure 1-(b)] strongly supported the formation of a 1:1 chelate complex between Li⁺ and the imino ester **8Ba**.

**Figure 1.** ¹H-NMR studies of **8Ba** before and after addition of LiClO₄. (a) The spectral and conformational change. (b) a continuous variation method.

Based on the present results, synthetic studies of various optically active α -amino acids by means of chiral PLP (and PMP) model compounds are now in progress.

References and Notes

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