Tetrahedron Letters, Vol.31, No.43, pp 6141-6144, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

SELECTIVE HYDROGENATION OF POLYNITROAROMATIC DERIVATIVES WITH NOBLE METAL CATALYSTS IN THE PRESENCE OF CATALYTIC AMOUNTS OF IRON

George Theodoridis,* Mark C. Manfredi, and Jessica D. Krebs

Agricultural Chemical Group, FMC Corporation, P.O. Box 8
Princeton, New Jersey 08543

ABSTRACT: Hydrogen over PtO_2, 5%Pd(c), $PdCl_2$, or 5%Rh(Al_2O_3), in the presence of catalytic amounts of iron and under mild reaction conditions, resulted in the selective reduction of a variety of polynitroaromatic compounds in high yields.

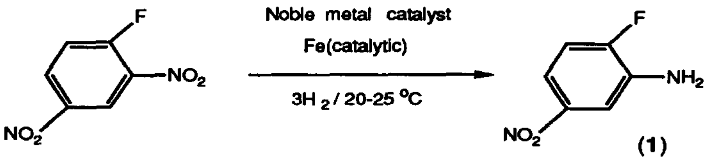
Synthesis of 2-fluoro-5-nitroaniline (**1**), an intermediate in the preparation of herbicides[1,2] and relatively inexpensive when obtained from the selective reduction of 2,4-dinitrofluorobenzene (Sanger's Reagent), was limited to the stoichiometric use of stannous chloride[3,4] in hydrochloric acid or iron in acetic acid.[2] These reductions suffer from labor intensive product work-up, and from yields not high enough to be of interest on an industrial scale.

A survey of the literature immediately reveals that catalytic hydrogenation is not a generally useful approach for selectively reducing substituted dinitrobenzene to nitroaniline derivatives. Preparation of nitroaniline derivatives have, in the past, largely been limited to the reduction of di- and trinitroaromatic compounds with sulfides in a basic medium.[5] Limitations of this method include poor yields and laborious product purification.

More recently a number of catalytic hydrogenations have been reported to selectively reduce polynitrobenzenes.[6-12] Our attempts to apply these procedures to the selective reduction of 2,4-dinitrofluorobenzene met with no success. In all cases, complex tarry mixtures of starting material, both fluoronitroaniline isomers, the fluorodiaminobenzene derivative, and several unidentified products were obtained.

We would like to report a novel method for the catalytic and selective reduction of 2,4-dinitrofluorobenzene using a mixture of a metal catalyst such as PtO_2, 5%Pd(c), $PdCl_2$, or 5%Rh(Al_2O_3) and a catalytic amount of iron in ethanol/glacial acetic acid at room temperature and hydrogen at low pressure. The best results were obtained with $PdCl_2$/Fe. The presence of both acetic acid and iron is crucial; their exclusion from the reaction resulted in low yields of 2-fluoro-5-nitroaniline (**1**) (16-31% yield), longer reaction times, and the formation of highly insoluble tars. The hydrogenation was easily controlled by allowing the reaction mixture to absorb the stoichiometric quantity of hydrogen -- i.e., 3 moles of hydrogen per mole of dinitroarene -- required to reduce one of the nitro groups. Larger quantities of hydrogen than the stoichiometric amount resulted in further reduction of the nitroaniline derivative to the corresponding phenylenediamine product. The replacement of ethanol with dimethoxyethane resulted in lower yields (Table 1).

TABLE 1



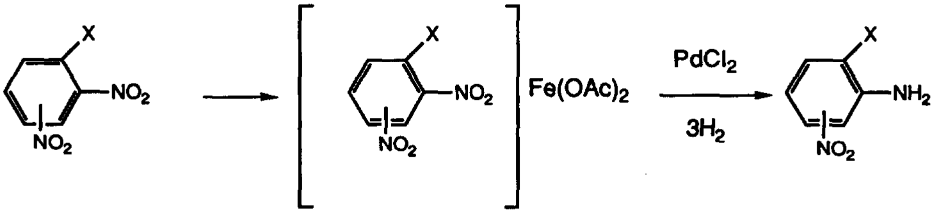
(1)

EXPERIMENT	NOBLE METAL CATALYST (g)	SOLVENT (mL) ETHANOL	SOLVENT (mL) ACETIC ACID	ISOLATED YIELD[a,b](%)	REACTION TIME (minutes)	BLANK[c](%)
1	$PdCl_2$ (0.35)	100	100	87 (80)[d]	45	16
2	5%Pd(c) (0.5)	100	100	79	36	18
3	PtO_2 (0.45)	100	100	79	35	31
4	5%Rh(Al_2O_3) (0.5)	100	100	73	65	18
5	$PdCl_2$ (0.35)	100 dimethoxyethane	100	70	80	-
6	$PdCl_2$ (0.35)	200	-	20	-	-

[a] Hydrogenation conditions: 2,4-dinitrofluorobenzene 18.61 g , 0.10 mole ; 5-45 psi H_2; 20-25°C; Fe 1.4 g, 0.025 mole. [b] Yield of 2-fluoro-5-nitroaniline after purification by silica gel chromatography. [c] Isolated yields when Fe powder was excluded from the reaction. Reaction times range from 100 to 200 minutes. [d] Yields of 2-fluoro-5-nitroaniline when iron powder was replaced with $Fe(OAc)_2$. Reaction conditions: 2,4-dinitrofluorobenzene 18.61g, 0.10 mole; 5-45 psi H_2; 20-25°C; $Fe(OAc)_2$ 4.34g, 0.025 mole.

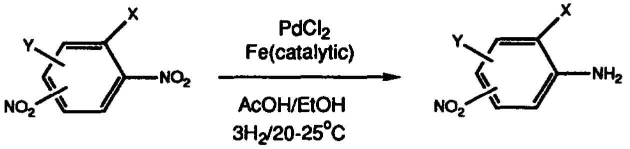
At this stage of our investigations there is no definite evidence for the detailed mechanism by which catalytic amounts of iron give the high degree of selectivity observed in the hydrogenation of polynitroaromatic compounds with noble metal catalysts. One possible mechanism, suggested by previous studies on the interaction of aromatic nitro compounds with transition metals,[12,13] is the complexation of the dinitroaromatic compound with a catalytically active iron species followed by hydrogenation to the corresponding nitroaniline derivative. The catalytically active iron species is possibly $Fe(OAc)_2$, formed from the reaction of iron in acetic acid. When iron powder was replaced with $Fe(OAc)_2$, comparable results were obtained (Table 1, exp. # 1, yield in parentheses). In addition to selectively reducing only one of the nitro groups of dinitroarenes, varying degrees of regioselectivity were obtained in the hydrogenation of several 2,4-dinitrosubstitutedbenzene derivatives to 2-substituted-5-nitroaniline. The highest 2-substituted-5-nitroaniline : 3-nitro-4-substitutedaniline isomer ratio was obtained when X = OH (40:1) followed by X = F (16:1) and X = Cl (3:1) (Table 2). The electronic properties of the X group are likely to play an important role in determining the degree of regioselectivity, though further work is required to establish any definite trends.

$$Fe + 2AcOH \longrightarrow Fe(OAc)_2$$

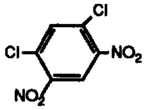
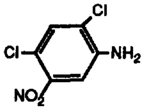
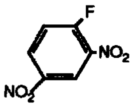
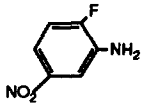
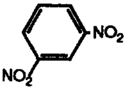
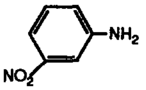
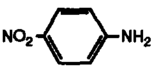
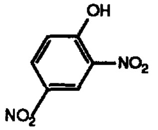
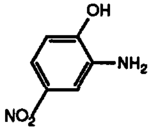
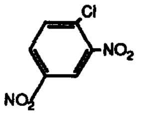
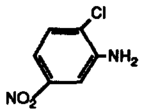


X = H, F, Cl, OH

TABLE 2



X = H, Cl, F, OH
Y = H, Cl

STARTING MATERIAL	MAIN PRODUCT	MELTING POINT (°C)(Lit.mp)	ISOMER RATIO[a]	ISOLATED YIELD[b,c,d](%)	BLANK[e](%)
		104-105(108)[f]	–	90	16
		99-100(101.5)[3]	16:1	87	16
		110-111(110-111)[g]	–	80	21
		146-147(148)[h]	–	80	14
		142-143(142-143)[i]	40:1	79	42
		118-119(119)[4]	3:1	61	11

---

[a] Refers to the ratio of 2-substituted-5-nitroaniline : 3-nitro-4-substitutedaniline. [b] Hydrogenation conditions : Dinitroarene 0.10 mole; 5-45 psi H_2 ; 20-25°C ; Fe 1.40g, 0.025 mole; $PdCl_2$ 0.35g, 0.0020 mole; acetic acid 100 mL; ethanol 100 mL. [c] After purification by silica gel chromatography. [d] The nitroanilines were identified by comparison of TLC, NMR, and mp of authentic samples. Satisfactory analysis was obtained for main products. [e] Isolated yields obtained when Fe powder was excluded from the reaction. [f] Islam, A.M.; Hassam, E.A.; Hannout, I.B.; Morad, M.Y., J.Chem. U.A.R., 1970, 13, 297. [g] Vorontzov, I.I., J. Chem. Ind., 1930, 7, 2145. [h] Votocek, E.; Burda, J.,Ber., 1915, 48, 1004. [i] Hartman, W.W.; Silloway, H.L., Organic Syntheses, Collect. Vol. III, Wiley , New York, N.Y., 1955, p 82.

Selective catalytic hydrogenation was previously achieved by varying the reaction solvents,[6] the pH,[7,8] and the source of hydrogen,[9-10] or by using a homogeneous catalyst.[12] An extensive literature search has shown that this is the first report of a procedure in which a transition metal such as iron, in catalytic amounts, and a noble metal catalyst were combined to provide a highly selective hydrogenation of dinitroaromatic compounds.

Representative Experimental Procedure.

Powdered iron (1.40g, 0.025 mole) and $PdCl_2$ (0.35g, 0.002 mole) were ground together with a mortar and pestle. This mixture was placed in a 500 mL Parr hydrogenation reactor equipped with a thermocouple and a cooling jacket to monitor and regulate the reaction temperature. Ethanol (100 mL) and glacial acetic acid (100 mL) were added, followed by 2,4-dinitrofluorobenzene (18.61g, 0.10 mole). The reaction was allowed to proceed for 75 minutes during which 3 equivalents of hydrogen were taken up at 5-45 psi of pressure. The temperature was maintained between 20-25°C. The solution was filtered, diluted with water (400 mL), and extracted with ether. The organic layer was dried ($MgSO_4$) and removed under reduced pressure. The residue was washed with water and dried to give 14.75g of an orange solid, 95% yield. This material was 94% of the desired isomer, compound (1), and 6% of 3-nitro-4-fluoroaniline as determined by NMR.[14] Column chromatography (silica gel, CH_2Cl_2/heptane 80/20) afforded 13.53g (87%) of **2-fluoro-5-nitroaniline**, m.p. 99-100°C (lit.[3]m.p.101.5°C). The NMR spectra were determined on a Nicolet QE 300 NMR spectrometer and reference to TMS. ^{1}Hnmr ($CDCl_3$): 4.12 (bs, 2H, NH_2), 7.09 (t, 1H, Aromatic), 7.57-7.69 (m, 2H, Aromatic). Anal.Calcd. for $C_6H_5FN_2O_2$: C,46.16; H,3.22; N,17.94; F,12.17; Found: C,46.35; H,2.93; N,17.85; F,12.15.

Acknowledgement. The author thanks the FMC Corporation for permission to publish this paper.

References.

1. Theodoridis, G., FMC Corporation, U.S. Patent 4,868,321 (1989).
2. Takemoto, I.; Fukushima, M., Sumitomo Chemical Co., European Patent Application 127,079 (1984).
3. Swarts, F., Rec.Trav.Chim., 1915, 35, 142.
4. Blanksma, J.J.; Van Den Broek, W.J.; Hoegen, D., Rec.Trav.Chim., 1946, 65, 329.
5. For a review see: Schroter, R. 'Amine durch Reduktion', Methoden der Organishcen Chemie, ed. Eugen Muller, Georg Thieme Verlag, Stuttgart, 1957, 11/1, p. 474 ff.
6. Lyle, R.E.; LaMattina, J.L., Synthesis, 1974, 726.
7. Brunner, W.H.; Halasz, A., U.S. Patent 3,088,978 (1963).
8. Jones, W.H.; Pines, S.H.; Sletzinger, M., Ann. N.Y. Acad. Sci., 1973, 214, 150.
9. Terpko, M.O.; Heck, R.F., J.Org.Chem., 1980, 45, 4992.
10. Miesel, J.L.; O'Doherty, G.O.P.; Owen, J.M., Catalysis in Organic Synthesis, eds. Rylander, P.N., and Greenfield, H., Academic Press, New York, 1976, p. 273.
11. Pitre, D.; Lorenzotti, E., Chimia, 1965, 19, 462.
12. Knifton, J.F., J.Org.Chem., 1976, 41, 1200.
13. Izakovich E.N.; Khidekel M.L., Russian Chemical Reviews, 1988, 57, 419.
14. Both fluoronitroaniline isomers were identified by comparisons of TLC, NMR, and mp of authentic samples (Aldrich Chemicals).

(Received in USA 11 January 1990; accepted 17 July 1990)