Palladium-catalysed Transfer Hydrogenation of Azobenzenes and Oximes using Ammonium Formate†

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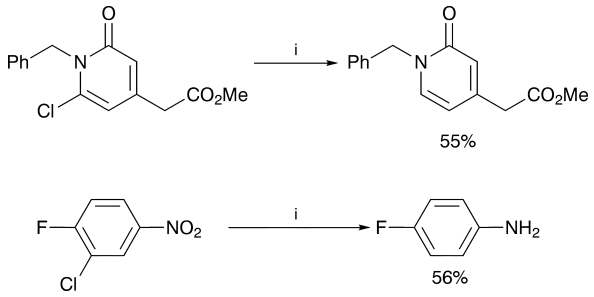
The reductive cleavage of azobenzenes, including the reduction of oximes to their corresponding amines, has been achieved with Pd^0 using ammonium formate as hydrogen source.

The reduction of aromatic azo and azoxy compounds has received a good deal of attention, both preparatively and analytically.[1] It proceeds *via* the hydrazo derivative to the amine or a mixture of two amines when the original azo compound is unsymmetric. Azobenzene undergoes reductive cleavage to aniline with a number of reagents, such as metal–acid combinations and on transfer hydrogenation over Pd.[2] Reductive cleavage of azo- and azoxy-benzenes continues to be used in connection with structural determinations of azo dyes. More recently, Cp_2TiBH_4 has been reported to reduce azobenzenes to the corresponding amines.[3]

Catalytic transfer hydrogenation with Pd/C as catalyst and ammonium formate as hydrogen source has found widespread use in the reduction of various functionalities.[4] This forms a safe alternative to the use of hydrogen gas. We have recently reported the regiospecific reductive ring opening of epoxides and glycidic esters under transfer hydrogenation using ammonium formate.[5] In this paper, we wish to report that Pd/C catalyses the reductive cleavage of various azobenzenes as well as the reduction of various oximes to the corresponding amines in moderate yields, using ammonium formate as H_2 source.

Table 1 summarizes the results of the reductive cleavage of the N=N of azobenzenes to give the corresponding amines, using 4 equiv. of ammonium formate at ambient temperature. It is to be noted that reducible groups such as Cl and NO_2 also underwent facile reduction under the reaction conditions employed. However, it is remarkable that selective reduction of a C–Cl bond over a C–F or a C–N (debenzylation) bond[6] has been achieved with the present system (Scheme 1).

The reduction of various carbon–nitrogen systems to saturated derivatives with various reducing agents provides highly useful processes for the preparation of amines and related functionalities.[7] The reduction of oximes and subsequent cleavage of the N–O bond to afford primary amines occurs with a variety of potent hydride reagents, including $LiAlH_4$.[8] Table 2 gives the various oximes that underwent



Scheme 1 i, HCO_2NH_4 (2 mol), 10% Pd/C (cat.), MeOH, heat, 5–6 h

reduction with 2 equiv. of ammonium formate at the reflux temperature to produce the corresponding amines in moderate yields. Further, it is to be noted that C=N has been reduced preferentially over C=C (entries 4 and 5, Table 2). The yield in the case of oxime reduction is only moderate owing to the instability of the amines under the reaction conditions, possibly giving other side products. In conclusion, we have shown that the ammonium formate–Pd/C system is a versatile, selective and rapid method for catalytic hydrogenation of N=N and C=N functionalities.

Experimental

All mps reported are uncorrected. IR spectra were recorded neat or as Nujol mulls (in case of solid samples) on a Perkin Elmer Infrared model 137-E. The ^1H NMR spectra were recorded on Varian FT 80A and Bruker 200 MHz instruments. ^{13}C NMR were obtained on a Bruker 200 MHz instrument. The chemical shifts (ppm) were reported with Me_4Si as the internal standard. The mass spectra (MS) were recorded on an automated Finnigan-MAT 1020 C mass spectrometer using an ionization energy of 70 eV.

General Experimental Procedure for the Reduction of Azobenzene.—A mixture of azobenzene (1.82 g, 0.01 mol), ammonium formate (2.52 g, 0.04 mol) and 10% Pd/C (180 mg) in MeOH (20 ml) was stirred at room temperature for 5 h. The progress of the reaction was monitored by TLC. After the reaction was complete, the catalyst was filtered off and the crude product was purified by flash chromatography. Yield: 63%.

General Experimental Procedure for the Reduction of Oximes.—A mixture of acetophenone oxime (1.35 g, 0.01 mol), ammonium

Table 1 Pd-catalysed transfer hydrogenation of azobenzenes using ammonium formate as H_2 source

Entry	Substrate	Products[a] (% yield)[b]
1	Azobenzene	Aniline (63)
2	4-Aminoazobenzene	Aniline (31) + 1,4-diaminobenzene (64)
3	4-Hydroxyazobenzene	Aniline (29) + 4-aminophenol (54)
4	4-Methyl-4′-hydroxyazobenzene	*p*-Toluidine (31) + 4-aminophenol (47)
5	4-Chloro-4′-hydroxyazobenzene	Aniline (25) + 4-aminophenol (48)
6	4-Nitro-4′-hydroxyazobenzene	1,4-Diaminobenzene (49) + 4-aminophenol (34)
7	2-Methoxy-4′-hydroxyazobenzene	*o*-Anisidine (30) + 4-aminophenol (64)
8	2-Nitro-4-methoxy-4′-hydroxyazobenzene	3,4-Diaminoanisole (21) + 4-aminophenol (55)
9	Acetophenone azine	α-Methylbenzylamine (30)

[a]Characterized by IR, ^1H and ^{13}C NMR and MS. [b]Isolated after chromatographic purification.

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Table 2 Pd-catalysed transfer hydrogenation of oximes using ammonium formate

Entry	Substrate	Product[a]	Yield (%)
1	Benzaldoxime	Benzylamine	42
2	Acetophenone oxime	α-Methylbenzylamine	41
3	Cyclohexanone oxime	Cyclohexylamine	42
4	β-Ionone oxime	2-Amino-4-(2,6,6-trimethylcyclohex-1-en-1-yl)but-3-ene	29
5	Carvone oxime	1-Amino-2-methyl-5-(1-methylethenyl)cyclohex-2-ene	22
6	Methylphenylglyoxalate oxime	2-Phenylglycine methyl ester	45
7	Ethyl (4-methoxyphenyl)glyoxalate oxime	4-Methoxyphenylglycine ethyl ester	55

[a]Characterized by IR, ^{1}H and ^{13}C NMR and MS. [b]Isolated after chromatographic purification.

formate (1.26 g, 0.02 mol) and 10% Pd/C (135 mg) in MeOH (20 ml) was boiled under reflux for 5 h. The progress of the reaction was monitored by TLC. After the reaction was complete, the catalyst was filtered off and the crude product was purified by flash chromatography. Yield: 41%.

2-*Phenylglycine methyl ester*. ν_{max}/cm^{-1} 3500–3300, 1740, 1600, 1450, 1400, 1250, 1180, 1100, 1000, 740; δ_H (200 MHz, $CDCl_3$) 2.7 (2 H, br, s, NH_2), 3.70 (3 H, s, OMe), 4.6 (1 H, s > CH), 7.35 (5 H, s, Ar-H); *m*/*z* 165 (M^+, 100%), 150 (13%), 135 (4%), 121 (6%), 105 (8%), 91 (6%), 77 (8%).

α-*Methylbenzylamine*. ν_{max}/cm^{-1} 2500–3500, 1600, 1450, 1300, 1000, 700; δ_H (200 MHz, $CDCl_3$) 1.45 (3 H, s, Me), 1.5 (3 H, s, Me), 3.1–3.5 (2 H, br s, NH_2), 4.1–4.25 (1 H, q, *J* 3.5 Hz, 7CH, 7.4 (5 H, s, Ar-H); *m*/*z* 121 (M^+, 4%), 120 (M − 1, 12%), 106 (100%), 79 (52%), 66 (35%).

4-*Methoxyphenylglycine ethyl ester*. ν_{max}/cm^{-1} 3500–3300, 1740, 1600, 1250, 1050, 820; δ_H (200 MHz, $CDCl_3$) 1.3–1.4 (3 H, t, *J* 3 Hz, CH_3), 4.3 (3 H, s, OMe), 4.2–4.4 (H, q, *J* 4 Hz, CH_2), 4.45 (1 H, s, > CH), 6.9–6.95 (2 H, d, *J* 8 Hz, ArH), 7.3–7.35 (2 H, d, *J* 8 Hz, Ar-H); *m*/*z* 209 (M^+, 2%) 208 (M-1, 33%), 164 (4%), 145 (5%), 136 (12%), 111 (12%), 97 (25%), 83 (35%), 77 (12%), 57 (100%).

1-*Amino*-2-*methyl*-5-(1-*methylethenyl*)*cyclohex*-2-*ene*. ν_{max}/cm^{-1} 2500–3500, 1610, 1450, 1390, 950, 500; δ_H (200 MHz, $CDCl_3$) 1.2–1.35 (1 H, m, CH), 1.75 (3 H, s, CH_3), 1.9 (3 H, s, CH_3), 2.05–2.4 (4 H, M, 2 > CH_2), 3.2–3.3 (1 H, dd, *J* 3 and 5 Hz, > CH—), 4.65 (2 H, m =CH_2), 6.0–6.1 (1 H, m =CH—), 10.1 (2 H, br, s, NH_2); *m*/*z* 151 (M^+, 2%), 150 (M − 1, 9%), 135 (5%), 124 (5%), 109 (5%), 99 (9%), 93 (9%), 84 (29%), 69 (100%).

2-*Amino*-4-(2,6,6-*trimethylcyclohex*-1-*en*-1-*yl*)*but*-3-*ene*. ν_{max}/cm^{-1} 3000–3500, 1600, 1450, 940, 500; δ_H (90 MHz, $CDCl_3$): 0.7–0.85 (4 H, m, CH_2), 1.6–1.7 (9 H, s, 3Me), 2–2.1 (3 H, m, CH_2), 2.3–2.9 (3 H, m, CH_3), 4.6 (2 H, s, CH_2), 5.8 (2 H, dd, J 3 and 5 Hz, =CH—), 8.9–9.0 (2 H, br, s, NH_2); *m*/*z* 193 (M^+, 12%), 192 (M − 1, 100%), 160 (40%), 146 (5%), 134 (8%), 120 (5%), 105 (10%), 91 (15%), 77 (12%).

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