

## Mild, Zinc-Induced Defluorination of Butatrienes: Stereoselective Formation of Divinylacetylene Derivatives

Peter A. Morken, Donald J. Burton,\* and Dale C. Swenson

Department of Chemistry, University of Iowa, Iowa City, Iowa 52242

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Defluorination of  $R(\text{Ph})\text{C}=\text{C}=\text{C}(\text{Ph})\text{R}$  [ $R = \text{C}_2\text{F}_5$  (**3b**);  $R = n\text{-C}_3\text{F}_7$  (**3c**)] was accomplished under remarkably mild conditions: Zn/rt/18 h. Reaction of pure (*E*)- or (*Z*)-**3b** with Zn gave in both instances 89–96% (*E,E*)- $\text{CF}_3\text{CF}=\text{C}(\text{Ph})\text{C}=\text{C}(\text{Ph})=\text{CF}_3$  in greater than 95% isomeric purity. The latter product was characterized by X-ray crystallography. Similarly, treatment of pure (*E*)- or (*Z*)-**3c** with Zn gave 70–93%  $\text{CF}_3\text{CF}_2\text{CF}=\text{C}(\text{Ph})\text{C}=\text{C}(\text{Ph})=\text{CF}_2\text{CF}_3$  in 95% isomeric purity, although the stereochemistry could not be determined. A single electron transfer (SET) mechanism is proposed for the defluorination reaction.

### Introduction

Because of the strong bond between fluorine and carbon,<sup>1,2</sup> defluorination processes are difficult to accomplish and have been achieved by four general strategies: utilization of (a) high temperatures (300–700 °C), (b) powerful reducing agents, or (c) transition-metal complexes or (d) employment of a reactive substrate. The high-temperature iron defluorination reaction of perfluorocyclohexane derivatives is of commercial importance, especially for the preparation of fluorinated aromatic compounds.<sup>3</sup> More recently, activated carbon<sup>4</sup> and an expired fluorination catalyst,  $\text{CsCoF}_3$ ,<sup>5</sup> have been utilized for similar transformations. While high-temperature techniques are useful for the preparation of aromatic compounds, the analogous defluorination of fluorinated alkenes can be complicated by side reactions at the required temperatures. For example, pyrolysis of tetrafluoroethylene tetramer in an Fe or Pt tube gives a diene and its cyclobutene isomer, the latter from electrocyclic rearrangement of the diene.<sup>6</sup> The defluorination reaction is possible under milder temperatures when more powerful reducing agents are employed, including electropositive elements such as Na,<sup>7</sup> and Mg.<sup>9</sup> Sodium benzophenone radical anion defluorinates saturated perfluorocarbons.<sup>10</sup> Benzoin dianion<sup>11</sup> and  $\text{Li}/\text{NH}_3$ <sup>12</sup> reduce poly(tetrafluoro-

ethylene). Transition metals including  $\text{CpFe}(\text{CO})_2^-$  have also been utilized for defluorination reactions.<sup>13</sup> Divalent lanthanoid complexes were recently reported to defluorinate perfluoroolefins,<sup>2</sup> and  $\text{LiAlH}_4/\text{CeCl}_3$  reduces aliphatic and aromatic carbon–fluorine bonds.<sup>14</sup>

The defluorination reaction can be accomplished under less forcing conditions if a more reactive fluorinated substrate is employed. Substrates with an element of unsaturation or a tertiary or quaternary carbon are more susceptible to defluorination *via* an SET mechanism.<sup>10,13a,15,16</sup> Thus, hexadecafluorobicyclo[4.4.0]dec-1(6)-ene was defluorinated by Zn in DMF at 80 °C, while perfluorodecalin did not react under similar conditions.<sup>16</sup> A single electron transfer (SET) mechanism was proposed by the authors, and a radical intermediate was trapped by  $\text{C}_6\text{H}_5\text{NO}$  and observed by ESR. The  $(\text{CF}_3)_2\text{CF}$  group in polyfluoroaromatic compounds has also been defluorinated by Zn under mild conditions (50 °C).<sup>17</sup> Arenethiolate nucleophiles have been proposed to react with perfluorodecalin *via* an SET mechanism; perfluorocyclohexane, with no tertiary centers, does not react under similar conditions.<sup>15</sup> Quantum mechanical calculations have confirmed the observed trend (3° > 2° carbon) of reactivity to SET reaction.<sup>18</sup> The reduction of butatrienes and hexapentaenes has been accomplished with  $\text{Zn}/\text{ZnCl}_2/\text{H}_2\text{O}$  or  $\text{Al-Hg}$ .<sup>19</sup>

### Results and Discussion

We recently reported the preparation and exploratory reactions of fluorinated 1,2,3-butatrienes, available by treatment of ( $\alpha$ -bromovinyl)zinc reagents with a catalytic amount of cuprous bromide (eq 1).<sup>20</sup> Fluorinated butatrienes **3a–d** were available in multigram quantities and

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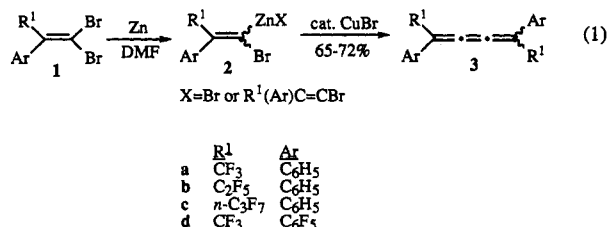
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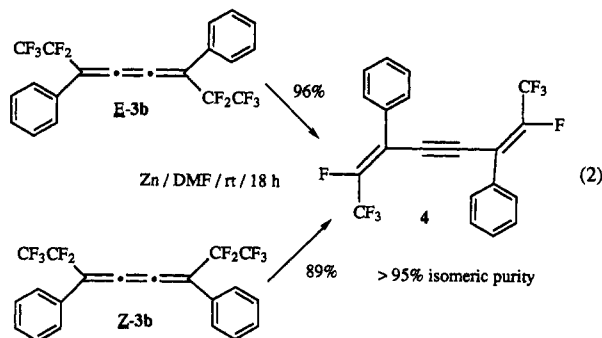
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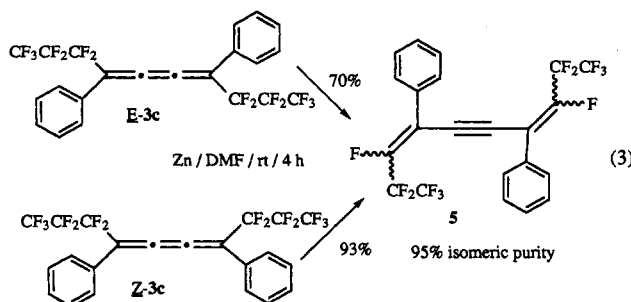


are readily separated in high purity to the individual isomers, which were characterized by X-ray crystallography. The ( $\alpha$ -bromovinyl)zinc reagents (**2a-d**) were easily prepared by addition of a slight excess (1.2–2 equiv) of zinc to 1,1-dibromoalkenes **1a-d** in DMF. The best yields of **3a-d** were obtained when the excess zinc metal was removed by filtration prior to treatment of the ( $\alpha$ -bromovinyl)zinc reagents with cuprous bromide. When an unfiltered solution of **2b** was treated with cuprous bromide and stirred overnight at room temperature, several products which were not readily purified by silica gel chromatography were formed. Surprisingly, fractional recrystallization of the impure organic materials gave white and yellow crystals, which were manually separated. The yellow crystals were found to be (*E*)- and (*Z*)-**3b**. The white crystals, on the other hand, were determined by GC-MS and  $^{19}\text{F}$ ,  $^{13}\text{C}$ , and  $^1\text{H}$  NMR to be the symmetrical product **4**. The *E* stereochemistry about both double bonds was elucidated by X-ray analysis<sup>21</sup> (Figure 1).

We thus began a detailed study of this novel reaction and found that **3b** underwent defluorination under mild conditions, Zn/25 °C/18 h, to afford the novel divinylacetylene derivative **4** in excellent yield. Significantly, treatment of either pure (*E*)- or (*Z*)-**3b** with Zn gave the *E, E* isomer in greater than 95% isomeric purity (eq 2).



The *E* or *Z* isomers of **3c** also underwent Zn-induced defluorination, affording divinylacetylene derivative **5** as a (95:5:trace) mixture of isomers (eq 3).



Although the major isomer could be isolated by silica gel chromatography, attempts to recrystallize a sample for

(21) Detailed X-ray crystallographic data for **4** will be published.

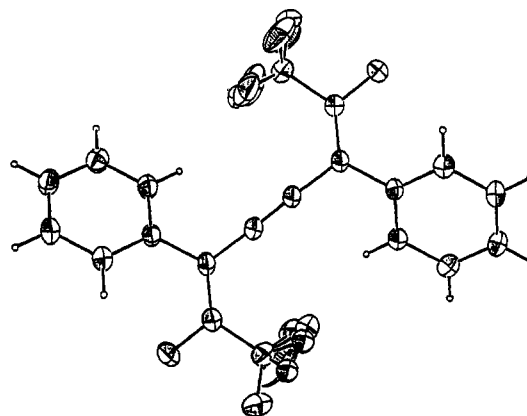
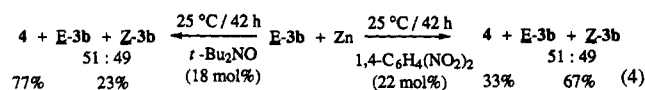


Figure 1. ORTEP drawing of (*E,E*)- $\text{CF}_3\text{CF}=\text{CPh}-\text{C}\equiv\text{CCPh}=\text{CF}_3$  (**4**).

X-ray analysis were not successful. However by analogy to (*E,E*)-**4**, it is likely that **5** is the *E,E* stereoisomer.

The defluorination reaction of (*E*)- and (*Z*)-**3a** and **3d** was complicated by side reactions. This result can be attributed to the susceptibility of the expected product,  $\text{CF}_2=\text{C}(\text{Ph})\text{C}\equiv\text{CC}(\text{Ph})=\text{CF}_2$  (**6**), to nucleophilic attack at the less sterically demanding difluoromethylene group. A complex mixture of products was observed by  $^{19}\text{F}$  NMR analysis after treatment of **3a** with Zn in DMF,  $\text{CH}_3\text{CN}$ , or TG. A trace of a product with a  $m/z$  of 302, consistent with the molecular formula of **6**, was observed by GC-MS analysis in the  $\text{CH}_3\text{CN}$  experiment. However, the major products had masses consistent with the addition of 1 or 2 equiv of HF to **6** (isomers of  $m/z = 322, 342$ ). Complex mixtures of products were still observed by  $^{19}\text{F}$  NMR when the defluorination was carried out in TG or  $\text{CH}_3\text{CN}/(\text{CH}_3)_3\text{SiBr}$  (fluoride anion scavenger).

**Mechanism of Defluorination.** Isomerization of the butatriene was observed when the (*E*)-**3b**/Zn reaction mixture was monitored by  $^{19}\text{F}$  NMR before complete consumption of butatriene had occurred, which implies that one of the steps of the reaction is reversible. The thermodynamic equilibration ratio of (*E*)-**3b**:(*Z*)-**3b** was determined to be 48:52 (110 °C/triglyme).<sup>20</sup> When the reaction of (*E*)-**3b** and Zn was carried out in the presence of single electron transfer (SET) scavengers<sup>22</sup> such as *p*-dinitrobenzene or di-*tert*-butyl nitroxide, incomplete conversion of (*E*)-**3b** was observed (eq 4).<sup>23</sup>



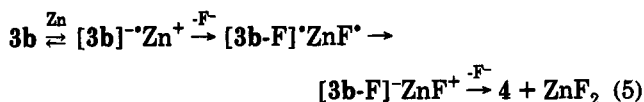
Thus, the mechanism is envisioned to involve a reversible electron transfer from Zn to **3b** to afford a radical anion which can return to either isomer of **3b** or lose fluoride anion to give a radical, which after accepting another electron loses a second fluoride anion en route to **4** (eq 5). The high susceptibility of **3b** to the defluorination reaction may be attributed to the low LUMO level of **3b**, which is a consequence of the extended conjugation<sup>24</sup> of the butatriene and the presence of the two perfluoroalkyl

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(24) For example, (*E*)-**3b** exhibits a  $\lambda_{\text{max}} = 377$  ( $\epsilon = 37\,600$ ).<sup>19</sup>

groups.<sup>25</sup>



**Conclusion.** The defluorination reaction of fluorinated butatrienes **3b** and **3c** has been discovered to proceed under the mildest reported conditions: Zn/rt/18 h. The ease of defluorination reaction of these substrates is attributed to the high susceptibility of the fluorinated butatrienes toward electron transfer reaction. The defluorination reaction of **3b** and **3c** proceeds with greater than 95% stereoselectivity to afford symmetrical divinylacetylene derivatives.

### Experimental Section

**General.** <sup>19</sup>F NMR were recorded on a JEOL FX90Q (83.81 MHz) or Bruker AC-300 (282.44 MHz) spectrometer, and <sup>1</sup>H/<sup>13</sup>C NMR (75.48 MHz) and <sup>1</sup>H NMR (300.17 MHz) spectra were recorded on the AC-300 spectrometer. All samples were taken in CDCl<sub>3</sub> solvent and all chemical shifts are reported in parts per million downfield (positive) of the standard: TMS for <sup>1</sup>H and <sup>13</sup>C; CFCl<sub>3</sub> for <sup>19</sup>F NMR. FT-IR spectra were recorded as CCl<sub>4</sub> solutions and reported in wavenumbers (cm<sup>-1</sup>). GC-MS spectra were obtained at 70 eV in the electron impact mode. High resolution mass spectral determinations were made at the University of Iowa High Resolution Mass Spectrometry Facility or the Midwest Center for Mass Spectrometry, the latter with partial support by the National Science Foundation, Biology Division (Grant No. DIR9017262). DMF (CaH<sub>2</sub>) was distilled at reduced pressure and silica gel (EM) was 70–230-mesh ASTM. Zinc (325 mesh, Aldrich) was activated by washing the solution with dilute HCl and then drying *in vacuo* at room temperature. Butatrienes **3a–d** were prepared as described earlier.<sup>20</sup>

**(E,E)-1,1,1,2,7,8,8,8-Octafluoro-3,6-diphenylocta-2,6-dien-4-yne (4).** A 2-neck 25-mL flask equipped with a Teflon-coated stir bar, Ar tee, and septum was charged with (*Z*)-**3b** (0.24 g, 0.54 mmol), activated Zn (0.06 g, 0.9 mmol), and DMF (3.5 mL). The solution immediately turned light green in color. After the mixture was stirred at room temperature for 18 h, the black mixture was transferred to a silica gel (75 g) column and eluted with hexane. Eluents with similar UV-active TLC spots were combined and the solvent was removed by rotary evaporation and exposure to a vacuum (1 mmHg/25 °C/1 min) to afford 0.21 g (96%) of **4** as a white solid, mp 79–80 °C. The isomeric purity was determined to be greater than 95% by <sup>19</sup>F NMR analysis.

Recrystallization from hexane gave pure **4** for X-ray analysis: <sup>1</sup>H NMR δ 7.59 (m, 2H), 7.42 (m, 3H); <sup>19</sup>F NMR δ -67.6 (d, 7.3 Hz, 3F), -120.3 (d, 7.3 Hz, 1F); <sup>13</sup>C NMR δ 149.8 (dq, 275, 38.8 Hz), 130.9, 130.1, 129.1, 129.0, 128.9, 128.8, 119.0 (qd, 274, 40.0 Hz), 111.2 (d, 20.3 Hz), 90.4 (dd, 7, 4 Hz); GC-MS 403 (M + 1, 61%), 334 (16), 265 (100), 201 (20), 151 (49), 132 (22), 77 (18), 51 (33); FTIR (CCl<sub>4</sub>) 3064.6 (vw), 1952.9 (vw), 1449.5 (w), 1349.3 (s), 1291.3 (vs), 1153.9 (vs); HRMS calcd for C<sub>20</sub>H<sub>10</sub>F<sub>8</sub> 402.0655, obsd 402.0673.

Similarly, **4** (0.23 g, 89% yield) was prepared from (*E*)-**3b** (0.28 g, 0.64 mmol), activated Zn (0.08 g, 1 mmol), and DMF (5.5 mL). The isomeric distribution and spectroscopic data were identical to those described for (*Z*)-**3b**.

**1,1,1,2,2,3,8,9,9,10,10,10-Dodecafluoro-4,7-diphenyldeca-3,7-dien-5-yne (5).** A 2-neck 25-mL flask equipped with a Teflon-coated stir bar, Ar tee, and septum was charged with (*Z*)-**3c** (0.15 g, 0.28 mmol), activated Zn (0.0228 g, 0.35 mmol), and DMF (2 mL). The solution immediately turned light green in color. After the solution was stirred at room temperature for 4 h, the black mixture was isolated as described for **4** to afford 0.13 g (93%) **5** as an oil. The isomeric purity was determined to be 95% by <sup>19</sup>F NMR analysis: <sup>1</sup>H NMR δ 7.56 (m, 2H), 7.37 (m, 3H); <sup>19</sup>F NMR δ -84.2 (s, 3F), -117.8 (bs, 1F), -118.0 (d, 10 Hz, 2F); <sup>13</sup>C NMR δ 149.4 (dt, 274, 28 Hz), 131.4, 130.1, 129.1, 129.0, 128.8, 118.8 (qt, 288, 37 Hz), 114.0 (d, 22.0 Hz), 109.3 (tqd, 260, 40, 37 Hz), 90.7 (t, 9 Hz); GC-MS 502 (M<sup>+</sup>, 100%), 433 (12), 382 (19), 264 (74), 162 (58), 77 (14); FTIR (CCl<sub>4</sub>) 3064.9 (vw), 2362.1 (vw), 1700.4 (w), 1330.5 (m), 1218.5 (vs), 1176.6 (s), 1034.3 (m); HRMS calcd for C<sub>22</sub>H<sub>10</sub>F<sub>12</sub> 502.0591, obsd 502.0577.

Similarly, **5** (0.31 g, 70% yield) was prepared from (*E*)-**3c** (0.48 g, 0.89 mmol), activated Zn (0.10 g, 1.5 mmol), and DMF (4 mL). The isomeric distribution and spectroscopic data were identical to those described for (*Z*)-**3c**.

**Reaction of (*E*)-CF<sub>3</sub>(C<sub>6</sub>H<sub>5</sub>)C=C=C(C<sub>6</sub>H<sub>5</sub>)CF<sub>3</sub> (**3a**) with Zn.** A 2-neck 25-mL flask equipped with a Teflon-coated stir bar, N<sub>2</sub> tee, and septum was charged with (*E*)-**3a** (0.06 g, 0.2 mmol), activated Zn (0.02 g, 0.3 mmol), and DMF (2 mL). The solution turned green after 2 min, and <sup>19</sup>F NMR analysis after 10 min revealed a complex reaction mixture.

(*E*)-**3a** (0.16 g, 0.47 mmol) was similarly treated with activated Zn (0.17 g, 2.6 mmol) in CH<sub>3</sub>CN (7.5 mL). Compound **3a** was consumed after reflux the solution for 3 h and then stirring for 16 h at 25 °C. <sup>19</sup>F NMR analysis of the mixture revealed four signals: δ -60.1 (s, 16%), -69.8 (d, ~10 Hz, 35%), -75.2 (s, 29%), and -78.8 (s, 20%). The DMF was removed by low pressure distillation (0.5 mmHg/40 °C) and the residue was purified by silica gel (100 g) chromatography. No fraction could be obtained pure, and GC-MS analysis of the fractions indicated that seven or more products had formed, including compounds with mass/charge ratios of 302, 322, and 342.

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