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Synthetically Useful Reactions with Metal Boride and Aluminide Catalysts

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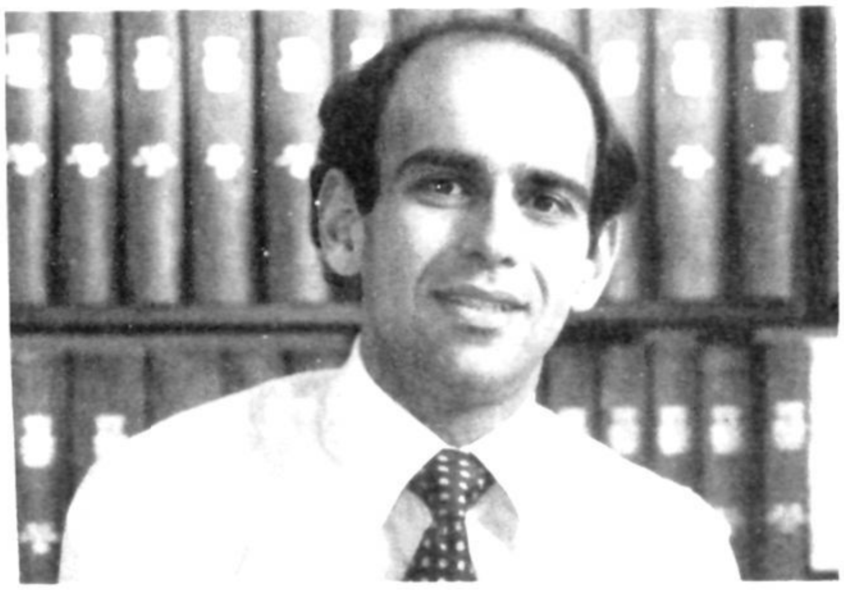
I. Introduction

A. Background

Since the pioneering discovery of nickel-catalyzed hydrogenation by Paul Sabatier, for which he won the Nobel Prize in 1912, organic chemists have been fascinated with transition metals and their compounds as promoters for other synthetically important reductions. In the past 40 years, metal hydrides, particularly sodium borohydride and lithium aluminum hydride, have emerged as preeminent reducing agents in modern organic chemistry.[1,2] These are extraordinarily versatile reagents capable of reducing most functional groups. Moreover by attaching organic ligands at boron or aluminum or changing the metal counterion, one can modulate the scope, regio-, and stereoselectivity of such



Bruce Ganem was born in Boston, MA, in 1948 and attended Harvard College. After graduate study with Gilbert Stork at Columbia University and a National Institutes of Health postdoctoral fellowship with W. S. Johnson at Stanford, he joined the Cornell faculty in 1974 where he became Professor of Chemistry in 1980. Dr. Ganem's early scientific interests in natural products synthesis, synthetic methodology, and bioorganic chemistry have led recently to new interdisciplinary forays into biochemistry, enzymology, and immunology. Current interests include studies on the shikimic acid biosynthetic pathway, the mechanism and function of carbohydrate-processing enzymes, new chemistry of naturally occurring polyamines, and the design and assembly of well-characterized synthetic vaccines.

John O. Osby was born in Denver, CO, in 1958. He received his B.A. degree in Chemistry in 1980 from The Johns Hopkins University. After a one-year industrial position in inorganic analytical chemistry, he entered Cornell University where he joined Professor Bruce Ganem's research group. Dr. Osby's graduate work focused on the mechanism of cobalt(II)- and nickel(II)-promoted sodium borohydride and lithium aluminum hydride reductions. He received his Ph.D. degree in 1985, and has since joined the Dow Chemical Company as a research chemist in Midland, Michigan.

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reductions. Literally hundreds of substituted boron and aluminum hydrides have been described in the chemical literature and dozens are now commercially available.[3,4]

More recently, transition metal salts have been used as catalysts or additives in conjunction with $NaBH_4$ and $LiAlH_4$ to modify or enhance the properties of these reagents. Nearly every conceivable combination of salt and hydride has been investigated with the concomitant development of many useful new synthetic methods.[5] The resulting systems are complex, however, and in most cases virtually nothing is known about mechanism or reactive intermediates. Boron and aluminum hydrides may combine with metal halides in several different ways: (1) simple metathesis (e.g., $LiCl + NaBH_4$, $LiBH_4 + NaCl$),[6] (2) reduction of the metal halide to the metal,[7] (3) conversion of metal halide to metal hydride,[8] (4) some combination of (2) and (3), viz., $FeCl_3 + LiBH_4 \rightarrow Fe(BH_4)_2$,[9] or (5) formation of a boride[10] or aluminide.[11] Furthermore, it is often unclear whether the metal salt serves a true catalytic function or whether some transient, metalloidal complex formed in situ is the actual reducing agent. Recently we had occasion to probe the mechanism of several transition-metal-assisted hydride reductions which are of particular interest to synthetic organic chemists.[12-14] The unambiguous involvement of metal borides and aluminides in case after case we studied prompted us to organize the present review.

B. Catalyst Preparation

1. Borides

Historically, borides were first produced by the combination of boron with metallic or metalloidal elements less electronegative than itself. For the most part, borides are very hard, high-melting, refractory substances whose structures and stoichiometries do not conform to the ordinary concepts of valence. Borides with low boron-to-metal ratios (M_4B, M_3B, M_2B) contain isolated boron atoms, however as the proportion of boron increases (M_3B_2, M_4B_3, M_3B_4), borides with single and double chains of borons appear. Borides with formulae like MB_4, MB_6, and MB_{12} exist in three-dimensional arrays with open networks of boron atoms interpenetrating a regular metal atom lattice.[15,16]

The industrial synthesis of borides usually involves (1) reduction of metal oxides using a mixture of boron carbide and carbon, (2) electrolysis, or (3) direct reaction of the elements. Some borides prepared in this fashion possess good electrical and thermal conductivity properties while others show promise as high-temperature semiconductors. A much simpler synthesis was discovered by H. I. Schlessinger in his pioneering work on borohydrides.[10] Combinations of cobalt or nickel (or other metal salts) with aqueous $NaBH_4$ deposit finely divided black precipitates of Co_2B and Ni_2B (eq 1).

$$4NaBH_4 + 2NiCl_2 + 9H_2O \rightarrow Ni_2B + 3H_3BO_3 + 4NaCl + 12.5H_2 \quad (1)$$

Because they actively catalyzed the decomposition of borohydride,[10] these borides have been commonly used as a practical, controlled source of hydrogen (eq 2).

$$NaBH_4 + 2H_2O \rightarrow NaBO_2 + 4H_2 \quad (2)$$

Other versions of this synthesis have been conducted in alcoholic or ether solvents, under an inert atmosphere like nitrogen, or under hydrogen pressure.[17] Borides have been deposited in the presence of a second (promoter) metal,[18] on inert solid supports,[19] or as colloidal suspensions on solvent-swollen polymers.[20] As will be seen, small variations in the method of preparation can dramatically affect the activity, selectivity, physical, and chemical properties of the boride.[21] Cobalt(II), nickel(II), and copper(II) salts uniformly produce borides when treated with $NaBH_4$ in protic solvents. Iron(III), ruthenium(III), rhodium(III), palladium(II), osmium(VIII), iridium(IV), and platinum(IV) salts afford black precipitates which catalyze $NaBH_4$ decomposition. They may be borides, zerovalent metals, or a mixture (see Table I).[5,22]

TABLE I. NABH$_4$ Reduction of Transition-Metal Cations

metal	element	boride	metal	element	boride
Fe(III)	Fe(0)	Fe(B)	Pd(II)	Pd(0)	Pd(B)
Co(II)		Co_2B	Ag(I)	Ag(0)	
Ni(II)		Ni_2B	Os(VIII)	Os(0)	Os(B)
Cu(II)	Cu(0)	Cu(B)	Ir(IV)	Ir(0)	Ir(B)
Ru(III)	Ru(0)	Ru(B)	Pt(II)	Pt(0)	Pt(B)
Rh(III)	Rh(0)	Rh(B)			

2. Aluminides

The first aluminides of iron and cobalt were reported 30 years ago by Schaeffer and Stewart.[9,11] Reaction of $CoBr_2$ with $LiAlH_4$ in ether gave two mol of hydrogen and a black, pyrophoric precipitate of $CoAl_2$. Likewise $LiAlH_4$ reacted with $FeCl_3$ to give as the ultimate products aluminum, $FeAl_2$, LiCl, and H_2 (eq 8). A series of five discrete processes was proposed to account for the overall stoichiometry in the latter process (eq 3–7).

$$FeCl_3 + LiAlH_4 \rightarrow FeCl_2 + AlH_3 + LiCl + {}^1/{}_2H_2 \quad (3)$$

$$FeCl_2 + 2LiAlH_4 \rightarrow LiCl + FeAl_2H_8 \quad (4)$$

$$FeAl_2H_8 \rightarrow FeAl_2H_6 + H_2 \quad (5)$$

$$FeAl_2H_6 \rightarrow FeAl_2 + 3H_2 \quad (6)$$

$$AlH_3 \rightarrow Al + 1.5H_2 \quad (7)$$

$$\text{overall:}\ FeCl_3 + 3LiAlH_4 \rightarrow 3LiCl + FeAl_2 + Al + 6H_2 \quad (8)$$

C. Catalyst Composition and Properties

1. Borides

The actual composition of borides prepared from inorganic salts depends to a great extent on the specific mode of preparation. Maybury, Mitchell, and Hawthorne analyzed nickel and cobalt borides prepared in ethanol under N_2 using excess $NaBH_4$ and concluded that the stoichiometries Ni_2B and Co_2B inadequately represented their constitution. Besides containing solvent and adsorbed hydrogen, which was released upon heating, the solids were contaminated with tightly trapped NaCl. Freshly precipitated cobalt boride in water slowly liberated hydrogen with formation of boric acid. On the basis of the metal:boron ratio and the amounts of H_2 evolved, the formulae $(Ni_2B)_2H_3$ and $(Co_2B)_5H_3$ were suggested.[23]

The effect of solvent on boride activity and selectivity was first demonstrated by C. A. Brown and H. C. Brown who prepared a series of hydrogenation catalysts by the reaction of $NaBH_4$ with $Ni(OAc)_2$. "P-1" nickel boride prepared in water was considerably more active than Raney nickel and exhibited a markedly lower tendency to isomerize olefins. "P-2" nickel boride prepared in ethanol could selectively hydrogenate olefins and dienes of different substitution patterns, and converted alkynes stereoselectively into *cis*-alkenes.[24] The cis–trans selectivity achieved with P-2 boride could further be improved by the addition of catalyst modifiers such as ethylenediamine.[25]

Most borides of interest have been prepared in protic solvents and are stable to air. However the reaction of $CoBr_2$ with $LiBH_4$ in anhydrous ether formed a greyish-white solid at low temperature, presumed by analogy with other systems to be a cobalt borohydride. Upon warming to room temperature, the solid darkened and hydrogen evolution commenced. Ultimately a black, pyrophoric precipitate of CoB_2 remained which reacted with methanol to form $(CH_3O)_3B$ along with elemental cobalt and hydrogen.[11] To our knowledge, the catalytic properties of this potentially very active boride have not been explored.

Many borides prepared in alcohol or water can be filtered and stored moist without problem. However when dry, they become pyrophoric.[23] They are insoluble in base but hydrolyze readily in acid with vigorous H_2 evolution. X-ray diffraction analysis reveals their structures to be amorphous.[26,27] Certain preparations of nickel boride, however, become crystalline when heated to 250 °C or higher. These crystalline materials have been identified as mixtures of Ni and Ni_2B or Ni_3B. While loss of boron with concomitant crystallization of the structure has been confirmed by several groups,[21] it remains to be seen whether these more ordered borides retain their former activity.

Recently Okamoto et al. have used X-ray photoelectron spectroscopy to examine the surface structure of amorphous nickel boride and nickel phosphide catalysts.[28-30] Studies of the former revealed that surface nickel existed in three forms: Ni(0), nickel oxide (NiO), and boron-bound nickel. Two forms of boron were detected, regardless of the solvent or metal salt used: nickel-bound boron (designated B-I boron) and BO_2^- (designated B-II boron). Analogous components were observed for cobalt boride.

Why does catalyst activity vary so markedly with the method of boride preparation? In the first place, surface contamination by spectator ions such as Na^+ and Cl^- can dramatically reduce activity. The lower the ion's solubility in the boride-forming solvent, the higher its concentration as a surface contaminant. Secondly, two lines of evidence suggest that maximizing boron-bound nickel is the key to preparing active catalysts.[28] (1) Catalytic activity (in hydrogenation reactions) decreases with increasing nickel oxide content, which in turn depends strongly on the starting nickel salt. For example, boride made from nickel chloride contains 17% nickel oxide and is a good catalyst, whereas that from nickel formate contains 85% nickel oxide and is only very weakly active in alkene hydrogenations. (2) The surface concentration of B-I boron (boron-bound nickel) is heavily dependent on the choice of solvent and metal salt. While the boron 1s binding energy for B-I boron in each catalyst remains constant (independent of the precursor salt, reaction temperature and amounts of $NaBH_4$), the specific activity of catalysts increases linearly with B-I boron content. This correlation best explains, for example, why P-1 nickel boride is a more active hydrogenation catalyst than P-2 nickel boride, since the former contains 40% higher levels of B-I boron than the latter. Okamoto et al. conclude that boron bound to nickel (B-I boron) donates electrons to the nickel, resulting in electron-rich sites on the catalyst. The electron-withdrawing effect of phosphorous creates the opposite trend in nickel phosphides. Table II summarizes the surface features of some common borides prepared by reducing metal salts in water.[28] It provides valuable insight to the experimentalist wishing to produce a catalyst possessing specific, well-defined characteristics.

TABLE II. Surface Characterization of Metal Borides

catalyst	precursor	metal %[a]	B/M ratio[b]	%B–I	%B–II	B–H/M[c]
Ni_2B	$Ni(OAc)_2$	61	0.54	51	49	0.45
	$NiSO_4$	86	0.55	58	42	0.37
	$NiCl_2$	83	0.47	56	44	0.32
	$NiBr_2$	77	0.38	56	44	0.27
	$Ni(HCO_2)_2$	ca. 15				
	$Ni(NO_3)_2$	ca. 0				
Co_2B	$CoSO_4$	83	0.37	56	44	0.25
	$CoCl_2$	83	0.38	51	49	0.24
	$Co(HCO_2)_2$	81	0.39	48	52	0.23
	$CoBr_2$	85	0.25	53	47	0.17
	$Co(OAc)_2$	ca. 10				
FeB	$FeCl_2$	81	0.29	22	78	0.08
PdB	$PdCl_2$	94	0.02	67	13[d]	0.01
PtB	H_2PtCl_6	83	0.01	27	13[d]	<0.01

[a] Fraction of metal in total surface metal. [b] Total boron:total metal in surface. [c] Fraction of boron bonded to metal. [d] Remainder is hydrogen.

2. *Aluminides*

Little is known about the surface structure of transition metal aluminides. Cobalt aluminide prepared from $CoBr_2$ and $LiAlH_4$ (see section B.2) has recently been analyzed by argon plasma emission spectroscopy and assigned the empirical formula $CoAl_{1.6}$. However this composition was markedly dependent on the reaction solvent (THF or ether), the specific cobalt(II) salt employed, and even the manner and rate of mixing.[14] Combining solid $CoBr_2$ with diethyl ether solutions of $LiAlH_4$ led to precipitates with high average aluminum content, whereas mixing homogeneous THF solutions of $CoCl_2$ and $LiAlH_4$ resulted in finely divided cobalt aluminide with the lowest aluminum content ($CoAl_{1.1}$). Judging from trends in nickel borides and phosphides, the higher electron density on aluminum should result in even greater electron donation to metals in the corresponding aluminides. We are actively exploring new uses of $NiAl_x$.

D. Useful Reducing Systems

Most of the methods described in this review involve the use of sodium borohydride with borohydride-reduced catalysts. This reducing agent is a colorless, crystalline, high-melting solid which is soluble in water, alcohols, liquid ammonia, ethers, dimethyl sulfoxide, and many other common solvents.[3a] Besides being relatively inexpensive, it is not shock or oxygen sensitive, making it an ideal reagent for use even on an industrial scale.[31]

The combination of $NaBH_4$ with an appropriate metal salt will generally form a black precipitate of the corresponding boride in water or alcohols. However in the presence of complexing ligands,[32] or in good donor solvents like *N,N*-dimethylformamide or *N,N*-dimethylacetamide,[33-35] soluble metal (hydride, borohydride?) species are produced which can catalyze homogeneous hydrogenations or other hydride reductions. The catalytic activity of these species has been reviewed elsewhere.[36] **Caution**: *Concentrated solutions of $NaBH_4$ in DMF in the absence of reducible substrate are unsafe at elevated temperatures. Violent exothermic reactions can occur, generating flammable gases. Dissolving $NaBH_4$ in DMF on a large scale with inefficient cooling is hazardous. To avoid a potential violent reaction, the use of N,N-dimethylacetamide is recommended, especially in processes being conducted at elevated temperature.* This is not to say, however, that borides cannot be prepared in one solvent and then used to catalyze reactions in another. Very little work (besides our own recent effort)[14] has been reported in this area, but more can be expected now that the essential catalytic role of borides has been demonstrated.

Cobalt and nickel borides containing promoter metals such as chromium, molybdenum, tungsten, vanadium, manganese, or rhodium have been synthesized by coreduction of the cobalt or nickel salt with chromium sulfate, sodium molybdate, sodium tungstate, ammonium vanadate, manganese chloride, or rhodium chloride. Analysis of the resulting black precipitates reveals about 2% by weight of promoter. Interestingly, $NaBH_4$ will not reduce any of these promoter salts (except for rhodium) in the absence of Co(II) or Ni(II).[18,21]

Teranishi et al. have prepared cobalt–nickel binary boride catalysts by reducing equimolar mixtures of $Co(Ac)_2$ and $Ni(OAc)_2$ with $NaBH_4$ in water. Such hybrid borides displayed enhanced catalytic hydrogenation activity but selectivity proved superior using cobalt boride containing traces of promoter metals.[37]

For the most part, metal-assisted $NaBH_4$ reductions are carried out using a stoichiometric quantity (sometimes greater) of the metal salt together with excess (2–10 mol equiv) of $NaBH_4$. We have now shown that in many instances reactions can be conducted satisfactorily using much less metal. Since the boride is deposited in situ with concomitant H_2 evolution, good stirring of the heterogeneous system is essential.

II. Reactions Involving Borides and Aluminides

A. Hydrogenation of Alkenes and Alkynes

Many combinations of a transition metal salt with $NaBH_4$ or $LiAlH_4$ promote the reduction of unsaturated compounds, though not all involve borides or aluminides.[5,21] In some cases, premade metal catalysts are used under an atmosphere of hydrogen, while in others the direct reduction of unsaturated compounds by "MX_2-$NaBH_4$" is reported without mentioning whether black precipitates form or hydrogen is evolved—observations which might shed light on questions of mechanism. Borides of nickel, cobalt, palladium, and rhodium along with aluminides of cobalt, nickel, and iron have seen the most widespread use.

1. Borides

The use of nickel boride prepared from $MX_2/NaNH_4$ as heterogeneous hydrogenation catalysts was first reported by Paul et al.[18] These catalysts, together with their "promoted" analogues doped with chromium, molybdenum, tungsten, vanadium, or manganese, formed finely divided black precipitates which when dried under nitrogen were neither pyrophoric nor ferromagnetic. While unpromoted nickel boride was about as active as Raney nickel in the hydrogenation of safrole, furfural, and benzonitrile, it exhibited superior catalyst life. Nickel boride could also selectively hydrogenate alkenes in the presence of ketones, alcohols, and ethers with no detectable hydrogenolysis.[38] Promoted nickel boride was even more active than Raney nickel in most hydrogenations.

Koritala and Dutton prepared Ni_2B by reducing nickel acetate with aqueous $NaBH_4$ under N_2 to produce commercially useful catalysts.[39] In the selective hydrogenation of soybean oil, this boride produced 80–90% mono- or diunsaturated esters and virtually no stearic acid.

In dimethylformamide (DMF) or dimethylacetamide, reduction of $CoCl_2$ or $NiCl_2$ with $NaBH_4$ produced dark brown/black solutions which comprised quite efficient systems for alkene hydrogenation.[33] Suspected to be cluster compounds, the active species are borderline homogeneous/heterogeneous catalysts. Rigorous exclusion of air apparently precluded boride formation in DMF.

In the systematic study of olefin heterogeneous hydrogenation using nickel boride noted earlier,[24,25] C. A. Brown and H. C. Brown observed that P-1 nickel boride (under H_2 in ethanol, room temperature, 1 atm) was considerably more reactive than commercially Raney nickel towards less reactive alkenes like cyclopentene, cyclohexene, and cyclooctene. The P-1 boride was much less likely to isomerize reactive alkenes, and permitted the selective hydrogenation of unconjugated dienes.[24a] Thus 2-methyl-1,5-hexadiene gave pure 2-methyl-1-hexene in 93% yield while 4-vinylcyclohexene afforded ethylcyclohex-3-ene in 99% yield.

When nickel acetate was reduced with $NaBH_4$ in ethanol, the activity of the resulting P-2 nickel boride proved very sensitive to steric hindrance and olefin substitution pattern (Table III). Strained double bonds were readily reduced. Little or no hydrogenolysis of benzylic, allylic, or propargylic compounds was observed, and the partial reduction of dienes and terminal alkynes to monoenes was easily achieved (Table IV). Moreover when P-2 nickel boride was used in conjunction with ethylenediamine, it selectively reduced disubstituted alkynes to *cis*-alkenes in high yield (Table V).[25]

The reduction of diphenylacetylene and methyl hex-3-ynoate to the corresponding *cis*-alkenes has also been accomplished using $NaBH_4/PdCl_2$ in a mixture of polyethylene glycol and CH_2Cl_2.[40] As regards mechanism, the authors noted that "the $PdCl_2$ apparently dissolved completely...but it is not clear whether or not Pd-black [or boride] was generated."

Recently two publications describing the direct reduction of alkenes by $NaBH_4$–$CoCl_2$ in protic or aprotic solvents appeared. In 1979 Chung reported that alcoholic $NaBH_4$–$CoCl_2$ could selectively reduce alkynes as

TABLE III. Hydrogenation of Representative Substrates over 5.0 Mmol of P-2 Ni[a]

compd	initial rate,[b] mmol/min	$T_{50\%}$,[c] min
1-octene	5.3	4.3
3-methyl-1-butene	2.0	10
3,3-dimethyl-1-butene	0.53	48
2-methyl-1-pentene	0.13	720
2-methyl-2-pentene	0.01*	>24 h
2,3-dimethyl-2-butene	0	∞
cis-2-pentene	0.31	120
trans-2-pentene	0.08*	>8 h
cyclopentene	0.6	8.0
cyclohexene	0.08*	>8 h
cycloheptene	2.1	13
cyclooctene	0.67	40
norbornene	5.6	3.4[e]
α-methylstyrene[d]	0.25	120
benzene	0	∞

[a] 40.0 mmol of substrate, 0.8 min, 95% ethanol at 25 °C, 730-mm pressure. [b] Average from 0.0 to 0.2 H_2. * denotes values measured between 0.0 and 0.05 or 0.1 H_2. [c] Time for uptake of 20.0 mmol of H_2. [d] No reduction of aromatic ring. [e] May reflect slight amount of diffusion limitation.

well as mono- and disubstituted alkenes in the presence of more highly substituted olefins.[41] The selective monohydrogenation of limonene was described (see Table VI). No mechanism was proposed, but a cobalt hydride species was invoked as the active reducing agent. In 1984 Satyanarayana and Periasamy reported the solvent dependency of this reduction and contended that reaction of $NaBH_4$ with $CoCl_2$ produced either "CoH_2" (in THF:CH_3OH) or "BH_3" (in THF). Selective hydrogenation of mono- and disubstituted alkenes in CH_3OH (Table VII) was ascribed to the former species.[42]

Earlier this year Osby et al. demonstrated that the selective hydrogenation of limonene with ethanolic $CoCl_2$/$NaBH_4$ could equally well be achieved under heterogeneous conditions using preformed Co_2B and H_2 gas.[14] The boride alone (1 equiv) was incapable of reducing limonene. Homogeneous hydrocobaltation may be considered unlikely since $CoCl_2$ formed Co_2B so rapidly that "CoH_2" species would have been fleeting intermediates at best. Nucleophilic attack by $NaBH_4$ on a homogeneous alkene–cobalt complex also seemed improbable for the same reasons. While $NaBH_4$ might conceivably attack a heterogeneous alkene–Co_2B complex, the fact that limonene could not be reduced over Co_2B using $NaBH_4$ or $LiBH_4$ in either THF or 12:1 THF:CH_3OH (where H_2 evolution is suppressed) rendered this a remote possibility. Thus it would appear, in the two systems reported,[41,42] that $NaBH_4$ functioned solely as a source of H_2 via decomposition over Co_2B.

Russell, Hoy, and Cornelius have surveyed the hydrogenation of nitrogen- and oxygen-containing unsaturated compounds over nickel boride [premade from $Ni(OAc)_2$ and $NaBH_4$ in ethanol or water and then filtered]. Unsaturated amines, amides, ethers, esters, aldehydes, ketones, alcohols, and diols all gave high yields of single compounds resulting from alkene reduction. No hydrogenolysis products were detected by gas chromatography. Only *trans*-cinnamic acid, 1,2-epoxybutane and 2-methyl-1,2-epoxypropane failed to be reduced and controls showed they were not catalyst poisons. Unsaturated nitriles have hydrogenated to saturated primary amines.[43]

TABLE IV. Selective Hydrogenations over P-2 Nickel

compd[a]	product (%)
1-hexyne	*n*-hexane (16)
	1-hexene (68)
	1-hexyne (16)
3-hexyne	*n*-hexane (1)
	cis-3-hexene (96)
	tert-3-hexene (3)
	3-hexyne (0)
1-octene + 2-methyl-1-pentene	*n*-octane (48)
	1-octene (2)
	2-methylpentane (3)
	2-methyl-1-pentene (47)
1-octene + cyclohexene	*n*-octane (49)
	1-octene (1)
	cyclohexane (2)
	cyclohexene (48)
norbornene + cyclopentene	norbornane (47)
	norbornene (3)
	cyclopentane (2)
	cyclopentene (48)
2-methyl-1,5-hexadiene	2-methylnexane (2)
	2-methyl-1-hexene (96)
	other methylhexenes (2)
	2-methyl-1,5-hexadiene (0)
4-vinylcyclohexene	ethylcyclohexane (2)
	4-ethylcyclohexene (97)
	vinylcyclohexane (1)
	4-vinylcyclohexene (0)
isoprene	2-methylbutene (4)
	methylbutenes (91)
	isoprene (5)
1,3-cyclohexadiene[b]	cyclohexane (2)
	cyclohexene (89)
	1,3-cyclohexadiene (0)
	benzene (9)
5-methylenenorbornene	methylnorbornanes (1)
	methylnorbornenes (2)
	2-methylenenorbornane (96)
	5-methylenenorbornene (1)
endo-dicyclopentadiene (2)	tricyclodecane (2)
	dihydro (3) (>97)
	other dihydro (<1)
	dicyclopentadiene (0)
1-penten-3-ol[c]	*n*-pentane (0)
	3-pentanol (100%)
1-vinylcyclohexanol[c]	ethylcyclohexane (0)
	1-ethylcyclohexanol (100)
3-methyl-1-pentyn-3-ol[d]	3-methylpentane (0)
	3-methyl-3-pentanol (100)
1-ethynylcyclohexanol[d]	ethylcyclohexane (0)
	1-ethylcyclohexanol (100)

[a] Hydrogenation of 40.0 mmol of substrate (40.0 mmol of each in mixtures) over 5.0 mmol of P-2 nickel in 95% ethanol at 25 °C, 1 atm; 40 ± 0.8 mmol of hydrogen used. [b] 32.0 mmol of hydrogen. [c] Hydrogen uptake 40.0 mmol. [d] Hydrogen uptake 80.0 mmol.

TABLE V. Stereospecific Reduction of $R^1C{\equiv}CR^2$ by P-2 Ni-eda[a]

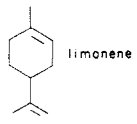
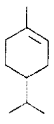
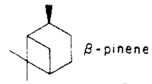
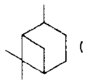
substrate (mmol)	P-2Ni, mmol	% olefin[b]	*cis*:*trans*[b]	total yield, (%)
hex-3-yne (40)	5.0	98	97:1	>95[b]
hex-3-yne (200)	10.0	97	ca. 200:1	>95[b] (80)[c]
1-phenylpropyne (100)	5.0	96	ca. 200:1	>95[b]
hex-3-yn-1-ol (40)	5.0	98	>100:1	94[c]

[a] Amine used was 2–3 × molar amounts of catalyst. There is no evidence that this excess is required. [b] GLC analysis. [c] Isolated yield.

Catalytic quantities (0.1–0.25 equiv) of nickel, cobaltous, cupric, and palladium(II) salts with $NaBH_4$ also reduced methyl cinnamate to methyl hydrocinnamate,[44] and carda-16,20(22)-dienolide to card-17(20)-enolides.[45]

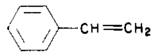
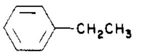
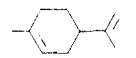
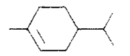
Selective reduction of an alkene by $NaBH_4$ in the

TABLE VI. Reduction of Alkenes and Alkynes by $NaBH_4$ and Co(II)[a]

entry	substrate	product, % yield	mol ratios of substrate/Co(II)/$NaBH_4$	reacn time, h	$T_{1/2}$
1	styrene	ethylbenzene (>98)^b	1/1/2	3.5	<10 min
2	1-octene	*n*-octane (>98)^{b,d}	1/1/2	3	<10 min
3	1-dodecene	*n*-dodecane (95)^{c,d}	1/1/2	3	
4	norbornene	norbornane (>98)^b	1/1/2	3	
5	norbornadiene	norbornane (>98)^b	1/1/2	2.5	
6	cyclohexene	cyclohexane (>98)^b	1/1/2	20	~2 h
7	*cis*-stilbene	1,2-diphenylethane (>98)^b	1/1/2.5	16	<2 h
8	*trans*-stilbene	1,2-diphenylethane (45)^b	1/1/2.5	16	~20 h
9		 (79)^c	1/0.5/1	12.5	~6 h
10		 (44)^c	1/0.5/1	20	
11	1-methylcyclohexene	no reaction	1/1/3	19	
12	α-pinene	no reaction	1/1/2	24	
13	cholesterol	no reaction	1/1/2	23	
14	cholesteryl acetate	no reaction	1/1/2	24	
15	lanosterol	no reaction	1/1/2	24	
16	1-octyne	*n*-octane (>98)^b	1/0.1/1	3	
17	1-octyne	1-octene (>95)^b *n*-octane (trace) 1-octyne (trace)	1/0.1/0.5	3	
18	1,2-diphenylacetylene	*cis*-stilbene (30)^{b,c} *trans*-stilbene (10) 1,2-diphenylethane (10) 1,2-diphenylacetylene (50)	1/0.1/0.5	11	
19	cyclohexanone	cyclohexanone (~30) cyclohexanol (~70)	1/1/2	10	

[a] All the reactions were run in EtOH (see text). [b] Determined by VPC. [c] Determined by NMR. [d] $CoCl_2 \cdot 6H_2O$ and anhydrous $CoBr_2$ could be used interchangeably.

TABLE VII. Hydrogenation of Alkenes with $NaBH_4/CH_3OH$-$CoCl_2$ in THF[a]

alkene	reacn time, h[b]	product[c]	yield,[d] %
$CH_3(CH_2)_7CH{=}CH_2$	3	$CH_3(CH_2)_7CH_2CH_3$	80
	3		65
(*E*) $CH_3(CH_2)_2$	8	$CH_3(CH_2)_6CH_3$	70
α-pinene	12	no reaction	
cholesterol	12	no reaction	
	8		75

[a] The reactions were carried out using 10 mmol of $CoCl_2$, 20 mmol of $NaBH_4$, 60 mmol of CH_3OH and 20 mmol of alkene in THF (40 mL). [b] Time taken after the addition of the alkene into the mixture containing $NaBH_4$-CH_3OH-$CoCl_2$ in THF. [c] The products were identified by spectral data (IR ^1H NMR and ^{13}C NMR) and comparison with the data reported in the literature. [d] Yields are of the isolated and distilled products.

presence of a ketone carbonyl would be unusual. In fact, β-sulfenylated α,β-unsaturated ketones were reduced by using $CoCl_2$ or $NiCl_2/NaBH_4/CH_3OH$ to give the corresponding saturated, desulfurized ketones in excellent yield.[46] However β-dialkylamino-α,β-unsaturated ketones, normally resistant to $NaBH_4$, afforded the corresponding saturated γ-amino alcohols in high yield with $FeCl_3/NaBH_4/CH_3OH$. The authors noted the reddish brown color at the start ($FeCl_3$–enaminoketone complexes) became pale green, but no precipitate of the boride appeared. Nickel and cobalt salts were not as effective.[47] It would be interesting to compare these results with reductions using premade borides.

2. Aluminides

In 1965, Takegami et al. reported systematic studies on the hydrogenation of olefins using various mixtures of $FeCl_3/LiAlH_4$ or $CoCl_2/LiAlH_4$ in THF under H_2.[48] In both cases, the most active catalyst resulted from equimolar mixtures of metal chloride and $LiAlH_4$. Alkenes were classified into three groups according to decreasing ease of reduction by the iron (hydride or aluminide) system: (1) styrene, α-methylstyrene, safrole, isosafrole, indene, anethole, and isoprene were quickly reduced under most conditions; (2) cyclohexene and limonene were only partly reduced; (3) α-pinene, squalene, and furan were not reduced at all. Moreover catalytic activity was killed off when reductions of vinyl acetate, ethyl acrylate, allyl chloride, and acrylonitrile were attempted with the iron-based precipitate. The more active cobalt aluminide smoothly reduced cyclohexene, limonene, α-pinene, squalene, and even furan, albeit more slowly.

Ashby and Lin studied the reduction of alkenes and alkynes by $LiAlH_4$ in combination with first-row transition metal salts.[49] Equimolar mixtures of $LiAlH_4$ reacted with $TiCl_3$, VCl_3, $CrCl_3$, $FeCl_2$, $FeCl_3$, $CoCl_2$, or $NiCl_2$ in THF at low temperature and quantitatively reduced alkenes to alkanes (Table VIII). However when catalytic amounts of the metal halides were used, only $CoCl_2$, $NiCl_2$, and $TiCl_3$ gave alkanes in high yield. Few experimental details were reported. To determine the nature of reactive intermediates, product mixtures were quenched with D_2O and analyzed by gas chromatography–mass spectrometry. Reduction of 1-octene using stoichiometric amounts of $FeCl_2$ or catalytic

TABLE VIII. Reactions of Alkanes with $LiAlH_4$-Transition-Metal Halides

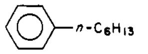
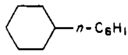
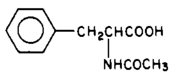
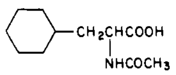
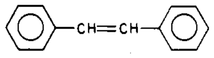
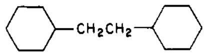
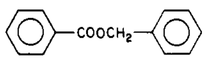
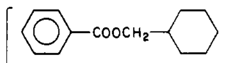
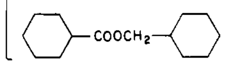
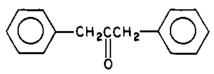
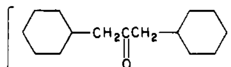
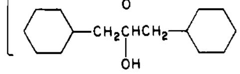
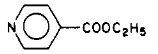
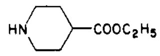
metal halide	alkene	reacn time, h	substrate recovery, %	alkane	yield,[c] %
$FeCl_2$[a]	styrene	24	0	ethylbenzene	95
$CoCl_2$[b]			5		92
$NiCl_2$[b]			0		92
$TiCl_3$[b]			0		94
$FeCl_2$[a]	1-hexene	24	2	hexane	97
$CoCl_2$[b]			0		97
$NiCl_2$[b]			0		97
$TiCl_3$[b]			0		96
$FeCl_2$[a]	*cis*-2-hexene	24	0	hexane	98
$CoCl_2$[b]			70		32
$CoCl_2$[a]			0		98
$NiCl_2$[b]			70		28
$NiCl_2$[a]			3		95
$TiCl_3$			80		18
$FeCl_2$[a]	*trans*-2-hexene	24	0	hexane	99
$CoCl_2$[a]			0		96
$NiCl_2$[a]			0		95
$TiCl_3$[a]			10		90
$FeCl_3$[a]	2-ethyl-1-hexene	24	20	3-methylheptane	80
		48	0		95
$CoCl_2$[b]		48			35
$CoCl_2$[a]		24	0		98
$NiCl_2$[b]		48			15
$NiCl_2$[a]		24	18		82
		48	0		95
$TiCl_3$[b]		48			10
$TiCl_3$[a]		24	10		88
		48	2		94
$FeCl_2$[a]	cyclohexene	24	0	cyclohexane	96
$CoCl_2$[b]		48	45		55
$CoCl_2$[a]		24	0		96
$NiCl_2$[b]		48	60		40
$NiCl_2$[a]		24	2		94
$TiCl_3$[b]		48	95		0
$TiCl_3$[a]		24	60		45
		48	0		95

[a] The molar ratio of $LiAlH_4$-metal halide-olefin is 1.0:10:2.0. [b] The molar ratio of $LiAlH_4$-metal halide-olefin is 1.0:0.1:2.0. [c] Of alkane.

amounts of $CoCl_2$ or $NiCl_2$ gave only 12-26% octane-d_1, whereas 93% deuterium incorporation was observed using $TiCl_3$. On the basis of these data, the reactive species was presumed to be a transition metal hydride, with homolytic dissociation of an intermediate transition metal-alkyl species and subsequent hydrogen abstraction from solvent accounting for the low deuterium content of the products. However, diphenylacetylene was reduced exclusively to *cis*-stilbene by $LiAlH_4$-$NiCl_2$, suggesting a more traditional heterogeneous hydrogenation mechanism for this process.

Ueno and Miya have shown that when excess sodium bis(2-methoxyethoxy)aluminum hydride (SMEAH, Vitride, Red-Al) reacted with $CoCl_2$ or $Co(acac)_2$ in THF, a black precipitate was deposited with evolution of hydrogen.[50] The solid actively catalyzed reduction of styrene, ethyl acrylate, and cyclohexene under an atmosphere of hydrogen. No appreciable deactivation of the catalyst was observed during reduction, and samples more than 2 months old retained activity when stored under argon. Exposure to 1,3-cyclooctadiene (1,3-COD) did change the catalyst's properties: before exposure it failed to reduce cyclooctene, whereas after reduction of 1,3-COD, the catalyst smoothly hydrogenated cyclooctene to cyclooctane. While this behavior was not fully rationalized, cobalt hydride or a cobalt-bridged aluminum hydride were suggested as reactive intermediates.

TABLE IX. Reduction of Aromatic Compounds with $NaBH_4$-$RhCl_3$ in EtOH

arom. compds.	temp, °C	products	yield, %
	40		quant
	30		94
	40		quant
	40	 	75 25
	5	 	22 21
	40		50

B. Reduction of Arenes

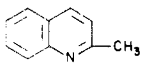
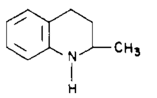
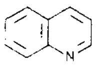
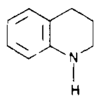
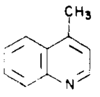
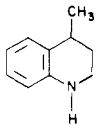
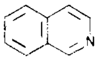
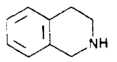
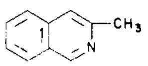
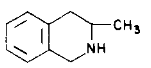
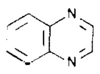
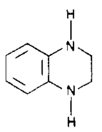
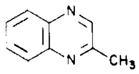
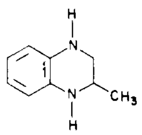
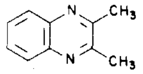
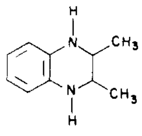
In examining the hydrogenolysis of aryl ketones by $NaBH_4$-noble metal salts, Nishiki et al. observed that aromatic rings were readily saturated when treated with $NaBH_4/RhCl_3$/ethanol in the absence of added hydrogen.[51] Black precipitates were noted upon addition of $NaBH_4$. Carboxylic acids, esters, and amides were unaffected by the reducing agent. In studies with β-phenethyl alcohol, the optimum yield of β-cyclohexylethyl alcohol (100%) required stoichiometric quantities of $RhCl_3$. The stereochemistry of reduction of *p*-*tert*-butylphenol and *p*-*tert*-butyltoluene proved temperature-dependent over the range from -30 °C to 60 °C, with the cis isomers generally predominating. Best results were achieved with monosubstituted benzenes and pyridines (Table IX).

Grundy et al. discovered that benzene was reduced to cyclohexane using $RhCl_3/NaBH_4$/EtOH at 30 °C.[52] Gas chromatographic analysis showed that both cyclohexene and cyclohexadiene were absent in the reaction mixture. This process also worked, but less well, with $RuCl_3$ or $IrCl_3$. In all cases, the metal which had precipitated by the end of the reduction was inactive, suggesting, in accordance with earlier workers, that reduction was stoichiometric both in $NaBH_4$ and in metal.

The partial hydrogenation of several polycyclic aromatic hydrocarbons has also been achieved using $RhCl_3/NaBH_4$.[53]

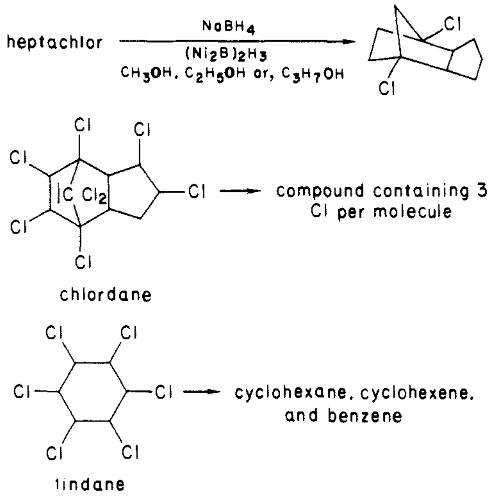
Reduction of heterocyclic compounds using $CoCl_2$, $NiCl_2$, $CuCl_2$, or $CrCl_3$ in conjunction with $NaBH_4$ has been described by Nose and Kudo.[54] Best results were obtained with $NiCl_2$ and excess $NaBH_4$ in CH_3OH at room temperature. Conversion of several quinolines, isoquinolines, and quinoxalines to their tetrahydro derivatives are summarized in Table X. Contrary to the authors' mechanistic claims, several observations in the reduction of quinaldine (entry 1, Table X) suggested that Ni_2B and not $NiCl_2$ complexes were reduced by $NaBH_4$: (1) the reduction was catalytic in $NiCl_2$; (2) in all reductions, exothermic formation of the characteristic boride was accompanied with vigorous H_2 evo-

TABLE X. Reduction of Heterocycles with $NiCl_2/NaBH_4$

compd	mmol	$NaBH_4$, mmol	$NiCl_2$, mmol	solvent	temp	product	yield, %
	8	32	1.4	MeOH	RT[a]		93.5
	8	32	4	MeOH	RT		82.8
	8	80	8	MeOH	RT		83.0
	8	96	8	MeOH	RT		86.7
	8	96	8	MeOH	RT		96.1
	8	160	16	MeOH	RT		54.2
	8	160	16	MeOH	RT		52.4
	8	64	8	MeOH	RT		99.2

[a] RT = room temperature.

TABLE XI. Reduction of Polychlorinated Organics with $NiCl_2/NaBH_4/CH_3OH$



lution; (3) controls further indicated quinaldine was not reduced by catalytic hydrogenation over Ni_2B; (4) tetrahydroquinaldine was produced (31% yield) by using preformed Ni_2B and excess $NaBH_4$. The yield of desired product was somewhat lower, probably because working with the premade boride avoided the uncontrolled temperature rise during exothermic boride formation.

C. Reduction of Halides

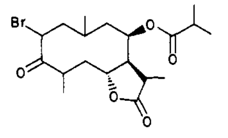
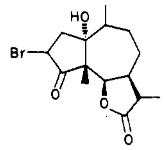
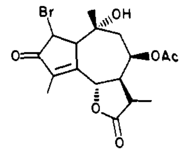
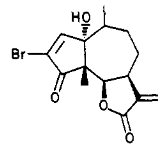
1. Borides

Ordinarily sodium borohydride will not reduce unactivated organic halides. However Dennis and Cooper reported that the combination of Ni_2B catalyst with $NaBH_4$ in alcohol reductively dechlorinated toxic polychlorinated hydrocarbon pesticides (Table XI).[55] Besides the examples shown, both DDT and 2,4-D were extensively dechlorinated. Nickel boride prepared in anhydrous CH_3OH liberated more free chloride than did reductions in ethanol or 2-propanol. The presence of water-retarded reduction, and dehalogenation was less effective using $CoCl_2$, $MnSO_4$, or $FeSO_4$. This method has also found application in the detoxification of polychlorinated biphenyls.[56,57]

In contrast with an earlier report,[33] combining $NiCl_2$ with $NaBH_4$ (1.5 mol equiv) in DMF with no special precautions to exclude air generated a black precipitate of nickel boride which stoichiometrically reduced α-halo ketones to ketones (Table XII).[58] Reaction of *vic*-dibromides using the same procedure afforded alkenes in 80–90% yield. Alkyl chlorides were inert to this boride while bromides and iodides were reduced in only poor yield. In related work, Lin and Roth reacted $(Ph_3P)_2NiCl_2$ with $NaBH_4$ in DMF or THF to reduce aryl bromides. Tris(triphenylphosphine)nickel(0) was suggested to be the active catalyst.[59]

In a recent study of the $PdCl_2/NaBH_4/CH_3OH$ system, Satoh et al. found that aryl chlorides like β-chloronaphthalene and methyl *p*-chlorobenzoate were efficiently reduced to the corresponding arenes.[60] The same method selectively dechlorinated 5,7-dichloro-

TABLE XII. **Reduction of α-Halo Ketones with Nickel Boride**[a–e]

entry	α-halo ketone reduced	% yield[f]
1	2-chlorocyclohexanone	75
2	2-bromocyclohexanone	90
3	2α-bromocholestan-3-one	95
4	3β-acetoxy-7α-bromocholestan-6-one	95
5	*p*-bromophenacyl bromide	98
6	phenacyl bromide	98
7	α-bromocamphor	NR[g]
8	2α-chlorocholest-4-en-3-one	70
9	 9	85
10	 10	90
11	 11	95
12	 12	50

[a] All compounds were characterized by direct comparison (TLC, IR, NMR, and MS) with the authentic samples. [b] Yields refer to the isolated products of >90% purity. [c] Nickel chloride refers to the hexahydrate. [d] The rest of the material in case of entry 8 and 12 was the unreacted starting α-haloketone. [e] Substrates at entry 9, 10, 11, and 12 were prepared from the natural products available in our laboratory. [f] Of parent ketone. [g] NR = no reaction.

6,8-difluoro-1,4-dimethylnaphthalene to 5,7-difluoro-1,4-dimethylnaphthalene in 82% yield.[61]

2. *Aluminides*

Combinations of $LiAlH_4$ with Co(II), Ni(II), Fe(II), Fe(III), Mn(II), Ti(III), Cr(III), and V(III) halides in THF have been studied extensively by Ashby et al. as reducing agents for alkyl halides or tosylates, and aryl halides.[62] Of these, only the $CoCl_2$-, $NiCl_2$-, and $TiCl_3$-based systems were active with *catalytic* quantities of the transition metal salt (Table XIII).

Using the reduction of bromocyclohexane with $CoCl_2/LiAlH_4$ as a representative case, Osby et al. demonstrated that the black precipitate of cobalt aluminide was primarily responsible for cyclohexane formation.[14] The lithium borohydride reduction of halides like 1-chlorodecane was also promoted by CoAl in THF at 65 °C. Studies using $LiAlD_4$ with *cis*- and *trans*-4-bromo-*tert*-butylcyclohexane showed reduction occurred with complete stereochemical scrambling. Apparently THF and *not* the aluminum hydride served as the hydrogen donor in this radical process. In fact, stoichiometric amounts of CoAl were sufficient to reduce *cis*-4-bromo-4-deuterio-*t*-butylcyclohexane to a 43:57 mixture of *cis*- and *trans*-4-deuterio-*tert*-butylcyclohexane. Two plausible mechanisms were proposed (Figure 1): (1) halogen atom transfer from the alkyl halide to a metal radical on the aluminide surface, or (2) oxidative addition of the cobalt catalyst into the carbon–halogen bond. The latter process, besides involving a homolytic alkylcobalt cleavage well-known in the chemistry of vitamin B_{12} and its analogues, was favored by several additional lines of evidence.[63] Both mechanisms correctly rationalize the secondary role of $LiAlH_4$ in regenerating active (reduced) aluminide catalyst.

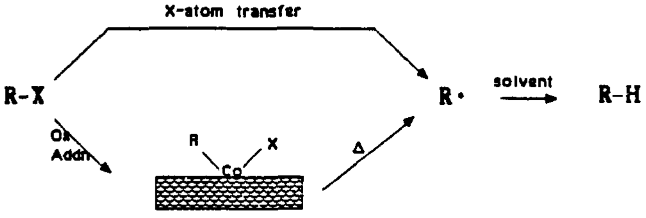


Figure 1. Mechanism of alkyl halide reduction.

A Japanese group recently reported that alkyl and aryl halides (including fluorides) were smoothly reduced using $CeCl_3/LiAlH_4$ in dimethoxyethane (DME) or THF at reflux (Table XIV).[64] Experiments with $LiAlD_4$ furnished products with no detectable deuterium incorporation (Table XIV, entries 4 and 10), again suggesting a radical pathway with H atom abstraction from DME or THF.

D. Reduction of Nitriles

In 1969 Satoh and Suzuki reported that nitriles (along with nitroarenes and amides) were reduced to primary amines by transition metal salt–$NaBH_4$ systems.[65] They found that $CoCl_2$ (2 equiv)/$NaBH_4$ (10 equiv) in CH_3OH was a particularly effective combination, which has since been applied to a wide variety of cases (Table XV).[66–76] Because nitro group reduction required elevated temperatures, the selective reduction of *p*-nitrophenylacetonitrile to *p*-nitrophenethylamine was readily achieved. In a preliminary communication about the mechanism of this reaction,[12] Heinzman and Ganem concluded that the cobalt boride formed in situ served as a true catalyst, strongly coordinating nitriles and activating them towards reduction by $NaBH_4$. Possible homogeneous and heterogeneous hydrogenations were unambiguously ruled out. Subsequent kinetic studies using benzonitrile indicated that at high nitrile:catalyst ratios, the rate of nitrile reduction was independent of its concentration. Moreover the rate of reduction exhibited a first-order dependence on $NaBH_4$ concentration over a 4-fold concentration range and several half-lives of benzonitrile. When the nitrile was reduced with equimolar mixtures of $NaBH_4$ and $NaBD_4$, a primary isotope effect ($k_H/k_D = 3.3$) was observed, consistent with rate-determining hydride attack on the coordinated nitrile by dissolved, uncoordinated borohydride.[14,63] An optimized reduction procedure was developed using catalytic quantities of Co_2B in 2:1 THF:H_2O and avoiding the harshly acidic workup of Satoh and Suzuki.[65]

Besides $NaBH_4$, certain amine boranes like *tert*-butylamine–borane (TAB) were found to reduce nitriles in CH_3OH in the presence of Co_2B (Table XVI). Although stoichiometric quantities of the boride were

TABLE XIII. Reduction of Halides by $LiAlH_4$–Transition-Metal Chlorides at Room Temperatures in THF Solvent[a]

expt	halide substrate[d]	transition metal chloride[b]	reacn time, h	product	yield, %
1	1-chlorodecane[e]	None	24	*n*-decane	68
2		VCl_3			75
3		$CrCl_3$			90
4		$MnCl_2$			19
5		$FeCl_3$			100
6		$FeCl_2$			95
7		$FeCl_2$[c]			85
8		$CoCl_2$[c]			100
9		$NiCl_2$[c]			100
10		$TiCl_3$[c]			100
11	1-bromodecane[e]	None	1	*n*-decane	92
12		VCl_3			40
13		$CrCl_3$			65
14		$MnCl_2$			43
15		$FeCl_3$			50
16		$FeCl_2$			100
17		$FeCl_2$[c]			90
18		$CoCl_2$			98
19		$CoCl_2$[c]			98
20		$NiCl_2$			100
21		$NiCl_2$[c]			100
22		$TiCl_3$			96
23		$TiCl_3$[c]			98
24	1-iododecane	None		*n*-decane	98
25		$FeCl_2$			98
26		$CoCl_2$[c]			98
27		$NiCl_2$[c]			98
28		$TiCl_3$[c]			100
29	1-fluorodecane	None	24	*n*-decane	0
30		$FeCl_2$			16
31		$CoCl_2$[c]			10
32		$NiCl_2$[c]			7
33		$TiCl_3$[c]			9
34	*n*-octyltosylate	None	24	*n*-octane	92
35		$FeCl_2$			25
36		$CoCl_2$[c]			100
37		$NiCl_2$[c]			98
38		$TiCl_3$[c]			54
39	3-bromooctane	None	24	*n*-octane	75
40		$FeCl_2$			90
41		$CoCl_2$			98
42		$NiCl_2$			92
43		$TiCl_3$			88
44	bromocyclohexane	None	24	cyclohexane	0
45		$FeCl_2$			97
46		$CoCl_2$			99
47		$NiCl_2$			99
48		$TiCl_3$			100
49	chlorocyclohexane	None	24	cyclohexane	0
50		$FeCl_2$			98
51		$CoCl_2$			92
52		$CoCl_2$[c]			3
53		$NiCl_2$			95
54		$NiCl_2$[c]			5
55		$TiCl_3$			95
56		$TiCl_3$[c]			95
57	1-bromoadamantane	None	24	adamantane	70
58		$FeCl_2$			100
59		$CoCl_2$			100
60		$NiCl_2$			100
61		$TiCl_3$[c]			100
62	chlorobenzene	None	24	benzene	0
63		$FeCl_2$			72
64		$CoCl_2$			25
65		$CoCl_2$[c]			0
66		$NiCl_2$			100
67		$NiCl_2$[c]			0
68		$TiCl_3$[c]			45
69	bromobenzene	None	24	benzene	0
70		$FeCl_2$			80
71		$CoCl_2$			74
72		$CoCl_2$[c]			23
73		$NiCl_2$			100
74		$NiCl_2$[c]			87
75		$TiCl_3$[c]			91
76	iodobenzene	None	24	benzene	38
77		$FeCl_2$			98
78		$CoCl_2$			98

TABLE XIII (Continued)

expt	halide substrate[d]	transition metal chloride[b]	reacn time, h	product	yield, %
79		$NiCl_2$			100
80		$TiCl_3$[c]			92

[a] All reactions were carried out in THF at −78 °C for 10 min and then warmed to room temperature by removing the cooling bath. The reaction time was counted beginning with the period at −78 °C. Yields were determined by GLC using a suitable internal standard. [b] Molar ratio of $LiAlH_4$ to transition metal chloride is 1:1, except when noted. [c] Used 10% molar equivalent. [d] Halide substrate was used in equivalent molar amount to $LiAlH_4$ except when noted. [e] Halide substrate was $^1/_2$ equiv with respect to $LiAlH_4$.

TABLE XIV. Reduction of Organic Halides with $LiAlH_4$-$CeCl_3$

entry	substrate	conditions[a]	product	yield, %[b,c]
1	$CH_3(CH_2)_{11}F$	THF, reflux, 3 h	$C_{12}H_{26}$	90 (>99)
2	1-fluoronaphthalene	DME, reflux, 3 h	naphthalene	94 (>99)
3[d]	1-fluoronaphthalene	DME, reflux, 3 h	naphthalene	0
4	1-fluoronaphthalene	DME, reflux, 3 h[e]	naphthalene[f]	92
5	2-fluorobiphenyl	DME, reflux, 5 h[g]	biphenyl	94 (98)
6	1-chloronaphthalene	THF, reflux, 3 h	naphthalene	95 (>99)
7[d]	1-chloronaphthalene	THF, reflux, 3 h	naphthalene	37
8	4,4′-dichlorobiphenyl	DMF, reflux, 3 h	biphenyl	92 (>99)
9	2,4-dichlorophenol	THF, reflux, 20 h	4-chlorophenol	81

[a] A molar ratio of 1:4.5:1.5 substrate/$LiAlH_4$/$CeCl_3$ was used unless otherwise stated. [b] Isolated yield. [c] The figures in parentheses indicate the yields determined by GLC. [d] The reaction was carried out in the absence of $CeCl_3$ under the same conditions. [e] $LiAlD_4$ was used in place of $LiAlH_4$. [f] The product was identified by ^1H NMR and mass spectra. [g] Under irradiation with a 200-W W-lamp.

TABLE XV. Reduction of Nitriles Using $CoCl_2$–$NaBH_4$

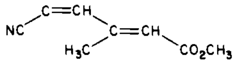
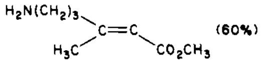
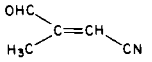
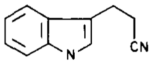
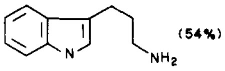
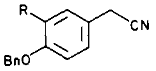
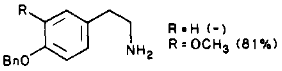
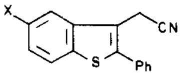
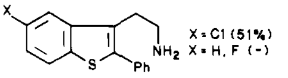
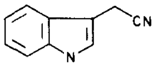
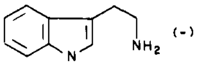
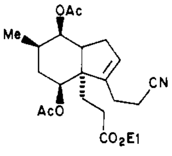
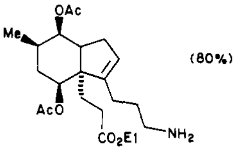
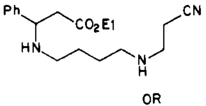
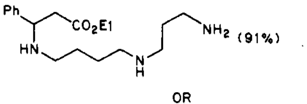
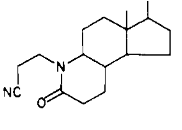
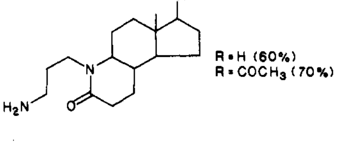
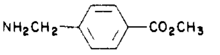
nitrile	product (yield)	ref
C_6H_5CN	$C_6H_5CH_2NH_2$ (72%)	65
C_6H_5CN	$C_6H_5CH_2NH_2$ (91%)	14
p-NO_2-C_6H_4CN	p-$NO_2C_6H_4CH_2NH_2$ (60%)	65
p-OH-C_6H_4CN	p-OH-$C_6H_4CH_2NH_2$ (70%)	65
β-cyanopyridine	β-aminomethylpyridine (35%)	65
furonitrile	furfurylamine (75%)	65
$C_6H_5CH_2CN$	$C_6H_5CH_2CH_2NH_2$ (74%)	12
CH_2=CHCN	CH_2=$CHCH_2NH_2$ (70%)	65
	 (60%)	12
	$CH_3CH(CH_2OH)CH_2CH_2NH_2$ (80%)	66
$NC(CH_2)_2NH(CH_2)_3NH(CH_2)_4NH_2$	$H_2N(CH_2)_3NH(CH_2)_3NH(CH_2)_4NH_2$ (70%)	67
n-$C_7H_{15}CN$	n-$C_7H_{15}CH_2NH_2$ (80%)	65
$C_6H_5CH(OH)CN$	$C_6H_5CH(OH)CH_2NH_2$ (80%)	65, 68
n-$C_6H_{13}CH(OH)CN$	n-$C_6H_{13}CN(OH)CH_2NH_2$ (77%)	68
	 (54%)	69
		70 71
		72
	 (-)	73
	 (80%)	74
		75
		76

TABLE XVI. **Reduction of Organic Compounds Using Co_2B–TAB**

substrate	conditions[a]	product (yield, %)
PhCN	2 equiv TAB, 3 h	$PhCH_2NH_2$ (75%)
$PhCH_2CN$	2 equiv TAB, 7 h	$PhCH_2CH_2NH_2$ (88)
$CH_3(CH_2)_4CN$	2 equiv TAB, 2.5 h	$CH_3(CH_2)_5NH_2$ (81)
	4 equiv TAB, 12.5 h	 (75)
$PhCONH_2$	2 equiv TAB, 3 h	NR[b]
$PhCH{=}CHCO_2CH_3$	2 equiv TAB, 3 h	$PhCH{=}CHCO_2CH_3$ (75)
$CH_3(CH_2)_5C{\equiv}CH$	2 equiv TAB, 2 h	octene (25)[c] octane octyne (75)

[a] All reactions were run with 1 equiv of Co_2B at reflux in CH_3OH under N_2. [b] No reaction. [c] Yield determined by GC.

necessary,[12] "spent" boride from TAB nitrile reductions still actively catalyzed reduction of nitriles by $NaBH_4$. This unusual behavior was later attributed to pH differences between the two reactions.[14] When the pH of TAB–CH_3OH solutions was brought to ca. 8–9 (as in $NaBH_4$–CH_3OH mixtures), the reduction of benzonitrile to benzylamine became catalytic in Co_2B. Since TAB did not decompose to liberate H_2, little or no reduction of alkenes or alkynes occurred, making it a much more selective method (Table XVI).

E. Reduction of Nitro Compounds

1. Nitroarenes

The reduction of aromatic nitro compounds to amines is an important synthetic reaction, especially in large-scale pharmaceutical and industrial chemical processes. Suspensions of tin and iron in acid are commonly employed, as is catalytic hydrogenation. A special example of the latter method is the use of $NaBH_4$ with Pd/C catalyst in protic solvents in converting nitrobenzene to aniline.[77]

The combination of $NaBH_4$ with transition metal salts to reduce nitroarenes has been investigated in detail. In 1962 Brown and Sivasankaran reported that platinum metal salts (e.g. Ru, Rh, Pd, Os, Ir, Pt), when treated with aqueous or ethanolic $NaBH_4$, formed finely divided black precipitates which catalytically reduced nitrobenzene to aniline as $NaBH_4$ decomposed to H_2.[22b,78] In 1969, Satoh and Suzuki described several examples of the same reaction using $CoCl_2/NaBH_4$ in either CH_3OH or dioxane (Table XVII) at 40–100 °C.[65] Yields were modest, and both gas evolution and the formation of black precipitates were noted. In 1970, upon reinvestigating this process, the same research group found that products varied with the reaction conditions and with the choice of metal salt. Nitroarenes furnished azoxy compounds by using $CoCl_2$ (Table XVIII) and amines by using $CuCl_2$.[79] Experimental details rationalized the apparent contradiction in the cobalt experiments: the later paper[79] described the addition of $NaBH_4$ at 20 °C to a stoichiometric mixture of nitrobenzene and $CoCl_2$ in CH_3OH slowly enough to prevent formation of a black precipitate. In the absence of boride, $NaBH_4$ reduction of an unspecified homogeneous cobalt complex must have occurred. Recently Osby noted the same anomalous behavior in the complexation of *nitroalkanes* with Co(II) salts (vide infra).[63]

Nickel chloride exhibited no such peculiarities, and has been used with $NaBH_4$ to reduce nitroarenes to anilines in good yield (Table XIX).[80] Nickel boride supported on charcoal converted *p*-nitrophenylglycosides to *p*-aminophenylglycosides.[81] Other nitroarene reductions using $CuCl/NaBH_4/EtOH$ and $FeCl_3/NaBH_4/EtOH$ have been reported which also probably involve boride catalysts.[82,83]

Numerous homogeneous systems comprised of $NaBH_4$ in combination with soluble transition metal complexes have also been developed for nitro group reductions, but are reviewed elsewhere.[5]

2. Nitroalkanes

Nitroaliphatic compounds have traditionally been reduced to amines by high-pressure hydrogenation, $LiAlH_4$ or aluminum amalgam. More recently, the use of transfer hydrogenation[84] and of low-valent titanium reagents[85] has been recommended. In 1985 Osby and Ganem reported that $NiCl_2/NaBH_4/CH_3OH$ rapidly reduced a variety of primary, secondary, and tertiary nitroalkanes to amines at room temperature (Table XX).[13] Nickel boride, prepared in situ, was the active catalyst, requiring dissolved $NaBH_4$ (and not H_2) as the reducing agent. The reagent selectively reduced nitrocyclohexane in the presence of hexanenitrile. While methanolic $CoCl_2/NaBH_4$ completely failed to reduce nitroalkanes (no boride was formed), premade Co_2B with $NaBH_4$ did slowly convert nitrocyclohexane to cyclohexylamine; however, no selectivity between nitriles and nitro compounds could be achieved.[63]

F. Reduction of Other Nitrogeneous Functional Groups

1. Amides

Besides nitriles and nitro compounds, Satoh and Suzuki reported that primary amides were also reduced to amines using $CoCl_2/NaBH_4/CH_3OH$.[65] However Heinzman and Ganem were unable to reproduce the reduction of benzamide to benzylamine (60% yield reported)[65] even in the presence of excess boride.[12] Other workers have apparently had similar difficulties.[86]

2. Oximes

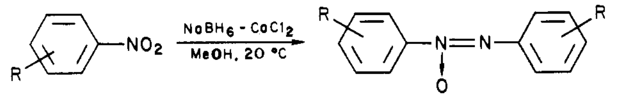
In 1984, Ipaktschi observed that saturated and unsaturated oximes were exhaustively reduced to satu-

TABLE XVII. **Reduction of Aromatic Nitro Compounds with $NaBH_4$–$CoCl_2$ System**

nitro compd	product	solvent (temp)	yield, %
p-$NO_2C_6H_4CH_2CN$	*p*-$NH_2C_6H_4(CH_2)_2NH_2$	CH_3OH (40°)	50
o-$NO_2C_6H_4COOH$	*o*-$NH_2C_6H_4COOH$	dioxane (bp)[a]	40
p-$NO_2C_6H_4OH$	*p*-$NH_2C_6H_4OH$	dioxane (bp)	35
p-$HOC_6H_4CH_2CH(NO_2)CH_3$	*p*-$HOC_6H_4CH_2CH(NH_2)CH_3$	C_2H_5OH (bp)	45
p-$NO_2C_6H_4SO_3H$	*p*-$NH_2C_6H_4SO_3H$	C_2H_5OH (bp)	38

[a] Boiling point.

TABLE XVIII. Reduction of Monosubstituted Nitrobenzenes to Azoxybenzenes with Samarium Borohydride–Cobaltous Chloride



	yield,[a] %	Hammett's constant σ
p-CO_2Me	87	+0.636
p-CO_2Et	86	+0.522
p-CN	86	+0.628
p-Cl	79	+0.227
p-CO_2H	71	+0.132
H	62	+0
p-Me	40	−0.170
p-OMe	19	−0.263
m-Cl	84	+0.378
m-CO_2Me	84	+0.315

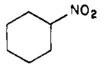
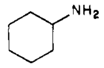
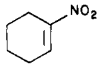
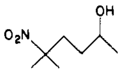
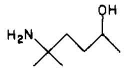
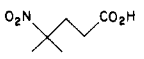
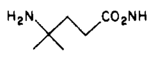
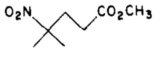
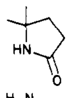
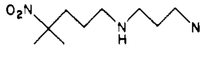
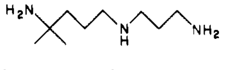
[a] Of azoxy compound.

TABLE XIX. Reduction of Aromatic Nitro Compounds with $NaBH_4$–$NiCl_2$

nitro compd[a]	$NiCl_2 \cdot 6H_2O$, mmol	$NaBH_4$,[b] mmol	product (prim amine)	
			R	yield, %
H	16	64	H	76.3
p-CH_3	16	32	p-CH_3	95.0
m-CH_3	16	32	m-CH_3	94.6
o-CH_3	16	32	o-CH_3	80.5
p-CH_3O	16	32	p-CH_3O	88.9
p-Cl	16	32	p-Cl	89.1
p-OH	16	32	p-OH	88.2
p-COOH	16	32	p-COOH	77.6
o-COOH	8	32	o-COOH	85.6
1-nitronaphthalene[c]	16	32	1-naphthylamine[c]	85.5

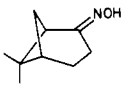
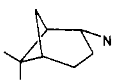
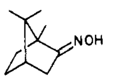
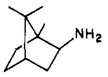
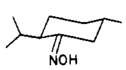
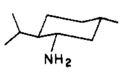
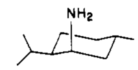
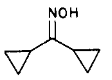
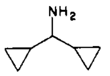
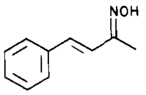
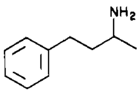
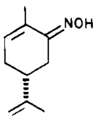
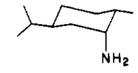
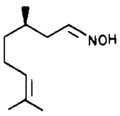
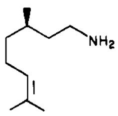
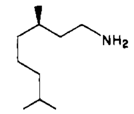
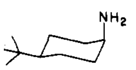
[a] The amount of nitro compound was 8 mmol. [b] The reaction time was 30 min, and the reaction temperature was 20 °C. [c] The chemical name.

TABLE XX. $NaBH_4$–Ni_2B Reductions of Nitro Aliphatic Compounds

reactant[a]	product[b]	yield[c]
		68%[d]
	**2**	66%[d]
$C_8H_{17}NO_2$ **6**	$C_8H_{17}NH_2$ **7**	61%
		76%
		64%
		50%[e]
		69%

[a] All reductions were carried out according to the representative proceudre in section IIE2. [b] Products were identified by comparison with authentic samples, where possible. Satisfactory IR, NMR, and mass spectra were obtained for all new compounds. [c] Yields reported are for isolated, pure compounds. [d] Isolated as its HCl salt; lower yields are due to appreciable water solubility of this product. [e] Product stirred for 2 days at room temperature before workup.

TABLE XXI. Reduction of Oximes with $NiCl_2/NaBH_4$

substrate	product	yield, %
		94
		92
	  (1:2)	92
		70
		95
	  (1:1)	90
	  (1:1)	95
	  (62:38)	95

rated amines at −30 °C using $NiCl_2/NaBH_4/CH_3OH$ (Table XXI). Unsaturated oximes furnished allylic amines when the reduction was carried out with $MoO_3/NaBH_4$. Moreover the stereochemistry of reduction was decidedly different with the two reagent systems. While the reduction mechanisms were not established, the $NiCl_2$ method was shown not to involve heterogeneous hydrogenation.[87]

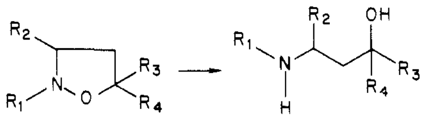
3. Azoxy, Azo, Nitroso Compounds, and Hydroxylamines

In their 1969 survey of heterogeneous boride catalysts, Pratt and Swinden found that Co_2B catalyzed the decomposition of H_2O_2 and promoted the reduction of nitrate to ammonia in the presence of $NaBH_4$. While hydrazine hydrate was catalytically decomposed to ammonia (inter alia) by the boride, the same mixture quantitatively reduced azobenzene to hydrazobenzene in ethanol, apparently by transfer hydrogenation.[88] The combination of $CoCl_2$ with $NaBH_4$ in CH_3OH (−60 °C) was later shown to reduce azoxybenzenes, azobenzenes, and nitrosobenzenes to hydrazobenzenes. Prolonged reduction of the hydrazo compounds at room temperature led to the corresponding anilines. However aliphatic azo compounds like 2,3-diazanorbornene and *trans*-di-1-adamantyldiazene did not react.[89] More recently the same reduction of nitroso-, azoxy-, azo-, and hydroxylaminobenzene to aniline was achieved with $NiCl_2/NaBH_4/CH_3OH$.[80]

4. Isoxazolidines

In studying the use of nitrone cycloadditions for the synthesis of anatoxin-A, Tufariello et al. found that anhydrous $NiCl_2/LiAlH_4$ reductively cleaved isoxazolidines to aminoalcohols (Table XXII). Substituting anhydrous $CoCl_2$ for $NiCl_2$ considerably attenuated the yield of isolated product.[90]

TABLE XXII. **The Reduction of Isoxazolidines** with $NiCl_2$–$LiAlH_4$



substituents[a]	product, % yield
R_1, R_2 = Ph, R_3 = H, R_4 = *n*-Bu	92
R_1, R_2 = $(CH_2)_4$, R_3 = H, R_4 = Ph	87
R_1, R_2 = $(CH_2)_4$, R_3 = H, R_4 = $PhCH_3I$ salt	76
R_1, R_2 = $(CH_2)_4$, R_3 = H, R_4 = *n*-Bu	97
R_1, R_2 = $(CH_2)_4$, R_3, R_4 = Ph	95

[a] The isoxazolidines were prepared by nitrone–alkene cycloaddition reactions.

G. Deoxygenation Reactions

1. Sulfoxides

A recent review on sulfoxide reduction comprehensively tabulated methods involving low-valent metals such as $CrCl_2$, $TiCl_2$, $TiCl_4$, $Mo(CO)_6$, $Fe(CO)_5$, and others.[91] In 1971 Chasar noted that dialkyl, arylalkyl, and diaryl sulfoxides were quantitatively reduced to sulfides within 1 h using $CoCl_2$ (2 equiv) with $NaBH_4$ (10 equiv) in ethanol at room temperature (Table XXIII). However with dibenzylsulfoxide and tetramethylenesulfoxide, cleavage reactions producing volatile byproducts were suggested to account for the low mass recovery and poor yield of sulfide.[92] Chung and Han recently rediscovered this method and reported several additional examples.[93] Some hydrogenolysis of dibenzyl sulfoxide to benzyl mercaptan was detected. Cobalt boride, noted by both groups, was apparently catalytic (entry 3, Table XXIII). Sulfones were not affected.

The mechanism of sulfoxide reduction has been investigated by Osby.[63] Neither Co_2B alone (premade in EtOH, washed) nor boride under an atmosphere of H_2 was capable of reducing di-*n*-butyl sulfoxide in the normal reaction period (2 h), although di-*n*-butyl sulfide was produced in 35% yield after 2 days. In sharp contrast, mixtures of Co_2B and $NaBH_4$ furnished the sulfide in 50–60% yield. As mentioned earlier, working with premade boride avoided the initial temperature rise and resulted in moderately slower reaction rate. Thus Osby's work demonstrated that two reduction mechanisms were possible, but that the $NaBH_4$-based process was faster than heterogeneous hydrogenation.

In dimethyl sulfoxide solvent, the combination of $NaBH_4$ with $CoCl_2$ or $CeCl_3$ selectively reduced aldehydes in the presence of ketones. Also α,β-unsaturated ketones were converted predominantly to allylic alcohols. Not surprisingly, copious quantities of dimethyl sulfide were also produced.[94]

2. Phosphine Oxides

Phosphine oxides were rapidly deoxygenated to the corresponding phosphines using $LiAlH_4/CeCl_3/THF$.[64]

3. Ethers and Esters

While P-2 nickel boride does not hydrogenolyze allylic, propargylic, and benzylic substituents, recent developments in boride chemistry have made this transformation possible. In 1984, Ipaktschi found that $NiCl_2/NaBH_4/CH_3OH$ constituted an effective system for reductive removal of allylic, propargylic, and benzylic acetate esters (Table XXIV).[95] Equimolar amounts of the unsaturated ester and $NiCl_2$, when treated with excess $NaBH_4$ (10 equiv) for 30 min at 0 °C, afforded (mixtures of) alkenes and alkanes. Likewise cinnamyl alcohol furnished a 1:1 mixture of 1-phenylpropane and 1-phenylpropene. Interestingly, *p*-anisyl acetate was reduced in CH_3OD to a 35:65 mixture of mono and undeuterated 4-methylanisole. More highly deuterated species were not detected.

Using nickel boride prepared in anhydrous diglyme from $NiCl_2$ and $NaBH_4$, Sarma and Sharma showed that the ease of reductive removal of allylic substituents followed the order: allylic $OCH_3 < OH < OSiMe_3 < OCOCH_3 < OCOCF_3$. In comparing nickel boride with Raney nickel, the former was judged superior for reductive removal of an allylic acetate whereas the latter more efficiently deoxygenated allylic benzyl ethers. Consistent with earlier findings, reductions of 3β-acetoxycholest-4-ene run in CH_3CH_2OD resulted in only 20% deuterium incorporation.[96] The same workers reported the reductive cleavage of allylic alcohols to alkenes in a one-pot process via the corresponding trimethylsilyl ethers (Table XXV).[97]

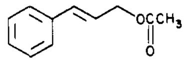
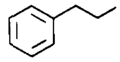
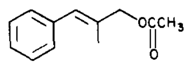
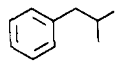
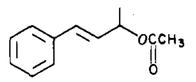
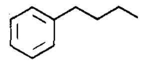
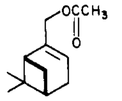
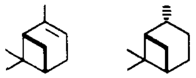
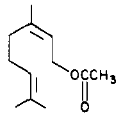
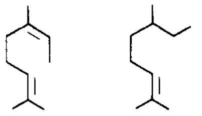
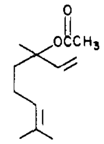
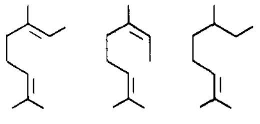
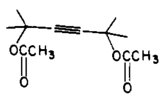
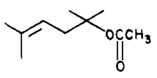
4. Aryl Ketones

Aromatic ketones like benzophenone, fluorenone, and acetophenone and their corresponding benzylic alcohols can be reductively deoxygenated with $PdCl_2/NaBH_4/$

TABLE XXIII. **Reduction of Sulfoxides by $CoCl_2/NaBH_4/EtOH$**

entry	substrate	product (% yield)	mol ratios of sub/Co(II)/$NaBH_4$	reacn time, h
1	*p*-tolyl sulfoxide	starting material	1/0/2.7	48
2	*p*-tolyl sulfoxide	*p*-tolyl sulfide (95)	1/1/2.7	4
3	*p*-tolyl sulfoxide	*p*-tolyl sulfide (60)	1/0.1/2.7	48
4	phenyl sulfoxide	phenyl sulfide (90)	1/1/2.7	4
5	*p*-chlorophenyl sulfoxide	*p*-chlorophenyl sulfide (96)	1/1/2.7	4
6	*n*-butyl sulfoxide	*n*-butyl sulfide (80)	1/1/2.7	4
	n-butyl sulfoxide	*n*-butyl sulfide (98)	1/2/10	2
7	benzyl sulfoxide	benzyl sulfide (72)	1/1/2.7	5
8	phenyl vinyl sulfoxide	phenyl ethyl sulfide (60)	1/2/5	4
9	phenyl vinyl sulfoxide	phenyl ethyl sulfide (56) phenyl ethyl sulfoxide (44)	1/1/2.7	4
10	phenyl methyl sulfoxide	phenyl methyl sulfide (98)	1/2/10	2
11	dibenzyl sulfoxide	dibenzyl sulfide (10)	1/2/10	2
12	thioxanthine sulfoxide	thioxanthone (100)	1/2/10	2
13	$(CH_2)_4SO$	-	1/2/10	2
14	diphenyl sulfone	diphenyl sulfone (100)		

TABLE XXIV. Reduction of Allylic and Propargylic Acetates Using $NiCl_2/NaBH_4$

reactant	product	% yield
		93
		>95
		87
	 (1:1)	>95
	 (60:40)	90
	 (38:19:43)	
		

CH_3OH at room temperature.[60] Hindered steroidal ketones were also reduced to alcohols in good yield. A black precipitate noted during reduction was termed elemental palladium, but may well have been palladium boride.[78]

H. Desulfurization Reactions

The first use of Ni_2B to desulfurize organic structures was reported in 1963 when Truce and Perry reduced thioketals and thioacetals with excess $NiCl_2/NaBH_4$ in EtOH under N_2 at reflux.[98] That method was later extended to the desulfurization of mercaptans, sulfides, and sulfoxides in good yield.[99] Besides ease of preparation, Ni_2B offered several advantages over Raney nickel, among them: (1) the boride could selectively remove a single sulfur from a thioketal, and (2) desulfurization could be accomplished in the presence of sulfones.

A later study described the desulfurization of heterocyclic thiols with Ni_2B at reflux in ethylene glycol or in aqueous solution at 200 °C.[100] Yields were not as high as those obtained using Raney nickel. Paz et al. also used $NiCl_2/NaBH_4$ to desulfurize peptides for mass spectrometric sequence analysis.[101]

In 1973 Boar et al. desulfurized ethylene dithioacetals and hemithioacetals with Ni_2B and noted that the rate of reduction decreased as borohydride decomposition raised the pH of the medium. Optimum reaction conditions were developed, consisting of ethylene glycol or ethanol–boric acid as solvent, and the method was then applied to a new synthesis of triterpene-2-enes.[102]

The reductive fission of sulfides and thioketals with $CuCl_2$ (2 equiv) and $LiAlH_4$ (4 mole equiv) has been investigated by Mukaiyama et al.[103] Benzophenone ethylene dithioketal, diphenylmethyl phenyl sulfide, and several 2-pyridyl sulfides were reductively desulfurized at reflux in THF after 3 h. Yields were enhanced when $ZnCl_2$ was added to the medium. Narasaka et al. later reported the total synthesis of *α-cis*-bergamotene using this method.[104]

TABLE XXV. Nickel Boride Reduction of Me_4Si Ethers of Allylic Alcohols

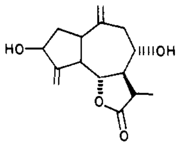
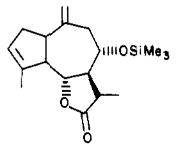
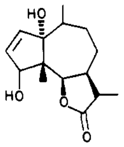
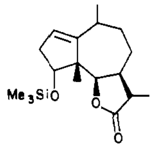
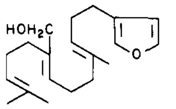
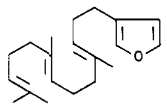
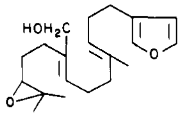
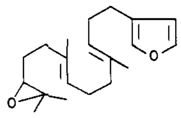
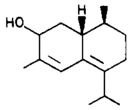
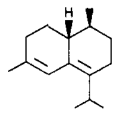
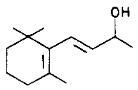
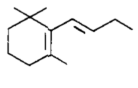
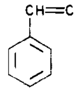
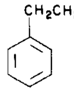
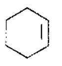
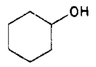
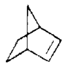
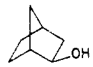
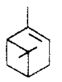
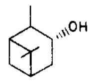
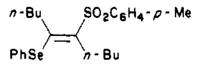
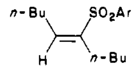
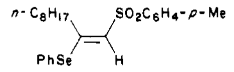
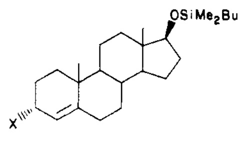
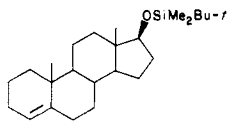
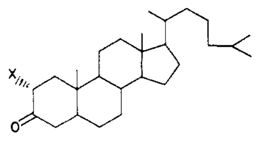
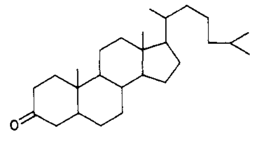
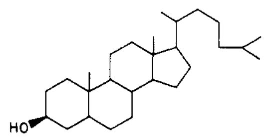
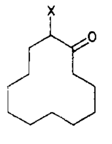
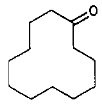
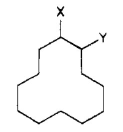
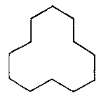
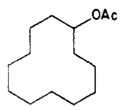
entry	substrate	product	time, h	yield, %
1	cholest-4-en-3β-ol	cholest-4-ene	6	80
2	cholest-5-en-4β-ol	cholest-5-ene	6	50
3			3	60
4			3	60
5			1	80
6			1.5	80
7			2	75
8			6	30

TABLE XXVI. Hydroboration of Alkenes with $CoCl_2/NaBH_4$[a]

alkene	product[b]	yield, %[c]
$CH_3(CH_2)_7CH{=}CH_2$	$CH_3(CH_2)_7CH_2CH_2OH$	70
		68[d]
		85
		90
		70

[a] The reactions were carried out using 40 mmol of alkenes, 20 mmol of $NaBH_4$ and 10 mmol of $CoCl_2$ in THF (40 mL) under nitrogen atmosphere. THF used was distilled over benzophenone–sodium. Cobalt(II) chloride supplied by Alfa-USA and the sample prepared by the dehydration of $CoCl_2{\cdot}6H_2O$ using 2,2-dimethoxypropane work equally well. Sodium borohydride supplied by Fluka-Switzerland and the sample supplied by Loba-Cheme-India give identical results. [b] Products obtained after oxidation with H_2O_2/NaOH. The products were identified by spectral data (IR, ^1H NMR and ^{13}C NMR) and comparison with the data reported in the literature. [c] Yields are of the isolated and distilled products. [d] The isomeric 1-phenylethanol is present to the extent of 18%. Products in other cases contain only small amount of the isomeric alcohols (<5%).

TABLE XXVII. Reductive Deselenization with $NiCl_2/NaBH_4$

selenide	product	yield
		95%
	$n\text{-}C_{10}H_{21}SO_2C_6H_4\text{-}p\text{-}Me$	80%
$PhSe\text{-}(CH_2)_{11}CO_2Me$	$CH_3(CH_2)_{10}CO_2CH_3$	90%
 X = o-$NO_2C_6H_4Se$ X = p-$NO_2C_6H_4Se$		83–91%
 X = PhSe		60%
		34%
 X = PhSe		93%
 X = p-$NO_2C_6H_4Se$, Y = H X = PhSe, Y = Cl		71–100%
X = PhSe, Y = OAc		50%

The combination of $FeCl_2$ with sodium triethylborohydride on alumina in benzene–THF at room temperature turned black and desulfurized thiols and thionoketones in a heterogeneous reaction. The order of mixing proved very important in this process: much lower conversions resulted when the $FeCl_2$ was first deposited on alumina. Yields were also poorer with lithium triethylborohydride.[105]

I. Miscellaneous Reactions

1. Formation of Amine Boranes

A new synthesis of amidine-based amine boranes was recently reported by Okamoto et al. These useful reducing agents, customarily prepared under aprotic conditions, were easily produced by treating the corresponding amines (2-aminopyridine, 2-aminopyrimidine) with excess $NaBH_4$ and $^1/_2$ mol equiv of $CoCl_2$ in aqueous solvent.[106] Use of $FeSO_4$ also gave amine boranes in good yield. However, 4-aminopyridine and 2-aminomethylpyridine did not form borane complexes, suggesting that metal–amidine chelation played an important mechanistic role.

Osby et al. showed that Co_2B was formed in this process and altered the normal mode of borohydride decomposition in water or alcohol. For instance, 2-aminopyridine alone had no effect on the rate of H_2 evolution from an aqueous solution of $NaBH_4$, nor did was any amine borane formed. However mixing the amine with $CoCl_2$ or Co_2B caused considerable foaming and afforded the corresponding amine borane.[14]

2. Hydroboration

In 1984, Satyanarayana and Periasamy reported that alkenes like 1-decene could be hydroborated by using a combination of $CoCl_2$ (0.5 mol equiv) and $NaBH_4$ (1 mol equiv) in anhydrous THF.[42] The intermediate, presumed to be an organoborane, underwent protonolysis (with 3 N HCl) or oxidation (with H_2O_2) to afford n-decane (40–50%) or 1-decanol (70%), respectively (Table XXVI). Few experimental details were recorded.

This system was reinvestigated by Osby et al. who showed it to be a complex heterogeneous reaction in which a fine black precipitate of cobalt boride slowly formed alongside undissolved $NaBH_4$ and $CoCl_2$.[14] Nevertheless the supernatant retained its characteristic blue color, even after prolonged reaction. Controls showed that BH_3, if generated in situ, would continue to react with $CoCl_2$ to form more boride. Efforts to trap BH_3 using 1,5-cyclooctadiene were inconclusive.

3. Epoxide Opening

The reduction of epoxides to alcohols has been achieved by using $NiCl_2/LiAlH_4$ in THF at room temperature. Whereas $LiAlH_4$ alone reduced styrene oxide to α-phenylethanol, the $NiCl_2/LiAlH_4$ system afforded β-phenylethanol exclusively (95% yield).[90] The same primary alcohol was obtained with Raney nickel.

4. Deselenation

In 1984, Back published a convenient method for the reductive deselenization of alkyl, allyl, and alkenyl selenides with $NiCl_2/NaBH_4$ in THF–CH_3OH at 0 °C. Little or no alkene reduction was observed under these conditions, and selenides could be cleaved in the presence of the analogous sulfides, presumably because of the greater C–S bond strength. Sulfones, ketones, and acetates also resisted reduction (Table XXVII).[107]

J. Conclusion

It is apparent from the literature reviewed here that transition metal borides and aluminides constitute an exciting variety of active heterogeneous catalysts. With a growing appreciation of the factors which govern catalyst activity and selectivity, the chemist may now rationally design specific borides or aluminides by proper choice of reagents and careful adjustment of reaction conditions. Many such materials have already found application in industrial chemical processes. Others await discovery as key catalysts for new and emerging synthetic chemical methods.

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