Pergamon

Tetrahedron Letters 42 (2001) 1983–1985

TETRAHEDRON LETTERS

Direct conversion of aryl nitro compounds to formanilides under catalytic transfer hydrogenation conditions

T. V. Pratap and S. Baskaran*

Department of Chemistry, Indian Institute of Technology Madras, Chennai 600 036, India

Received 17 November 2000; accepted 9 January 2001

Abstract—A direct and mild route to formanilides from aromatic nitro compounds bearing different functional groups under catalytic transfer hydrogenation (CTH) conditions is described.

1. Introduction

Formanilides have been widely used in the synthesis of biologically active compounds[1] such as *N*,*N*–diaryl ureas,[2] cancer chemotherapeutic agents[3] and quinolone antibacterials.[4] They also constitute important precursors in the synthesis of fungicides and herbicides.[5] In addition, *N*-formyl compounds are found to be the constituents of fragrant flowers,[6] thus finding an application in the perfume industry. Furthermore, *N*-formyl compounds are Lewis bases, which are known to catalyze allylation[7] and hydrosilylation[8] of carbonyl compounds. Various methods have been reported for the selective reduction[9] of aryl nitro compounds to anilines as well as *N*-formylation of anilines with different formylating agents.[10] However, the direct conversion[11] of aryl nitro compounds to formanilides would be an ideal choice for this class of important compounds.

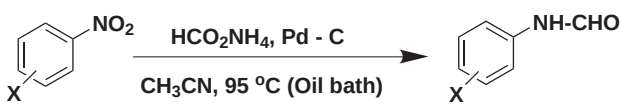
During the course of our study on the catalytic transfer hydrogenation (CTH) of aryl nitro compounds with the ammonium formate/Pd–C system,[12] we made the interesting observation that ammonium formate in an aprotic solvent like acetonitrile can function as a formylating agent[13] apart from being a source of hydrogen. Based on this observation, we have developed a novel and highly selective procedure for the direct conversion of aryl nitro compounds to formanilides in acetonitrile under CTH conditions (Scheme 1).

The selectivity and mildness of this one step reductive *N*-formylation methodology was tested with a variety of aromatic nitro compounds having different sensitive functional groups and the results are illustrated in Table 1.

The dehalogenation[14] of aromatic chloro compounds has been reported in methanol under CTH conditions, however the chloro functional group was found to be inert under our reaction conditions (entry 4). The mildness of the CTH reaction in acetonitrile was further tested with oxime and keto derivatives (entries 5, 8 and 9). Unlike the Pd/C–H_2 system, chemoselective transformation of aryl nitro compounds to the corresponding *N*-formanilides was achieved in the presence of ketone functionality as shown in Scheme 2.[15] In the case of *p*-nitro acetophenone (entry 9), in addition to the *N*-formyl product (46%), the intermediate *p*-amino acetophenone was isolated in 28% yield. The selectivity of this methodology is further exemplified in the case of entry 5, where the reducible oxime[16] functional group was found to be stable under the reaction conditions.

2. Typical experimental procedure

To a stirred solution of *p*-nitrotoluene (100 mg, 0.73 mmol) in dry acetonitrile (3 mL) was added 10% Pd/C (20 mg) followed by anhydrous ammonium formate (460 mg, 7.3 mmol). The resultant heterogeneous reaction mixture was allowed to reflux at 95°C (bath tem-



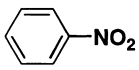
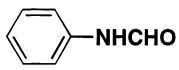
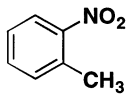
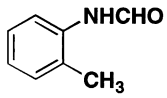
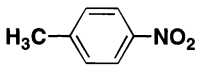
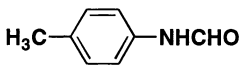
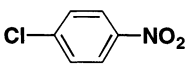
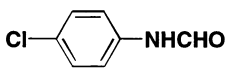
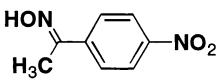
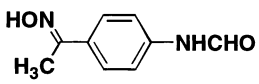
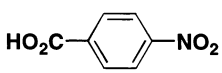
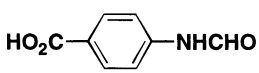
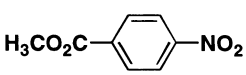
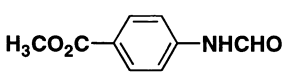
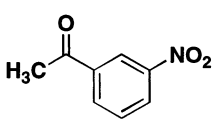
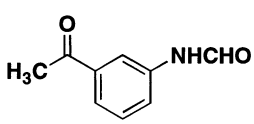
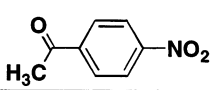
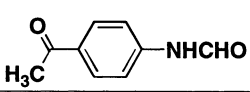
Scheme 1.

Keywords: reductive *N*-formylation; catalytic transfer hydrogenation; formanilides; aromatic nitro and ammonium formate.

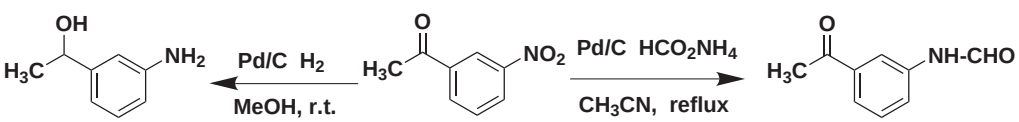
* Corresponding author. Fax: 0091-44-235 2545; e-mail: sbhaskar@iitm.ac.in

0040-4039/01/$ - see front matter
PII: S0040-4039(01)00049-1

Table 1. Reductive *N*-formylation of aryl nitro compounds under catalytic transfer hydrogenation conditions

Entry	Substrate	Time (h)	Product [a]	Yield (%)	M. P. (°C)
1		14		70	48 – 50
2		16		75	58 – 60
3		7		89	51 – 53
4		12		91	104 -106
5		20		93	142-144
6		14		40	258 - 260
7		24		94	123 -125
8		10		75	92 – 94
9		16		46[b]	104 -105

[a] Satisfactory spectroscopic data were obtained for all the purified products.
[b] In addition, *p*–amino acetophenone was isolated in 28% yield.



Scheme 2.

perature). After 7 h, the reaction mixture was diluted with ethyl acetate (15 mL) and the catalyst was removed by filtration through a pad of Celite. The filtrate was washed with water (2×10 mL), dried (anhyd. Na_2SO_4) and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel using 40% ethyl acetate in hexane as an eluent to furnish the pure product (85 mg, 86%) as colorless crystals, mp 51–53°C.

In conclusion, we have developed a facile and highly selective methodology for the direct conversion of aryl nitro compounds to the corresponding formanilides in good yields under catalytic transfer hydrogenation conditions.

Acknowledgements

We thank Professor K. K. Balasubramanian for his constant encouragement and generous gift of chemicals. T.V.P. (JRF) thanks CSIR, New Delhi for a research fellowship.

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