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REDUCTIVE DIMERIZATION OF IMINES IN A Pb/Al BIMETAL REDOX SYSTEM

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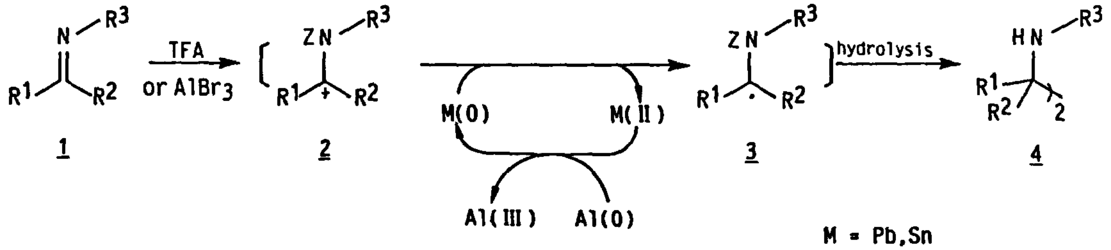
Reductive dimerization of N-alkylimines into vicinal diamines has been performed by the action of a catalytic amount of lead(II) bromide and aluminum (1 equiv.) in THF containing trifluoroacetic acid (TFA) or aluminum(III) bromide.

Despite the frequent occurrence of vicinal diamine units in natural products and medicinal agents,[1] only a few methods are available for the preparation of vicinal diamines.[2] Apparently, the reductive dimerization of imines is a straightforward route to vicinal diamines. However, unlike pinacolization of carbonyl compounds, the reductive coupling of imines had been rare.[3] Recently, two new methods, the niobium(IV) promoted dimerization of N-trimethylsilylimines[4] and the reductive dimerization of N-methylbenzylimine with titanium(0),[5] for access to vicinal diamines from imines have been reported. These reports prompted us to describe here a simple and efficient synthesis of vicinal diamines **4** by reductive coupling of N-alkylimines **1** in a Pb/Al bimetal redox system containing TFA or aluminum(III) bromide (Scheme 1).[6]

A typical reaction procedure is as follows. A mixture of imine **1a** (R^1 = Ph, R^2 = H, R^3 = Bn, 1 mmol), lead(II) bromide (0.05 mmol), aluminum (1 mmol) and TFA (1.1 mmol) in THF (1.5 ml) was stirred at ambient temperature for 6 h.



M = Pb,Sn
Z = H or $^-AlBr_3$

Scheme 1

After evaporation of most of the solvent, the residue was diluted with ether (5 ml) and treated under vigorous stirring with aqueous potassium hydroxide (10% w/v, 6 ml) for 5 min. The usual workup of the mixture followed by column chromatography (SiO_2, hexane/AcOEt: 4/1) afforded vicinal diamine **4a** (R^1 = Ph, R^2 = H, R^3 = Bn; 82%).[7]

The Pb/Al bimetal redox system is the best choice among reductants examined so far (Table 1). The combination of lead(II) chloride or tin(II) salts with aluminum is also effective for the reductive coupling of imine **1a**, affording **4a** (59-73%) (entries 2-4), whereas other metal salts, e.g., titanium(IV) chloride, niobium(V) chloride, zinc(II) chloride and cerium(III) fluoride, are incompetent for this purpose (entries 5-8). When magnesium or zinc metal is used as a reductant, the reductive coupling of **1a** proceeds slowly, and the addition of lead(II) bromide slightly accelerates this reaction (entries 9-12). In the combination of lead(II) or tin(II) salts with aluminum (entries 1-4), formation of small particles of lead or tin metal on aluminum surface is observed. The *in situ* generated metals must be much more active than commercial ones (>99.9% pure); indeed, neither commercial lead nor tin metal can effect any coupling reaction of **1a** (entries 13 and 14).

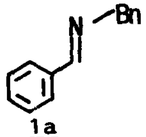
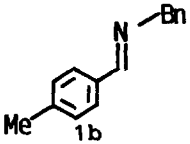
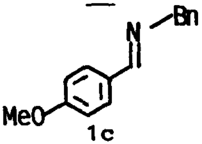
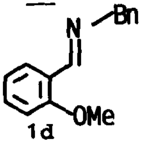
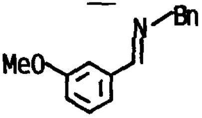
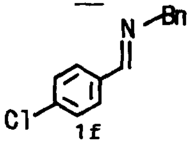
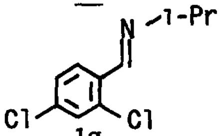
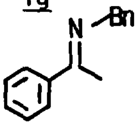
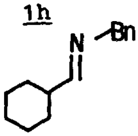
Table 1. Reductive Dimerization of Imine **1a** with Metal and Metal Salt-Metal[a)]

Entry	MX_n/M[b)]	Time(h)	Yield(%)[c]	Entry	MX_n/M[b)]	Time(h)	Yield(%)[c)]
1	$PbBr_2/Al$	6	82	8	CeF_3/Al	8	--[d)]
2	$PbCl_2/Al$	25	59	9	$PbBr_2/Zn$	18	63
3	$SnBr_2/Al$	3	73	10	none/Zn	26	65
4	$SnCl_2/Al$	3	66	11	$PbBr_2/Mg$	18	75
5	$TiCl_4/Al$	21	--[d)]	12	none/Mg	24	40
6	$ZnCl_2/Al$	25	--[d)]	13	none/Sn	30	--[d)]
7	$NbCl_5/Al$	24	--[d)]	14	none/Pb	22	--[d)]

a) Carried out in the manner as described in the text unless otherwise noted.
b) Metal Salt (0.05 equiv)/Metal (1 equiv). c) Isolated yields of dimer **4b**.
d) Imine **1a** was recovered (>90%).

The present Pb/Al bimetal redox system can be successfully applied to the reductive coupling of aromatic imines **1** (Table 2, entries 1-8). Under the reduction conditions, chlorine atoms on the aromatic nuclei were retained intact (entries 7 and 8). Interestingly, ketimine **1h** and aliphatic imine **1i** afforded no detectable amount of dimers **4** even after heating to reflux with 3 equiv. of TFA for 18 h. Satisfactory results were obtained when aluminum(III) bromide was used in place of TFA (entries 9 and 10); thus, upon heating to reflux, a combination of lead(II) bromide, aluminum, and aluminum(III) bromide (0.05 : 1 : 0.5) promoted the desired coupling reaction to give **4** in satisfactory yields.

Table 2. Reductive Coupling of Imines in a $PbBr_2/Al/TFA$ or $AlBr_3$ System[a)]

Entry	Imine 1	Acid (mmol)	Temp.	Time[b)] (h)	Product 4[c)] (Yield %)
1	 1a	TFA (1.1)	r.t.	6	82
2	1a	TFA (0.1)	r.t.	6	73
3	 1b	TFA (1.1)	r.t.	6	84
4	 1c	TFA (1.1)	r.t.	10	79
5	 1d	TFA (1.1)	r.t.	6	62
6	 1e	TFA (1.1)	r.t.	6	65
7	 1f	TFA (1.1)	r.t.	6	81
8	 1g	TFA (1.1)	r.t.	6	78
9	 1h	$AlBr_3$ (0.5)	reflux	2	90
10	 1i	$AlBr_3$ (0.5)	reflux	15	63

a) Carried out in the manner described in the text unless otherwise noted. b) The reaction was continued until most of 1 was consumed. c) Isolated yields after column chromatography (SiO_2; hexane/AcOEt: 4/1).

Although the reaction mechanism is still unclear, it is likely that the formation of vicinal diamines **4** proceeds through the following steps: generation of iminium ions **2** by the action of TFA or aluminum(III) bromide, subsequent one electron reduction with lead(0) to radical **3**, and finally coupling of **3** leading to diamine **4** (Scheme 1). The lead(II) generated in the second step would be reduced with aluminum to lead(0) as a mediator. In this Pb/Al bimetal redox system, aluminum(III) salts accumulated in the media would play a role, in the generation of iminium ion **2**, but the addition of TFA or aluminium(III) bromide is indispensable to initiate the reaction. Actually, the reductive coupling of imines **1** can be achieved with less than 0.5 equiv. of TFA or alumium(III) bromide (Table 2, entries 2, 9, and 10), while absence of the acid resulted in the almost complete recovery of imine **1**.

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5) C. Betschart and D. Seebach, Helv. Chim. Acta, 70, 2215 (1987): titanium(0) is prepared from titanium(IV) chloride and magnesium (1/2 mol/mol) imediately before use.
6) The previous papers on the Pb/Al bimetal redox system: H. Tanaka, S. Yamashita, Y. Katayama, and S. Torii, Chem. Lett., 1986, 2043; H. Tanaka, S. Yamashita, Y. Ikemoto, and S. Torii, ibid., 1987, 673; H. Tanaka, S. Yamashita, H. Hamatani, Y. Ikemoto, and S. Torii, Syn. Commun., 17, 789 (1987); H. Tanaka, H. Dhimane, Y. Ikemoto, and S. Torii, Chem. Express, 2, 487 (1987).
7) Diamine **4a** was a mixture of dl and meso isomers (4 : 6); 500 MHz ^{1}H NMR ($CDCl_3$): (dl isomer) δ = 3.28 (d, J = 13.8 Hz, 2H), 3.56 (d, J = 13.8 Hz, 2H), 3.78 (s, 2H), 6.70-7.35 (m, 20H); (meso-isomer) δ = 3.47 (d, J = 13.4 Hz, 2H), 3.64 (d, J = 13.4 Hz, 2H), 3.69 (s, 2H), 6.70-7.35 (m, 20H).

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