Samarium/NBS system mediated dimerisation of imines: a convenient route to vicinal diamines

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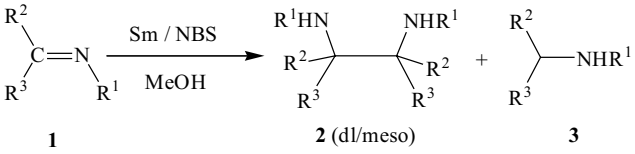
A convenient, efficient and stereoselective synthesis of vicinal diamines in satisfactory yields by dimerisation of imines mediated by a Sm/NBS system has been performed.

Keywords: samarium, NBS, imine, dimerisation, stereoselectivity

The vicinal diamine functionality is present in many compounds of biological significance[1] and is now playing a more and more important role in stereocontrolled organic synthesis and analytical and medicinal chemistry.[2] Various substrates such as olefins and 1, 2-dicarbonyl compounds have been employed to form vicinal diamines.[3] A typical procedure for synthesis of vicinal diamines is by the direct reductive dimerisation of imines promoted by reductants or systems such as SmI_2,[4] $SmBr_2$,[5] indium,[6] a Pb/Al bimetallic redox system,[7] a Zn–Cu couple,[8] niobium(IV) chloride,[9] low-valent titanium,[10] active manganese[11] and electrochemical reduction.[12]

Samarium diiodide and organosamarium compounds have been widely employed as useful reagents in organic synthesis.[13] However, relatively few reports on the direct use of samarium metal in organic synthesis have been reported, because the surface of samarium metal is inactive.[14a] In order to improve the reactivity of samarium, some additives, such as I_2,[14b] $TiCl_4$,[14c] TMSCl[14d] or $CoCl_2$,[14e] *etc*., have been added. NBS was recently introduced by Banik *et al*.[15] to promote the pinacol coupling of aryl aldehydes. Banik *et al.* claimed that samarium dibromide ($SmBr_2$) could be generated *in situ* from a Sm/NBS system in methanol.[15] Although SmI_2 or $SmBr_2$[16a] were considered as powerful reagents to promote the reductive coupling of imines to form vicinal diamines, the complicated preparation and their high sensitivity to air and water has limited their utility.[16] Samarium metal is stable in air and has strong reducing power (Sm^{3+}/Sm = –2.41V), providing a more convenient reducing source for use in synthesis. Here we wish to report the use of the Sm/NBS system for the reductive coupling of imines to form vicinal diamines in methanol (Scheme 1). This methodology has advantages over the existing methods because of easy handling, mild conditions and good stereoselectivity, whilst, avoiding the complicated preparation of samarium dibromide.



Scheme 1

Results and discussion

The purpose of the present research was to determine if the Sm/NBS system could promote dimerisation of imines and to investigate the stereoselectivity of the reaction. Our first attempt used *N*-benzylidene-aniline (**1a**) as the substrate. To optimise the reaction conditions, the solvents and the ratio of samarium to NBS were investigated. Firstly, we tried to examine the effects of different solvents on the reaction using the Sm/NBS system (Table 1). As shown in Table 1, when THF was used as solvent, only traces of vicinal diamine were detected, which was possibly due to the poor solubility of NBS in THF. The yield could be increased by using methanol as solvent (entry 6). Subsequently, the effects of the ratio of samarium to NBS were investigated. When the ratio of Sm/NBS was 3/0.6, product **2a** was obtained with good yield. The yield decreased when the ratio was reduced, so the optimised condition was chosen as shown in entry 6.

To explore the scope of the protocol, experiments were carried out using a variety of imines. According to Table 2, all the aryl aldimines underwent dimerisation to give vicinal diamines in moderate to good yields, but the alkyl aldimines and ketimine could not be dimerised. The products were obtained as diastereoisomeric (*dl/meso*) mixture. The ratios of *dl/meso* were determined by ^{1}H NMR and ranged from 0.26 to 0.63.[18-20] Traces of the byproduct **3** were also detected in the reactions.

Table 1 Reductive dimerisation of *N*-benzylidene-aniline (**1a**) under different conditions mediated by a Sm/NBS system[a]

Entry	Reagent (Sm/NBS)[b]	Solvent	Time/h	Yield(%) of **2a**	Yield(%) of **3a**
1	3/0.6	THF	2	<5	<5
2	3/0.6	H_2O/THF(1: 10)	3	Trace	Trace
3	3/0.6	H_2O/MeOH(10: 1)	3	Trace	Trace
4	3/0.6	H_2O/MeOH(1: 10)	1	28	15
5	3/0.6	MeOH[c]	0.5	70	11
6	3/0.6	MeOH[c]	0.5	65	15
7	3/0.5	MeOH[c]	0.5	65	14
8	2.5/0.4	MeOH[c]	0.5	60	14
9	2.5/0.3	MeOH[c]	0.5	55	15
10	2/0.3	MeOH[c]	0.5	40	14

[a]The reaction was carried out at room temperature.
[b]Ratio of amounts/mmol.
[c]Reagent grade methanol was used without further purification.

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Table 2 Reductive dimerisation of imines to vicinal diamines mediated by the Sm/NBS system[a]

Entry	R^1	R^2	R^3	Time/h	Product	Yield/%[a]	Ratio/*dl/meso*[b]
a	Ph	Ph	H	0.5	**2a**	65	27/73
b	*o*-ClC_6H_4	Ph	H	0.5	**2b**	63	25/75
c	Ph	*p*-MeC_6H_4	H	1	**2c**	67	21/79
d	Ph	*p*-ClC_6H_4	H	1.5	**2d**	61	30/70
e	Ph	*o*-$MeOC_6H_4$	H	0.5	**2e**	73	23/77
f	*p*-ClC_6H_4	Ph	H	1	**2f**	65	39/61
g	$PhCH_2$	Ph	H	1	**2g**	72	34/66
h	Ph	*o*-HOC_6H_4	Me	2	**2h**	None[b]	–
j	Ph	Ph	Me	2	**2i**	None[b]	–
k	Ph	$PhCH_2CH_2$	H	24	**2j**	None[b]	–

[a]Isolated yield based on imines. [b]90% of the starting material was recovered.

Although the detailed mechanism of the reductive dimerisation reaction has not been elucidated,[17] the formation of vicinal diamines (*dl/meso*) may be described as shown in **Scheme 2**. Firstly, samarium dibromide ($SmBr_2$) is generated *in situ*; then a Sm(II)-bound anion radical (**4**) is formed *via* single electron transfer (SET) from $SmBr_2$ to the imine. The anion radical (**4**) forms intermediate **5a** or **5b** by a radical coupling process. Compared to **5b**, the formation of intermediate **5a** is favoured, so the major product observed is the *meso*-configuration (Path A). Of course, the simple reduction product **3** can be obtained as a side-product by direct protonation of radical 4.

Conclusion

We have developed a facile method for the conversion of imines into the corresponding vicinal diamines by reductive dimerisation mediated by the Sm/NBS system in methanol. The advantages of the present method are simple operation, mild reaction, satisfactory yields and good stereoselectivity. Further studies on the application of the Sm/NBS system are now progressing in our laboratory.

Experimental

Melting points were recorded on a Digital Melting Point Apparatus WRS-1B and are uncorrected. IR spectra were recorded using KBr pellets on a Nicolet AVATAR 370 FI–infrared Spectrophotometer. ^{1}H NMR spectra were recorded on a VARIAN Mercury plus-400 instrument using $CDCl_3$ as the solvent with TMS as an internal standard. All reagents were commercially available. Methanol was reagent grade and used without purification. Imines were prepared according to the literature.[18]

General procedure for the preparation of vicinal diamines from the dimerisation of imines mediated by a Sm/NBS system in methanol

To a mixture of imine (1.0 mmol) and samarium (3.0 mmol, 0.460 g) in MeOH (10 ml) was added NBS (0.6 mmol, 0.108 g) in MeOH (2 ml) at room temperature under a nitrogen atmosphere. The reaction was monitored by TLC. After completion the reaction mixture was quenched with saturated NH_4Cl(aq) solution and extracted with $CHCl_3$ (25 ml×3). The organic phase was washed with brine and dried over sodium sulfate. After concentration in a vaccuum, the residue was purified by preparative TLC using cyclohexane: ethyl acetate (15 : 1) as eluent to afford product **2**.

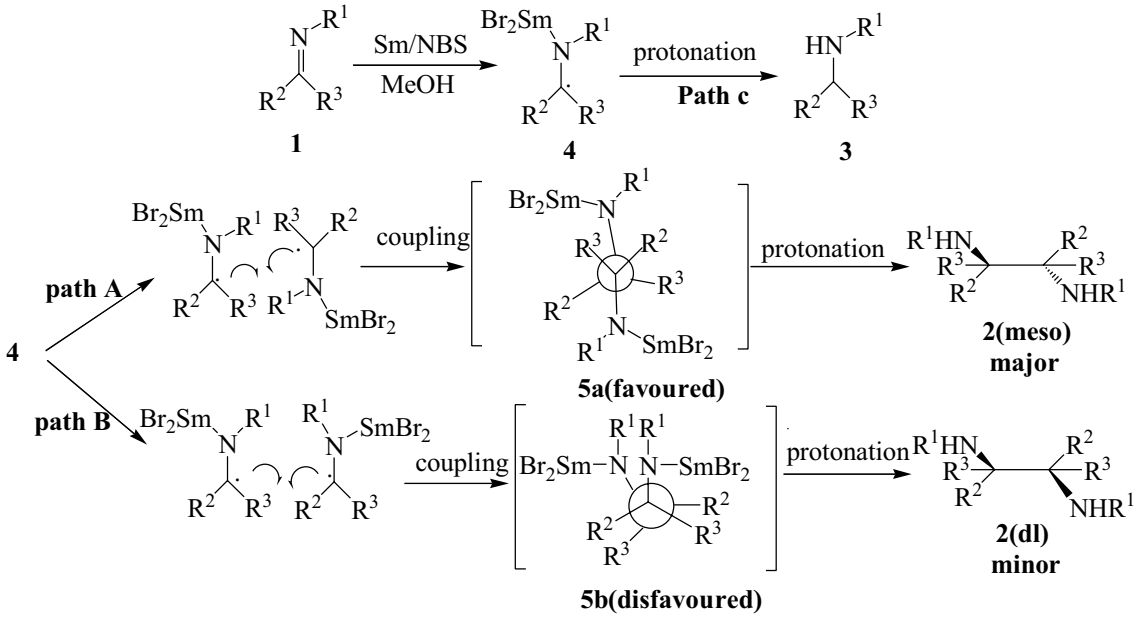
Compound **2a**: Obtained as a 27 : 73 ratio of *dl/meso* diastereoisomers. m.p. 158–159°C. (lit[20b] 152.5–153.5°C for *dl* and 169–170°C for *meso*). IR (KBr) ν_{max}: 3410(NH), 3037(CH) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ(ppm) 4.54(s, 1.08H, *dl*), 4.96(s, 2.92H, *meso*), 6.64–7.24(m, 20H);

Compound **2b**: Obtained as a 25 : 75 ratio of *dl/meso* diastereo isomers.(lit[10b]) IR(neat) ν_{max}: 3394(NH), 2915(CH) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ(ppm) 4.12(m, 2H), 4.27(s, 0.5H, *dl*), 4.84(s, 1.5H, *meso*), 6.60–7.49 (m, 18H);

Compound **2c:** Obtained as a 21 : 79 ratio of *dl/meso* diastereoisomers. m.p. 127–128°C. (lit[20a]131–131.5°C for *dl* and 138.5–141°C for *meso*). IR (KBr) ν_{max}: 3410(NH), 3011(CH) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ(ppm) 2.29(s, 3H), 2.34 (s, 3H), 4.10 (m, 2H), 4.51 (s, 0.42H, *dl*), 4.92(s, 1.58H, *meso*), 6.45–7.10 (m, 18H);

Compound **2d**: Obtained as a 30 : 70 ratio of *dl/meso* diastereoisomers. (lit[19]) IR (KBr) ν_{max}: 3378(NH), 3010(CH) cm^{-1};^{1}H NMR ($CDCl_3$): δ(ppm) 4.46(s, 0.6H, *dl*), 4.56(m, 2H), 4.91(s, 1.4H, *meso*), 6.53–7.25 (m, 18H);

Compound **2e**: Obtained as a 23 : 77 ratio of *dl/meso* diastereoisomers; m.p. 149–150°C. (lit[10b] *dl/meso* diastereoisomers 147°C). IR (KBr) ν_{max}: 3421(NH), 3040(CH) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ(ppm) 3.59(s, 3H), 3.62 (s, 3H), 4.16(s, 2H), 5.07(s, 0.46H, *dl*), 5.41 (s, 1.54H, *meso*), 6.43–7.31 (m, 18H);



Scheme 2

Compound **2f**: Obtained as a 39 : 61 ratio of *dl/meso* diastereoisomers m.p. 147°C. (lit[20a] 137°C for *dl* and 198-199 °C for *meso*); IR (KBr) ν_{max}: 3480(NH), 3025, 3005(CH) cm^{-1}; ^1H NMR ($CDCl_3$): δ(ppm) 4.12 (s, 2H), 4.50(s, 0.78H, *dl*), 4.90(s, 1.22H, *meso*), 6.40–7.21(m, 18H);

Compound **2g**: Obtained as a 34 : 66 ratio of *dl/meso* diastereoisomers; m.p. 158–159°C (lit[4]151–153°C). IR (KBr) ν_{max}: 3370(NH), 3025(CH) cm^{-1}; ^1H NMR($CDCl_3$): δ(ppm) 1.87 (m, 2H), 3.40 (B part of an AB system, J = 8.4 Hz, 2H), 3.52 (B part of an AB system, J = 8.4 Hz, 2H), 3.74(s, 0.68H, *dl*), 3.79(s, 1.32H, *meso*), 6.96–7.43(m, 20H);

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