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THE REDUCTION OF NITROBENZENES BY TRIETHYLSILANE USING WILKINSON'S CATALYST

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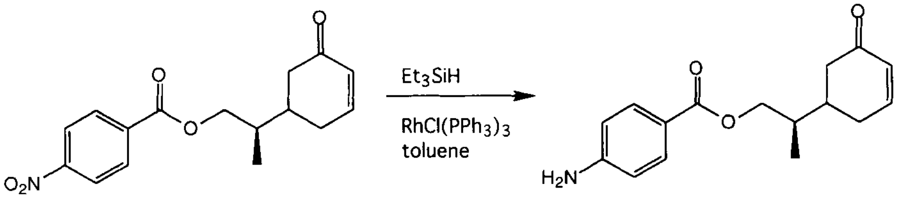
ABSTRACT : Aromatic nitro compounds are effectively reduced to anilines by triethylsilane using Wilkinson's catalyst.

The reduction of nitrobenzenes to anilines is one the most important reactions in aromatic chemistry[1]. The most common methods for nitro group reduction employ a metal (iron or zinc) in acid[2], reduction with hydrogen and a metal catalyst[3], or with disulfide (Zinin reaction)[4]. The recent reports for the reduction of aromatic nitro groups using Baker's yeast[5a] and N,N-dimethylhydrazine[5b] underscore the continuing importance of this process. In developing a formal synthesis of (+)-juvabione based on organo-manganese arene chemistry[6], we inadvertently discovered conditions for the reduction of the aromatic nitro group using triethylsilane catalyzed by Wilkinson's catalyst, $RhCl(PPh_3)_3$[7]. Examination of the literature revealed only one report for the reduction nitrobenzene with triethylsilane catalyzed by $RhCl(PPh_3)_3$ (no solvent), with the authors reporting poor yields of the aniline and N-triethylsilylaniline[8,9]. Since we uncovered a rather surprising chemoselectivity in which the NO_2 group was reduced preferentially to the α, β unsaturated ketone, we



decided to explore the limitations and optimal conditions of this reaction. This paper reports the preparation of aromatic amines from the corresponding aromatic nitro compounds by the reduction with triethylsilane in the presence of Wilkinson's catalyst.

We initially investigated the optimum reaction conditions for the reduction of 4-nitro-o-xylene to 1,2-dimethylaniline (Table 1). 4-Nitro-o-xylene, triethylsilane (at least five equivalents), Wilkinson's catalyst (at least 0.01 equivalents) and the aromatic solvent were refluxed for 1-6 hours to give a crude mixture of reduction products (vide infra) which were treated first with methanolic HCl and then with sodium hydroxide to give 1,2 dimethylaniline. Reduction in refluxing toluene with 0.02 equivalents of Wilkinson's catalyst gave the highest and most reproducible yields of the aniline product. When the reaction was conducted at lower temperatures and/or lower catalyst concentrations, the starting nitro compound was often recovered. Higher catalyst concentrations led to an inevitable contamination of the aniline with

Table 1. Reduction of 4-Nitro-o-Xylene.

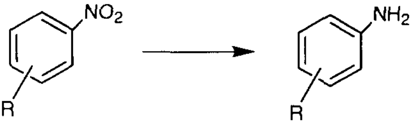
Solvent mL	Temp °C	Catalysis equiv.	Et_3SiH equiv.	time hr	3.4-Dimethyl aniline %
benzene(10mL)	80	0.01	5.0	360	73
toluene(10mL)	80	0.01	5.0	360	not complete
toluene(10mL)	110	0.01	8.0	360	76
toluene(20mL)	110	0.01	8.0	360	not complete
toluene(10mL)	110	0.02	5.0	240	82
toluene(10mL)	110	0.05	5.0	120	89[1]
toluene/EtOAc(10mL)	105	0.02	5.0	240	78

[1] GC showed the presence of triphenylphosphine oxide

triphenylphosphine oxide. We also found that "old" $RhCl(PPh_3)_3$ was an ineffective catalyst for the reduction of the aromatic nitro compounds[10]. When tri(isopropyl)silane[11] or diphenylsilane[12] was used in place of triethylsilane, the starting aromatic nitro compound was recovered.

Our results for the reduction of a variety of aromatic nitro compounds are summarized in Table 2. The reduction of alkyl-substituted aromatic nitro compounds (entries 2-7) to the corresponding anilines proceeded in good yields, although we noted that longer reaction times were required for the more sterically hindered nitro compounds. 4-Chloronitrobenzene (entry 9) was successfully reduced, but the reduction of 4-bromonitrobenzene was complicated by the reduction of the carbon-bromine bond. Both p-nitrobenzaldehyde (entry 11) and p-nitroacetophenone (entry 12) gave low yields of the corresponding aniline product due to competitive reduction

Table 2. Reduction of Aromatic Nitro Compounds[a]



Entry	R=	Time(hr)	Yield of amine[b]
1	H	2	86
2	4-CH_3	2	90
3	3,4-di CH_3	4	82
4	2,4-di CH_3	2	83
5	2,6-di CH_3	3	83
6	3,5-di CH_3	3	85
7	2,4,6-tri CH_3	6	75
8	4-OCH_3	2	86
9	4-Cl	2	71
10	4-Br	2	-[c]
11	4-CHO	3	-[c]
12	4-$COCH_3$	3	-[c]
13	3-$COCH_3$	2	71
14	4-CO_2CH_3	2	49
15	4-CN	2	-[d]

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a) Conditions: 1) aromatic nitro compound (10 mmol), toluene (10 mL), triethylsilane (8 mL, 5 equiv.), and $RhCl(PPh_3)_3$ (184 mg, 0.02 equiv.); 2) HCl, CH_3OH; 3) OH^-.

b) Isolated yields.

c) Low yield of aniline product due to reduction of the R group.

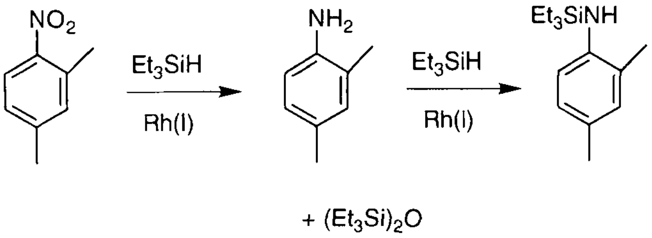
d) Aromatic nitro compound was recovered in high yield.

of the carbonyl group. In the case of p-nitrobenzaldehyde, the aldehyde group was reduced much more quickly than the nitro group as determined by ^1H NMR analysis. The reduction of electron-poor carbomethoxynitrobenzenes (entries 13 and 14) proceeded in moderate yield but p-cyanonitrobenzene did not undergo reduction at all.

We conducted a series of competition experiments in order to more fully define the chemoselectivity of the reduction process. As noted earlier, the carbonyl group (entries 11 and 12) was reduced faster or as fast as the nitro group. Competitive reduction experiments between carvone (1,4-reduction prevails under these conditions[13]) and 4-nitro-o-xylene established that the alpha, beta-unsaturated moiety was reduced 1.6 times faster than the nitro group. Reduction of carvone and methyl 4-nitrobenzoate showed only a slight preference for the reduction on the nitro group. As expected, the methyl 4-nitrobenzoate reduces twice as fast as 4-nitro-o-xylene. Although our interest in this reduction procedure was piqued by the unexpected chemoselectivity in the reduction of the juvabione intermediate, we have been unable to demonstrate and develop conditions for the selective reduction of the nitro group over the carbonyl group. The juvabione intermediate remains inexplicably a unique case of the selective reduction of a nitro group in the presence of a ketone by triethylsilane and Wilkinson's catalyst.

Selective reductions of inseparable mixtures of nitro aromatics (generated by the relatively unselective electrophilic nitration reaction) have proven to be a useful chemical procedure for the preparation of isomerically pure anilines.[14] Given the sensitivity of this reduction process to the steric environment of the nitro group (e.g. entry 7), we briefly investigated the competitve reduction of isomeric nitro aromatics. The reduction of a 85:15 mixture of 4-nitro-m-xylene and 2-nitro-m-xylene (1 mol% $RhCl(PPh_3)_3$, 10 min, 110°C) gave 2,4-dimethylaniline (69% yield based on 4-nitro-m-xylene) in greater than 98% isomeric purity.[15]

We have not examined the mechanism for this reduction process in detail but we have made the following observations. The major products before the work-up procedure are the N-triethylsilylaniline (verified by ^1H NMR and GC/MS) and hexaethyldisiloxane, $[(CH_3CH_2)_3Si]_2O$, along with small and variable amounts of the aniline. Examination of the reduction reaction mixture of 4-nitro-m-xylene at short reaction times (5-30 minutes) by GC indicated that the initial reduction product was 2,4-dimethylaniline with smaller amounts of (N-triethylsilyl)-2,4-dimethylaniline. As the reaction proceeds aniline is apparently converted into the corresponding N-triethylsilylaniline by the well-precedented reaction of N-H groups with silanes and transition metal catalysis.[16]



Despite the bewildering number of possible intermediates in the reduction of nitro groups,[17] we have not observed any other intermediates by ^1H NMR.

The results presented in this paper describe an efficient method for the reduction of aromatic nitro compounds to the corresponding anilines. The chemoselectivity and regioselectivity exhibited make this method a potentially useful procedure for selective reductions of aromatic nitro compounds to the corresponding anilines.

Typical Procedure for Aromatic Nitro Group Reduction. To a flame dried flask equipped with a magnetic stirrer, condenser, and argon inlet was added the 4-nitro-o-xylene (1.51 g, 10 mmol), toluene (10 mL), triethylsilane (8 mL, 50 mmol), and $RhCl(PPh_3)_3$ (184 mg, 0.2 mmol). The reaction mixture was heated to reflux until the reaction was judged to be complete (ca. 4h) by GC (HP Ultra 1 column, 50°C to 280°C @ 20 °C/min.). The solvent was removed *in vacuo* and the residue was stirred for 2 hours at room temperature in 10 ml of methanol and 12N HCl (3 ml). The mixture was then extracted with water (100 ml) and ethyl ether (2 X 100 ml). The aqueous layer was neutralized to pH 8 with 50% aqueous NaOH. The aqueous layer was extracted with ethyl ether (2 X 100 ml) and the combined ether layer washed with water (100 ml). The ethereal solution was dried over magnesium sulfate, filtered, and the solvent removed in vacuo to give 3,4 dimethylaniline (0.91 g, 82%). 3,4 Dimethylaniline: IR (KBr) 3377, 3194, 2918, 1632, 1509, 1462 cm^{-1}. ^1H NMR ($CDCl_3$, 400MHz) δ 6.89 (d, J=8.4Hz, 1H), 6.48 (s, 1H), 6.43 (dd, J=2.0, 7.6Hz, 1H), 3.44 (s, 2H), 2.16 (s, 3H), 2.14 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.25, 137.31, 130.28, 126.43, 116.87, 112.64, 19.80, 18.69.

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References

1. Larock, R. C. *Comprehensive Organic Transformations*, VCH: New York, 1989, pp 411-415.

2. Mahood, S. A.; Schaffner, P. V. L. *Org. Synth. Coll. Vol. 2*, **1943**, 160; Fox, B. A.; Threlfall, T. L. *Org. Synth. Coll. Vol. 5*, **1973**, 346.

3. Secrist III, J. A.; Logue, M. W. *J. Org. Chem.* **1973**, 37, 335.

4. Porter, H. K., *Organic Reactions*, John Wiley & Sons. vol. 20, pp 455.

5. Baik, W.; Han, J. L.; Lee, K. C.; Lee, N. H.; Kim, B. H. ; Hahn, J. *Tetrahedron Lett.* **1994**, 35, 3965.

6. Miles, W. H.; Brinkman, H. R. *Tetrahedron Lett.* **1992**, 33, 589.

7. Brinkman, H. R. Doctoral Thesis, Seton Hall University, South Orange, NJ, 1992.

8. Andrianov, K. A.; Sidorov, V. I.; Filimonova, M. I. *Zh. Obshch. Khim.*, **1977**, 47(2), 485; *Chem Abstr.* **1977**, 25, 190078c.

9. For further examples of rhodium catalyzed reductions of nitro groups and related reactions see: Liou, K. F.; Cheng, C. H. *J. Org. Chem.* **1982**, 47, 3018. Mahdavi, F.; Bruton, T. C.; Li, Y. *J. Org. Chem.* **1993**, 58, 744. Gargulak, J. D.; Berry, A. J.; Noirot, M. D.; Gladfelter, W. L. *J. Am. Chem. Soc.* **1992**, 114, 8933.

10. "Old" $RhCl(PPH_3)_3$ did not appear (spectrochemically) different from "new" $RhCl(PPh_3)_3$.

11. Triisopropylsilane was also recovered.

12. Attempted reduction with diphenylsilane led to the violent evolution of a gas, presumably hydrogen as the result of the dehydrogenative coupling of diphenysilane by $RhCl(PPh_3)_3$. See Brown-Wensley, K. A. *Organometallics* **1987**, 6, 1590.

13. Ojima, I.; Kogure, T. *Organometallics* **1982**, 1, 1390.

14. Nickson, T. E. *J. Org. Chem.* **1986**, 51, 3903.

15. Nickson (ref 14) reported a "poor yield" of the 2-nitro-m-xylene using the Zinin reaction.

16. For examples of the silylation of amines (a) Bonar-Law, R.P.; Davis, A.P.; Dorgan, B.J.

Tetrahedron Lett. **1990**, 31,6721; (b) Matarasso-Tchiroukhine, E. *J. Chem. Soc., Chem. Commun.* **1990**, 681; (c) Yamamoto, K.; Takemae, M. *Bull. Chem. Soc. Jpn.* **1989**, 62, 2111. For related examples of the silylation of alcohols (a) Gregg, B.T.; Cutler, A.R. *Organometallics* **1994**, 13, 1039; (b) Doyle, M.P.; High, K.G.; Bagheri, V.; Pieters, R.J.; Lewis, P.J.; Pearson, M.M. *J. Org. Chem.* **1990**, 55, 6082; (c) Ojima, I.; Kogure, T.; Nihonyanagi, M.; Kono, H.; Inaba, S.; Nagai, Y. *Chem Lett.* **1975**, 501.

17. Feuer, H. Ed., *The Chemistry of the Nitro and Nitroso Groups*, Interscience: New York, 1970.

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