Binary Regiocontrol in the Reaction between Pentadienyltin and Imines by Lewis Acids and *N*-Substituents

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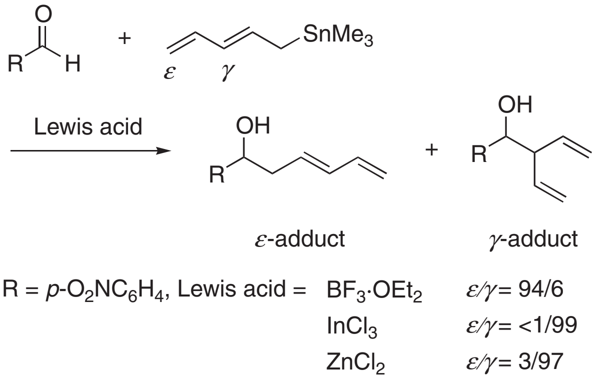
(Received October 2, 2003; CL-030929)

Binary regiocontrolled pentadienylation of imines with a pentadienyltin reagent was achieved. While *N*-phenyl imines afforded ε-adducts (1,3-dienes) exclusively under Lewis acidic conditions, the combination of *N*-tosyl imines and indium or zinc chloride as a Lewis acid gave γ-adducts (1,4-dienes) preferentially.

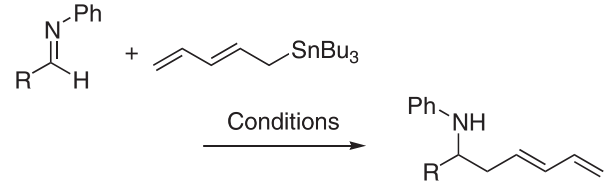
Imines are accepted as versatile starting materials for the synthesis of nitrogen containing compounds.[1] Among various nucleophilic reagents applied to them, allylic metals[2] are most widely used and give successful results. As an extension of such reaction, their vinylogues, pentadienylmetals, are also attractive owing to their synthetic potential to introduce a C_5 unit and a diene functionality. Accordingly, because we have already developed a method to control the ε/γ-regioselectivity in the pentadienylation of aldehydes and ketones with pentadienyltin reagents[3,4] (Scheme 1), we have focused on the pentadienylation of imines in a regiocontrolled fashion. We herein describe the results of the Lewis acid-promoted reactions between various imines and pentadienyltin.



Scheme 1. Binary regioselective pentadienylation of aldehyde.

As a typical and simple imine, benzalaniline was employed at first to the previously reported reaction systems (Table 1, R = Ph); $BF_3 \cdot OEt_2$-promoted reaction in dichloromethane (conditions A)[3a,3b] and $InCl_3$-promoted reaction in acetonitrile (conditions B).[3b] It was very acceptable that the ε-adduct was exclusively obtained (78%) when $BF_3 \cdot OEt_2$ was used (Table 1). However, it was an unexpected result that only the ε-adduct was obtained again (64%) even in the $InCl_3$-promoted reaction, because the corresponding reaction of aldehydes afforded the γ-adducts in very high regioselectivity as depicted in Scheme 1.[3b] Other *N*-phenyl imines, such as aromatic, α, β-unsaturated, and aliphatic ones, also gave only ε-adducts in both the BF_3-promoted and the $InCl_3$-promoted pentadienylation reactions as shown in Table 1.

Table 1. Pentadienylation of *N*-phenylimines



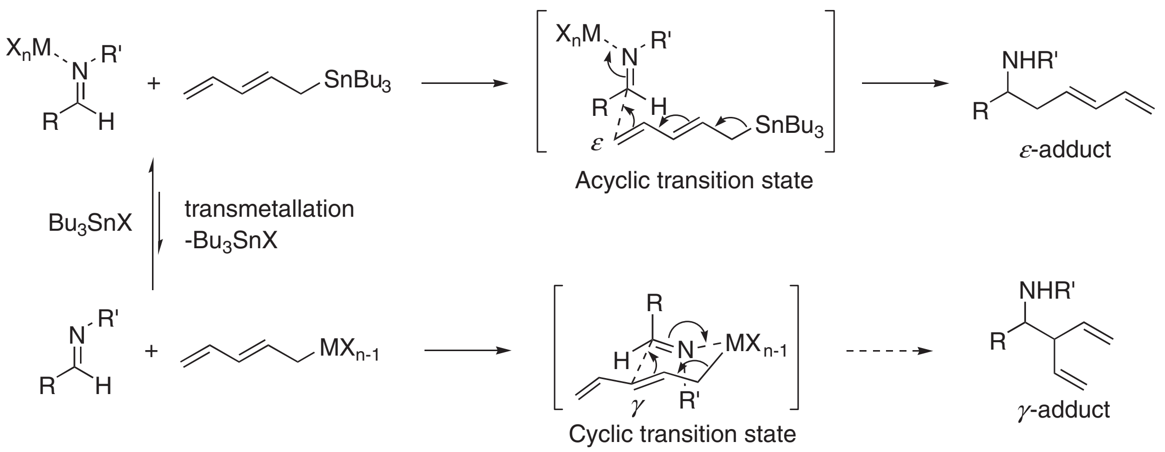
Imine/R	Product ratio, ε/γ (yield/%)	
	A ($BF_3 \cdot OEt_2$)	**B** ($InCl_3$)
p-$O_2NC_6H_4$	>99/1 (98)	>99/1 (51)
C_6H_5	>99/1 (78)	>99/1 (64)
PhCH=CH	>99/1 (63)	>99/1 (78)
$(CH_3)_3C$	>99/1 (42)	>99/1 (51)
n-C_6H_{13}[a]	>99/1 (64)	>99/1 (57)

Conditions: **A**. $BF_3 \cdot OEt_2$ in CH_2Cl_2, −78 °C, 4 h. **B**. $InCl_3$ in CH_3CN, rt, 4 h. [a]Yields were determined as the corresponding acetamide.

The reason why the $InCl_3$-promoted reaction did not gave the γ-adduct at all is not clear so far, but we tentatively postulate the following reaction paths as shown in Scheme 2. When $InCl_3$ is used, tributylpentadienyltin would be equilibrated with pentadienylindium chloride ($MX_n = InCl_3$) given by the transmetallation,[5] where the former would be the major species.[6] When the indium reagent reacts with an aldehyde,[3b] the 6-membered cyclic transition state would be adopted to afford the γ-adduct. However, in the reaction with imines of lower reactivity such as *N*-phenyl imines ($R' = Ph$), the cyclic transition state may not be favored[7] because of the steric congestion of the γ-position of the pentadienyl moiety and the axially located substituents R and R′. Thus the reaction from the $InCl_3$-coordinated imine and the tin reagent via the acyclic transition state would be much faster.

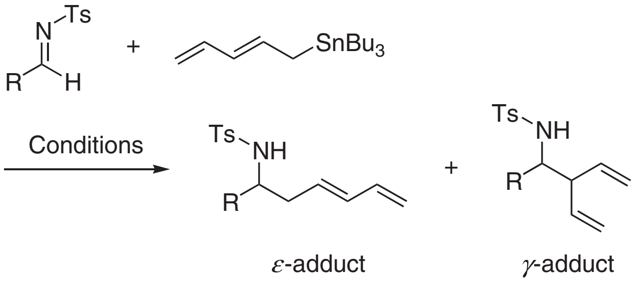
Standing on this consideration, we assumed that the unreactiveness of the indium reagent toward an imine could be overcome if the imine is more reactive. Therefore, we next planned the application of *N*-sulfonylimines[8] as reactive imines. They may be also advantageous for the transmetallation because the coordination of a Lewis acid to them is less favorable than to the *N*-phenylimines due to the electron-withdrawing group on the nitrogen.

The results of the reactions with *N*-tosylimines are collected in Table 2. $ZnCl_2$ was also used for the present reaction, which also showed γ-selectivity in the reaction with aldehydes.[3a] Most of the reactions we attempted proceeded in good to high yields. As we expected, very high γ-selectivity was realized in the both $InCl_3$- and $ZnCl_2$-mediated reactions with various imines such



Scheme 2. Plausible reaction pathways for ε- and γ-adducts.

Table 2. Regiocontrolled pentadienylation of *N*-Sulfonylimines



Imine/R	Product ratio, ε/γ (yield/%)		
	A ($BF_3 \cdot OEt_2$)	**B** ($InCl_3$)	**C** ($ZnCl_2$)
p-$O_2NC_6H_4$	65/35 (76)	<1/99 (98)	<1/99 (97)
C_6H_5	87/13 (94)	<1/99 (80)	<1/99 (95)
p-$CH_3C_6H_4$	88/12 (94)	<1/99 (81)	<1/99 (97)
2-furyl	92/8 (99)	<1/99 (97)	<1/99 (93)
PhCH=CH	86/14 (66)	<1/99 (77)	<1/99 (94)
n-C_6H_{13}	72/28 (86)	<1/99 (89)	<1/99 (92)
cyclo-C_6H_{11}	87/13 (91)	19/81 (65)	1/99 (69)

Conditions: **A**. $BF_3 \cdot OEt_2$ in CH_2Cl_2, −78 °C, 4 h. **B**. $InCl_3$ in CH_3CN, 0 °C, 3 h. **C**: $ZnCl_2$ in Et_2O, rt, 12 h.

as aromatic, unsaturated, and aliphatic ones. The electronic effect of aromatic imines did not affect the regioselectivity. In contrast, BF_3-mediated reactions showed good to high ε-selectivity. This preference of regioselectivity is very similar to that of aldehydes. Thus Scheme 2 explains the present Lewis acid-dependence of the regioselectivity; $BF_3 \cdot OEt_2$ as a non-transmetallating Lewis acid took the path through the acyclic transition state, whereas $InCl_3$ and $ZnCl_2$ underwent the transmetallation to take the cyclic transition state path. The reaction of *tert*-butyl imine (*t*-BuCH=NTs) which is not included in Table 2 was sluggish probably due to its serious steric congestion.

These results clearly indicate that the regioselectivity in the pentadienylation can be controlled not only for the reaction of aldehydes but also for that of imines. It should be stressed that the regioselectivity for the imines is controlled by the combination of the Lewis acids and the *N*-substituents. This means that *N*-tosylimines have substantially different reactivity than *N*-phenylimines. Because almost complete ε/γ-regiocontrol has been achieved and the *N*-substituents can be utilized as protecting and/or functional groups for further transformation, more practical application of the present stereocontrolled pentadienylation would be possible in the syntheses of the nitrogen containing compounds, which is in progress in our laboratory.

References and Notes

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7 Poor reactivity via the cyclic transition state was supported by the $SnCl_4$ mediated reaction, where the reactive species is confirmed trichloropentadienyltin.[9] The reaction with benzalaniline afforded only 17% of the ε-adduct after 4 h at −78 °C.

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Published on the web (Advance View) January 8, 2004; DOI 10.1246/cl.2004.108