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Vanadium(I) Chloride and Lithium Vanadium(I) Dihydride as Selective Epimetallating Reagents for π- and σ-Bonded Organic Substrates[‡]

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Dedicated to Professor Dr. Udo H. Brinker on the occasion of his 65th birthday

Keywords: Vanadium(I) chloride / Lithium vanadium(I) dihydride / Epimetallation / Cleavage of carbon-heteroatom bonds / Reductive dimerization

Subvalent vanadium(I) salts, of empirical formulas, VCl, vanadium(I) chloride and $LiVH_2$, lithium vanadium(I) dihydride, whose efficient preparation, structural constitution and mode of reaction toward certain organic substrates have been described in a preceding article, are here evaluated in their reactions toward a wide variety of π- and σ-bonded organic substrates, namely carbonyl, imine, azo, alkene, 1,3-diene, nitrile π-bonds and C–X, C–O, C–N and N–N σ-bonds. Compared with the high reactivity of CrCl and $LiCrH_2$ reagents in attacking both types of bonds, the VCl and $LiVH_2$ reagents were much milder and selective in epimetallating π-bonds, often forming the 1:1 adduct of $LiVH_2$ and π-bonded substrate as the major product. Finally, the vanadium reagents showed little tendency to cleave C–O, C–S and C–N bonds and a smaller scope in cleaving C–X bonds than their chromium counterparts. Because of their selectivity these vanadium reagents offer the following preparative promise: 1) smooth McMurry carbonyl coupling to their reductive dimers; 2) deoxygenation of epoxides; 3) selective aromatic C–X reduction; 4) high yields of epimetallated carbonyls or imines as intermediates to α-hydroxy and α-amino acids; 5) 1,4-reductions of 1,3-alkadienes; 6) reductive dimerization of nitriles to ketones; 7) 1,4 or 1,*n*-epimetallations leading to acyloins or indoles; and 8) reductive dimerizations of azines to produce unusual imidazole derivatives. In explaining the greater kinetic stability of the 1:1 $LiVH_2$ adduct with carbonyl or imine substrates it is pointed out that such epimetallated adducts from $LiVH_2$ would likely be diamagnetic, whereas such adducts from $LiCrH_2$ have an unpaired electron on the Cr center and hence would rupture, so that the electron would be on the C center.

Introduction

Transition metals, especially in the colloidal state, have proved to be outstanding hydrogenation catalysts for over a century. Then just over 50 years ago, the revolutionary researches of Karl Ziegler and of Guilio Natta have shown that subvalent transition metal salts, when combined with main group metal alkyls, can serve as potent and stereoselective oligomerization and polymerization catalysts for a wide range of unsaturated hydrocarbons.[2] The swift worldwide impact of their research is reflected in the mere ten years extending from their initial publications of success to the awarding of their joint Nobel Prize in 1963. In the ensuing 35 years it has become the chief endeavor of industrial and academic chemists alike to elucidate the molecular mechanisms of Ziegler–Natta processes.[3] As a fertile offshoot of that investigation, such studies have led to the synthesis of many subvalent transition metal complexes and a fundamental examination of their reactions with unsaturated organic substrates. The principal and pioneering effort in this field, launched independently in 1973 by the research groups of Mukaiyama, of Tyrlik and of McMurry, involved subvalent titanium reagents of uncertain oxidation state and their efficiency in reductively dimerizing ketones into olefins.[4] Following their lead, many researchers began to explore the reducing action of subvalent transition metal reagents encompassing divalent complexes of titanium, chromium and vanadium for organic transformations. The copious literature on such research has been meticulously reviewed.[5] In these studies the actual oxidation state of the transition metal remained uncertain, as with Ti, or was no lower than divalent, as with Cr and V.

About 15 years ago we recognized the need to find a general methodology able to generate such transition reductants in defined low oxidation state efficiently and with a minimum of main-group metal reductant or Lewis acid as

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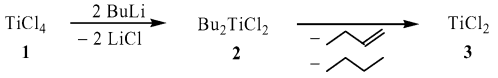
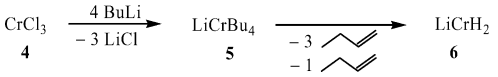
impurities. This requisite process has proved to be *alkylative reduction*.[6] Illustrated in Equation (1) for $TiCl_2$ (**3**),[7] it appears to be generally applicable to early transition metal salts, such as Ti(*i*-OPr)$_2$,[8] $ZrCl_2$,[9] Zr(OEt)$_2$,[10] $HfCl_2$[9] and CrCl.[11] The reaction occurs by the partial alkylation of $TiCl_4$ (**1**) in THF at –78 °C by *n*-butyllithium and the subsequent loss of butyl radicals from **2** above 0 °C.



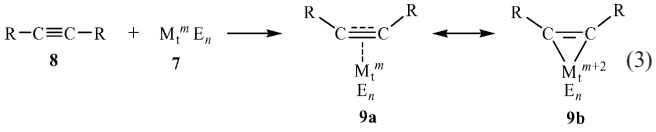
(1)

In an important modification, the interaction of the initial $CrCl_3$ (**4**) or $TiCl_4$ (**1**) salt with four or five equivalents of *n*-butyllithium, respectively, appears to form a lithium alkylmetallate (**5**) in Equation (2), whose reductive dealkylation leads to the lithium metal hydride, $LiCrH_2$ (**6**).[12] The corresponding reactions starting with $TiCl_4$ would produce $LiTiH_3$, but this hydride has been found to be stable only below 0 °C.[13]



(2)

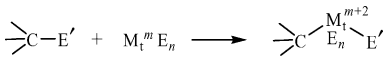
Such resulting subvalent transition-metal complexes, $M_t^mE_n$ (**7**), can add, in varying individual scope, to a range of π-bonded systems (C=C, C≡C, C=O, C=N and C≡N bonds) to form adducts. Such an adduct with an alkyne (**8**), for example, can be considered, on the one extreme, as a simple π complex (**9a**), where there is relatively little net electron density transferred from the metal (oxidation no. *m*, with increase ≈ 0) [Equation (3)]. In another resonance contribution, however, much electron transfer from the metal may lead to the bonding in **9b**, which resembles that of a metallocycle (oxidation no. *m* increase approaching 2).



(3)

Whether one of these two resonance forms is the better approximation of **9** can only be decided by assessing the structural and chemical properties of individual complexes.[14] If, for example, the bond length in **9** approximates that of a C=C bond in a cyclopropene and if in reactions of **9**, insertions or cleavages, seem to be occurring at two separate C–M bonds, then structure **9b** is a more reliable structural representation. The term proposed for the addition of the metal complex $M_t^mE_n$ onto a π-bond to form a metallocycle like **9b** is epimetallation.[14]

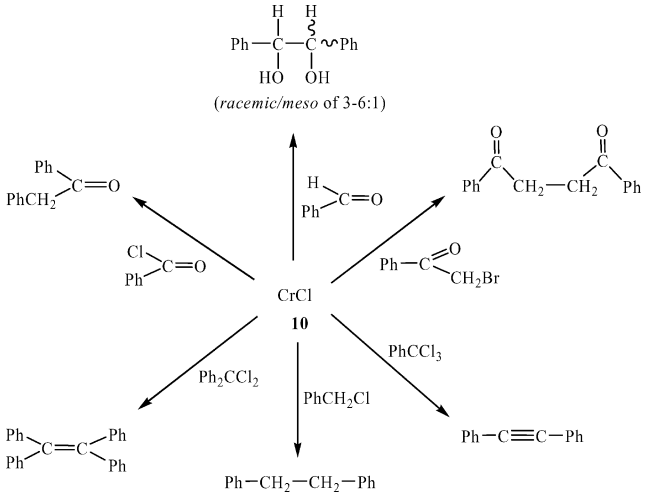
In an analogous reaction of a generalized subvalent transition metal complex, $M_t^mE_n$, with a σ C–E′ bond (E′ = C, O, N, X), leading to cleavage [Equation (4)], such a reaction may also be viewed as an epimetallation.[14]



(4)

Purpose of the Present Study

Of all of the foregoing subvalent transition-metal complexes prepared by our group thus far, the two most active reagents for epimetallating π-bonded substrates and for cleaving σ-carbon–heteroatom (O, N, S, X) bonds have been found to be chromium(I) chloride (**10**)[11] and lithium chromium(I) dihydride (**6**).[12] Illustrative of the wide scope of high-yielding reactions achievable with CrCl (**10**) are those given in Scheme 1.[11] But lithium chromium(I) dihydride (**6**) was thereafter shown to surpass in reactivity any neutral subvalent transition metal complex yet prepared by us, including CrCl. Reagent **6** can for example: 1) cleave the σ-C–O bond or C–S bond in dibenzofuran or in dibenzothiophene, respectively; 2) cleave the σ-C–N bond in benzylamine and deaminate the compound completely; 3) initiate polymerization of styrene or methyl methacrylate; and 4) dehalogenate aromatic halides, all reactions indicative of the extraordinary reducing action of **6**.[12]



Scheme 1.

This great reactivity of these two chromium reagents in the epimetallation of π- and σ-bonds of carbon roused our interest in the corresponding reagents of vanadium, VCl (**11**) and $LiVH_2$ (**12**). In the preceding publication in this series[1] we have described the preparation and structural characterization of these vanadium reagents. The significance of these transition metal complexes lies in their being the first chromium or vanadium reductants shown to exist in a univalent oxidation state. Although VCl gives no clear indication of being paramagnetic, $LiVH_2$ exhibits an EPR spectrum consistent with the presence of an anion having a linear H–V–H structure and two unpaired electrons. Both reagents have been shown to undergo epimetallations involving radical intermediates.

With this insight into the compositions and modes of reaction of VCl (**11**) and $LiVH_2$ (**12**), we have now under-

taken a survey of their reductions of selected organic substrates. The goal of this study has been to learn what differences would exist between the reactivity of these vanadium reagents and their chromium counterparts, where the metal nuclei differ by only one proton, V with the atomic number of 23 and Cr with that of 24. As to their lithium metal dihydrides, we now could compare the chemical reactivity of the free radical $LiCrH_2$ with that of the biradical $LiVH_2$.

Results and Discussion

Reductions of Organic Substrates with Vanadium(I) Chloride (11)

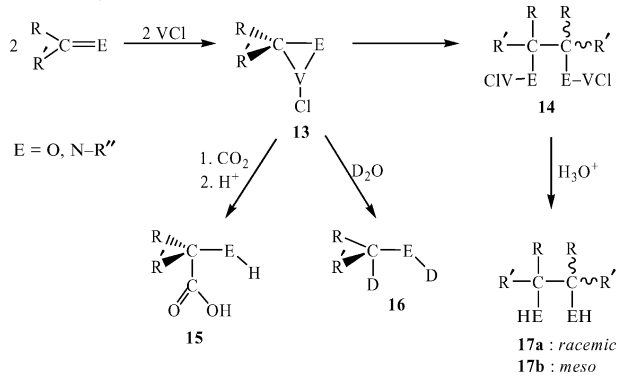
A variety of typical organic π- and σ-bonded functional groups was allowed to react with a THF solution of two equiv. of VCl (**11**) at 25 °C for 12 h (Table 1). All the sub-

Table 1. Reductions of π- and σ-bonded organic substrates with vanadium(I) chloride (VCl, **10**).

Entry	Substrate[a]	Product(s)	Yield[b]
1	benzaldehyde	benzyl alcohol	20
		1,2-diphenyl-1,2-ethanediol (2:1, *rac*/*meso*)	63
2	acetophenone	1-phenylethanol	45
		2,3-diphenyl-2,3-butanediol (1.2:1.0, *rac*/*meso*)	55
3	benzophenone	diphenylmethanol	51
		1,1,2,2-tetraphenyl-1,2-ethanediol	33
4	9-fluorenone[c]	9,9′-bifluorenyl-9,9′-diol	43
		9,9′-bifluorenylidene	32
		9,9′-bifluorenyl	16
		9-fluorenol	5
		fluorene	4
5	9-fluorenone[d]	9,9′-bifluorenylidene	99
6	*N*-benzylidenemethylamine	benzyl(methyl)amine	48
		1,2-bis(methylamino)-1,2-diphenylethane (1.0:2.3, *rac*/*meso*)	52
7	benzonitrile	benzyl phenyl ketone	3
		butyl phenyl ketone	10
8	carbon dioxide	pentanoic acid	17
9	azobenzene	aniline	75
		hydrazobenzene	25
10	*E*-stilbene oxide	stilbene (*E*/*Z* = 97:3)	100
11	acenaphthylene	acenaphthene	62
12	styrene	polystyrene (atactic)	100
13	1,1-diphenylethene	1,1-diphenylethane	30
14	*Z*-stilbene	stilbene (*E*/*Z* = 97:3)	100
15	4-phenyl-1-butene	(*E*)-1-phenyl-1-butene	64
		(*E*)-1-phenyl-2-butene	10
		1-phenylbutane	26
16	(*E*,*E*)-1,4-diphenyl-1,3-butadiene	(*E*)-1,4-diphenyl-1-butene	39
		1,4-diphenyl-2-butene (*E*/*Z* = 1:1)	22
17	diphenylacetylene	1,2-diphenylethene (*E*/*Z* = 1:1)	8
18	benzyl chloride	toluene	24
		1,2-diphenylethane	76
19	benzal chloride	benzyl chloride	77
		meso-1,2-dichloro-1,2-diphenylethane	23
20	dichloro(diphenyl)methane	tetraphenylethene	92
		diphenylmethane	1
21	9-bromofluorene	fluorene	35
		9,9′-bifluorenyl	65
22	iodobenzene	biphenyl	8
		benzene	8
23	4-iodoanisole	anisole	43
24	4-bromotoluene	4,4-dimethylbibenzyl	3
		toluene	5
25	2-bromobiphenyl	biphenyl	100

[a] Unless otherwise noted, a typical reaction run involved 1.5–3.0 mmol of organic substrate and two molar equivs. of VCl (**10**) in 30 mL of anhydrous, deoxygenated THF, which mixture was allowed to stir for 12 h at 25 ± 5 °C before being hydrolyzed by H_2O or aqueous 1 N HCl. After extraction of products into ether, the dried organic extract was evaporated, the residue weighed and the product(s) analyzed directly by ^1H and ^{13}C NMR spectroscopy. In necessary situations, *racemic*- and *meso*-isomers were separated by column chromatography and their relative amounts assessed by methine CH integrations in the 4.0–5.0 ppm ^1H region (diols) or the 3.5–4.1 ppm region (dianilines). [b] The difference between the total percentage of product(s) and 100% represents the percentage of remaining starting material. [c] In this run workup of a reaction sample taken after 30 min with CO_2 and hydrolysis led to about 10% yield of 9-hydroxy-9-fluorenecarboxylic acid. In an alternative workup with D_2O a comparable yield of 9,0-dideuterio-9-fluorenol was obtained. These results provide evidence for the intermediacy of vanadacycle **13** (Scheme 2). [d] In this run a ratio 1.25:1.00 molar equivalents of **10** to 1.00 equiv. of 9-fluorenone was employed.

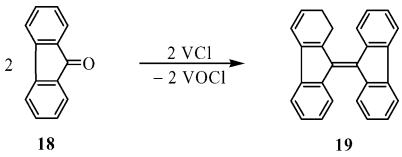
strates with C=O and C=N bonds underwent either epimetallation or reductive dimerization completely (Scheme 2).



Scheme 2.

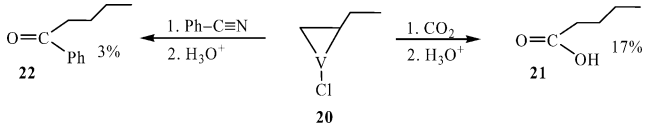
Similar observations have been noted with CrCl but the reductive dimer amounts to 90% or greater with this reagent. The epimetallated product of benzaldehyde, acetophenone, benzophenone, 9-fluorenone and *N*-benzylidenemethylamine with VCl, on the other hand, amounted to 20%, 45%, 51%, 43% and 48%, respectively, of the products (Entries 1–4, 6). This epimetallated product **13** appears to lead to the dimer **14** relatively slowly. In certain runs, support for such a vanadacyclopropane intermediate **13** was obtained by treating **13** with CO_2 to produce the hydroxy acid **15** (E = O in Entry 4) or hydrolyzing with D_2O to form **16** (Entry 4). Finally, treating **14** with H_2O resulted in a mixture of the *racemic* and *meso* diols or diamines **17**. But in contrast with the high *rac*/*meso* ratios of **17** obtained with CrCl (3.0–6.0:1.0), the *rac*/*meso* ratios from VCl were much less selective (1–2:1.0). By employing a larger excess of VCl, the epimetallated product **13** could be further favored over **14**. But the CrCl reagent is clearly the choice for fostering the reductive dimer and hence the resulting racemic dimer **17a**.

One special advantage of VCl may be the smooth dimerizing deoxygenation of certain ketones with VCl in refluxing THF. Use of 1.25 equiv. of VCl with 9-fluorenone (**18**) gives essentially a quantitative yield of 9,9′-bifluorenylidene (**19**) (Entry 5) [Equation (5)].



(5)

One peculiarity of the THF solution of VCl as prepared is the presence of about 20% of the epimetallated product of VCl with 1-butene (**20**). The intermediate **20** can be trapped by carbonation to pentanoic acid (**21**) (Entry 8) or with benzonitrile to produce butyl phenyl ketone (**22**) (Entry 7). If desired, any **20** in the VCl solution can be removed by disrupting **20** by THF evaporation in vacuo and thereafter adding fresh THF (Scheme 3).



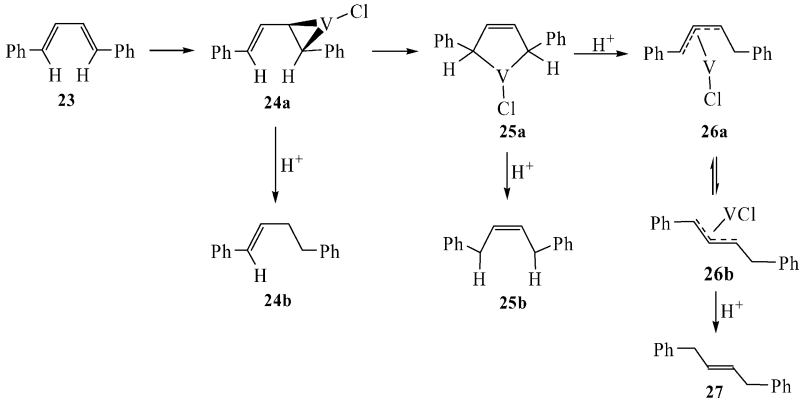
Scheme 3.

Although the N=N bond of azobenzene (Entry 9) and the strained C=C bond of acenaphthene (Entry 11) can be epimetallated readily, C=C or C≡C bonds are not easily attacked (Entries 13, 14, 15 and 17). Instead, VCl appears to act as a source of free radicals and effects the isomerization of (*Z*)-stilbene to (*E*)-stilbene, the polymerization of styrene and the C=C bond migration and (*Z*,*E*)-isomerization of 4-phenyl-1-butene (Entries 14, 12, 15).

A typical conjugated diene, such as (*E*,*E*)-1,4-diphenyl-1,3-butadiene (**23**), does undergo ready epimetallation, apparently involving rearrangement of the 1,2-epimetallated intermediate (**24a**) to 1,4-epimetallated intermediate (**25a**) and of vanadocycle **25a** to **26a** + **26b** (Entry 16).

Protonation of **26b** could produce **25b** or **27** (Scheme 4). Although the epimetallation of **23** with VCl provides an interesting study of organometallic rearrangements, such reduction of 1,3-dienes seems to offer no clean route as a preparative procedure.

Finally, the epimetallations of certain σ-bonded substrates has appeal in preparative reductions. Epoxides such



Scheme 4.

as (*Z*)-stilbene oxide undergo smooth deoxygenation to the thermodynamic mixture of 97:3 of *E*/*Z*-stilbenes (Entry 10). Benzylic halides are dimerized principally to reduced dimers (Entries 18–21) but as with carbonyl substrates, monomeric reduction to hydrocarbon or halide occurs in significant amounts (benzyl chloride: 24% toluene; benzal chloride: 77% benzyl chloride; 9-bromofluorene: 35% fluorene in Entries 18, 19, 21). Thus VCl is again less selective than CrCl for such reductive dimerizations. The inadequacy of VCl either for the dehalogenation or reductive dimerization of aromatic halides is reflected in the low yields and selectivity shown in Entries 22, 23 and 24. However, halonaphthalenes and halobiphenyls undergo high-yielding formation of the corresponding hydrocarbon (Entry 25).

Reductions of Organic Substrates with Lithium Vanadium(I) Dihydride (12)

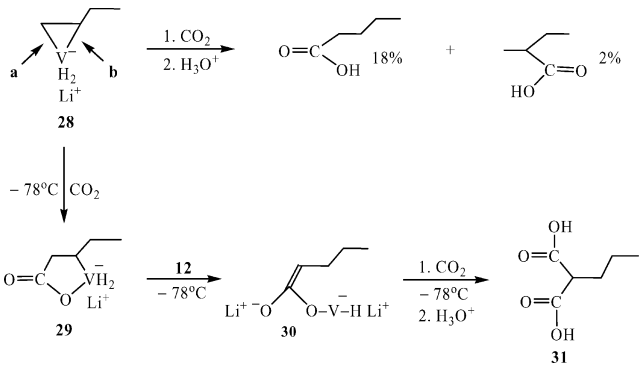
Carbonyl and Imino Derivatives: A selected variety of π-bonded organic substrates was treated with a THF solution of two equiv. of $LiVH_2$ (**12**) at 25 °C for 18 h (Table 2). As with VCl in THF, the starting $LiVH_2$ contained a considerable proportion of the epimetallated adduct with 1-butene (**28**) (Scheme 5). The presence of **28** was revealed in the reactions of **12** with CO_2: for carbonations begun at –78 °C and continued up to 25 °C (Entry 2), CO_2 insertions at both bond **a** and bond **b** occurred, resulting in the isolation of pentanoic acid (18%) and 2-methylbutanoic acid (2%). Interestingly,

Table 2. Reductions with lithium vanadium(I) dihydride, $LiVH_2$ (**12**).

Entry	Substrate[a]	Product(s)	Yield[b]
1	carbon dioxide (–78 °C)	propylmalonic acid	35
2	carbon dioxide (–78 °C to 25 °C)	pentanoic acid	18
		2-methylbutanoic acid	2
3	benzonitrile[c]	butyl phenyl ketone	55
		benzyl phenyl ketone	45
4	benzonitrile[d]	benzyl phenyl ketone	90
5	benzylideneaniline	1,2-dianilino-1,2-diphenylethane (67:33, *rac*/*meso*)	91
		N-benzylaniline	6
6	2-naphthylideneaniline	1,2-dianilino-1,2-di-2-naphthylethane (100:0, *rac:meso*)	51
		N-2-naphthylmethylaniline	49
7	*N*-benzylidenemethylamine	*N*-benzylmethylamine	50
		1,2-bis(*N*-methylamino)-1,2-diphenylethane (100:0 *rac:meso*)	50
8	(*E*,*E*)-benzaldehyde azine	4,5-diphenyl-1,3-bis(phenylmethylimino)-tetrahydroimidazole (73:27 *rac:meso*)	65
		benzaldehyde	10
9	9-fluorenylideneaniline	*N*-(9-fluorenyl)aniline	95
10	9-fluorenylideneaniline[e]	9,*N*-dideuterio-*N*-(9-fluorenyl)aniline	95
11	azobenzene	hydrazobenzene	85
		aniline	15
12	9-fluorenone	9-fluorenol	84
13	9-fluorenone[e]	9,*O*-dideuterio-9-fluorenol	82
14	benzophenone	diphenylmethanol	87
15	benzophenone[e]	α-*O*-dideuteriodiphenylmethanol	85
16	acetophenone	1-phenylethanol	30
		2,3-diphenyl-2,3-butanediol (81:19 *rac:meso*)	70
17	benzaldehyde	benzyl alcohol	29
		1,2-diphenyl-1,2-ethanediol (80:20)	71
18	α-bromoacetophenone	1,2-dibenzoylethane	70
		acetophenone	30
19	2-(*N*-ethanoylamino)benzophenone	2-methyl-3-phenylindole	85
		2-(*N*-acetamido)diphenylmethanol	15
20	(±) camphor	*endo*-2-borneol	70
		exo-2-borneol	30
21	benzil	benzoin	94
22	adamantanone	adamantanol	100
23	2-benzoylpyridine	2-(α-hydroxylbenzyl)pyridine	95
24	(*E*,*E*)-1,4-diphenyl-1,3-butadiene	1,4-diphenyl-2-butene (83:17 *E*/*Z*)	82
		1,4-diphenyl-1-butene	12
25	benzal chloride	stilbene (6.5:1.0, *E*/*Z*)	94
26	tetrahydrofuran	1-butanol	—

[a] As with the runs with VCl in Table 1, all the foregoing runs involved a 1:2 molar equivalent ratio of organic substrate: $LiVH_2$ (**12**) with 1.5–3.0 mmol of organic substrate in 30–40 mL of pure THF for 12 h at 25 ± 5 °C. It is important to note that VCl_4 was the starting material employed for the alkylative reduction with *n*-butyllithium to prepare the $LiVH_2$ (**12**) used in the foregoing reactions; cf. the detailed procedure in ref.[1]. [b] Cf. footnote ***b*** in Table 1. [c] The solution of the $LiVH_2$ (**12**) in THF was used directly after the reaction of VCl_4 with five equivalents of *n*-butyllithium without any attempt to remove the 1-butene by-product. [d] The solution of the $LiVH_2$ (**12**) in THF was freed of solvent and any epimetallated 1-butene under reduced pressure and the residual $LiVH_2$/LiCl solid was then redissolved in anhydrous THF that had been freshly distilled under argon. [e] Workup with D_2O.

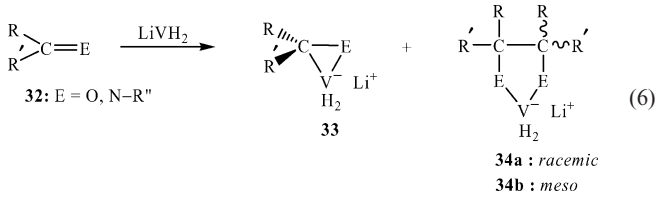
when the carbonation was conducted at –78 °C only (Entry 1), then a 35% yield of propylmalonic acid (**31**) was formed.



Scheme 5.

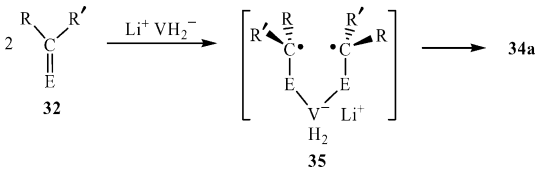
Apparently the carbonated intermediate **29** isomerized with enolate salt **30** being formed and the further carbonation of **30** then ensued. Intermediate **28** also interfered in reactions of **12** with benzonitrile: instead of the desired reduction by **12** (cf. infra), benzonitrile inserted almost quantitatively into **28** at bond **a** to form butyl phenyl ketone upon hydrolysis (cf. Scheme 3). This interference in reagent **12** could be obviated by simply removing all the THF under reduced pressure and readding fresh THF.

One of the striking differences in the reaction of $LiVH_2$ with carbonyl and imine substrates (**32**), vs. that of $LiCrH_2$, is the greater selectivity of $LiVH_2$ for forming the 1:1 epimetallated product [**33**, equation (6)]. The bonding in intermediate **33** was corroborated in several reactions by deuteriolytic workup to provide the expected dideuterio reduction product or by carbonation to yield the α-hydroxy or α-amino acid [cf. supra, Scheme 2 and ref.[14] (Entries 5, 6, 7, 9, 10, 12, 13, 14, 16, 17)].



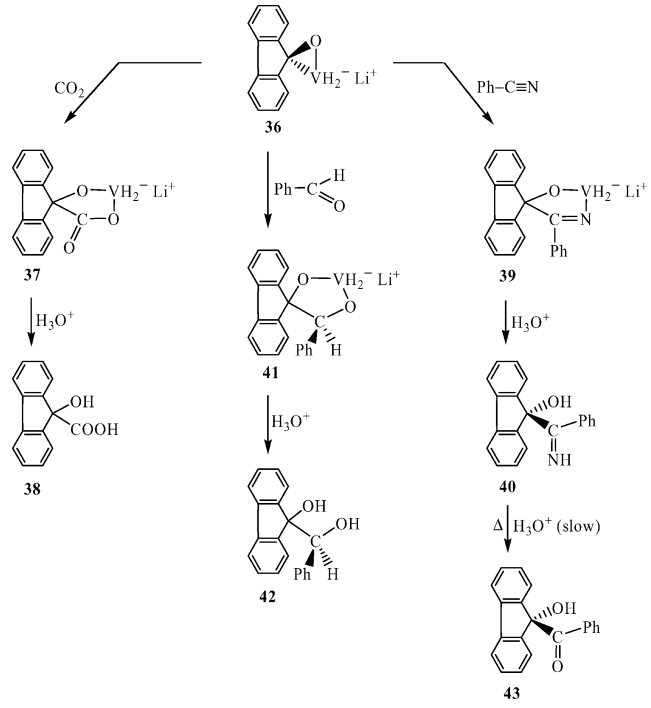
(6)

In the reductive dimer formed in such reactions in yields ranging from 10% to 70%, the racemic stereochemistry was favored by 2–4 to 1.0 and in certain cases, exclusively over the *meso* (Entries 5–7). This stereoselectivity could result from the steric orientation of the R and R′ substituents in the transition state (**35**) for C–C bond formation [Equation (7)]. Although the reduced dimers constitute a smaller proportion of the products, in some cases they are separable from the monomeric product and resolvable into *racemic* and *meso* isomers by column chromatography (Entries 5, 6, 7, 16 and 17).



(7)

The great preference for forming epimetallated monomer is displayed with rigid and sterically hindered carbonyl and imino derivatives, such as 9-fluorenone and 9-fluorenylidene aniline (Entries 9, 10, 12 and 13). Epimetallated intermediate **36**, for example, formed from 9-fluorenone (**18**) in over 80%, serves as a practical precursor to α-hydroxy acid **38**, via **37**,[15] to α-benzoyl alcohol **43**, via **39**, and potentially to the unsymmetrical pinacol **42**, via **41**[13] (Scheme 6), all in good yield. Such reactions of epimetallated adduct **36** appear to be feasible with corresponding adducts of hindered ketones like adamantanone, benzophenone and 2-benzoylpyridine.

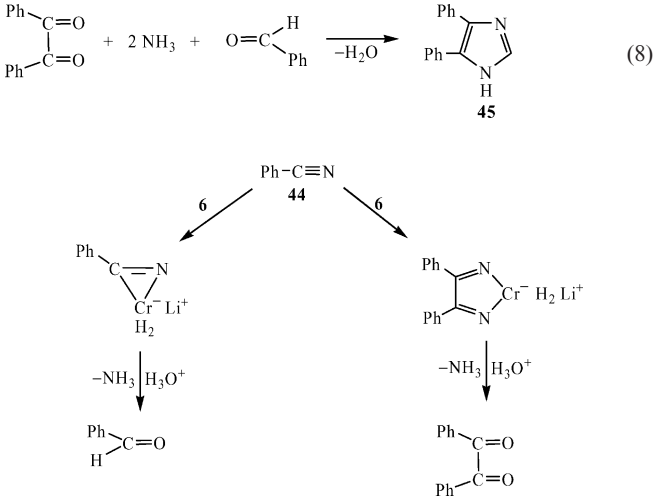


Scheme 6.

Reactions of Benzonitrile

The reaction of benzonitrile (**44**) with $LiVH_2$ forms a sharp contrast with the vigorous and variegated reactions of $LiCrH_2$ with such a nitrile. At 25 °C in THF the latter reagent converts 75% of benzonitrile, after hydrolysis, into a mixture of benzaldehyde, benzil, 2,4,6-triphenyl-1,3,5-triazine and 2,4,5-triphenylimidazole, in varying proportions depending on the molar ratio of **6**/nitrile.[12] First of all, it is clear that the imidazole (**45**) is an artifact produced during hydrolysis by the Radziszewski reaction[16] [Equation (8)].

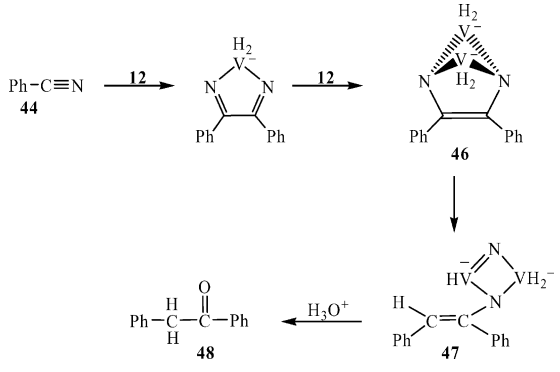
The requisite benzaldehyde and benzil arise apparently from the epimetallation and reductive dimerization of benzonitrile by $LiCrH_2$ (**6**) (Scheme 7), respectively.



(8)

Scheme 7.

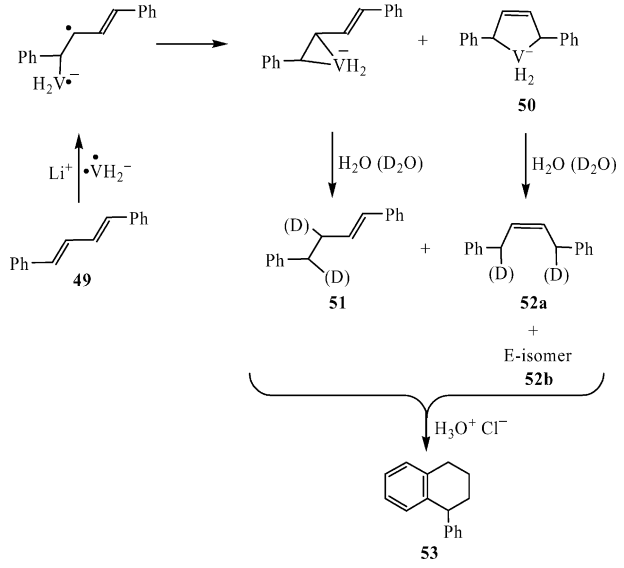
The $LiVH_2$ reagent, on the other hand, converts benzonitrile into a product yielding upon hydrolysis benzyl phenyl ketone (**48**) in high yield. This unprecedented reductive dimerization may occur by the following pathway (Scheme 8). The rearrangement of bridged dimer **46** to enamine **47** would yield upon hydrolysis, **48**. This novel reductive dimerization of nitriles may prove applicable to the useful cyclization of α,ω-dinitriles. Reminiscent of the Thorpe dimerization of nitriles or the Thorpe–Ziegler cyclization of α,ω-dinitriles, this process differs from them in not involving an enolizable α-carbon–hydrogen bond and thus in no loss of a carbon atom.[17]



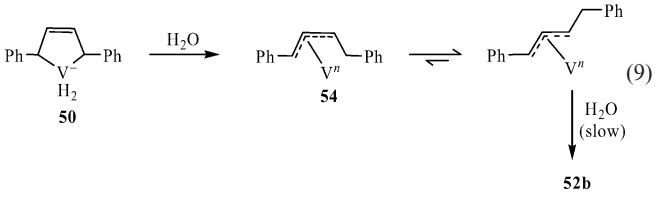
Scheme 8.

1,2-Epimetallation vs. 1,4-Epimetallation in Conjugated Substrates

Because $LiVH_2$ is known to have the biradical VH_2 anion, attack of **12** on conjugated systems (Scheme 9), such as 1,4-diphenyl-1,3-butadiene (**49**) could well result in 1,2- and 1,4-epimetallations. The latter mode of addition would be revealed by *cis*-geometry of the olefin formed upon hydrolysis (**52a**). Initial runs of the reaction in fact gave the *cis*-isomer of 1,4-diphenyl-2-butene (**52a**) as the principal product, as well as (*E*)-1,4-diphenyl-1-butene as the minor (**51**). But surprisingly, 1-phenyl-1,2,3,4-tetrahydronaphthalene (**53**) was a significant by-product. However **53** was shown to be an artifact produced by the 6 N aq. HCl used in the hydrolysis, which cyclized **51** and/or **52** into **53**. Use of water alone then yielded 82% of a *Z*/*E* mixture of 1,4-diphenyl-2-butene in a 83:17 ratio of **52a** and **52b** and 12% of (*E*)-1,4-diphenyl-1-butene (**51**). Treatment of a reaction sample with D_2O and subsequent ^1H and ^2H NMR spectral analysis showed the presence of deuterium at C^3 and C^4 in **51** and C^1 and C^4 in **52a**. The small content of *E*-isomer **52b** in **52** is ascribed to the relatively slow protolysis by H_2O of the two V–C bonds in **50**, by neutral H_2O, permitting *Z*/*E* isomerization of the intermediate **54** [Equation (9)]. Further studies of the reaction $LiVH_2$ with such conjugated dienes may lead to a useful method for *cis*-1,4-reductions.

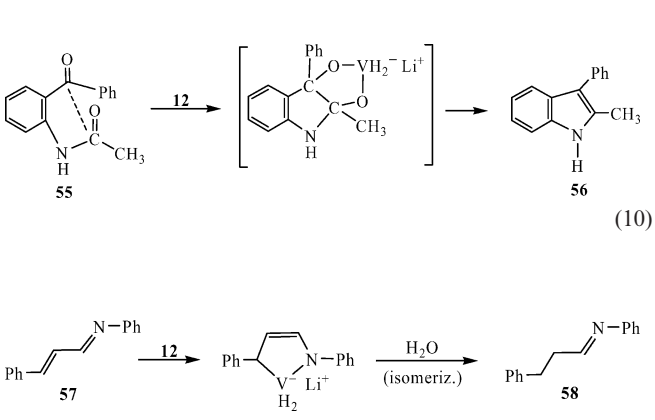


Scheme 9.



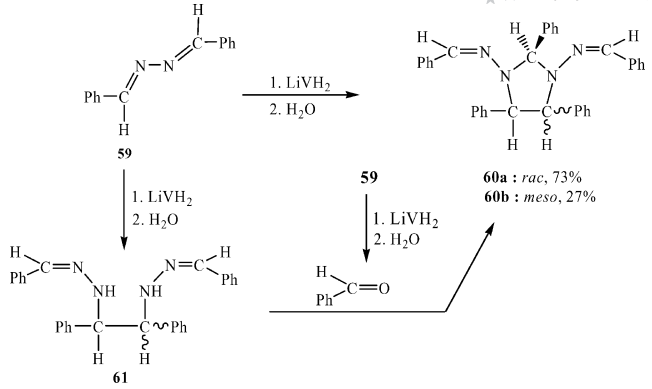
(9)

Analogous reactions of **12** involving intramolecular 1,4- or 1,*n*-epimetallations are: a) the reduction of benzil to benzoin (Entry 21); b) the coupling of the two carbonyl groups in 2-(ethanoylamino)benzophenone (**55**) to produce the indole **56** (Equation 10, Entry 19);[18] and c) the reaction of **12** with cinnamaldehyde anil (**57**) (1:1) to yield principally **58** (Equation 11).



(10)

(11)



Scheme 10.

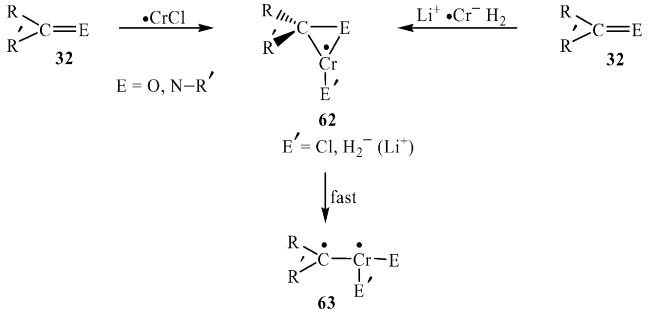
Coupling or σ-epimetallation of benzylic and α-bromocarbonyl derivatives by **12** (1:2 molar ratio) occurs in good to high yields. Examples are the reactions of benzyl chloride to bibenzyl (100%), of benzal chloride to (*E*)-stilbene (94%), of benzo trichloride to stilbene (84% and *E*/*Z* ratio of 5.3:1.0) and bibenzyl (12%), of dichlorodiphenylmethane to 1,1,2,2-tetraphenylethene (93%) and of α-bromoacetophenone to 1,2-dibenzoylethane (70%). Aromatic halides on the other hand were coupled and dehalogenated in low yields. In pointed contrast to $LiCrH_2$, finally, $LiVH_2$ failed to cleave the C–O, C–N and C–S bonds of aromatic ethers, amines or sulfides, confirming the chromium reagent as much more reactive in σ-bond epimetallations.[12] The THF solvent underwent reductive cleavage to form 1-butanol only with slow-reacting organic substrates.

A final such striking example of the selectivity of $LiVH_2$ in the coupling of imines is the good yield (68%) of **60** as a 73:27 mixture of *racemic* and *meso* isomers after reaction of (*E*,*E*)-benzalazine (**59**) with **12** and hydrolysis. That **60** could be formed in such a high yield with relatively little cleavage of the weak N–N bond in any precursors is a further indication of the milder reducing action of **12**. It is likely that **60** is actually formed in the hydrolysis step, where the coupled intermediate **61** undergoes a condensation reaction with the benzaldehyde arising from the reductive cleavage of **59** and subsequent hydrolysis (Scheme 10).

Possible Sources of the Reactivity Differences Between Vanadium(I) Chloride (11) and Lithium Vanadium(I) Dihydride (12) vis-à-vis their Chromium Counterparts

The discernible atomic differences between the empirical formulas of the vanadium(I) reagents, VCl (**11**) and $LiVH_2$ (**12**), and their chromium(I) counterparts, CrCl (**10**) and $LiCrH_2$ (**6**) are the following: 1) $LiVH_2$ has one less proton in the metal nucleus (23) than does chromium(24); 2) $LiVH_2$ has two unpaired electrons, while $LiCrH_2$ has only one unpaired electron; 3) on the Allred–Rochow scale, the chromium center is somewhat more electronegative (1.56) than the vanadium center (1.45); and 4) the atomic radius of the vanadium atom is slightly larger (1.34 Å) than that of chromium (1.27 Å). Nothing is known about the degree of association or ion-clustering of any of the four reagents, nor the degree of solvation with the THF medium.

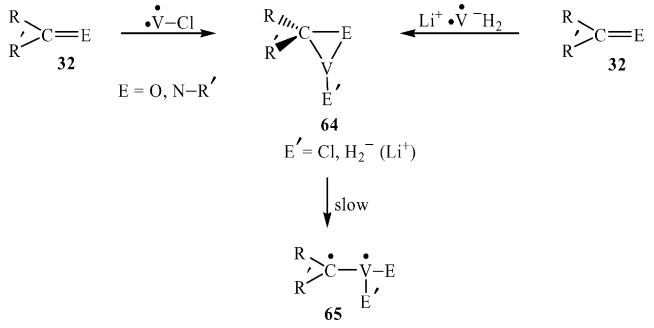
Of the above differences between these vanadium and chromium reagents, we proposed that the principal contributing factor to the greater reactivity of $LiCrH_2$ is the single available unpaired electron on Cr(I). With CrCl, the unpaired electron may not be available until a dimer or oligomer $(CrCl)_n$ dissociates. In either case, when monomeric (·CrCl) or $LiCrH_2$ engages in oxidative addition or epimetallation (Scheme 11), the intermediate formed, **62**, should still possess an unpaired electron. With an unpaired electron the epimetallated adduct **62** should tend to rupture rapidly to yield radical **63**, where the free electron can be transferred to carbon, where delocalization and electronegativity would enhance radical stability.



Scheme 11.

In sharp contrast, biradical Li^+ **:**VH_2 and potentially available biradical **:**VCl, could epimetallate **32** with complete pairing of available electrons in **64** (Scheme 12). Formation of diamagnetic **64** should contribute to its kinetic stability and thus slow down its conversion to open-chain biradical **65**. This proposal would explain why the epimetallated products from **32** and $LiVH_2$ are often the major products (**33**), while **32** and $LiCrH_2$ often yield more of the reductive dimers (**34**).

Finally, the reasons for the greater reactivity of $LiCrH_2$ over $LiVH_2$ in the epimetallation or cleavage of σ-bonds [see Equation (4)] and the nature of the reaction mechanism remain unclear and are the goal of continuing studies.



Scheme 12.

Experimental Section

General Experimental Procedures and Starting Materials: All procedures involving the purification of reaction solvents, distillation of reagents, the preparations of vanadium(I) chloride (**11**), lithium vanadium(I) dihydride (**12**) and their subsequent measurements or reactions with organic substrates were conducted under a positive atmospheric pressure of anhydrous, deoxygenated argon employing vacuum techniques and with standard Schlenk apparatus. The drying and deoxygenation of argon, as well as the solvents, such as tetrahydrofuran, toluene and hexane, used in the reactions were carried out according to established procedures.[19]

The *n*-butyllithium in hexane was purchased from Sigma–Aldrich in Sure Seal™ bottles and was used at the stated concentration as received, uniformly 2.5 M. The anhydrous vanadium(III) chloride was purchased from Sigma–Aldrich at 97% purity and the vanadium(IV) chloride in at least 99% purity.

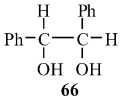
Preparations of Vanadium(I) Chloride (12) and Lithium Vandium(I) Dihydride (12) and Their Gasometric, Infrared Spectroscopic and Electronic Paramagnetic Resonance Analyses: Detailed procedures for the preparation of VCl (**11**) in THF from VCl_3 or VCl_4, as well as the preparation of $LiVH_2$ (**12**) from VCl_4 (the preferred method), are given in the preceding publication.[1] Likewise, all apparatus and instrumentation required for the gasometric, IR spectral and EPR analyses are described or specified in the same reference.

Product Identification from the Reactions of VCl (11) or $LiVH_2$ (12) with Various Organic Substrates in THF: Product identification of known compounds was achieved principally by comparison of ^1H and ^{13}C NMR spectra of such reaction products with those spectra of authentic compounds given in the literature.[20,21] Similarly, product yields from such reactions were calculated based on integration of the respective NMR proton peaks, except for carboxylic acids, where the yields were based on the weight of product obtained.

The ^1H NMR spectroscopic data are reported on the δ scale in parts per million with reference to an internal standard of tetramethylsilane (TMS) for solutions in deuteriated chloroform ($CDCl_3$) or deuteriated dimethyl sulfoxide ([D_6]DMSO) solvent. The ^{13}C NMR spectroscopic data are reported on the δ scale in parts per million with reference to deuteriated solvents. Coupling constants between adjacent, chemical different Hs and falling in the usual range have been omitted. In the next section ^1H and ^{13}C NMR spectroscopic data are given for the unusual organic products and for the stereochemical assignments of the *meso*- and *racemic*-isomers obtained.

^1H and ^{13}C NMR Spectral Data of Unusual Organic Products Encountered in This Study: The ^1H and ^{13}C NMR spectra of certain organic products, which were obtained in this investigation of the reduction capabilities of VCl (**11**) and $LiVH_2$ (**12**) (Table 1 and Table 2) and are not found in standard spectral compilations,[20,21] are given here. The following ^1H and ^{13}C (decoupled) NMR spectra were recorded with a Bruker AM-360 spectrometer at 360 MHz in $CDCl_3$ solution in ppm on the δ scale.

Such data served to verify the correct overall structures of the reaction products, as well as assessing the *racemic*/*meso* isomeric ratio where such stereochemical variation was possible, as in the bimolecular reductions of aldehydes, aldimines and unsymmetrical ketones, exemplified by benzaldehyde, benzylidenemethylamine and acetophenone, respectively (Entries 1, 6, 2 in Table 1; Entries 17, 5, 16 in Table 2). From the known ^1H NMR spectra of *meso*- and *rac*-isomers of benzaldehyde's dimeric diol, the methine H on the chiral carbon in racemic isomer **66** occurs at a lower field, 4.67 ppm than the methine H in the *meso* isomer, 4.82 ppm.



The dimers of benzylidenemethylamine show a similar relationship: *racemic* methine H at δ = 3.63 ppm and the *meso* methine H at δ = 4.05 ppm. From the integration of such peaks, the *rac*-*meso* isomeric ratio was estimated. In the case where only one methine H singlet was found in this region, as with the dimer from 2-naphthylideneaniline, it was assumed that the *rac*-isomer was formed exclusively due to steric hindrance in the bimolecular coupling (compare transition state **35**).

9,9′-Bifluorenylidene: ^1H NMR: δ = 8.36 (3, 4 H), 7.67 (d, 4 H), 7.30 (t, 4 H), 7.19 (dd, 4 H) ppm. ^{13}C NMR: δ = 141.32, 141.0, 138.29, 129.13, 126.82, 126.71, 119.86 ppm.

9,9′-Bifluorenyl: ^1H NMR: δ = 7.64 (d, 4 H), 7.26 (t, 4 H), 7.08 (t, 4 H), 6.95 (d, 4 H), 4.83 (s, 2 H) ppm. ^{13}C NMR: δ = 144.67, 141.54, 127.27, 126.69, 124.07, 119.62, 49.84 ppm.

9,9′-Bifluorenyl-9,9′-diol: ^1H NMR: δ = 7.38 (m, 5 H), 7.24 (m, 6 H), 7.06 (m, 5 H), 3.17 (s, 2 H) ppm.

***rac*-1,2-Diphenylethane-1,2-diol:** ^1H NMR: δ = 7.23–7.11 (m, 10 H), 4.67 (s, 2 methine H), 2.92 (s, 2 H) ppm. ^{13}C NMR: δ = 139.89, 127.87, 126.92, 79.64 ppm.

***meso*-1,2-Diphenylethane-1,2-diol:** ^1H NMR: δ = 7.33–7.23 (m, 10 H), 4.82 (s, 2 methine H), 2.37 (s, 2 H) ppm.

***rac*-2,3-Diphenylbutane-2,3-diol:** ^1H NMR: δ = 7.25–7.13 (m, 10 H), 2.54 (s, 2 H), 1.49 (s, 6 methyl H). ^{13}C NMR: 143.46, 127.35, 127.15, 127.03, 78.85, 24.95 ppm.

***meso*-2,3-Diphenylbutane-2,3-diol:** 7.25–7.13 (m, 10 H), 2.54 (s, 2 H), 1.49 (s, 6 methyl H). ^{13}C NMR: δ = 143.46, 127.35, 127.15, 127.03, 78.6 (diagnostic for *meso*), 24.95 ppm.

***rac*-1,2-Bis(methylamino)-1,2-diphenylethane:** ^1H NMR: δ = 7.55–7.33 (m, 10 H), 3.63 (s, 2 methine H), 2.08 (6 H), 1.51 (2 H, br. s). ^{13}C NMR: 140.7, 128.4, 127.6, 126.6, 70.9, 34.3 ppm.

***meso*-1,2-Bis(methylamino)-1,2-diphenylethane:** ^1H NMR: diagnostic singlet for 2 methine H at δ = 4.05 ppm.

(*E*)-1,4-Diphenyl-1-butene: ^1H NMR: δ = 7.34–7.16 (m, 10 H), 6.41 (d, 1 H), 6.25 (dt, 1 H), 2.79 (t, 2 H), 2.52 (q, 2 H). ^{13}C NMR: 141.17, 137.7, 129.9, 128.5, 128.3, 126.9, 125.9, 125.86, 35.9, 34.87 ppm.

(*Z*)-1,4-Diphenyl-2-butene: ^1H NMR: δ = 7.15 (s, 10 H), 5.70 (t, 2 H), 3.4 (d, 4 H) ppm.

(*E*)-1,4-Diphenyl-2-butene: ^{1}H NMR: δ = 7.21 (br. s, 10 H), 5.66 (m, 2 H), 3.39 (d, 4 H) ppm.

***rac*-1,2-Dianilino-1,2-diphenylethane:** ^{1}H NMR: δ = 7.27–7.14 (m, 10), 7.10–7.06 (t, 4 H), 6.67 (t, 2 H), 6.51 (d, 4 H), 4.57 (s, 2 methine H). ^{13}C NMR: 146.9, 139.9, 129.1, 128.4, 127.5, 118.1, 114.1, 64.0 ppm.

***meso*-1,2-Dianilino-1,2-diphenylethane:** ^{1}H NMR: δ = 7.05–7.01 (m, 10 H), 6.93 (q, 4 H), 6.63 (t, 2 H), 6.48 (d, 4 H), 4.94 (s, 2 methine H) ppm.

***rac*-1,2-Dianilino-1,2-di(2-naphthyl)ethane (assumed stereochemistry):** ^{1}H NMR: diagnostic one singlet at δ = 5.55 ppm for 2 methine H.

Specific Procedures for Certain Reductions with Lithium Vanadium(I) Dihydride (12): Although the general procedures described in footnote [a] of Tables 1 and 2 are sufficient for guidance in conducting most reductions with VCl (**11**) or $LiVH_2$ (**12**), certain reductions with $LiVH_2$ require the more detailed descriptions given here.

Reactions of (*E*,*E*)-Benzaldehyde Azine (59) with $LiVH_2$ (12). a) 1:1 Ratio of 59 and 12: A solution of $LiVH_2$ (**12**, 4.8 mmol) in 40 mL of THF was treated with a solution of the azine (1.00 g, 4.8 mmol) in 20 mL of THF at 25 ± 5 °C for 12 h. Hydrolysis of the reaction mixture with 1.0 N aqueous HCl, ether extraction, drying of the ether extract and removal of the ether gave an organic residue of 410 mg (51% calculated as **60a** and **60b** with the assumption 3 equiv. of **59** are theoretically required to produce 1.0 equiv. of **60**). Flash column chromatography on silica gel using a 1:50 ethyl acetate/hexane eluent gave a composition of 65% of *rac*-4,5-diphenyl-1,3-bis(phenylmethylimino)tetrahydroimidazole (**60a**), 24% of *meso*-4,5-diphenyl-1,3-bis(phenylmethylimino)tetrahydroimidazole (**60b**), 8% benzaldehyde and 1% of the azine.

Basification of the original aqueous layer and ether extraction yielded 100 mg of benzylamine and the *rac*/*meso*-1,2-diphenyl-1,2-ethylenediamines in yields of about 6% of each.

***meso*-4,5-Diphenyl-1,3-bis(phenylmethylimino)tetrahydroimidazole (60b):** ^{1}H NMR ($CDCl_3$): δ = 8.00 (d, 2 H), 7.90–7.00 (m 30 H), 5.60 (s, 1 H), 5.10 (s, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 139.9, 137.8, 135.9, 129.0–126.2, 102.7, 86.4, 76.4, 69.7 ppm.

***rac*-4,5-Diphenyl-1,3-bis(phenylmethylimino)tetrahydroimidazole (60a):** ^{1}H NMR ($CDCl_3$): δ = 7.72 (d, 2 H), 7.70–7.02 (m, 28 H), 6.93 (s, 1 H), 4.88 (s, 1 H), 4.68 (d, 1 H), 4.66 (d, 1 H) ppm.

Samples of (**60a**) and (**60b**), separated by column chromatography on silica gel with an eluent of ethyl acetate and hexane in a 1:50 ratio, were separately subjected to mass spectrometry (70 eV, electrospray with NaI). Both presented similar spectra: (529) [M + Na], (530) [M + 1 + Na], (506) [M], (505) [M –1], (402) [M –104] (-PhCH=N), (403) [M –103] (-PhCH≡N), (–299) [M] (loss of Ph and PhCH=N). Such fragments are consistent with the structures of **60a** (*rac*) and **60b** (*meso*), which can lose H^+, Ph–C^+=NH and Ph–C≡N sequentially, at the weak PhHC=N–N bonds.

b) 1:2 Ratio of 59 and 12: In a similar experiment to investigate the effect of stoichiometry on product distribution and yield, a solution of the azine (540 mg, 2.6 mmol) in 5 mL THF, was admixed with a solution of LiVH2 (5.1 mmol) in 40 mL THF and treated at room temperature for 12 h. Upon hydrolysis of the black reaction mixture a vigorous exothermic reaction characterized by gas evolution ensued. Hydrolytic workup gave 300 mg of a light brown solid (≈ 65% as **60a** and **60b**) as the neutral organic extract consisting of 10% benzaldehyde, 60% of **60a** and 5% of **60b**. On the other hand 140 mg of a pale yellow liquid as the aqueous organic extract was found to be benzylamine in 25% overall yield.

Reactions of Benzonitrile (44) with $LiVH_2$ (12) Prepared from VCl_4. a) Reagent $LiVH_2$ Containing 1-Butene: A solution of $LiVH_2$ (2.4 mmol) in 40 mL THF was treated with benzonitrile (0.12 mL, 1.2 mmol) at room temperature for 12 h. Hydrolytic workup yielded 240 mg of a light red liquid consisting of 45% benzyl phenyl ketone and 55% of butyl phenyl ketone.

b) Reagent $LiVH_2$ Freed of 1-Butene: In an effort to prevent the interference of 1-butene with product distribution, a solution of $LiVH_2$ (**12**) (2.0 mmol) in 20 mL THF was subjected to reduced pressure at room temp. and most of the volatiles removed. Then fresh dry and deoxygenated THF (distilled under argon) was added and the resulting solution was again allowed to react with benzonitrile (0.20 mL, 1.0 mmol) at room temperature for 12 h. Hydrolytic workup afforded 280 mg of a reddish liquid consisting of essentially pure benzyl phenyl ketone and amounting to a 90% yield.

Reactions of 9-Fluorenone (18) with $LiVH_2$ (12) and Treatment of the Resulting Epimetallated Adduct 36 with Benzonitrile: A solution of $LiVH_2$ (**12**, 3.2 mmol) in 10 mL of THF was allowed to react with a solution of 9-fluorenone (**18**, 288 mg, 1.6 mmol) in 5 mL of THF for 6 h at 25 ± 5 °C. Thereupon the resulting reaction mixture was treated with benzonitrile (**44**, 165 mg, 1.6 mmol) and the solution stirred for an additional 12 h. Usual hydrolytic workup with 0.1 N aqueous HCl and ether extraction yielded 242 mg of 9-benzimidyl-9-fluorenol (**40**) in 97% purity, containing 2% of 9-fluorenol and 1% of fluorene as impurities. The overall yield of ketimine **40** was 60%.

9-Benzimidyl-9-fluorenol (40): ^{1}H NMR ($CDCl_3$): δ = 7.59–7.53 (m, 2 H), 7.46–7.39 (m, 2 H), 7.33–7.26 (m, 5 H), 7.03 (t, 2 H), 6.93 (m, 2 H), 6.44 (s, 1 H), 5.18 (br., 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 157.7, 145.7, 140.8, 130.6, 129.4, 128.2, 127.9, 127.6, 127.2, 124.5, 120.0, 83.8 ppm.

The ketimine **40** proved resistant to hydrolysis and refluxing a sample in 3 N aqueous H_2SO_4 for several hours, basifying with aqueous NaOH and isolating the organic product gave only a 45% yield of 9-benzoyl-9-fluorenol (**43**) after column chromatographic purification, m.p. 120–122 °C.

9-Benzoyl-9-fluorenol (43): ^{1}H NMR ($CDCl_3$): δ = 7.74 (m, 2 H), 7.41 (td, 2 H), 7.35 (m, 2 H), 7.31–7.20 (m, 5 H), 7.07 (m, 2 H), 5.67 (br., 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 199.7, 146.0, 141.2, 133.0, 129.9, 129.2, 128.7, 128.2, 124.5, 120.8, 86.52 ppm.

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