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Enantioselective vanadium-catalyzed transformations. An update

Hélène Pellissier

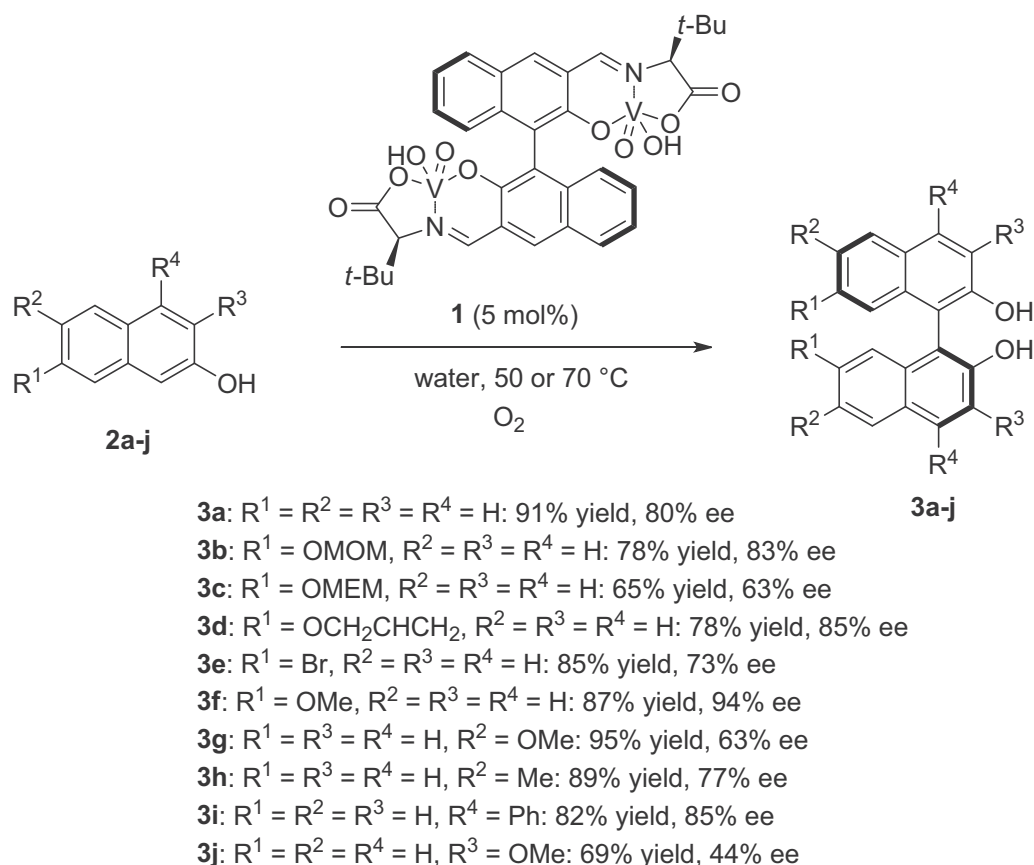
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1. Introduction

While asymmetric metal catalysis has been widely developed with spectacular successes throughout the last decades [1], the special use of vanadium has remained silent for a long time in spite

of its involvement in many fields, such as in biochemistry. Indeed, vanadium participates in redox processes catalyzed by enzymes, such as bromoperoxidase and nitrogenase [2]. Moreover, in chemistry vanadium presents the advantage to be less moisture sensitive than other metals. Another interest of vanadium is related to its wide range of oxidation states, allowing many vanadium complexes to be synthesized. Nowadays, the utility of vanadium complexes is well demonstrated in a myriad of organic transformations. In particular, asymmetric vanadium catalysis has gained significant importance in the last decade, with its successful application to various types of enantioselective reactions. Indeed, since the pioneering works reported by Sharpless in 1977, dealing with asymmetric epoxidations promoted by a proline-derived hydroxamic acid vanadium complex [3], many types of highly efficient enantioselective vanadium-catalyzed

Abbreviations: acac, acetylacetonate; Ar, aryl; BINOL, 1,1'-bi-2-naphthol; Bn, benzyl; Box, bisoxazoline; Bs, benzenesulfonyl; Bz, benzoyl; CHP, cumene hydroperoxide; Cy, cyclohexyl; DAC, 1,2-diaminocyclohexane; DCE, 1,2-dichloroethane; de, diastereomeric excess; Dec, decyl; DMA, dimethylacetamide; DMF, *N,N*-dimethylformamide; ee, enantiomeric excess; H₂BPDC, biphenyl-4,4'-dicarboxylic acid; Hex, hexyl; Lap, laponite; MEM, methoxyethoxymethyl; MOF, metal organic framework; MOM, methoxymethyl; Naph, naphthyl; Pent, pentyl; PS, polystyrene; r.t., room temperature; salen, salicylidenediamine; TBHP, *tert*-butyl hydroperoxide; TEA, trimethylamine; TMS, trimethylsilyl; Tol, tolyl.



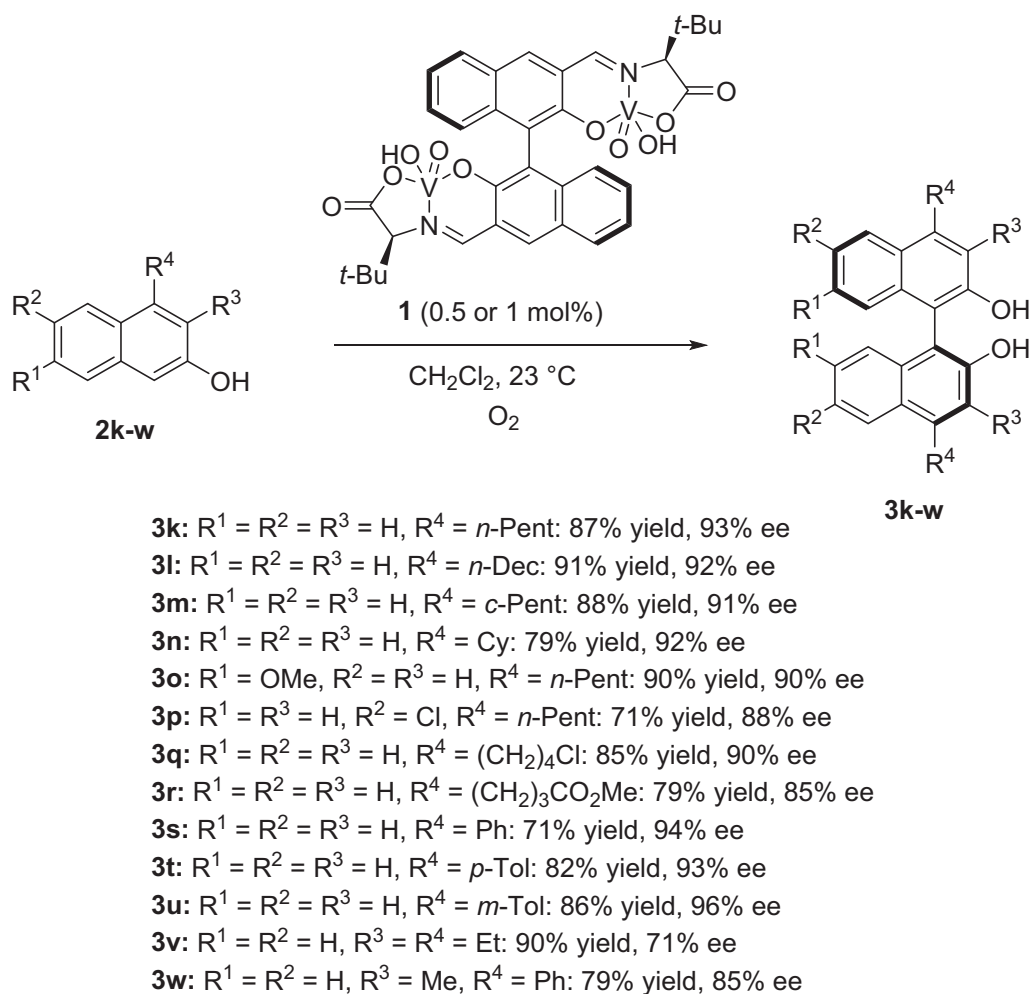
Scheme 1. Oxidative coupling of 2-naphthols catalyzed by dinuclear (*S*)-*tert*-leucine-derived Schiff base vanadium(V) complex **1** in water [7].

transformations have been developed, including asymmetric epoxidations, sulfide oxidations, α -hydroxy acid oxidations, but also carbon–carbon bond-forming reactions spanning from cyanations of aldehydes, Friedel–Crafts reactions, Michael additions, Mannich-type reactions, polymerizations, biaryl couplings to domino reactions among others [4], demonstrating the impressive potential of asymmetric vanadium catalysis [5]. Among relevant advances achieved in the last five years, are the first asymmetric oxidative couplings of 2-naphthols, phenols and *N*-benzylated 2-hydroxycarbazoles, asymmetric oxidation of sulfides, epoxidations of alkenes using TBHP as an oxidant, cyanosilylations of aldehydes using chiral porous metal–organic frameworks, domino epoxidation/intramolecular ring-opening reactions of indoles, domino oxidative coupling/intramolecular cyclization reactions of 2-hydroxybenzo[*c*]phenanthrenes and Strecker-type reactions of aldimines among other transformations. Most of chiral vanadium catalysts investigated in the last few years are mononuclear and based on Schiff base ligands, in addition to salen, hydroxamic acid, or bishydroxamic acid ligands. Along with these monometallic complexes, are bifunctional dinuclear vanadium catalysts introduced by the group of Sasai. These amino acid-derived Schiff base complexes exhibit two active sites attached to a binaphthyl-type skeleton to achieve dual activation especially in oxidative coupling reactions. This review updates the field of enantioselective vanadium-catalyzed reactions published since the beginning of 2015, since this area was most recently updated this year [6]. The review is divided into six parts, dealing successively with enantioselective vanadium-catalyzed oxidative couplings, sulfoxidations, epoxidations, cyanosilylations of aldehydes, domino reactions and miscellaneous reactions.

2. Enantioselective vanadium-catalyzed oxidative couplings

The BINOL motif is considered to be a privileged one for ligands in asymmetric catalysis [7]. The enantioselective oxidative coupling of 2-naphthols constitutes the most direct route to prepare chiral BINOL derivatives [8]. Especially, chiral vanadium complexes have been successfully applied to catalyze these reactions. For example, in 2015 Sasai et al. described the enantioselective oxidative coupling of 2-naphthols performed in water in the presence of dinuclear vanadium complex **1** [9]. This amino acid-derived Schiff base catalyst was earlier developed by these authors starting from VOCl₃, (*S*)-*tert*-leucine and (*R*)-3,3'-diformyl-2,2'-dihydroxy-1,1'-binaphthyl [10]. As shown in Scheme 1, the reaction of 2-naphthols **2a-j** occurred at 50 or 70 °C in the presence of 5 mol% of catalyst **1** under an O₂ atmosphere, providing the corresponding chiral (*S*)-BINOLs **3a-j** in both moderate to excellent yields (65–95%) and enantioselectivities (44–94% ee). The reaction conditions were compatible with a range of 2-naphthols exhibiting either electron-withdrawing or electron-donating groups in different positions, yielding the corresponding BINOL derivatives **3b-i** in good to high enantioselectivities (63–94% ee) combined with good yields (65–95%). The lowest enantioselectivity (44% ee) was obtained in the reaction of 3-methoxy-2-naphthol **2j**.

Later in 2017, the same catalyst **1** was investigated by Oh and Takizawa in similar reactions performed in dichloromethane as a solvent [11]. Interestingly, in this case only 0.5 mol% of catalyst loading was sufficient to promote the formation of a range of (*S*)-BINOLs **3k-w** in both good to high yields (71–91%) and enantioselectivities (71–96% ee), as depicted in Scheme 2. For example, 4-alkyl-2-naphthols **2k-n** gave the corresponding chiral BINOL



Scheme 2. Oxidative coupling of other 2-naphthols catalyzed by dinuclear vanadium(V) complex **1** in dichloromethane [11].

derivatives with uniformly excellent enantioselectivities (91–93% ee) and yields (79–91%). The lowest yield (71%) was obtained in the reaction of chlorinated substrate **2p** which required 1 mol% instead of 0.5 mol% of catalyst loading to afford the corresponding product in high enantioselectivity (88% ee). This higher catalyst loading was also necessary in the reaction of aryl-substituted 2-naphthols **2s–u** to give the corresponding products **3s–u** in good to high yields (71–86%) and very good enantioselectivities (93–96% ee).

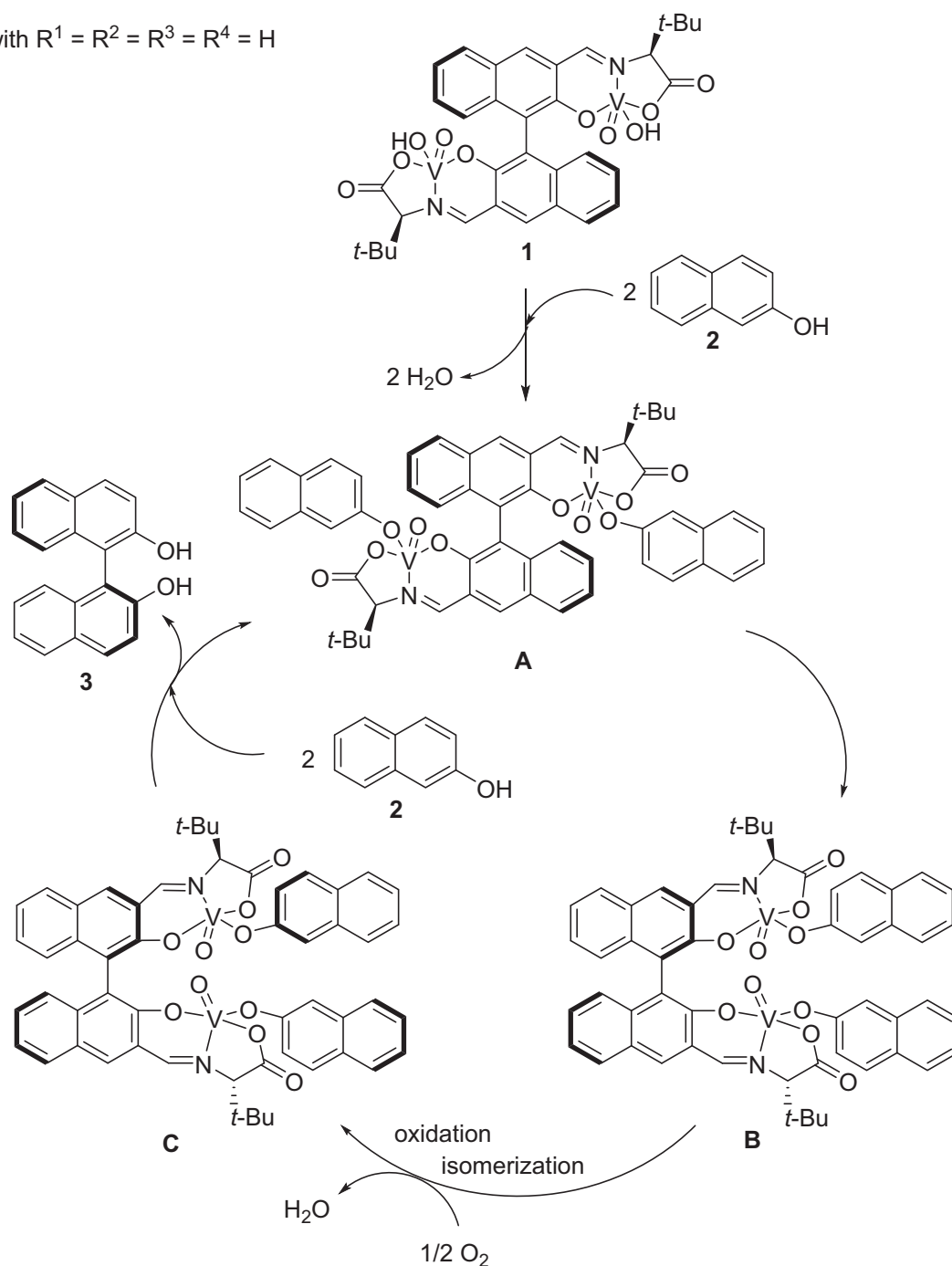
The authors proposed a mechanism depicted in **Scheme 3** based on dual activation and intramolecular manner coupling of the dinuclear catalyst with two molecules of the 2-naphthol [11]. Indeed, dinuclear vanadium(V) complex **1** reacted with two molecules of 2-naphthol **2** to give intermediate **A**. The C1 positions of 2-naphthol molecules approached each other by rotation of the binaphthyl axis of the catalyst, resulting in the formation of intermediate **B**. The latter was then intramolecularly coupled after a single electron transfer to a vanadium(V) species. The (*S*)-BINOL **3** was then released from **C** and vanadium(V) species was regenerated after isomerization of the coupling product and oxidation of the vanadium(IV) species.

In the same study, these authors performed the same reactions by using mononuclear vanadium (V) complexes [11]. Among them, catalyst **4** employed at 5 mol% of catalyst loading in tetrachloromethane at 23 °C provided the best results. Unlike dinuclear

catalyst **1**, the use of mononuclear Schiff base catalyst **4** generated enantiomeric (*R*)-BINOLS *ent*-**3k–w**. In all cases of substrates studied, (*R*)-BINOL derivatives *ent*-**3k–w** were achieved in slightly lower enantioselectivities (27–87% ee) and yields (62–93%) than (*S*)-BINOL products **3k–w** (**Scheme 2**), as shown in **Scheme 4**. The lowest enantioselectivities (27–46% ee) were observed in the reaction of 2-naphthol substrates bearing a methyl ester (**2r**, $\text{R}^4 = (\text{CH}_2)_3\text{CO}_2\text{Me}$) or an ethyl/phenyl group at the 3-position (**2v–w**, $\text{R}^4 = \text{Et}$, Ph).

Sasai et al. demonstrated that oxidative couplings of 2-naphthols into chiral BINOLs followed two different mechanisms according to the mononuclear or dinuclear nature of the vanadium catalyst employed as promoters [12]. Indeed, while a dual activation occurred with a dinuclear complex, a single 2-naphthol activation was involved by using a mononuclear vanadium complex. With the mononuclear catalyst, only one molecule of naphthol is coordinated to the catalyst center whereas two molecules of naphthol were simultaneously activated by the dinuclear complex. In the first case, an intermolecular coupling of the mononuclear catalyst and a second equivalent of naphthol occurs while an intramolecular coupling underwent in the second case. The mechanism based on an intermolecular coupling via single 2-naphthol activation is depicted in **Scheme 5** [11]. Mononuclear vanadium(V) complex **4** added a first molecule of 2-naphthol **2** to give intermediate **D**. The latter subsequently coupled with a second molecule of 2-naphthol **2** to provide

with $R^1 = R^2 = R^3 = R^4 = H$



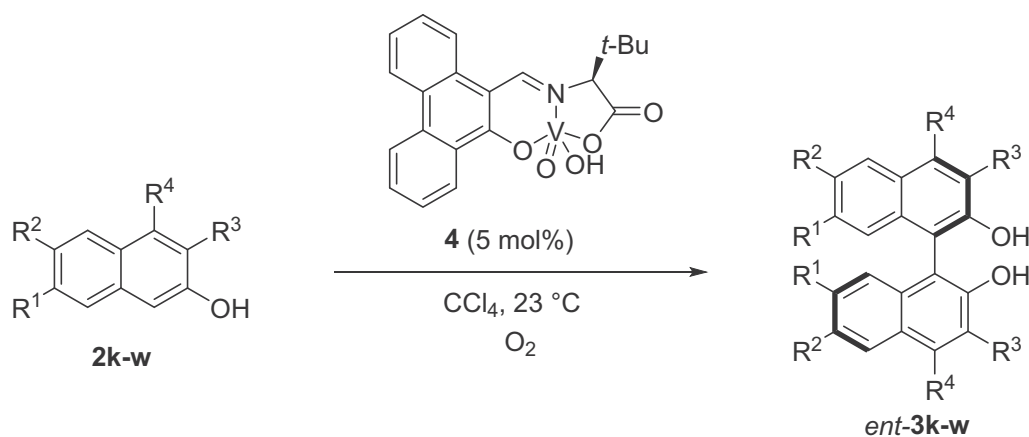
Scheme 3. Mechanism for oxidative coupling of 2-naphthol catalyzed by dinuclear vanadium(V) complex **1** [11].

intermediate **E** which finally released (*R*)-BINOL derivatives *ent*-**3** and regenerated intermediate **D**.

Earlier in 2015, another type of mononuclear vanadium catalyst earlier developed by Chen et al. [13], such as chiral tridentate oxido vanadium(IV) complex **5** derived from 2-hydroxy-1-naphthaldehyde and valine, was investigated by the same authors to promote the enantioselective coupling of 4-aryl-2-naphthols **2i**, **t,aa-ad** [14]. The process was performed at room temperature in the presence of 10 mol% of catalyst **5** in a mixture of tetrachloroethane and dichloromethane as solvent, leading to the corresponding 4,4'-biaryl-1,1'-binaphthols *ent*-**3i**, **t,aa-ad** in uniformly

excellent yields (85–98%) and low to high enantioselectivities (23–80% ee). The best result (98% yield, 80% ee) was achieved in the reaction of substrate **2ab** bearing a heteroaromatic group (Ar = 2-thienyl), as illustrated in Scheme 6.

In 2017, Kozłowski et al. reported the first highly enantioselective phenol oxidative coupling based on the use of 20 mol% of novel mononuclear catalyst **6** generated by ligand design [15]. In the presence of AcOH and LiCl as additives in toluene at 0 °C to room temperature and under an O_2 atmosphere, a range of diversely substituted phenols **7a-h** were coupled into the corresponding chiral 2,2'-dihydroxy-1,1'-binaphthyl products **8a-h** with both moderate



- 3k:** $R^1 = R^2 = R^3 = \text{H}$, $R^4 = n\text{-Pent}$: 91% yield, 87% ee
3l: $R^1 = R^2 = R^3 = \text{H}$, $R^4 = n\text{-Dec}$: 87% yield, 87% ee
3m: $R^1 = R^2 = R^3 = \text{H}$, $R^4 = c\text{-Pent}$: 92% yield, 86% ee
3n: $R^1 = R^2 = R^3 = \text{H}$, $R^4 = \text{Cy}$: 83% yield, 85% ee
3o: $R^1 = \text{OMe}$, $R^2 = R^3 = \text{H}$, $R^4 = n\text{-Pent}$: 88% yield, 82% ee
3p: $R^1 = R^3 = \text{H}$, $R^2 = \text{Cl}$, $R^4 = n\text{-Pent}$: 79% yield, 81% ee
3q: $R^1 = R^2 = R^3 = \text{H}$, $R^4 = (\text{CH}_2)_4\text{Cl}$: 74% yield, 84% ee
3r: $R^1 = R^2 = R^3 = \text{H}$, $R^4 = (\text{CH}_2)_3\text{CO}_2\text{Me}$: 85% yield, 27% ee
3s: $R^1 = R^2 = R^3 = \text{H}$, $R^4 = \text{Ph}$: 91% yield, 82% ee
3t: $R^1 = R^2 = R^3 = \text{H}$, $R^4 = p\text{-Tol}$: 86% yield, 83% ee
3u: $R^1 = R^2 = R^3 = \text{H}$, $R^4 = m\text{-Tol}$: 93% yield, 80% ee
3v: $R^1 = R^2 = \text{H}$, $R^3 = R^4 = \text{Et}$: 62% yield, 46% ee
3w: $R^1 = R^2 = \text{H}$, $R^3 = \text{Me}$, $R^4 = \text{Ph}$: 85% yield, 27% ee

Scheme 4. Oxidative coupling of 2-naphthols catalyzed by mononuclear Schiff base vanadium(V) complex **4** in tetrachloromethane [11].

to high yields (56–89%) and enantioselectivities (50–89% ee), as depicted in Scheme 7. The lowest enantioselectivities (50–60% ee) were observed in the reaction of substrates exhibiting an hydrogen atom (**7b**, $R^2 = \text{H}$) or a phenyl group (**7g**, $R^1 = \text{Ph}$) at the *meta*-position of the phenol.

The importance of mono- and dimeric resorcinols is related to their use as chiral metal ligands, organocatalysts but also as biologically active products [16]. In 2018, mononuclear catalyst **9** earlier developed by Kozłowski et al. [15a] was applied by these authors to the oxidative coupling of chiral resorcinol **10**, providing the corresponding chiral tetraphenol **11** in good yield (67%) and high diastereoselectivity (88% de), as depicted in Scheme 8 [17]. In this case, the process employed AcOH as additive and chlorobenzene as solvent at 0 °C. Importantly, this reaction constituted the key step of a total synthesis of natural product chaetoglobin A.

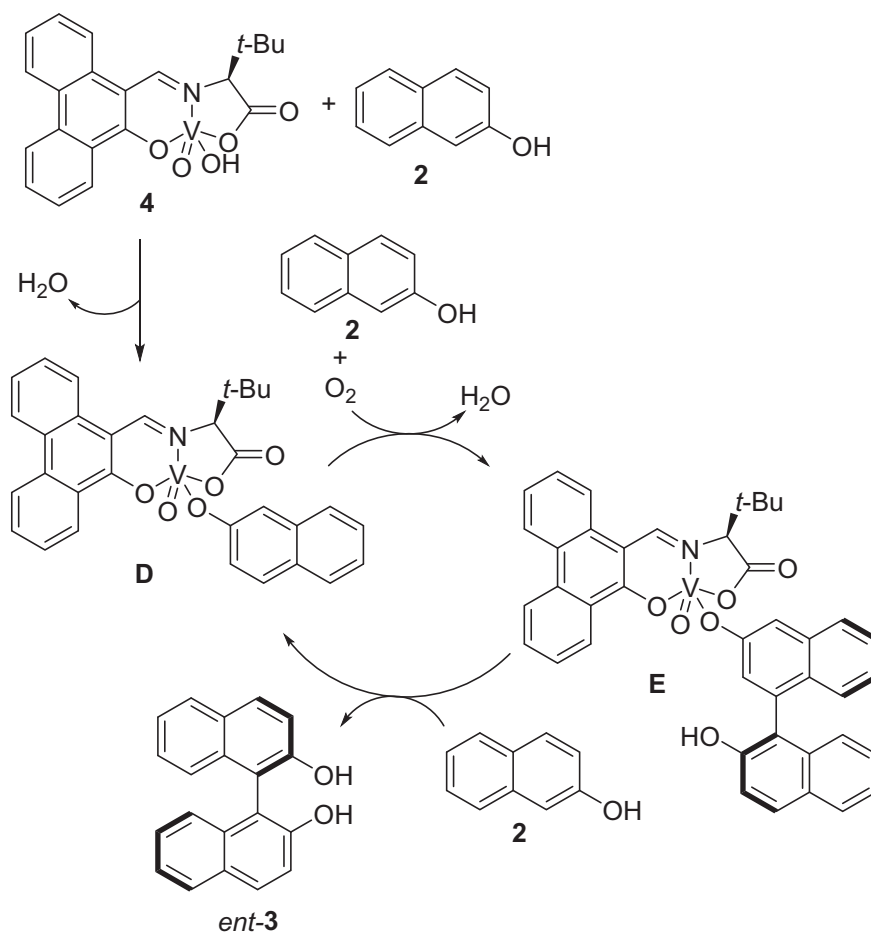
More recently, Sasai and Takizawa developed a more general asymmetric oxidative coupling of resorcinols **7g,o-aa** catalyzed by novel designed dibrominated dinuclear vanadium(V) complex **12** in toluene [18]. The process was performed under air in the presence of 5 mol% of this catalyst at 70 °C, leading to the corresponding chiral biresorcinols **8g,o-aa** in low to excellent yields (29–93%) and moderate to very high enantioselectivities (36–97% ee), as illustrated in Scheme 9. Moderate to high yields (29–93%) combined with uniformly high enantioselectivities (76–97% ee) were observed in the reaction of a range of resorcinols **7p-x** exhibiting many types of substituents at different positions of

the aryl group (Ar). The lowest enantioselectivities (36–70% ee) were observed in the reaction of bulkier substrates **7g** and **7aa** exhibiting an *ortho*-substituent ($R^2 = \text{Me}$ or Br). It was proposed that the reaction evolved through intramolecular coupling. Dinuclear vanadium(V) complex **12** added two molecules of resorcinol **7** to give the corresponding intermediate which was then submitted to a rotation of the binaphthyl axis, resulting in the formation of intermediate **F**. The latter was then intramolecularly coupled to give final chiral biresorcinol **8** (Scheme 9).

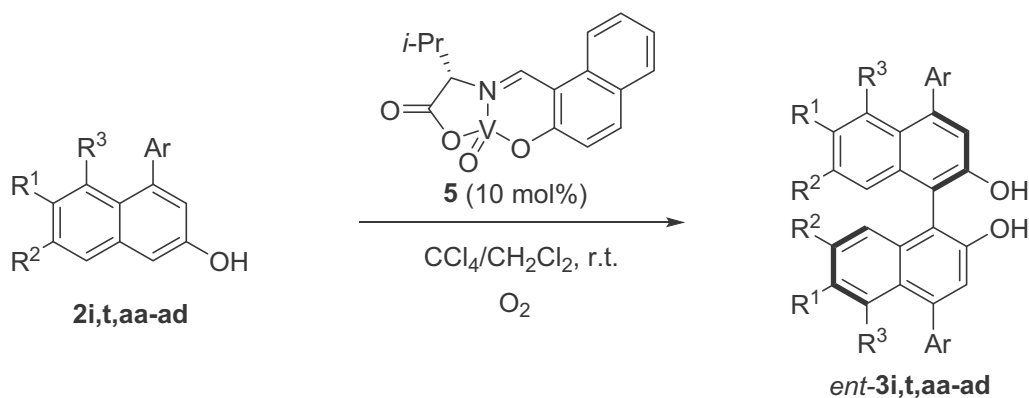
Earlier in 2017, Kozłowski et al. designed novel mononuclear vanadium(V) complex **13** to promote the oxidative coupling of another type of substrates, such as *N*-benzylated 2-hydroxycarbazoles **14a-l** [15]. As illustrated in Scheme 10, the reaction of these compounds performed at 0 or –15 °C in chlorobenzene with 20 mol% of catalyst **13** in the presence of AcOH as a superstoichiometric additive under O_2 atmosphere afforded the corresponding chiral coupled products **15a-l** in moderate to high yields (45–91%) and good to excellent enantioselectivities (74–96% ee). The reaction of a substrate bearing an allyl group instead of a methyl group adjacent to the phenol also occurred smoothly, providing the corresponding product **15b** in both high yield (75%) and enantioselectivity (83% ee). The lowest enantioselectivities (74–76% ee) were observed in the reaction of substrates **14k-l** exhibiting a methyl or methoxy substituent ($R^2 = \text{Me}$, OMe).

In 2017, Takizawa and Sasai employed dinuclear vanadium complex **1** to promote the first enantioselective oxidative coupling

with $R^1 = R^2 = R^3 = R^4 = H$

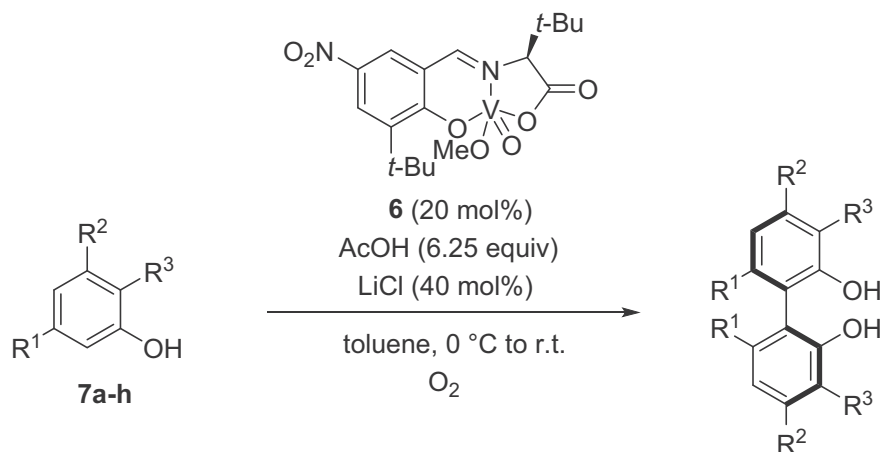


Scheme 5. Mechanism for oxidative coupling of 2-naphthols catalyzed by mononuclear vanadium(V) complex **4** [11].



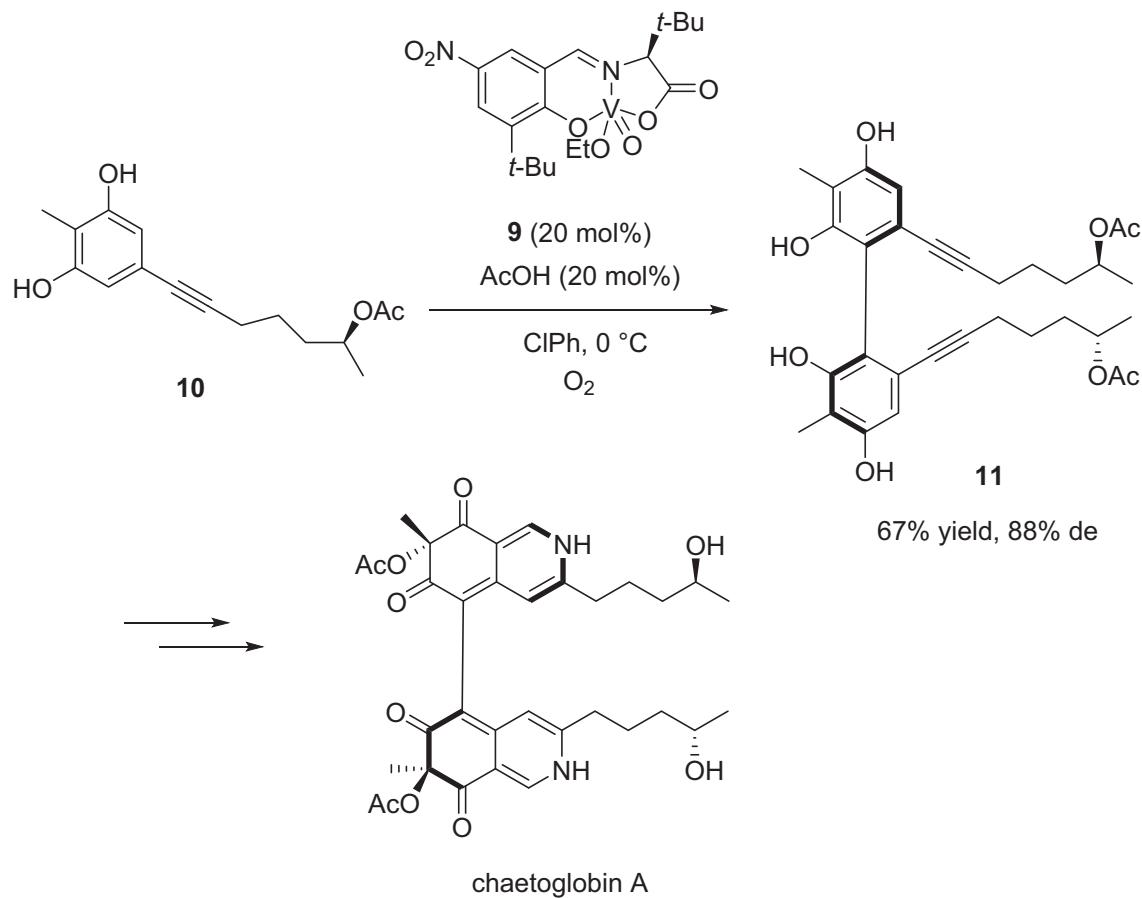
ent-3i: $R^1 = R^2 = R^3 = H$, Ar = Ph: 85% yield, 65% ee
ent-3t: $R^1 = R^2 = R^3 = H$, Ar = *p*-Tol: 90% yield, 74% ee
ent-3aa: $R^1 = R^2 = R^3 = H$, Ar = *p*-ClC₆H₄: 95% yield, 71% ee
ent-3ab: $R^1 = R^2 = R^3 = H$, Ar = 2-thienyl: 98% yield, 80% ee
ent-3ac: $R^1 = R^2 = OMe$, $R^3 = H$, Ar = *p*-ClC₆H₄: 97% yield, 56% ee
ent-3ad: $R^1 = R^2 = Me$, $R^3 = H$, Ar = *p*-ClC₆H₄: 98% yield, 23% ee

Scheme 6. Oxidative coupling of 4-aryl-2-naphthols catalyzed by mononuclear oxidovanadium(IV) complex **5** in dichloromethane/tetrachloroethane solvent mixture [14].

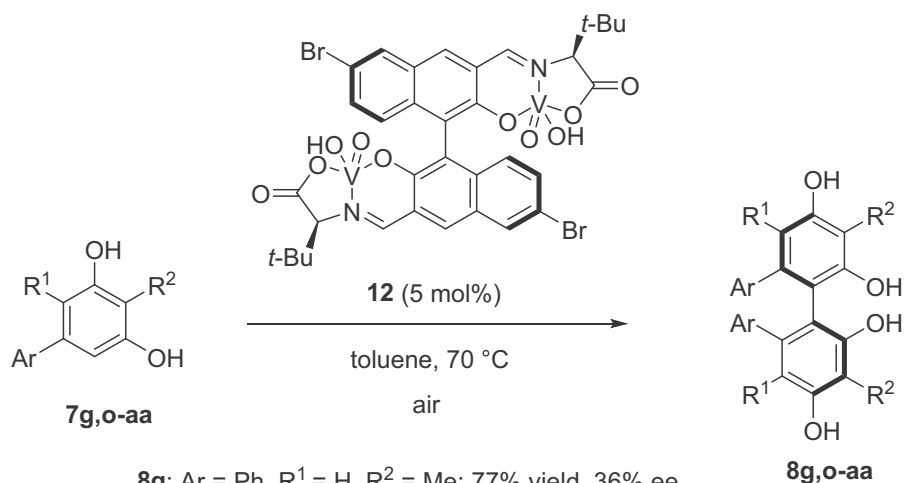


- 8a:** $R^1 = R^2 = R^3 = \text{Me}$: 89% yield, 83% ee
8b: $R^1 = R^3 = \text{Me}$, $R^2 = \text{H}$: 100% conversion, 60% ee
8c: $R^1 = R^2 = \text{Me}$, $R^3 = \text{allyl}$: 56% yield, 77% ee
8d: $R^1 = R^2 = \text{Me}$, $R^3 = n\text{-Pr}$: 80% yield, 72% ee
8e: $R^1 = R^3 = \text{Me}$, $R^2 = \text{OMe}$: 80% yield, 82% ee
8f: $R^1 = R^3 = \text{Me}$, $R^2 = \text{OH}$: 81% yield, 86% ee
8g: $R^1 = \text{Ph}$, $R^2 = \text{OH}$, $R^3 = \text{Me}$: 65% yield, 50% ee
8h: $R^1 = n\text{-Hex-C}\equiv\text{C}$, $R^2 = \text{OH}$, $R^3 = \text{Me}$: 66% yield, 89% ee

Scheme 7. Oxidative coupling of phenols catalyzed by mononuclear vanadium(V) complex **6** in toluene [15].

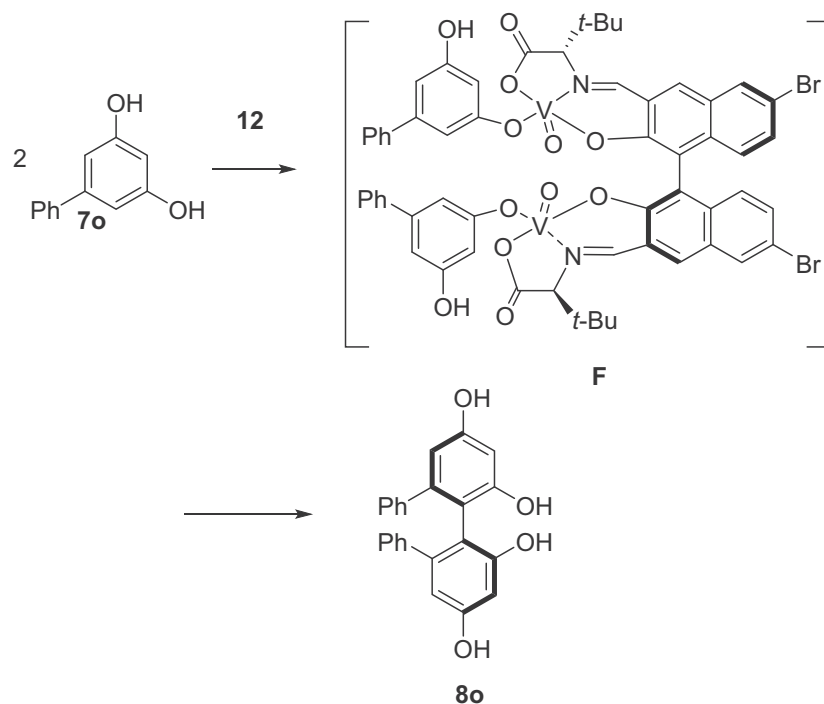


Scheme 8. Oxidative coupling of a chiral resorcinol by using mononuclear vanadium(V) complex **9** in chlorobenzene and synthesis of chaetoglobin A [17].

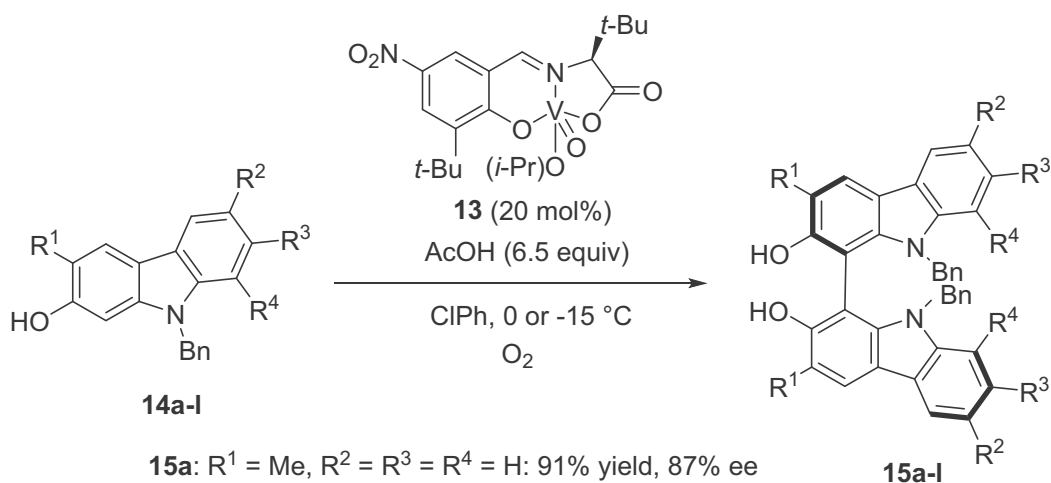


- 8g:** Ar = Ph, R¹ = H, R² = Me: 77% yield, 36% ee
8o: Ar = Ph, R¹ = R² = H: 80% yield, 97% ee
8p: Ar = *o*-FC₆H₄, R¹ = R² = H: 87% yield, 97% ee
8q: Ar = *m*-Tol, R¹ = R² = H: 42% yield, 90% ee
8r: Ar = *m*-MeOC₆H₄, R¹ = R² = H: 75% yield, 93% ee
8s: Ar = *m*-FC₆H₄, R¹ = R² = H: 70% yield, 87% ee
8t: Ar = *m*-ClC₆H₄, R¹ = R² = H: 29% yield, 76% ee
8u: Ar = *p*-Tol, R¹ = R² = H: 91% yield, 95% ee
8v: Ar = *p*-MeOC₆H₄, R¹ = R² = H: 93% yield, 96% ee
8w: Ar = *p*-FC₆H₄, R¹ = R² = H: 83% yield, 80% ee
8x: Ar = *p*-ClC₆H₄, R¹ = R² = H: 75% yield, 77% ee
8y: Ar = 2-Naph, R¹ = R² = H: 78% yield, 85% ee
8z: Ar = Ph, R¹ = Me, R² = H: 93% yield, 88% ee
8aa: Ar = Ph, R¹ = H, R² = Br: 49% yield, 70% ee

proposed mechanism with **7o**:

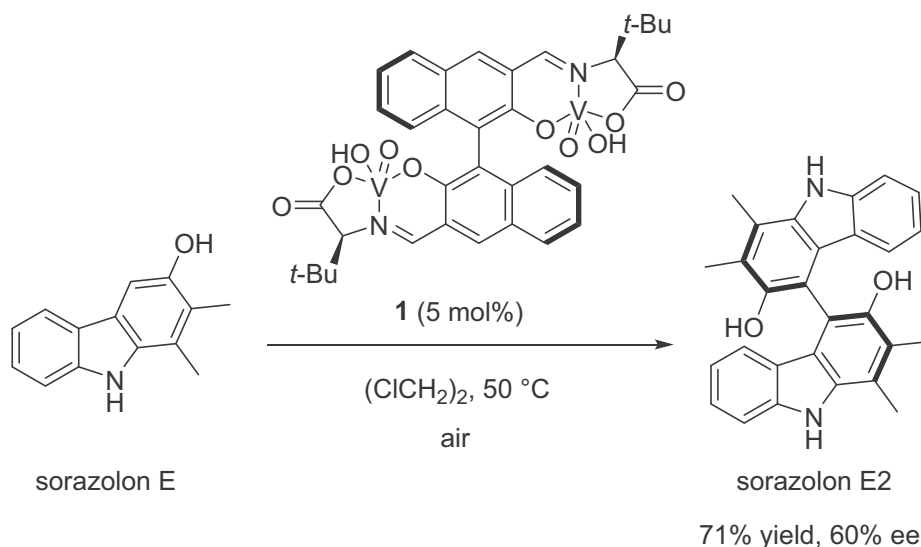


Scheme 9. Oxidative coupling of resorcinols catalyzed by dibrominated dinuclear vanadium(V) complex **12** in toluene [18].



- 15a:** R¹ = Me, R² = R³ = R⁴ = H: 91% yield, 87% ee
15b: R¹ = allyl, R² = R³ = R⁴ = H: 75% yield, 83% ee
15c: R¹ = Me, R² = CF₃, R³ = R⁴ = H: 70% yield, 93% ee
15d: R¹ = Me, R² = R⁴ = H, R³ = CF₃: 60% yield, 94% ee
15e: R¹ = Me, R² = CO₂t-Bu, R³ = R⁴ = H: 67% yield, 96% ee
15f: R¹ = Me, R² = Bz, R³ = R⁴ = H: 76% yield, 85% ee
15g: R¹ = Me, R² = R⁴ = H, R³ = F: 73% yield, 92% ee
15h: R¹ = Me, R² = F, R³ = R⁴ = H: 87% yield, 92% ee
15i: R¹ = Me, R² = R³ = H, R⁴ = F: 80% yield, 91% ee
15j: R¹ = Me, R² = Ph, R³ = R⁴ = H: 70% yield, 82% ee
15k: R¹ = Me, R² = Me, R³ = R⁴ = H: 45% yield, 76% ee
15l: R¹ = Me, R² = OMe, R³ = R⁴ = H: 82% yield, 74% ee

Scheme 10. Oxidative coupling of *N*-benzylated 2-hydroxycarbazoles catalyzed by mononuclear vanadium(V) complex **13** in chlorobenzene [15].

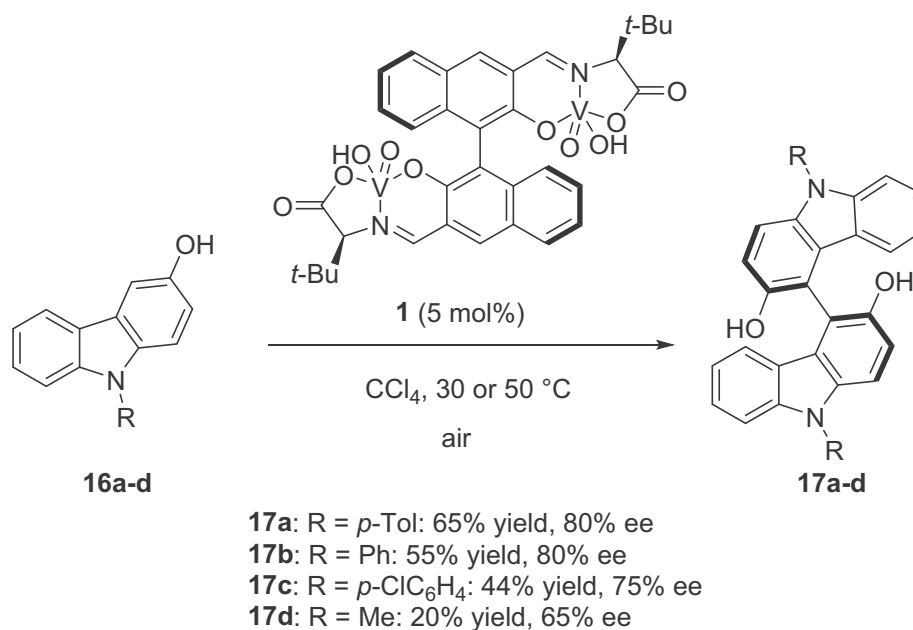


Scheme 11. Synthesis of sorazolon E2 through oxidative coupling of sorazolon E catalyzed by dinuclear vanadium(V) complex **1** in dichloroethane [19].

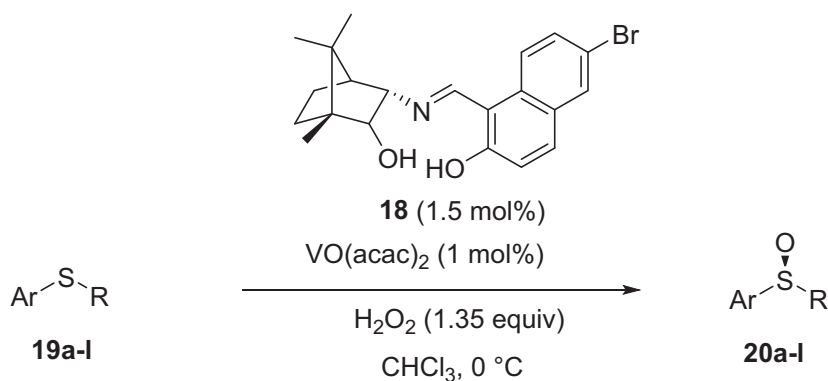
of a 3-hydroxycarbazole such as sorazolon E [19]. The reaction was carried out at 50 °C in dichloroethane as solvent in the presence of 5 mol% of catalyst **1**. It afforded the corresponding chiral dimeric sorazolon E named sorazolon E2 in good yield (71%) and enantio-


selectivity (60% ee), as illustrated in Scheme 11. This natural product is known to exhibit antibacterial and cytotoxic activities.

In spite of the biological roles of bihydroxycarbazoles, only rare methodologies are available to prepare them in enantiopure form.



Scheme 12. Oxidative coupling of 3-hydroxycarbazoles catalyzed by dinuclear vanadium(V) complex **1** in tetrachloromethane [20].

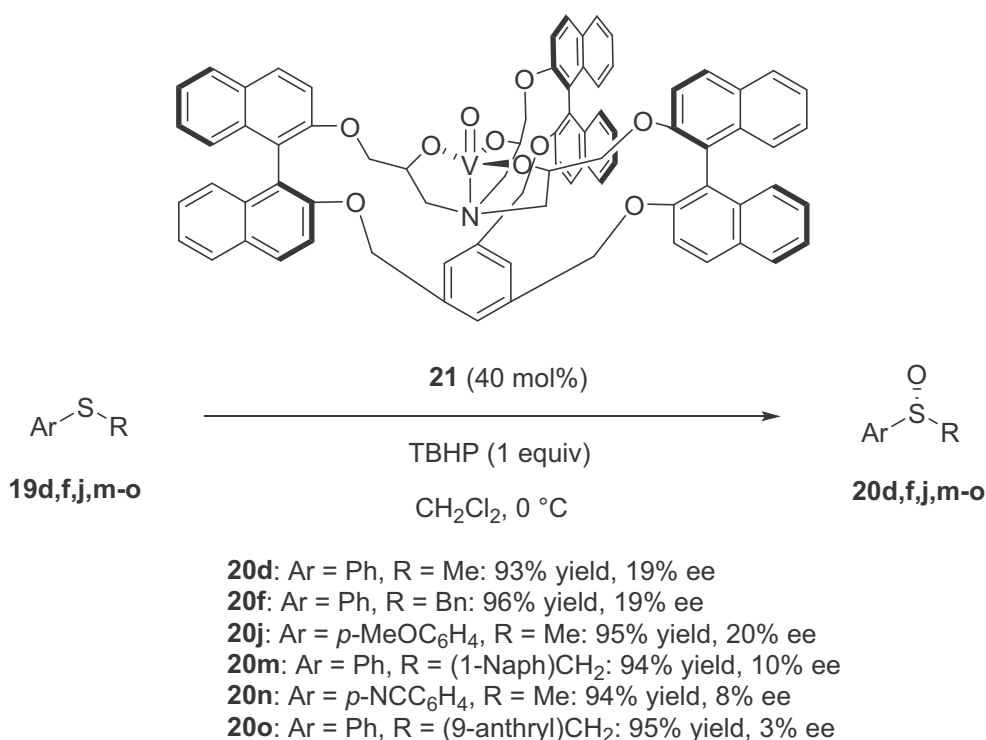


- 20a:** Ar = 2-Naph, R = Et: 74% yield, 94% ee
20b: Ar = 2-Naph, R = Me: 72% yield, 97% ee
20c: Ar = 1-Naph, R = Et: 68% yield, 88% ee
20d: Ar = Ph, R = Me: 63% yield, 88% ee
20e: Ar = Ph, R = *n*-Bu: 60% yield, 88% ee
20f: Ar = Ph, R = Bn: 63% yield, 92% ee
20g: Ar = *p*-Tol, R = Me: 73% yield, 85% ee
20h: Ar = *m*-Tol, R = Me: 74% yield, 86% ee
20i: Ar = *p*-BrC₆H₄, R = Me: 67% yield, 94% ee
20j: Ar = *p*-MeOC₆H₄, R = Me: 60% yield, 89% ee
20k: Ar = *p*-O₂NC₆H₄, R = Me: 67% yield, 85% ee
20l: Ar = , R = Me: 73% yield, 85% ee

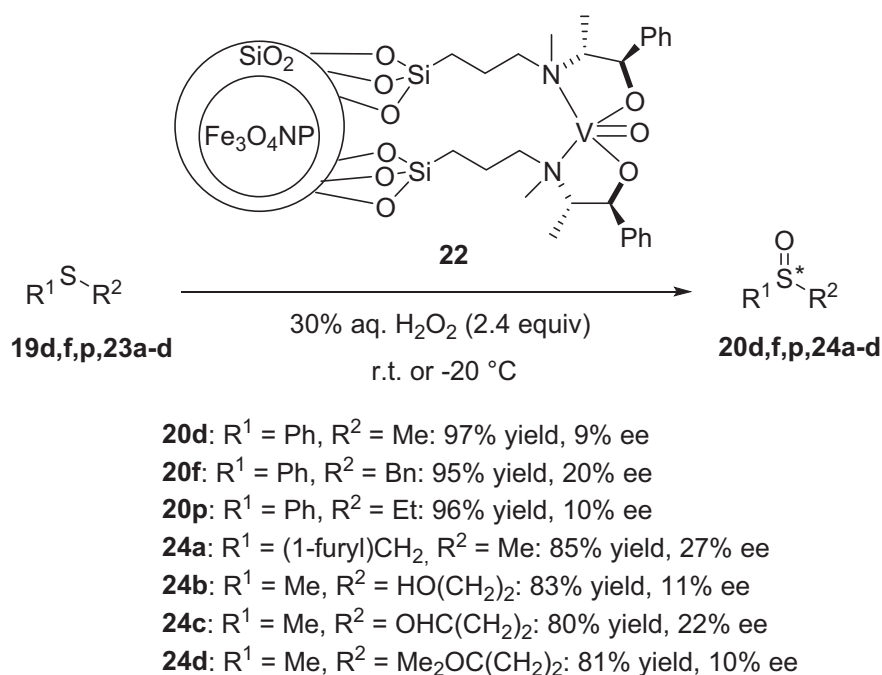
Scheme 13. Sulfoxidation of alkyl aryl sulfides with H₂O₂ in the presence of vanadium camphor-based Schiff base catalyst **18** [26].

Thus, the same authors extended the scope of their synthesis of sorazolone **E2** [20]. As depicted in [Scheme 12](#), the same catalyst **1** was applied to promote at the same catalyst loading (5 mol%) the asymmetric oxidative coupling of several *N*-protected

3-hydroxycarbazoles **16a-d** in tetrachloromethane as solvent. Performed at 30 or 50 °C, the reaction readily afforded the corresponding chiral bihydroxycarbazoles **17a-d** in low to good yields (20–65%) and good to high enantioselectivities (65–80% ee).



Scheme 14. Sulfoxidation of alkyl aryl sulfides with TBHP in the presence of supramolecular oxidovanadium catalyst **21** [28].

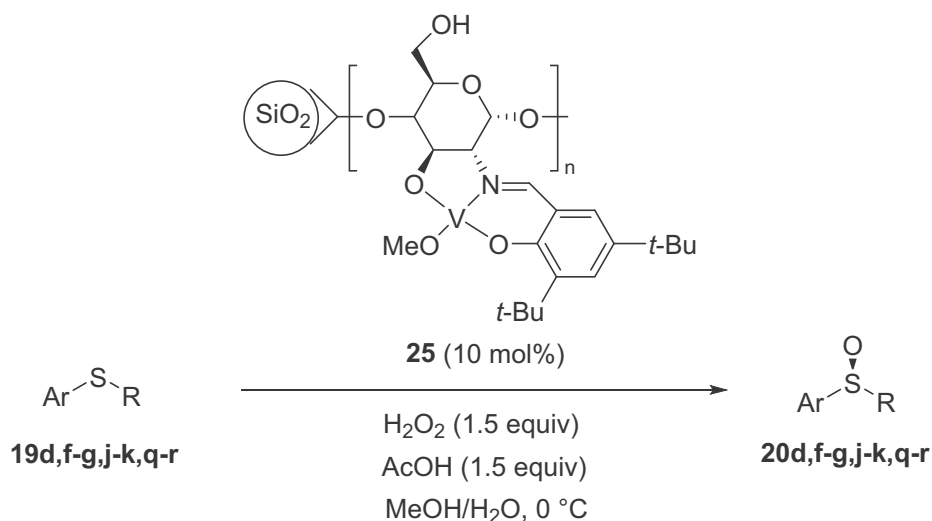


Scheme 15. Sulfoxidation of alkyl aryl and dialkyl sulfides with H₂O₂ in the presence of (+)-pseudoephedrine-derived vanadium catalyst **22** immobilized on magnetic nanoparticles [32].

3. Enantioselective vanadium-catalyzed sulfoxidations

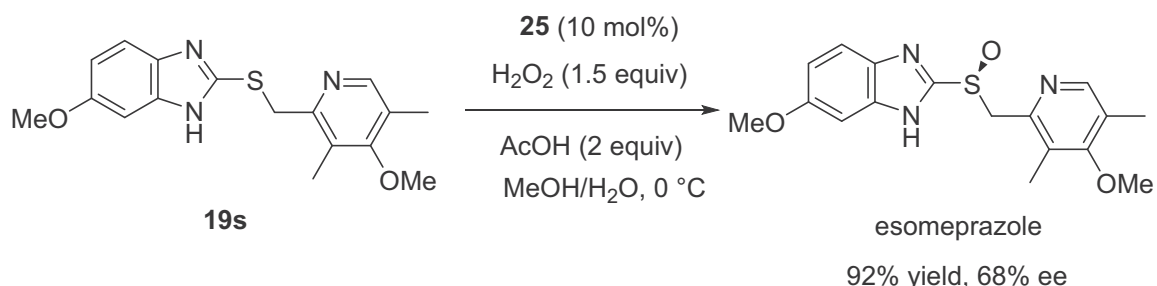
Chiral sulfoxides are widely employed in asymmetric synthesis as chiral auxiliaries, chiral ligands, and are also present in many drug structures [21]. A common methodology to prepare chiral sul-

foxides is the metal-catalyzed asymmetric oxidation of sulfides [22]. Among metals employed to catalyze these reactions, chiral vanadium catalysts derived from salen ligands were early used by Nakajima et al. in 1986 with moderate enantioselectivities ($\leq 42\%$ ee) [23]. Ever since, significant advances have been achieved



20d: Ar = Ph, R = Me: 93% yield, 63% ee
20f: Ar = Ph, R = Bn: 77% yield, 61% ee
20g: Ar = *p*-Tol, R = Me: 70% yield, 42% ee
20j: Ar = *p*-MeOC₆H₄, R = Me: 63% yield, 45% ee
20k: Ar = *p*-O₂NC₆H₄, R = Me: 95% yield, 67% ee
20q: Ar = *p*-ClC₆H₄, R = Me: 93% yield, 64% ee
20r: Ar = *m*-ClC₆H₄, R = Me: 91% yield, 61% ee

synthesis of esomeprazole:



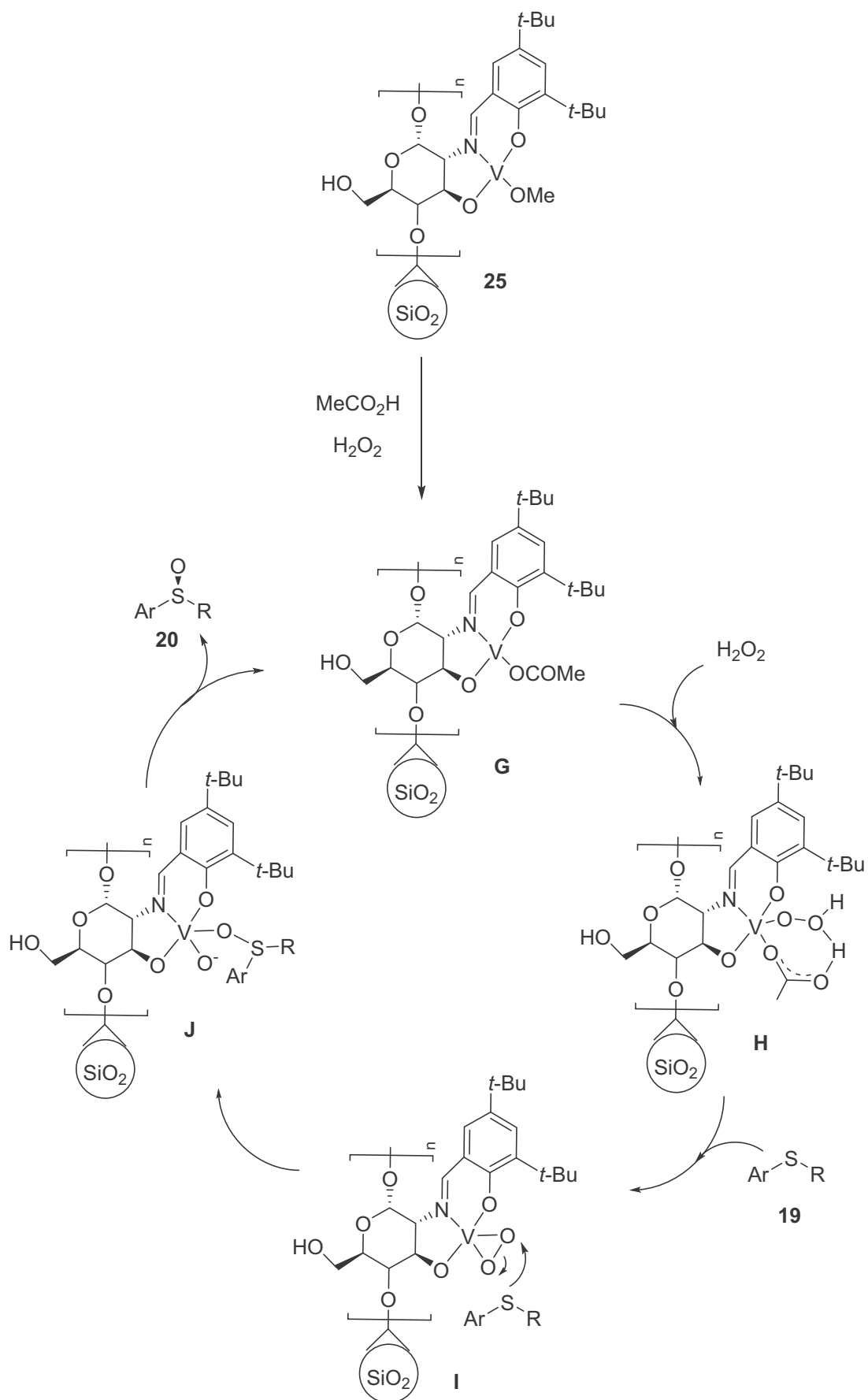
Scheme 16. Sulfoxidation of alkyl aryl sulfides with H₂O₂ in the presence of silica supported Chitosan@vanadium catalyst **25** and synthesis of esomeprazole [33].

in this field, such as the use of vanadium complexes of chiral Schiff bases by Bolm group in 1995 in combination with hydrogen peroxide as oxidant, providing remarkable enantioselectivities (>99% ee) [24]. Later, this methodology has been submitted to modifications [25]. For example, in 2016 Chen and Boobalan designed a novel camphor-based Schiff base ligand **18** to be employed in combination with VO(acac)₂ as a precatalyst to promote the asymmetric sulfoxidation of alkyl aryl sulfides with H₂O₂ as an oxidant [26]. As illustrated in Scheme 13, when employed at 1.5 mol% of catalyst loading and combined with 1 mol% of VO(acac)₂ in chloroform at 0 °C, it promoted the enantioselective sulfoxidation of a range of alkyl aryl sulfides **19a-l** with hydrogen peroxide to give the corresponding (*S*)-configured sulfoxides **20a-l** in good yields (60–74%) and uniformly high enantioselectivities (85–97% ee).

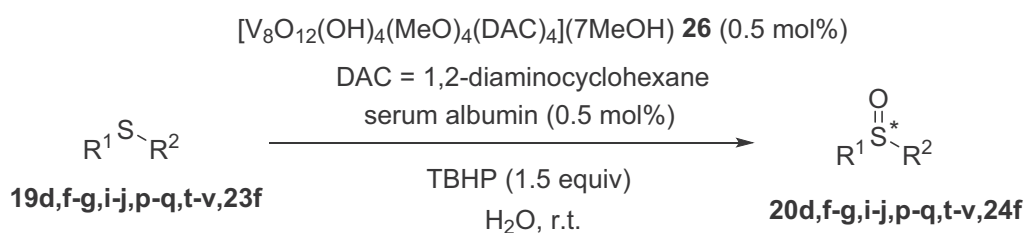
Supramolecular vanadium complexes have been applied to the selective oxidation of sulfides into sulfoxides [27]. For example, Martinez et al. reported in 2017 the synthesis of a novel

supramolecular chiral oxidovanadium catalyst **21** that was further investigated as promotor for the sulfoxidation of sulfides [28]. When 40 mol% of this catalyst was applied at 0 °C in dichloromethane as a solvent to promote the sulfoxidation of alkyl aryl sulfides **19d,f,j,m-o** with *tert*-butyl hydroperoxide (TBHP) as an oxidant, it afforded the corresponding (*R*)-sulfoxides **20d,f,j,m-o** in uniformly excellent yields (93–96%) albeit combined with low enantioselectivities (3–20% ee), as depicted in Scheme 14.

Chiral vanadium catalysts have been immobilized on different types of materials, such as mesoporous silica [29], polysiloxane [30], and more recently magnetic nanoparticles [31]. For example, Rostami reported in 2015 the synthesis of a novel chiral nanocatalyst to be used for the first time in sulfoxidations [32]. This chiral oxo-vanadium (+)-pseudoephedrine complex **22** immobilized on magnetic nanoparticles was applied to promote the asymmetric oxidation of alkyl aryl **19d,f,p** and dialkyl sulfides **23a-d** with



Scheme 17. Mechanism for sulfoxidation of alkyl aryl sulfides with H₂O₂ in the presence of silica supported Chitosan@vanadium catalyst **25** [33].



with bovin serum albumin:

20d: $R^1 = \text{Ph}$, $R^2 = \text{Me}$: 70% yield, 77% ee (*R*)

20g: $R^1 = p\text{-Tol}$, $R^2 = \text{Me}$: 97% yield, 58% ee (*R*)

20i: $R^1 = p\text{-BrC}_6\text{H}_4$, $R^2 = \text{Me}$: 95% yield, 57% ee (*R*)

20t: $R^1 = m\text{-BrC}_6\text{H}_4$, $R^2 = \text{Me}$: 96% yield, 75% ee (*R*)

24f: $R^1 = \text{Bn}$, $R^2 = \text{Me}$: 94% yield, 11% ee (*S*)

with porcine serum albumin:

20j: $R^1 = p\text{-MeOC}_6\text{H}_4$, $R^2 = \text{Me}$: 93% yield, 68% ee (*R*)

20p: $R^1 = p\text{-ClC}_6\text{H}_4$, $R^2 = \text{Me}$: 94% yield, 60% ee (*R*)

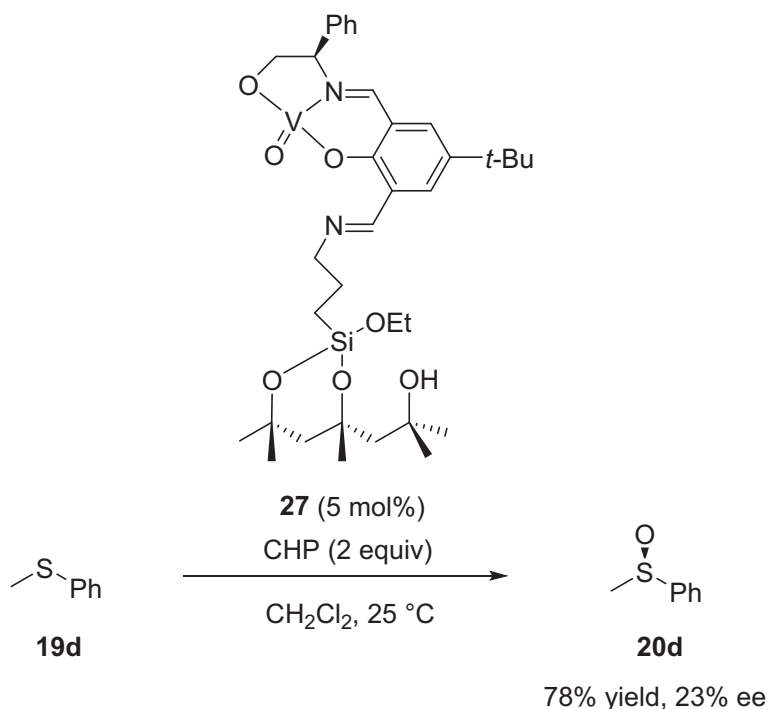
20q: $R^1 = m\text{-ClC}_6\text{H}_4$, $R^2 = \text{Me}$: 88% yield, 23% ee (*R*)

20u: $R^1 = o\text{-ClC}_6\text{H}_4$, $R^2 = \text{Me}$: 90% yield, 36% ee (*R*)

with rabbit serum albumin:

20v: $R^1 = \text{Ph}$, $R^2 = \text{CH}_2=\text{CH}$: 86% yield, 29% ee (*S*)

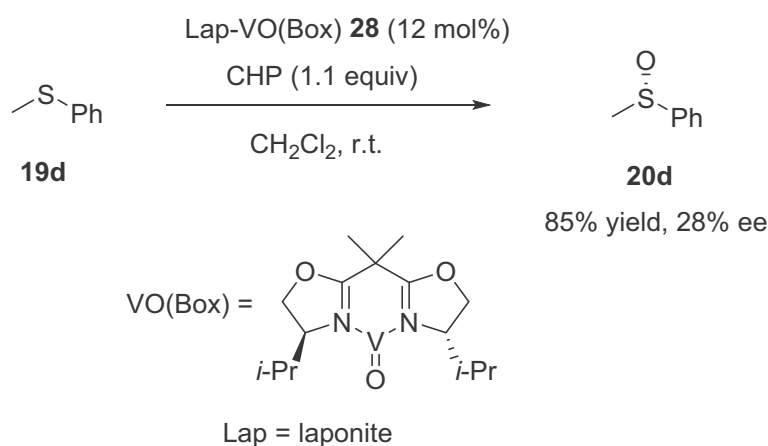
Scheme 18. Sulfoxidation of alkyl aryl sulfides and a dialkyl sulfide with TBHP in the presence of V(IV)₈ cluster catalyst **26** and serum albumins [34].



Scheme 19. Sulfoxidation of methyl phenyl sulfide with CHP in the presence of Schiff base-derived vanadium catalyst **27** immobilized on mesoporous MCM-41 [35].

H_2O_2 at room temperature or -20°C . The reaction led to the corresponding chiral sulfoxides **20d,f,p** and **24a-d** with high yields (95–97% for **20d,f,p** and 80–85% for **24a-d**) combined with low enantioselectivities (9–20% ee for **20d,f,p** and 10–27% ee for **24a-**

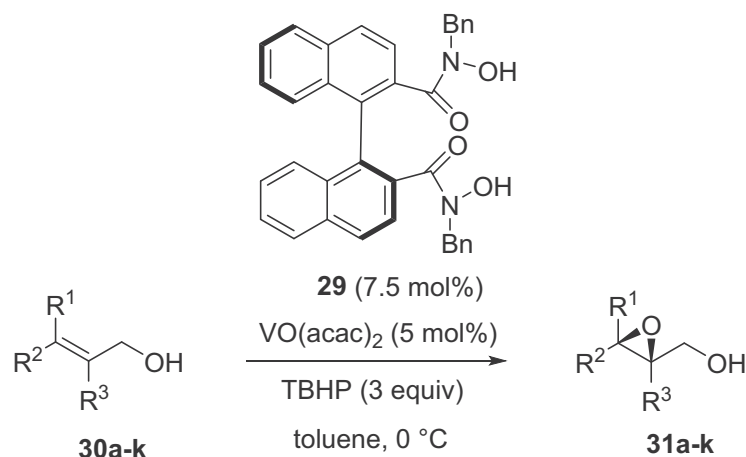
d), as shown in Scheme 15. In spite of providing a low enantioselectivity level, this novel catalyst could be recovered by using an external magnet and reused for up to twenty times with little loss of activity and enantioselectivity.



Scheme 20. Sulfoxidation of methyl phenyl sulfide with CHP in the presence of bisoxazoline-derived vanadium catalyst **28** immobilized on laponite [36].

In 2017, Shen et al. introduced a novel type of heterogeneous catalysts, such as silica-supported Chitosan@vanadium complex **25**, to be employed in the catalysis of the asymmetric sulfoxidation of alkyl aryl sulfides with hydrogen peroxide [33]. The formation of this catalyst was initiated by the formation of covalent SiO₂-O bonds between SiO₂ and D-glucosamine-derived polyoside Chitosan bearing hydroxyl and amino groups. Then, the formed

SiO₂-Chitosan complex was reacted with salicylaldehydes to give the corresponding SiO₂-Chitosan-Schiff base complex. The latter subsequently reacted with NH₄VO₃ to give silica-supported Chitosan@vanadium complex **25**. When 10 mol% of this catalyst was applied at 0 °C in the presence of AcOH as additive in aqueous methanol as a solvent to promote the sulfoxidation of alkyl aryl sulfides **19d,f-g,j-k,q-r**, it afforded the corresponding sulfoxides



- 31a:** R¹ = H, R² = Ph, R³ = Me: 87% yield, 92% ee
31b: R¹ = H, R² = R³ = Ph: 95% yield, 87% ee
31c: R¹ = R³ = H, R² = Ph: 29% yield, 82% ee
31d: R¹ = Ph, R² = R³ = H: 18% yield, 89% ee
31e: R¹ = Me, R² = (Me)₂C=CH(CH₂)₂, R³ = H: 89% yield, 98% ee
31f: R¹ = (Me)₂C=CH(CH₂)₂, R² = Me, R³ = H: 95% yield, 84% ee
31g: R¹ = R² = Me, R³ = H: 60% yield, 80% ee
31h: R¹ = H, R², R³ = (CH₂)₄: 52% yield, 83% ee
31i: R¹ = R³ = H, R² = *n*-Pr: 75% yield, 80% ee
31j: R¹ = *n*-Pr, R² = R³ = H: 86% yield, 87% ee
31k: R¹ = R² = H, R³ = Ph: 20% yield, 21% ee

Scheme 21. Epoxidation of allylic alcohols in the presence of binaphthylbis-hydroxamic acid ligand **29** [40].

(*S*)-**20d,f-g,j-k,q-r** in good to excellent yields (63–95%) and moderate enantioselectivities (42–67% ee). As shown in Scheme 16, sulfides **19k,q,r** exhibiting electron-withdrawing substituents on the phenyl group provided better enantioselectivities (61–67% ee) than sulfides **19g,j** bearing electron-donating substituents (42–45% ee). Importantly, it was possible to recycle and reuse the catalyst for five times without significant loss of catalyst in quantity and catalytic activity. The methodology was applied to the synthesis of esomeprazole drug starting from alkyl aryl sulfide **19s** in high yield (92%) and 68% ee (Scheme 16).

A mechanism was proposed by the authors to rationalize the stereoselectivity of this reaction (Scheme 17) [33]. In a first time, catalyst **25** was converted into intermediate **G** which then underwent heterolysis of the O-O bond to give intermediate **H**. The latter oxidized sulfide **19** into chiral sulfoxide **20** through transition state **I** and active complex **J**, releasing intermediate regenerated **G**.

Earlier in 2016, these reactions were also performed in the presence of novel achiral cluster anadium catalyst **26** based on 1,2-diaminocyclohexane (DAC) [34]. Actually, the chirality of the process was induced by chiral serum albumins. The reaction employed TBHP as oxidant and was performed at room temperature in aqueous media. As depicted in Scheme 18, a range of alkyl aryl sulfides **19d,f-g,i-j,p-q,t-v** underwent asymmetric oxidation to give the corresponding chiral sulfoxides **20d,f-g,i-j,p-q,t-v** in good to excellent yields (70–97%) combined with low to good enantioselectivities (11–77% ee). The lowest enantioselectivity (11% ee) was observed in the reaction of dialkyl sulfide **23f** albeit providing product **24f** in excellent yield (94%).

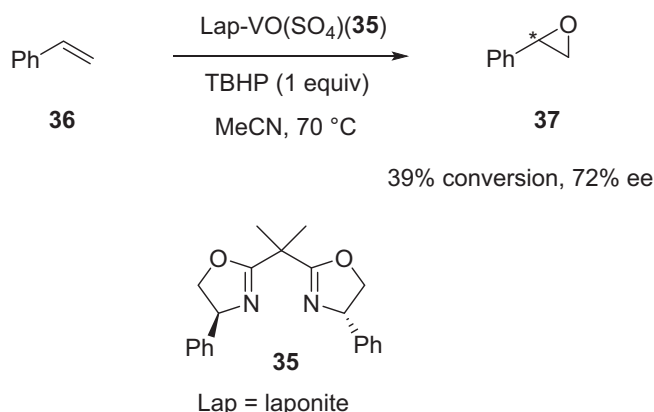
In 2016, another heterogeneous vanadium catalyst immobilized through covalent bonds on mesoporous silica support MCM-41 was developed by Zid et al. [35]. This complex **27** was generated through the formation of covalent bonds between two hydroxyl groups of MCM-41 and Si atom of 3-aminopropyltriethoxysilane to give the corresponding 3-aminopropyl silyl-functionalized silica which subsequently reacted with a diformylphenol to afford final supported Schiff base- vanadium catalyst **27**. The latter was investigated to promote the asymmetric sulfoxidation of methyl phenyl sulfide **19d**. As illustrated in Scheme 19, the use of 5 mol% of this catalyst in the presence of cumene hydroperoxide (CHP) as oxidant in dichloromethane as solvent at 25 °C allowed the corresponding (*R*)-sulfoxide **20d** to be synthesized in good yield (78%) and low enantioselectivity (23% ee). In comparison with the neat complex,

catalytic studies showed that anchoring of VO(Schiff base) complex on functionalized silica provided a slight improvement in enantioselectivity (23% ee vs 13% ee) which was attributed to the support effect of the heterogeneous recyclable catalyst **27**.

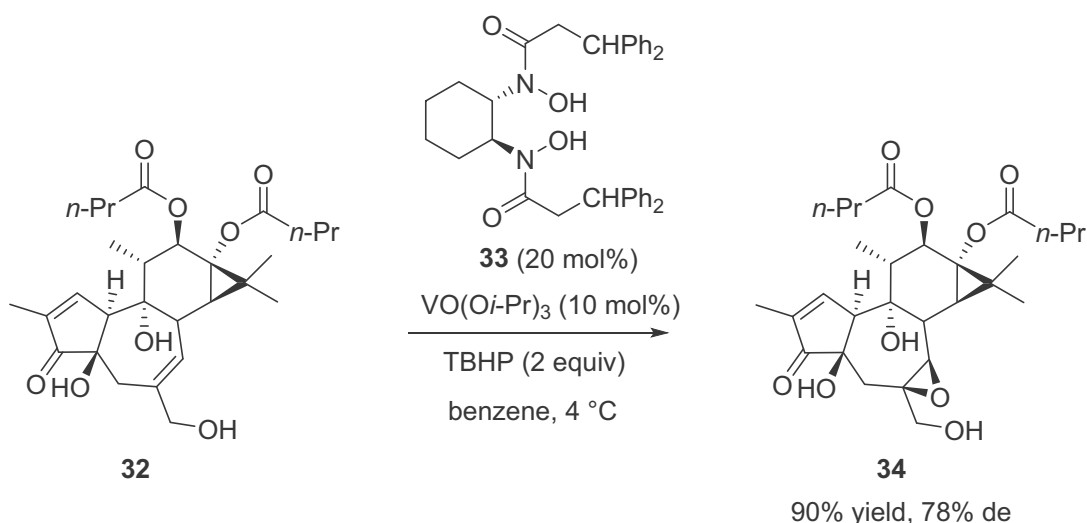
A slightly higher enantioselectivity (28% ee) was later described by this group for the same reaction catalyzed by a novel bisoxazoline-derived chiral vanadium catalyst **28** immobilized on laponite by non-covalent electrostatic interaction (cationic exchange into clays) not requiring a covalent bond between the ligand and the support [36]. When performed in the presence of 12 mol% of catalyst **28** in dichloromethane as solvent at 25 °C, the reaction of methyl phenyl sulfide **19d** afforded the corresponding (*S*)-sulfoxide **20d** in high yield (85%) and 28% ee (Scheme 20). It must be noted that the recovered catalyst was less active, without vanadium leaching due to the stability of its interaction with the support. The enantioselectivity was also reduced, demonstrating the decomplexation of the chiral ligand.

4. Enantioselective vanadium-catalyzed epoxidations

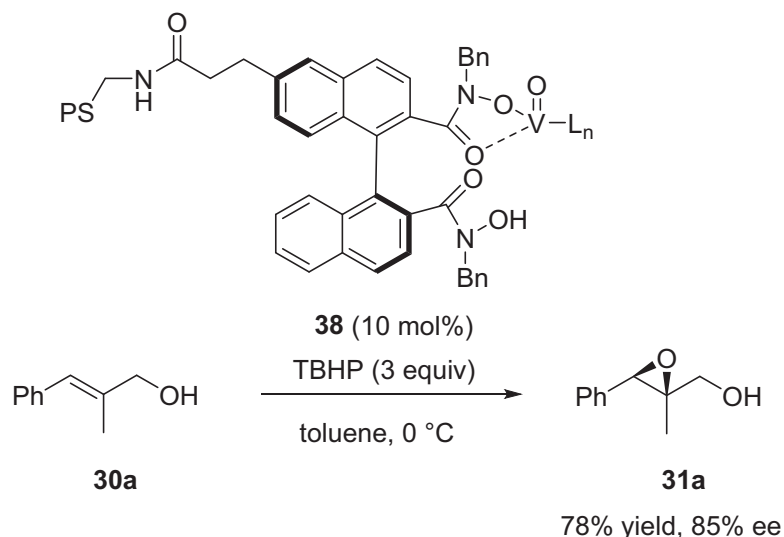
Chiral epoxides are widely employed as starting materials in the preparation of many important products [37]. The Katsuki and



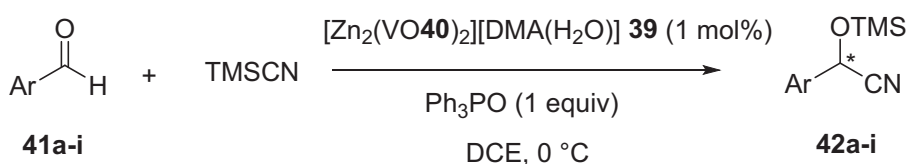
Scheme 23. Epoxidation of styrene on vanadium bis(oxazoline)-derived catalyst **35** immobilized on laponite [43].



Scheme 22. Epoxidation of a tiglane in the presence of bishydroxamic acid ligand **33** [41].

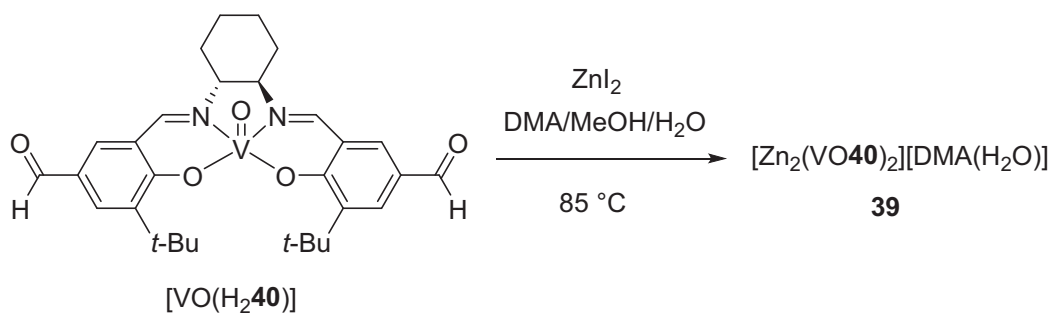


Scheme 24. Epoxidation of an allylic alcohol on vanadium binaphthylbishydroxamic acid-derived catalyst **38** immobilized on polymer [44].



- 42a:** Ar = Ph: 93% conversion, 92% ee (S)
42b: Ar = *p*-BrC₆H₄: 94% conversion, 92% ee (S)
42c: Ar = *p*-Tol: 90% conversion, 92% ee (S)
42d: Ar = *m*-MeOC₆H₄: 92% conversion, 95% ee (S)
42e: Ar = *p*-MeOC₆H₄: 90% conversion, 94% ee (S)
42f: Ar = 1-Naph: 91% conversion, 92% ee (R)
42g: Ar = 2-Naph: 90% conversion, 95% ee (S)
42h: Ar = 2-thiophenyl: 92% conversion, 92% ee (S)
42i: Ar = 9-anthryl: 62% conversion, 35% ee (S)

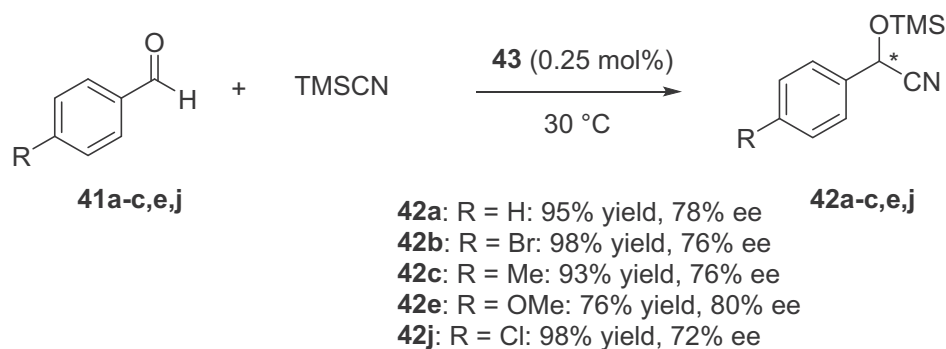
preparation of catalyst [Zn₂(VO**40**)₂][DMA(H₂O)] **39**:



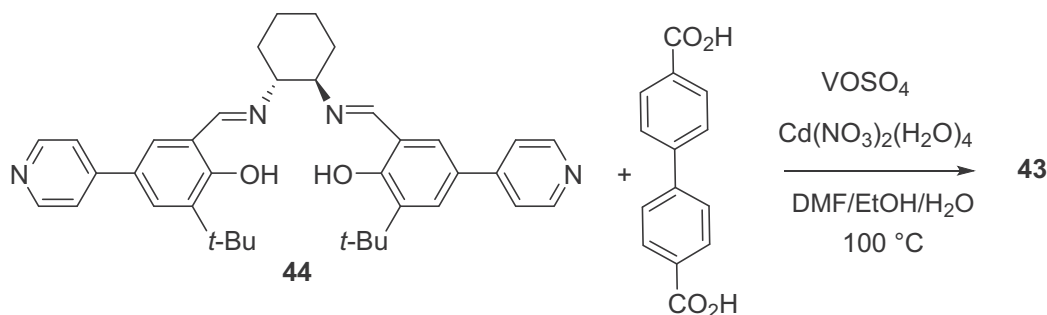
Scheme 25. Cyanosilylation of aromatic aldehydes in the presence of porous metal–organic framework **39** incorporating two [VO(salen)] units [46].

Sharpless methodology remains the most popular methodology to synthesize these products through asymmetric titanium-catalyzed oxidation of allylic alcohols [38]. Sharpless also successfully investigated vanadium in these reactions [3], and other groups later [39]. Among them, Noji et al. reported in 2015 the use of a novel

chiral vanadium catalyst in situ generated from 5 mol% of VO(acac)₂ and 7.5 mol% of chiral binaphthylbishydroxamic acid ligand **29** in the asymmetric epoxidation of allylic alcohols **30a-k** with TBHP as an oxidant [40]. As illustrated in Scheme 21, the reaction of a range of 2,3,3-trisubstituted allylic alcohols **30a-b,e-h**



preparation of catalyst **43**:



Scheme 26. Cyanosilylation of benzaldehydes in the presence of salen-derived vanadium **43** based on metal-organic frameworks [47].

performed in toluene at 0 °C led to the corresponding (2*R*)-epoxy alcohols **31a-b,e-h** in uniformly high enantioselectivities (80–98% ee) combined with moderate to excellent yields (52–95%). In contrast, a much lower enantioselectivity (21% ee) was observed in the reaction of geminal disubstituted allylic alcohol **30k** which also provided the lowest yield (20%). Other disubstituted allylic alcohols **30c-d,i,j** reacted smoothly to give the corresponding chiral epoxides **31c-d,i,j** with high enantioselectivities (80–89% ee) and low to high yields (18–86%).

In 2015, a double induction was described by Wender et al. in the asymmetric epoxidation of chiral tiglane **32** [41]. Indeed, the epoxidation of this compound with TBHP as oxidant was promoted by a chiral vanadium catalyst in situ generated from 10 mol% of VO(Oi-Pr)₃ and 20 mol% of chiral bishydroxamic acid ligand **33** [42]. Performed at 4 °C in benzene as a solvent, it yielded the corresponding biologically interesting epoxide **34** as almost single diastereomer (78% de) in excellent yield (90%), as depicted in Scheme 22.

Later in 2018, Fraile et al. developed chiral vanadium complexes derived from bis(oxazoline) ligand **35** immobilized on laponite through non-covalent cation exchange to be investigated in the asymmetric epoxidation of styrene **36** with TBHP as an oxidant [43]. The process was performed in acetonitrile at 70 °C, producing the corresponding chiral epoxide **37** with moderate conversion (39%) and enantioselectivity (72% ee), as shown in Scheme 23. The recovery of the catalyst was not fully demonstrated.

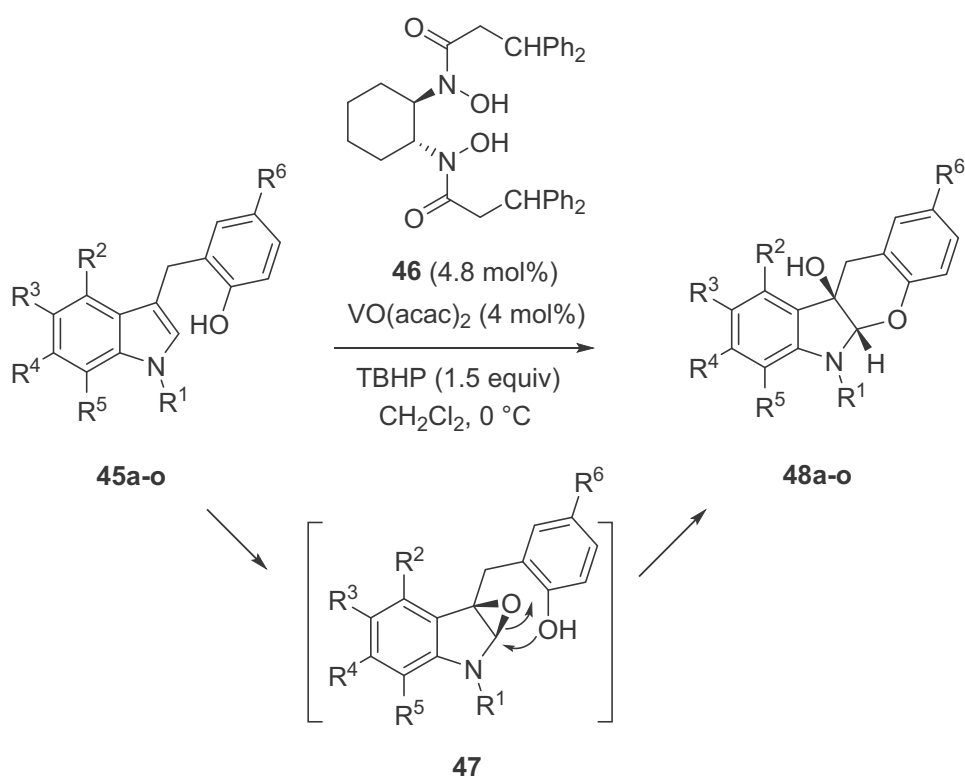
More recently in 2019, Noji et al. developed polymer-supported vanadium complex **38** derived from a chiral binaphthylbis-hydroxamic acid ligand which was investigated in the asymmetric epoxidation of allylic alcohol **30a** [44]. Employed at 10 mol% of catalyst loading in toluene at 0 °C in the presence of TBHP as oxidant, it afforded the corresponding chiral epoxide **31a** in both good yield (78%) and enantioselectivity (85% ee), as illustrated in

Scheme 24. Interestingly, catalyst **38** could be recyclable and reused for up to five times.

5. Enantioselective vanadium-catalyzed cyanosilylations of aldehydes

Various asymmetric metal-catalyzed cyanosilylations of aldehydes have been successfully developed in the last decade [45]. In 2015, Cui et al. designed novel metal organic frameworks (MOFs) incorporating chiral [VO(salen)] units which were applied after oxidation to catalyze the asymmetric cyanation of aromatic aldehydes [46]. Among them, catalyst **39** was synthesized by reaction of [VO(H₂**40**)] with ZnI₂ at 85 °C (Scheme 25). When applied at 1 mol% of catalyst loading in dichloroethane as a solvent at 0 °C in the presence of PPh₃O and TMSCN to the asymmetric cyanosilylation of a wide variety of aromatic aldehydes **41a-h**, it afforded the corresponding (*S*)-products **41a-h** in both uniformly excellent yields (90–94%) and enantioselectivities (92–95% ee). The lowest enantioselectivity (35% ee) was observed in the reaction of 9-anthraldehyde **41i**. The authors demonstrated that it was possible to recover the catalyst by simple filtration and reuse it without significant deterioration of the catalytic activity.

With the aim of developing even greener catalytic systems, Van Der Voort et al. reported the synthesis of another novel metal-organic framework to be used under solvent-free conditions [47]. As illustrated in Scheme 26, MOF catalyst **43** was prepared from VOSO₄, chiral ligand H₂**44**, Cd(NO₃)₂(H₂O)₄ and biphenyl-4,4'-dicarboxylic acid. When only 0.25 mol% of this catalyst was applied to promote the cyanosilylation of benzaldehydes **41a-c,e,j** at 30 °C, the corresponding chiral cyanides **42a-c,e,j** were produced in high yields (76–98%) and enantioselectivities (72–80% ee). The heterogeneous nature of the reaction was demonstrated by recyclability



- 48a:** R¹ = R² = R³ = R⁴ = R⁵ = R⁶ = H: 58% yield, 95% ee
48b: R¹ = Me, R² = R³ = R⁴ = R⁵ = R⁶ = H: 62% yield, 86% ee
48c: R¹ = Bn, R² = R³ = R⁴ = R⁵ = R⁶ = H: 89% yield, 90% ee
48d: R¹ = *p*-MeOC₆H₄, R² = R³ = R⁴ = R⁵ = R⁶ = H: 64% yield, 88% ee
48e: R¹ = 1-Naph, R² = R³ = R⁴ = R⁵ = R⁶ = H: 71% yield, 92% ee
48f: R¹ = R² = R⁴ = R⁵ = R⁶ = H, R³ = Cl: 47% yield, 90% ee
48g: R¹ = R² = R³ = R⁵ = R⁶ = H, R⁴ = Cl: 58% yield, 94% ee
48h: R¹ = R² = R³ = R⁵ = R⁶ = H, R⁴ = F: 53% yield, 95% ee
48i: R¹ = R² = R³ = R⁵ = R⁶ = H, R⁴ = Br: 58% yield, 95% ee
48j: R¹ = R² = R⁴ = R⁵ = R⁶ = H, R³ = Br: 45% yield, 97% ee
48k: R¹ = R³ = R⁴ = R⁵ = R⁶ = H, R² = Br: 78% yield, 98% ee
48l: R¹ = R² = R³ = R⁴ = R⁶ = H, R⁵ = Br: 57% yield, 95% ee
48m: R¹ = R² = R³ = R⁴ = R⁶ = H, R⁵ = Me: 52% yield, 94% ee
48n: R¹ = Bn, R² = R³ = R⁴ = R⁵ = H, R⁶ = Cl: 83% yield, 92% ee
48o: R¹ = Bn, R² = R³ = R⁴ = R⁵ = H, R⁶ = Br: 77% yield, 94% ee

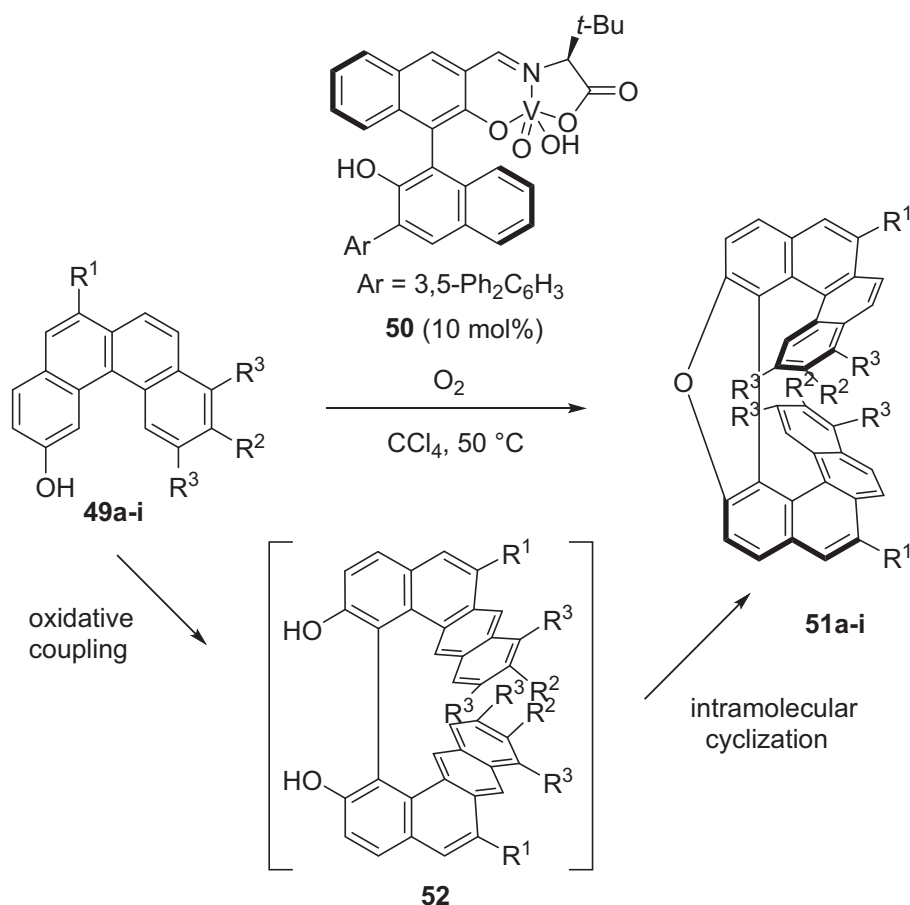
Scheme 27. Domino epoxidation/intramolecular ring-opening reaction of indoles in the presence of bishydroxamic acid ligand **46** [49].

and reusability of the catalyst. Indeed, both its activity and enantioselectivity were found unchanged for up to two cycles. However, in the third run, the values of yield and enantioselectivity excess decreased, probably because of modification of the surrounding environment of the chiral centers or undesirable adsorption of organic compounds by the MOF catalyst.

6. Enantioselective vanadium-catalyzed domino reactions

So far, only few asymmetric domino reactions have been catalyzed by chiral vanadium complexes in comparison with other metals [48]. Among them, an enantioselective domino epoxida-

tion/intramolecular ring-opening reaction of indoles was developed by You et al., in 2015 [49]. It employed a combination of 4.8 mol% of designed C₂-symmetric bishydroxamic acid ligand **46** with 4 mol% of VO(acac)₂ as precatalyst. The reaction was performed at 0 °C in dichloromethane as solvent in the presence of TBHP as oxidant. A variety of unprotected (R¹ = H) as well as *N*-protected indoles **45a-o** were tolerated. A first epoxidation step led to the corresponding intermediate epoxide **47** which further underwent an intramolecular ring-opening reaction to afford the final chiral domino products **48a-o**. As shown in Scheme 27, these products were obtained in moderate to high yields (45–89%) and uniformly high enantioselectivities (86–98% ee).



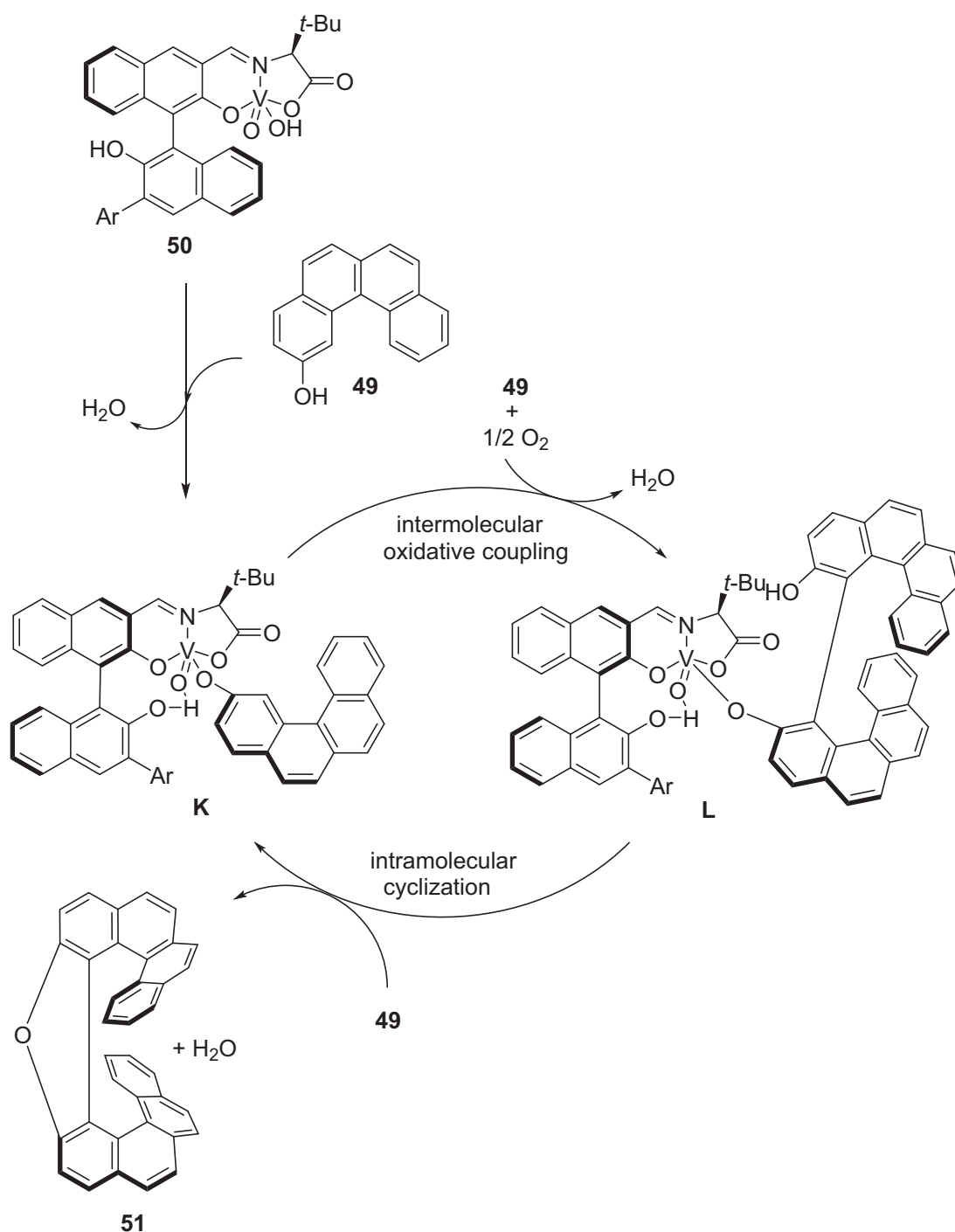
- 51a:** $\text{R}^1 = \text{R}^2 = \text{R}^3 = \text{H}$: 86% yield, 78% ee
51b: $\text{R}^1 = \text{Ph}$, $\text{R}^2 = \text{R}^3 = \text{H}$: 72% yield, 45% ee
51c: $\text{R}^1 = p\text{-Tol}$, $\text{R}^2 = \text{R}^3 = \text{H}$: 61% yield, 44% ee
51d: $\text{R}^1 = p\text{-FC}_6\text{H}_4$, $\text{R}^2 = \text{R}^3 = \text{H}$: 68% yield, 50% ee
51e: $\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{R}^3 = \text{H}$: 70% yield, 88% ee
51f: $\text{R}^1 = n\text{-Hex}$, $\text{R}^2 = \text{R}^3 = \text{H}$: 72% yield, 76% ee
51g: $\text{R}^1 = \text{Br}$, $\text{R}^2 = \text{R}^3 = \text{H}$: 56% yield, 94% ee
51h: $\text{R}^1 = \text{R}^3 = \text{H}$, $\text{R}^2 = \text{Me}$: 68% yield, 80% ee
51i: $\text{R}^1 = \text{R}^2 = \text{H}$, $\text{R}^3 = \text{Me}$: 84% yield, 60% ee

Scheme 28. Domino oxidative coupling/intramolecular cyclization reaction of 2-hydroxybenzo[*c*]phenanthrenes in the presence of binaphthyl vanadium catalyst **50** [50].

In 2016, Sasai and Takizawa described another asymmetric domino reaction catalyzed by a newly designed chiral vanadium complex [50]. As depicted in Scheme 28, the process consisted in an enantioselective domino oxidative coupling/intramolecular cyclization reaction of 2-hydroxybenzo[*c*]phenanthrenes **49a-i** promoted by chiral preformed binaphthyl vanadium catalyst **50**. The reaction was performed at 50 °C under O_2 atmosphere in tetrachloromethane as solvent and led to the corresponding chiral oxa [9]helicenes **51a-i** in good to high yields (56–86%) and moderate to excellent enantioselectivities (44–94% ee). After a first oxidative coupling of **49a-i** which gave intermediate **52**, an intramolecular cyclization occurred to afford domino products **51a-i**. The lowest enantioselectivities (44–50% ee) were obtained in the reaction of phenyl-, *p*-tolyl- and *p*-fluoro C_6H_4 -substituted substrates **49b-d**.

To explain these results, the authors proposed the mechanism depicted in Scheme 29 based on a radical-anion coupling with one molecule of vanadium catalyst [50]. The reaction began with the reaction of catalyst **50** with 2-hydroxybenzo[*c*]phenanthrene **49** to give intermediate **K**, which subsequently underwent an intermolecular oxidative coupling with a second equivalent of 2-hydroxybenzo[*c*]phenanthrene **49** through a single electron transfer to a vanadium(V) species. Then, oxidation of vanadium(IV) by O_2 generated intermediate **L**. Subsequently, intramolecular cyclization assisted by vanadium(V) afforded final domino product **51** and released regenerated intermediate **K**. It seemed that the hydroxy group on the binaphthyl ligand in the vanadium catalyst increased the Lewis acidity of vanadium through an intramolecular hydrogen bond in intermediates **K** and **L**.

with $R^1 = R^2 = R^3 = H$



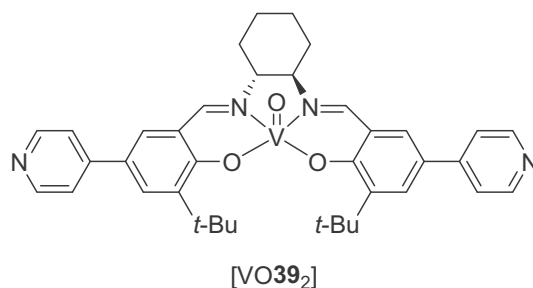
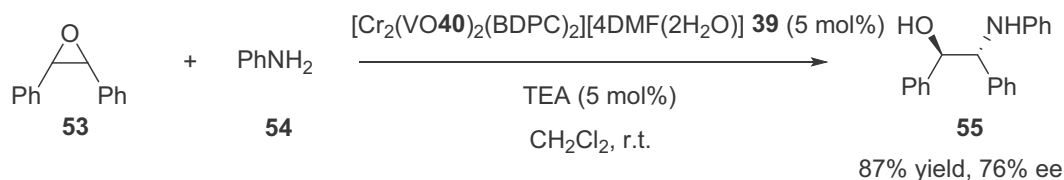
Scheme 29. Mechanism for domino oxidative coupling/intramolecular cyclization reaction of 2-hydroxybenzo[c]phenanthrenes [50].

7. Miscellaneous enantioselective vanadium-catalyzed transformations

MOF **39** (Scheme 20) was also employed by Cui and Liu at 5 mol % of catalyst loading to promote the asymmetric ring-opening reaction of *cis*-stilbene oxide **53** with aniline **54** [46]. As illustrated in Scheme 30, the reaction was performed at room temperature in dichloromethane as solvent in the presence of TEA as base, yielding

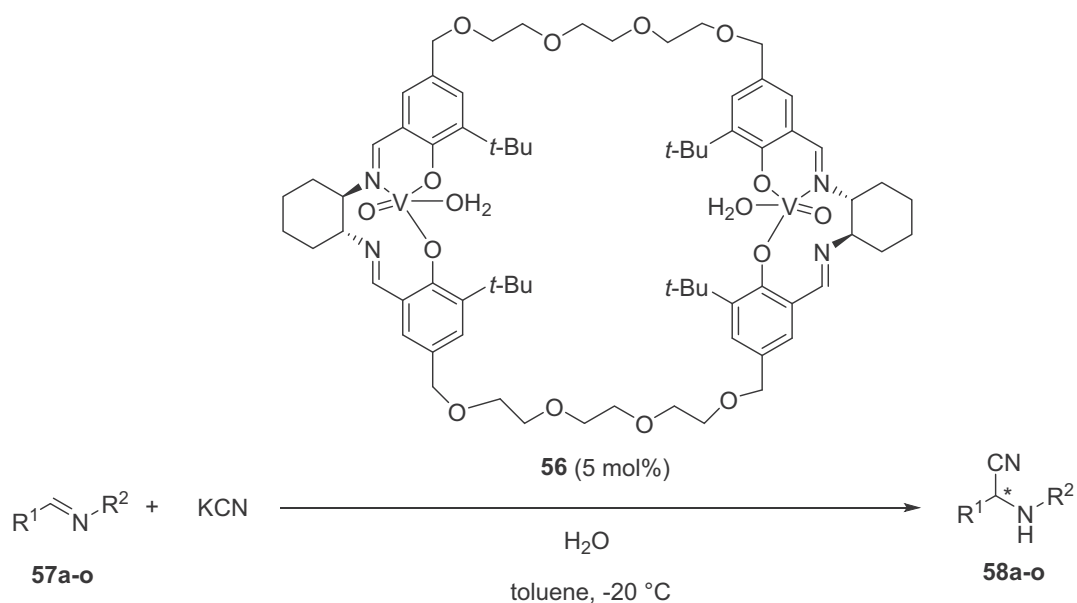
the corresponding chiral 1,2-amino alcohol **55** in both good yield (87%) and enantioselectivity (76% ee).

In 2015, Khan et al. reported the synthesis of novel chiral macrocyclic dimeric salen complex **56** [51]. This catalyst was found highly efficient to promote the asymmetric Strecker-type reaction of aromatic aldimines **57a-n** with potassium cyanide in toluene at -20 °C in the presence of water as additive, as illustrated in Scheme 31. The process afforded the corresponding chiral



H₂BDPC: diphenyl-4,4'-dicarboxylic acid

Scheme 30. Ring-opening reaction of *cis*-stilbene oxide with aniline in the presence of MOF **39** [46].



- 58a:** R¹ = Ph, R² = Bn: 89% yield, 84% ee
58b: R¹ = *p*-Tol, R² = Bn: 91% yield, 93% ee
58c: R¹ = *m*-Tol, R² = Bn: 84% yield, 79% ee
58d: R¹ = *o*-Tol, R² = Bn: 88% yield, 90% ee
58e: R¹ = *p*-MeOC₆H₄, R² = Bn: 90% yield, 91% ee
58f: R¹ = *m*-MeOC₆H₄, R² = Bn: 86% yield, 80% ee
58g: R¹ = *o*-MeOC₆H₄, R² = Bn: 90% yield, 89% ee
58h: R¹ = *p*-FC₆H₄, R² = Bn: 87% yield, 92% ee
58i: R¹ = *p*-ClC₆H₄, R² = Bn: 83% yield, 91% ee
58j: R¹ = Ph, R² = CH(Ph)₂: 92% yield, 96% ee
58k: R¹ = *p*-Tol, R² = CH(Ph)₂: 90% yield, 93% ee
58l: R¹ = *o*-MeOC₆H₄, R² = CH(Ph)₂: 89% yield, 99% ee
58m: R¹ = *p*-BrC₆H₄, R² = CH(Ph)₂: 86% yield, 87% ee
58n: R¹ = Naph, R² = CH(Ph)₂: 84% yield, 90% ee
58o: R¹ = *t*-Bu, R² = CH(Ph)₂: 71% yield, 91% ee

Scheme 31. Strecker-type reaction of aldimines in the presence of macrocyclic dimeric salen catalyst **56** [51].

N-benzylimines **58a-n** in both high yields (83–92%) and enantioselectivities (79–99% ee) when 5 mol% of catalyst **56** was used. The catalyst system tolerated various types of substituents on different positions of the phenyl ring of *N*-benzylimines as well as *N*-(1,1-diphenylmethylamine)-substituted imines. Moreover, dialkyl imine **57o** reacted smoothly to give the corresponding chiral amine **58o** in good yield (71%) and high enantioselectivity (91% ee). The recyclability and reuse of the catalyst was demonstrated by the authors. It was found that the catalyst could be recycled up to five runs with retention of enantioselectivity.

8. Conclusions

This review collects the results published in the last five years in the field of enantioselective vanadium-catalyzed transformations, demonstrating that vanadium is becoming capable of replacing other transition metals. Indeed, a range of highly enantioselective vanadium-catalyzed reactions of many types have been recently developed, providing a novel potential for catalysis and demonstrating that this original field is growing rapidly. Among these novel results, are the first asymmetric oxidative couplings of 2-naphthols, phenols and *N*-benzylated 2-hydroxycarbazoles achieved with up to 96, 97 and 96% ee, respectively. Excellent enantioselectivities have also been reported in the asymmetric oxidation of sulfides (97% ee), epoxidations (98% ee) by using TBHP as an oxidant, cyanosilylations of aldehydes (95% ee) by using a chiral porous metal-organic framework, domino epoxidation/intramolecular ring-opening reactions of indoles (98% ee), domino oxidative coupling/intramolecular cyclization reactions of 2-hydroxybenzo[*c*]phenanthrenes (94% ee) and Strecker reactions of aldimines (99% ee). On the basis of advantages of vanadium catalysts compared to other metals, such as high range of oxidation states and low moisture sensitivity level, novel vanadium chiral systems will be developed in the future to perform even more new transformations in unexplored fields, such as C–C bond formations, and apply them in the total synthesis of important products. Efforts will have to be made to develop more kinetic and mechanistic studies to disclose the roles of chiral vanadium complexes and for designing more efficient and selective ligands so far limited to Schiff base, salen, hydroxamic acid or bishydroxamic acid ligands. This should lead to developments toward better discerning the chemistry of vanadium and structure–activity relationships. Moreover, synthesizing multimetallic vanadium catalysts also constitutes a challenge to better know nuclearity effects caused by metal–metal interactions, and know how supported systems operate. Advanced spectroscopic techniques will also help to gain insight into catalyst behavior.

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