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LETTERS

Deiodination of 5-iodopyrrole-2-carboxylates using sodium formate catalyzed by palladium complexes: preparation of 5-unsubstituted pyrrole-2-carboxylates

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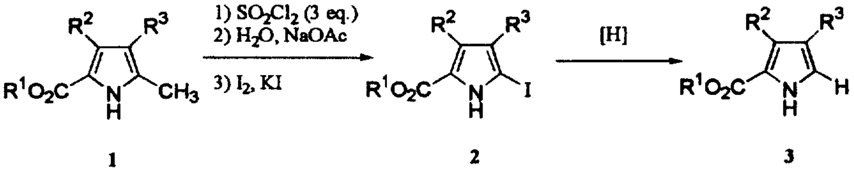
Abstract

5-Iodopyrrole-2-carboxylates are deiodinated with sodium formate in the presence of a catalytic amount of either $PdCl_2(Ph_3P)_2$ or $Pd(Ph_3P)_4$ to give the corresponding 5-unsubstituted pyrrole-2-carboxylates in good yields.

Keywords: dehalogenation; pyrrole; palladium; palladium compounds.

5-Unsubstituted pyrrole-2-carboxylates (**3**) are important precursors to the dipyrromethanes used in the stepwise synthesis of porphyrins or linear tetrapyrroles.[1] The ester group at the 2-position serves as a blocking group and is removed when necessary during the course of the porphyrin synthesis. Methods of synthesizing these pyrroles directly using isocyanoacetates and nitroalkenes have been developed in recent years.[2] However, some commonly used 5-unsubstituted pyrrole-2-carboxylates (**3**) are still prepared by the traditional method of removing the 5-methyl group from a 5-methylpyrrole-2-carboxylate (**1**) using a series of reactions:[3,4] trichlorination, hydrolysis, decarboxylative iodination, and reduction/deiodination (Scheme 1).



Scheme 1.

The final step of deiodination can be achieved by different methods. 5-Iodopyrroles bearing a *tert*-butyl ester group or an ethyl ester group are usually deiodinated using hydrogen with PtO_2[5,6] or Pd/C.[7] However, this method is not suitable for 5-iodopyrroles with a benzyl ester group because of the possible

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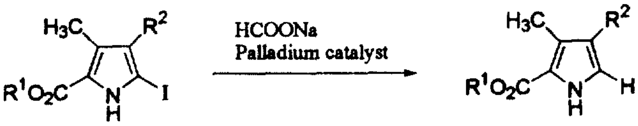
cleavage of this group under the reaction condition.[2b] Zinc dust with acetic acid can be used to achieve deiodination without the cleavage of a benzyl ester group.[4] 5-Iodopyrroles have also been deiodinated using HI/H_3PO_2 in acetic acid.[3]

It has been reported that various formates can be used to dehalogenate some aryl halides in the presence of a palladium catalyst.[8,9] However, this dehalogenation method has not been studied using the pyrrole system. Here we report an efficient procedure of deiodinating 5-iodopyrrole-2-carboxylates using sodium formate and a catalytic amount of either $PdCl_2(Ph_3P)_2$ or $Pd(Ph_3P)_4$ to give good yields of the corresponding 5-unsubstituted pyrroles (Scheme 2). Unlike the previous methods, this method is compatible with all the common ester groups (methyl, ethyl, *tert*-butyl, or benzyl) found in pyrroles that are used in porphyrin synthesis.



4a: R^1 = $-CH_2Ph$, R^2 = $-CH_2CH_2CO_2CH_3$
4b: R^1 = $-CH_2CH_3$, R^2 = $-CH_2CH_3$
4c: R^1 = $-C(CH_3)_3$, R^2 = $-CH_3$

5a: R^1 = $-CH_2Ph$, R^2 = $-CH_2CH_2CO_2CH_3$
5b: R^1 = $-CH_2CH_3$, R^2 = $-CH_2CH_3$
5c: R^1 = $-C(CH_3)_3$, R^2 = $-CH_3$

Scheme 2.

5-Iodopyrroles **4a**,[10] **4b**,[3] and **4c**[11] were smoothly deiodinated using sodium formate and a catalytic amount of either $PdCl_2(Ph_3P)_2$ or $Pd(Ph_3P)_4$ in DMF at 110°C. The results are summarized in Table 1. The reaction is usually complete within 3 h (monitored by TLC) to give the product in yields ranging from 78 to 88%. At temperatures below 110°C, deiodination occurred either very sluggishly or not at all. When 1-butanol was used as solvent, deiodination of **4a** was complete in 4 h at 110°C, but transesterification of the methyl ester with 1-butanol also occurred. In the absence of sodium formate (with palladium catalyst only), the reaction did not proceed. However, rather interestingly, when triethylamine was used in place of sodium formate, deiodination did occur to some extent, and the reason for this is still unclear. Ammonium formate was also used in this study, but the product yields were inconsistent among various trials.

A typical procedure for the deiodination is as follows: Benzyl 5-iodo-4-(2-methoxycarbonyethyl)-3-methylpyrrole-2-carboxylate (**4a**) (350 mg, 0.82 mmol), $Pd(Ph_3P)_4$ (49 mg, 0.042 mmol), and sodium formate (95 mg, 1.4 mmol) were mixed in a round-bottomed flask and flushed with argon. DMF (5 mL) was added and the reaction was stirred at 110°C. The progress of the reaction was monitored by TLC. After the reaction was complete, the mixture was diluted with dichloromethane and washed with water (twice). The organic layer was dried over anhydrous Na_2SO_4. The resulting crude product (a brown oil) was purified by column chromatography (silica gel, 20:80% ethyl acetate:hexane) to give the product (**5a**) as a light tan oil (221 mg) –88% yield.

In summary, 5-iodopyrrole-2-carboxylates can be smoothly deiodinated using sodium formate with a catalytic amount of either $PdCl_2(Ph_3P)_2$ or $Pd(Ph_3P)_4$ to give the corresponding 5-unsubstituted pyrrole-2-carboxylates, useful precursors in porphyrin synthesis. This method provides an alternative procedure to deiodinate 5-iodopyrroles and is compatible with most ester groups. More importantly, because benzyl esters are not cleaved in the reaction, this procedure is particularly useful for iodopyrroles bearing a benzyl ester (such as **4a**).

Table 1
Deiodination of 5-iodopyrrole-2-carboxylates using sodium formate

Pyrrole	**Catalyst**	**Solvent**	**Temperature**	**Time**	**Product**	**Isolated Yield**
4a	A	THF	reflux	4.5 h	**5a**[3]	0%
4a	B	DMF	100 °C	20 h	**5a**	0%[a]
4a	A	DMF	60 °C	4 h	**5a**	0%
4a	A	DMF	110 °C	3 h	**5a**	78%
4a	B	DMF	110 °C	5 h	**5a**	88%
4a	C	DMF	110 °C	2.5 h	**5a**	0%
4b	A	DMF	110 °C	1 h	**5b**[3]	80%
4b	B	DMF	110 °C	1.5 h	**5b**	82%
4c	A	DMF	110 °C	1 h	**5c**[11]	87%

[a] Sodium formate was not used in this reaction
A = $PdCl_2(Ph_3P)_2$
B = $Pd(Ph_3P)_4$
C = $Pd(OAc)_2$
THF = tetrahydrofuran
DMF = *N,N*-dimethylformamide

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