Lanthanoid Metal Promoted Reaction of Diaryl Ketones and Thioketones with Isocyanides

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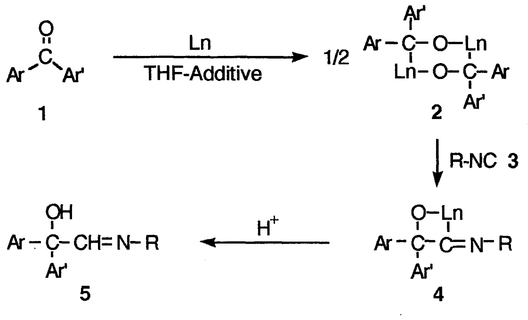
Ytterbium and samarium metals promote the coupling reaction of diaryl ketones and thioketones with isocyanides, leading to 2,2-diaryl-2-hydroxyethylideneamines and 2-amino-1,1-diarylethylene, respectively, in fairly good yields.

Previously, we found that diaryl ketones were reduced with lanthanoid metals such as ytterbium and samarium to give dianion complexes **2**, which reacted with various electrophiles at the carbonyl carbon.[1] The complexes **2** included the divalent lanthanoids and their dimeric structure was determined by X-ray analyses.[2] Diaryl thioketones reacted also with lanthanoid metals in a similar manner.[3] In order to get further information on the reactivities of the complexes **2**, we have investigated their reaction with isocyanides, since it has been known that isocyanides insert into carbon-lanthanoid(III) bond[4] whereas R-NC bond is reductively cleaved by divalent lanthanoids.[5] We report herein a coupling reaction of diaryl ketones and thioketones with isocyanides via insertion reaction of isocyanides to the complexes **2**.

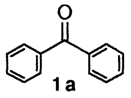
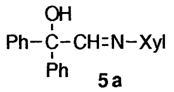
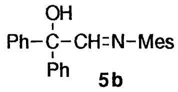
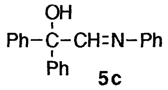
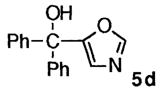
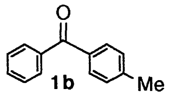
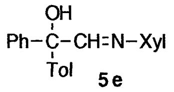
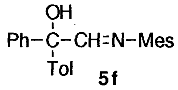
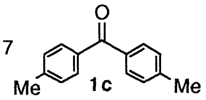
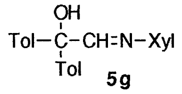
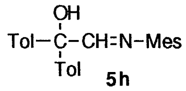
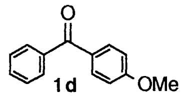
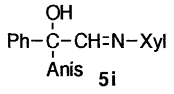
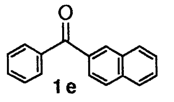
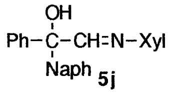
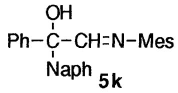
Treatment of 2,6-xylyl isocyanide (**3a**) with benzophenone-Yb complex **2a**, generated from Yb metal and an equimolar amount of benzophenone, at -35 °C in THF/HMPA and subsequent hydrolysis gave 2,2-diphenyl-2-hydroxyethylidene-2,6-dimethylaniline (**5a**) in 69% yield (Scheme 1). The yield decreased as the reaction temperature increased. Other highly coordinating additives such as 1,3-dimethyl-2-imidazolidinone (DMI) and *N,N'*-dimethylpropyleneurea (DMPU) could be used instead of HMPA, but in the absence of these additives the reaction became sluggish and the yield decreased. Sm metal also promoted the reaction to afford the product **5a** in 59 % yield under the identical conditions. Deuterolysis of the reaction mixture resulted in 81% deuterium incorporation at the iminium carbon of **5a**. Thus the reaction is likely to proceed via oxymetallacycle intermediate **4a**, which is formed by insertion of isocyanide **3a** into the carbon-Yb (II) bond of the complex **2a**.



Scheme 1.

The results of the coupling reaction of diaryl ketones **1** with various isocyanides **3** using Yb metal are summarized in Table 1. The reaction with 2,6-xylyl and mesityl isocyanides (**3a**) and (**3b**) afforded the coupling products **5** in fairly good yields as

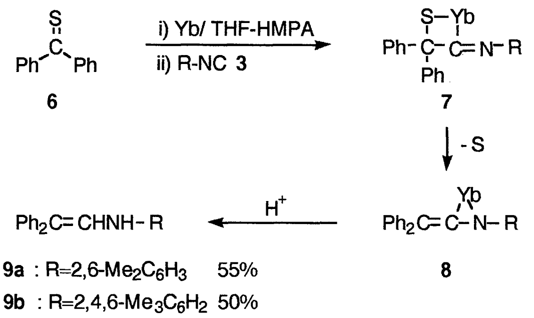
Table 1. Yb Metal Promoted Coupling Reaction of Diaryl Ketones with Isocyanides[a]

Run	Ketone	Isocyanide	Product	Yield/%[b]
1	 1a	2,6-$Me_2C_6H_3NC$ 3a	 $\mathrm{Ph{-}C(OH)(Ph){-}CH{=}N{-}Xyl}$ 5a	69 (76)[c]
2		2,4,6-$Me_3C_6H_2NC$ 3b	 $\mathrm{Ph{-}C(OH)(Ph){-}CH{=}N{-}Mes}$ 5b	64[d]
3		C_6H_5NC 3c	 $\mathrm{Ph{-}C(OH)(Ph){-}CH{=}N{-}Ph}$ 5c	23
4		EtO_2CCH_2NC 3d	 5d	20
5	 1b	3a	 $\mathrm{Ph{-}C(OH)(Tol){-}CH{=}N{-}Xyl}$ 5e	67
6		3b	 $\mathrm{Ph{-}C(OH)(Tol){-}CH{=}N{-}Mes}$ 5f	63
7	 1c	3a	 $\mathrm{Tol{-}C(OH)(Tol){-}CH{=}N{-}Xyl}$ 5g	66
8		3b	 $\mathrm{Tol{-}C(OH)(Tol){-}CH{=}N{-}Mes}$ 5h	68
9	 1d	3a	 $\mathrm{Ph{-}C(OH)(Anis){-}CH{=}N{-}Xyl}$ 5i	34
10	 1e	3a	 $\mathrm{Ph{-}C(OH)(Naph){-}CH{=}N{-}Xyl}$ 5j	60 (45)[c]
11		3b	 $\mathrm{Ph{-}C(OH)(Naph){-}CH{=}N{-}Mes}$ 5k	55

[a] The reaction was carried out as described in the text. [b] GC yield based on the ketone. [c] DMI was used instead of HMPA. [d] Two equivalents of the isocyanide were used.

shown in Table 1. However phenyl isocyanide (**3c**) gave the product **5c** in lower yield (Run 3).[6] In the reaction with ethyl isocyanoacetate (**3d**), no expected product was obtained (Run 4). Instead, 5-(diphenylhydroxymethyl)oxazole (**5d**) was formed, presumably by the fast nucleophilic addition of the complex **2a** to the ester moiety of **3d**,[1] followed by cyclization.[7]

When the reaction of thiobenzophenone (**6**) with the isocyanides **3a** and **3b** was carried out similarly, except for the treatment of **6** with Yb metal at -35 °C for 4 h,[3] secondary enamines **9a**[8] and **9b** were obtained in 55% and 50% yields, respectively (Scheme 2). In these reactions, insertion of the isocyanides **3** to the dianion complex of **6** would lead to the intermediates **7**, which were readily desulfurized to yield the products **9** via ketenimine-Yb complexes **8**.[3,9]



Scheme 2.

Next we studied the reaction of the complexes **2** with carbon monoxide, which was reported to react with organolanthanoids via insertion[10] or reduction modes[11], depending on the complexes. Exposure of **2a** to carbon monoxide resulted in the quantitative recovery of benzophenone (**1a**), although benzhydrol was formed in quantitative yield in the absence of it. Apparently, the complex **2a** acted as a reductant, but the products derived from carbon monoxide could not be captured.

General procedure for the Yb metal promoted coupling reaction of the ketone **1** with the isocyanide **3** is as follows: Methyl iodide (2 μL) was added under argon to a slurry of Yb metal (173 mg, 1 mmol) in HMPA (1 mL) to activate the metal. Then THF (4 mL) and diaryl ketone (1 mmol) was added successively. The reaction commenced within a few minutes and stirring was continued for 2 h at room temperature. Resulting deep red homogeneous solution was cooled to -35 °C. Isocyanide (1 mmol) in THF (2 mL) was added to the solution and the mixture was stirred for 2 h at this temperature. After addition of water (0.2 mL), the mixture was filtered through florisil. The filtrate was dried ($MgSO_4$), concentrated *in vacuo*, and chromatographed on silica gel using hexane-ethyl acetate eluent to provide analytically pure compound **5**.

In summary, diaryl ketone and thioketone-lanthanoid complexes react with isocyanides to afford unprecedented coupling products, but in contrast they are converted to the starting ketones and thioketones with carbon monoxide.

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6 Since this reaction was relatively complicated, it was unclear whether the competitive reduction of the isocyanide **3c** with **2a** took place as previously reported,[5] or not. The reaction with *tert*-butyl isocyanide gave also an untractable mixture.

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8 Compound **9a**: ^{1}H NMR ($CDCl_3$) δ 2.26 (6H, s, 2Me), 5.36 (1H, d, J = 11.9 Hz, NH), 6.77 (1H, d, J = 11.9 Hz, CH=C), 7.10-7.50 (13H, m, Ar); ^{13}C NMR ($CDCl_3$) δ 18.8 (2CH_3), 113.8 (4°), 123.6, 124.6, 125.3, 126.8, 128.2, 128.8, 129.2, 130.5, 131.0 (4°), 131.5, 138.7 (4°), 140.5 (4°), 141.9 (4°); MS (70 eV) m/e 299 (M^+). Satisfactory elemental analysis was obtained as an *N*-acetyl compound.

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