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Design and synthesis of dinuclear hemisalen complex on hexaarylbenzene scaffold

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ABSTRACT

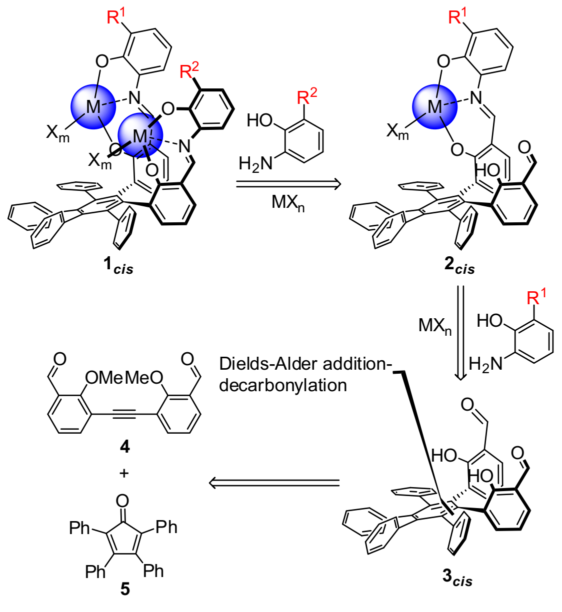
The dinuclear vanadium(V) dihemisalen complexes on the hexaarylbenzene scaffold were designed and synthesized, where the characteristic behaviors were found in the complexation of the dihemisalen ligand with $VO(O^iPr)_3$.

Differentiation of dual sites of transition metals provides a useful system for catalytic reaction and molecular recognition due to the electronic and/or steric effects. Well-organized dinuclear metals are also found in active sites of enzymes to catalyze unique reactions.[1] So far, a variety of dinuclear catalysts have been developed in selective transformations.[2] In the previous study, we envisioned that the controlled arrangement of two metals on the rigid scaffold is able to give spatially regulated reaction sites. The bis-biphenol ligand on a hexaphenyl benzene scaffold was employed for the cross-pinacol coupling reaction.[3]

Vanadium(V) hemisalen complexes are known to catalyze oxidation reactions,[2e,4] such as oxidative coupling of naphthols,[2e,4b–d] asymmetric oxidative kinetic resolution of α-hydroxy esters,[4e] and oxidation of sulfides.[4a] The bimetallic complex, in which discriminated two hemisalen structures are three-dimensionally regulated through a suitable spacer unit, would lead to multifunctional catalysts depending on individual activated sites. In this context, the sterically controlled dinuclear complex $\mathbf{1}_{cis}$ bearing the hemisalen coordination moieties was designed (Scheme 1). Here, we report the synthesis of hemisalen vanadium(V) complexes on the hexaarylbenzene scaffold.

Our synthetic strategy is outlined in Scheme 1. The dinuclear complex $\mathbf{1}_{cis}$ is envisaged to be constructed via condensation of the monoaldehyde $\mathbf{2}_{cis}$ with various aminophenols, followed by complexation with a transition metal, such as a vanadium(V) compound. The monoaldehyde $\mathbf{2}_{cis}$ is similarly prepared from the dialdehyde $\mathbf{3}_{cis}$.[5] The dialdehyde $\mathbf{3}_{cis}$ would arise from the Diels–Alder addition-decarbonylation reaction[6] of the tolan **4** with tetraphenylcyclopentadienone (**5**).

Synthesis of **3** is shown in Scheme 2. 1,2-Bis(2-methoxyphenyl)ethyne (**6**)[7] was treated with BuLi, followed by trapping of DMF to give the dialdehyde **4** in 52% yield. The Diels–Alder addition-decarbonylation of **4** with the cyclopentadienone **5** in



Scheme 1. Synthetic strategy for $\mathbf{1}_{cis}$.

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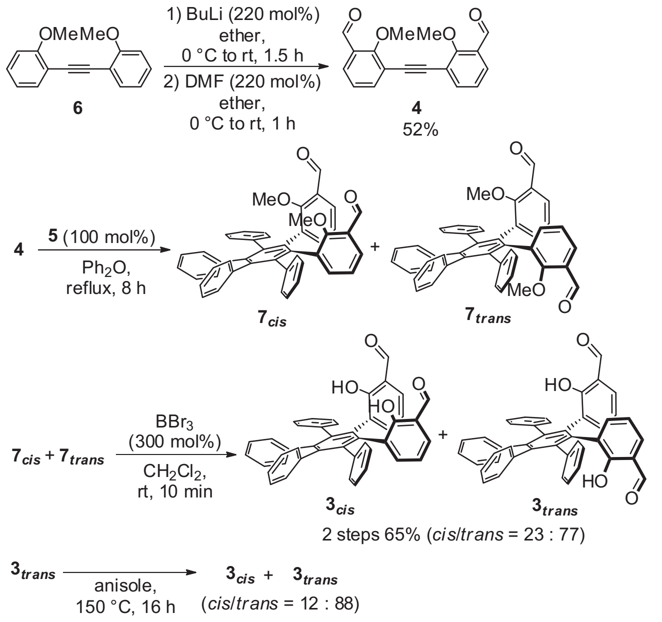
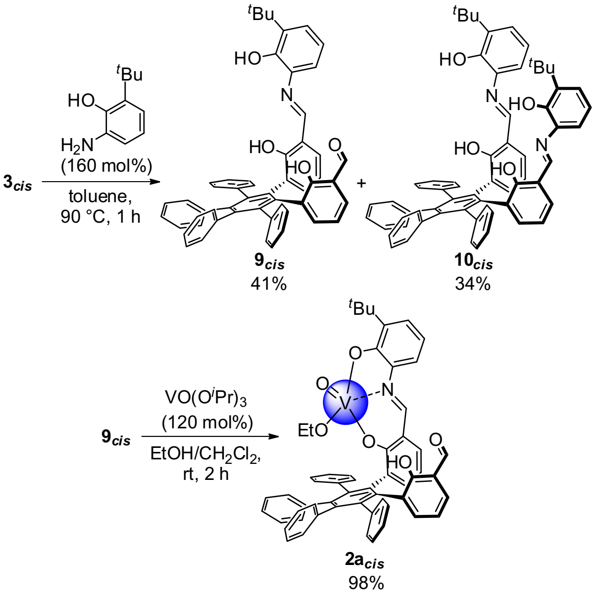


Scheme 2. Synthesis of **3**.



Scheme 4. Synthesis of $\mathbf{2a}_{cis}$.

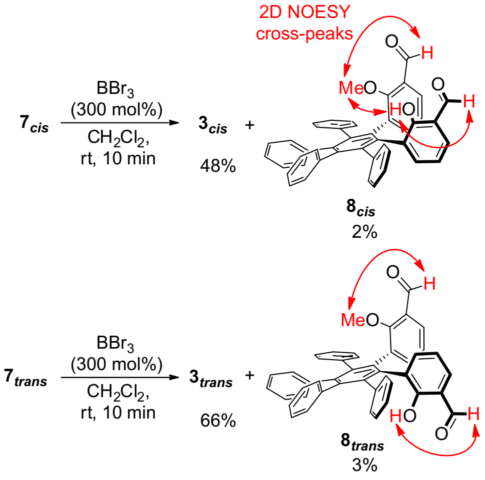
Ph_2O at reflux led to dimethoxyhexaarylbenzene **7** (a mixture of *cis* and *trans* isomers). The thus-obtained mixture of $\mathbf{7}_{cis}$ and $\mathbf{7}_{trans}$ was treated with BBr_3 to give hexaarylbenzene **3** (2 steps 65%, *cis*/*trans* = 23:77). The diastereomers were able to be separated by silica-gel chromatography. The gram scale synthesis was possible.

The structural assignment of the *cis*/*trans* isomers was determined by 2D NOESY experiments of the desymmetrized monomethoxy derivative **8** shown in Scheme 3. Dimethoxyhexaarylbenzenes $\mathbf{7}_{cis}$ and $\mathbf{7}_{trans}$ were separately treated with 3 equiv of BBr_3 to give disalicylaldehyde **3** and small amounts of the monomethoxy salicylaldehydes $\mathbf{8}_{cis}$ and $\mathbf{8}_{trans}$ (2% and 3% yields, respectively). The isomer $\mathbf{8}_{cis}$, in which cross-peaks were observed between the methoxy group and the hydroxyl one of another side in a 2D NOESY spectrum, was assigned as a *cis* isomer. The *cis*/*trans* determination of disalicylaldehyde **3** was carried out by the transformation from each isomer of the monomethoxy derivative **8** by deprotection.

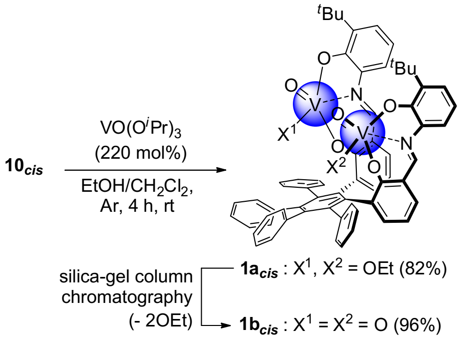
The *cis* isomer $\mathbf{3}_{cis}$ is a minor product in the Diels–Alder addition-decarbonylation reaction, however the treatment of $\mathbf{3}_{trans}$ in anisole at 150 °C for 16 h led to *cis* and *trans* isomers (Scheme 2, *cis*/*trans* = 12:88). On the other hand, this isomerization did not occur at 90 °C even after 24 h, indicating the conformational rigidity.

Condensation of disalicylaldehyde $\mathbf{3}_{cis}$ with 2-amino-6-*tert*-butylphenol led to the mono- and dihemisalen ligands $\mathbf{9}_{cis}$ and $\mathbf{10}_{cis}$ in 41% and 34% yields, respectively (Scheme 4). Complexation of the monohemisalen ligand $\mathbf{9}_{cis}$ with $VO(O^iPr)_3$ in the ethanol/dichloromethane solution gave mononuclear vanadium(V) complex $\mathbf{2a}_{cis}$ in 98% yield.[8] Electrospray ionization (ESI) mass (positive mode) of $\mathbf{2a}_{cis}$ in ethanol mainly detected the peak corresponding to the monoethoxide complex ($[\mathbf{2a}_{cis}+Na]^+$ 902.3). Thermogravimetry (TG) analysis showed the mass loss corresponding to 1 equiv of ethanol at 250–350 °C. In addition, ^1H NMR spectrum in $CDCl_3$/CD_3OD also supports the coordination of one ethanol.[9] On the other hand, two sharp signals assigned to CHO protons (δ 9.49 and 9.46) were observed in ^1H NMR spectrum. Two distinct resonances (−520 and −526 ppm) were also observed in the ^{51}V NMR spectrum. These results may suggest the formation of the *endo* and *exo* diastereomers as reported by Chakravorty.[10]

The dihemisalen ligand $\mathbf{10}_{cis}$ was complexed with $VO(O^iPr)_3$ to give the dinuclear vanadium(V) complex $\mathbf{1a}_{cis}$ in 82% yield. Elemental analysis supports the formula of the diethoxide complex $\mathbf{1a}_{cis}$ (Anal. Calcd. for $C_{68}H_{62}N_2O_8V_2$: C, 71.82; H, 5.50; N, 2.46. Found: C, 71.58; H, 5.32; N, 2.47). TG analysis of $\mathbf{1a}_{cis}$ showed the mass loss corresponding to 2 equiv of ethanol. ^1H NMR spectrum



Scheme 3. Structural assignment of **8**.



Scheme 5. Synthesis of $\mathbf{1a}_{cis}$ and $\mathbf{1b}_{cis}$.

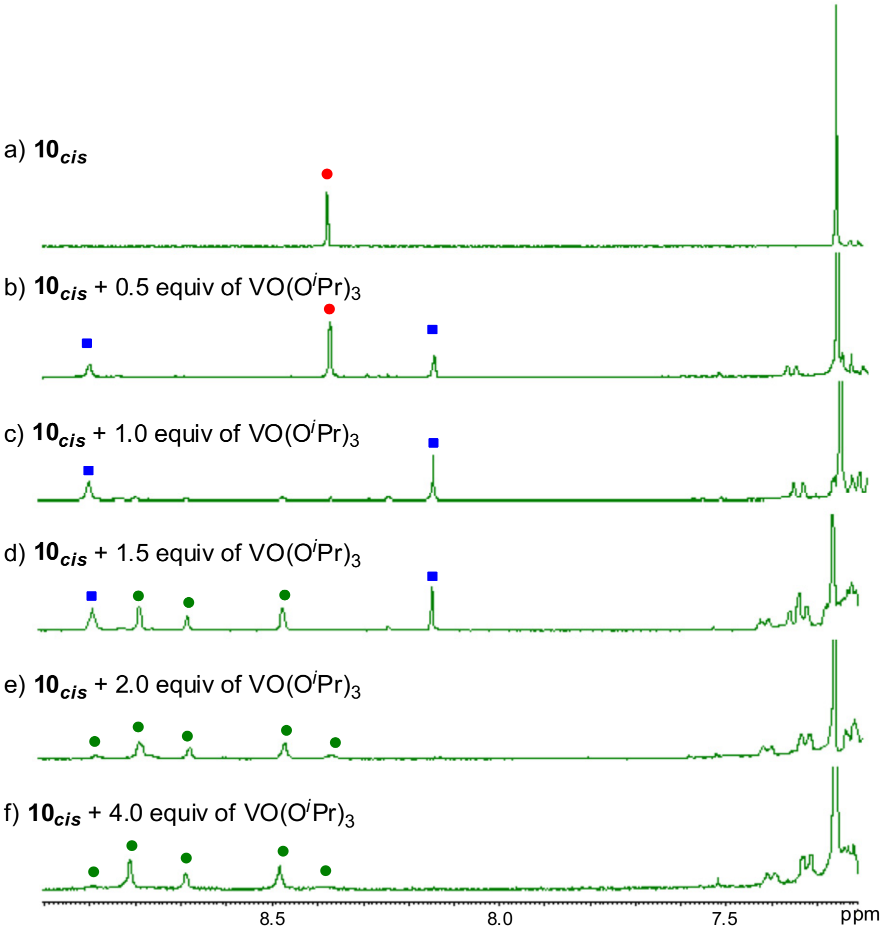
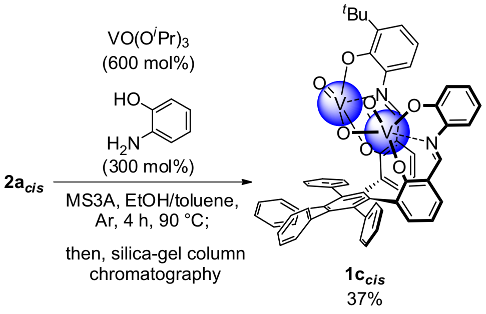


Figure 1. ^{1}H NMR spectra for the complexation of **10**$_{cis}$ with VO(O^{i}Pr)$_3$. Each reaction was carried out in ethanol/dichloromethane at room temperature for 1 h under argon. Then, the solvent was replaced by CDCl$_3$/CD$_3$OD (20:1) for the ^{1}H NMR study.

in CDCl$_3$/CD$_3$OD also indicates 2 equiv of ethoxides. On the other hand, ^{1}H and ^{51}V NMR spectra in CDCl$_3$/CD$_3$OD suggest a mixture of the diastereomers or the V–O–V linked complex. In the ESI mass (positive mode) spectra of **1a**$_{cis}$ in ethanol, both the diethoxide complexes ([M+Na]$^+$ 1159.3) and the V–O–V linked complex ([M-2EtO+O+Na]$^+$ 1085.2) were observed. One of the plausible structures for **1a**$_{cis}$ is shown in Scheme 5.[11] The coordinated ethoxides in **1a**$_{cis}$ were lost by the silica-gel column chromatography to give the complex **1b**$_{cis}$. Matrix-assisted laser desorption ionization time-of-flight (MALDI TOF) mass (negative mode) spectra are consistent with the expected value for the V–O–V linked dinuclear complex ([**1b**$_{cis}$]$^-$ 1062.0, see the Supplementary data). The peaks of hydroxide were not observed in the IR spectrum of **1b**$_{cis}$. The obtained compound is likely to have the V–O–V linked structure, as reported in the Refs. 4d,12.



Scheme 6. Synthesis of **1c**$_{cis}$.

Complexation of the dihemisalen ligand **10**$_{cis}$ with VO(O^{i}Pr)$_3$ was also followed by ^{1}H NMR (Fig. 1). The singlet peak for CHN protons (●) in the aldimine moiety was decreased by the addition of a half equivalent of VO(O^{i}Pr)$_3$ with the concomitant appearance of the new signals (■) assignable to the monometallic complexes (Fig. 1b). Then, an equimolar mixture of **10**$_{cis}$ and VO(O^{i}Pr)$_3$ almost induced the convergence to these peaks (■) (Fig. 1c). When one and a half equivalents of VO(O^{i}Pr)$_3$ were added, the peaks corresponding to the dinuclear hemisalen complexes appeared (●) (Fig. 1d). These three singlets and two broad peaks (●) grew with two equivalents of VO(O^{i}Pr)$_3$ (Fig. 1e), where the vanadium(V) dihemisalen complexes may exist as a mixture of the three diastereomers (*endo-endo*, *exo-exo*, and *endo-exo*) and the V–O–V linked structure. ESI mass (positive mode) supports the formation of both the diethoxide complexes **1a**$_{cis}$ ([M+Na]$^+$ 1159.3) and the V–O–V linked structure ([M-2EtO+O+Na]$^+$ 1085.2) in ethanol. Use of more than 2 equiv of VO(O^{i}Pr)$_3$ did not induce the new peaks (Fig. 1f).

Based on the synthetic plan shown in Scheme 1, the desymmetrized dinuclear complex **1c**$_{cis}$ was synthesized by the treatment of monoaldehyde **2a**$_{cis}$ with 2-aminophenol and VO(O^{i}Pr)$_3$ (Scheme 6). After the reaction, the reaction mixture was purified by silica-gel column chromatography. ^{1}H NMR spectrum of **1c**$_{cis}$ showed the absence of ethoxide. IR spectrum of **1c**$_{cis}$ did not show the peaks assignable to hydroxide. MALDI TOF mass (negative mode) spectra also supported the expected value for the V-O-V linked desymmetrized dinuclear complex **1c**$_{cis}$ ([**1c**$_{cis}$]$^-$ 1006.1, see the Supplementary data).[12]

In summary, the dinuclear vanadium(V) dihemisalen complexes on the hexaarylbenzene scaffold were designed and synthesized, where the characteristic behaviors were found in the complexation of the dihemisalen ligand with $VO(O^iPr)_3$. Furthermore, the desymmetrized vanadium(V) complex **1c**$_{cis}$ was formed from the key intermediate **3**$_{cis}$. These complexes are considered to be of potential to promote various reactions including the pinacol coupling through dual activation by metals. Further investigation on the application of the dinuclear hemisalen complexes for catalysis is now in progress.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2012.07.127.

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