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Samarium diiodide/Nickel diiodide an efficient system for homo and heterocoupling reactions of imines.

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Abstract

Samarium diiodide in the presence of a catalytic amount of nickel diiodide mediates a very fast dimerization of imines into vicinal diamines and the mixed coupling of imines and ketones to give β-amino alcohols.

Keywords: Samarium diiodide; Nickel diiodide; Imines; Amino alcohols.

The pinacolic coupling of carbonyl compounds has been widely developed [1,2]. A great variety of metal reagents has been proposed to carry out this transformation. For instance, inter and intra molecular pinacol coupling reactions of aldehydes and ketones, are promoted by low valent lanthanide species [3,4]. In contrast, the reductive dimerization of imines into vicinal diamines has received less attention. However, very recently several reagents such as activated manganese [2], titanium derivatives [5] or zinc powder [6] as well as ytterbium metal [7] and samarium diiodide [8] have been used. With the latter compound, the reaction is slow and must be performed with an excess of the reagent in refluxing THF [9] or with activated imines [8,10]. The coupling of an imine and a ketone to give an amino alcohol is an even more complicated problem. Naphthalene lithium [11] niobium trichloride [12] titanium salts [13] and electroreductive coupling methods [14] have been used. Imamoto has described a procedure to couple benzophenone or fluorenone anil with cyclohexanone using SmI_2 in refluxing THF, but the method is not efficient for other imines [15]

Recently, we have reported that the addition of catalytic amounts of NiI_2 strongly accelerates a variety of samarium diiodide mediated reactions [16] We now wish to report that the SmI_2/(NiI_2-catalytic) system promotes very fast homocoupling reactions of imines into vicinal

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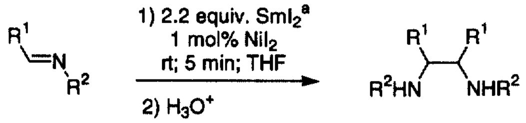
diamines and heterocoupling reactions between imines and ketones.

As indicated in Table 1, we have been able to couple a variety of aromatic imines, with reaction times of less than 5 min at r.t. (instead of 6-12 h in refluxing THF in the absence of NiI_2) [9], to give diamines in good to excellent isolated yields. The vicinal diamines are obtained as a diastereomeric (*meso/dl*) mixture. We have observed that the reactions need one equivalent of SmI_2 per imine, however, better isolated yields are obtained with an excess of reagent (typically 95% instead of 75%). It is worth noting that with these aromatic aldimines, monoamines which could arise from a competitive unimolecular reduction of imines are not detected. This is in contrast with a ketimine such as *N*-cyclohexylidenephenylamine, where *N*-cyclohexylphenylamine is exclusively obtained.

Table 1
Reductive Coupling of Aldimines into Vicinal Diamines.



Imine: R^1, R^2	Isolated yield of diamine (%)	*meso:dl* ratio[b]
Ph, Ph	91	54:46
p-$MeOC_6H_4$, Ph	87	47:53
Ph, *p*-$MeOC_6H_4$	90	48:52
Naphthyl, Ph	95	50:50
Ph, Et	95	63:37
Ph, Bu	78	72:28
Ph, Pr	85	57:43
Ph, Pr^i	95	62:38
Ph, Pentyl	89	62:38
Ph, Bu^t	95	57:43
o-$MeOC_6H_4$, Pr^i	95	58:42
Ph, Cyclopropyl	93	63:37
Ph, Cyclopentyl	98	62:38
Ph, Cy	95	67:33
Ph, *p*-$MeC_6H_4CH_2$	88	50:50

a) In a Schlenk tube under argon, to a solution of SmI_2 (2.2 10^{-3} mol) in THF (22 mL) was added a solution of NiI_2 (2.2 10^{-5} mol) in THF (2.2 mL). The imine (10^{-3} mol) in THF (2 mL) was added dropwise over 5 min, then the reaction was quenched with HCl (0.1 M). Stirring was continued for 30 min until a clear solution was obtained which was extracted with ether. The pH of the aqueous phase was adjusted to neutrality by the addition of saturated aqueous $NaHCO_3$ (a samarium hydroxyde precipitate was observed). The aqueous phase was extracted with ether and the combined ethereal extracts were washed with sodium thiosulfate and brine then dried ($MgSO_4$). The solvents were removed under reduced pressure to give the crude product which was purified by flash chromatography on silica gel

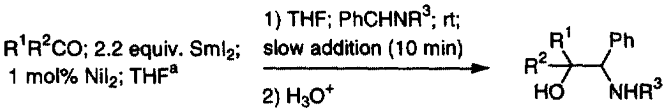
b) The stereochemical assignments were made as indicated in ref 4, from resonances of the benzylic protons.

To the best of our knowledge, the SmI_2/(NiI_2 catalytic) system is the most efficient in promoting the reductive coupling of aromatic aldimines into vicinal diamines.

A similar catalytic effect of nickel diiodide is not observed for the pinacolization of non-aromatic ketones in THF. These reactions are very slow and need at least 24 h to go to completion. We took advantage of this fact to perform heterocoupling reactions between aromatic aldimines and non aromatic ketones.

With this methodology we were pleased to obtain a variety of β-amino alcohols in good isolated yields, Table 2.

Table 2
Reductive Coupling of Aldimines with Ketones.



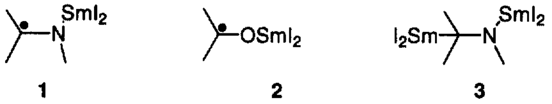
Ketone	Imine: R^3	Ketone:Imine ratio	Isolated yield in amino alcohol (%)
propanone	Pr^i	10	80
2-octanone	Pr^i	2	74[b]
dicyclopropylketone	Pr^i	6	84
cyclobutanone	Pr^i	2	76
cyclopentanone	Pr^i	2	67
cyclohexanone	Pr^i	2	68
cyclohexanone	Bu	2	73
cyclohexanone	Pent	2	64
cycloheptanone	Pr^i	2	60
propanone	Bu^t	10	0[c]
propanone	Cyclopentyl	10	58
propanone	Cy	10	63
propanone	Ph	10	15

a) The experimental procedure is similar to the one described in Table 1 note a), except that the ketone is mixed with samarium diiodide before addition of the imine.
b) Mixture of diastereomers.
c) The vicinal diamine is exclusively obtained.

To ensure the success of the heterocoupling, the imine, in THF, must be slowly added (over about 10 min) to a mixture of ketone (in excess), SmI_2 and NiI_2 (1 mol%) in THF at 0°C. The reactions are fast, being over at the end of the addition of the imine. The only by-product is the vicinal diamine (typically 5-10%, except for *N*-benzylideneaniline where 80% of the diamine was observed). A variety of ketones can be used, but reactions with acetophenone fail because of the fast competing homocoupling reaction of the ketone [3]. Under the same conditions, the reaction between octanal and *N*-benzylideneisopropylamine gives the amino alcohol in modest yield (22%).

The precise role of NiI_2 in these reactions has not yet been established. However, it seems that this additive facilitates single electron transfer from SmI_2 to organic species. A possible reaction pathway, for the coupling of imines could be *via* a single electron transfer to give a radical anion intermediate **1** (Figure 1). This species could undergo dimerization to give a diamine or coupling with a ketyl radical **2** to give an amino alcohol. Alternatively, the radical anion **1** could be reduced to a dianion **3**, which could then add to an imine or a ketone. As pinacolic coupling products of ketone are not obtained in THF, it can be assumed that ketyl radicals **2** are not formed in appreciable amounts. Therefore, the formation of amino alcohols through coupling of radicals can be ruled out. This suggests the formation of amino alcohols could occur through reaction of dianion **3** with a ketone. However, in the presence of EtOD in large excess (100 equiv. per *N*-benzylideneisopropylamine) the homocoupling of the imine still readily occurs without reduction to the monoamine and any incorporation of deuterium. Consequently, the possibility that homocoupling products may be formed through a coupling of radicals **1** cannot be ruled out.

Figure 1



To conclude, coupling reactions of imines mediated by SmI_2 are strongly accelerated in the presence of NiI_2. Moreover, the heterocoupling between a ketone and an imine can be readily performed with the SmI_2/(NiI_2-catalytic) system. We are currently trying to improve stereoselectivity of the reactions and to achieve a SmI_2-catalytic version of these reactions.

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