Selective Reduction of the Nitro-group Using $Co_2(CO)_8$-H_2O[†]

Hee-Yoon Lee[*] and Mihyun An

Center for Molecular Design and Synthesis, Department of Chemistry & BK21 School of Molecular Science, Korea Advanced Institute of Science and Technology, Daejeon 305-701, Korea

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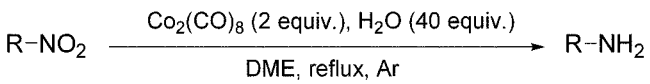
Recently, we reported a new reducing agent prepared from $Co_2(CO)_8$ and H_2O for the selective 1,4-reduction of α,β-unsaturated carbonyl compounds[1] as well as a tandem reductive Pauson-Khand reaction.[2] We became interested in the reduction power especially the reactivity and the selectivity of this new reducing agent in reducing other functional groups.

Reduction of aromatic nitro compounds to amines is a very useful synthetic transformation for which a vast array of reagents has been developed.[3] Though the most general methodology for this conversion is catalytic hydrogenation[4] as it is an economical and effective method, particularly in large scale reactions, the reaction has a limited utility in the presence of other reducible functional groups.[5] The selective reduction of nitro group in presence of other reducible functional groups were also achieved using metal based reduction systems.[6] However, the selective reduction of the nitro group in presence of carbonyl group could not easily be attainable under these conditions. Therefore we became interested in a possibility of the selective reduction of nitro groups in presence of other reducible functional groups including carbonyl groups and halides.

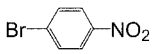
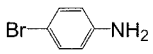
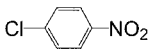
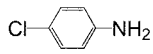
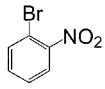
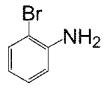
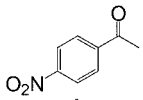
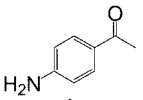
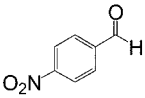
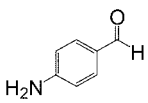
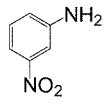
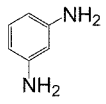
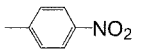
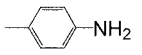
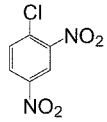
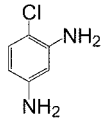
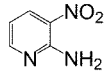
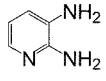
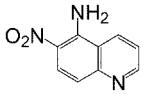
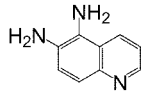
Herein, we report that various nitro compounds are selectively and readily reduced to their corresponding amino derivatives in presence of other functional groups.

The reaction was tested on *p*-chloronitrobenzene with the reaction conditions used in the previous report of unsaturated carbonyl compound reduction.[1] Since the nitro group requires more reducing agent than unsaturated carbonyl groups, 2 equivalent of $Co_2(CO)_8$ was used for the reaction with the corresponding amount of water. Dimethoxyethane (DME) was used as the solvent since DME was the optimal solvent for the reduction of the unsaturated carbonyl compounds. To our delight, the reaction completed in 30 minutes and the reaction mixture contained only the desired aniline compound without any trace of other byproducts. When a less amount than 2 equivalent of $Co_2(CO)_8$ was used, the reduction was not complete. Then, the reaction was applied to aromatic nitro



Scheme 1

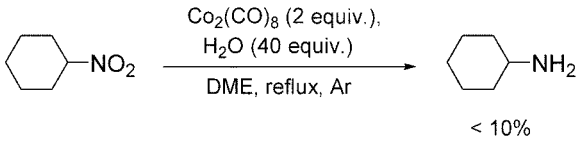
Table 1.

entry	substrate	product	yield (isolate)
1	 **1**	 **1a**	80
2	 **2**	 **2a**	99 (100% conversion)
3	 **3**	 **3a**	58
4	 **4**	 **4a**	83
5	 **5**	 **5a**	80
6	 **6**	 **6a**	93 (100% conversion)
7	 **7**	 **7a**	100
8	 **8**	 **8a**	100[a]
9	 **9**	 **9a**	50 (100% conversion)
10	 **10**	 **10a**	70

[a] 4 equiv. of $Co_2(CO)_8$ and 80 equiv. of H_2O were used.

[†]Dedicated to Professor Yong Hae Kim for his distinguished achievements in organic chemistry.

[*]Corresponding Author. e-mail: leehy@kaist.ac.kr



Scheme 2

compounds with various functional groups (Table 1).

In most cases, all the nitro compound was consumed within 30-60 min. The results in the table showed that a wide variety of substituted nitrobenzenes were reduced in almost quantitative yields.

Under the reaction conditions, other reducible groups were not affected at all. Halogenated nitro compounds were reduced to the amino compounds without losing halides (entries 1, 2, 3 and 8). When various halides were reacted under the current reduction conditions, only benzyl bromide was reduced to toluene quantitatively. Bromotetradecane and bromobenzene were not reduced at all by $Co_2(CO)_8$-H_2O. Nitro compounds containing carbonyl groups were reduced to the corresponding amino compounds (entries 4 and 5). The reduction of carbonyl groups to the corresponding alcohols was not observed. Even the aldehyde group was intact under the reaction conditions.

Dinitro compound was completely reduced using 4 equiv. of $Co_2(CO)_8$ and 80 equiv. of H_2O (entry 8). Selective partial reduction of a nitro group in presence of the other could not be accomplished with using 2 equivalent of $Co_2(CO)_8$. Only a mixture of all the possible products with starting material was obtained.

The pyridine ring did not affect the reduction of the nitro group at all (entries 9 and 10). Low yield of the product in entry 9 appears to be due to chelation of the product to the metal as the reaction was complete and the recovery of the product was not good. The similar result was observed when other metal reducing agents were used. The product seemed to be physically adsorbed onto the cobalt complex and could not be effectively extracted with organic solvent.

Contrary to aromatic nitro compounds, the present procedure was not efficient in the reduction of aliphatic nitro compounds as the reduction of nitrocyclohexane led to the isolation of only a small amount of the desired aminocyclohexane, though the reaction was clean and complete. The aliphatic amine product seemed to be absorbed onto the cobalt complex tightly. Further study to find a method for decomplexation of the alkyl amine product from cobalt complex would extend the current reduction protocol to the reduction of nitro-alkanes.

These results indicate that $Co_2(CO)_8$-H_2O is a versatile reducing system for wide variety of aromatic nitro compounds in the presence of other functional groups. The reaction can easily be applicable to a large scale synthesis of aniline compounds as the reaction set-up, sequence and work-up is simple and straightforward. Therefore this procedure does bear a general use for a large scale preparation of aromatic amines specifically in cases where selective, rapid, mild reduction is required.

Experimental Section

The general procedure for the reduction. $Co_2(CO)_8$ (169 mg, 0.50 mmol) was dissolved in a round bottom flask charged with Ar atmosphere in DME (0.50 mL) A solution of 1-bromo-4-nitrobenzene (**1**) (50 mg, 0.25 mmol) and water (178 μL, 9.9 mmol) were added, and the mixture was heated to reflux for 1 h. Upon completion of the reaction, the mixture was cooled to room temperature and was concentrated *in vacuo*. Purification by flash chromatography (SiO_2, EtOAc/Hexane = 1/2) afforded 4-bromoaniline (**1a**) (80% yield) as a solid.

Compound 1a: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23-7.18 (m, 2H), 6.55-6.51 (m, 2H), 3.62 (bs, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 145, 131, 117, 110.

Compound 2a: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.09-7.04 (m, 2H), 6.58-6.53 (m, 2H), 3.60 (bs, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 144, 129, 122, 116.

Compound 3a: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (dd, J = 7.98, 1.35 Hz, 1H), 7.11-7.05 (m, 1H), 6.73 (dd, J = 6.57, 1.43 Hz, 1H), 6.62-6.59 (m, 1H), 3.96 (bs, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 144, 132, 128, 119, 115, 109.

Compound 4a: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (d, J = 8.60 Hz, 2H), 6.58 (d, J = 8.59 Hz, 2H), 4.22 (bs, 2H), 2.44 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 196, 151, 130, 126, 113, 25.

Compound 5a[4]**:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.73 (s, 1H), 7.66 (d, J = 8.48 Hz, 2H), 6.67 (d, J = 8.46 Hz, 2H), 4.26 (bs, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 190, 152, 132, 128, 114.

Compound 6a: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.90 (t, J = 7.91 Hz, 1H), 6.10-6.06 (m, 2H), 5.98-5.97 (m, 1H), 3.43 (bs, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 147, 130, 105, 101.

Compound 7a: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.96 (d, J = 8.11 Hz, 2H), 6.60 (d, J = 8.24 Hz, 2H), 3.39 (bs, 2H), 2.24 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 143, 129, 127, 115, 20.

Compound 8a: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.71-6.65 (m, 3H), 3.25 (bs, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 135, 120, 119, 118, 117, 116.

Compound 9a: ^{1}H NMR (300 MHz, DMSO) δ 7.24-7.21 (m, 1H), 6.65-6.62 (m, 1H), 6.33-6.29 (m, 1H), 5.23 (bs, 2H), 4.53 (bs, 2H). ^{13}C NMR (75 MHz, DMSO) δ 148, 135, 130, 118, 113.

Compound 10a: ^{1}H NMR (300 MHz, DMSO) δ 8.41-8.42 (m, 1H), 8.29-8.26 (m, 1H), 7.19-7.12 (m, 3H), 4.95 (bs, 2H), 4.81 (bs, 2H). ^{13}C NMR (75 MHz, DMSO) δ 145, 130, 129, 126, 121, 119, 118. IR (KBr) 3377, 3206, 2362, 2344. HRMS (EI): m/z calcd ($C_9H_9N_3$) 159.0796, found 159.0797.

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