APPLIED ORGANOMETALLIC CHEMISTRY, VOL. 9, 461–466 (1995)

A New Reduction System by the Combination of Lanthanoid Metals (Ln) and LnI_2: Deoxygenative Coupling of Amides to *vic*-Diaminoalkenes

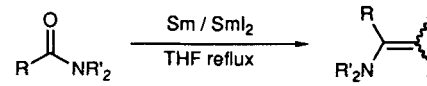
Akiya Ogawa,* Taizoh Nanke, Noriaki Takami, Masahito Sekiguchi, Nobuaki Kambe and Noboru Sonoda*
Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565, Japan

Deoxygenative coupling of aromatic amides takes place successfully by the use of a mixed system comprising of ytterbium metal and ytterbium diiodide, providing the corresponding *vic*-diaminoalkenes in good yields. The same reaction does not take place if Yb metal or YbI_2 is used alone. These results suggest novel enhancement of reducing ability by the combination of ytterbium(0) and ytterbium(II) diiodide. The Yb/YbI_2 system is also effective for dethiolative coupling of thioamides, as sulfur analogues of amides. This paper also deals with reductive coupling of thioamides and selenoamides by using an Sm/SmI_2 mixed system.

Keywords: ytterbium–ytterbium diiodide; *vic*-diaminoalkene; deoxygenative coupling; amide; samarium–samarium diiodide; thioamide; selenoamide

INTRODUCTION

The organic chemistry of rare-earth elements has been growing in recent years, because of the many synthetic applications of these elements and their inorganic and organic compounds.[1–4] Among the rare-earth reagents developed, samarium diiodide (SmI_2) is widely employed as a useful one-electron transfer reagent in organic synthesis.[1,2,4,5] A variety of organic functional groups such as organic halides and carbonyl compounds can be reduced easily by SmI_2 under mild conditions.[6,7] For example, aldehydes and ketones can be reduced to the corresponding alcohols or reductive coupling products. Contrary to this, there are only very limited examples reported to date of the reduction of amides by using SmI_2. SmI_2 itself cannot reduce amides at all; recently Kamochi and Kudo reported that the reaction system comprising SmI_2 and base[8] (or acid[9]) is effective for the reduction of primary and secondary amides to the corresponding amines or alcohols. Recently, we have disclosed the first example of deoxygenative coupling of *N*,*N*-disubstituted amides by an unprecedented Sm/SmI_2 system as indicated in Eqn [1].[10]



[1]

It is noteworthy that the present amide coupling proceeds only in the presence of both samarium (Sm) metal and SmI_2. A similar pronounced effect by the combination of Sm metal and SmI_2 is also observed in the reduction of organic halides.[11] These findings led us to examine whether other rare-earth metals and their halides exhibit a similar enhanced reducing ability toward the amide coupling reaction. Herein we report that the Yb/YbI_2 system indicates a higher reducing ability, compared with Yb (or YbI_2) alone, in the reductive coupling of amides.[10,11] Also, this paper describes how such reagents, comprising Ln metal and Ln halides, can be employed for the efficient reductive coupling of chalcogen analogues of amides, i.e. thioamides and selenoamides.[12]

EXPERIMENTAL

Unless otherwise noted, materials were obtained from commercial suppliers and purified by distillation or recrystallization. Ytterbium powder

* Authors to whom correspondence should be addressed.

CCC 0268–2605/95/050461–06

Received 1 July 1994
Accepted 25 July 1994

(99.9%) was purchased from Aldrich and was used without further purification. Samarium powder in oil (99.9%), cerium powder in oil (99.9%), and lanthanum powder in oil (99.9%) were purchased from High Purity Chemicals or Aldrich, and were used after washing with dry pentane, followed by drying under reduced pressure. Ytterbium diiodide (YbI_2), samarium diiodide (SmI_2), cerium triiodide (CeI_3), and lanthanum triiodide (LaI_3) were prepared by the reaction of the corresponding metals with 1,2-diiodoethane in freshly distilled (sodium/benzophenone ketyl)–THF.[6,13] Thioamides were prepared from the corresponding amides by using Lawesson's reagent [2,4-bis(4-methoxyphenyl)-1,3 - dithia - 2,4 - diphosphetane - 2,4 - disulfide].[14] Selenoamides were synthesized according to the literature.[15]

^{1}H NMR spectra were recorded on a JEOL JNM-GSX-270 (270 MHz) spectrometer using $CDCl_3$ as the solvent with Me_4Si as the internal standard. ^{13}C NMR spectra were taken on a JEOL JNM-GSX-270 using $CDCl_3$ as the solvent. Chemical shifts in ^{13}C NMR were measured relative to $CDCl_3$ and converted to δ (Me_4Si) value by using δ ($CDCl_3$) = 76.9 ppm. IR spectra were determined on a Perkin–Elmer Model 1600 spectrometer. Melting points were determined on a Yanagimoto micro melting point apparatus. Mass spectra were obtained on a JEOL JMS-DX303 in the analytical section of our department. Elemental analyses were also performed there.

Representative procedure for the deoxygentive coupling of amides with Yb/YbI_2

Synthesis of 1,2-Dipiperidinostilbene (2a)

In a 20 ml two-necked flask equipped with a condenser were placed, under an argon atmosphere, ytterbium (Yb) powder (0.7 mmol), 1,2-diiodoethane (0.3 mmol), and THF (3 ml). The mixture was heated at 67 °C for 1 h with magnetic stirring, and, at this stage, Yb/YbI_2 reagent was then prepared. To the THF solution of Yb/YbI_2 was added benzoylpiperidine **1a** (0.5 mmol), and the resulting solution was stirred at 67 °C for 4 h. After the reaction was complete, saturated $NaHCO_3$ (40 ml) was added to the reaction mixture, and the products were extracted with diethyl ether (20 ml × 3). The combined extracts were dried ($MgSO_4$), and the solvent was evaporated. Purification by column chromatography on basic alumina (activity I, Merck Art. 02069) containing 15 wt % of water using hexane as an eluent provided 38 mg (0.11 mmol, 43%) of 1,2-dipiperidinostilbene **2a** (E/Z = 84:16, a yellow solid, m.p. 112.0–112.5 °C).

^{1}H NMR (270 MHz, $CDCl_3$) [*E*-isomer]: δ 1.27 (brs, 12H), 2.29 (brs, 8H), 7.05–7.19 (m, 2H), 7.19–7.35 (brd, 8H). Nuclear Overhauser enhancement (NOE) experiment: Irradiation of the *o*-phenyl multiplet at δ 7.05–7.35 resulted in a 7% enhancement of the signal at δ 2.29 (methylene broad singlet). [*Z*-isomer]: δ 1.50 (brs, 12H), 2.91 (brs, 8H), 6.83–6.97 (m, 6H), 6.97–7.05 (m, 4H). ^{13}C NMR (68 MHz, $CDCl_3$) [*E*-isomer]: δ 24.43, 27.18, 52.91, 126.21, 127.64, 129.68, 136.52, 142.35. [*Z*-isomer]: δ 24.76, 26.98, 51.90, 125.43, 127.06, 131.31, 137.71, 140.61; IR (NaCl): 3054, 3018, 2929, 2850, 2812, 1594, 1489, 1442, 1378, 1228, 1194, 1112, 755, 670 cm^{-1}. MS (EI), *m/z* 346 (M^+, 100).

Analysis: calcd for $C_{24}H_{30}N_2$: C, 83.19; H, 8.73; N, 8.08. Found: C, 82.99; H, 8.69; N, 8.02%.

1,2-Bis(diethylamino)stilbene (2b)

A pale yellow oil. ^{1}H NMR (270 MHz, $CDCl_3$) [*E*-isomer]: δ 0.84 (t, 12H, J = 7.1 Hz), 2.54 (q, 8H, J = 7.0 Hz), 7.16–7.40 (m, 10H). [*Z*-isomer]: δ 1.07 (t, 12H, J = 6.8 Hz), 3.03 (q, 8H, J = 7.0 Hz), 6.91–7.04 (m, 10H). ^{13}C NMR (68 MHz, $CDCl_3$) [*E*-isomer]: δ 14.27, 46.44, 126.00, 127.48, 130.08, 135.46, 141.97; [*Z*-isomer]: δ 14.79, 44.28, 125.01, 126.93, 131.84, 132.52, 140.70. IR (NaCl): 3075, 3055, 2964, 2926, 2865, 1595, 1542, 1443, 1375, 1227, 1200, 1070, 744, 699 cm^{-1}. MS (EI), *m/z* 322 (M^+, 58).

Analysis: calcd for $C_{22}H_{30}N_2$: C, 81.94; H, 9.38; N, 8.69. Found: C, 81.85; H, 9.45; N, 8.70%.

1,2-Dipiperidino-1,2-bis(*p*-methylphenyl)ethene (2c)

A yellow solid. ^{1}H NMR (270 MHz, $CDCl_3$) [*E*-isomer]: δ 1.35 (brs, 12H), 2.35 (brs, 14H), 7.10–7.23 (m, 8H). NOE experiment: irradiation of the *o*-tolyl multiplet at δ 7.10–7.23 resulted in an 8% enhancement of the signal at δ 2.35 (methylene singlet). [*Z*-isomer]: δ 1.56 (brs, 12H), 2.19 (s, 6H), 2.96 (brs, 8H), 6.80–7.00 (m, 8H). ^{13}C NMR (68 MHz, $CDCl_3$) [*E*-isomer]: δ 21.25, 24.51, 27.23, 52.82, 128.35, 129.55, 135.55, 135.97, 139.57. [*Z*-isomer]: δ 21.12, 24.81, 27.00, 51.90, 127.86, 131.09, 134.70, 137.28, 137.74. IR

(KBr): 3018, 2926, 2849, 2778, 1580, 1506, 1446, 1377, 1252, 1229, 1193, 1115, 1105, 1031, 999, 851, 820, 764, 721, 543, 494 cm^{-1}. MS (EI): *m/z* 374 (M^+, 100).

Analysis: calcd for $C_{26}H_{34}N_2$: C, 83.37; H, 9.15; N, 7.48. Found: C, 83.39; H, 9.19; N, 7.22%.

(*Z*)-1,2-Dipiperidino-1,2-di(α-naphthyl)ethene [(*Z*)-2d]

M.p. 174.7–175.5 °C (a yellow solid). ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.58 (brs, 12H), 3.04 (m, 8H), 6.78 (t, 2H, J = 7.81 Hz), 7.00–7.52 (m, 8H), 7.59 (d, 2H, J = 7.81 Hz), 8.26 (d, 2H, J = 8.3 Hz). ^{13}C NMR (68 MHz, $CDCl_3$): δ 24.91, 26.92, 49.81, 124.07, 124.61, 124.93, 125.10, 126.52, 127.21, 127.88, 128.61, 130.48, 133.00, 137.64. IR (KBr): 3046, 2931, 2849, 2802, 1592, 1504, 1451, 1380, 1234, 1197, 1120, 1112, 776 cm^{-1}. Assignment of stereochemistry of **2d** was determined by the IR absorbance of the C=C stretching frequency (1592 cm^{-1}). MS (EI): *m/z* = 446 (M^+, 100); exact mass calcd for $C_{32}H_{34}N_2$ 446.2722; found 446.2730.

Isolation of (*E*)-**2d** could not be attained. The following ^{1}H and ^{13}C NMR spectra were obtained by using a mixture of *E*- and *Z*-isomers. [*E*-isomer]: ^{1}H NMR (270 MHz, $CDCl_3$): δ 0.98 (m, 12H), 2.39 (m, 8H), 7.21–8.55 (m, 14H). ^{13}C NMR (68 MHz, $CDCl_3$): δ 24.31, 26.47, 51.62, 125.01, 125.28, 125.36, 125.45, 127.01, 128.09, 128.73, 133.27, 134.17, 136.37, 139.44.

***N,N'*-Dimethyl-5,6-diphenyl-1,2,3,4-tetrahydropyrazine (2e)**

M.p. 118–118.5 °C (a colorless solid). ^{1}H NMR (270 MHz, $CDCl_3$): δ 2.32 (s, 6H), 2.97 (s, 4H), 7.00–7.13 (m, 10H). ^{13}C NMR (68 MHz, $CDCl_3$): δ 42.10, 46.65, 125.57, 127.36, 130.43, 130.87, 138.99. IR (KBr): 2921, 2941, 2862, 2840, 2794, 1590, 1567, 1489, 1456, 1446, 1344, 1323, 1300, 1120, 1018, 753, 699 cm^{-1}. MS (EI): *m/z* 264 (M^+, 100).

Analysis: calcd for $C_{18}H_{20}N_2$: C, 81.78; H, 7.63; N, 10.60. Found: C, 81.58; H, 7.63; N, 10.41%.

Reductive coupling of thioamides with Sm/SmI$_2$

In a 20-ml two-necked flask equipped with a condenser were placed, under an argon atmosphere, Sm powder (1.25 mmol), 1,2-diiodoethane (0.55 mmol), and THF (5.5 ml). The mixture was heated at 67 °C for 1 h with magnetic stirring, and, at this stage, Sm/SmI$_2$ reagent was then prepared. To this solution was added *p*-chlorothiobenzoylpiperidine **1f'** (1 mmol), and the resulting solution was stirred at 67 °C for 2 h. Workups similar to those described in the amide coupling provide 216 mg (0.52 mmol, 52%) of 1,2-di-*p*-chlorophenyl-1,2-dipiperidinoethene (**2f**): a yellow solid.

^{1}H NMR (270 MHz, $CDCl_3$) [*E*-isomer]: δ 1.37 (brs, 12H), 2.34 (brs, 8H), 7.15–7.40 (m, 8H). [*Z*-isomer]: δ 1.58 (brs, 12H), 2.96 (brs, 8H), 7.00 (brs, 8H). ^{13}C NMR (68 MHz, $CDCl_3$) [*E*-isomer]: δ 24.27, 27.07, 52.91, 127.92, 130.71, 131.71, 135.68, 140.57. [*Z*-isomer]: δ 24.58, 26.89, 51.70, 127.52, 121.18, 132.34, 136.85, 138.94. IR (KBr): 2928, 2849, 2810, 1486, 1448, 1378, 1227, 1196, 1114, 1088, 835, 426 cm^{-1}. MS (EI): *m/z* 414 (M^+, 100).

Analysis: calcd for $C_2H_{28}N_2Cl_2$: C, 69.39; H, 6.79; N, 6.74. Found: C, 69.79; H, 6.84; N, 6.70%.

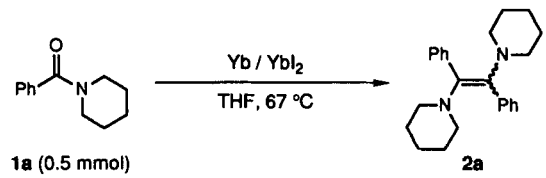
Deselenative coupling of selenoamides using Sm/SmI$_2$ was performed similarly.

RESULTS AND DISCUSSION

In order to clarify whether the Yb/YbI$_2$ mixed system exhibits a pronounced effect on the amide coupling, the reaction of benzoylpiperidine (**1a**) with Yb metal and/or YbI$_2$ was examined.[4] (For representative examples of synthetic reactions using ytterbium, see Refs 16 and 17.) As indicated in Table 1, the reduction of **1a** using Yb metal or YbI$_2$ alone did not proceed at all (runs 1 and 3), whereas the Yb/YbI$_2$ mixed reagents could reduce benzoylpiperidine to afford 1,2-dipiperidinostilbene (**2a**) in 56% yield (run 2).

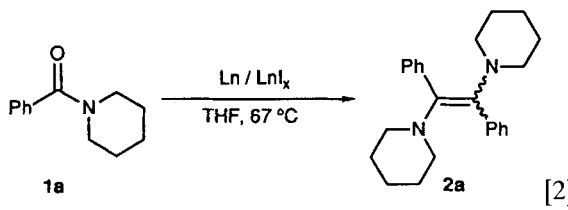
Although the yield of the deoxygenative coupling product (**2a**) was lower in comparison with the case using Sm/SmI$_2$ reported previously (Eqn [2]),[10] these results clearly indicate the enhancement of the reducing ability in the amide coupling reaction by the combination of Yb metal and YbI$_2$. Similarly some other rare-earth mixed systems were attempted. However, La/LaI$_3$ exhibited only a slight effect on the desired amide coupling reaction, and no reaction was observed in the case of Ce/CeI$_3$ (see Eqn [2]).

Table 1 Deoxygenative coupling of benzoylpiperidine by using ytterbium reagents



Run	Yb (mmol)	YbI_2 (mmol)	Additive	time (h)	Yield of **2a** (%)[a]	*E*/*Z*[a]
1	0.0	0.6	None	15	NR	—
2	0.4	0.3	None	4	56[b]	84/16
3	0.5	0.0	None	1	NR	—
4	0.0	0.6	Na (1.0 mmol)	0.5	21	84/16
5	0.0	0.6	Mg (3.0 mmol)	22	NR	—

[a] Determined by ^{1}H NMR. NR, No reaction. [b] Isolated yield of **2a** was 43% (see Experimental section).



[2]

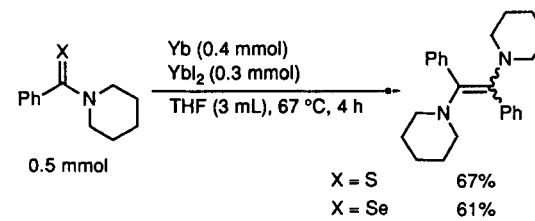
Sm / SmI_2	1 h	92%
La / LaI_3	14 h	3%
Ce / CeI_3	15 h	no reaction
Sm / cat. SmI_2	2 h	61%
Mg / SmI_2	2 h	72%

When sodium (Na) was employed, instead of Yb metal, for the reaction of **1a** with YbI_2, a complex mixture containing small amounts of the desired **2a** was formed (run 4 in Table 1). This is probably due to the further reduction of **2a** by Na (or Na/YbI_2). On the other hand, magnesium (Mg) metal did not cause amide coupling with YbI_2 (run 5).

Deoxygenative coupling of several aromatic amides was examined by the use of Yb/YbI_2 and the corresponding coupling products (**2b–2e**) were obtained in moderate yields (Table 2). Bis(benzoyl)ethylenediamine (**1e**) underwent intramolecular coupling to give the tetrahydropyrazine derivative **2e** (run 4). These results do suggest that Yb/YbI_2 is promising as a new reducing system in organic synthesis, while the reducing ability of Yb/YbI_2 appears to be a little lower compared with that of Sm/SmI_2.

As mentioned in the previous paper, amide coupling using Sm/SmI_2 proceeded smoothly to afford higher yields of *vic*-diaminoalkenes.[10] The samarium system worked well even in the presence of a catalytic amount of SmI_2. Moreover, the combination of SmI_2 and Mg metal was also effective for the amide coupling reaction (Eqn [2]).

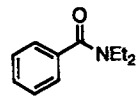
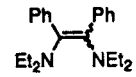
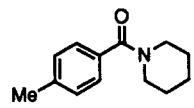
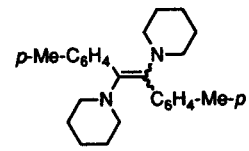
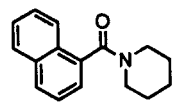
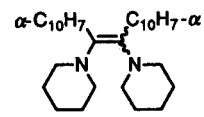
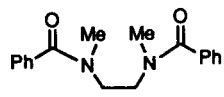
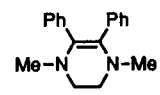
As an extension of our interest in the reduction systems made up of Ln(0) and Ln(II), we next examined the reduction of thioamides and selenoamides as amide analogues bearing a soft metal–carbon double bond.[18–20] Table 3 represents the dethiolative coupling reaction of thiobenzoylpiperidine (**1a′**) using Sm/SmI_2 under several different conditions. Treatment of **1a′** with Sm/SmI_2 at 67 °C for 2 h led to the formation of 1,2-dipiperidinostilbene (**2a**) quantitatively (run 2). As can be seen from runs 1–3, again, both Sm metal and SmI_2 were essential for the dethiolative coupling of the thioamide. The yields of **2a** are dependent on the amounts of Sm metal employed (run 4). The coupling reaction of **1a′** with Sm metal also proceeded smoothly by the use of a catalytic amount of SmI_2 (run 5). As well as Sm/SmI_2, Yb/YbI_2 was operative on the thioamide coupling reaction (Eqn [3]).



[3]

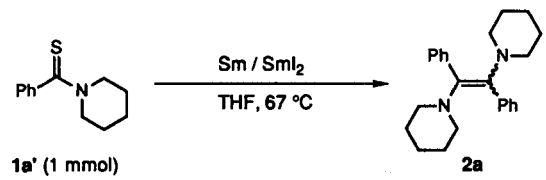
Furthermore, deselenative coupling of selenoamides was examined by using the Sm/SmI_2 or Yb/YbI_2 system. As the result, selenobenzoylpiperidine (**1a″**) underwent reduction easily to

Table 2 Yb/YbI$_2$-induced deoxygenative coupling amides[a]

Run	Amide		Product		Yield (%)[b]	*E*/*Z*[c]
1		**1b**		**2b**	45 (63)	40/60
2		**1c**		**2c**	42 (66)	89/11
3		**1d**		**2d**	34[d]	
4		**1e**		**2e**	23	

[a] Reaction conditions: amide (0.5 mmol), Yb (0.4 mmol), YbI$_2$ (0.3 mmol), THF (3 ml), 67 °C, 4 h. [b] Isolated (NMR) yield. [c] *E*/*Z* ratio was determined by ^{1}H NMR. [d] Only the *Z*-isomer was isolated. It was difficult to isolate the *E*-isomer in pure form.

Table 3 Dethiolative coupling of benzoylthiopiperidine by using samarium reagents

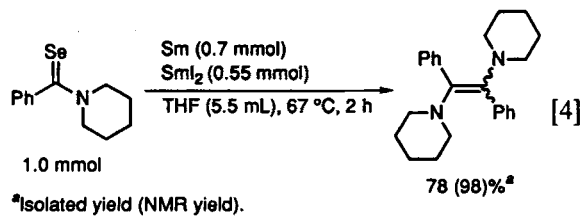


1a' (1 mmol) **2a**

Run	Sm (mmol)	SmI$_2$ (mmol)	THF (ml)	Time (h)	Yield of **2a** (%)[a]	*E*/*Z*
1	0.0	1.2	12.0	2	NR	—
2	0.7	0.55	5.5	2	82 (99)	83/17
3	0.5	0.0	2.0	2	NR	—
4	0.3	2.2	22.0	3	(52)	83/17
5	1.0	0.2	2.0	3	(95)	67/33
6[b]	1.0	0.3	3.0	3	52 (87)	80/20

[a] Isolated yield (^{1}H NMR yield). [b] *p*-Chlorothiobenzoylpiperidine was used as the substrate.

give **2a** in good yields (Eqns [3] and [4]).



[4]

In conclusion, a new reduction system, i.e. Yb/YbI$_2$, has been developed, which is effective for the reductive coupling of aromatic amides and their chalcogen analogues.

Acknowledgements This research was supported in part by a Grant-in-Aid for Scientific Research on the Priority Area 'New Development of Rare Earth Complexes' No. 06241247 from the Ministry of Education, Science and Culture, Japan. Thanks are due to the Instrumental Analysis Center, Faculty of Engineering, Osaka University, for assistance in obtaining mass spectra on a JEOL JMS-DX303.

REFERENCES

1. H. B. Kagan and J. L. Namy, *Tetrahedron* **42**, 6573 (1986).
2. G. A. Molander, *Chem. Rev.* **92**, 29 (1992).
3. T. Imamoto, in: *Comprehensive Organic Synthesis*, Trost, B. M. (ed.), Pergamon, Oxford, 1991, Vol. 1, pp. 231–250.
4. G. A. Molander, in: *Comprehensive Organic Synthesis*, Trost, B. M. (ed.), Pergamon, Oxford, 1991, Vol. 1, pp. 251–282.
5. J. Inanaga, *Rev. Heteroatom. Chem.* **3**, 75 (1990).
6. P. Girard, J. L. Namy and H. B. Kagan, *J. Am. Chem. Soc.* **102**, 2693 (1980).
7. J. Inanaga, M. Ishikawa and M. Yamaguchi, *Chem. Lett.* 1485 (1987).
8. Y. Kamochi and T. Kudo, *Tetrahedron Lett.* **32**, 3511 (1991).
9. Y. Kamochi and T. Kudo, *Tetrahedron* **48**, 4301 (1992).
10. A. Ogawa, N. Takami, M. Sekiguchi, I. Ryu, N. Kambe and N. Sonoda, *J. Am. Chem. Soc.* **114**, 8729 (1992).
11. A. Ogawa, T. Nanke, N. Takami, Y. Sumino, I. Ryu and N. Sonoda, *Chem. Lett.* 379 (1994).
12. M. Sekiguchi, A. Ogawa, N. Kambe and N. Sonoda, *Chem. Lett.* 315 (1991).
13. T. Imamoto, T. Kusumoto, Y. Hatanaka and M. Yokoyama, *Tetrahedron Lett.* **23**, 1353 (1982).
14. S. Raucher and P. Klein, *Tetrahedron Lett.* **21**, 4061 (1980).
15. A. Ogawa, J. Miyake, N. Kambe, S. Murai and N. Sonoda, *Bull. Chem. Soc. Jpn.* **58**, 1448 (1985).
16. Y. Fujiwara, K. Takaki and Y. Taniguchi, *J. Alloys Comp.* **192**, 200 (1993).
17. Z. Hou, K. Takamine, O. Aoki, H. Shiraishi, Y. Fujiwara and H. Taniguchi, *J. Org. Chem.* **53**, 6077 (1988) and references therein.
18. Y. Makioka, S. Uebori, M. Tsuno, Y. Taniguchi, K. Takaki and Y. Fujiwara, *Chem. Lett.* 611 (1994).
19. Y.-S. Liu, M.-Z. Bei, Z.-H. Zhou, K. Takaki and Y. Fujiwara, *Chem. Lett.* 1143 (1992).
20. Y. Makioka, Y.-S. Liu, M.-Z. Bei, Z.-H. Zhou, T. Shindo, Y. Taniguchi, K. Takaki and Y. Fujiwara, *Nippon Kagaku Kaishi* 475 (1993).