# Reaction of Yb-Imine Complexes with Isocyanates. Novel Synthesis of α-Aminoacetamides

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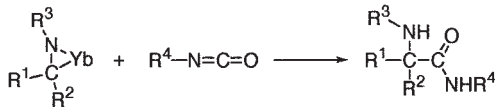
Yb(II)-imine complexes, prepared from Yb metal and aromatic imines in THF and HMPA, reacted with isocyanates to give α-aminoacetamides. This method provides a novel synthetic route to α-amino-substituted acetamide derivatives.

Organic synthesis using lanthanoid metals or reagents has been developed extensively.[1] In our study on the development of organic synthesis using lanthanoid metals, we have found that the reaction of Yb metal and an aromatic ketone gives a Yb-ketone complex via two-electron transfer.[2] This Yb complex reacts with various electrophiles including carbon electrophiles, indicating a "umpoled" dianionic character. Similarly, Yb metal reacts with an aromatic imine to form the corresponding Yb-imine complex.[3] This Yb-imine complex has relatively strong basicity compared with the Yb-ketone complex. Therefore, the Yb-imine complex abstracts protons from acetone to lead to the reduced amine.[4] The Yb-imine complex also catalyzes the isomerization of terminal alkynes to internal alkynes and the dehydrogenative coupling reaction of terminal alkynes and hydrosilanes.[5]

On the other hand, the reaction forming the C–C bond is one of important synthetic methods. However, there is only one example that the Yb-imine complex reacts with carbon electrophiles.[6] The Yb-imine complexes prepared *in situ* afford α-aminoacetic acid derivatives by the reaction with $CO_2$. If the Yb-imine complexes attack nucleophilically to the cumulene bond of isocyanates, the reaction will lead to the formation of α-aminoacetamides as shown in Scheme 1. Here we report a simple and novel synthesis of α-aminoacetamides from imines and isocyanates by using Yb metal.

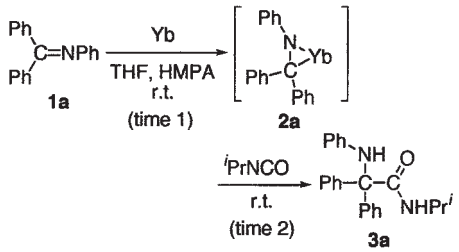


**Scheme 1.**

The synthesis of α-aminoacetamides in this study consists of the following two steps: the preparation of the Yb-imine complex and the reaction with an isocyanate. This one-pot synthesis can be conducted as follows.

Yb metal (0.25 mmol) and *N*-(diphenylmethylene)aniline (**1a**, 0.25 mmol) were placed under Ar and then THF (1.0 mL), hexamethylphosphoramide (HMPA, 0.25 mL) and MeI (3.0 μL, an activating agent of Yb) were added successively. The solution of the Yb-imine complex was prepared by stirring the mixture for the time indicated in Table 1 (time 1). The reaction of the Yb-imine complex was conducted by adding isopropyl isocyanate (0.50 mmol) and by stirring the mixture for the time indicated in Table 1 (time 2). The reaction mixture was quenched with $H_2O$ (0.1 mL). The resulting precipitates were filtered off and the filtrate was analyzed by GC. Column chromatography on silica gel afforded *N*-isopropyl-2,2-diphenyl-2-(phenylamino)acetamide (**3a**)[7] as crystals. The results are given in Table 1.

**Table 1.** Optimization of reaction conditions[a]



| Entry | Time 1/h | Time 2/h | Yield/%[b] |
|---|---|---|---|
| 1 | 1 | 1 | 49 |
| 2 | 2 | 1 | 96 |
| 3 | 3 | 1 | 99 |
| 4 | 6 | 1 | 89 |
| 5 | 8 | 1 | 69 |
| 6 | 3 | 0.5 | 75 |
| 7 | 3 | 0.75 | 90 |
| 8 | 3 | 1.5 | 89 |
| 9 | 3 | 2 | 64 |

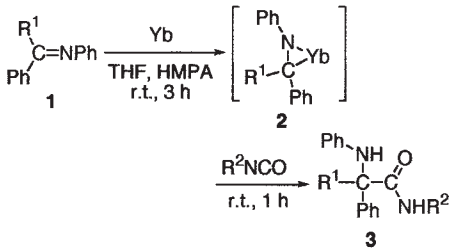
[a]Conditions: Yb (0.25 mmol), **1a** (0.25 mmol), THF (1.0 mL), HMPA (0.25 mL), $^i$PrNCO (0.5 mmol), MeI (3.0 μL). [b]GC yield.

The best result was obtained in the case requiring 3 h for the first step (time 1) and 1 h for the second step (time 2).

Next, we examined the additives except HMPA. In the absence of HMPA, the yield of aminoacetamide **3a** was 34%. Addition of 1,3-dimethylimidazolidin-2-one or dimethoxyethane was not effective in the formation of **3a**. Other additives such as *N*,*N*-dimethylacetamide, *N*,*N*′,*N*′-tetramethylurea and trimethyl phosphate retarded the formation of **3a**. As the result, HMPA is essential for this aminoacetamide synthesis.

The optimized conditions were employed for the reaction of various Yb-imine complexes and isocyanates. The results are given in Table 2. 4-Methyl and methoxy-substituted aromatic imines (**1b** and **1c**) reacted with isopropyl isocyanate to give the corresponding α-aminoacetamides (**3b** and **3c**)[7] in 60 and 45% yields, respectively. The reaction of Yb-imine complexes **2a**–**2c** with propyl and hexyl isocyanates proceeded smoothly to give the corresponding aminoacetamides (**3d**–**3g**). However, the reaction with phenyl isocyanate did not provide the aminoacetamide even in the prolonged reaction time.

**Table 2.** Reaction of Yb-imine complexexs **3** with isocyanates[a]




| Entry | $R^1$ | $R^2$ | Product | Yield/%[b] |
|---|---|---|---|---|
| 1 | 4-$MeC_6H_4$ | $(CH_3)_2CH$ | **3b** | 60 |
| 2 | 4-$MeOC_6H_4$ | $(CH_3)_2CH$ | **3c** | 45 |
| 3 | Ph | $CH_3CH_2CH_2$ | **3d** | 49 |
| 4 | Ph | $CH_3(CH_2)_4CH_2$ | **3e** | 23 |
| 5 | 4-$MeC_6H_4$ | $CH_3(CH_2)_4CH_2$ | **3f** | 26 |
| 6 | 4-$MeOC_6H_4$ | $CH_3(CH_2)_4CH_2$ | **3g** | 27 |

[a]Conditions: Yb (0.25 mmol), **1** (0.25 mmol), THF (1.0 mL), HMPA (0.25 mL), $R^2NCO$ (0.5 mmol), MeI (3.0 μL). [b]GC yield.

In summary, we have found a new approach to α-aminoacetamides by using Yb-imine complexes and isocyanates. Although the reactivity of isocyanates to the Yb-imine complexes is similar to that of $CO_2$, this reaction provides a very simple and one-pot synthesis of highly substituted α-aminoacetamides. This simple and convenient procedure will be applied to the synthesis of functionalized aminoacetamides in near future.

## References and Notes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7 Spectral data of representative α-aminoacetamides **3** are as follows. **3a**: mp 170–171 °C; IR (KBr) $\nu_{max}$ ($cm^{-1}$) 3382 (N–H), 1670 (C=O); $^1$H NMR ($CDCl_3$) $\delta$ 1.02 (d, $J$ = 7 Hz, 6H), 4.07 (sept, $J$ = 7 Hz, 1H), 5.13 (br s, 1H), 6.34 (br s, 1H), 6.43 (d, $J$ = 7 Hz, 2H), 6.62 (t, $J$ = 7 Hz, 1H), 6.98 (d, $J$ = 7 Hz, 2H), 7.12–7.29 (m, 6H), 7.54 (d, $J$ = 7 Hz, 4H); $^{13}$C NMR ($CDCl_3$) $\delta$ 22.2, 41.8, 71.1, 115.8, 118.2, 122.4, 128.1, 128.4, 128.6, 141.5, 144.6, 170.6. Found: C, 80.08; H, 7.04; N, 8.10%. Calcd for $C_{23}H_{24}N_2O$: C, 80.20; H, 7.02; N, 8.13%. **3b**: mp 170–171 °C; IR (KBr) $\nu_{max}$ ($cm^{-1}$) 3382 (N–H), 1649 (C=O); $^1$H NMR ($CDCl_3$) $\delta$ 1.02 (d, $J$ = 7 Hz, 6H), 2.30 (s, 3H), 4.07 (sept, $J$ = 7 Hz, 1H), 5.13 (br s, 1H), 6.34 (br s, 1H), 6.44 (d, $J$ = 7 Hz, 2H), 6.64 (t, $J$ = 7 Hz, 1H), 7.00 (t, $J$ = 7 Hz, 2H), 7.09–7.52 (m, 9H); $^{13}$C NMR ($CDCl_3$) $\delta$ 20.4, 22.2, 41.8, 71.1, 115.8, 118.2, 127.4, 128.1, 128.4, 128.6, 128.9, 137.3, 138.5, 141.4, 144.6, 144.7, 170.8. Found: C, 80.34; H, 7.29; N, 7.76%. Calcd for $C_{24}H_{26}N_2O$: C, 80.41; H, 7.31, N, 7.81%. **3c**: mp 133–135 °C; IR (KBr) $\nu_{max}$ ($cm^{-1}$) 3382 (N–H), 1649 (C=O); $^1$H NMR ($CDCl_3$) $\delta$ 1.05 (d, $J$ = 7 Hz, 6H), 3.77 (s, 3H), 4.07 (sept, $J$ = 7 Hz, 1H), 5.26 (br s, 1H), 6.38 (br s, 1H), 6.43 (d, $J$ = 7.5 Hz, 2H), 6.64 (t, $J$ = 7.5 Hz, 1H), 6.80 (t, $J$ = 7.5 Hz, 2H), 7.00–7.52 (m, 9H); $^{13}$C NMR ($CDCl_3$) $\delta$ 22.3, 41.8, 55.2, 70.6, 113.5, 115.8, 118.1, 127.5, 128.2, 128.4, 128.6, 129.8, 133.3, 141.6, 144.6, 158.7, 170.1. Found: C, 76.80; H, 6.95; N, 7.40%. Calcd for $C_{24}H_{26}N_2O_2$: C, 76.98; H, 7.00; N, 7.48%.