



A convenient AIBN-initiated radical addition of ethyl iododifluoroacetate to alkenes

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ABSTRACT

The AIBN-initiated addition of ethyl 4-iodo-2,2-difluoroacetate to a variety of alkene substrates is described. The addition generally led to the corresponding addition products in good to excellent yields and various functional groups could be tolerated under the reaction conditions.

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1. Introduction

The synthesis of fluorinated compounds is of importance across a number of areas, notably in pharmaceutical, agrochemical, and materials chemistry [1]. An important subset of fluorinated compounds contains a difluoromethylene (CF₂) group [2]. This group can be obtained by direct fluorination of ketones [3], or by a building block approach using appropriately fluorinated synthons [4]. For the syntheses of α,α -difluoroesters **3** (Scheme 1), (m)ethyl bromo and iodo difluoroacetate **1a,b** are useful building blocks, with the desired products accessible via a Reformatsky or aldol-type reaction or via a radical-mediated addition to alkenes.

A Reformatsky process is typically performed using **1** [2,5], and leads to adducts **2c**, of which the alcohol group subsequently needs removing to obtain **3**. This is typically achieved by a 2-step Barton-McCombie reduction process [6] via a thiocarbamate [7] or a thiocarbonate [8] derivative. Alternatively, a radical-mediated addition reaction using **1a,b** leads to adducts **2a** or **2b**, with subsequent reduction of the halide required to obtain **3**. A range of initiators have been reported, such as copper [9], sodium dithionite

[10], and triethylborane [11]. In the majority of cases, **1b** is used as reagent. Subsequent reduction of **2b** to **3** is reported using NiCl₂·6H₂O [9c]. In addition, Burton has also reported an addition process of **1b** to alkenes leading directly to products **3** using NiCl₂·6H₂O/Zn [12], and Taguchi has reported the direct formation of the reduced product **3** when the electron deficient acrylamide was used, with Sn as reagent [9b].

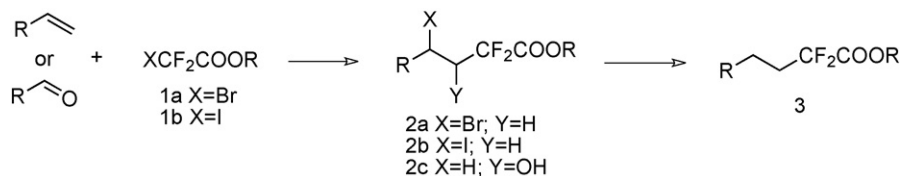
In our hands, addition of **1b** to alkenes using NiCl₂·6H₂O/Zn appeared to be a rather capricious process, presumably due to the quality of the Zn metal used and/or inadequate Zn-activation. We wish to report a convenient, high-yielding alternative in that radical-mediated addition of **1b** to alkenes was found to proceed by simply using AIBN as initiator. Subsequent iodide reduction to afford difluoroalkane **3** was achieved in high yields using NiCl₂·6H₂O/Zn or Et₃B/Bu₃SnH.

2. Results and discussion

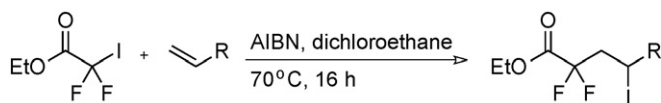
2.1. AIBN-initiated addition of ethyl 4-iodo-2,2-difluoroacetate to alkenes

AIBN is a commonly employed radical initiator in organic synthesis. Several examples of AIBN-initiated addition of perfluoroalkyl iodides to alkenes have been reported in the literature,

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Scheme 1.



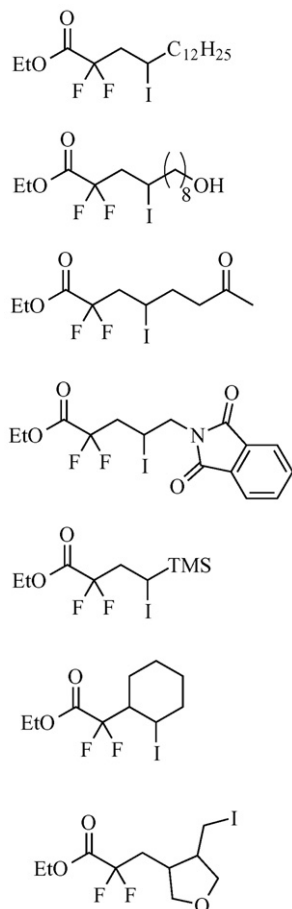
Scheme 2.

the earliest of which was reported in the 1960s [13]. To the best of our knowledge, this reagent has not yet been applied in radical additions involving iododifluoroacetates such as **1b**, though an AIBN-initiated allylation involving allyltin has been described starting from a 2-bromo-2,2-difluoroacetamide derivative [14].

We were thus pleased to find that when difluoroacetate **1b** was reacted with a range of alkene substrates **4–10** with AIBN, the addition products **11–17** were generally formed in good to excellent yields (Scheme 2 and Table 1). Unfortunately, when ethyl bromodifluoroacetate was submitted under these reaction conditions no reaction was observed.

In most cases, a slight excess of difluoroacetate **1b** was required in order to achieve optimum results (Entries 2–8). When 1.5 equivalents of tetradecene **4** and 1.0 equivalent of iododifluoroacetate **1b** were treated with AIBN (10%), a modest 54% yield of product **11** was obtained (Entry 1). On the other hand, using a small

Table 1
AIBN-initiated addition of difluoroacetate **1b** to alkene substrates



Entry	Alkene	Equiv	AIBN (mol%)	1b (equiv)	Product	Yield ^a (%)
1	Tetradecene 4	1.5	10%	1.0		54
2	4	1.0	10%	1.5	11	77

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