



Palladium-catalyzed cyclocarbonylation of (*Z*)-3-iodo-3-trifluoromethyl allylic alcohols producing 3-trifluoromethyl-2(5*H*)-furanones (γ -lactones)

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Received 9 April 2001; revised 20 June 2001; accepted 28 June 2001

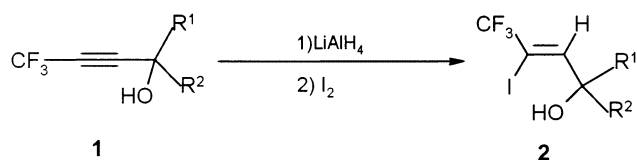
Abstract—The reaction of (*Z*)-3-iodo-3-trifluoromethyl allylic alcohols **2** and CO in the presence of catalytic Pd(PPh₃)₄ afforded 3-trifluoromethyl-2(5*H*)-furanones (γ -lactones) **3**. © 2001 Elsevier Science Ltd. All rights reserved.

2(5*H*)-Furanones (γ -lactones) have been of interest for many years due to their biological activity.¹ Transition metal catalyzed cyclocarbonylation reactions represent a useful method for the preparation of a variety of γ -lactones.² Considerable attention has been given to trifluoromethyl-containing organic compounds as agrochemical and pharmaceutical agents due to their unique properties arising from altered electron density, acidity, and lipophilicity.³ Accordingly, the development of newer methods for the synthesis of trifluoromethyl-containing organic compounds continues to be an important area of research in agricultural, medicinal, and organic chemistry.⁴ Although the preparation of α -trifluoromethyl- γ -lactones⁵ using different methodologies are well documented, to the best of our knowledge, there is only one example of the synthesis of a perfluoroalkyl-containing γ -lactone in low yield through a palladium-catalyzed cyclocarbonylation reaction in which the initial stage of the reaction (the carbo-metallation step) may involve radical character.⁶ We report herein a successful cyclocarbonylation of trifluoromethyl-containing allyl alcohols **2** to form 3-trifluoromethyl-2(5*H*)-furanones (γ -lactones) **3**.

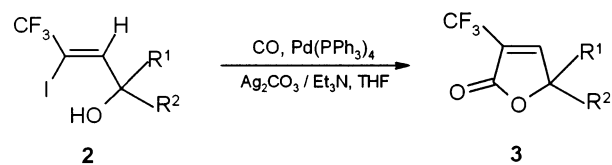
(*Z*)-3-Iodo-3-trifluoromethyl allylic alcohols **2** were prepared in high yields by treatment of trifluoromethyl

propargylic alcohols **1** with lithium aluminium hydride followed by iodide (Scheme 1).⁷

The transition metal catalyzed carbonylation of organic halides is one of the most versatile and convenient processes for the introduction of a carbonyl group into a molecule.⁸ However, there are only a few examples of carbonylation of fluorinated organic halides.⁹ (*Z*)-3-Iodo-3-trifluoromethyl allylic alcohols **2** are different from the usual vinylic (aryl) halides (triflates) for palladium-catalyzed carbonylation reactions. Once the α -trifluoromethylvinylpalladium(II) intermediate is formed, fluorine may easily leave as fluoride anion because of the β -electron effect. Based on these considerations, the reaction conditions for the cyclocarbonylation of **2** were explored using (*Z*)-3-iodo-4,4,4-trifluoro-1-cyclohexyl-2-buten-1-ol **2a** as a model substrate (Scheme 2). Initially, the typical



Scheme 1.



Scheme 2.

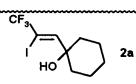
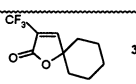
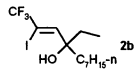
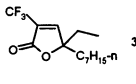
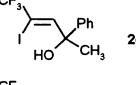
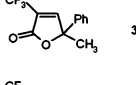
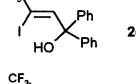
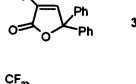
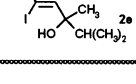
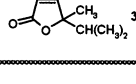
Keywords: cyclocarbonylation; γ -lactones; trifluoromethyl-containing compounds.

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Table 1. Cyclocarbonylation optimization using **2a**

Entry	Catalyst (5 mol%)	Base	Pressure (atm)	Time (h)	Isolated yield of 3a (%)
1	Pd(PPh ₃) ₂ Cl ₂	Et ₃ N (2.0 equiv.)	1	48	NR
2	Pd(PPh ₃) ₄	Et ₃ N (2.0 equiv.)	1	48	31
3	Pd(PPh ₃) ₄	Ag ₂ CO ₃ (2.0 equiv.)	1	48	75
4	Pd(PPh ₃) ₄	Ag ₂ CO ₃ (2.0 equiv.)	10	24	80
5	Pd(PPh ₃) ₄	Ag ₂ CO ₃ (0.1 equiv.) and Et ₃ N (2.0 equiv.)	10	24	82

Table 2. Palladium-catalyzed cyclocarbonylation of tertiary allylic alcohols **2** to 3-trifluoromethyl-2(5*H*)-furanones **3**

Entry	Alcohol 2	2(5 <i>H</i>)-Furanones 3	Isolated Yield (%)
1			82
2			81
3			58
4			80
5			71

reaction conditions for the cyclocarbonylation of iodoallyl alcohols were tested.¹⁰ Treatment of **2a** with 1 atm of CO in THF in the presence of Pd(PPh₃)₂Cl₂ (5 mol%) and triethylamine (2.0 equiv.) at room temperature for 48 h resulted in no reaction (Table 1, entry 1). When Pd(PPh₃)₂Cl₂ was replaced by Pd(PPh₃)₄ under the conditions of entry 1, **2a** was cyclocarbonylated to produce 3-trifluoromethyl-2(5*H*)-furanone **3a** in 31% yield along with unreacted **2a** (Table 1, entry 2). When the reaction temperature was increased to 80°C, ¹⁹F NMR monitoring of the reaction mixture revealed that the trifluoromethyl group had disappeared. To improve the yield of the cyclocarbonylation, the use of different bases was examined. We were pleased to find that **3a** was isolated in 75% yield with little unreacted **2a** using Ag₂CO₃ as base instead of triethylamine under the conditions of entry 3 (Table 1). Increasing the CO pressure to 10 atm under the conditions of entry 4 resulted in complete conversion of **2a** in 24 h (Table 1, entry 4). Furthermore, the use 0.1 equiv. of Ag₂CO₃ and 2.0 equiv. of triethylamine as co-bases under the conditions of entry 5 led to complete conversion of **2a** and **3a** in 82% yield (Table 1). Obviously, from an economical and an efficiency point of view, the reaction conditions described in entry 5 were chosen as optimized conditions for the cyclocarbonylation of **2a**.

Under the optimized conditions established for **2a** (10 atm of CO, 0.1 equiv. of Ag₂CO₃, 2.0 equiv. Et₃N, and 5 mol% Pd(PPh₃)₄ in THF at room temperature), the cyclocarbonylation of various (*Z*)-3-iodo-3-trifluoromethyl allylic alcohols **2** was investigated. The results are summarized in Scheme 2 and Table 2. Ter-

tiary allylic alcohols can be converted into the corresponding 3-trifluoromethyl-2(5*H*)-furanones, but secondary allylic alcohols were unreactive under the typical cyclocarbonylation conditions.

In conclusion, we have developed a practical route to 3-trifluoromethyl-2(5*H*)-furanones through the palladium-catalyzed cyclocarbonylation of (*Z*)-3-iodo-3-trifluoromethyl allylic alcohols.

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