

# Preparative-scale one-pot syntheses of hexafluoro-1,3-butadiene

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Received 22 January 2008; accepted 24 January 2008

Available online 3 February 2008

## Abstract

Hexafluoro-1,3-butadiene, with its negligible global warming potential, is required in quantities for application in plasma dielectric etching in semiconductor industry and as gaseous microbubble suspension contrast agents in diagnostic ultrasound imaging. Three efficient protocols for the preparation of perfluoro-1,3-butadiene in 62–70% overall yields have been described. They involve the coupling of (1) iodotrifluoroethylene (ITFE) with activated copper, (2) trifluorovinylzinc bromide in the presence of copper (II) or iron (III) salts and (3) trifluorovinylzinc chloride, prepared from 1,1,1,2-tetrafluoroethane (HFC 134a) in the presence of copper (II) or iron (III) salts.

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*Keywords:* Etching-gases; Ultrasound contrast agents; Gaseous microbubbles; Hexafluoro-1,3-butadiene; Coupling reaction; Bromotrifluoroethylene

## 1. Introduction

Fluoroorganic molecules have found applications as pharmaceuticals, agrochemicals, and valuable materials in electronics industry [1]. Noteworthy examples of the latter application are gaseous fluorocarbons utilized for plasma dielectric etching. Of the several dry-etching-gases, hexafluoro-1,3-butadiene ( $C_4F_6$ , **1**) with Xe and Ar as carrier gas is preferred due to its negligible global warming potential (GWP) [2,3]. Chatterjee et al. have reported an 80% decrease in global warming plasma emissions from a  $C_4F_6$ -based etching process compared to  $C_3F_8$  etching process [3]. This material has a very short atmospheric lifetime, decomposing within 2 days. Perfluorocarbon gases, including  $C_4F_6$  have recently been exploited to generate stable gaseous microbubble suspensions as ultrasonic contrast agents in diagnostic molecular imaging [4].

Haszeldine and co-workers reported the first synthesis of **1** more than half a century ago from chlorotrifluoroethylene (CTFE), via the corresponding 1,2,3,4-tetrahalogenobutane, prepared by the treatment with iodine monochloride or monobromide, followed by reacting with mercury in UV light or zinc in dioxane. The dehalogenation of the tetrahalo

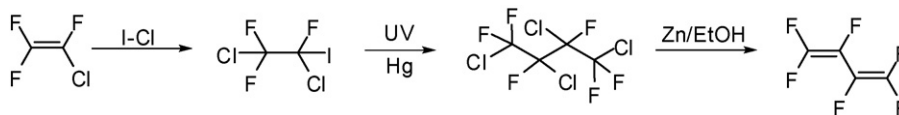
derivative was achieved using zinc in ethanol (Scheme 1) [5]. A modified synthesis of **1** from the disodium salt of octafluorohexane-1,6-dioic acid via decarboxylation and defluorination was also reported by Haszeldine (Scheme 2) [6]. Dedek and Chvatal [7] developed a cumbersome process for the preparation of **1** by the initial addition of 1,2-dibromo-1-chlorotrifluoroethane to chlorotrifluoroethylene under ultraviolet radiation to obtain a mixture of products, including 1,4-dibromo-2,3-dichlorohexafluorobutane (Scheme 3). This was isolated and treated with zinc and ethanol to provide **1**. Copper and iron-mediated coupling of perfluoroalkenyl iodides and bromides are known [8]. During an attempted preparation of trifluorovinylcopper reagent from iodotrifluoroethylene (ITFE), Burton and Hansen [9] recognized its dimerization [10].

Due to the industrial importance of **1**, there are a few recent protocols described in patent literature for its preparation [11–13]. Two of these involve the preparation of **1** via the dehalogenation of 1,4-dihaloctafluorobutadiene and the third patent [13] describes the preparation of **1** from 1,2-dibromotetrafluoroethane via isomerization, dehalogenation and dimerization using cupric bromide.

As part of our program in fluoroorganic chemistry, we were interested in developing a simple cost-effective synthesis of **1** from bromotrifluoroethylene for large-scale applications. Following are the details of our study on the preparative-scale synthesis of hexafluoro-1,3-butadiene.

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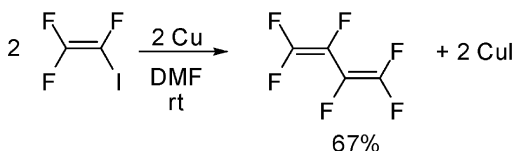
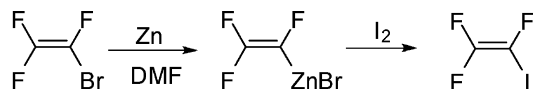
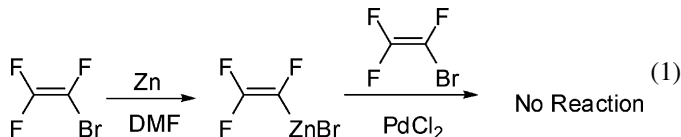
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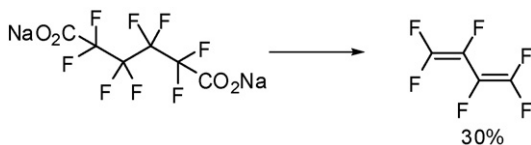
Scheme 1.

## 2. Results and discussion

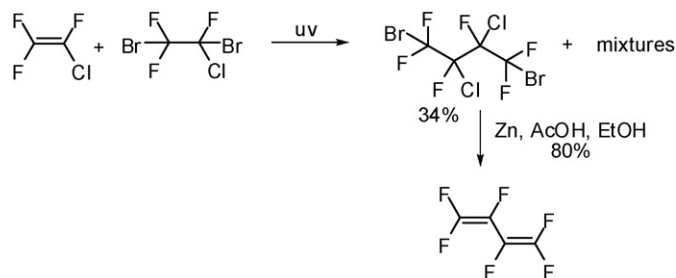
We undertook a systematic study to realize a one-pot synthesis of **1** that can be scaled up. Initially, our focus was on the transition metal-catalyzed coupling of the haloolefins. To this end, we attempted a Negishi coupling [14] of trifluorovinylzinc bromide with BTFE in the presence of palladium chloride. However, no formation of **1** was observed (Eq. (1)). We utilized other palladium salts, such as palladium acetate and nickel salts, such as nickel chloride to no avail. Since vinyl iodides serve as better coupling partners, ITFE was prepared from BTFE using zinc and iodine. Similar attempts to couple ITFE using palladium and nickel salt catalysts also failed to provide **1**. We then sought to dimerize ITFE in the presence of activated copper powder in dimethylformamide (DMF), on the basis of the observation of Burton et al. [8], and achieved the coupled product in 67% isolated yield (Eq. (2)).



Encouraged by this result, we directed our efforts towards an efficient synthesis of **1** from BTFE, avoiding the preparation of ITFE. Screening of several metal salts, solvents, and temperature were performed for arriving at the optimal conditions for the desired dimerization. Indeed, our goal was achieved in the presence of copper (II) salts, such as copper acetate, bromide, or triflate and iron (III) salts, such as ferric chloride or bromide, in DMF as solvent. The dimerized product



Scheme 2.



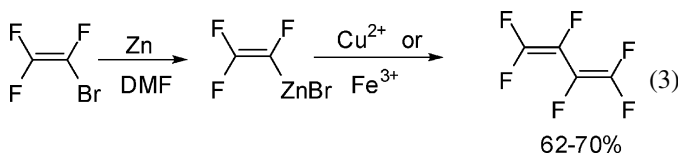
Scheme 3.

Table 1  
Preparation of hexafluoro-1,3-butadiene from trifluoroethenezinc halides<sup>a</sup>

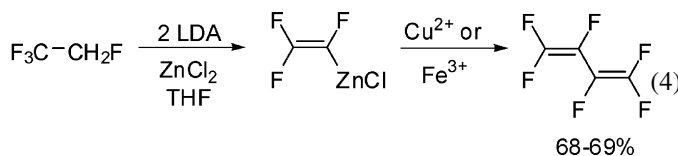
Entry	TFEZnX X	Metal salt	C <sub>4</sub> F <sub>6</sub> yield (%)
1	Cl	CuBr <sub>2</sub>	69
2	Cl	FeCl <sub>3</sub>	68
3	Br	CuBr <sub>2</sub>	68
4	Br	Cu(OAc) <sub>2</sub>	68
5	Br	Cu(OTf) <sub>2</sub>	62
6	Br	FeBr <sub>3</sub>	68
7	Br	FeCl <sub>3</sub>	70

<sup>a</sup> Reaction condition: metal salt (0.03 mol) was added to TFEZnX (0.03 mol) in DMF (50 mL) at RT and hexafluoro-1,3-butadiene was collected simultaneously at  $-78^{\circ}\text{C}$ .

**1** was realized in 62–70% isolated yields and 100% chemical purity in all of the cases (Eq. (3)).



We then attempted a cost-effective synthesis of **1** from the corresponding trifluorovinylzinc chloride utilizing a simple preparation from 1,1,1,2-tetrafluoroethane (HFC-134a) [15]. The dimerization was attempted in the presence of Cu(II) or Fe(III) salts, as in the case of Eq. (3). Much to our satisfaction, we achieved the preparation of **1** in 69–70% yield (Eq. (4)). The results are summarized in Table 1.



## 3. Conclusion

In summary, we have developed a simple, practical and high yielding procedure for a one-pot preparation of hexafluoro-

obutadiene by the coupling of iodotrifluoroethylene in the presence of activated copper or from bromotrifluoroethylene or 1,1,1,2-tetrafluoroethane via the coupling of the trifluorovinylzinc halides (chloride or bromide), in the presence of copper (II) or iron (III) salts. All of these procedures were repeated several times and reproduced. These protocols are amenable to scaling up and the yields can be improved by carrying out the reactions in well-sealed conditions [16]. The negligible global warming potential of  $C_4F_6$  with the required process performance, an efficient alternative to  $CF_4$ ,  $CHF_3$ , and  $C_4F_8$ , should make this procedure attractive.

#### 4. Experimental

Bromotrifluoropropene and HFC-134a were obtained as a gift from Great Lakes Chemical Corporation (Chemtura). All other chemicals were purchased from various commercial sources. The  $^{19}F$  ( $CFCl_3$  or trifluoroacetic acid internal standard) nuclear magnetic resonance (NMR) spectrum was plotted in  $CDCl_3$  on a Varian Gemini-300 spectrometer (282 MHz) with a Nalorac-quad probe.

The Zinc dust used for the reactions was activated [17] by stirring 100 g of zinc powder with 50 mL of 10% dilute hydrochloric acid for 2–4 min, filtering and washing with 100 mL of water, followed by 50 mL of acetone and drying in oven (130–140 °C) for 1 h.

The copper powder used for the reactions was activated as follows [18]. 20 g of copper powder was treated with 200 mL of 2% solution of iodine in acetone for 10 min. This resulted in the formation of a rather grayish color due to the formation of copper iodide. The activated copper was filtered and washed with 100 mL of 1:1 solution of conc. HCl in acetone. The copper iodide gets dissolved and the residual copper is filtered, washed with acetone, and dried under vacuum at 40–50 °C for immediate in the next step.

##### 4.1. Preparation of hexafluoro-1,3-butadiene

###### 4.1.1. From iodotrifluoroethylene

Activated copper powder (8.5 g, 132 mmol) was placed in 50 mL of dry DMF in a 100 mL RB flask having a side arm fitted with dry ice condenser. Trifluorovinyl iodide, prepared from the corresponding bromide using a literature procedure [19] (25 g, 120 mmol) was added slowly to this mixture and kept stirring at RT. A slightly exothermic reaction initiated after 15 min, which was left stirred for 1 h and the product was collected using a cold trap kept at  $-78$  °C. b.p.  $5-6$  °C (lit. [7]  $5.8$  °C). Yield: 6.5 g (67%). The  $^{19}F$  NMR spectral data matched with that reported in the literature [20].

###### 4.1.2. From bromotrifluoroethylene

Under stirring, activated zinc (2 g, 30 mmol) and dry DMF (30 mL) were placed in a 3-necked 100 mL RB flask fitted with a dry ice condenser, followed by the slow addition of bromotrifluoroethylene (5.3 g, 33 mmol), at RT. The reaction mixture was warmed to 30 °C (inside temperature). After 15 min, the reaction initiated, with the temperature rising to

$\sim 70$  °C, which was controlled by keeping the RB flask in ice-water. The reaction mixture turned brown and was stirred further for 1 h at RT, completing the formation of the trifluorovinylzinc bromide.

The flask was now fitted with an addition funnel and while the reaction mixture is cooled to 0–5 °C, and applying vacuum using a water aspirator pump (100 mm Hg), 33 mmol of ferric salt ( $FeCl_3$  or  $FeBr_3$ ) or cupric salt ( $Cu(OTf)_2$  or  $Cu(OAc)_2$ ) was added slowly, maintaining the reaction temperature below 5 °C.  $FeCl_3$  is soluble in DMF and can be added as a solution. Most of hexafluorobutadiene was collected in a trap cooled using dry ice-acetone ( $-78$  °C). The rest of the product was collected by warming the reaction to 40 °C and stirring for 2 h (all the while applying vacuum). The reaction was repeated several times and the yield of the reactions ranges between 62–70% (see Table 1).

###### 4.1.3. From HFC-134a

Under nitrogen, to a 100 mL RB flask having side-arm and fitted with dry ice condenser, 4.2 g (32 mmol) of anhydrous zinc chloride, 30 mL of dry THF were added. The suspension was cooled to 10 °C and HFC-134a (36 mmol) was added slowly. LDA (64 mmol) (lithium diisopropyl amine 1.8 M solution) is added slowly through a syringe to the above HFC-134a/ $ZnCl_2$  slurry, while maintaining the temperature  $< 15$  °C. (The tip of the needle was dipped into THF to avoid decomposition of trifluorovinyl lithium formed by reaction of HFC-134a with LDA). The reaction mixture was stirred for 1 h and allowed to warm to room temperature. After that reaction mixture was cooled to 0–5 °C, and applying vacuum (100 mm Hg), 33 mmol of ferric salt ( $FeCl_3$  or  $FeBr_3$ ) or cupric salt (Copper triflate or  $Cu(OAc)_2$ ) was added slowly, maintaining the reaction temperature below 5 °C. The reaction was stirred at 40 °C for 2 h and the product collected using a trap cooled at  $-78$  °C. The reaction was repeated several times to confirm the yields (68–69%, Table 1).

#### Acknowledgements

We gratefully acknowledge Chemtura for financial support and the gift of BTFE and HFC-134a for this research.

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