Tetrahedron Letters 53 (2012) 3798–3801

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Simultaneous dehalogenation and hydrogenation reduction of halogen-heteroaromatic aldehydes

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ARTICLE INFO

Article history:
Received 7 March 2012
Revised 3 May 2012
Accepted 11 May 2012
Available online 17 May 2012

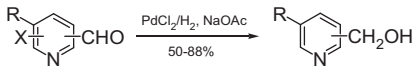
Keywords:
Halogen-heteroaromatic aldehydes
Palladium catalysts
Hydrogen
Dehalogenation
Hydrogenation

ABSTRACT

Treatment of halogen-heteroaromatic aldehydes with catalytic amount of $PdCl_2$ under atmosphere pressure of hydrogen in base medium (sodium acetate) leads to the corresponding dehalogenated primary alcohols. The reaction system was especially effective for the heteroaromatic compounds bearing aldehyde groups and halides (bromo- or chloro-functions).

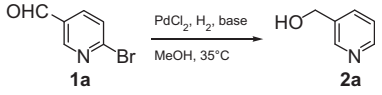
Hydrodehalogenation of aryl halides has been recognized as an important chemical transformation in organic synthesis as well as in the industrial applications.[1] Bromo- or chloro-substituents often severed as excellent blocking groups on aromatic rings.[2] Consequently, a wide variety of hydrodehalogenation reaction systems have been reported to perform this transformation. Among these catalytic systems, the reactions were usually performed with transition metal catalysts (e.g., Ni, Pd) and hydrogen sources (e.g., polymethylhydrosiloxane, H_2, hydrazine).[3,4] However, there were few reports on hydrodehalogenation of heteroaromatic halides due to the proximity of a coordinating heteroatom to the metal center.[5,6] What is more, there were no reports on simultaneous hydrogenation and dehalogenation of halogen-heteroaromatic aldehydes.

When initial hydrodehalogenation of 6-bromonicotinaldehyde was conducted, dehalogenation and hydrogenation of aldehyde to primary alcohol happened simultaneously using catalytic amount of $PdCl_2$ at room temperature under atmospheric pressure of hydrogen in base medium. According to the literature, most hydrogenations of heteroaromatic aldehydes require vast amounts of catalyst, high temperature and/or, high hydrogen pressure.[7] Herein, we wish to develop a general procedure for the $PdCl_2$-catalyzed simultaneous dehalogenation and hydrogenation of halogen-heteroaromatic aldehydes that operated under mild conditions. In addition, this method could be applied to a variety of halogen-heteroaromatic aldehydes (Scheme 1).



Scheme 1. Dehalogenation and hydrogenation of halogen-heteroaromatic aldehydes.

Table 1
Optimization of reaction conditions[a]



1a 2a

Entry	Cat. (mol %)	Solvent	Base	Yield[b] (%)
1	2	MeOH	NaOAc	42
2	5	MeOH	NaOAc	78
3	10	MeOH	NaOAc	79
4	5	MeOH	DBU	75
5	5	MeOH	Et_3N	53
6	5	MeOH	TMEDA	15
7	5	MeOH	K_2CO_3	Trace
8	5	MeOH	^tBuOK	Trace
9	5	MeOH	None	Trace
10	5	^iPrOH	NaOAc	34
11	5	Dioxane	NaOAc	7.5

[a] Reaction conditions: 5 mmol of **1a** in given solvent (30 mL), 10 mmol of base, 2–10 mol % $PdCl_2$, H_2 (1 atm), 4 h, 35 °C.
[b] Isolated yield.

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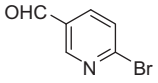
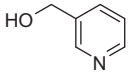
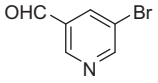
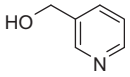
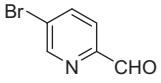
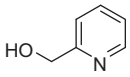
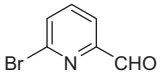
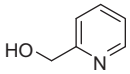
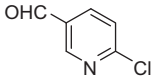
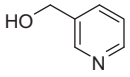
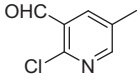
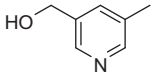
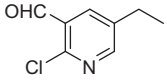
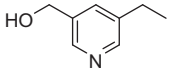
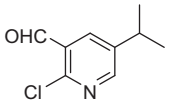
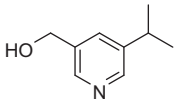
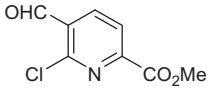
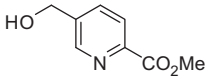
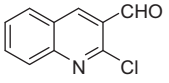
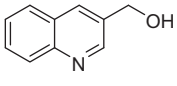
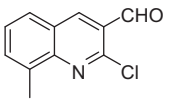
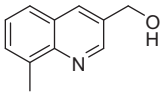
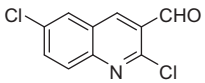
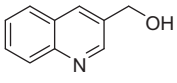
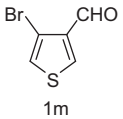
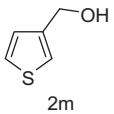
http://dx.doi.org/10.1016/j.tetlet.2012.05.054

A series of reactions were undertaken to test the effect of catalyst loading amount, bases, and solvents. A preliminary survey of catalytic efficiency with different loadings of catalyst was performed on the model reaction involving 6-bromonicotinaldehyde as the substrate, sodium acetate as the base, and methanol as the solvent under an atmospheric pressure of hydrogen.[8] As shown in

Table 2
One-pot dehalogenation and hydrogenation of halogen-heteroaromatic aldehydes[a]

Entry	Reactant	Product	Cat. (mol %)	Time (h)	Yield[b] (%)
1	 1a	 2a	5	4	78
2	 1b	 2a	5	2	83
3	 1c	 2c	5	4	83
4	 1d	 2c	5	2	0
5	 1e	 2a	5	2	88
6	 1f	 2f	5	2	76
7	 1g	 2g	5	3	87
8	 1h	 2h	5	2	85
9	 1i	 2i	5	3	88
10	 1j	 2j	10	3	84
11	 1K	 2k	10	3	61
12	 1l	 2j	10	2	86
13	 1m	 2m	20	12	50

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