

Intermolecular Heterocoupling Reaction between *N*-Sulfonylimines and Aliphatic Ketones Promoted by Samarium(II) Iodide

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N-sulfonylimines (**1**) were induced by samarium(II) iodide to produce radical anion intermediates (**2**) *in situ*, which were trapped by aliphatic ketones (**4**) to afford heterocoupling products β -sulfonamido alcohols (**5**) in moderate to good yields under mild and neutral conditions.

Keywords *N*-Sulfonylimines, samarium(II) iodide, radical anion intermediates, ketones, heterocoupling products, β -sulfonamido alcohols

Samarium diiodide as a powerful one-electron transfer reductant has been extensively applied to organic synthesis in the last decade. Because of its mild and neutral reaction conditions as well as excellent selectivity, the novel reactions and various chemical transformations induced by samarium diiodide are daily on the increase, for example, radical cyclizations,¹ ketyl-olefin coupling reactions,² pinacolic coupling reactions,³ Barbier-type reactions,⁴ aldol-type reactions,⁵ Reformatsky-type reactions⁶ and reductive coupling cyclizations,⁷ *etc.*

As mentioned above, the ketyl-olefin coupling reactions promoted by samarium diiodide have been widely developed.⁸ However, the cross-coupling reaction of ketones and imines has received less attention. Imamoto has described a procedure to couple benzophenone or fluorenone anil with cyclohexanone using SmI₂ in refluxing THF, but the method is not efficient for other imines.⁹ Kise has promoted electroreductive coupling of aromatic imines with electrophiles in the presence of chlorotrimethylsilane.¹⁰ Recently, Machrouhi reported that samarium diiodide/nickel diiodide system could in-

duce coupling reactions of imines and aliphatic ketones.¹¹ However, to the best of our knowledge, there is no report on the coupling reactions between *N*-sulfonylimines and other substrates promoted by SmI₂.

N-sulfonylimines are powerful synthetic intermediates and are used in numerous reactions, for example, addition reactions as carbonyl equivalents¹² or in ene¹³ reactions, inverse electron-demand Diels-Alder reaction-sA¹⁴ and [2 + 2] cycloaddition reactions.¹⁵ However, there are relatively few reports on the reactions involving in radical process. Very recently, in our experiments we found that SmI₂ could easily promote dimerization of *N*-sulfonylimines (**1**) into vicinal disulfamines (Scheme 1).

According to the mechanism of pinacol coupling reactions of aldehydes and dimerization of imines,^{16,17} it is reasonable to suggest that the reaction proceeds *via* a radical anion intermediate **2**. If the intermediate **2** is existing, then we think it may be trapped by other substrates (such as ketones). In our work, when 1 mmol *N*-sulfonylimines (**1**) and 1.2 mmol ketones (**4**) are added to 2.2 mmol SmI₂ solution, just as our prediction, the reaction afforded β -sulfonamido alcohols (**5**) in moderate to good yields under mild and neutral conditions (Scheme 2).

Table 1 summarizes our results and reaction conditions on the *N*-sulfonylimine-ketone reductive coupling. When **1** and **4** were heated at 60°C with SmI₂ under nitrogen, compounds **5** were obtained in moderate to good

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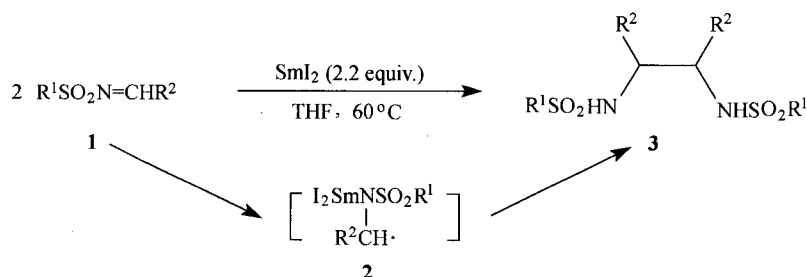
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yields. If the reaction was carried out at room temperature, it was still available while needed longer time (Entry 11). The coupling reaction could be accelerated by the addition of hexamethylphosphoramide (HMPA) to

the reaction mixture (Entry 12). Attempts to induce the cross coupling between *N*-sulfonylimine and acetophenone were unsuccessful because of the fast homocoupling reaction of the ketone.³

Scheme 1



Scheme 2

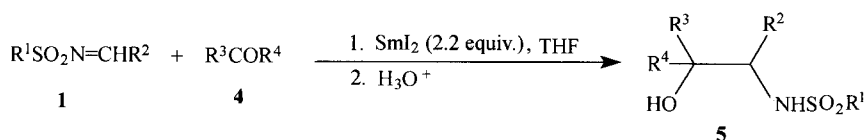


Table 1 Heterocoupling reaction of *N*-sulfonylimines (1) and ketones (4) induced by SmI_2

Entry	R ¹	R ²	R ³	R ⁴	T (°C)	t (h)	Yield (%) ^a
1	<i>p</i> -CH ₃ C ₆ H ₄	Ph	Me	Et	60	10	76 (5a)
2	<i>p</i> -CH ₃ C ₆ H ₄	Ph	Me	<i>n</i> -Pr	60	10	72 (5b)
3	<i>p</i> -CH ₃ C ₆ H ₄	<i>p</i> -CH ₃ C ₆ H ₄	Me	<i>n</i> -Pr	60	10	74 (5c)
4	<i>p</i> -CH ₃ C ₆ H ₄	<i>p</i> -ClC ₆ H ₄	Me	<i>n</i> -Pr	60	12	68 (5d)
5	<i>p</i> -CH ₃ C ₆ H ₄	<i>p</i> -CH ₃ OC ₆ H ₄	Me	Et	60	8	74 (5e)
6	Ph	Ph	Me	Et	60	10	71 (5f)
7	Ph	Ph		-(CH ₂) ₅ -	60	10	80 (5g)
8	Ph	<i>p</i> -CH ₃ C ₆ H ₄	Me	<i>n</i> -C ₅ H ₁₁	60	10	76 (5h)
9	Ph	<i>p</i> -ClC ₆ H ₄	Me	<i>n</i> -C ₅ H ₁₁	60	12	75 (5i)
10	Ph	<i>p</i> -CH ₃ OC ₆ H ₄	Me	<i>n</i> -Bu	60	8	70 (5j)
11	<i>p</i> -CH ₃ C ₆ H ₄	Ph	Me	<i>n</i> -Pr	r. t.	20	70
12	<i>p</i> -CH ₃ C ₆ H ₄	Ph	Me	<i>n</i> -Pr	60	5	74 ^b

^aIsolated yields. ^bHMPA was added.

In the cross-coupling reaction, when the addition of **1** was two hours later than the addition of ketones, the reaction could still give β -sulfonamido alcohols (**5**) in good yields; if the addition of **1** was two hours early than that of ketones (**4**), both disulfamides and heterocoupling products were obtained. So we hold that the reaction proceeds *via* the intermediate **2** rather than a ketyl radical intermediate. According to previous work reported,¹¹ a possible mechanism was presented in Scheme 3.

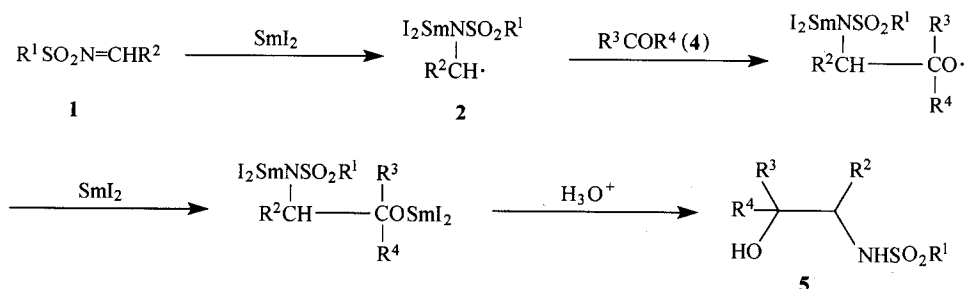
To conclude, the heterocoupling between *N*-sulfonylimines (**1**) and ketones (**4**) can be readily performed by SmI_2 to give β -sulfonamido alcohols (**5**) which has not been achieved previously by other reductants. Further studies on the heterocoupling reaction between *N*-sulfonylimines and other substrates are now in

progress.

Experimental

Tetrahydrofuran (THF) was distilled from sodium-benzophenone immediately prior to use. All reactions were conducted under a nitrogen atmosphere. Melting points were uncorrected. Infrared spectra were recorded on an IR-408 spectrometer in KBr with absorption in cm^{-1} . ¹H NMR spectra were recorded on a Bruker AC-80 spectrometer as CDCl_3 solutions. *J* values are in Hz. Chemical shifts are expressed downfield from internal tetramethylsilane. Mass spectra were recorded on a HP 5989B MS spectrometer. Microanalysis was carried out on a Carlo-Erba 1106 instrument.

Scheme 3



General procedure

In a Schlenk tube under a dry nitrogen atmosphere, to a solution of SmI_2 (2.2 mmol) and ketones (1.2 mmol) in THF (20 mL) was slowly added (over 20 min) a solution of *N*-sulfonylimines (1 mmol in 2 mL THF). The reaction mixture was heated at 60°C for given hours showed in the Table 1. Then the reaction was quenched with HCl (0.1 mol/L). Stirring was continued for 30 min until a clear solution was obtained which was extracted with ethyl acetate (2×30 mL). The pH value of the aqueous phase was adjusted to neutrality by addition of saturated aqueous NaHCO_3 . The aqueous phase was extracted with ethyl acetate (20 mL) and the combined extracts were washed with sodium thiosulfate and brine, then dried over MgSO_4 . After evaporating the solvent under reduced pressure, the crudeproduct was purified by preparative TLC on silica gel using ethyl acetate-cyclohexane (1:2) as eluent.

5a Colorless crystal, m. p. $110\text{--}112^\circ\text{C}$; ^1H NMR (CDCl_3 , 80 MHz) δ : 7.88—6.80 (m, 9H, ArH), 6.12 (br, 1H, NH), 4.68 (br, 1H, OH), 4.08 (s, 1H, CH), 2.30 (s, 3H, CH_3), 1.28 (q, $J = 7$ Hz, 2H, CH_2), 1.17 (s, 3H, CH_3), 0.88 (t, $J = 7$ Hz, 3H, CH_3); IR (KBr) ν : 3525 (br, OH), 3250 (br, NH), 3040 (ArH), 2960, 1600, 1500, 1450, 1380cm^{-1} ; MS m/z (%): 316 ($\text{M}^+ - \text{OH}$, 1.82), 260 (10.12), 73 (34.64); Anal. calcd for $\text{C}_{18}\text{H}_{23}\text{NO}_3\text{S}$: C 64.84, H 6.95, N, 4.20; found C — OH, 1.02), 364 ($\text{M}^+ - \text{OH}$, 2.76), 296 (21.54), 294 (57.76), 73 (34.64); Anal. calcd for $\text{C}_{19}\text{H}_{24}\text{ClNO}_3\text{S}$: C 59.75, H 6.33, N 3.67; found C 59.63, H 6.42, N 3.75.

5e Colorless crystal, m. p. $150\text{--}152^\circ\text{C}$; ^1H NMR (CDCl_3 , 80 MHz) δ : 7.72—6.60 (m, 8H, ArH), 6.16 (br, 1H, NH), 4.72 (br, 1H, OH),

64.75, H 6.84, N 4.26.

5b Colorless crystal, m. p. $162\text{--}164^\circ\text{C}$; ^1H NMR (CDCl_3 , 80 MHz) δ : 7.68—7.83 (m, 9H, ArH), 6.18 (br, 1H, NH), 4.55 (br, 1H, OH), 4.15 (s, 1H, CH), 2.28 (s, 3H, CH_3), 1.60—0.76 (m, 10H, O — C(CH_3) $_3\text{H}_7\text{-n}$); IR (KBr) ν : 3525 (br, OH), 3290 (br, NH), 3050 (ArH), 2950, 1600, 1500, 1460, 1380cm^{-1} ; MS m/z (%): 330 ($\text{M}^+ - \text{OH}$, 2.02), 260 (12.38), 87 (32.56); Anal. calcd for $\text{C}_{19}\text{H}_{25}\text{NO}_3\text{S}$: C 65.68, H 7.25, N, 4.03; found C 65.86, H 7.14, N 4.11.

5c Colorless crystal, m. p. $188\text{--}190^\circ\text{C}$; ^1H NMR (CDCl_3 , 80 MHz) δ : 7.80—6.62 (m, 8H, ArH), 6.02 (br, 1H, NH), 4.50 (br, 1H, OH), 4.10 (s, 1H, CH), 2.32 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 1.62—0.75 (m, 10H, O — C(CH_3) $_3\text{H}_7\text{-n}$); IR (KBr) ν : 3500 (br, OH), 3300 (br, NH), 3050 (ArH), 2950, 1600, 1500, 1460, 1380cm^{-1} ; MS m/z (%): 344 ($\text{M}^+ - \text{OH}$, 1.63), 274 (8.68), 87 (76.01); Anal. calcd for $\text{C}_{20}\text{H}_{27}\text{NO}_3\text{S}$: C 66.45, H 7.53, N 3.87; found C 66.20, H 7.42, N 3.95.

5d Colorless crystal, m. p. $149\text{--}151^\circ\text{C}$; ^1H NMR (CDCl_3 , 80 MHz) δ : 7.68—6.62 (m, 8H, ArH), 6.06 (br, 1H, NH), 4.60 (br, 1H, OH), 4.03 (s, 1H, CH), 2.30 (s, 3H, CH_3), 1.64—0.77 (m, 10H, O — C(CH_3) $_3\text{H}_7\text{-n}$); IR (KBr) ν : 3500 (br, OH), 3250 (br, NH), 3050 (ArH), 2952, 1600, 1500, 1492, 1380cm^{-1} ; MS m/z (%): 366 ($\text{M}^+ + 2$), 4.25 (s, 1H, CH), 3.75 (s, 3H, OCH_3), 2.30 (s, 3H, CH_3), 1.30 (q, $J = 7$ Hz, 2H, CH_2), 1.18 (s, 3H, CH_3), 0.88 (t, $J = 7$ Hz, 3H, CH_3); IR (KBr) ν : 3525 (br, OH), 3250 (br, NH), 3050 (ArH), 2952, 1610, 1510, 1450, 1380cm^{-1} ; MS m/z (%): 346 ($\text{M}^+ - \text{OH}$, 1.22), 290 (43.02), 73 (38.78); Anal. calcd for $\text{C}_{19}\text{H}_{25}\text{NO}_4\text{S}$: C 62.79, H 6.93, N

3.85; found C 62.95, H 6.77, N 3.76.

5f Colorless crystal, m. p. 166—168°C; ^1H NMR (CDCl_3 , 80 MHz) δ : 7.88—6.80 (m, 10H, ArH), 6.10 (br, 1H, NH), 4.70 (br, 1H, OH), 4.20 (s, 1H, CH), 1.28 (q, $J = 7$ Hz, 2H, CH_2), 1.16 (s, 3H, CH_3), 0.88 (t, $J = 7$ Hz, 3H, CH_3); IR (KBr) ν : 3525 (br, OH), 3250 (br, NH), 3040 (ArH), 2960, 1600, 1500, 1450, 1380 cm^{-1} ; MS m/z (%): 302 ($\text{M}^+ - \text{OH}$, 2.54), 246 (23.67), 73 (38.04); Anal. calcd for $\text{C}_{17}\text{H}_{21}\text{NO}_3\text{S}$: C 63.92, H 6.63, N 4.39; found: C 63.74, H 6.78, N 4.50.

5g Colorless crystal, m. p. 108—110°C; ^1H NMR (CDCl_3 , 80 MHz) δ : 7.70—6.70 (m, 9H, ArH), 6.15 (br, 1H, NH), 4.70 (br, 1H, OH), 4.18 (s, 1H, CH), 1.68—1.22 (m, 10H, $-(\text{CH}_2)_5-$); IR (KBr) ν : 3525 (br, OH), 3260 (br, NH), 3040 (ArH), 2940, 1600, 1580, 1500, 1450, 1380 cm^{-1} ; MS m/z (%): 328 ($\text{M}^+ (\text{OH}, 1.59)$), 246 (8.32), 99 (66.21); Anal. calcd for $\text{C}_{19}\text{H}_{23}\text{NO}_3\text{S}$: C 66.06, H 6.71, N 4.05; found C 66.24, H 6.54, N 4.23.

5h Colorless crystal, m. p. 196—198°C; ^1H NMR (CDCl_3 , 80 MHz) δ : 7.70—6.80 (m, 9H, ArH), 6.22 (br, 1H, NH), 4.82 (br, 1H, OH), 4.28 (s, 1H, CH), 2.30 (s, 3H, CH_3), 1.70—0.77 (m, 14H, O - C (CH_3) $\text{C}_5\text{H}_{11-n}$); IR (KBr) ν : 3500 (br, OH), 3260 (br, NH), 3050 (ArH), 2940, 1610, 1580, 1510, 1450, 1380 cm^{-1} ; MS m/z (%): 358 ($\text{M}^+ - \text{OH}$, 1.68), 260 (28.74), 115 (41.32). Anal. calcd for $\text{C}_{21}\text{H}_{29}\text{NO}_3\text{S}$: C 67.17, H 7.78, N 3.73; found: C 67.33, H 7.84, N 3.59.

5i Colorless crystal, m. p. 208—210°C; ^1H NMR (CDCl_3 , 80 MHz) δ : 7.70—6.70 (m, 9H, ArH), 6.15 (br, 1H, NH), 4.70 (br, 1H, OH), 4.04 (s, 1H, CH), 1.68—0.77 (m, 14H, O - C (CH_3) $\text{C}_5\text{H}_{11-n}$); IR (KBr) ν : 3500 (br, OH), 3260 (br, NH), 3050 (ArH), 2950, 1600, 1500, 1490, 1400, 1380 cm^{-1} ; MS m/z (%): 380 ($\text{M}^+ + 2 - \text{OH}$, 0.84), 378 ($\text{M}^+ - \text{OH}$), 282 (0.87), 280 (2.01), 115 (86.50); Anal. calcd for $\text{C}_{20}\text{H}_{26}\text{ClNO}_3\text{S}$: C 60.67, H 6.62, N 3.54; found C 60.87, H 6.78, N 3.46.

5j Colorless crystal, m. p. 168—170°C; ^1H NMR (CDCl_3 , 80 MHz) δ : 7.70—6.64 (m, 9H, ArH), 6.12 (br, 1H, NH), 4.70 (br, 1H, OH), 4.24 (s, 1H, CH), 1.76—0.77 (m, 12H, O - C (CH_3) C_4H_9-n); IR (KBr) ν : 3520 (br, OH), 3250

(br, NH), 3050 (ArH), 2950, 1610, 1580, 1510, 1450, 1380 cm^{-1} ; MS m/z (%): 360 ($\text{M}^+ - \text{OH}$, 1.77), 276 (12.25), 101 (26.42); Anal. calcd for $\text{C}_{20}\text{H}_{27}\text{NO}_4\text{S}$: C 63.64, H 7.21, N 3.71; found C 63.39, H 7.33, N 3.59.

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