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HOMOGENEOUS HYDROGENATION OF NITROALIPHATIC COMPOUNDS CATALYZED BY GROUP VIII TRANSITION METAL PHOSPHINE COMPLEXES

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Abstract. A variety of Group VIII transition metal phosphine complexes were shown to be active catalysts for hydrogenation of nitroaliphatic compounds. The catalysis was determined to be homogeneous based on results of selective catalyst poisoning experiments using dibenzo[a,e]cyclooctatetraene and Hg. A deuterium labeling study showed that in the absence of added base the primary hydrogenation pathway does not involve intermediates containing C=N bonds.

INTRODUCTION

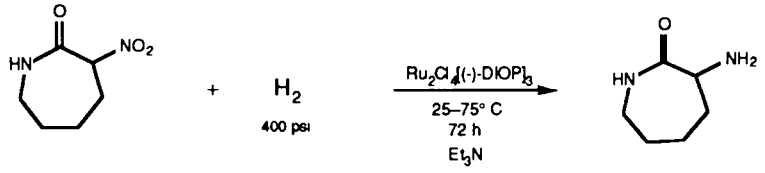
The catalytic hydrogenation of aromatic nitro compounds to amines has long been recognized as one of the most facile processes in heterogeneous catalysis.[1] However, hydrogenation of aliphatic nitrocompounds[2] using heterogeneous catalysts is significantly more sluggish. While the reaction can be effected in good yields, it requires higher temperatures and pressures, longer reaction times, and often the presence of acid.[1a,3] One hypothesis put forth to explain this difference in reactivity is that the aliphatic amine products, being more basic than aromatic amines, are more effective at binding to and poisoning active catalytic sites.[4] Acid is believed to increase the yield by protonating the amine product, rendering it incapable of poisoning the catalyst.

In contrast to the work on heterogeneous catalytic hydrogenation of aliphatic nitro compounds to amines, few reports using homogeneous catalysts exist. While several authors have reported on the reductive carbonylation of nitroaliphatics,[5] these systems involve reaction conditions substantially different from those typical for catalytic hydrogenation, probably involve nitrene-like intermediates, and as such would be expected to result in differing products and selectivities. The earliest report[6] of homogeneous catalytic hydrogenation involves use of a cyanocobalt complex in strongly basic media to reduce

1. (a) Rylander, P. "Catalytic Hydrogenation in Organic Synthesis"; Academic Press: New York, 1979; p. 113. Freifelder, M. "Catalytic Hydrogenation in Organic Synthesis"; Wiley: New York, 1978; p. 26. (b) Anton, D. R.; Crabtree, R. H. *Organometallics* **1983**, *2*, 855.
2. We define aliphatic nitro compounds as those compounds containing a nitro group attached to an aliphatic (sp^3-hybridized) carbon, regardless of any other functionality in the molecule.
3. (a) Suggitt, R. M. U.S. Patent 3 845 130, 1974. (b) Iffland, D. C.; Cassis, F. A. *J. Am. Chem. Soc.* **1952**, *74*, 6284. (c) Tyrone, P. F. U.S. Patent 2 587 572, 1952.
4. Yao, H.-C.; Emmett, P. H. *J. Am. Chem. Soc.* **1961**, *83*, 796.
5. Alper, H.; Amaratunga, S. *Tet. Lett.* **1980**, *21*, 2603.
6. Murakami, M.; Kawai, R.; Suzuki, K. *Nippon Kagaku Zasshi* **1963**, *84*, 669, *C.A.* **1964**, *60*, 4053b.

$EtNO_2$ to $EtNH_2$. Significant amounts of EtOH and acetaldehyde were also produced. The same catalyst promoted hydrogenation of t-$BuNO_2$ to t-$BuNH_2$ in 13% yield. The $RhCl_3$(pyridine)$_3$/$NaBH_4$ catalyst system developed by McQuillen was found to catalyze the hydrogenation of nitrocyclohexane to cyclohexylamine,[7] but more recent work by Crabtree suggests that that catalyst system is in fact heterogeneous.[1a] Knifton[8] found that nitrododecanes were hydrogenated to amines in the presence of 1 to 33 mole% $RuCl_2(PPh_3)_3$. Turnover numbers were significant when 200 mole % strong base (KOH) were present, but no demonstration of equally high numbers was made in the absence of base. Knifton postulates that the nitronate salt is more reactive toward hydrogenation than the nitro form, and basic reaction conditions are therefore preferred. This raises concerns about achieving efficient catalysis for base-sensitive nitrocompounds such as 1,2-nitroalcohols.

A chiral ruthenium dimer, Ru_2Cl_4[(-)-DIOP]$_3$, was used by Monsanto workers[9] to asymmetrically hydrogenate 3-nitrocaprolactam to (+)-3-aminocaprolactam (39% e.e.), a precursor to L-lysine.



As with the previous case, two equivalents of base, albeit a weak one (Et_3N), were added to the reaction mixture. Due to the high acidity of the α-proton of α-nitroketones, this undoubtedly deprotonates the substrate to generate the nitronate, which the authors believed was a necessary first step. Other types of aliphatic nitro compounds were claimed but not substantiated by experimental results or details. Klabunovskii et al.[10] have reported a similar transformation using $PdCl_2$ as the catalyst and S-α-phenethylamine as the chiral auxiliary in a 0.18:1.5 ratio relative the the nitro compound. An 11% e.e. was reported. They also report that α-nitrocaprolactam is *not* hydrogenated in the presence of a rhodium catalyst.

While the work reported herein was in progress, Bose and Saha[11] described a Pd-based system that reduced a variety of nitro-substituted hydrocarbons to the corresponding amines. They found that while yields were high and turnovers significant, the reaction only proceeded well when highly polar, coordinating solvents (DMF, DMSO) were employed, which served to keep the catalyst, $Pd_2(BOP)_2(OAc)_2$ (BOP = 2-benzoylpyridine), in solution.

Based on these reports, we wished to establish whether conditions and catalysts more typical of those used to homogeneously hydrogenate olefins could be applied to aliphatic

7. Love, C. J.; McQuillen, F. J. *J.Chem. Soc. Perkin Trans. 1* **1973**, 2509.
8. Knifton, J. F. In "Catalysis in Organic Synthesis 5th", Rylander, P. N., Ed; p. 257. Knifton, J. F. *J. Org. Chem.* **1975**, *40*, 519.
9. Bachman, G. L.; Sabacky, M. J.; Eur. Patent Appl. 0 083 332, 1983.
10. Klabunovskii, E. I.; Gogoladze, D. D.; Levitina, E. S.; Karpeiskaya, E. I.; Godunova, L. F.; Kaigorodova, L. N.; Chivadze, G. O. *Izv. Akad. Nauk SSSR Ser. Khim.* **1987**, 1597.
11. Bose, A.; Saha, C. R. *Chem. Ind. (London)* **1987**, 199.

nitro compounds, and whether base-sensitive nitro compounds such as 1,2-nitroalcohols could survive these conditions and form aminoalcohols.

RESULTS AND DISCUSSION

2-Nitro-1-butanol was chosen as the initial substrate for study, due primarily to the commercial importance of the D-form of its reduction product, 2-amino-1-butanol.[12] Table 1 shows that when the nitroalcohol was hydrogenated in the presence of a variety of "typical" hydrogenation catalyst systems, moderate to good yields of the aminoalcohol were indeed obtained.

Table 1. Hydrogenation of 2-Nitro-1-butanol[a]

Catalyst	Amount Catalyst (mole %)	Reaction Time (h)	Reaction Temperature (° C)	Hydrogen Pressure (psi)	Yield	Turnover #
$Rh_2Cl_2(NBD)_2/Ph_2PCH_2CHMePPh_2$ (1/1)[b]	5%	20	60	1000	78%	16
$Rh_2Cl_2(NBD)_2/PPh_3$ (1/1)[b]	4%	16	50	1000	36%	9
$Rh_2Cl_2(NBD)_2$/DIOP (1/1)[b,c]	5%	65	80	400	57%	11
$Ir_2Cl_2(COD)_2$/PPFA (1/2)[d]	0.5%	16	50	1000	67%	134
$Ir_2Cl_2(COD)_2$/PPFA (1/2)	1%	16	50	1000	65%	65
$Ir_2Cl_2(COD)_2$/BPPFA (1/2)[e]	1%	16	50	1000	56%	56
$Ir_2Cl_2(COD)_2$/DIOP (1/2)	1%	16	50	1000	54%	54
$Ir_2Cl_2(COD)_2$/DIPHOS (1/2)[f]	1%	16	50	1000	47%	47
$Ir_2Cl_2(COD)_2$/DIPHOS (1/4)	1%	16	50	1000	24%	24
$PdCl_2(PhCN)_2$/BPPFOH (1/1)[g]	0.5%	18	75	1000	41%	82

[a] Reactions run in EtOH with substrate concentration of 0.2 – 0.4 *M*. Yields determined by capillary GC using dodecane as an internal standard. [b] Solvent EtOH/Toluene 1/1. [c] DIOP = S,S-2,3,O-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane. [d] PPFA = (R)-α-[(S)-2-(diphenylphosphine)ferrocenyl]ethyldimethylamine. [e] BPPFA = (R)-α-[(S)-2,1'-bis (diphenylphosphine) ferrocenyl]ethyldimethylamine. [f] DIPHOS = bis(1,2-diphenylphosphino)ethane. [g] BPPFOH = (R)-α-[(S)-2,1'-bis(diphenylphosphine)ferrocenyl]ethanol.

The metal phosphine complexes were formed in situ by charging the organometallic precursor containing an easily displaceable ligand (norbornadiene, 1,4-cyclooctadiene, PhCN) and the phosphine to the reaction. In most cases the pressure of H_2 was 1000 psig; pressures below 400 psig resulted in no or very slow reactions. Turnover numbers, calculated by determining the molar ratio of desired product to catalyst, while modest, were clearly indicative of catalytic activity. The reaction produced few other products detectable by GC, although n-propylamine and MeOH, which would have resulted from reduction of 1-nitropropane and formaldehyde (retro-Henry products from 2-nitro-1-butanol)[13] would

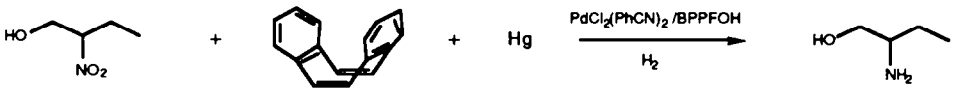
12. Windholz, M., Ed. "The Merck Index," 10th ed; Merck & Co. Inc.: Rahway, N.J., 1983; p. 63. Grayson, M. Ed. "Kirk-Othmer Encyclopedia of Chemical Technology," 3rd ed.; Wiley: New York, 1978; Vol. 2, p. 362.
13. Baer, H. H.; Urbas, L. In "The Chemistry of the Nitro and Nitroso Groups"; Feuer, H., Ed.; Krieger: Huntington, N.Y., 1981; Part 2, Chapter 3, p. 113.

have escaped detection due to co-elution with solvent. When toluene was used as a co-solvent, a significant amount of methylcyclohexane was detected, resulting from toluene hydrogenation. While a variety of chiral phosphines were tested, in no case did the 2-amino-1-butanol produced have an e.e. in excess of 5%.

While the metal complex which is initially added to these reaction systems is soluble one cannot *a priori* rule out the possibility that under these reducing conditions the complex is forming enough of a metal (0) precipitate[4] or colloid[5,14] to be responsible for the observed catalysis. In fact, heterogeneous catalysts are so active for aromatic nitro hydrogenation that observation of formation of aniline from nitrobenzene has been proposed as a test for the presence of a heterogeneous catalyst.[15] Since the goal in this work has been to develop homogeneous catalysts with which to realize the enhanced selectivity and activity they are noted for, it became important to demonstrate that our catalysts were in fact homogeneous. A variety of tests have been described to distinguish between heterogeneous and homogeneous catalysts,[1b,16] but perhaps the most definitive are two complimentary procedures developed by Crabtree[1b] and Whitesides.[17] Crabtree showed that dibenzo[a,e]cyclooctatetraene (DCT) poisons homogeneous hydrogenations catalysts based on iridium and rhodium, irreversibly occupying two coordination sites on the metal. DCT had no effect on the heterogeneous catalysts Crabtree studied. In contrast, liquid Hg was shown to inhibit heterogeneous catalysts, but have no effect on homogeneous catalysts.

Table 2 shows the effect that additions of DCT and Hg had on yields of 2-amino-1-butanol when $PdCl_2$(S,R-BPPFOH) was used as the catalyst.

Table 2. Selective Poisoning of Pd(II)-catalyzed Reduction of 2-Nitro-1-butanol[a]



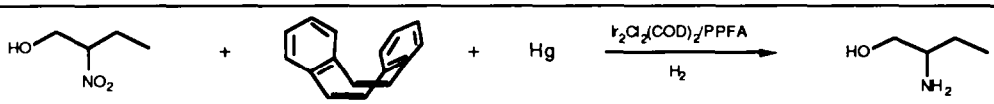
Relative Molar Ratios:				Yield
100	-	-	0.5/0.5	41±5 %[b]
100	-	1600	0.5/0.5	36±4 %[c]
100	0.5	-	0.5/0.5	< 10%
100	1.0	-	0.5/0.5	0 %

[a] Reactions run in EtOH with 0.34 M nitrobutanol; 50° C, 1000 psi, 16 h. [b] Reaction temperature 75° C, time 18 h. [c] Reaction temperature 75° C.

14. Yao, H.-C.; Emmett, P. H. *J. Am. Chem. Soc.* **1959**, *81*, 4125. Dunworth, W. P.; Nord, F. F. *ibid.* **1950**, 72, 4197.
15. See ref. 1b. However, this is probably not a valid assumption, in light of the work of Mestroni (Mestroni, G.; Zassinovich, G.; del Bianco, C.; Camus, A. *J. Mol. Catal.* **1983**, *18*, 33), who observed that Ir(I) catalyzed hydrogen transfer from isopropanol to nitrobenzene. The reported dependence of selectivity and rate vs. ligand make it unlikely that the active catalyst is heterogeneous in that system.
16. Laine, R. M. *J. Mol. Catal.* **1982**, **14**, 137.
17. Foley, P.; DiCosimo, R.; Whitesides, G.M. *J. Am Chem Soc.* **1980**, *102*, 6713. Whitesides, G. M.; Hackett, M.; Brainard, R. L.; Lavalleye, J.-P. P. M.; Sowinski; A. F.; Izumi, A. N.; Moore, S. S.; Brown, D. W.; Staudt, E. M. *Organometallics* **1985**, *4*, 1819.

It is clear that addition of Hg had no effect on the reaction, suggesting that the Pd responsible for catalytic hydrogenation is not heterogeneous. When DCT was added, however, the yield dramatically decreased, consistent with catalysis by a homogeneous complex. In Table 3, analogous results are presented for hydrogenation catalyzed by in situ-generated IrCl(COD)(S,R-PPFA).

Table 3. Selective Poisoning of Ir(I)-catalyzed Reduction of 2-Nitro-1-butanol[a]



Relative Molar Ratios:				Yield
100	-	-	1.0/1.0	67±8%
100	-	1600	0.5/0.5	43±5%[b]
100	0.5	-	0.5/0.5	50%
100	1.0	-	0.5/0.5	0 %

[a] Reactions run in EtOH with 0.21 *M* nitrobutanol; 50° C, 1000 psi, 16 h. [b] Reaction temperature 75° C.

In this case the evidence is more ambiguous. Addition of Hg causes a measurable but not complete loss of yield, as does addition of a 1:1 molar ratio of DCT to Ir. However, a 2:1 molar ratio has a dramatic effect, completely inhibiting the reaction. Thus the mostly likely course is a homogeneous one, although an additional complexity arises relating to the number of equivalents of DCT necessary to poison the system, which must relate to the number of available coordination sites on the Ir during the catalytic cycle (*vide infra*).

The hydrogenation of 1-phenyl-2-nitropropane provides amphetamine, the prototype drug for an important class of sympathomimetic agents.[18] Table 4 summarizes results using several catalyst systems.

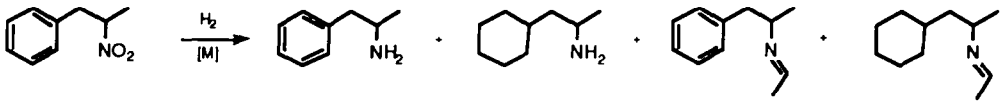
Table 4. Hydrogenation of 1-Phenyl-2-nitropropane[a]

Catalyst	Catalyst Amount (mole %)	Reaction Time (h)	Reaction Temperature (° C)	Hydrogen Pressure (psi)	Yield	Turnover #
$Rh_2Cl2(NBD)_2/Ph_2PCH_2CHMePPh_2$ (1/1)	2%	16	60	1000	58%	29
$Rh_2Cl2(NBD)_2/Ph_2PCH_2CHMePPh_2$ (1/1)[b]	2%	16	60	1000	50%	25
$Rh_2Cl2(NBD)_2$/DIOP (1/1)	2%	16	60	1000	53%	26
$Ir_2Cl_2(COD)_2/(PPh2CHMe)_2$ (1/2)	1%	16	60	1000	45%	45
$PdCl_2(PhCN)_2$/PPFA (1/1)	1%	16	60	1000	44%	44
$PtCl2(PhCN)_2$/PPFA (1/1)	1%	16	60	1000	42%	42

[a] Reactions run in EtOH with substrate concentration of 0.12 *M*, 1.0 equivalents LiOMe. Yields determined by capillary GC using dodecane as an internal standard. [b] Solvent EtOH/Toluene (1/1).

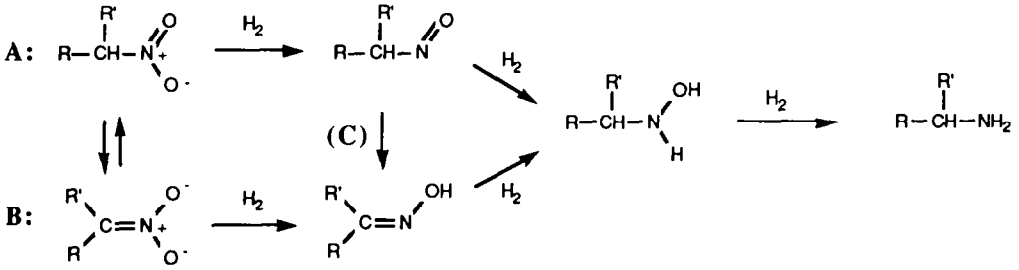
18. Lednicer, D.; Mitscher, L. A. "The Organic Chemistry of Drug Synthesis"; Wiley: New York, 1980; Vol. 2. p. 47.

Yields were moderate, and again the turnover numbers demonstrated that the metal was involved in a substantial number of cycles. Since this substrate does not decompose in the presence of base, we were able to perform the hydrogenations in the presence of LiOMe, forcing formation of the nitronate salt prior to reduction (*vide infra*). Again, no e.e's greater than 5% were detected. The reduction afforded, in addition to the desired amphetamine, products derived from both aromatic ring reduction and imine formation.



Imine formation must arise by catalytic dehydrogenation of the ethanol solvent,[19] generating acetaldehyde, which can react with the amine to form the observed imine products. Systems containing rhodium usually produced substantial amounts of the ring-hydrogenated products. This is not surprising, in light of aromatic ring reduction catalyzed by similar complexes at much lower pressures.[20]

Mechanism. The mechanistic steps involved in the reduction of an aliphatic nitro group to an amine have, to our knowledge, never been well defined, although homogeneous hydrogenation of aromatic nitro groups have been proposed to proceed via nitroso and hydroxylamine intermediates.[21] A key to the mechanism for aliphatic compounds is the effect of the hydrogenation on the carbon center bound to the nitro group (*ipso* carbon). Two basic types of pathways can be considered: one (B) which involves any sp^2-hybridized *ipso* carbon intermediate, and another (A) which does not.

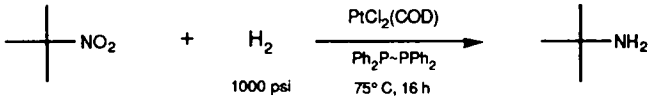


The practical effects that distinguish these two pathways are that (1) the α-hydrogen of the amine is not necessarily the hydrogen that originated in the α position of the nitro compound if the B manifold is entered at any point and (2) the initial stereochemistry at the *ipso* carbon of the nitro compound is lost if the B manifold is entered at any point. An important consequence of latter is that only by entering manifold B can one hope to achieve an asymmetric synthesis of amines from nitro compounds, as is seen in the Monsanto L-lysine

19. Strathdee, G.; Given, R. *Can. J. Chem.* **1974**, *52*, 2216.
20. Landis, C. R.; Halpern, J. *Organometallics* **1983**, *2*, 840. Pieta, D.; Trzediak, A. M.; Zoilkowski, J. *J. Mol. Catal.* **1983**, *18*, 193.
21. Khandual, P.; Saha, C. R. J. Indian Chem. Soc. 1986, 901. Mestroni *et al.* in ref. 15.

synthesis. Thus, addition of base should enhance the potential for entering manifold B and achieving an asymmetric synthesis, although this presents a problem with base-sensitive nitroalcohols. Even in the absence of base, it is still possible for the reaction to proceed via B rather than A. A low concentration of the nitronic acid and/or nitronate is expected to be in equilibrium with the nitro form,[22] and could hydrogenate at a faster rate. Alternatively, manifold B could be entered by rearrangement of an initially formed nitroso compound to an oxime (C). Such rearrangements are known thermally,[23] although rates are slow enough that hydrogenation might be expected to successfully compete with rearrangement under our conditions.

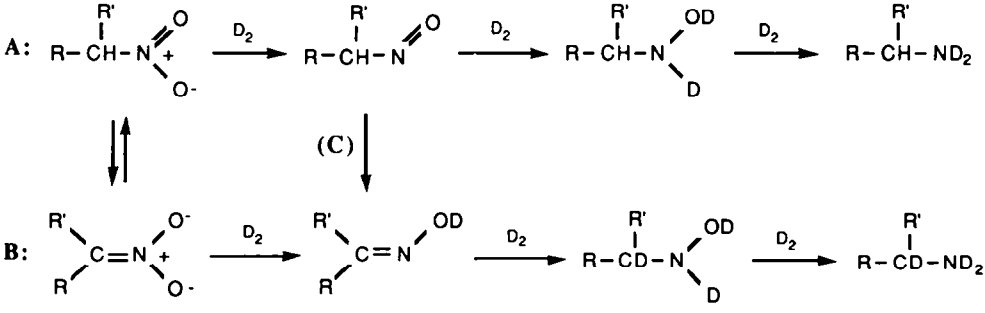
In order to define the pathway involved, initially an attempt was made to reduce a compound structurally incapable of passing through any intermediate involving an sp^2-hybridized *ipso* carbon, 2-methyl-2-nitropropane.



11 %

Under conditions that typically gave ~50% yields of amines from other nitro compounds, t-butylamine was formed in only 11% yield. Unreacted starting material accounted for most of the remainder. While it is tempting to ascribe the low yield to the inability of the molecule to enter a more facile reduction mode involving an sp^2-hybridized *ipso* carbon, it is also possible that manifold A is preferred, and the low yield is due to the steric demand of the substrate.

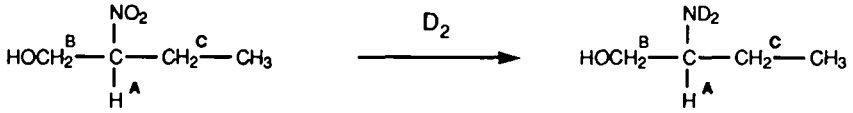
A more probing test that could be directly applied to a substrate of interest, 2-nitro-1-butanol, was to examine the deuterium incorporation into the product when D_2 was used as the reducing agent rather than H_2. Any entry into manifold B would cause deuterium to be incorporated at the ipso carbon in the product when the C-N double bond was reduced.



22. Nielson, A. T.; Cordes, H. F. *Tetrahedron* **1964**, *20 suppl. 1*, 235.
23. Mackor, A.; De Boer, Th. J. *Recl. Trav. Chim. Pays-Bas.* **1970**, *89*, 164.

The hydrogenation was run using $Ir_2Cl_2(COD)_2$/(PPFA) as the catalyst, and 1000 psi D_2. The 2-amino-1-butanol in the crude product was analyzed using ^1H NMR to determine the deuterium incorporation at each position. In addition, signals due to unreacted starting material were examined for signs of deuterium incorporation (Table 5)

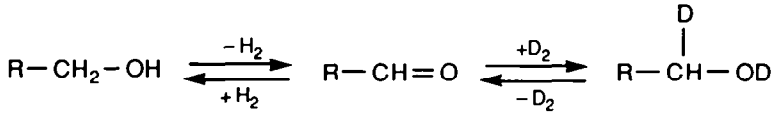
Table 5. Deuterium Incorporation During Reduction of 2-Nitro-1-Butanol[a]



Relative NMR Integrations:		
H^A:	0.60	0.76
H^B:	0.88	0.93
H^C:	1.00	1.00

[a] Reactions run in EtOH with substrate concentration of 0.34 *M*, 1.0 mole % catalyst, 1/1 ratio metal complex/phosphine.

It was found that 24% deuterium had been incorporated on the A carbon of the product. Unfortunately, the deuterium incorporation could not be unequivocally ascribed to D_2 reduction of an sp^2-hybridized intermediate, because 40% exchange had occurred on the A carbon of the starting material. This can be ascribed to exchange of the acidic α-proton of the nitro compound with exchangeable amino deuteria, promoted by the basic amine product.[24] In addition, the hydroxymethyl hydrogens also had incorporated some deuterium. This is most likely a result of dehydrogenation of the alcohol, followed by deuteration.[25]



Thus, while no definitive conclusion can be drawn about the process responsible for the 26% deuterium incorporation at the *ipso* carbon in the product, it is possible to maintain that

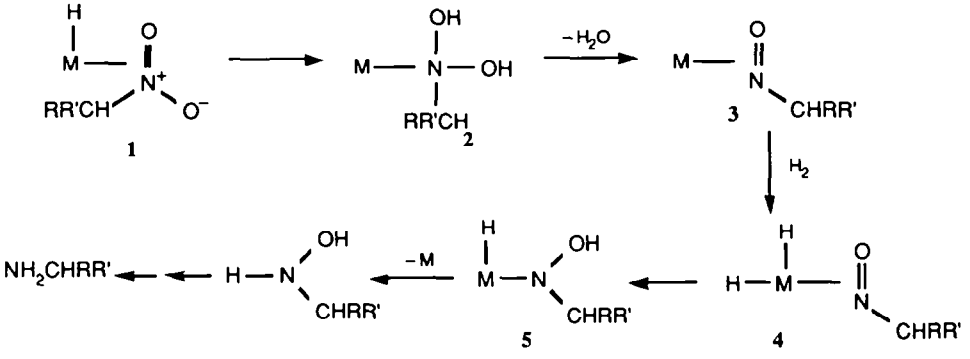
24. A referee has pointed out that participation of the ethanol solvent in exchange processes may complicate interpretation of this data. The exchangeable proton on ethanol should not interfere since it only dilutes the effect of the exchangeable amine deuteria deuterating the starting material. It is possible that dehydrogenation of ethanol contaminates D_2 with H_2 during the course of the reaction. However, we believe that this process is slow relative to reduction, and its effects are minimized by stopping the reaction prior to completion.

25. Group VIII complexes which are catalysts for homogeneous hydrogenation are often active hydrogen transfer catalysts. Martinelli, F.; Mestroni, G.; Camus, A.; Zasinovich, G. *J. Organomet. Chem.* **1981**, *220*, 383. Garnett, J. L.; Hodges, R. J.; Kenyon, R. S.; Mervyn, A *J. Chem. Soc., Perkin Trans. 2* **1979**, 885.

at a minimum, 76% of the reaction occurs via a pathway excluding an sp²-hybridized ipso carbon intermediate. Thus for this system the primary mechanism must involve interaction of the nitro group with the metal center, and successive reduction steps affect only the nitrogen-containing functional group (manifold A).

Mechanisms for the homogeneous hydrogenation can be proposed based on the preceding discussion. Since we have shown that catalysis is predominantly homogeneous rather than heterogeneous, we can use as models known pathways for homogeneous hydrogenation by Group VIII transition metal complexes. The mechanism must account for the variation in number of equivalents of DCT required to inhibit the reaction for Pd and Ir and the deuterium incorporation results indicating a major pathway which excludes and sp²-hybridized *ipso* carbon intermediate.

Scheme 1



Coordination of the nitro compound to the active metal hydride would give **1** (coordination via the N=O bond is an arbitrary, but reasonable, representation). Hydride transfer to one oxygen and protonation of the other either by solvent, or in the case of Ir, by the acidic Ir dihydride,[26] would generate the metal-bound dihydroxylamine **2**. Dehydration would lead to the nitroso complex **3**. Dihydrogen addition to the metal center followed by insertion into the N=O bond would lead to **5**. Reductive elimination would produce a hydroxylamine, which would proceed by an unspecified pathway to the amine.

The Ir/PPFA-catalyzed process was found to be unaffected by 1 equivalent of DCT, but completely inhibited by 2 equivalents. This is consistent with Scheme 1, since the ability of **3** (where M = Ir) to add dihydrogen would be unaffected by ligands occupying three sites (two for DCT and one for the monophosphine PPFA), whereas 2 equivalents of DCT would occupy four sites alone, PPFA a fifth, and 6-coordinate Ir could not then accommodate both substrate and hydrogen. However for the Pd/BPPFOH system, the four sites occupied by DCT and BPPFOH (a diphosphine) would keep **3** from proceeding to **4**, and thus shut down the cycle, an effect that was in fact observed.

26. Anton, D. R.; Crabtree, R. H. *Organometallics* **1983**, 2, 855.

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EXPERIMENTAL

General. Organometallic complexes (Alfa), phosphines (Chemical Dynamics), dodecane (Aldrich, 99%) and EtOH (USI, 200 proof) were used as received. 2-Nitro-1-butanol[27] was distilled before use (b.p. 57–61°C, 1 mm Hg; CAUTION: Explosions have been reported if 2-nitro-1-butanol is distilled above 100°C). 1-Phenyl-2-nitropropane was prepared from 1-phenyl-2-nitropropene (Alfa) by the method of Pakrashi et al.[28] DCT was used as received.[29] Gas chromatographic analyses were carried out on a Varian 6000 GC equipped with FID detectors and a DB-5 capillary column (30 m, 0.25 mm ID, 0.25 μm df). GC/MS analyses were performed using the same column on a Hewlett Packard 5993 GC/MS. 400 MHz ^{1}H NMR spectra were recorded on a Brucker AM 400 NMR.

2-Amino-1-butanol. Standard Hydrogenation Procedure. In a typical run, a 130 ml. capacity stainless steel autoclave was charged with 502.4 mg. (4.22 mmoles) 2-nitro-1-butanol, 14.1 mg. (0.021 mmoles) $Ir_2Cl_2(COD)_2$, 18.5 mg. (0.042 mmoles) (R)-(S)-PPFA, 110.5 mg. dodecane (GC internal standard), and 25 ml. EtOH. The reactor was sealed, pressurized to 1000 psi with H_2, then heated at 50° C for 16 h with stirring. The reactor was then cooled to room temperature, depressurized, and the contents analyzed by capillary gas chromatography. A yield of 67% 2-amino-1-butanol was determined. In some cases, the identity of the 2-amino-1-butanol was verified by removing the volatiles by rotary evaporation, and isolating the product by vacuum distillation.

Catalyst Poisoning Experiments. These experiments were run according to the standard procedure above, except that either DCT or Hg was added to the reactor in the amounts shown in Tables 3 and 4.

Deuterium Labelling Experiments. These experiments were run according to the standard procedure above, except that deuterium was substituted for hydrogen. 400 MHz ^{1}H NMR analysis of the crude product allowed determination of deuterium incorporation by peak integration relative to the CH_2 ^{C} group.

1-Methyl-2-phenylethylamine (Amphetamine). Standard Hydrogenation Procedure. A 130 ml. capacity stainless steel autoclave was charged with 0.500 g. (3.03 mmoles) 1-phenyl-2-nitropropane, 13.8 mg. (0.030 mmoles) $Rh_2Cl_2(NBD)_2$,12.4 mg. (0.030 mmoles) R-Prophos, 0.150 g. dodecane (GC internal standard), and 25 ml. EtOH. 7.1 ml. of a 2.4 *M* solution of LiOMe in MeOH (2.9 mmoles) was added. The autoclave was sealed, pressurized to 1000 psi with H_2, then heated to 60 °C for 16 hours with stirring. After cooling to room temperature and depressurizing, the contents were analyzed by capillary GC and GC/MS. A yield of 58% amphetamine was determined, along with peaks characterized by GC/MS as 1-methyl-2-cyclohexylethylamine, N-ethylidene-1-methyl-2-cyclohexylethylamine, and N-ethylidene-1-methyl-2-phenylethylamine. The identity of the latter was confirmed by matching GC retention times with a authentic sample prepared from the reaction of amphetamine with acetaldehyde.

27. We thank G. O'Neill, Organic Chemicals Division, W. R. Grace & Co. for a sample of 2-nitro-1-butanol.
28. Bhattacharjya, A.; Mukhopadhyay, R.; Pakrashi, S. C. *Synthesis* **1985**, 886.
29. We thank R. H. Crabtree, Yale University, for a gift of DCT.