Cadmium Chloride-Zinc Catalysed Selective Reduction of Nitro Aromatics to Azoxy Compounds

Bipul Baruah, Anima Boruah, Dipak Prajapati, and Jagir S. Sandhu*
Regional Research Laboratory, Jorhat 785 006, Assam, India

(Received December 11, 1995)

Treatment of aromatic nitro compounds with cadmium chloride-metallic zinc combination systems has been shown to display a good reaction selectivity in the formation of symmetrical azoxy compounds in high yields.

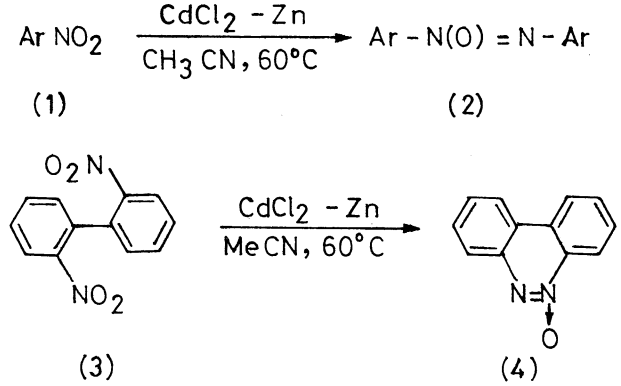
The formation of azo and azoxy compounds from nitro aromatics has been known for many decades[1]. However, the type of dimeric product can vary, not only with change of substituent in the aromatic ring, but also with the reaction conditions. Thus, in aqueous alkali, 2-nitrotoluene yields a salt of anthranilic acid[2], whereas, in the presence of diphenylamine 2,2'-dinitrobibenzyl is formed[3]. With 4-nitrotoluene in methanolic alkali the reaction course alters, 4,4'-dinitrobibenzyl being accompanied by 4,4'-dinitrostilbene[4]. The precise nature of the product depends upon the presence or absence of aerial oxygen[5], radical anions having been detected[6] as intermediates. Herein we wish to disclose the first example of cadmium chloride-metallic zinc combination can be utilised for the selective reduction of aromatic nitro compounds both inter and intramolecularly to the corresponding azoxy compounds in high yields. It may be mentioned that there are some naturally occurring azoxybenzenes which possess potent biological properties[7]. Also, metal-catalyzed reactions is of interest because of its relevance to the enzymatic degradation of nitrogen containing compounds in biological systems. Their utility in liquid crystals is also well known.[8]

Table Cadmium chloride-zinc catalysed reduction of **1** to **2**[a] and **3** to **4**[d]

Entry	Ar in **1**	Time[b] (h)	mp (°C)	Yield[c] (%)
1	Ph	1	35-36[14a]	80
2	4-ClC_6H_4	1	154-156[14a]	70
3	4-BrC_6H_4	1.5	173-175[14c]	72
4	3-ClC_6H_4	1.5	96-97[14a]	65
5	4-MeC_6H_4	1	66-68[14a]	85
6	4-EtC_6H_4	1	110-112[14b]	80
7	4-$OMeC_6H_4$	1.5	116-118[14c]	80
8	4-IC_6H_4	1.5	209-210[14d]	72
9	4-$MeCOC_6H_4$	1.5	192-194[14g]	80
10	4-MeOOC.CH=CHC_6H_4	1.5	57-58[14f]	70

[a]Products were identified by the comparision of IR and NMR spectra and melting points with those of authentic samples. [b]Increasing the time of reaction had no significant effect on the yield and resulted in minor amount of decomposition. [c]Isolated yields. [d]For product **4** mp 138-139 °C, Yield 50%.

In a typical experiment, to a suspension of metallic zinc powder (195 mg, 3 mmol) in dry acetonitrile (20 ml) was added cadmium chloride (402 mg, 2 mmol) followed by nitrobenzene (246 mg, 2 mmol). The reaction mixture was stirred at 60°C for 1 h under nitrogen atmosphere, until most of nitrobenzene was consumed. Usual workup of the mixture followed by extraction with chloroform and purification by column chromatography on silica gel gave azoxybenzene 80% yields exclusively and there was no evidence for the formation of N-phenylhydroxylamine or azobenzene or aniline. Under the same conditions without metallic zinc or without cadmium chloride no reduced products were formed and the nitrobenzene being recovered intact. The reaction also proceed when lesser amount of cadmium chloride (1 mmol) was used in the above reaction and azoxybenzene was isolated in about 60% yields. Various substituted nitrobenzenes were then reduced to the corresponding azoxy compounds, typical results are being shown in the Table. The use of other divalent metal salts in combination with metallic zinc, such as magnesium, zinc or mercury halides are not effective and produces mixture of products along with totally reduced primary amines.



In the case of methyl 4-nitrocinnamate the reaction occurred selectively at the nitro group and the carbon-carbon double bond in the substrate was not effected. High yields of azoxy compounds are obtained from nitro aromatics with ether or alkyl substituent, the positional relationship of the substituent in no way influencing the overall reaction. Both bromo and iodo-substituted nitro aromatics react smoothly with retention of the halogen, instead of its elimination.[9] The carbonyl group in p-nitroacetophenone remain intact and the corresponding 4,4'-

diacetyl azoxybenzene was obtained in 80% yields exclusively.[10] It was also found that this novel reduction system can be conveniently used to perform reductive intramolecular cyclisation of O,O'-dinitrobiphenyls to the corresponding benzo (c) cinnoline N-oxides **4** in 50% yields. Therefore the reaction is general and can be employed for the synthesis of symmetrically substituted azoxybenzenes.

In conclusion, the present new method employing cadmium chloride-zinc combination has some notable advantages compared with other methods. For example in the reduction of bromo or iodo nitrobenzene by Mg, Tl or Al reagents, the halogens were usually eliminated or complex products were formed and in the reduction of alkyl substituted nitrobenzene by sodium alcoholate polymers were usually formed.[11] In contrast, in our examples none of these side reactions were observed. Therefore the present method demonstrate the novelty of cadmium chloride-zinc combination system which exercises unique selectivity and constitutes a useful alternative to the commonly accepted procedure for the synthesis of various azoxybenzenes[12] and benzo(c) cinnoline N-oxides.[13]

We thank the Department of Science and Technology (DST), New Delhi, for financial support to this project.

References

1 P. Buck, *Angew. Chem. Int. Ed. Engl.*, **8**, 120 (1969); H. Zollinger, Azo and Diazo Chemistry, Ch. 9, Interscience, N.Y. (1961).

2 J. D. Loudon and G. Tennant, *Quart. Rev.*, **18,** 389 1964).

3 F.W. Bergstrom, I. M. Granara and V. Erickson, *J. Org. Chem.*, **7,** 98 (1942).

4 H. Klinger, *Ber. Dtsch. Chem. Ges.*, **16,** 941 (1883); O. Fischer, E. Hepp, *Ber. Dtsch. Chem. Ges.*, **26,** 2231 (1893).

5 T. Tsuruta, T. Fueno and J. Furukawa, *J. Am. Chem. Soc.*, **27**, 3265 (1955).

6 G. A. Russell, and E. G. Janzen, *J. Am. Chem. Soc.*, **89**, 300 (1967).

7 S. Murata, M. Miura, and N. Nomura, *J. Org. Chem.*, **54**, 4700 (1989).

8 J. P. Snyder, V. T. Bandurco, F. Darack, and H. Olsen, *J. Am. Chem. Soc.*, **96**, 5158 (1974).

9 A. McKillop, and R. A. Raphad, *J. Org. Chem.*, **35**, 1671 (1970); J. F. Corbett, *Chem. Commun.*, **1968,** 1257.

10 For the reduction of carbonyl group to hydroxy in azoxybenzene formation see: K. Oke, H. Takahashi, S. Uemura, and N. Sugita, *J. Chem. Soc., Chem. Commun.*, **1988,** 591.

11 C. M. Sutter, and F. B. Danis, *J. Am. Chem. S0c.*, **50**, 2733 (1928); I. Shimao, *Nippon Kagaku Kaishi*, **1974,** 515.

12 For pre-existing methods see: K. F. Keirstead, *Can. J. Chem.*, **31**, 1064 (1953); P. T. Lansbury, and J. O. Peterson, *J. Am. Chem. Soc.*, **85**, 2236 (1963); H. C. Brown, P. M. Weissman, and N. M. Yoon, *J. Am. Chem. Soc.*, **88**, 1458 (1966); R. O. Hutchins, D. W. Lamson, L. Rua, C. Milewski, and B. Maryanoff, *J. Org. Chem.*, **36**, 803 (1971); T. S. Suzuki, and T. Okada, *Chem. Ind.*, **1970,** 1926.

13 For some recent reports see: H. R. Sonawane, A. V. Pol, P. P. Moghe, S. S. Biswas, and A. Sudalai, *J. Chem. Soc., Chem. Commun.*, **1994,** 1215; S. Sakaue, T. Tsubakino, Y. Nishiyama, and Y. Ishii, *J. Org. Chem.*, **58**, 3633 (1993); C. Paradisi, G. Gonzalez-Trueba, and G. Scorrano, *Tetrahedron Lett.*, **34**, 877 (1993).

14 For literature melting points see; a) P. H. Gore, and O. H. Weelar, *J. Am. Chem. Soc.*, **78**, 2160 (1956); b) E. Bamberger, *Chem. Ber.*, **59**, 481, (1926); c) R. S. Porter, and J. E. Johnson, *J. Phys. Chem.*, **66**, 1826 (1962); d) E. Bamberger, and W. Hama, *Ann.*, **165**, 189 (1873); f) D. Vorlander, *Ber.*, **39**, 803 (1906); g) H. Tani, S. Tanaka, and F. Toda, *Bull. Chem. Soc. Jpn.*, **36**, 1267 (1963).