Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters 47 (2006) 9245–9248
Tetrahedron Letters

Palladium(0)-catalyzed addition of $CFBr_3$ to olefins: synthesis of 1,1,3-tribromo-1-fluoroalkanes and 1,2-difluoroalkenes

B. Rama Raju, E. K. Pramod Kumar and Anil K. Saikia*

Department of Chemistry, Indian Institute of Technology Guwahati, Guwahati 781 039, India

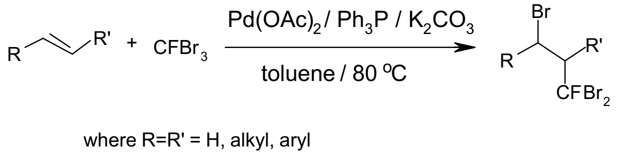
Received 14 March 2006; revised 17 October 2006; accepted 26 October 2006

Abstract—It has been observed that Pd(0) can be used as a catalyst for the addition of $CFBr_3$ to olefins to give 1,1,3-tribromo-1-fluoroalkanes with good yields. Both terminal and internal olefins react under these conditions. Treatment of the addition product with zinc and methanol gave 1,2-fluoroalkenes.

The introduction of fluorine(s) into organic materials is prevalent in fields such as pharmacology or functionalized materials because of the unique biological and physical properties of the resulting compounds.[1] Several β-fluorophenethylamines,[2] 3-fluoroalkylamines,[3] and vinyl fluorides,[1c,4] have been shown to be irreversible inhibitors of certain enzymes. 1,2-Difluoroethylenes are especially interesting intermediates in organic chemistry due to their use in fluorinated analogues of natural products,[5] polymers[6] and liquid crystals.[7] In particular, reactions using fluoroorganometallic reagents derived from fluorohalohydrocarbons are versatile for constructing fluorinated target molecules.[8] There are a few methods reported for the addition of perfluoroalkyl monobromides to olefins catalyzed by radical initiators.[9] However, reports on the metal catalyzed addition of fluorohaloalkanes to olefins are few.[10] In this letter we report the palladium(0)-catalyzed addition of $CFBr_3$ to various olefins and subsequent reduction of the addition products with Zn and methanol to give 1,2-difluoroolefins.

In continuation of our interest in Freon,[11] we required a method for the addition of $CFBr_3$ to olefins. Following a literature procedure for the addition of perfluoroalkyl monobromide under free radical conditions,[9] where $CFBr_3$ was treated with olefin in the presence of sodium dithionite, the reaction resulted in a complex mixture. A variety of addition reactions of organic halides to alkenes catalyzed by palladium(0) have been reported.[12] Klabunde and Low have studied the stabilities and properties of some oxidative addition products of palladium and perfluoroalkyl halides.[13] They studied various fluorohaloalkanes, however, there was no mention of $CFBr_3$. Taking cues from this and in continuation of our own work on palladium-catalyzed reactions,[14] it was envisaged that palladium(0) might be a suitable reagent for the addition reaction of $CFBr_3$ to olefins. Thus, when $CFBr_3$ was treated with olefins in the presence of a catalytic amount of palladium(II) acetate, triphenylphosphine and anhydrous potassium carbonate in toluene at 80 °C, the corresponding addition products were obtained in good yields.[15] The reaction is represented in Scheme 1.

To generalize the reaction, various olefins were reacted with $CFBr_3$ as shown in Table 1. It was observed that both terminal and internal olefins could be converted to the corresponding fluorobrominated alkanes. In both cases, no Heck products (olefins) were isolated. Terminal olefins gave only one product whereas cyclic olefins



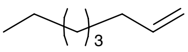
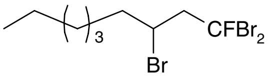
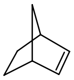
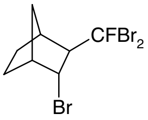
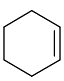
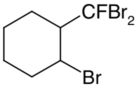
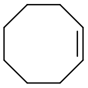
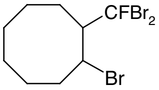
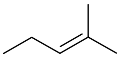
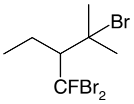
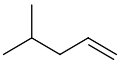
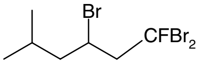
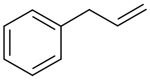
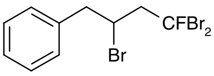
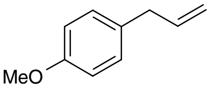
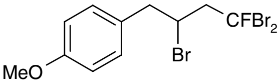
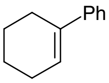
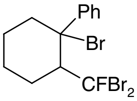
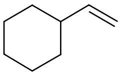
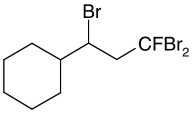
Scheme 1.

Keywords: Tribromofluoromethane; Palladium; Catalyst; Addition; Olefins; Reduction; Zinc–methanol.

* Corresponding author. Tel.: +91 361 2582316; fax: +91 361 2690762; e-mail: asaikia@iitg.ernet.in

0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.10.145

Table 1. Palladium catalyzed addition of $CFBr_3$ to olefins

Entry	Substrate (**a**)	Time (h)	Product (**b**)	Yield[a] (%)
1		30		79
2		16		79
3		31		78
4		49		96
5		27		63[b]
6		21		79
7		15		81
8		17		75
9		71		33
10		18		85

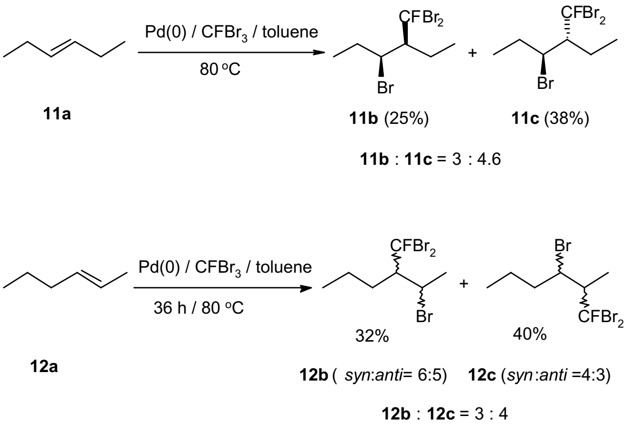
[a] Isolated yields. Compounds were characterized by IR, ^1H, ^{13}C and ^{19}F NMR.
[b] Determined by ^1H NMR.

gave *cis* and *trans* products. Internal olefins gave a mixture of diastereomers.

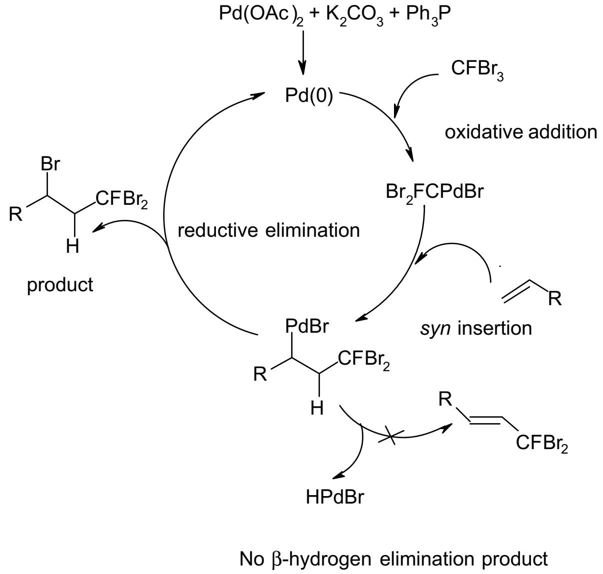
trans-3-Hexene **11a** gave diastereomers[16] **11b** and **11c** in a ratio of 3:4.6.[17] The unsymmetrical olefin **12a** gave a mixture of four isomers[16] (Scheme 2). It was observed that CF_2Br_2 did not react with olefins under these reaction conditions due to the instability of the $CFBr_2PdBr$ species.[13]

The mechanism of the reaction may be as follows (Scheme 3). The first step is the oxidative addition of palladium(0) to $CFBr_3$ followed by olefin insertion. Reductive elimination of palladium(II) to palladium(0) with addition of bromine gives the product. With unfunctionalized olefins, the insertion occurs placing the $CFBr_2$ group at the less-substituted position of the olefin. Thus, the regioselectivity of the insertion is controlled by steric, not electronic factors with these substrates. β-Hydrogen elimination as occurs in the Heck reaction does not take place.

The reduction of 1,1,3-tribromo-1-fluoroalkanes with Zn and methanol gave *cis*- and *trans*-1,2-difluoroolefins (Scheme 4).[18]



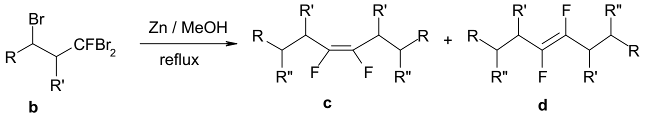
Scheme 2.



Scheme 3.

Compound **2b** on refluxing with zinc and methanol for 18 h gave *cis*-**2c** (23%) and *trans* olefin **2d** (44%). On the other hand, refluxing for 52 h gave *cis*-**2e** (21%) and *trans*-**2f** (48%). Similarly, compound **3b** on refluxing for 22 h with Zn and methanol gave *cis*-**3c** (18%) and *trans*-**3d** (36%) whilst **4b** gave *cis*-**4c** (24%) and *trans*-**4d** (43%) (Scheme 5). The structures of all the compounds were determined by ^{1}H, ^{13}C and ^{19}F NMR spectroscopy. Single crystal X-ray determinations for adducts **2c**, **2d** and **3c** also confirmed the *cis* and *trans* product stereochemistries (Figs. 1–3).[19]

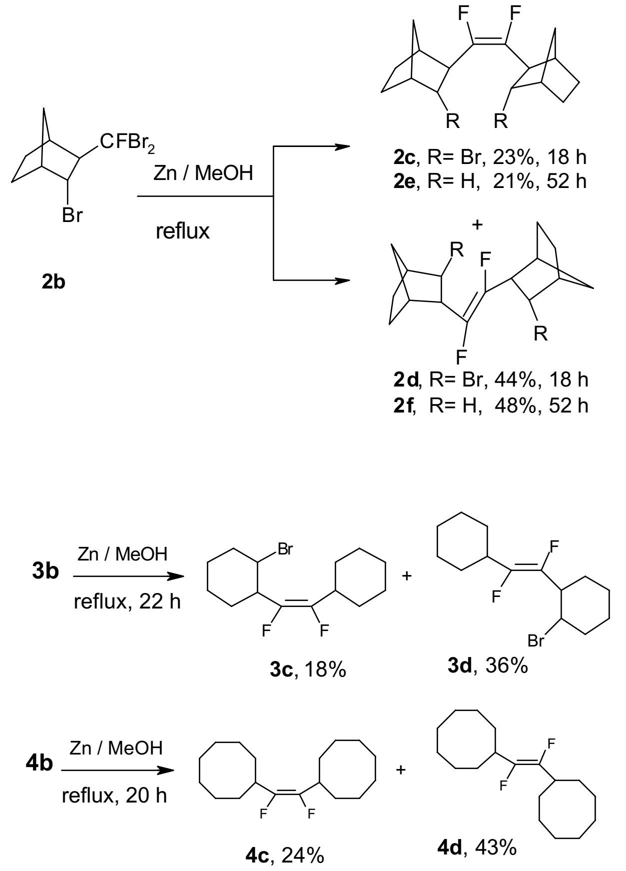
In summary, we have developed an efficient method for the introduction of tribromofluoromethane into various olefins. The products can be elaborated into more complex structures by further reactions at bromine. In addition, we have described a method for the preparation of 1,2-difluoroolefins, which could be applied in polymers and liquid crystal displays (LCD).



Substrate	Product			Time / h	Yield (%)^a	
	R	R'	R"		c	d
1b	CH$_3$(CH$_2$)$_5$	H	H	14	28^b	44^b
6b	(CH$_3$)$_2$CHCH$_2$	H	H	28	26	38
7b	C$_6$H$_5$–CH$_2$	H	H	10	28	36
10b	C$_6$H$_{11}$	H	H	9	28	37
11b	C$_2$H$_5$	C$_2$H$_5$	Br	8	—	62

^{a} Isolated yield.
^{b}Determined by ^{1}H and ^{19}F NMR.

Scheme 4.



Scheme 5.

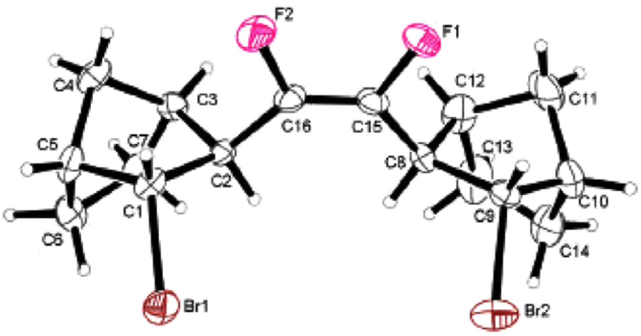


Figure 1. The ORTEP structure of *cis*-**2c**.

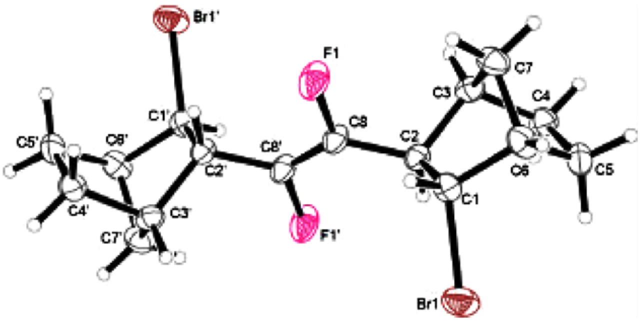


Figure 2. The ORTEP structure of *trans*-**2d**.

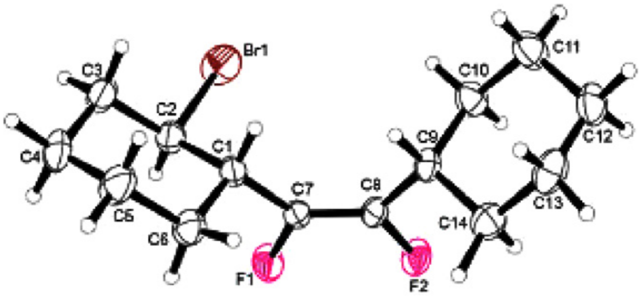


Figure 3. The ORTEP structure of *cis*-**3c**.

Acknowledgements

This work was supported by the Council of Scientific and Industrial Research (CSIR), New Delhi (Grant No. 01(1809)/02/EMR II). Authors gratefully acknowledge the X-ray facility provided by the Department of Science and Technology (DST), under the FIST programme.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.10.145.

References and notes

1. (a) Welch, J. T.; Eswarakrishnan, S. *Fluorine in Bioorganic Chemistry*; John Wiley & Sons: NY, 1990; (b) *Biomedical Frontiers of Fluorine Chemistry*; Ojima, I., McCarthy, J. R., Welch, J. T., Eds.; ACS Symposium Series 639; ACS: Washington, DC, 1996; (c) McCarthy, J. R.; Matthews, D. P.; Stemerick, D. M.; Huber, E. W.; Bey, P.; Lippert, B. J.; Snyder, R. D.; Sunkara, P. S. *J. Am. Chem. Soc.* **1991**, *113*, 7439–7440.
2. LeTourneau, M. E.; McCarthy, J. R. *Tetrahedron Lett.* **1984**, *25*, 5227–5230.
3. McDonald, I. A.; Lacoste, J. M.; Bey, P.; Wagner, J.; Palfreyman, M. G. *J. Am. Chem. Soc.* **1984**, *106*, 3354–3356.
4. McCarthy, J. R.; Matthews, D. P.; Edwards, M. L.; Stemerick, D. M.; Jarvi, E. T. *Tetrahedron Lett.* **1990**, *31*, 5449–5452.
5. (a) Zhang, Q.; Lu, L. *Tetrahedron Lett.* **2000**, *41*, 8545–8548; (b) Colmenares, L. U.; Zou, X.; Liu, J.; Asato, A. E.; Liu, R. S. H. *J. Am. Chem. Soc.* **1999**, *121*, 5803–5804.
6. (a) Hetakeyama, J.; Watanabe, J.; Harada, Y. U.S. Patent Appl. Publ. 2001010890, 2001; *Chem. Abstr.* **2001**, *135*, 144695; (b) Groh, W.; Herbrechtsmeier, P.; Heumueller, R.; Theis, J.; Wieners, G. Ger. Offen, 19901018, 1990; *Chem. Abstr.* **1991**, *114*, 144260.
7. (a) Shimizu, T.; Yokokoji, O.; Kumai, S. Jpn. Kokai Tokkyo Koho 1996, 20 pp., Patent appl. JP 08119887; *Chem. Abstr.* **1996**, *125*, 128460; (b) Yokokoji, O.; Shimizu, T.; Kumai, S. Jpn. Kokai Tokkyo Koho 1996, 14 pp., Patent appl. JP 08059525; *Chem. Abstr.* **1996**, *125*, 45736; (c) Shinya, S.; Yokokouji, O.; Miyajima, T.; Koh, H.; Machida, K. Eur. Pat. Appl. 1993, 19 pp.; EP 560382; *Chem. Abstr.* **1994**, *120*, 91031; (d) Wang, Y.; Lu, L.; Burton, D. J. *J. Org. Chem.* **2005**, *70*, 10743–10746.
8. (a) Burton, D. J.; Yang, Z. Y.; Morken, P. A. *Tetrahedron* **1994**, *50*, 2993–3063; (b) Kuroboshi, M.; Yamada, N.; Takebe, Y.; Hiyama, T. *Tetrahedron Lett.* **1995**, *36*, 6271–6274; (c) Shimizu, M.; Takebe, Y.; Kuroboshi, M.; Hiyama, T. *Tetrahedron Lett.* **1996**, *37*, 7387–7390.
9. (a) Liu, J.-T.; Sui, G.-D.; Chen, G.; Huang, W.-Y. *J. Fluorine Chem.* **1999**, *93*, 49–51; (b) Dmowsski, W.; Ignatowska, J. *J. Fluorine Chem.* **2003**, *123*, 37–42; (c) Dmowsski, W.; Ignatowska, J.; Piasecka-Maciejewska, K. *J. Fluorine Chem.* **2004**, *125*, 1147–1151.
10. (a) Dolbier, W. R., Jr.; Burkholder, C. R. *J. Org. Chem.* **1990**, *55*, 589–594; (b) Dolbier, W. R., Jr.; Wojtowicz, H.; Burkholder, C. R. *J. Org. Chem.* **1990**, *55*, 5420–5422; (c) Burton, D. J.; Kehoe, L. J. *Tetrahedron Lett.* **1966**, 5163–5167; (d) Wu, S.-H.; Liu, W.-Z.; Jiang, X.-K. *J. Org. Chem.* **1994**, *59*, 854–857.
11. Saikia, A. K.; Tsuboi, S. *J. Org. Chem.* **2001**, *66*, 643–647.
12. (a) Tsuji, J. *Palladium Reagents and Catalysts*; John Wiley & Sons: UK, 2004; pp 105–176; (b) Tsuji, J.; Sato, K.; Nagashima, H. *Chem. Lett.* **1981**, 1169–1170.
13. Klabunde, K.; Low, J. Y. F. *J. Am. Chem. Soc.* **1974**, *96*, 7674–7680.
14. Bosco, J. W. J.; Saikia, A. K. *Chem. Commun.* **2004**, 1116–1117.
15. A mixture of 1-octene (100 mg, 0.89 mmol) and CFBr$_3$ (300 mg, 1.12 mmol) was added to a reaction flask containing Pd(OAc)$_2$ (4.00 mg, 0.018 mmol), Ph$_3$P (9.35 mg, 0.036 mmol) and K$_2$CO$_3$ (246 mg, 1.78 mmol) in distilled and degassed toluene (2 ml). The reaction mixture was heated with stirring at 80 °C (oil bath) under an N$_2$ atmosphere. The progress of the reaction was monitored by TLC using hexane as the eluent. After completion, the reaction mixture was neutralized with 5% HCl. The product was extracted with ethyl acetate and the organic fraction washed with brine and water. The organic layer was dried (Na$_2$SO$_4$) and evaporated to leave the crude product which was purified by short column chromatography over silica gel using hexane as the eluent to give 269 mg (79%) of the pure product (Table 1, entry 1). ^{1}H NMR (400 MHz, CDCl$_3$): δ 0.88 (t, $J = 6.8$ Hz, 3H, –CH$_3$), 1.25–1.38 (m, 6H, 3–CH$_2$–), 1.46–1.59 (m, 2H, –CH$_2$–), 1.85–1.93 (m, 2H, –CH$_2$–), 3.27–3.47 (m, 2H, –CH$_2$–), 4.20 (m, 1H, –CH–); ^{13}C NMR (100 MHz, CDCl$_3$): δ 14.21, 22.70, 27.21, 28.53, 31.70, 38.61, 49.72, 60.52 (d, $J = 17.6$ Hz), 93.2 (d, $J = 319.6$ Hz); ^{19}F NMR (376 MHz, CDCl$_3$): δ 114.97 (t, $J = 17.29$ Hz, 1F, –CFBr$_2$); IR (neat): 2927, 2860, 1459, 1122, 997, 766 cm^{-1}.
16. The configurations of the cis–trans isomers were determined from the ^{1}H NMR coupling constants. Compound **13b** has a vicinal coupling constant of 6.8 Hz (cis), whereas compound **13c** shows a 10.8 Hz (trans) coupling for the same protons.
17. The ratio was determined by 400 MHz ^{1}H NMR.
18. A mixture of **2b** (100 mg, 0.27 mmol) and powdered zinc (27 mg, 0.41 mmol) in methanol (5 ml) was refluxed for the time specified in Scheme 4. The solid material was filtered and washed with ethyl acetate (3 × 10 ml) and the filtrate was evaporated to dryness and purified by thin layer chromatography to give the products.
19. Crystallographic data for compounds **2c**, **2d** and **3c** have been deposited with the Cambridge Crystallographic Data Centre as Supplementary publication numbers CCDC, 610506, 610505 and 610507, respectively.