

# Reductive Dimerization and Reduction of Imines Using Lanthanum Metal

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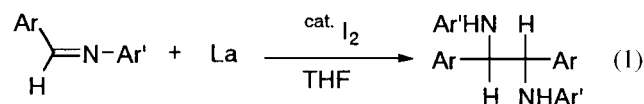
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**ABSTRACT:** The treatment of *N*-benzylideneaniline (**1a**) with a half-equivalent of lanthanum metal and a catalytic amount of iodine gave the reductive dimerization product of **1a**, a vic-diamine, in good yield. Various vic-diamines were synthesized from aldimines in this manner in moderate to good yields. Our findings suggest that electrons of a zero-valent lanthanum metal were efficiently utilized in this reductive dimerization. In the reaction of ketimines, however, a similar reductive dimerization did not take place, and the corresponding amines were formed as the sole products. © 2002 Wiley Periodicals, Inc. *Heteroatom Chem* 13:131–135, 2002; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.10007

## INTRODUCTION

Lanthanoid metal salts and organolanthanoid compounds have often been used in organic synthesis [1]. In particular, low-valent lanthanoid species having strong reducing ability, which were generated in situ by the reaction of lanthanoids with various reagents, have been widely used in organic synthesis [2]. Since these reagents have already lost one or two electrons of the zero-valent metal in the preparation step, before use as the reagent, these reductions usually required stoichiometric or an excess amount of lanthanoid reagents to produce a good yield of product by these methods. If three electrons,

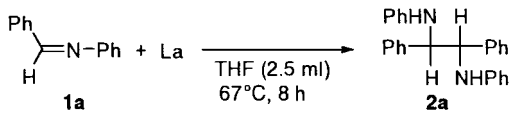
which may be supplied during the change from zero-valent metal to the stable trivalent ion, can be used directly in organic reactions, it is expected that the organic chemistry using lanthanoid compounds as reducing agents will be widely expanded. Hitherto, the use of ytterbium [3], samarium [4], and cerium [5] metals as agents in organic reactions have been reported; however, efficient use of the electrons of the lanthanoid metal has been extremely limited [6]. To establish a new method for the efficient use of the available electrons of lanthanum and related metals, we examined first the use of lanthanum metal itself, which has the largest redox potential [7] and can be purchased at the cheapest price of all lanthanoid metals [8]. We found that the reductive dimerization of aldimines with lanthanum metal occurred, accompanied by the efficient transfer of available electrons from the metal to the substrate (Eq. (1)).



## RESULTS AND DISCUSSION

The treatment of *N*-benzylideneaniline (**1a**) with lanthanum metal was examined under various reaction conditions and the results are listed in Table 1. *N*-Benzylideneaniline (**1a**) was treated with lanthanum metal (1 equiv.) in THF at 67°C for 8 h; however, reductive dimerization and/or reduction products were not obtained and the starting material was recovered (entry 1). We have already reported

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**TABLE 1** Reaction of *N*-Benzylideneaniline (**1a**) with Lanthanum Metal under Various Reaction Conditions


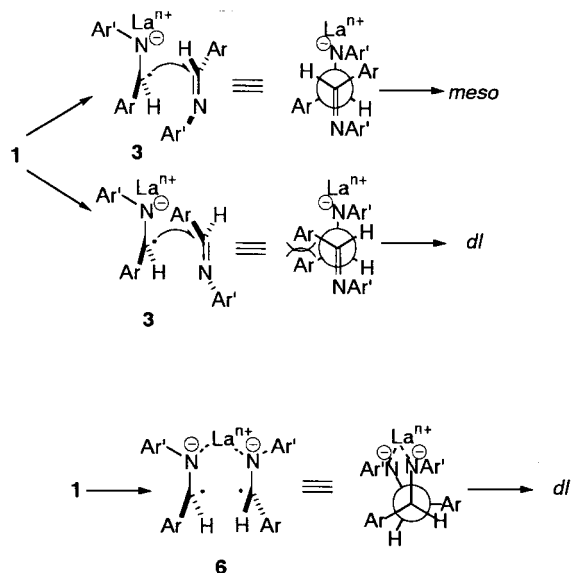
Entry	<b>1a</b> (mmol)	La (mmol)	I <sub>2</sub> (mmol)	Yield (%) <sup>a</sup> ( <i>dl</i> : <i>meso</i> )
1	2.0	2.0	—	0
2	2.0	4.0	0.8	87 <sup>b</sup> (55:45)
3	2.0	2.0	0.4	87 (49:51)
4	2.0	1.0	0.2	178 (33:67)

<sup>a</sup>GC yield based on lanthanum being assumed to function as a one electron donor atom. Parenthesis shows the ratio of *dl* and *meso* determined by <sup>1</sup>H NMR.

<sup>b</sup>GC yield based on imine.

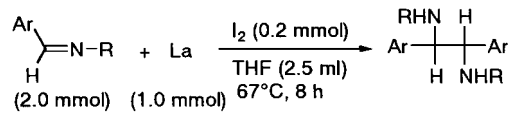
that the addition of a catalytic amount of iodine dramatically enhances the reaction of carbonyl compounds with lanthanum metal [9]. The reaction was then carried out in the presence of 0.2 equiv. of iodine, and the diamine (**2a**), the reductive coupling product of **1a**, was obtained in 87% yield (entry 2) [10]. To determine the possibility of the efficient use of several electrons present in a zero-valent lanthanum metal, we examined the reaction of **1a** with a 0.5 equiv. of lanthanum metal. When **1a** was allowed to react with a 0.5 equiv. amount of lanthanum metal in the presence of a catalytic amount of iodine, **2a** was produced in 178% yield (based on the presumption of only one electron being available from each atom of the lanthanum metal used) (entry 4). This yield clearly proves that about two electrons of the lanthanum metal were efficiently utilized in this coupling reaction. In addition, the diastereomeric ratio of the *vic*-diamine was affected by the amount of lanthanum metal used. The reductive dimerization reaction using a 0.5 equiv. of lanthanum metal gave the *meso*-isomer preferentially [12], and the *dl*-diamine was preferentially formed with use of 2 equiv. of lanthanum metal (entries 2 and 4). Although, at the present time, we cannot explain the reason why the diastereomeric ratio was affected by the amount of lanthanum metal used, the *meso* selectivity may be explained by consideration of the reaction path, including the addition of the ketyl like intermediate **3**, which was generated via the one electron transfer from lanthanum metal to **1**, to the carbon–nitrogen double bond of another imine (Scheme 1) [13].

Various aldimines were allowed to react with a 0.5 equiv. of lanthanum metal in the presence of a catalytic amount of iodine, and the results are shown in Table 2. When methyl and methoxy substituted

**SCHEME 1**

*N*-benzylideneanilines were treated with 0.5 equiv. of lanthanum metal, the corresponding *vic*-diamines were formed in moderate to good yields (entries 1, 2, 3, and 5). On the contrary, the reaction of an *N*-benzylideneaniline derivative containing a strongly electron withdrawing group such as a nitro did not occur (entry 4). In the case of an *N*-alkyl substituted aldimine, the yield of *vic*-diamine was very low because of various side reactions (entry 6).

Unlike aldimines, the reaction of *N*-diphenylmethylenedianiline (**4a**) with lanthanum metal did not produce the dimerized product, but obtained the reduction product, the amine **5a**, in 82% yield (entry 1 in Table 3). Ketimines **4b** and **4c** were also

**TABLE 2** Reductive Dimerization of Various Aldimines with Lanthanum Metal


Entry	Ar	R	Product	Yield (%) <sup>a</sup> ( <i>dl</i> : <i>meso</i> )
1	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	C <sub>6</sub> H <sub>5</sub>	<b>1b</b>	154 (39:61)
2	<i>o</i> -MeC <sub>6</sub> H <sub>4</sub>	C <sub>6</sub> H <sub>5</sub>	<b>1c</b>	125 (>99:<1)
3	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	C <sub>6</sub> H <sub>5</sub>	<b>1d</b>	125 (38:62)
4	<i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	C <sub>6</sub> H <sub>5</sub>	<b>1e</b>	n.r.
5	C <sub>6</sub> H <sub>5</sub>	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	<b>1f</b>	104 (39:61)
6	C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	<b>1g</b>	— <sup>b</sup>

<sup>a</sup>Isolated yield based on lanthanum being assumed to function as a one electron donor atom. Parenthesis shows the ratio of *dl* and *meso* determined by <sup>1</sup>H NMR.

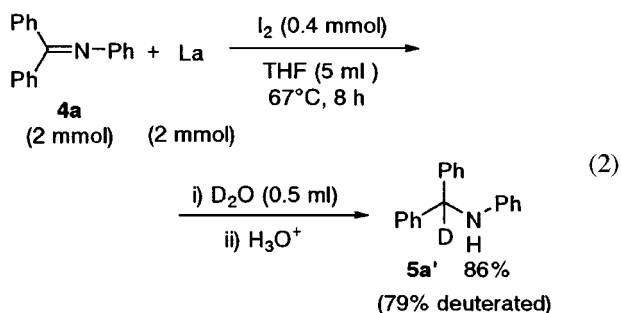
<sup>b</sup>Various complex mixtures were formed.

**TABLE 3** Reduction of Various Ketimines with Lanthanum Metal

Entry	Substrate	Time (h)	Yield (%) <sup>a</sup>
1	<b>4a</b>	8	82
2	<b>4b</b>	8	82
3	<b>4c</b>	24	48

<sup>a</sup>Isolated yield based on ketimine.

reduced by lanthanum metal to give the corresponding amines in 82 and 48% yields, respectively (Table 3). In order to better understand the reaction pathway, when the reaction was quenched with D<sub>2</sub>O instead of H<sub>2</sub>O, the amine **5a'**, in which the deuterium atom was introduced onto the carbon atom, was obtained in 86% yield (Eq. (2)).



Fujiwara and co-workers have reported that the reaction of **4a** with Yb metal in the presence of a catalytic amount of MeI gave **5a** in a good yield [14]. In this work, they proposed that **5a** was formed by the hydrolysis of the Yb(II) *N*-diphenylmethyleneaniline dianion. Recently, they succeeded in isolating the Yb(II) *N*-diphenylmethyleneaniline dianion by the reaction of **4a** with Yb metal in the presence of HMPA [15]. We then assumed that the formation of the amine as described above might occur through a similar lanthanum intermediate.

We have found that lanthanum metal can be used as an efficient reducing agent of imines in the presence of a catalytic amount of iodine. The results

shown here provide a new way of using lanthanum metal in organic synthesis.

Further studies on the utilization of lanthanum metal in organic synthesis are now in progress.

## EXPERIMENTAL

### Instruments

<sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a JEOL JNM-GSX-400 (400 MHz) spectrometer using CDCl<sub>3</sub> as a solvent with tetramethylsilane as the internal standard. FT-IR spectra were obtained on a Perkin Elmer Model PARAGON 1000 spectrophotometer. Mass spectra were measured on a Shimadzu Model QP-5050A instrument. Gas chromatography (GC) was carried out on a Shimadzu GC-14A instrument equipped with a flame ionizing detector and using a capillary column (Hicap-CBP-1-S25-025, 0.25 mm × 25 m).

### Reagents

Imines were prepared by the reaction of amines with carbonyl compounds. Iodine and lanthanum metal were commercially available high grade products and were used without purification. The other reagents and solvents were purified by the usual methods before use.

### General Procedure of the Reductive Dimerization of Aldimines with Lanthanum Metal in the Presence of a Catalytic Amount of Iodine

Lanthanum powder (139 mg, 1 mmol) was placed in a three-necked flask. Iodine (51 mg, 0.2 mmol), THF (2.5 ml.), and the aldimine (2 mmol) were added to the flask, and the mixture was stirred at 67°C for 8 h under a nitrogen atmosphere. The color of the solution gradually darkened. After the reaction was completed, methanol and silica gel were added and the mixture was stirred for 0.5 h. The resulting mixture was filtered and the filtrate was concentrated. Purification of the residue by column chromatography on silica gel afforded the corresponding *vic*-diamine. Products **2a** [16] and **2b-d** [17] were characterized by comparison of their spectral data with those of authentic samples. The structures of the products were assigned by their <sup>1</sup>H and <sup>13</sup>C NMR and IR spectra.

### General Procedure of the Reduction of Ketimines with Lanthanum Metal in the Presence of a Catalytic Amount of Iodine

Lanthanum powder (278 mg, 2 mmol) was placed in a three-necked flask. Iodine (102 mg, 0.4 mmol), THF

(5.0 ml.), and the ketimine (2 mmol) were added to the flask, and the mixture was stirred at 67°C for 8 or 24 h under a nitrogen atmosphere. The color of the solution gradually darkened. After the reaction was completed, methanol and silica gel were added and the mixture was stirred for 0.5 h. The resulting mixture was filtered and the filtrate was concentrated. Purification of the residue by column chromatography on silica gel afforded the corresponding amine. Products **5a** [18], **5b** [19], and **5c** [18] were characterized by comparison of their spectral data with those of authentic samples. The structures of the products were assigned by their <sup>1</sup>H and <sup>13</sup>C NMR and IR spectra.

*1,2-Diphenyl-N,N'-bis(4-methoxyphenyl) ethylenediamine (2f) (a mixture of dl and meso isomers).* <sup>1</sup>H NMR  $\delta$ : 3.64 (s, 6H, OCH<sub>3</sub>), 4.34 (br s, 2H, NH), 4.45 (s, 0.78H, CH), 4.87 (s, 1.22H, CH), 6.46–7.21 (m, 18H, Ar); <sup>13</sup>C NMR  $\delta$ : 55.8, 63.0, 65.1, 114.8, 114.9, 115.2, 115.6, 127.5, 127.6, 127.7, 128.3, 128.4, 128.7, 128.9, 138.7, 140.8, 152.3; IR: 3379, 3060, 3028, 3003, 2947, 2832, 1510, 1242, 1035, 821, 756 cm<sup>-1</sup>.

*N-Deuteriumdiphenylmethylaniline (5a').* <sup>1</sup>H NMR  $\delta$ : 4.18 (br s, 1H, NH), 6.49–7.34 (m, 15H, Ar); <sup>13</sup>C NMR  $\delta$ : 62.5 (t), 113.4, 117.6, 127.3, 128.3, 128.7, 129.1, 142.8, 147.3.

## ACKNOWLEDGMENT

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## REFERENCES

- [1] (a) Kagan, H. B. *New J Chem* 1990, 14, 453; (b) Curran, D. P.; Fevig, T. L.; Jasperse, C. P.; Totleben, M. J. *Synlett* 1992, 943; (c) Molander, G. A. *Chem Rev* 1992, 92, 29; (d) Kobayashi, S. *Synlett* 1994, 689; (e) Kamochi, Y.; Kubo, T. J. *Syn Org Chem Jpn* 1994, 52, 285; (f) Imamoto, T. *Lanthanides in Organic Synthesis*; Academic Press; New York, 1994; (g) Matsuda, Y. J. *Syn Org Chem Jpn* 1995, 53, 987; (h) Molander, G. A.; Harris, C. R. *Chem Rev* 1996, 96, 307; (i) Ito, Y.; Fujiwara, Y.; Yamamoto, T. In *Organic Synthesis by Means of Lanthanoids*; Kikan Kagaku Sousetu (Ed.); Gakkai Press Center, 1998, Vol. 37. (j) Kobayashi, S. *Lanthanide: Chemistry and Use in Organic Synthesis*; Springer-Verlag: Berlin, 1999 and references cited therein.
- [2] There are several methods for the generation of low-valent lanthanoid species.; (a) Sm/ICH<sub>2</sub>CH<sub>2</sub>I, Yb/ICH<sub>2</sub>CH<sub>2</sub>I, Eu/ICH<sub>2</sub>CH<sub>2</sub>I; Girard, P.; Namy, J. L.; Kagan, H. B. *J Am Chem Soc* 1980, 102, 2693; (b) Sm/CH<sub>2</sub>I<sub>2</sub>; Namy, J. L.; Girard, P.; Kagan, H. B. *Nouv J Chem* 1981, 5, 479; (c) Sm/I<sub>2</sub>; Imamoto, T.; Ono, M. *Chem Lett* 1987, 501; (d) Sm/HgI<sub>2</sub>; Deacon, G. B.; Forsyth, C. M. *Chem Lett* 1989, 837; (e) Sm/TMSCl/NaI; Akane, N.; Kanagawa, Y.; Nishiyama, Y.; Ishii, Y. *Chem Lett* 1992, 2431; (f) Sm/Et<sub>2</sub>AlI; Nishiyama, Y.; Shinomiya, E.; Kimura, S.; Ito, K.; Sonoda, N. *Tetrahedron Lett* 1998, 39, 3705; (g) Sm/SmBr<sub>3</sub>, SmBr<sub>3</sub>/BuLi; Yoshizawa, T.; Hatajima, T.; Amano, H.; Imamoto, T. *J. Chem Soc Jpn* 1993, 482; (h) SmBr<sub>3</sub>/Li; Lebrun, A.; Namy, J. L.; Kagan, H. B. *Tetrahedron Lett* 1993, 34, 2311; (i) Sm(OTf)<sub>3</sub>/BuLi; Fukuzawa, S.; Tsuchimoto, T.; Kanai, T. *Chem Lett* 1994, 1981; (j) Sm/SmI<sub>3</sub>; Ogawa, A.; Takami, N.; Sekiguch, M.; Ryu, I.; Kambe, N.; Sonoda, N. *J Am Chem Soc* 1992, 114, 8729; (k) Yb/BrCH<sub>2</sub>CH<sub>2</sub>Br; Watson, P. L.; Tulip, T. H.; Williams, I. *Organometallics* 1990, 9, 1999; (l) Yb/TMSBr; Taniguchi, Y.; Nakahashi, M.; Kuno, T.; Tuno, M.; Makioka, Y.; Takaki, K.; Fujiwara, Y. *Tetrahedron Lett* 1994, 35, 4111; (m) Yb/TMSSAr; Taniguchi, Y.; Nagata, K.; Kitamura, T.; Fujiwara, Y.; Deguchi, D.; Maruo, Y.; Makioka, Y.; Takaki, K. *Tetrahedron Lett* 1996, 37, 3465; (n) Yb(OTf)<sub>3</sub>/EtMgBr; Hanamoto, T.; Sugimoto, Y.; Sugino, A.; Inanaga, J. *Synlett* 1994, 377; (o) Tm/TmI<sub>3</sub>; Bochkarev, M. N.; Fedushkin, I. L.; Fagin, A. A.; Petrovskaya, T. V.; Ziller, J. W.; Broomhall-Dillard, R. N. R.; Evans, W. J. *Angew. Chem, Int Ed Engl* 1997, 36, 133; (p) Ce/I<sub>2</sub>; Imamoto, T.; Kusumoto, T.; Hatanaka, Y.; Yokoyama, M. *Tetrahedron Lett* 1982, 23, 1353.
- [3] Taniguchi, Y.; Takaki, K.; Fujiwara, Y. In *Reviews on Heteroatom Chemistry*; Oae, S. (Ed.); MYU: Tokyo, 1995; Vol. 12, p. 163 and Ref. [1](i) and references cited therein.
- [4] (a) Yanada, R.; Bessho, K.; Yanada, K. *Chem Lett* 1994, 1279; (b) Yanada, R.; Bessho, K.; Yanada, K. *Synlett* 1995, 443; (c) Yanada, R.; Bessho, K.; Yanada, K. *Synlett* 1995, 1261; (d) Yanada, R.; Negoro, N.; Yanada, K.; Fujita, T. *Tetrahedron Lett* 1996, 37, 9313; (e) Yanada, R.; Negoro, N.; Yanada, K.; Fujita, T. *Tetrahedron Lett* 1997, 38, 3271; (f) Ding, Z.-B.; Wu, S.-H. *Youji Huaxue* 17, 1997, 165; (g) Wang, L.; Zhang, Y. *Tetrahedron* 1998, 54, 11129.
- [5] (a) Imamoto, T.; Kusumoto, T.; Hatanaka, Y.; Yokoyama, M. *Tetrahedron Lett* 1982, 23, 1353; (b) Fukuzawa, S.; Fujinami, T.; Sakai, S. *J. Chem Soc, Chem Commun* 1986, 475; (c) Fukuzawa, S.; Sumimoto, N.; Fujinami, T.; Sakai, S. *J Org Chem* 1990, 55, 1328.
- [6] Examples on the efficient utilization of electrons of ytterbium and samarium metals have been shown; Jin, W.; Makioka, Y.; Kitamura, T.; Fujiwara, Y. *J Org Chem* 2001, 66, 514 and Ref [4] (a).
- [7] Marks, T. J. *Prog Inorg Chem* 1978, 25, 51.
- [8] We can obtain lanthanoid metals (–40 mesh, 99.9%) from Aldrich Chemical Co. (La: ¥ 26,300/25 g; Ce: ¥ 13,300/10 g; Sm: ¥ 14,300/10 g; Yb: ¥ 13,800/2 g).
- [9] Nishino, T.; Nishiyama, Y.; Sonoda, N. *Heteroatom Chem* 2000, 11, 81.
- [10] Fujiwara has reported that ytterbium metal assisted cross-coupling reactions of diaryl ketones with a variety of electrophiles [11]. In this reaction, 1–2 drops of methyl iodide were added to the reaction solution in order to activate the ytterbium metal used.
- [11] Hou, Z.; Takamine, K.; Aoki, O.; Shiraishi, H.; Fujiwara, Y.; Taniguchi, H. *J Org Chem* 1988, 53, 6077.

- [12] Hirao has recently reported that a highly *meso*-selective pinacol type coupling reaction of aldimines occurred by use of a  $\text{Cp}_2\text{VCl}_2/\text{Me}_3\text{SiCl}/\text{Zn}$  system.; Hatano, B.; Ogawa, A.; Hirao, T. *J Org Chem* 1998, 63, 9421.
- [13] In the case of *N*-(2-methylbenzylidene)aniline (**1c**), we propose that the addition of **3** to another **1c** was suppressed by the presence of the methyl group. Then the formation of **6** followed by coupling proceeded predominantly to give the *dl*-isomer (see compound **6** in Scheme 1).
- [14] Takaki, K.; Tsubaki, Y.; Tanaka, S.; Beppu, F.; Fujiwara, Y. *Chem Lett* 1990, 203.
- [15] Makioka, Y.; Taniguchi, Y.; Fujiwara, Y.; Takaki, K.; Hou, Z.; Wakatuki, Y. *Organometallics* 1996, 15, 5476.
- [16] Mangeney, P.; Tejero, T.; Alexakis, A.; Grosjean, F.; Normant, J. *Synthesis* 1988, 255.
- [17] Smith, J. G.; Ho, I. *J Org Chem* 1972, 37, 653.
- [18] Vetter, A. H.; Berkessel, A. *Synthesis* 1995, 419.
- [19] Imamoto, T.; Nishimura, S. *Chem Lett* 1990, 1141.