Selective synthetic methods using vanadium-mediated redox reactions*

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Abstract: Oxovanadium(V) compounds serve as Lewis acids with oxidation capability and induce one-electron oxidative transformations of organosilicons, organotins, organoaluminums, organoborons, organozincs, and/or their ate complexes. Low-valent vanadium-catalyzed stereoselective reductive transformations, including dehalogenation, pinacol coupling, and the related radical reaction, have been developed by constructing a multicomponent redox system in combination with a coreductant and an additive.

Keywords: Oxidation; reduction; oxovanadium; low-valent vanadium; radical; synthetic reaction.

INTRODUCTION

One-electron oxidation or reduction of organic compounds provides a useful route to generate cation radicals or anion radicals, respectively, as exemplified by Scheme 1. These methods are of potential utility in synthetic radical reactions. The redox properties of transition metals contribute to efficient one-electron reduction or oxidation reactions. In particular, the redox process of early transition metals, including titanium, vanadium, and manganese, has been employed from this point of view [1,2]. The redox properties are controlled by ligands, allowing a more efficient interaction between the orbitals of metals and substrates for facile electron transfer. Precise regulation of the redox process based on the electronic interaction between highest occupied molecular orbital (HOMO) and lowest occupied molecular orbital (LUMO) is required for this purpose, which allows us to develop novel and selective methods for oxidative or reductive transformations under redox potential control.
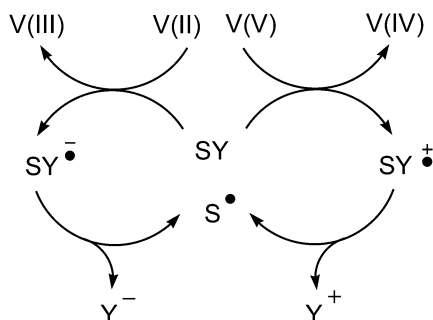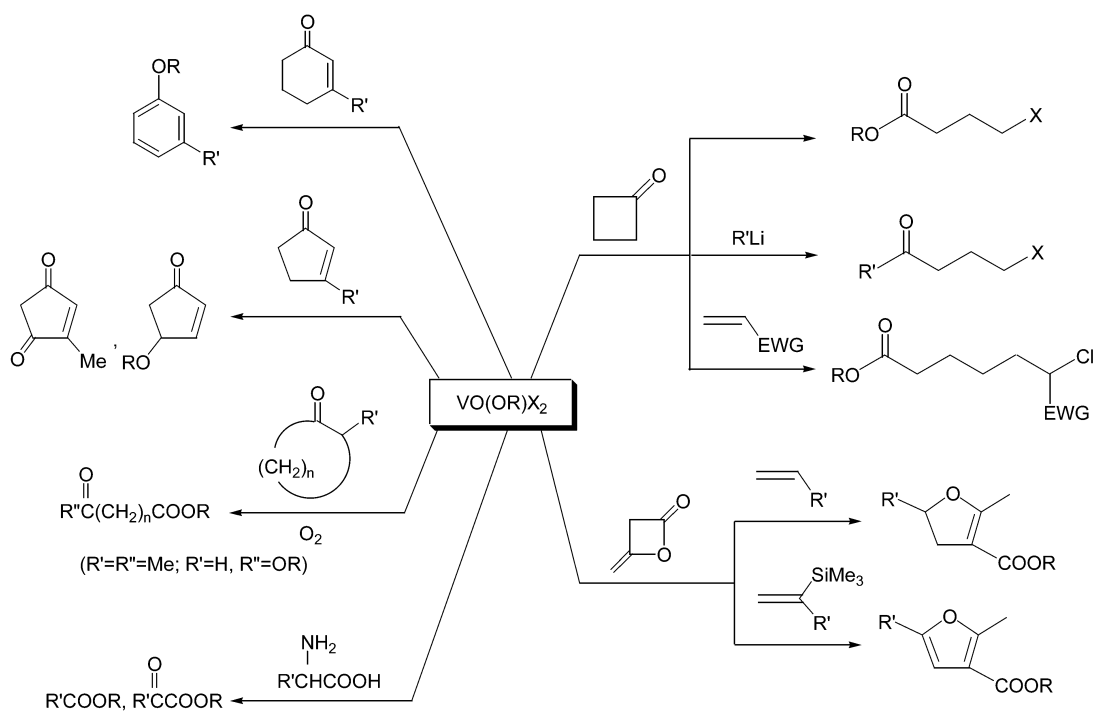
Scheme 1

OXOVANADIUM(V)-INDUCED OXIDATIVE TRANSFORMATIONS OF MAIN-GROUP ORGANOMETALLICS

Vanadium compounds in a high oxidation state are capable of inducing oxidative transformations. Pentavalent vanadium compounds are generally known to be one-electron oxidants which utilize the V(V)–V(IV) couple. The redox potential of this couple increases with acidity, so the reactions are usually carried out in acidic aqueous media.

A variety of oxidative transformations with vanadium oxidants have been developed in an organic solvent [2a], as exemplified by the oxidative coupling of phenols or naphthols [3]. The scope of synthetic reactions can be broadened by exploiting the versatility of vanadium compounds as an oxidant [4]. $VO(OR)X_2$ can act as a Lewis acid toward carbonyl compounds, which permits versatile oxidative transformations. Scheme 2 summarizes its synthetic utility: dehydrogenative aromatization, allylic oxidation, ring-opening oxygenation, oxidative decarboxylation, ring-opening oxidation, and so on [5,6]. In these transformations, one electron moves from the substrate to the Lewis acidic vanadium compound.
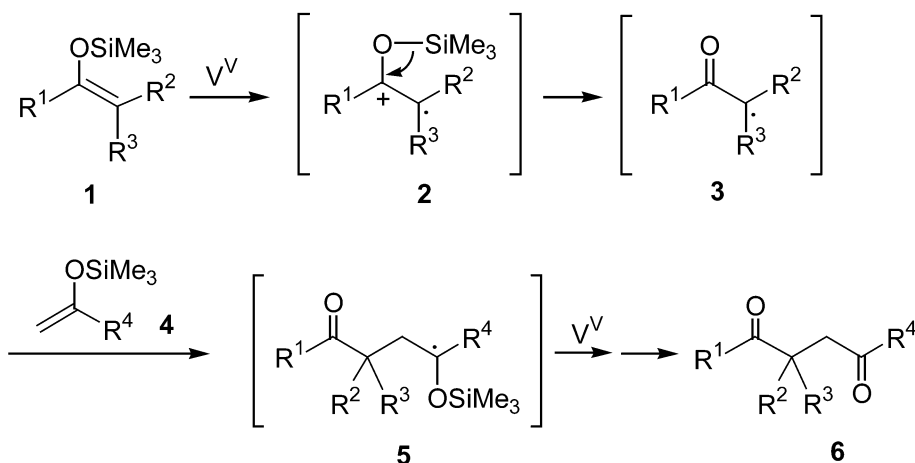

Scheme 2

Oxidation of main-group organometallic compounds with a metallic oxidant is considered to proceed via redox interaction between them, affording the corresponding radical species (Scheme 3). Another reaction path lies in the interaction between different metals to result in transmetallation. Such oxidative transformations induced by oxovanadium(V) compounds are described here.
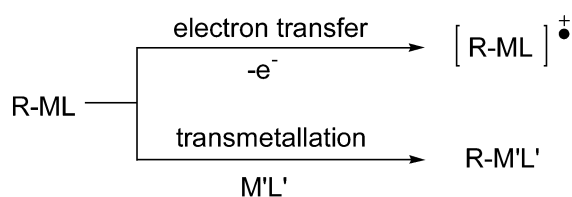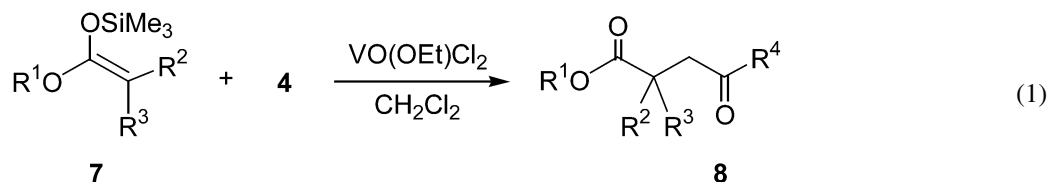
Scheme 3

## Oxidative transformations of organosilicon compounds

Silyl enol ethers are susceptible to one-electron oxidation [7]. $VO(OR)Cl_2$ [8] is capable of inducing chemoselective homo- or cross-coupling of silyl enol ethers **1** to give the corresponding 1,4-diketones **6** via regioselective carbon–carbon bond formation (Scheme 4) [9,10]. The radical cation **2**, obtained by one-electron oxidation, is desilylated to the radical **3**. The radical **3** adds intermolecularly to another silyl enol ether **4** to form the adduct **5**, which is further oxidized by the oxovanadium(V) species to form the cation. This cation undergoes desilylation to yield the 1,4-diketone **6**. The one-electron oxidation process depends on the redox potentials of both the substrates and oxovanadium(V) compounds. The more readily oxidizable silyl enol ethers work as radical precursors and the less oxidizable ones are radicophiles. The silyl ketene acetals **7** undergo more facile oxidation for the cross-coupling with the silyl enol ethers **4** to give the γ-keto esters **8** (eq. 1).


Scheme 4

(1)

This method is applied to the chemoselective oxovanadium(V)-induced cross-coupling reaction of silyl enol ethers and allylic silanes (Scheme 5) [11].
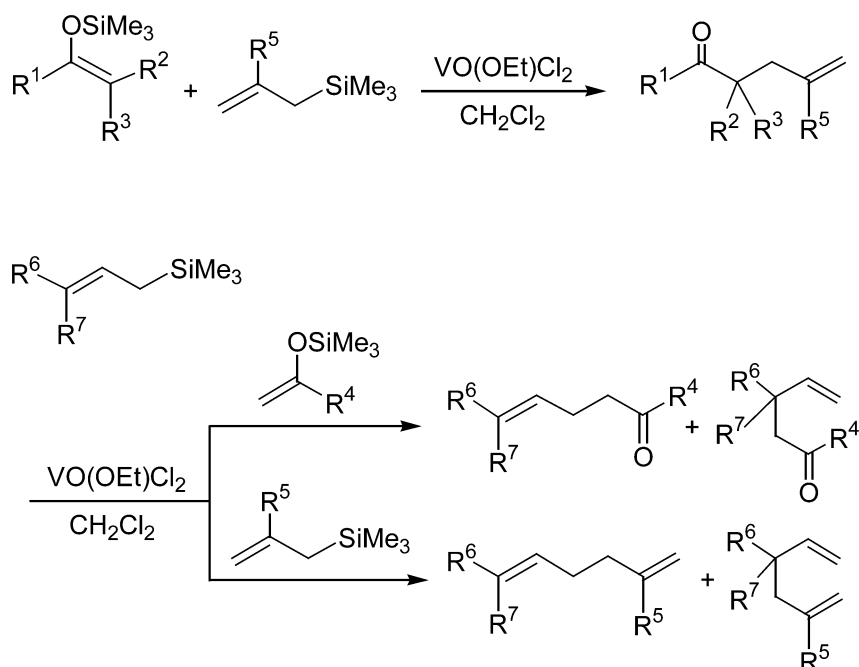
Scheme 5

Similar chemoselective oxidative desilylation is also observed with benzylic silanes. The electron-donating group on the arene ring lowers the ionization potential of the benzylsilane **9**, thus activating it for desilylation. The intermolecular regioselective coupling of the substituted benzylsilane occurs with an allylic silane or silyl enol ether (eq. 2) [12]. When the reaction of 4-methoxy-benzyltrimethylsilane with VO(OR)Cl$_2$ is carried out in *t*-BuOH under oxygen atmosphere, further oxidation occurs to give the benzaldehyde [13]. VO(OCH$_2$CF$_3$)Cl$_2$ [10] exhibits a higher reactivity than VO(OEt)Cl$_2$.

(2)
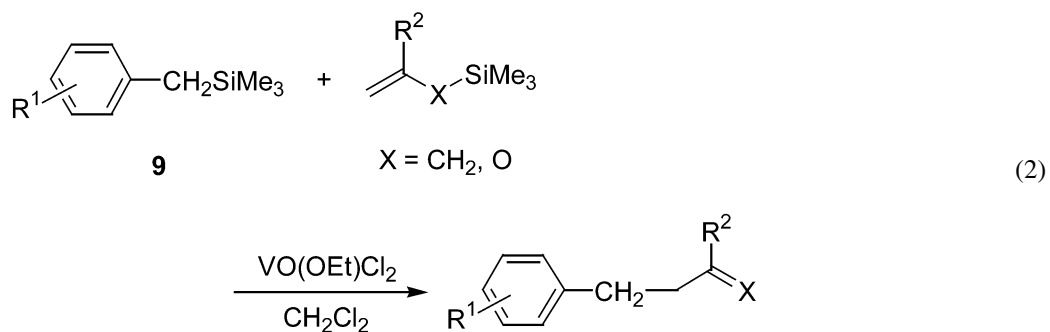
The redox potentials of organosilicon compounds, which are predicted from MOPAC-calculated ionization potentials, determine whether they act as radical precursors or acceptors. The oxovanadium(V) reagent, which differentiates the oxidation process effectively, is a versatile oxidant to promote the chemoselective coupling via oxidative desilylation of organosilicon compounds under controlled conditions. The reactivity order is as follows; VO(OR)Cl$_2$-AgOTf or Me$_3$SiOTf > VO(OR)Cl$_2$ > VO(OR)$_2$Cl > VO(OR)$_3$ [5]. Thus, the oxidation of organosilicon compounds provides a useful route to synthetic equivalents for cationic intermediates for the selective carbon–carbon bond formation.

Oxidative transformations of organotin compounds

Allylic and benzylic tins are known to undergo more facile oxidation than the corresponding silicon compounds [14], and are converted to the alcohols or their derivatives by a metallic oxidant such as Mn(IV), Ce(IV), Tl(III), or Fe(III) [15]. The oxidation of benzyltributyltins **10** with $VO(OCH_2CF_3)Cl_2$ in *t*-BuOH under oxygen atmosphere leads to the aldehydes (ketones) **11** and the corresponding carboxylic acids **12** (eq. 3) [13,16]. Furthermore, the catalytic reaction proceeds with $VO(OCH_2CF_3)Cl_2$. 1-Cyclopropyl-1-phenylmethyltributyltin is oxidized to the cyclopropyl ketone as a major product.


(3)
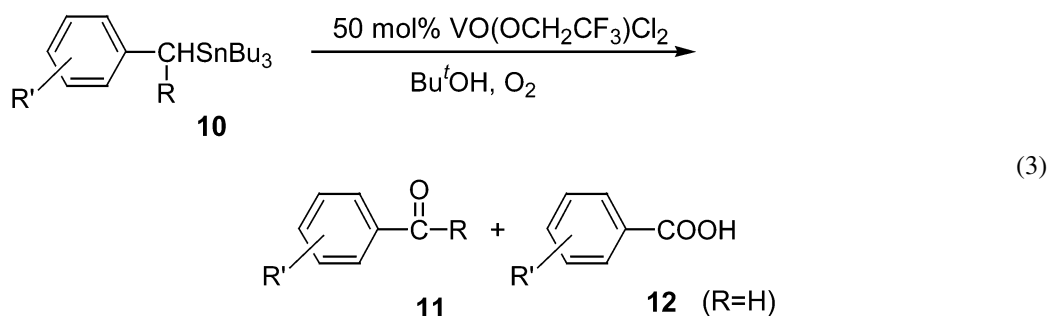
In the case of benzylic silanes, electron-transfer mechanism is considered to operate as mentioned above. Although benzyltin compounds undergo the more facile oxidation rather than benzylsilanes, an electron-transfer process may not be favorable, judging from the reactivities of the cyclopropyl-methyltin. Either electron-transfer process or homolytic scission of carbon–vanadium bond of a benzyl-vanadium species is suggested to be a minor pathway, and the ketone may be derived by transmetallation with nonradical process. A low-valent vanadium species generated in situ is oxidized under oxygen atmosphere to regenerate a vanadium species in its high oxidation state for catalytic reactions [16].

**Oxidative transformations of organoaluminum compounds**

The redox processes of organometallics are important in synthetic transformations, especially in transition-metal-induced reactions. The transition-metal-catalyzed cross-coupling reactions of main-group organometallic compounds with organic halides provide versatile synthetic tools in organic synthesis. As mentioned above, the transmetallation and/or electronic interaction can widen the reactivities of main-group organometallic compounds. One-electron oxidation of d°-transition-metal complexes such as titanocene, zirconocene, and platinum complex with a metallic oxidant permits synthetically useful transformations via organometallic radical cation species as key intermediates [17]. In these reactions, the selective coupling is achieved between two ligands on the transition metal, providing a method for carbon–carbon bond formation.

The usage of main-group organometallics is limited because of their restricted redox processes. Oxidation of organoaluminum compounds usually afford alcohols [18], but to the best of our knowledge, selective carbon–carbon bond formation of organic substituents on aluminum has not been investigated. The oxidation of the aryldiethylaluminums **13**, obtained from aryllithiums and diethylaluminum chloride, with $VO(OEt)Cl_2$ results in novel ethylation (Scheme 6) [19]. This method can be applied to a variety of arylaluminums bearing an electron-donating group, which permits the selective ligand coupling of the organic groups on aluminum.
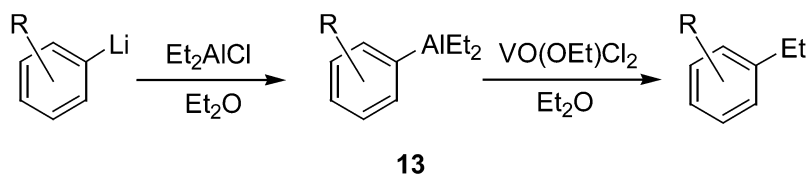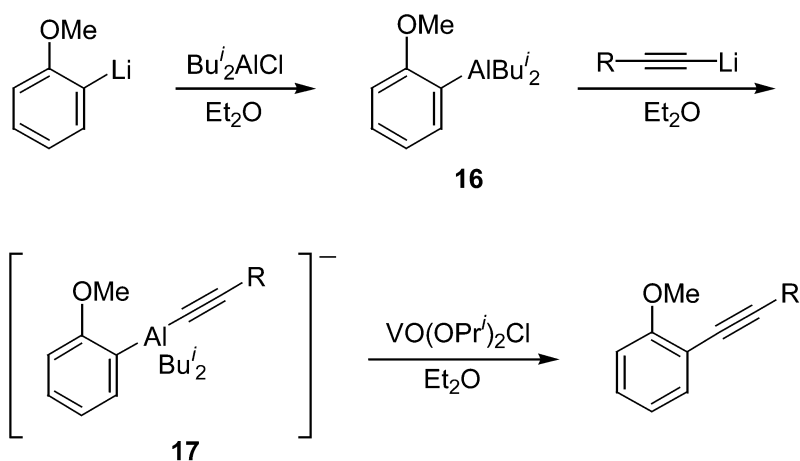
Scheme 6

The addition of 1-alkynyllithium to the 1-alkenylaluminum **14**, followed by treatment with VO(OEt)Cl$_2$, leads to the ligand coupling on aluminum, giving the corresponding *trans*-enyne **15** via chemoselective and stereoselective bond formation between *sp* and *sp*^{2} carbons (Scheme 7) [20].
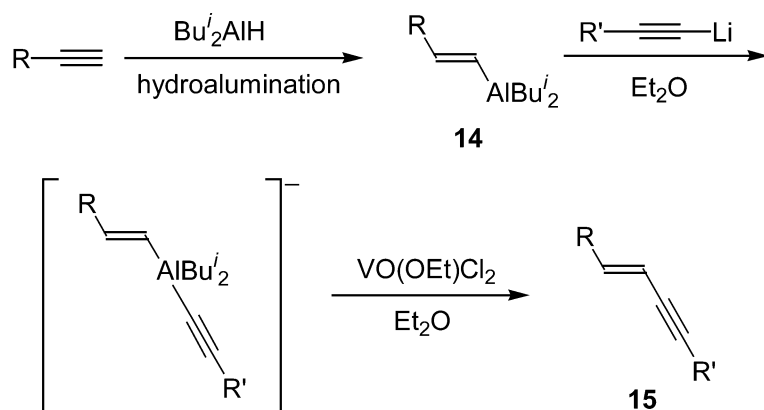
Scheme 7

The ate complex **17** derived from the aryl-substituted aluminum **16** undergoes similar ligand coupling with VO(OPr-*i*)$_2$Cl to give the aryl-1-alkynyl coupling product selectively (Scheme 8).
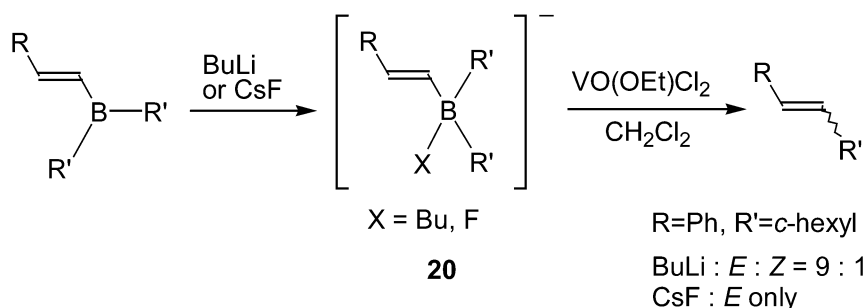

Scheme 8

Although the reaction mechanism is ambiguous, coordination of the oxo atom of the oxo-vanadium(V) species to organoaluminums seems to promote electron transfer or transmetallation for the oxidative coupling. The transformation is considered to be the first formal reductive elimination on aluminum [21].

Oxidative transformations of organoboron compounds

The organoboron compound **18**, derived from dicyclohexylborane and phenylacetylene or acetylenecarboxylic ester, is oxidized with $VO(OEt)Cl_2$ to give the (*E*)-ethenylcyclohexane **19** selectively without the formation of bi(cyclohexyl) and 1,4-butadiene derivative (eq. 4) [22]. When an equimolar mixture of bis(2-methylcyclohexyl)[(*E*)-2-phenylethenyl]borane and dicyclohexyl[(*E*)-2-(4-methylphenyl)ethnyl]borane is treated similarly, 1-methyl-2-(2-phenylethenyl)cyclohexane and [2-(4-methylphenyl)ethenyl]cyclohexane are predominantly produced, with only trace amounts of the cross-over products. The finding suggests that the coupling reaction proceeds mostly in an intramolecular path.

(4)

18　　**19**　*E* >98 %
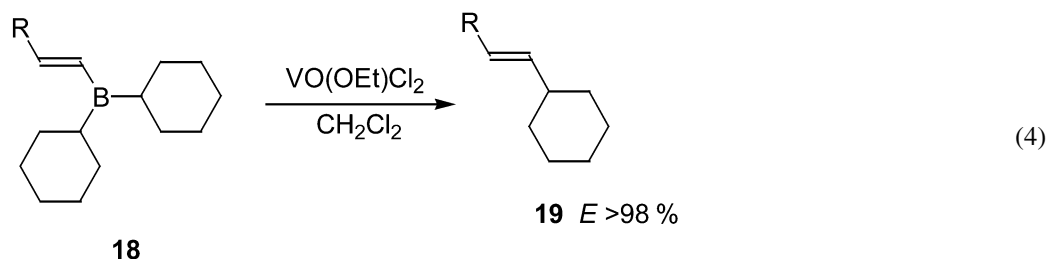
The ate complexes **20** of the organoborons undergo the more facile oxidation with $VO(OEt)Cl_2$, as observed in the oxidation of the aluminum ate complexes. The organic groups are effectively differentiated in the coupling reaction. Although the *Z*-isomer is obtained in a small amount, use of the organoborate derived from CsF [23] improves the stereoselectivity, giving the *E*-isomer exclusively (Scheme 9).


X = Bu, F

20

R=Ph, R'=*c*-hexyl

BuLi : *E* : *Z* = 9 : 1
CsF : *E* only

Scheme 9

Alkenyltrialkylborates have been reported to be oxidized to alkylated alkenes with I_2 or BrCN [24]. Biaryl formation also occurs by electrochemical, photochemical, and chemical oxidation, for example, with Ir(IV), of tetraarylborates [25]. The oxovanadium(V)-induced ligand coupling provides another effective method for the carbon–carbon bond formation on boron.

Oxidative transformations of organozinc compounds

Organozinc compounds can tolerate a broad range of functional groups. Cross-coupling reactions between organozinc reagents and electrophiles such as organic halides are catalyzed by transition-metal complexes [26]. However, examples for the selective cross-coupling of two ligands of organozinc compounds are limited to a few cases, which include 1,2-migration of zincate carbenoids and intramolecular coupling of organozinc compounds by organocopper reagents [27].

The organozinc compound **21a**, which is prepared in situ by transmetallation of the methylzinc chloride with the aryllithium, is oxidized with Cp_2FePF_6, to give the homo-coupling compound selectively. $AgBF_4$ serves as a useful oxidant to give the desired cross-coupling compound **22a**, probably via a one-electron oxidation process. Using $VO(OEt)Cl_2$ instead of $AgBF_4$, the cross-coupling reaction proceeds in preference to the homo-coupling reaction [28]. Higher selectivity for the cross-coupling is observed with $VO(OEt)Cl_2$ than with $VO(OPr-i)Cl_2$ or $VO(OPr-i)_2Cl$.

The coupling reaction of organozinc compounds **21** bearing an *o*-methoxy, *o*-phenyl, or *o*-methylthio group on the arene ring proceeds smoothly, but the *o*-cyano-substituted alkylarylzinc exhibits a lower reactivity, although organoaluminum compounds having an electron-withdrawing substituent do not undergo oxidative coupling under similar conditions. Alkyl and 1-alkynyl groups can couple with the aryl group successfully (Scheme 10).
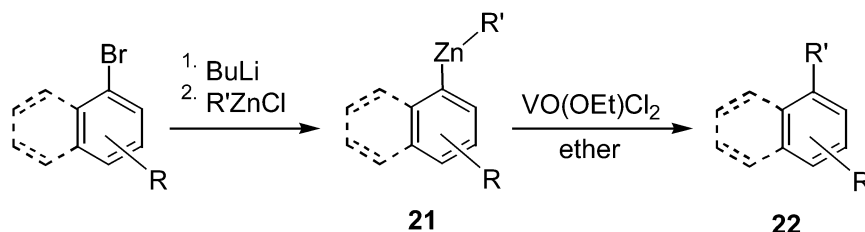
Scheme 10

Triorganozincates **23** are readily oxidized with $VO(OEt)Cl_2$ smoothly to give the cross-coupling compounds **22** (Scheme 11) [28].
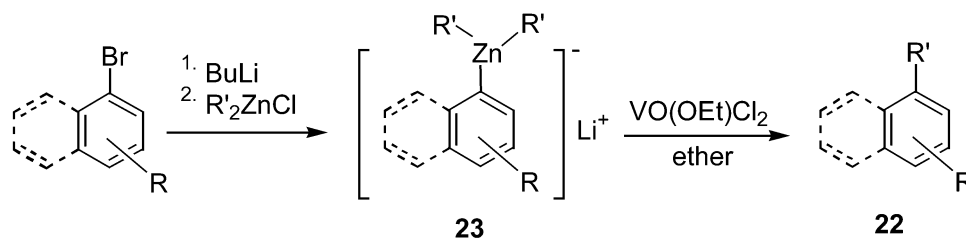
Scheme 11

To avoid the homo-coupling reaction of aryllithium compounds with oxovanadium(V) compounds [20], arylzincates from R_3ZnLi [29], and aryl iodides through iodine–zinc exchange can be used. Oxidation of the thus-obtained zinc ate complexes **23** results in the exclusive formation of the cross-coupling product **22** as shown in Scheme 12 [28].
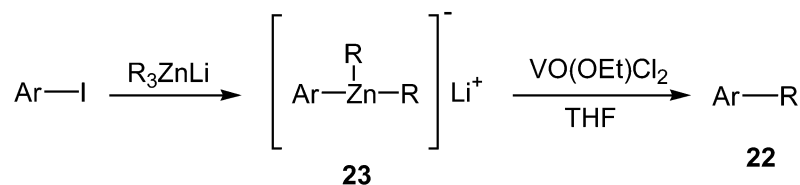
Scheme 12

The organozincates **24**, obtained from various bromoarenes and Me_4ZnLi_2 [29], are similarly oxidized with $VO(OEt)Cl_2$ to give the methylarene **22a** (Scheme 13) [30]. Thus, the coupling between sp^2-carbon (aryl group) and sp^3-carbon (methyl group) of aryltrimethylzincates is achieved chemoselectively.

Scheme 13

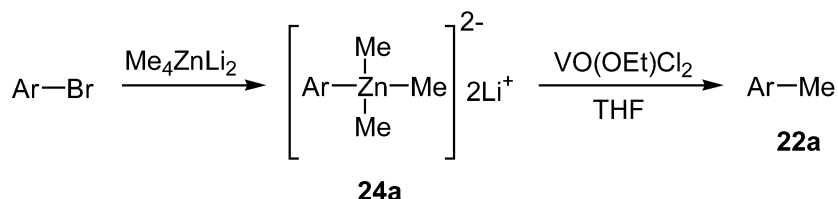The oxovanadium(V)-induced oxidative transformation is applied to the selective carbon–carbon bond formation between sp^3-carbons [30]. A bromine–zinc exchange reaction of **25** selectively occurs at the position cis to the phenyl group by treatment with Me_4ZnLi_2 [31]. The oxidation of the thus-obtained zincate **26** with $VO(OEt)Cl_2$ leads to the stereoselective formation of 1-bromo-1-methyl-2-phenylcyclopropane (**27**). On the other hand, when the reaction mixture is warmed up to 0 °C, followed by treatment of $VO(OEt)Cl_2$, dimethylation takes place to give the dimethylcyclopropane **29** via the organozinc **28** (Scheme 14).
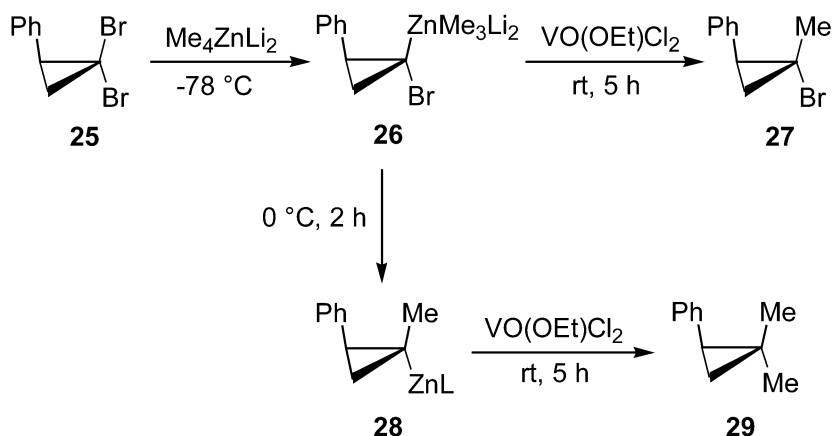
Scheme 14

Dialkylzinc reagent (R_2Zn) is recognized as a mild nucleophile in the presence of an additional promoter such as a Lewis acid [32]. Characteristics of oxovanadium(V) compounds as a Lewis acid and one-electron oxidant permit vicinal dialkylation at both the α and β positions of α,β-unsaturated carbonyl compounds with dialkylzinc reagents (Scheme 15) [33]. For example, reaction of 2-cyclohexenone with dimethylzinc in the presence of $VO(OEt)Cl_2$ affords 2,3-dimethylcyclohexanone. Use of a stronger Lewis acid, $VO(OEt)Cl_2 > VO(OPr-i)Cl_2 > VO(OPr-i)_2Cl$, gives a better result.
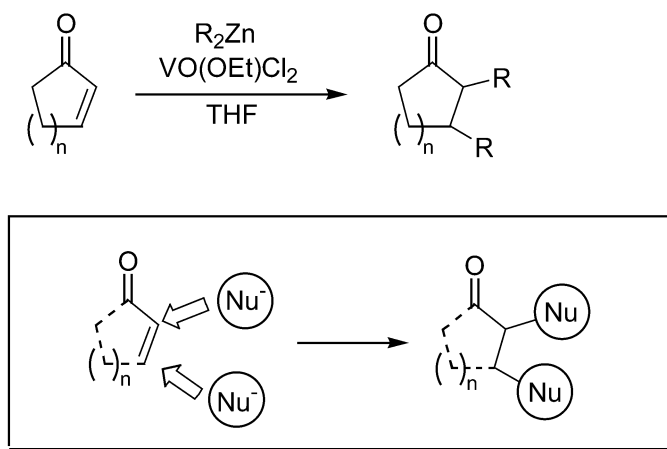
Scheme 15

This method can be applied to vicinal alkylation with triethylaluminum or triethylborane compounds as shown in eq. 5 [33]. In contrast, the similar oxidation reaction is not observed with organocuprate reagents.

(5)

R_nM: Et_3Al, Et_3B
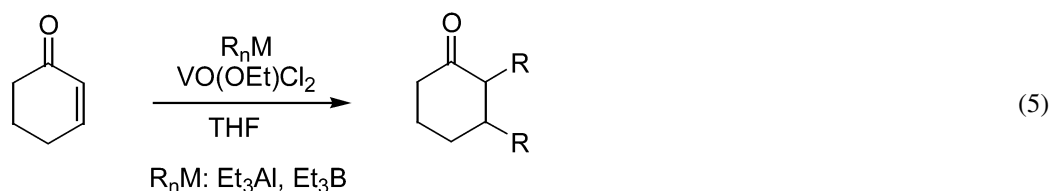
Contrary to dialkylzincs, lithium trialkylzincates (R_3ZnLi) have enough nucleophilicity for conjugate addition without the aid of a Lewis acid. Treatment with $R_2R'ZnLi$, followed by oxidation with $VO(OEt)Cl_2$, leads to the vicinal dialkylation to give the cycloalkanones **30** (Scheme 16). A better yield is obtained with the organozinc compound prepared from a $ZnCl_2$-TMEDA complex and BuLi. It is noteworthy that introduction of alkyl groups is differentiated regioselectively. For example, use of $BuMe_2ZnLi$ results in the selective formation of 3-butyl-2-methylcycloalkanone.
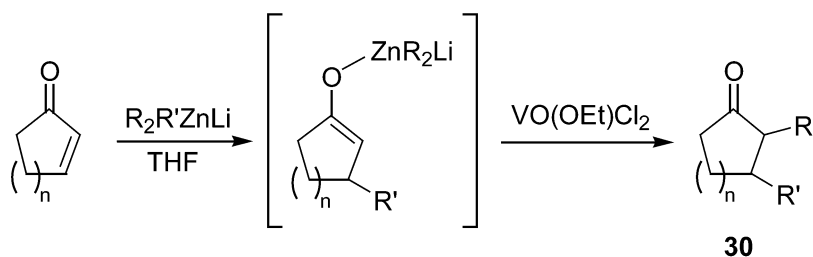
Scheme 16

Oxidative transformations of organozirconium compounds

The oxidation reaction of (*E*)-1-alkenylchlorozirconocenes with VO(OPr-*i*)$_2$Cl leads to the stereoselective homo-coupling product, the (*E,E*)-diene [34]. (*E*)-1-Alkenyl-1-alkynylzirconocenes undergo the oxovanadium(V)-induced cross-coupling of organic substituents on zirconium, to give the (*E*)-enynes stereoselectively.

CATALYTIC SYSTEM FOR REDUCTIVE TRANSFORMATIONS VIA ONE-ELECTRON TRANSFER

Synthetic limitation partially exists in the use of stoichiometric or excess amounts of metallic reductants or oxidants to complete the redox reaction. A catalytic system should be constructed to avoid the use of stoichiometric expensive and/or toxic metallic reagents. It is important to select stoichiometric co-reductants or cooxidants for the reversible cycle of a catalyst (Scheme 17). A metallic coreductant is ultimately converted to the corresponding metal salt in a higher oxidation state, which may work as a Lewis acid or, on the contrary, impede the reduction reaction. Taking these interactions into account, the requisite catalytic system is envisioned to be formed by multicomponent interaction. Steric control by means of coordination may permit the stereoselective and/or stereospecific transformations. An alternative method for recycling a catalyst is achieved by electrolysis [35].
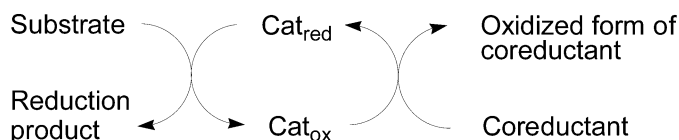
Scheme 17

Dehalogenative reduction

Homolytic cleavage of organic halides is induced by one-electron reduction to afford the corresponding radical intermediates. A catalytic dehalogenation is achieved in the vanadium-induced reduction. The highly stereoselective monodebromination of *gem*-dibromocyclopropane **31** to monobromide **32** proceeds with a catalytic amount of a low-valent vanadium species generated from VCl_3 or $CpV(CO)_4$ and Zn as a stoichiometric coreductant, in cooperation with diethyl phosphonate or triethyl phosphite (Scheme 18) [36]. The phosphonate or phosphite is likely to play an important role in the debromination step. The coordination to vanadium leads to a bulky and stronger reductant. The former effect is related to the stereoselectivity, since the bulky reductant is liable to approach the bromide from the less hindered side. Furthermore, a hydrogen source is assumed to be available from the phosphonate or phosphite [37] in the coordination sphere. In this manner, the ternary reductant system contributes to the stereoselective catalytic debromination.
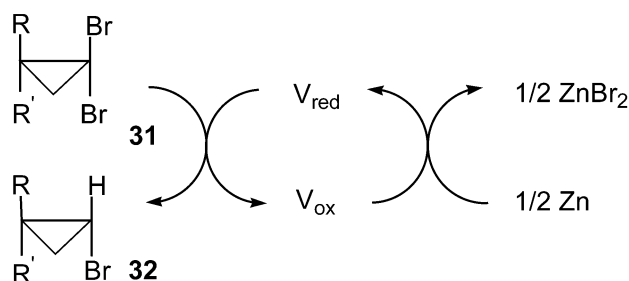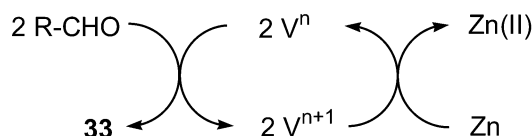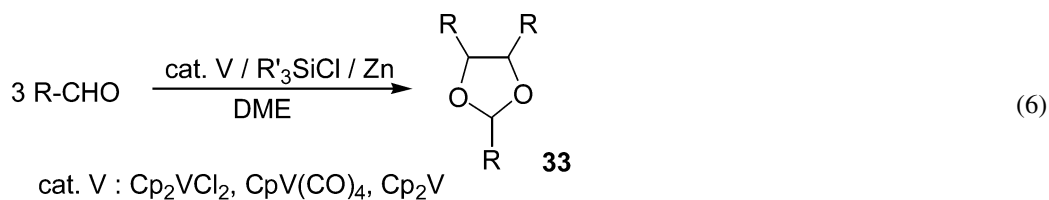

Scheme 18

The combination of YbI_2 catalyst and Al is effective for the photo-induced catalytic hydrogenative debromination of alkyl bromide [38]. In both vanadium- and ytterbium-catalyzed reactions, the multicomponent redox system is formed in an appropriate combination of a catalyst, a coreductant, and an additive.
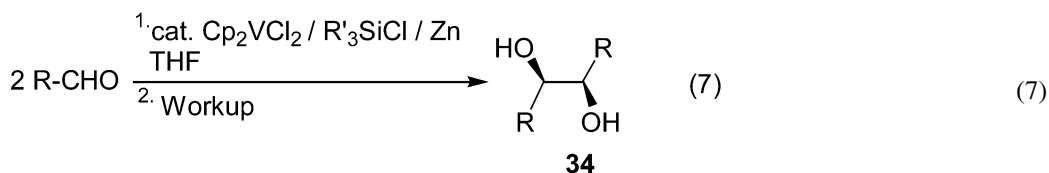
Pinacol coupling

The reductive dimerization of carbonyl compounds is a useful synthetic method for constructing vicinally functionalized carbon–carbon bonds. One-electron transfer from a metal to a carbonyl group generates the corresponding ketyl radical, which can dimerize to give either *dl-* or *meso*-1,2-diols. A complementary route to 1,2-diols has been developed by the osmium-catalyzed dihydroxylation of olefins [39]. For the former stoichiometric reductive dimerization, low-valent metals such as aluminum amalgam, zinc, titanium, vanadium, and samarium have been employed conveniently. For example, the pinacol coupling reaction using $TiCl_3/Zn$-Cu and $[V_2Cl_3(THF)_6]_2[Zn_2Cl_6]$ have been developed successfully for the synthesis of paclitaxel and C_2-symmetrical HIV protease inhibitors, respectively [40]. To synthesize such complicated compounds, the efficient control of the stereochemistry in the coupling reaction is of importance [41] in addition to the construction of a catalytic system for low-valent metals. The ternary system consisting of a catalytic metal, a chlorosilane, and a stoichiometric coreductant provides a catalytic process for the pinacol coupling. The homocoupling of aliphatic aldehydes is catalyzed by $CpV(CO)_4$ or Cp_2VCl_2 in the presence of Me_3SiCl and Zn in DME to give the 1,3-dioxolanes **33** via the coupling and acetalization (eq. 6) [42]. A vanadium catalyst is essential, although the combination of Zn and Me_3SiCl allows the reductive dimerization of aldehydes. The low-valent vanadium species mediating the electron transfer is generated in situ, and a reversible redox cycle is formed in the presence of Zn as a stoichiometric coreductant (Scheme 19).

$$3 \; R\text{-}CHO \xrightarrow[\text{DME}]{\text{cat. V / R'}_3\text{SiCl / Zn}} \mathbf{33} \qquad (6)$$

$$\text{cat. V : } Cp_2VCl_2, \; CpV(CO)_4, \; Cp_2V$$

$$2 \; R\text{-}CHO \qquad 2 \; V^n \qquad Zn(II)$$

$$\mathbf{33} \qquad 2 \; V^{n+1} \qquad Zn$$

Scheme 19

Use of THF as a solvent leads to the highly diastereoselective formation of the *dl-*1,2-diols **34** from secondary aliphatic aldehydes (eq. 7) [43]. The diastereoselectivity also depends on chlorosilanes: $PhMe_2SiCl$ is superior to Me_3SiCl. Cp_2TiCl_2 can be similarly employed as a catalyst [44].

$$2 \; R\text{-}CHO \xrightarrow[\text{2. Workup}]{\begin{array}{c}\text{1. cat. } Cp_2VCl_2 \text{ / R'}_3\text{SiCl / Zn} \\ \text{THF}\end{array}} \mathbf{34} \qquad (7) \qquad (7)$$

In the absence of a chlorosilane, a catalytic reaction is not observed. Silylation is considered to liberate the catalyst. The Lewis-acidic-like interaction of a chlorosilane with a carbonyl oxygen is suggested to facilitate the electron transfer to the carbonyl group, generating the stabilized silyloxyalkyl radical for dimerization. Another interaction with the vanadium catalyst is possible since the UV–vis spectrum of Cp_2VCl_2 changes on the addition of Me_3SiCl. The diastereoselectivity depends on the substituent of chlorosilanes, which implies its steric effect in the coupling step. Fürstner has independently developed a catalytic method for the McMurry coupling by using the similar ternary-component sys-

tem [45]. The oxoamide undergoes reductive cyclization to the indoles in the presence of a catalytic amount of $TiCl_3$, Zn, and a chlorosilane.

Based on these observations [42–45], a variety of modified catalytic systems have been investigated for the diastereoselective carbon–carbon bond formation. A trinuclear complex **35** derived from Cp_2TiCl_2 and $MgBr_2$ is considered to be an active catalyst for the *dl*-diastereoselective pinacol coupling of aromatic aldehydes [46]. The observed *dl* selectivity is explained by minimization of steric interference through *anti*-orientation in the intermediate **36**. Using *rac*-ethylenebis(η^5-tetrahydroindenyl-titanium) dichloride, the diastereoselective pinacol coupling of aromatic aldehydes also proceeds via **37** [47]. This method is applied to the enantioselective pinacol coupling by using a chiral catalyst **38** or **39** [48].
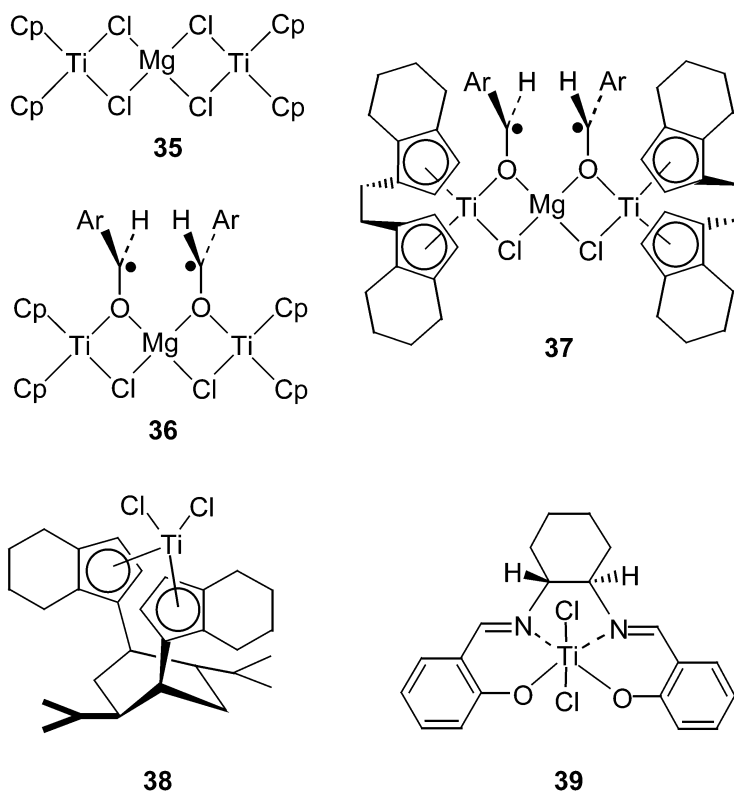
As shown in eqs. 8–9, 1,5- and 1,6-dialdehydes undergo annulative pinacol coupling to give cyclic *vic*-diols [49]. The vanadium-catalyzed intramolecular coupling reaction of 1,5-diketone also takes place with excellent selectivity (eq. 10) although the intermolecular coupling of ketones such as acetophenone results in low diastereoselectivity under the conditions [43a].

$$syn : anti = 89 : 11 \quad (8)$$

$$syn : anti = 52 : 48 \quad (9)$$

$$syn : anti = 91 : 9 \quad (10)$$
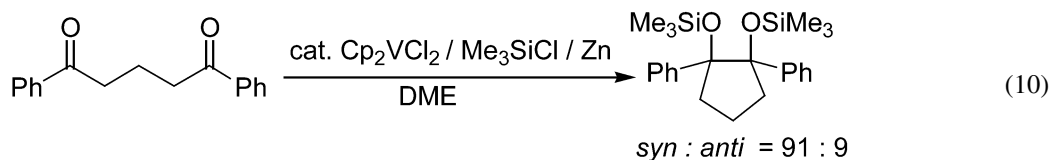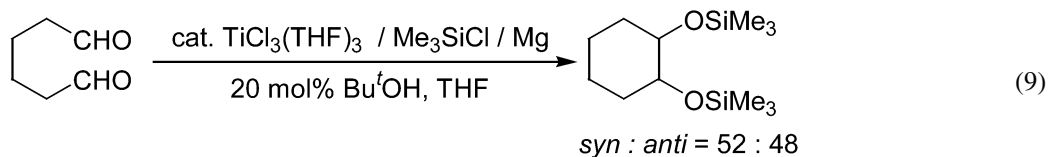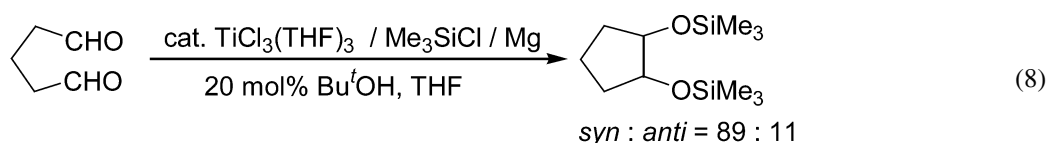
The ligand and additive effects are studied in the diastereoselective titanium-catalyzed coupling of aromatic aldehydes [49]. Higher selectivity is attained especially with $OC[N(Et)Ph]_2$ as a ligand. Substoichiometric quantities of a protic (t-BuOH, catechol, 2,2'-biphenol) or Lewis basic (DMF, N,N-dimethylacetamide) additive afford five- to ten-fold rate accelerations relative to the parent $TiCl_3(THF)_3$ catalyst.

A catalytic turnover is formed by protonation of the metal–oxygen bond instead of silylation. 2,6-Lutidine hydrochloride or 2,4,6-collidine hydrochloride behaves as an appropriate proton source in the Cp_2TiCl_2-catalyzed pinacol coupling of aromatic aldehydes in the presence of Mn [50].

Ac_2O or AcCl can be utilized instead of a chlorosilane in the vanadium- or titanium-catalyzed pinacol coupling reaction of aromatic aldehydes to give the diacetate **40** (eq. 11) [51].

40
$$dl : meso = 80 : 20 \quad (11)$$
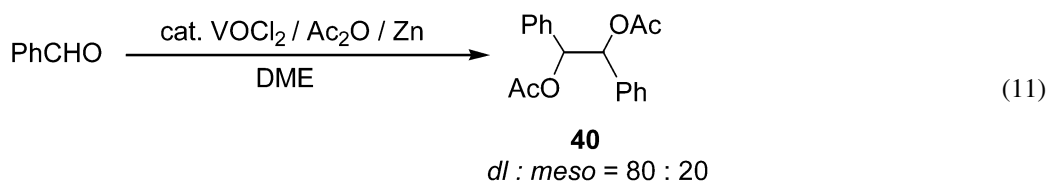
Low-valent lanthanides, represented by Sm(II) compounds, induce one-electron reduction. The recycling for the Sm(II) species is first performed by electrochemical reduction of the Sm(III) species [52]. In one-component cell electrolysis, the samarium-catalyzed pinacol coupling proceeds with sacrificial anodes of Mg or Al. Furthermore, redox interaction between Sm species and Mg allows the use of Mg as a reducing agent to form a ternary-component catalytic system for pinacol coupling in combination with Me_3SiCl as mentioned above [53]. A catalytic amount of Cr(II) salt or chromocene, Mn powder, and a chlorosilane are effective in the reductive coupling [54].

The coupling reaction of imines has been less investigated despite the frequent occurrence of *vic*-diamine units in naturally occurring compounds. A catalytic $PbBr_2$/Al system is effective for the coupling of aromatic imines in the presence of trifluoroacetic acid or $AlBr_3$ [55]. This recycling step is also performed using an undivided cell under constant current density [56]. A catalytic Cp_2TiCl_2/Sm system is effective to provide *dl*-diamines with moderate selectivity [57].

The $Cp_2VCl_2/R_3SiCl/Zn$ catalytic system can be also used for the reductive coupling of aldimines **41** (eq. 12) [58]. *meso*-Diastereoselectivity is observed in contrast to the coupling with catalytic Cp_2TiCl_2/Sm system. The selectivity depends on the substituents on both the nitrogen and silane atoms. The allyl or benzyl group on the nitrogen atom is advantageous for *meso* selection.

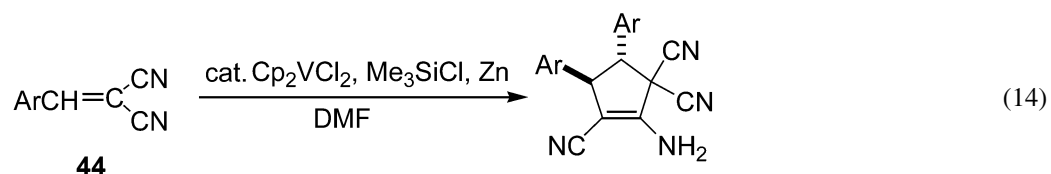$$2 \text{ Ar-CH=N-R} \xrightarrow[\text{2. Workup}]{\substack{\text{1. cat. Cp}_2\text{VCl}_2 \text{ / R}_3\text{SiCl / Zn} \\ \text{DMF}}} \begin{array}{c} \text{RNH} \quad \text{Ar} \\ \diagup\diagdown \\ \text{Ar} \quad \text{HNR} \end{array} \qquad (12)$$

41
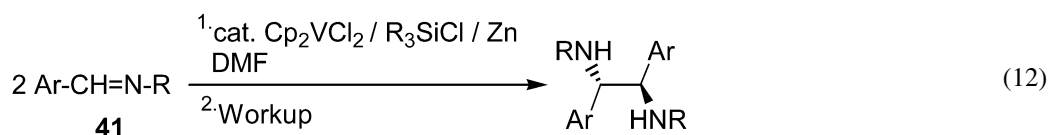
Radical cyclization

The above-mentioned reagent-controlled catalytic system is of synthetic potential in radical reactions. The generated ketyl radicals undergo the inter- and intra-molecular coupling with a variety of radical acceptors. A multicomponent catalytic reductant system consisting of catalytic SmI_2, Zn/Hg, LiI, and Me_3SiOTf induces the spirolactonization [59].

The reaction of the δ,ε-unsaturated aldehyde **42** with catalytic $Cp_2VCl_2/Me_3SiCl/Zn$ is conducted in THF to afford the cyclic alcohol **43** with excellent diastereoselectivity (eq. 13) [43]. The transformation is explained by 5-*exo*-cyclization of the radical anion intermediate, followed by chlorination.

$$\text{(13)}$$

42   **43**

$\alpha\text{-Me / }\beta\text{-Me} = 77 : 23$
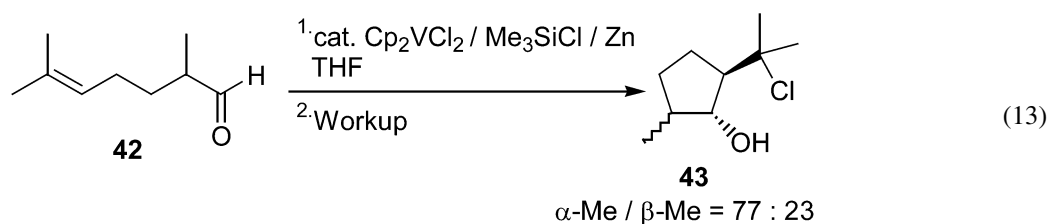
Catalytic cyclodimerization of the arylidene malononitriles **44** proceeds diastereoselectively in the presence of chlorotrimethylsilane as shown in eq. 14 [60].

$$\text{ArCH=C}\begin{array}{c}\text{CN}\\\text{CN}\end{array} \xrightarrow[\text{DMF}]{\text{cat. Cp}_2\text{VCl}_2, \text{ Me}_3\text{SiCl, Zn}} \begin{array}{c}\text{Ar}\quad\text{CN}\\ \text{Ar}\diagup\diagdown\text{CN}\\ \text{NC}\quad\text{NH}_2\end{array} \qquad (14)$$

44

This method is applied to the Cp_2TiCl_2-catalyzed reductive radical cyclization of the ketonitriles **45**, giving the 2-amino-3-cyano-2-cyclopenten-1-ols in moderate to good yields with high trans selectivity (up to 94 % trans, eq. 15) [61].

$$\text{(15)}$$

45
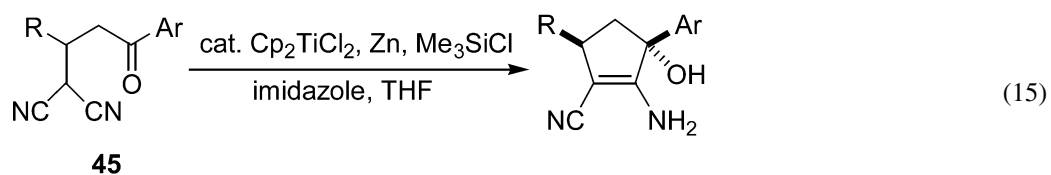
Olefinic iodoethers **46** similarly undergo the Cp_2TiCl_2-catalyzed reductive cyclization in the presence of Mn and Me_3SiCl (eq. 16) [62]. This protocol provides a versatile method for the selective formation of multisubstituted tetrahydrofurans **47**.

$$\text{(16)}$$

46   **47**
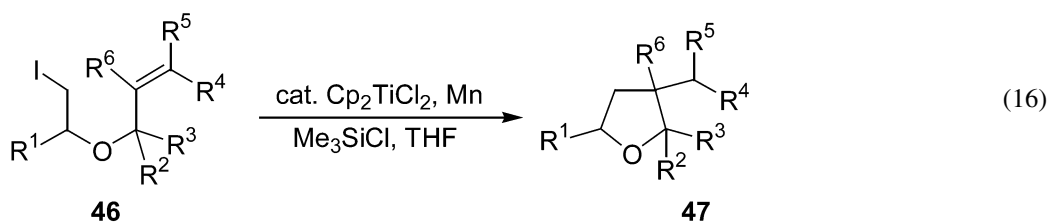
CONCLUSIONS AND OUTLOOK

Oxovanadium(V) compounds are potential Lewis acids with oxidation ability to induce the oxidation reactions of various main-group organometallic compounds based on their characteristics. Oxidation capability and redox potential are effectively controlled by the substituent of oxovanadium(V) compounds. The oxidative ligand coupling proceeds via the intermetallic interaction between vanadium species and main-group organometallics.

The multicomponent system consisting of a catalyst, a coreductant, and an additive cooperates with each other to construct the catalytic systems for efficient one-electron reduction [2,63]. In this system, the active catalyst is smoothly regenerated by redox interaction with the coreductant. The selection of the coreductant is, of course, important from this point of view. Furthermore, the oxidized form of the coreductant should not interfere with, but assist the reduction reaction or at least, be tolerant under the conditions. Additives, which are considered to contribute to the redox cycle, possibly facilitate the electron transfer and liberate the catalyst from the reaction adduct.

Both synthetic methods are expected to be promising in synthetic chemistry. These methods are complementary and useful to generate radical intermediates. Attainment of higher stereoselectivity is expected to be one of the coming goals in this field. Redox of vanadium compounds are also useful in the design of materials [64].

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