

## Nitroalkylation of Alkyl Iodides via Radical Reaction of Silyl Nitronates

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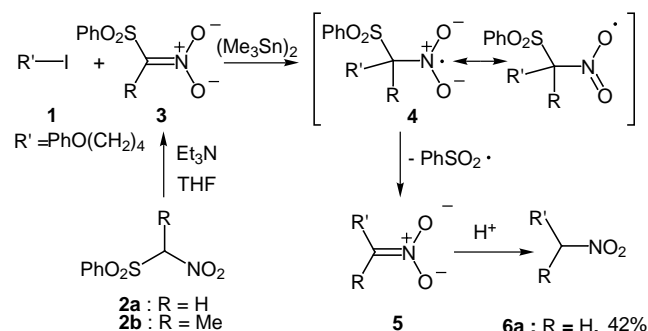
**Abstract:** Radical reaction of alkyl iodides with phenylsulfonyl substituted silyl nitronates in the presence of hexamethylditin at 300 nm afforded C-alkylated nitro compounds.

**Key words:** alkylation, halides, radical reactions, sulfones, tandem reactions

Alkylation of organonitro compounds through nitronates is a synthetically important reaction. The ambient nitronate ion can undergo C- and O-alkylation and the ratio is usually determined by the nature of a nitronate salt, a counter ion, and an alkylating agent.<sup>1</sup> The C-alkylation procedure via a double deprotonation of organonitro compounds has been widely utilized.<sup>2</sup> Michael addition and nitro-aldol reaction (Henry's reaction) of organonitro compounds give C-alkylated products and have found wide applications in organic synthesis as a carbon-carbon bond-forming reaction.<sup>3</sup> In addition, chain processes via anion-radical intermediates involving charge transfer or electron transfer from the nitronate ion to the alkylating agent nicely complement standard enolate alkylations, working well with tertiary alkyl and aryl halides.<sup>4</sup>

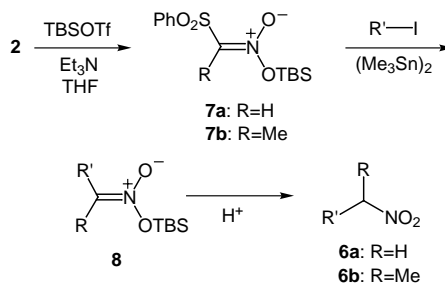
We have reported a novel free radical acylation approach involving the addition of alkyl radicals onto sulfonyl oxime ethers, in which the presence of a sulfonyl group was essential for the success of the radical acylation approach.<sup>5</sup> Since organonitro compounds are one of the most important functional groups for the formation of carbon-carbon bonds<sup>1</sup> and can be further converted into synthetically useful functional groups such as carbonyl<sup>6</sup> and amino groups,<sup>7</sup> we have studied the possibility of a nitroalkylation of an alkyl iodide. Our approach involves the addition of an alkyl radical onto the C=N bond of nitronates and the subsequent  $\beta$ -elimination of phenylsulfonyl radical to yield the desired organonitro compounds after hydrolysis of the resulting nitronates. In this approach, the addition step would be a rate-determining step and much slower than the  $\beta$ -elimination step. In order to check the efficiency of this approach, we initially used nitronate **3a** as a radical acceptor. When a mixture of 4-phenoxybutyl iodide, hexamethylditin (1.2 equiv), and nitronate **3a** (2.0 equiv), generated from  $\alpha$ -nitrosulfone **2a**<sup>8</sup> and triethylamine in THF, was irradiated at 300 nm for 5 h, one-carbon elongated organonitro compound **6a** was isolated in 42% yield along with the recovery of the starting material (44%). Under the present reaction conditions, the nitronate **3a** seemed to undergo decomposition to some extent. When the reaction was carried out in the ab-

sence of hexamethylditin, the desired product **6a** was not obtained, indicating the involvement of a radical mechanism.



Scheme 1

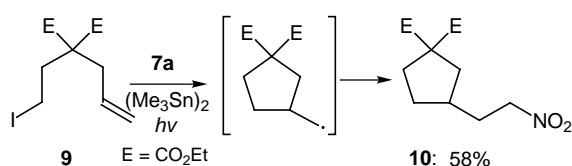
The use of silyl nitronates **7** as radical acceptors was next studied. When TMSCl was employed, the yield was improved to some extent, yielding **6a** in 50% yield. The use of TBSOTf gave slightly better results and the remaining reactions were carried out with TBSOTf. Thus, silyl nitronate **7** was generated by treatment of **2a** with TBSOTf (1.2 equiv) and triethylamine (1.2 equiv) in THF at  $-78^\circ\text{C}$  for 10 min. Treatment of 4-phenoxybutyl iodide in THF with silyl nitronate **7a** (2.0 equiv) and hexamethylditin (1.2 equiv) at 300 nm for 5 h afforded **6a** in 62% yield along with the recovery of the iodide (29%).<sup>9</sup> **7a** also underwent decomposition to some extent under the present condition.



Scheme 2

In order to obviate the problem of the decomposition of **7a** under photochemically initiated condition, when the same radical reaction was carried out in refluxing THF using

AIBN as an initiator, the reaction was messy and only a small amount of the desired product **6a** was obtained. To check the scope and limitations of the present method, the radical reactions were carried out with several alkyl iodides and the experimental results are summarized in the Table. For most of the cases observed, the reaction was complete within 5 h and **6** was obtained in moderate yield. Since the starting alkyl iodides were consistently recovered unchanged to some extent, the chemical yields of the organonitro compounds based on the consumed starting materials are much higher than the reported yields in the Table. As would be expected from the nature of the radical condition, the reaction worked well with primary (entries 1-4) or secondary alkyl iodides (entries 5-7) but somewhat less efficiently with tertiary alkyl iodide (entry 8). It is noteworthy that benzylic radical (entry 9) and  $\alpha$ -ester stabilized alkyl radical (entry 10) reacted with **3a**, yielding the corresponding organonitro compounds in reasonable yields. When the radical reaction was carried out with **3b** using 4-phenoxybutyl and cyclohexyl iodide under the same conditions, the desired organonitro compounds were obtained in 60% and 58% yield, respectively (entries 2 and 6). We briefly studied a sequential radical cyclization and nitromethylation approach, which would be unsuccessful with conventional synthetic methods. Treatment of **9** with **7a** and hexamethylditin in THF at 300 nm for 5 h afforded **10** in 58% yield along with the recovery of the starting material (25%).



In conclusion, we have developed a radical-mediated nitroalkylation method, which we believe has synthetic potential for the preparation of organonitro compounds. Further studies on the improvement and the synthetic utility of this method are in progress.

### Acknowledgement

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**Table** Preparation of Nitroalkanes from Alkyl Iodides

entry	substrate	product, yield <sup>a</sup>
	PhO(CH <sub>2</sub> ) <sub>4</sub> I	PhO(CH <sub>2</sub> ) <sub>4</sub> CH <sub>2</sub> NO <sub>2</sub> R
1		R = H 62% (29%)
2		R = CH <sub>3</sub> 60% (30%)
3		 62% <sup>b</sup>
4		 60% <sup>b</sup>
		 R
5		R = H 58% <sup>b</sup>
6		R = CH <sub>3</sub> 55%
7		 54% <sup>b</sup>
8		 42% (24%)
9		 46% (37%)
10		 48% <sup>b</sup>

<sup>a</sup>The numbers in parentheses indicate the yield of the recovered iodide.

<sup>b</sup>The unreacted starting material was not isolated.

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- (9) **A typical Procedure for the Preparation of 5-Nitro-1-phenoxy-pentane 3:** A degassed THF (2 mL) solution of 4-phenoxy-butyl iodide (110 mg, 0.4 mmol), freshly generated **2** (0.8 mmol), and hexamethylditin (159 mg, 0.48 mmol) in quartz tube was irradiated at Rayonet Photochemical Reactor equipped with 300 nm mercury UV lamp. After being irradiated for 5 h at room temperature, the reaction mixture was acidified with 10% aqueous HCl solution and concentrated under reduced pressure. Ethyl acetate (10 mL), water (3~4 drop), and potassium fluoride (174 mg, 3.0 mmol) were then added and the mixture was stirred for 1 h at room temperature. After the reaction mixture was filtered through a short column of silica gel, the filtrate was subjected to flash silica gel column chromatography (eluent: hexane: EtOAc = 3:1) to give 52 mg (62%) of **6a** as a colorless oil along with 32 mg (29%) of 4-phenoxybutyl iodide. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz) δ 1.53-1.65 (m, 2H), 1.76-1.87 (m, 2H), 2.01-2.12 (m, 2H), 3.96 (t, *J* = 6.2 Hz, 2H), 4.40 (t, *J* = 7.1 Hz, 2H), 6.84-6.96 (m, 3H), 7.23-7.31 (m, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz) δ 23.1, 27.1, 28.5, 67.1, 75.5, 114.4, 120.7, 129.4, 158.8; IR (NaCl) 2925, 1600, 1551, 1489, 1383, 1243 cm<sup>-1</sup>; HRMS (M<sup>+</sup>) calcd for C<sub>11</sub>H<sub>15</sub>NO<sub>3</sub>: 209.1052, found 209.0954.

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