

Rapid and Mild Generation of Carbon Radicals from *o*-(*o*-Iodophenyl)phenylthio Derivatives by an Anchimeric Approach

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Alkyl halides, especially iodides and bromides, are frequently utilized as precursors to generate various carbon-centered radicals. The usefulness

of these halo derivatives in radical reactions has been demonstrated in numerous synthetic examples and often reviewed in the chemical literature.^[1] There is, however, an inevitable drawback to the use of such reactive alkyl halides for radical reactions, and this is mainly due to the troublesome intervention of internal and/or external nucleophiles (e. g., alkoxides, amines, cyanide, enolates, etc.). To overcome this intrinsic problem, we initiated the search for a reactive alkyl iodide equivalent that is stable for ordinary nucleophilic attack. Herein we wish to report that *o*-(*o*-iodophenyl)phenylthio derivatives of the type **1a** (Figure 1) are highly effective with various functional group compatibility for the rapid generation of carbon radicals under mild conditions. This approach expands the scope of radical chemistry, since a variety of nucleophilic thiolations (thioacetalization, conjugate addition, epoxide opening, etc.) using arylthiol **1b** can be readily combined with the present radical generation process.

The requisite *o*-(*o*-iodophenyl)phenylthiol **1b** is conveniently prepared from *o*-(*o*-iodophenyl)aniline in a two-step sequence: (i) aqueous HCl, NaNO₂; then Na₂S₂,^[2] and (ii) LiAlH₄ in THF via the corresponding disulfide.

The relative reactivity of a series of alkyl derivatives, R-X [R = (CH₂)₅OCH₂Ph] including **1a**

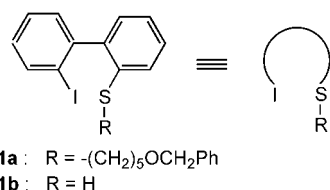
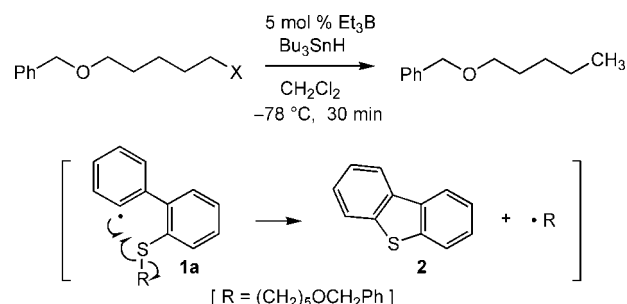


Figure 1. Structures of **1a** and **1b**

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(Scheme 1) has been examined by the radical reduction with Bu₃SnH (1.2 equiv) in the presence of catalytic Et₃B as radical initiator,^[3] and selected

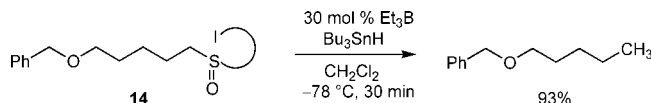
data are listed in Table 1. Alkyl iodide is rapidly reduced by Bu₃SnH (entry 1), but the reduction rate of the corresponding alkyl bromide is moderate (entry 2). Attempted reduction of other hetero-atom derivatives possessing phenylseleno and phenylthio groups results in recovery of most of the starting materials (entries 3 and 4).^[4] In marked contrast, however, the *o*-(*o*-iodophenyl)phenylthio derivative **1a** cleanly generates the corresponding carbon radicals under similar reaction conditions in very high yield (entry 5).^[5] The rapid generation of carbon radicals from **1a** is apparently ascribable to the facile formation of stable dibenzothiophene (**2**)^[6] as well as the higher reactivity of the iodobiphenyl moiety than that of ordinary aromatic iodides (entry 6 vs. 7).^[7,8]



Scheme 1. Evaluation of the relative reactivities of alkyl derivatives

Several characteristic features of the present approach have been noted. First, the *o*-(*o*-iodophenyl)phenylthio group of **3** is tolerant to the amino functionality. Obviously, the corresponding iodo derivative **4** is quite unstable, and hence synthetically not obtainable due to the facile intramolecular attack

tive sulfoxides such as **14** through the homolytic C–S=O bond cleavage by taking advantage of the remarkable reactivity of this system.^[16] Indeed, on reaction of **14** with Bu₃SnH (2 equiv) and cat. Et₃B (30 mol %) in CH₂Cl₂ at –78 °C for 30 min the corresponding reduction product was obtained in 93% yield (Scheme 5).



Scheme 5. Radical generation from a sulfoxide through homolytic C–S=O bond cleavage

Experimental Section

Intramolecular Radical Cyclization of **3a** (Scheme 2)

To a solution of *tertiary* amine **3a** (280 mg, 0.5 mmol) in CH₂Cl₂ (5 mL) was added Bu₃SnH (160 µL, 0.6 mmol) and a 1 M hexane solution of Et₃B (50 µL, 0.05 mmol) sequentially at room temperature under argon. The mixture was stirred for 1 h at room temperature and then poured into saturated NaHCO₃. Extractive workup was performed with ether and the combined extracts were dried over Na₂SO₄. Evaporation of the solvents and purification of the residual oil by column chromatography on silica gel (ether/hexane = 1 : 3 as eluant) gave the cyclic amine **6**; yield: 108.4 mg (0.435 mmol; 87%; E/Z = 56 : 44).

Acknowledgements

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References and Notes

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