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A Mild and Convenient Reduction of Aromatic and Heteroaromatic Aldoximes with Ammonium Formate/Pd

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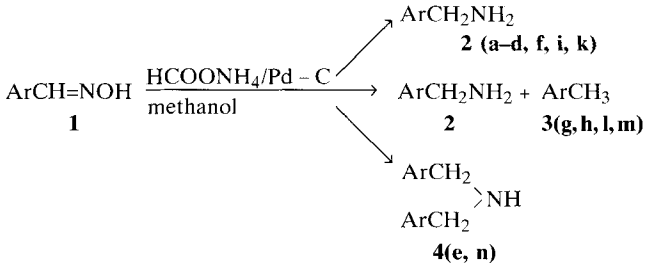
Traditional methods for the reduction of the aldoximes led to the formation of the amines or hydroxylamines, depending on the substrate used and the reaction conditions. Most of these works have been carried out using metal hydrides [1–6], molecular hydrogen under pressure in the presence of catalyst [7–9], sodium amalgam in alcohol [10], pyridine-BH_3 complex [11], $TiCl_3$-$NaBH_3CN$ system [12, 13], organolithium compounds [14], zinc dust in acetic acid [15], magnesium in ammonium acetate [16] or stannous chloride in HCl [17]. Unfortunately, many of these methods are deficients in some respects, such as low yields, long reaction time, expensive and not readily available reagents or severe reaction conditions.

In this communication, we report on a simple and mild method for the reduction of selected aromatic or heteroaromatic aldoximes using catalytic transfer hydrogenation. The reaction proceeds within 15 to 40 min. upon addition of ammonium formate to a suspension of palladium on carbon and substrate **1** in methanol at room temperature or at 50 °C.



	Ar		Ar
a	Ph	h	2-Naphthyl
b	m-Cl-C_6H_5	i	3-Pyridyl
c	m-NO_2-C_6H_5	k	4-Pyridyl
d	p-NO_2-C_6H_5	l	3-Quinolyl
e	o-OH-C_6H_5	m	4-Quinolyl
f	p-CH_3O-C_6H_5	n	2-Furyl
g	1-Naphthyl		

In the most cases (entries 1, 4, 5, 8, 9, 10, 12), the reaction leads to the formation of the corresponding primary (hetero)arylmethyl amines. The selectivity of this method towards several substituents present on the aromatic ring was examined. While the methoxy group remains unchanged and the p-methoxybenzylamine (entry 12) is produced, halo and nitro groups are readily eliminated (entry 8) or reduced (entries 9, 10) under reaction conditions [18]. In this way, not readily available p-amino- and m-aminobenzylamines can be directly obtained from the corresponding aldoximes.

The reduction of both 1- and 2-naphthaldoximes (entries 2, 3) give two compounds, the expected naphthylmethylamines and methylnaphthalenes as second products. Similar results were obtained in the case of 3- and 4- chinolinaldoximes (entries 6, 7). The corresponding quinolinmethylamines and methylquinolines were isolated from the reaction mixture. In the case of o-salicaldoxime (entry 11) and 2-furaldoxime (entry 13) an exothermic reaction took place, and unexpectedly secondary amines, di(o-hydroxybenzyl)amine and di(2-furylmethyl)amine were formed almost immediately as the only products of the reaction, in high yields.

The reaction can be applied as attractive laboratory method for the formation on the corresponding primary or secondary (hetero)-arylmethylamines. The advantages of this procedure are the avoidance of strong acid media and harsh reagents, the easy of manipulation, mild reaction conditions, good yield and finally no pressure apparatus is required. The reduction is in most cases uncomplicated by secondary amine formation (often a problem under classic hydrogenation conditions), and no reduction of aromatic ring takes place (sometimes a problem with pyridine).

Experimental

Hydrogenation of (Hetero)aryl Aldoximes 1 with $HCOONH_4$/Pd-C System

Typical procedure

To a magnetically stirred suspension of the appropriate aldoxime **1** (0.0025 mol) and 10 % palladium on carbon (0.15 g) in methanol (7 cm^3), anhydrous ammonium formate (0.01 mol) was added in one portion. The resulting reaction mixture (slightly exothermic in some cases) was stirred at room temperature or at 50 °C(see table) for 10–50 min., when TLC-chromatography indicated a consumption of the starting material. The catalyst was removed by filtration through Celite

Table 1 Hydrogenation of (Hetero)aryl Aldoximes (**1**) with $HCOONH_4$/Pd-C System

Entry	Substrate **1**[a] R–CH=NOH	Reaction time (min.)	cond. temp. (°C)	Product **2**[b]	Yield[c] (%)	m.p./b.p. (°C/torr)	m.p./b.p.	[Lit.]
1	Ph	30	r.t	Ph-CH_2NH_2	78	194–195 (picrate)	194 (picrate)	[19]
2	2-Naphthyl	25	50	2-Naphthyl-CH_2NH_2[d]	60	223-224	226	[20]
				2-Naphthyl-CH_3	35	37	37–38	[21]
3	1-Naphthyl	25	50	1-Naphthyl-CH_2NH_2[d]	56	221-222	223	[20]
				1-Naphthyl-CH_3	40	114/15	110/12	[22]
4	4-Pyridyl	20	r.t.	4-Pyridyl-CH_2NH_2	78	120/15	103/11	[23]
5	3-Pyridyl	30	r.t.	3-Pyridyl-CH_2NH_2	74	122/15	102/14	[23]
6	3-Quinolyl	15	50	3-Quinolyl-CH_2NH_2[d]	70	222–224 (x HCl)	225-230 (x HCl)	[24]
				3-Quinolyl-CH_3	15	184–185 (picrate)	187 (picrate)	[25]
7	4-Quinolyl	15	50	4-Quinolyl-CH_2NH_2[d]	63	203–206 (x HCl)	206–208 (x HCl)	[23]
				4-Quinolyl-CH_3	18	211–212 (picrate)	210–211 (picrate)	[26]
8	*m*-Cl-C_6H_5	30	rt.	*m*-Cl-$C_6H_5CH_2NH_2$	74	192–193 (picrate)	194 (picrate)	[19]
9	*m*-NO_2-C_6H_5	30	rt.	*m*-NO_2-C_6H_5-CH_2NH_2	72	151–152 (dipicr.)	148 (dipicr.)	[27]
10	*p*-NO_2-C_6H_5	40	r.t.	*p*-NO_2-C_6H_5-CH_2NH_2	68	261–265/760	268–270/760	[28]
11	*o*-OH-C_6H_5	10	rt.	*o*-OH-C_6H_5-CH_2 \ NH / *o*-OH-C_6H_5-CH_2	85	167–168	170	[29]
12	*p*-CH_3O-C_6H_5	50	r.t.	*p*-CH_3O-C_6H_5-CH_2NH_2	72	184–186 (picrate)	185 picrate)	[30]
13	2-Furyl	10	r.t	2-Furyl-CH_2 \ NH / 2-Furyl-CH_2	82	183–186 (x HCl)	186–187 (x HCl)	[31]

a) The substrates listed were prepared from the corresponding (hetero) aryl aldehydes and hydroxylamine hydrochloride; b) Products were characterized by IR, ^1H NMR, MS spectra and confirmed by direct comparison of their salts with authentic compounds; c) Yields of isolated products purified by distillation or crystallization, based on a single experiment; d) separated on the chromotography column using chloroform-aceton (9:1) as eluent.

and washed with methanol (5 cm^3). The filtrate was then alkalized with saturated aqueous Na_2CO_3 and extracted with $CHCl_3$ or CH_2Cl_2. The extract was dried over Na_2SO_4, the solvent evaporated and the residue purified by flash column chromatography or vacuum distillation to give pure product **2**.

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