

N-Sulfonylimines as an excellent acceptor for intermolecular radical reactions

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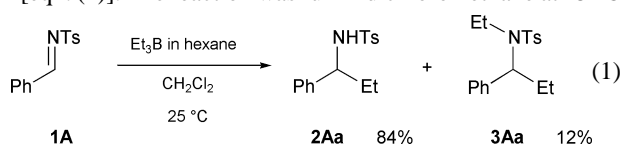
Received (in Cambridge, UK) 10th August 2000, Accepted 13th September 2000

First published as an Advance Article on the web

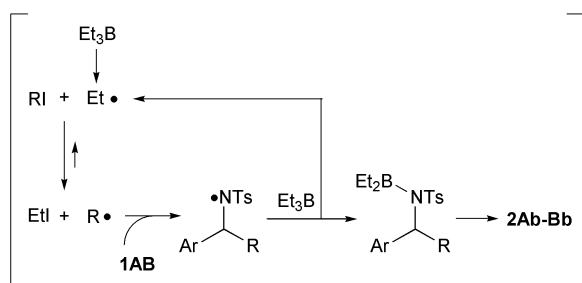
The intermolecular carbon radical addition to *N*-sulfonylimines proceeded effectively under either iodine atom-transfer reaction conditions or zinc-mediated aqueous-medium reaction conditions.

The carbon–nitrogen double bond of imine derivatives has emerged as a radical acceptor and, thus, numerous synthetically useful intramolecular carbon–carbon bond-forming reactions are available.¹ However, the intermolecular radical reaction of imine derivatives has not been widely investigated except for a few examples.² We reported recently that the intermolecular carbon radical addition to unactivated oxime ethers proceeded smoothly in the presence of $\text{BF}_3 \cdot \text{OEt}_2$;³ subsequently, the screening of more reactive imino radical acceptors has been the focus of our efforts. We now report an intermolecular radical reaction of electron deficient *N*-sulfonylimines which exhibit excellent reactivity toward nucleophilic alkyl radicals even in the absence of strong Lewis acids.

As a preliminary experiment, we investigated a simple intermolecular addition of an ethyl radical to *N*-sulfonylimine **1A** [eqn. (1)]. The reaction was run in dichloromethane at 25 °C



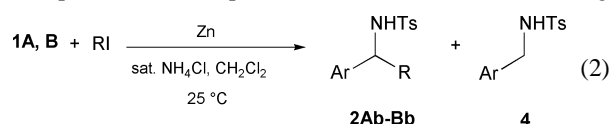
by using Et_3B as an ethyl radical source to give the desired ethylated product **2Aa** in 84% yield accompanied with a small amount of the diethylated product **3Aa**. It is important to note that the radical addition to benzaldehyde *O*-benzyloxime did not proceed under similar reaction conditions.³ Good chemical yields were also observed in the radical addition using different radical precursors such as isopropyl, cyclohexyl, and cyclopentyl iodides under the iodine atom-transfer reaction conditions in the absence of tin hydride (Scheme 1). We also examined the stannyl radical-mediated radical reaction of **1A**;



Scheme 1 Reagents and conditions: i, RI (30 equiv.), Et_3B 5 equiv. 3 times), CH_2Cl_2 , 25 °C; **2Ab**: R = Prⁱ (80%), **2Ac**: R = c-Hexyl (55%), **2Ad**: R = c-Pentyl (54%), **2Bb**: R = Prⁱ (89%).

however, the use of Bu_3SnH effected tin hydride-mediated reduction of the carbon–nitrogen double bond to give a significant amount of the corresponding *N*-sulfonylbenzylamine. Thus, the iodine atom-transfer reaction using RI and Et_3B in the absence of toxic tin hydride is an effective method for using *N*-sulfonylimine as a radical acceptor. Moreover, the reaction with more nucleophilic secondary alkyl radicals proceeded selectively and did not give the diethylated products, in contrast with the reaction with a primary ethyl radical. In this reaction, Et_3B would act as a reagent for trapping the intermediate aminyl radicals to regenerate an ethyl radical, and therefore more than a stoichiometric amount of Et_3B is required. As expected, *N*-sulfonylimine **1B**, which is activated by the intramolecular hydrogen bond by a 2-hydroxy group, was more reactive than *N*-sulfonylimine **1A** and therefore the isopropyl radical addition to **1B** proceeded effectively to give the desired product **2Bb** in 89% yield.

The use of water as a solvent has generated considerable interest from both economic and environmental points of view.⁴ We recently have demonstrated that radical reactions of imine derivatives such as oxime ethers, hydrazones, and nitrones proceed in aqueous media using Et_3B .⁵ In the case of *N*-sulfonylimine **1A**, a similar reaction procedure did not give good results in the radical addition reaction because of the competitive hydrolysis to TsNH_2 . On the other hand, we have now found that the formation of the desired alkylated products **2Ab–Af** was observed in the zinc-mediated radical reaction of **1A** in aqueous media [eqn. (2)].⁶ To a micro tube containing



N-sulfonylimine **1A**, PrⁱI, zinc, and dichloromethane as a co-solvent was added dropwise saturated aq. NH_4Cl over 15 min at 25 °C (Table 1, entry 1). The isopropylated product **2Ab** was obtained in 73% yield along with the reductive product **4** as a by-product. Not only a secondary alkyl but also the bulky *tert*-

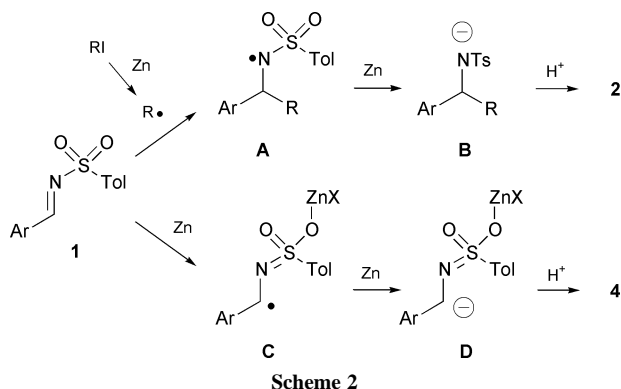
Table 1 Zinc-mediated radical addition to **1A**, **B** in aq. media^a

Entry	Sulfonylimine	RI	Yield (%) ^b	
			2	4
1	1A	Pr ⁱ I	2Ab 73	8
2	1A	c-Hexyl I	2Ac 71	12
3	1A	c-Pentyl I	2Ad 64	18
4	1A	Bu ^s I	2Ae 56	10
5	1A	Bu ^t I	2Af 66	20
6 ^c	1A	MeI	2Ag —	16
7	1B	Pr ⁱ I	2Bb 64	8
8 ^d	1A	Pr ⁱ I	No reaction	

^a Reactions of **1A** or **1B** (50 mg) were carried out with Zn (7 equiv.), RI (5 equiv.), and sat. NH_4Cl (1 cm³) in CH_2Cl_2 (0.1 cm³) at 25 °C. ^b Isolated yields. ^c ToSO_2NH_2 was obtained in 65% yield. ^d Reactions of **1A** (50 mg) were carried out with Zn (7 equiv.) and PrⁱI (5 equiv.) in CH_2Cl_2 (1 cm³) at 25 °C.

butyl radical worked well under similar reaction conditions (entries 1–5). The methylated product **2Ag** was not obtained in the reaction using a less reactive methyl radical because of the competitive hydrolysis and reduction (entry 6). The isopropyl radical addition to another *N*-sulfonylimine **1B** also proceeded smoothly (entry 7). However, the reaction of **1A** using zinc in dichloromethane in the absence of aq. NH_4Cl did not proceed (entry 8). The known examples of metal-mediated carbon–carbon bond-forming reactions in aqueous media are mainly limited to allylation of carbonyl compounds;⁷ thus, it is noteworthy that this reaction involves the alkylation of imine derivatives. The alkylation and reduction reactions would proceed as indicated in Scheme 2.

In conclusion, we have demonstrated the utility of *N*-sulfonylimines as radical acceptors under two different reaction conditions. These are the first examples of the reaction of *N*-



sulfonylimines with carbon radicals and are a convenient method for preparing a wide range of amine derivatives.

This work was supported by research grants from the Ministry of Education, Science, Sports and Culture of Japan and the Science Research Promotion Fund of the Japan Private School Promotion Foundation. Partial support for this work was also provided (to H. M.) by the Nissan Chemical Industries Award in Synthetic Organic Chemistry, Japan. H. M. gratefully acknowledges financial support from Takeda Science Foundation and Fujisawa Foundation, Japan.

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