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Synthesis of substituted cinnamic acids and cinnamonitriles via palladium catalyzed coupling reactions of aryl halides with acrylic acid and acrylonitrile in aqueous media

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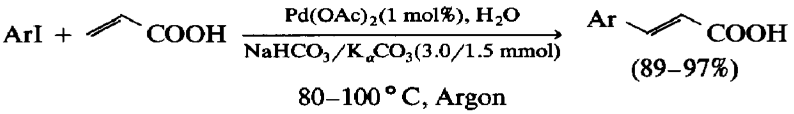
Abstract

The palladium-catalysed coupling reactions of aryl halides with acrylic acid and acrylonitrile in the presence of a base ($NaHCO_3$ or K_2CO_3) in water provide a novel and efficient and very simple method for the synthesis of substituted cinnamic acids and cinnamonitriles in high yields. $NaHCO_3$ or K_2CO_3 effectively acts as a base in the reaction at elevated temperature (80–100 ° C). The reaction can be carried out with higher velocity and at low temperature (50–60 ° C), using CH_3COOK as a base.

Introduction

The palladium catalysed coupling reactions of aryl halides with olefins (Heck reaction) have been studied extensively because of their wide application in organic synthesis [1–3]. The various types of olefins such as allylic alcohols [4–6]. α-β unsaturated aldehydes or ketones [7] have been used for the coupling reactions in which high yields of the arylated products are obtained. Thus, the palladium-catalyzed arylation of unsaturated compounds has proved to be useful reaction for the synthesis of a wide variety of olefinic compounds. In an earlier communication [8] we have reported the synthesis of substituted cinnamic acids via Heck reactions in aqueous media.

In the present communication we are dealing with the palladium catalyzed arylation of acrylic acid and acrylonitrile with aryl halides in aqueous media for the synthesis of substituted cinnamic acids and cinnamonitriles in high yields. We have examined the arylation of acrylic acid and acrylonitrile with *o*-, *m*-, *p*-iodobenzoic acid and *p*-iodophenol. The reaction proceeds selectively in the presence of a base ($NaHCO_3/K_2CO_3$) at elevated temperature to give the arylated product in high yields and practically without by-product formation (reactions 1 and 2).



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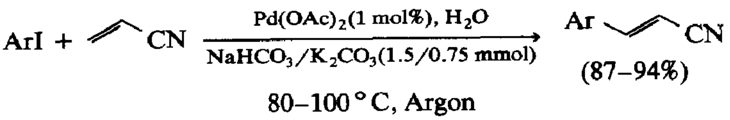
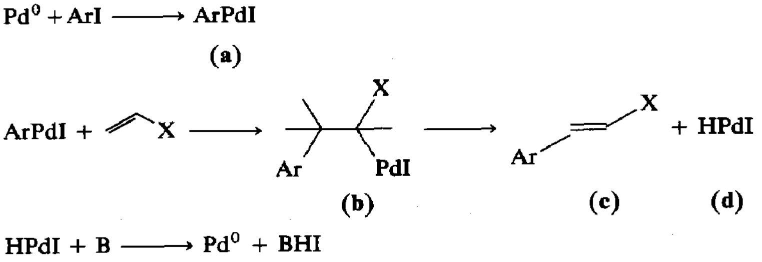


(2)

Ar = o-$HOOCC_6H_4$, m-$HOOCC_6H_4$, p-$HOOCC_6H_4$, p-HOC_6H_4

Results and discussion

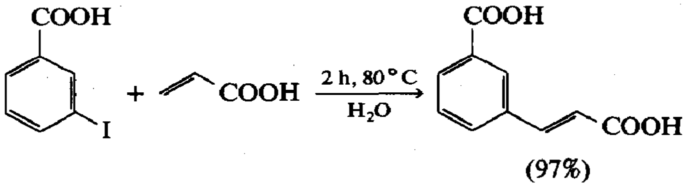
The catalytic cycle of the reaction is depicted in Scheme 1 (X = COOH, CN).



Scheme I

The palladium(0) complex is generated in situ from the initial palladium complex under the reaction conditions. ArI reacts with the palladium(0) complex under oxidative addition to give the arylpalladium complex (**a**). The arylpalladium complex (**a**) further adds to the olefin to give an intermediate alkylpalladium complex (**b**) which undergoes elimination of hydridopalladium halide (**d**) with the formation of an unsaturated compound (**c**). The hydridopalladium halide (**d**) reacts with the base and results in the recovery of the palladium(0) complex.

The selectivity and the rates of reactions 1 and 2 depend upon the nature of the substituent in aryl ring of ArI. For example, the reaction of *m*-iodobenzoic acid and acrylic acid proceeds smoothly and selectively in two hours at 80 ° C to give the product (reaction 3; Table 1, entry 1) in 97% yield, on the other hand the reaction of *o*-iodobenzoic acid and acrylic acid proceeds at 100 ° C in three hours to give the product in 89% yield (reaction 4, Table 1, entry 4). The requirement of rather rigorous conditions in the case of *o*-iodobenzoic acid may be due to steric hindrance.



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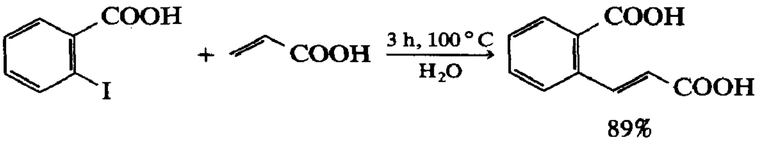
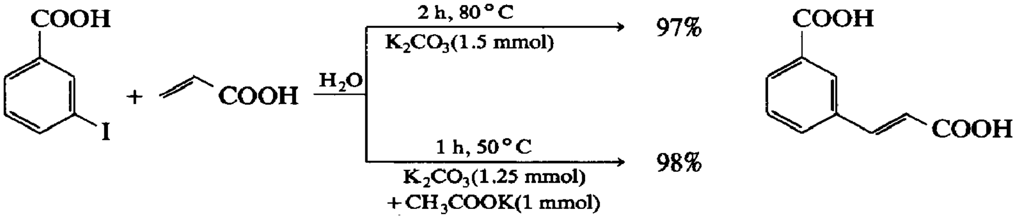


(4)

Sodium bicarbonate or potassium carbonate is an effective base in the reactions 1 and 2 because it forms water-soluble salts of the aryl iodides and acrylic acid and thus facilitates reaction in aqueous media.

It is of interest, from a synthetic viewpoint, to study the effect of potassium acetate on the selectivity and the rate of the reactions 1 and 2. To study this aspect we chose the reactions of *m*- and *o*-iodobenzoic acid with acrylic acid and acrylonitrile respectively (reactions 5 and 6; Table 1, entries 1, 2, 8 and 9). We found that in the presence of potassium acetate the reactions take place at low temperature and at higher rates.



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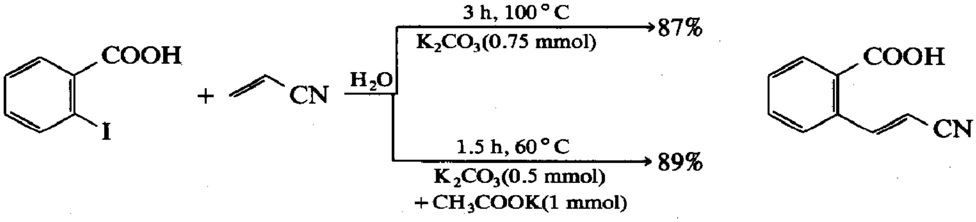
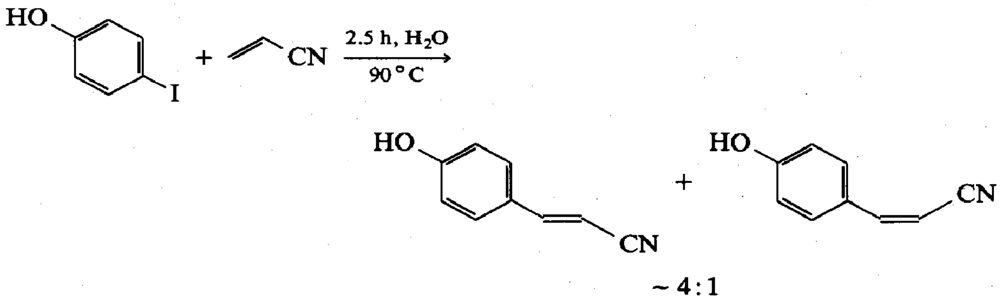


(6)

We compared the results obtained in the reactions of ArI with acrylic acid and acrylonitrile and found that in the case of acrylic acid only *trans*-isomer was formed (Table 1, entries 1–5), whereas in the case of acrylonitrile a mixture of *cis*- and *trans*-isomers was obtained (Table 1, entries 6–9). For example, the reaction of *p*-HOC_6H_4I and acrylonitrile gave the product containing *trans*- and *cis*-isomers (~ 4 : 1) (reaction 7; Table 1, entry 7). This phenomenon may be connected with the size of the X group in the olefin (CH_2=CH–X, X = COOH and CN). The intermediates A and B formed in the reaction are shown in Fig. 1 (the stability of A > B). In the case of acrylic acid, because of the bulky COOH group, strong interactions between the COOH and Ar groups take place and so elimination from the intermediate A occurs to give the *trans*-isomer only. On the other hand, in the case of acrylonitrile, because of less bulky CN group, less strong interactions (as compared to COOH



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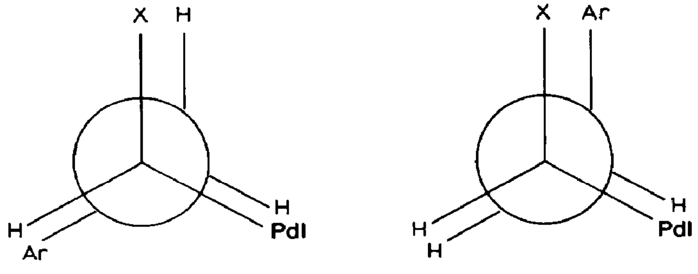

(A) (B)

Fig. 1.

group) between CN and AR groups take place and so elimination from both the intermediates **A** and **B** occurs to give the product containing *trans*- and *cis*-isomers (4 : 1) [9]

Experimental

The palladium complex. Pd(OAc)$_2$, and aryl iodides were prepared by standard procedures. Analytical grade NaHCO$_3$, K$_2$CO$_3$ and CH$_3$COOK were used. Acrylic acid, acrylonitrile, and water were distilled before use. The isolated products were identified from their elemental analyses, and by IR and NMR spectroscopy. The ratio of *trans* : *cis*-isomers (for the substituted cinnamonitriles) was determined by NMR spectroscopy.

Synthesis of m-HOOCC$_6$H$_4$CH=CHCOOH

(a) With m-iodobenzoic acid. A slurry of 2 ml of water, 0.207 g (1.50 mmol) of K$_2$CO$_3$, 0.103 ml (1.5 mmol) of acrylic acid, 0.248 g (1 mmol) of *m*-iodobenzoic acid, and 0.00224 g (0.01 mmol) of Pd(OAc)$_2$, a 5-ml round bottom flask, was stirred vigorously at 80 °C under argon. The mixture was tested by TLC to check

Table 1

Palladium catalyzed reactions of CH$_2$=CH–X with ArI [H$_2$O, NaHCO$_3$/K$_2$CO$_3$, Pd(OAc)$_2$, Argon]

Entry	Ar	X	Reaction temperature (°C)	Reaction time (h)	Isolated yield (%)
1	*m*-HOOCC$_6$H$_4$	COOH	80	2	97
2 [a]	*m*-HOOCC$_6$H$_4$	COOH	50	1	98
3	*p*-HOOCC$_6$H$_4$	COOH	80	2	90
4	*o*-HOOCC$_6$H$_4$	COOH	100	3	89
5	*p*-HOC$_6$H$_4$	COOH	80	2	94
6	*m*-HOOCC$_6$h$_4$	CN	90	2.5	90 [b]
7	*p*-HOC$_6$H$_4$	CN	90	2.5	94 [b]
8	*o*-HOOCC$_6$H$_4$	CN	100	3	87 [b]
9 [a]	*o*-HOOCC$_6$H$_4$	CN	60	1.5	89 [b]

[a] The reaction was carried out in the presence of CH$_3$COOK. [b] Contains a mixture of *cis*- and *trans*-isomers (1 : 4, determined by NMR spectroscopy).

for completion of the reaction (after 2 hours). The reaction mixture was cooled, filtered and the filtrate was treated with dilute HCl till it was acidic to litmus. The precipitate was filtered, washed with 3 × 5 ml of water, recrystallized, and dried under vacuum to give 0.186 g (97% yield) of *m*-$HOOCC_6H_4CH{=}CHCOOH$, m.p. 267 °C (10).

(b) With CH_3COOK as a base. A slurry of 2 ml of water, 0.173 g (1.25 mmol) of K_2CO_3, 0.103 ml (1.5 mmol) of acrylic acid, 0.248 g (1 mmol) of *m*-iodobenzoic acid, 0.098 g (1 mmol) of CH_3COOK and 0.00224 g (0.01 mmol) of $Pd(OAc)_2$ a 5-ml round bottom flask was stirred vigorously at 50 °C under argon. The reaction was complete after one hour (checked by TLC). The reaction mixture was cooled, filtered and the filtrate was treated with dilute HCl till it was acidic to litmus. The precipitate was filtered, washed with 3 × 5 ml of water, recrystallized and dried under vacuum to give 0.188 g (98% yield) of *m*-$HOOCC_6H_4CH{=}CHCOOH$, m.p. 267 °C (10).

Synthesis of p-$HOC_6H_4CH{=}CHCN$

A slurry of 2 ml of water, 0.104 g (0.75 mmol) of K_2CO_3, 0.099 ml (1.5 mmol) of acrylonitrile, 0.220 g (1 mmol) of *p*-iodophenol, and 0.00224 g (0.01 mmol) of $Pd(OAc)_2$ a 5-ml round bottom flask was stirred vigorously at 90 °C under argon. The reaction mixture was tested by TLC to check for completion of the reaction. The reaction was complete after 2.5 hours. The reaction mixture was cooled, filtered and the filtrate was treated with dilute HCl till it was acidic to litmus. The filtrate was extracted with 6 × 5 ml of ether. The ether solutions were combined, dried over $MgSO_4$, and evaporated to give 0.136 g (94% yield) of *p*-$HOC_6H_4CH{=}CHCN$ (11).

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