Tetrahedron Letters 50 (2009) 2925–2928

Contents lists available at ScienceDirect

Tetrahedron Letters

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

Solvent-free allylation and benzylation of aldimines mediated by zinc powder

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ARTICLE INFO

Article history:
Received 4 November 2008
Revised 26 March 2009
Accepted 27 March 2009
Available online 1 April 2009

ABSTRACT

A rapid and efficient procedure for allylation and benzylation of aldimines mediated by zinc powder under solvent-free conditions is described. The procedure is operationally simple, higher regioselective, and gives good to excellent yields.

Allylation and benzylation of imines are an established route to homoallylic and homobenzylic amines, which are fundamental building blocks for many biologically active compounds and the synthesis of many nitrogen containing natural products.[1–3] The reactions are generally carried out by addition of organometallic reagents to imines in the presence of acid catalysts in anhydrous organic solvents. Acid catalysts include $TiCl_4$, $BF_3.OEt_2$, $PdCl_2(PPh_3)_2$, $Pd_2(dba)_3$, or $PtCl_2(PPh_3)_2$.[1a,b,4] However, many of these reagents are expensive, hygroscopic, and difficult to handle. Therefore current investigation has focused on developing more benign protocols for the allylation of aldimines.[5] Solvent-free synthesis of homoallylic amines has also been considered.[6] However, the previous solvent-free method has certain drawbacks such as requirement of expensive Ga metal, supersonic irradiation with long reaction time, or unsatisfactory yields (especially with α,β-unsaturated and the –OH substituted imines). In this Letter, we report the reactions of allyllation and benzylation of aldimines mediated by zinc powder under solvent-free conditions. Allyl bromide and benzyl bromide can react with aryl aldimines without other assistance or any catalysts, and the reaction is completed within 20–30 min.[8]

Also, the reactions of organozinc reagents always require strict reaction conditions such as N_2 atmosphere, anhydrous solvent, and low temperature. However, our present route proceeds well in atmosphere at room temperature. The yields are high and the reaction time is very short.

Imines **1** listed in Table 1 were prepared by mixing various aldehydes with aniline in the presence of a catalytic amount of toluene-4-sulfonic acid at room temperature.[6] The furfuraldehyde imines (entries 8 and 9) were produced by grinding together furfuraldehyde with aniline with a mortar in an ice-bath.

We studied the reactions of allyl bromide and imines mediated by zinc powder under solvent-free conditions.[8] The range of different types of aryl aldimines studied in this reaction is summarized in Table 1. Imines containing both electron donating and electron-withdrawing groups in the aromatic rings proceeded smoothly. The corresponding homoallylic secondary amines were obtained in yields ranging from 76% to 94%. Other solventless methods[6] have been found to be unsuitable for the α,β-unsaturated and the –OH substituted imines. However, our approach only proceeded with 1,2-additions for α,β-unsaturated, and compatible with the –OH substituted imines, and the yields were high (Table 1, entries 5–7 and 10).

Compared to the extensive studies on the allylation of imines, the benzylation of imines has received much less scrutiny.[7] We report herein benzylation of imines under solvent-free conditions mediated by zinc powder. The results are listed in Table 2. Aromatic and hetoroaromatic imines gave the products in high yields (Table 2, entries 1–5, 7 and 8), and α,β-unsaturated imine only proceeded with 1,2-addition (Table 2, entry 6), while imines derived from hydroxyl substituted aldehydes did not give the desired product.

In conclusion, we have developed a new and simple procedure for the allylation and benzylation of aryl aldimines mediated by zinc powder under solvent-free and catalyst-free conditions at room temperature. The reaction here has the following advantages: mild conditions, short reaction time, environmentally benign procedure, and high yield.

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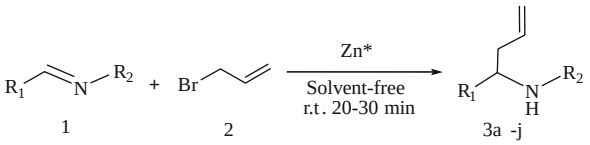
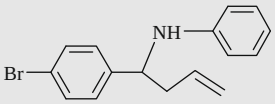
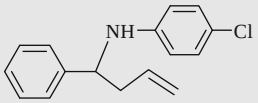
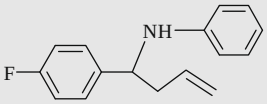
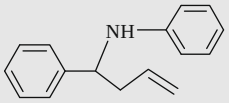
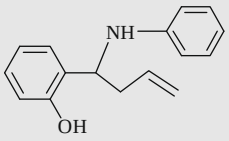
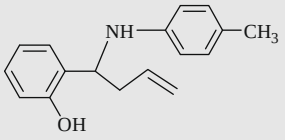
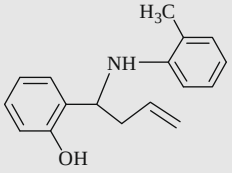
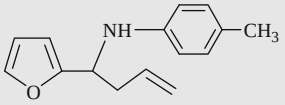
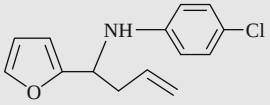
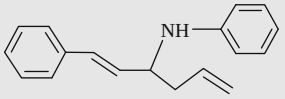
0040-4039/$ - see front matter © 2009 Published by Elsevier Ltd.
doi:10.1016/j.tetlet.2009.03.184

Table 1
Zinc powder mediated allylation of imines under solvent-free conditions[a]

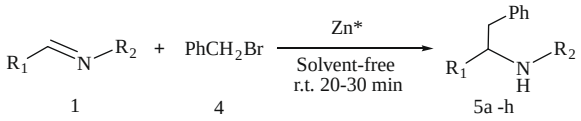


1 2 3a -j

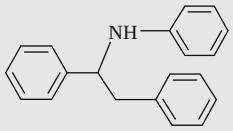
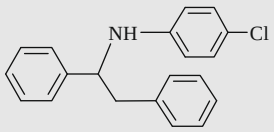
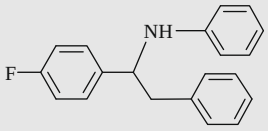
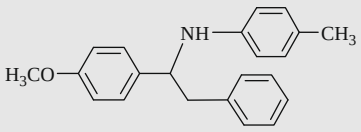
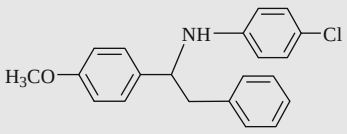
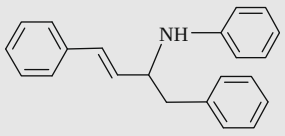
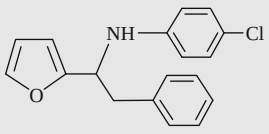
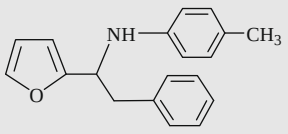
Entry	R_1	R_2	Product[b]		Yield[c] (%)
1	*p*-Br–C_6H_4	C_6H_5		**3a**	86
2	C_6H_5	*p*-Cl–C_6H_4		**3b**	93
3	*p*-F–C_6H_4	C_6H_5		**3c**	94
4	C_6H_5	C_6H_5		**3d**	91
5	*o*-OH–C_6H_4	C_6H_5		**3e**	88
6	*o*-OH–C_6H_4	*p*-CH_3–C_6H_4		**3f**	76
7	*o*-OH–C_6H_4	*o*-CH_3–C_6H_4		**3g**	82
8	2-Furyl	*p*-CH_3–C_6H_4		**3h**	85
9	2-Furyl	*p*-Cl–C_6H_4		**3i**	92
10	C_6H_5–CH=CH	C_6H_5		**3j**	88

[a] Reaction condition: activated zinc powder (6 mmol), imines (4 mmol), and allyl bromide (5 mmol) at room temperature for 20–30 min.
[b] All products were characterized by IR, ^{1}H NMR, ^{13}C NMR, and MS.
[c] Isolated yield.

Table 2
Zinc powder mediated benzylation of imines under solvent-free conditions[a]



1 4 5a -h

Entry	R_1	R_2	Product[b]		Yield[c] (%)
1	C_6H_5	C_6H_5		**5a**	87
2	C_6H_5	*p*-Cl–C_6H_4		**5b**	89
3	*p*-F–C_6H_4	C_6H_5		**5c**	83
4	*p*-CH_3O–C_6H_4	*p*-CH_3–C_6H_4		**5d**	94
5	*p*-CH_3O–C_6H_4	*p*-Cl–C_6H_4		**5e**	91
6	C_6H_5-CH=CH	C_6H_5		**5f**	72
7	2-Furyl	*p*-Cl–C_6H_4		**5g**	70
8	2-Furyl	*p*-CH_3–C_6H_4		**5h**	83

[a] Reaction condition: activated zinc powder(6 mmol), imines (4 mmol), and benzyl bromide (5 mmol) at room temperature for 20–30 min.
[b] All products were characterized by IR, ^{1}H NMR, ^{13}C NMR, MS.
[c] Isolated yield.

Acknowledgment

This work was supported by 'Qing Lan' Talent Engineering Funds of Lanzhou Jiaotong University.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.03.184.

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8. *General experimental procedure for preparation of homobenzylamine and homoallylamine*: Activated zinc powder[9,10] (0.39 g, 6 mmol) was placed in a dried round-bottomed flask fitted with a magnetic stir bar. Then imine (4 mmol) was added immediately. After this step, allyl (or benzyl) bromide (5 mmol) was added dropwise in 2 min and then stirred for 20–30 min at room temperature. After the reaction was completed, as indicated by TLC, saturated aqueous ammonium chloride was poured into the mixture and stirred for 5 min. Ethyl ether was added to the reaction mixture and the organic layer was separated. The organic extracts were dried over anhydrous $MgSO_4$. The residue was purified by column chromatograph on silica gel using petroleum/ethyl acetate as an eluent. Typical spectral data are as follows: *2-(1-(p-toluidino)but-3-enyl)phenol* (**3f**) oil, IR (ν/cm^{-1}): 3385, 1610, 1563, 1237; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 9.89 (br s, 2H, OH + NH), 7.24–6.65 (m, 8H), 5.87–5.77 (m, 1H), 5.29–5.24 (m, 2H), 4.26 (t, J = 6.8 Hz, 1H), 2.64 (t, J = 7.6 Hz, 2H), 2.21(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.7, 144.1, 134.3 130.8, 129.7, 128.5, 127.7, 126.1, 119.9, 119.6, 117.1, 116.9, 60.4, 41.4, 20.5; EI-MS: m/z (%) = 254 (M^++1, 0.41), 253 (M^+, 1.41), 212 (100.00), 91 (33.48), 77 (21.78); *N-(1,2-diphenylethyl)benzenamine* (**5a**) oil, IR (ν/cm^{-1}): 3413, 1643, 1605, 1465; 1H NMR (400 MHz, $CDCl_3$, TMS):δ 7.34–7.01 (m, 12H), 6.63–6.59 (m, 1H), 6.45–6.43 (m, 2H), 4.57 (t, J = 5.6 Hz, 1H), 4.10 (br s, 1H), 3.14–2.97 (m, 2H), 13C NMR (100 MHz, $CDCl_3$): δ 147.2, 143.3, 137.6, 129.1, 128.9, 128.53, 128.50, 127.0, 126.6, 126.4, 117.4, 113.6, 59.1, 45.1; EI-MS: m/z (%) = 273 [M^+] (1.57), 182 (100.00), 91 (63.28), 77 (50.38).
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