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# Heck reaction with ethyl (E)- and (Z)-3-fluoropropenoate

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#### ARTICLE INFO

#### ABSTRACT

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#### 1. Introduction

The Heck reaction holds a prominent position among the palladium-catalyzed carbon–carbon bond forming reactions [1,2]. Although a vast amount of information is available for the Heck reactions with regard to substrates and reaction conditions [3], very little is known about the use of mono-fluorinated alkene substrates. In 1991 Heitz and Knebelkamp reported that palladium-catalyzed coupling of aryl iodides with 1,1-difluoroethene showed coupling accompanied mostly by loss of a fluorine atom [4]. Ichikawa reported in 2006 several intramolecular cyclizations of 1,1-difluoroalkenes with palladium catalysis to also give products with loss of a fluorine atom [5].

#### 2. Results and discussion

Earlier we reported that the Heck reaction with 3-fluorobutenone (1) occurred easily to give the Z- arylated ketone (3) without loss of fluorine [6].



In 2011 we described the preparation of the fluoropropenoates *Z*-**4** and *E*-5, along with their behavior in 3+2 cycloaddition reactions [7]. We now extend our Heck procedure to the *E*- and *Z*-3-

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http://dx.doi.org/10.1016/j.jfluchem.2016.07.009 0022-1139/© 2016 Elsevier B.V. All rights reserved. fluoropropenoates, **4** and **5**. The results of this study provide a unique result in that in each case only the Z-6 isomer is obtained. Also the fluorinated compound is very reactive. Usually fluorinated substrates are very unreactive in the Heck reaction [8].

The use of monofluoro alkene substrates in the Heck reaction is relatively unknown. The reaction

between ethyl E-3-fluoropropenoate or ethyl Z-3-fluoropropenoate with iodobenzene and palladium

acetate produces only ethyl 3-fluoropropenoate (**Z**-**6**). Some loss of fluorine occurs from the *E* isomer.

Arylation of Z-**4** proceeds readily at  $90^{\circ}$  to give substitution at the 3-position and retention of the stereochemistry. A very small amount of material found was thought to come from arylation at the 2-position (less than 1%).



Arylation of **E-5** proceeds regioselectively at the 3-position. The alkene stereochemistry is inverted in the product which again is *Z*-**6** without formation of the *E* isomer. Product **7** is formed with loss of a fluorine atom.

PhI 
$$F$$
 E-5  $Pd(OAc)_2$ ,  $Et_3N$   $Ph_3P$ ,  $DMF$   $Ph_7$   $CO_2Et$   $Ph_7$   $Ph_7$ 

Control experiments showed that neither **Z-4** nor **E-5** were interconverted during the procedure. The same results were obtained at 50 °C and 90 °C. It is possible that the catalyst system causes the isomerization. The commonly accepted mechanism for the Heck reaction requires a *syn* elimination of HPdL from the intermediates *trans*-**A** and/or -**B** shown below [8,9]. Only *cis*-**B** can give the product observed (**Z-6**) for both cases, but *trans*-**A**, not - **B** should be formed from **Z-4**. Thus the results of this Heck procedure



Short Communication



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with fluorinated substrates **E-5** and **Z-4** are unique in that only **Z-6** is observed and that the fluorinated substrate is very reactive.



#### 3. Experimental procedure

3.1. Preparations of ethyl Z-3-fluoropropenoate (Z-4) and E-3-fluoropropenoate (E-5)

The preparations of ethyl Z-3-fluoropropenoate (Z-4) and E-3-fluoropropenoate (E-5) have been reported previously [7].

#### 3.2. General procedure for the palladium (II)-catalyzed heck reaction

Iodobenzene (**2**), ester **Z**-**4** or **E**-**5**, triethylamine, palladium (II) acetate, triphenylphosphine, and dimethyl formamide were weighed into a 10 ml round-bottomed vial in the ratio 1 mol: 3 mol: 3 mol: 0.05 mol: 0.1 mol, respectively. The vial was equipped with a triangular magnetic spinning bar and sealed with a screw cap. The reaction mixture was heated for 20 h at 90 °C (oil bath temperature), allowed to cool and then extracted with diethyl ether/water (30:70). The organic layer was washed with saturated NaHCO<sub>3</sub>, saturated NaCl, and several portions of water, and dried

over anhydrous  $Na_2SO_4$ . The residue formed after evaporation of the ether was chromatographed on 200–425 mesh silica gel eluting with a *n*-hexane/ethyl acetate mixture. Unreacted starting material was obtained at higher temperatures.

#### 3.3. Analytical data for Heck reaction products

#### 3.3.1. Ethyl Z-3-fluoro-3-phenylpropenoate (Z-6). (from Z-4)

Eluted with 9:1 hexane:ethyl acetate as a yellow liquid. 48% yield. <sup>1</sup>H NMR (CDCl<sub>3</sub>, TMS)  $\delta$  1.24 (t, 3H, CH<sub>3</sub>,  $J_{HH}$  = 4 Hz), 4.10, 4.10 (q, 2H, CH<sub>2</sub>,  $J_{HH}$  = 7 Hz), 6.25 (d, H, CH,  $J_{HH}$  = 3 Hz,  $J_{HF}$  = 15 Hz), 7.19 (m, 5H, aromatic); <sup>13</sup>C NMR  $\delta$  14.6 (s, CH<sub>3</sub>), 60.8 (s, CH<sub>2</sub>), 83.5 (CH, d, J = 5 Hz), 118.4 (CF, d, J = 5 Hz), 130.4-144.5 aromatic, 166.5 (C=O); <sup>19</sup>F NMR (CFCl<sub>3</sub>)  $\delta$  -70.1.

From E-5. Use of the E isomer in the procedure gave Z-6.

Ethyl cinnamate (**7**) was identified by comparison to an authentic sample prepared by the Heck procedure.

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