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Synthesis of Glycal-Based Chiral Benzimidazoles by $VO(acac)_2-CeCl_3$ Combo Catalyst and Their Self-Aggregated Nanostructured Materials

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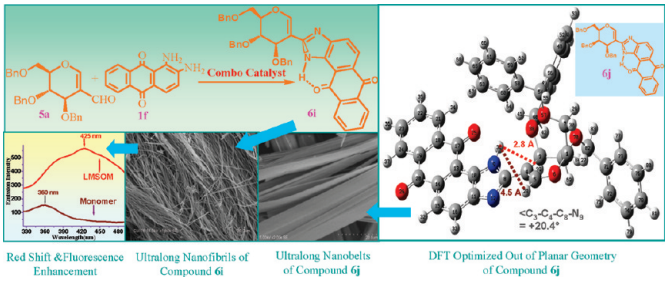

$VO(acac)_2-CeCl_3$ combo catalyst has been developed for chemoselective cyclocondensation *cum* oxidation under mild reaction conditions toward synthesis of a new class of optically pure compounds, 2-(2′-*C*-3′,4′,6′-tri-*O*-benzyl/methyl-glycal)-1*H*-benzimidazoles. It involves an operationally simple synthetic protocol efficient for the syntheses of a wide range of chiral benzimidazoles in high yields without formation of undesired 1,2-disubstituted and pseudoglycal byproducts. Vanadium(V) is found as active oxidant for the chemical processes which is investigated by UV absorption spectroscopy. Highly ordered one-dimensional low molecular mass organic nanostructured materials are fabricated by nanocrystallization of the chiral nanoscale building blocks. Theoretical calculation by the B3LYP/6-31G** level of theory of the glycal-based chiral benzimidazoles shows out of planar geometry of the 1*H*-anthra[1,2-*d*]imidazole-6,11-dione moiety, which is responsible for the strong self-aggregation to generate ultralong nanostructured materials. We have also found nice agreement between the theoretical results with the experimental observation in 2D-NOESY experiments. The photophysical property of the solid nanostructured materials is also reported.

Introduction

Cyclocondensation *cum* oxidation is a powerful synthetic tool in academic and industrial settings in producing essential heterocyclic moieties in one step.[1] Further, development of chemoselective mild catalytic processes with molecular oxygen as the stoichiometric reagent[2] is essential for achieving the acid and thermo-labile new chiral heterocycles. One important goal of achieving the designed compounds is to utilize them as chiral nanoscale building blocks for the construction of novel multifunctional supramolecular architecture possessing well-defined size, shapes, and physical properties as advanced organic functional materials for their unique optical, optoelectronic, and biological applications.[3,4b,4d]

The benzimidazole is a ubiquitous heterocyclic motif and many of its analogues have been extensively used in the

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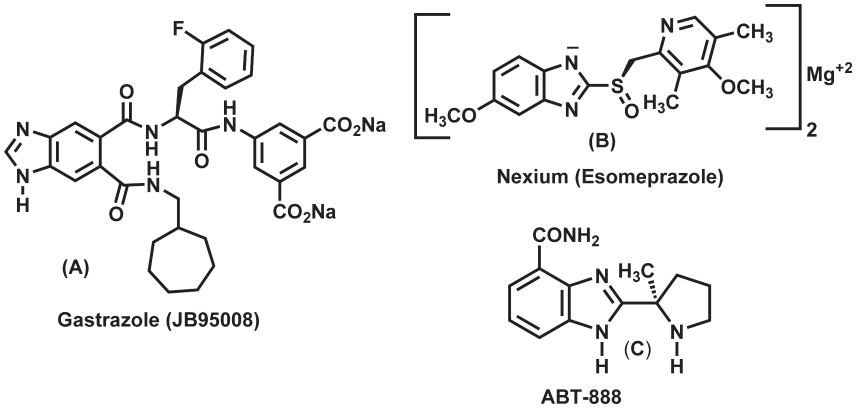

FIGURE 1. Biologically active chiral benzimidazoles.

treatment of viral, bacterial, and fungal infections.[5] Current studies in medicinal chemistry have demonstrated them as potential drug candidates for the pharmaceutical industry.[6] They have also widespread applications in fluorescence,[7] chemosensing,[8] crystal engineering,[9] and corrosion science.[10] Recent interest in chiral benzimidazoles can also be attributed to their asymmetric catalysis[11] and diverse biological activities.[12] It may be cited in this context that the chiral benzimidazoles like cholecystokinin-2 (CCK_2) receptor antagonist Gastrazole (JB95008)[12a] is used as a lead drug for treatment of pancreatic cancer, the proton-pump inhibitor Nexium[12c] (esomeprazole) is developed for acid-related diseases, and 2-[(*R*)-2-methylpyrrolidin-2-yl]-1*H*-benzimidazole-4-carboxamide (ABT-888)[12g] is currently undergoing clinical trials on humans for treatment of a variety of cancers (Figure 1). Looking into the novel pharmacological activities of the Nexium and ABT-888 possessing chiral substituents at C-2 positions of the benzimidazole scaffolds, we have envisioned that 2-substituted benzimidazoles bearing biocompatible chiral sugar moieties, conjugated olefinic double bonds, and electron withdrawing and donating functional groups should be potential candidates for new drug design and other applications. In a continuous effort to synthesize glycal-based new chiral heterocycles[4a−c] we are also looking for a chemoselective catalytic system under mild and acid free reaction conditions toward the new chiral benzimidazoles as there are some weaknesses in the current methods.

There are numerous accounts in the literature on the synthesis of benzimidazoles such as Philips method,[13] solid phase,[14] enzymatic,[15] and green approaches[16] involving cyclocondensation of ortho-aromatic diamines (OAD) with carboxylic acids, acid chlorides, or esters under harsher reaction conditions. Some of the syntheses are usually conducted

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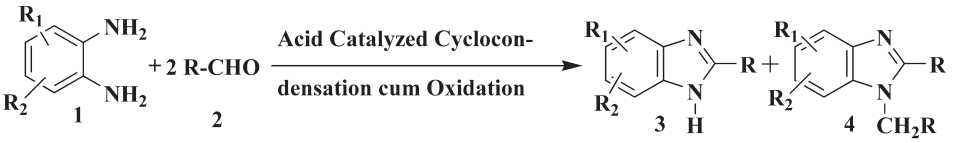
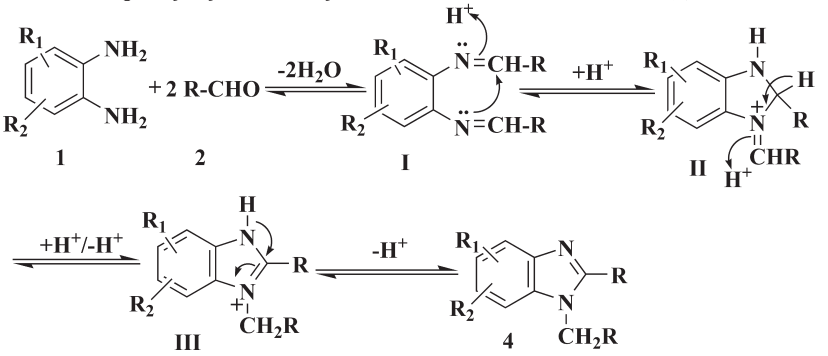
SCHEME 1. Generation of Undesired 1,2-Disubstituted Benzimidazoles under Acidic Conditions



Possible reaction path for formation of 1,2-disubstituted benzimidazoles (4)



in refluxing aqueous hydrochloric acid or phosphoric acid at 250 °C.[13] Another interesting depiction is the cyclocondensation of aldehyde with OAD under oxidative conditions (**3**, Scheme 1).[1,17,18] Most of the methods have limitations mainly in terms of drastic reagents used and reaction conditions, formation of undesired 1,2-disubstituted byproducts, and inapplicability toward synthesis of acid and/or thermo-labile compounds especially those possessing chiral center(s). The synthetic approaches under acids and heating conditions have suffered from the generation of a moderate to high percentage of undesired 1,2-disubstituted byproducts (**4**).[17,18] The path of their formation is possible through generation of diimine (**I**, Scheme 1), cyclization involving protonation, and subsequent tautomerization. New and straightforward chemoselective methods are thus highly desirable to access the chiral heterocyclic compounds under acid free mild reaction conditions.

However, recent investigations involving metal-catalyzed cyclization processes are very encouraging.[1,18] It is believed that the reactions proceed through formation of the Schiff's base and thus most of the metal-catalyzed syntheses are designed through initial synthesis of the Schiff's bases upon condensation of aldehyde with OAD and their subsequent oxidative ring closing by using more than the stoichiometric amount of metal oxidants like lead tetraacetate, nickel peroxide, active manganese dioxide, and barium manganate.[1a] Copper- and palladium-catalyzed synthesis of 2-substituted benzimidazoles *via* intramolecular cross-coupling of ortho aryl halide are also demonstrated.[18] Imidazoanthraquinone has been synthesized by Ooyama and co-workers utilizing 2 equiv of $Cu(OAc)_2$ at 90 °C in acetic acid medium.[18c] Shen and Driver have shown $FeBr_2$ (30 mol %)-mediated synthesis of benzimidazoles from 2-azidoarylimines.[1b] Bahrami and co-workers have established one large scale synthesis of the heterocycles by ceric ammonium nitrate (CAN) based on the Ce(IV)/Ce(III)-redox catalytic process guided oxidative cyclization of the Schiff's base intermediate using hydrogen peroxide as the stoichiometric oxidant.[1c] Diver et al. have reported the construction of *N*-substituted chiral benzimidazoles by palladium-catalyzed successive amination and imination of ortho-dibromoaromatic compounds followed by acid-catalyzed ring closure.[19] However, synthesis of sugar-based benzimidazoles was first reported more than one hundred years ago by Griess and Harrow through condensation of D-glucose and *o*-phenylenediamine (OPD) in the presence of hydrochloric acid to afford the open chain sugar derivative as the minor product, and in fact it was the first report for synthesis of benzimidazoles.[20a−c] Syntheses of several C_2- and N_1-benzimidazole nucleosides have been achieved in the intervening years to examine their potent biological activities.[19,20e,20f] Recently, Vojtech et al. has reported the synthesis of 2-*C*-glycosylated benzimidazoles by condensation of glycopyranosylmethanal dimethylacetal and OPD utilizing strongly acidic cation-exchange resin under refluxing conditions.[20d] In the present article we report the evolution of catalytic activity of the $VO(acac)_2$−$CeCl_3$ combo catalyst for chemoselective cyclocondensation *cum* oxidation of aldehydes with OAD under mild reaction conditions using molecular oxygen. This versatile chemoselective strategy provides direct access to the designed chiral heterocycles, 2-(2′-*C*-3′,4′,6′-tri-*O*-benzyl/methyl-glycal)-1*H*-benzimidazoles (**6**), toward cofacially self-aggregated novel 1D-nanostructured organic materials. For better understanding of the ground state geometries of the chiral benzimidazoles (**6**) and optoelectronic properties, the B3LYP-DFT/6-31G** level of theoretical calculations and their photophysical properties are investigated.

Result and Discussion

In a continuous effort to design and synthesize new heterocycles and studying of their supramolecular assemblies and photophysical properties[4] we have envisioned the synthesis of chiral benzimidazoles, 2-(2′-*C*-3′,4′,6′-tri-*O*-benzyl/methyl-glycal)-1*H*-benzimidazoles (**6**), possessing enyloxy

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TABLE 1. Development of Catalyst for Cyclocondensation *cum* Oxidation toward Benzimidazoles[a]

entry	reagents	condition	observation	yield (%)[b]
1	$PhI(OAc)_2$[c] or PhIO[c]	CH_2Cl_2, MS, rt, 24 h	intense coloration/no desired product found	
2	BiOCl[d] or $NaBiO_3$[d]	CH_2ClCH_2Cl, MS, rt, 24 h	no reaction	
3	$(NH_4)_2Ce(NO_3)_6$[d]	CH_2ClCH_2Cl, MS, rt, 24 h	no reaction	
4	$Al_2O_3-HClO_4$, AgF[d]	CH_2Cl_2, MS, rt, 72 h	slow conversion	40[f]
5	$Al_2O_3-HClO_4$, AgOTf[d]	CH_2Cl_2, MS, rt, 72 h	slow conversion	60[f]
6	$[Ir(COD)Cl]_2$,[d,e] IP[c]	CH_2Cl_2, MS, rt, 24 h	no reaction	
7	$VO(acac)_2$,[d] PhIO[c]	CH_2Cl_2, MS, rt, 24 h	polymerization	
8	$VO(acac)_2$[c]	CH_2Cl_2, MS, rt, 72 h	80% conversion	60[f]
9	$VO(acac)_2$,[d] $Ti(OBu)_4$[d]	CH_2Cl_2, MS, rt, 22 h	100% conversion	81[g]

[a]Unless otherwise noted, the reaction was conducted with **2a**. [b]Isolated yield of the pure compound **3a**. [c]Stoichiometric amount. [d]Catalytic amount (~20 mol %). [e]Reference 23. [f]No reaction with **5a**. [g]Treatment of **5a** afforded pure **6a** (yield: 34%).

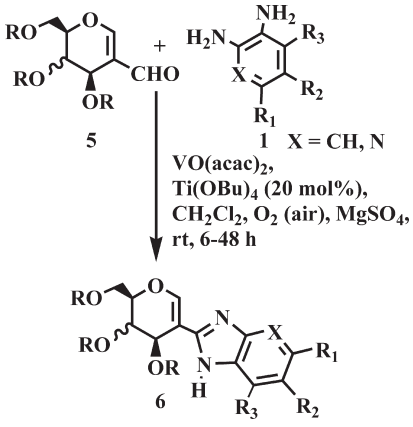
group conjugated to the benzimidazole motif with the expectation that the enyloxy group, chirality, and crowdedness in the glycal skeleton may play an important role in self-aggregation to obtain highly ordered organic nanostructured materials possessing dramatic enhancement in their optoelectronic properties. We are interested in synthesizing the chiral heterocycles (**6**) keeping the 1-position unsubstituted (N-*H*) for their further modifications to investigate its role in the formation of supramolecular architecture. In this context, an oxidative cyclization processes is sought for affording the sugar-based chiral benzimidazoles under acid free reaction conditions because the commonly used acids and metal Lewis acids are harmful to 2-*C*-glycal aldehydes (**5**) to generate the pseudoglycals through Ferrier rearrangement and sugar ring-opening.[21] In our attempts to synthesize (−)-2-(4*R*,5*R*-dibenzyloxy-6*R*-benzyloxymethyl-5,6-dihydro-4*H*-pyran-3-yl)-1*H*-benzimidazole (**6a**) from 2-*C*-formyl-(3,4,6-tri-*O*-benzyl)glucal (**5a**) and *o*-phenylenediamine (OPD), most of the commonly used reagents for synthesis of benzimidazoles are either inactive under the mild reaction conditions or prone toward generation of pseudoglycal byproducts through Ferrier rearrangement. Thus, initial exploration of the reaction is carried out by using potential chemoselective reagents and metal Lewis acid catalysts for this simultaneous condensation, cyclization, and oxidation of 4-bromobenzaldehyde (**2a**) with OAD to afford 2-(4′-bromophenyl)-1*H*-benzimidazole (**3a**) and the successful reagents are then applied to examine the efficiency in synthesis of the glycal-based chiral benzimidazole (**6a**). The representative results are summarized in Table 1. In many instances, the developed reagents are inactive for the synthesis of target compound **6a**. As for example, silver(I) salts are known as cyclization catalysts for alcohols with olefins[22] and we have found them as potential catalysts for the synthesis of the **3a** with moderate yield (entry 4,5, Table 1). Application of the combination of catalysts for synthesis of the chiral benzimidazole (**6a**) results in no reaction. We have explored the scope of

TABLE 2. Synthesis of 2-Substituted Benzimidazoles (3) by $VO(acac)_2-Ti(OBu)_4$

entry	R (**2**)	R_1, R_2 (**1**)	product (**3**)	time (h)	yield[a,b] (%)	ref
1	4-bromophenyl-	H, H	**3a**	18	83	25c
2	4-chlorophenyl-	H, H	**3b**	20	80	25a
3	4-nitrophenyl-	H, H	**3c**	22	78	26
4	phenyl-	H, H	**3d**	24	71	25c
5	4-methoxyphenyl-	H, H	**3e**	16	82	25c
6	4-bromophenyl-	Me, Me	**3f**	14	79	1b
7	2-furoyl-	H, H	**3g**	17	81	25b
8	4-methoxyphenyl-	H, CO_2H	**3h**	13	78	
9	4-cyanophenyl-	Me, Me	**3i**[c]	08	87	
10	4-methoxyphenyl-	COPh, H	**3j**[c]	17	91	
11	4-cyanophenyl-	COPh, H	**3k**[c]	16	90	

[a]Isolated yield of the pure compound. [b]Benzimidazoles were characterized by spectroscopic data and also by verification of their reported melting points where available. [c]Dichloromethane used as the reaction medium.

SCHEME 2. Synthesis of Glycal-Based Chiral Benzimidazoles by $VO(acac)_2-Ti(OBu)_4$



applying our recently developed oxidative cyclizing agent[4c,d] iodosobenzene and also with the combination of metal catalyst (entries 1 and 7, Table 1) to obtain the desired ubiquitous heterocyclic moiety in vain. It may be stated that vanadium is a biologically essential element[24a] and its higher oxidation state, especially $VO(acac)_2$, is effective for chemoselective oxidations,[24b] and C−C coupling reactions.[24c] Being inspired by these reports in the literature we have successfully used $VO(acac)_2$ for this reaction although the reaction is slow and incomplete even

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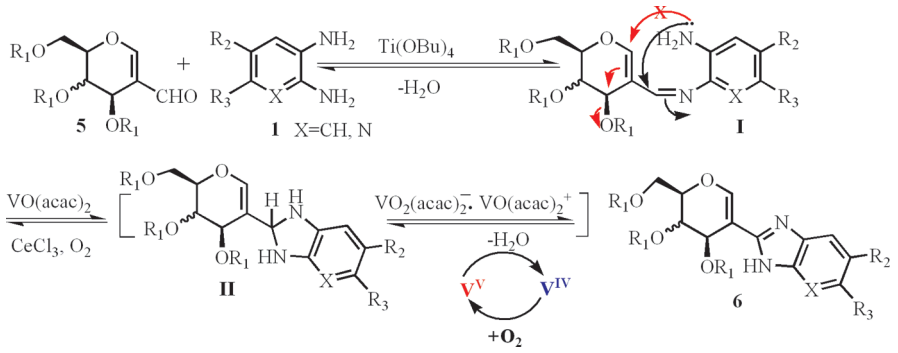
SCHEME 3. Proposed Path for Cyclocondensation *cum* Oxidation



after 72 h (entry 8, Table 1). We are encouraged to note that use of $Ti(OBu)_4$ as cocatalyst (entry 9), however, improves the reaction rate and yield. In the presence of 20 mol % of the cocatalyst the catalytic load of $VO(acac)_2$ is also reduced from the stoichiometric amount to 20 mol % (Table 2).

With this initial success, we have explored the versatility of the catalytic system $VO(acac)_2$−$Ti(OBu)_4$ by condensing various aldehydes with OAD at ambient temperature under oxygen (anhydrous air) affording the corresponding 2-substituted benzimidazoles (**3**, Table 2). In our initial experiments the cyclocondensation *cum* oxidation property of the catalytic system is confirmed by synthesis of the known benzimidazoles (**3a**−**g**,[1b,25,26] entries 1−7, Table 2). 1,2-Disubstituted byproducts (**4**, Scheme 1) are not found in this benign catalytic process. Tolerance of the functional groups on the aldehyde (**2**) and OAD (**1**) is also examined. Both the electron-rich and electron-deficient substituents are tolerated by the mild catalytic system. A fast reaction rate and excellent yield are obtained for all types of substrates. The moderate yield of compound **3d** (71%, entry 4, Table 2) may be attributed to the faster aerial oxidation of benzaldehyde during the oxidative cyclization processes.

Due to their structural feature, 2-*C*-glycal aldehydes (**5**) are very much inactive in forming the desired imine intermediates which are essential for this cyclocondensation *cum* oxidation reaction. Although the common benzimidazoles can be achieved with $VO(acac)_2$ (entry 8, Table 1), it fails to produce glycal-based chiral benzimidazoles due to the absence of the corresponding imine intermediate in the reaction mixture. After extensive studies we have found $Ti(OBu)_4$ (20 mol %) as condensing catalyst to afford the corresponding Schiff's base and hence the chiral benzimidazoles (**6**, Scheme 2). In this connection it may be referred that $Ti(OEt)_4$ has been used mainly by Ellman and co-workers[27] in condensing aldehydes with sulfonamide to the corresponding sulfinimines. Again, a large excess of $Ti(OEt)_4$ (2−5 equiv) is usually used for the generation of their imines.[28] In our experiments with OPD (**1a**), the simultaneous cyclization *cum* oxidation steps in neutral reaction conditions have been completed in 6−15 h (Scheme 3) in the presence of oxygen (dry air) at ambient temperature affording compounds **6a**−**c**,**f** in good isolated yield (70−77%, Table 3). This requires an almost stoichiometric amount of $VO(acac)_2$. The reaction proceeds well with methyl and pyridine analogues (**1b**−**d**) of OPD affording **6d**,**e**,**g** in 64−75% yield in 6−8 h. The reaction rate is, however, very slow (48 h) and low yielding (10−13%, entries 8 and 9, Table 3) while using OAD possessing an electron-withdrawing moiety like 4-benzoyl and benzoquinoyl (**1e**,**f**, Table 3).

We are looking for a robust catalytic system for improving the reaction rate and yield for the synthesis of the designed chiral benzimidazoles (**6h**,**i**, Table 3, entries 8 and 9) to built up UV and fluorescence active supramolecular self-assemblies for their potential uses as candidate materials in biological, optical, and electro-optical applications. Ceria (CeO_2) is a well-known additive as an oxygen storage *cum* release capacity material in the so-called three-way catalysts (TWC) used for oxidative exhaust treatment to eliminate pollutant produced in automobiles.[29] In recent times $CeCl_3$, the lower oxidation state of cerium, has attracted much attention from chemists because it shows excellent catalytic power for *cis*-dihydroxylation,[30] cyclization,[31] and various other interesting catalytic processes.[32] Excellent catalytic activity of $CeCl_3$ is usually observed in the presence of other metal cocatalysts or vice versa. This has prompted us to investigate the role of

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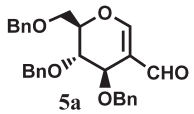
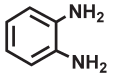
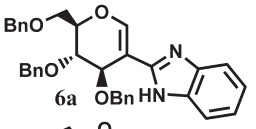
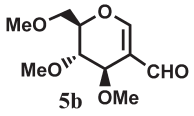
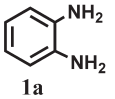
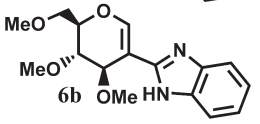
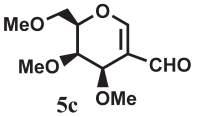
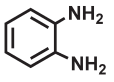
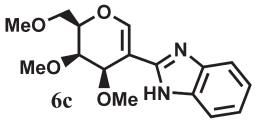
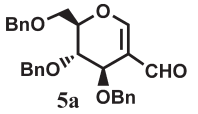
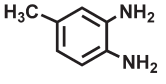
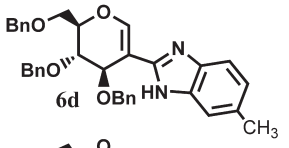
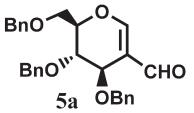
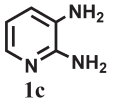
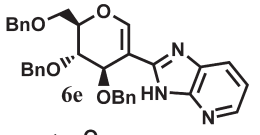
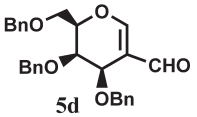
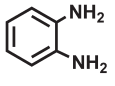
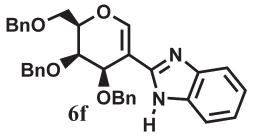
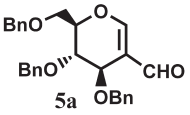
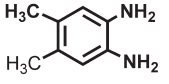
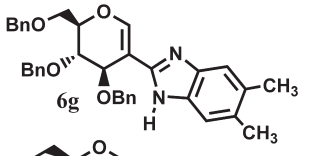
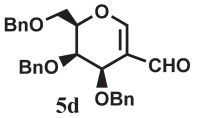
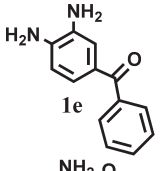
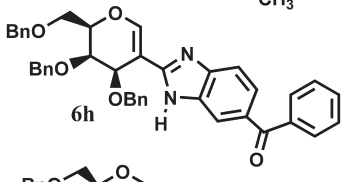
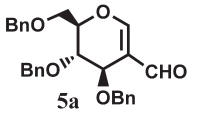
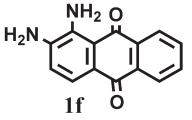
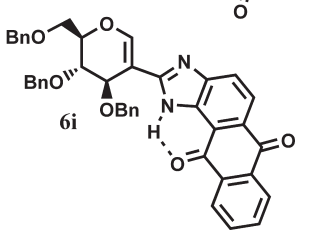
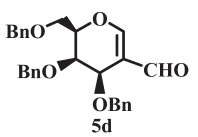
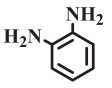
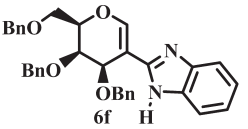
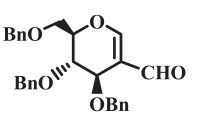
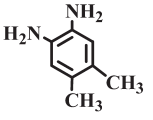
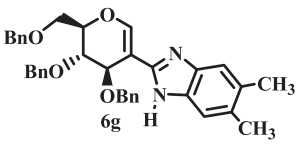
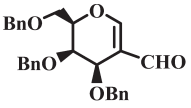
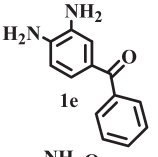
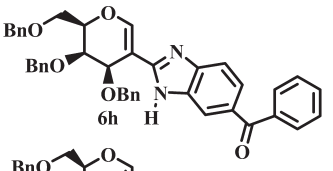
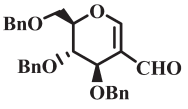
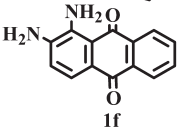
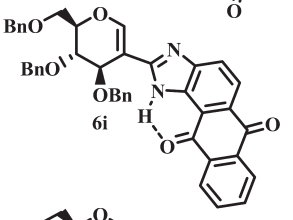
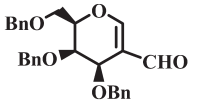
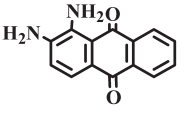
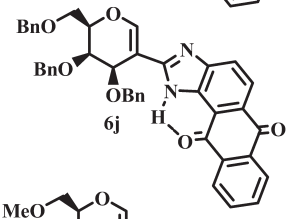
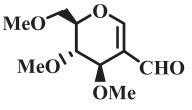
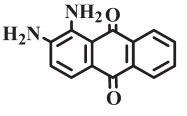
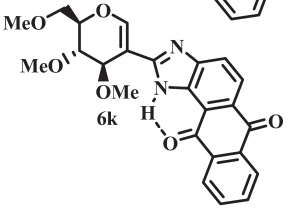
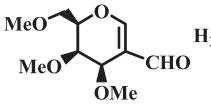
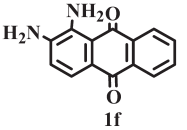
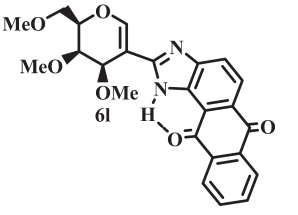
TABLE 3. Synthesis of Glycal-Based Chiral Benzimidazoles (6) by $VO(acac)_2-Ti(OBu)_4$

entry	2-*C*-glycal aldehyde (5)	o-aromaticdiamine (1)	chiral benzimidazoles (6)	time (h)	yield[a,b] (%)
1.	 5a	 1a	 6a	10	77
2.	 5b	 1a	 6b	6	70
3.	 5c	 1a	 6c	7	75
4.	 5a	 1b	 6d	6	71[c]
5.	 5a	 1c	 6e	7	75
6.	 5d	 1a	 6f	15	73
7.	 5a	 1d	 6g	8	64[c]
8.	 5d	 1e	 6h	48	10[d]
9.	 5a	 1f	 6i	48	13[d]

[a]Isolated yield of the pure compound. [b]Benzimidazoles were characterized by spectroscopic data. [c]Tetrahydrofuran used as reaction medium. [d]Yields were not improved even with use of 1.5 equiv of $VO(acac)_2$, tetrahydrofuran as solvent, and also increasing reaction temperature to 50 °C.

combo catalyst $CeCl_3-VO(acac)_2$ for this cyclocondensation *cum* oxidation of glycal-based Schiff's base intermediates utilizing atmospheric oxygen. We have found $VO(acac)_2-CeCl_3$ combo catalyst for the synthesis of the desired compounds. We are surprised to see that in presence of 5 mol % of $CeCl_3$ the catalytic loads of $VO(acac)_2$ and $Ti(OBu)_4$ are reduced from the stoichiometric amount to 30 mol %, and 20 mol % to 10 mol %, respectively (Table 4). The unique property of the robust combo catalyst is that the OAD of diverse molecular architectures are tolerated. The OAD with electron-deficient substituents like benzoyl and benzoquinoyl (entries 3−7, Table 4) and also electron-rich substituents (entry 2, Table 4) are consistent to follow the chemoselective catalytic cycle toward the chiral heterocycles (**6**). The reaction rate (9−20 h) and yield (59−68%, entries 3−7, Table 4) are significantly improved compared to the $VO(acac)_2$-catalyzed reactions (10−13%, entries 8 and 9, Table 3). Comparable yields are obtained for compounds **6f** and **6g** (entries 1 and 2) exhibiting the versatility of the combo catalyst for synthesis of a range of glycal-based chiral

TABLE 4. Synthesis of Chiral Benzimidazoles by $Ti(OBu)_4$ (10 mol %) and Combo Catalyst [$CeCl_3$ (5 mol %)−$VO(acac)_2$ (30 mol %)]

entry	2-*C*-glycal aldehyde (5)	o-aromaticdiamine (1)	chiral benzimidazoles (6)	time (h)	yield[a,b] (%)
1.	 5d	 1a	 6f	12	76[c]
2.	 5a	 1e	 6g	9	71
3.	 5d	 1e	 6h	12	65
4.	 5a	 1f	 6i	17	64
5.	 5d	 1f	 6j	17	62
6.	 5b	 1f	 6k	20	59[d]
7.	 5c	 1f	 6l	14	68[d]

[a]Isolated yield of the pure compound. [b]Benzimidazoles were characterized by spectroscopic data. [c]Same yield with acetonitrile as solvent. [d]Comparable yield with ethylene dichloride as the reaction medium.

benzimidazoles. We have explored the role of solvent and reaction temperature for enhancement of the reaction rate and reduction of the glycal substrate decomposition to obtain satisfactory yield. After extensive studies, polar aprotic solvent tetrahydrofuran, acetonitrile, and ethylene dichloride are found as good media at 50 °C for the combo catalytic processes. It is worth noting that only 5 mol % of $VO(acac)_2$ and 3 mol % of $CeCl_3$ are sufficient for the synthesis of 2-aryl-benzimidazoles (**3**) at room temperature in high yield (Table 5). Herein, $Ti(OBu)_4$ is not required because imine formation of common aldehydes occurs smoothly on mixing with OAD.

TABLE 5. Synthesis of 2-Arylbenzimidazoles by the Combo Catalyst [$CeCl_3$ (3 mol %)−$VO(acac)_2$ (5 mol %)]

entry	R (**2**)	R_1, R_2 (**1**)	product (**3**)	time (h)	yield[a,b] (%)	ref
1	4-bromophenyl-	H, H	**3a**	5	90	25c
2	4-nitrophenyl-	H, H	**3c**	7	94	26
3	4-methoxyphenyl-	H, H	**3e**	5	90	25c
4	4-bromophenyl-	Me, Me	**3f**	4.5	88	25d
5	4-cyanophenyl-	H, COPh	**3k**[c]	4	93	

[a]Isolated yield of the pure compound. [b]Benzimidazoles were characterized by spectroscopic data and also by verification of their reported melting points where available. [c]Tetrahydrofuran was used as the reaction medium.

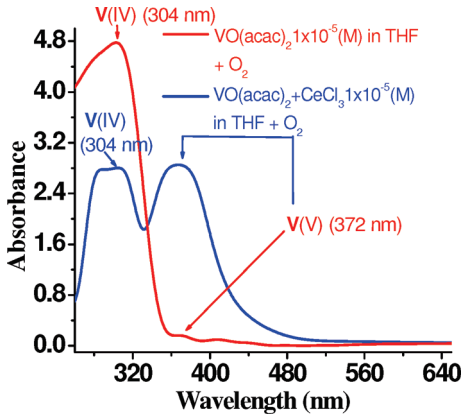


FIGURE 2. UV absorbance of the reagent containing V(IV) and V(V).

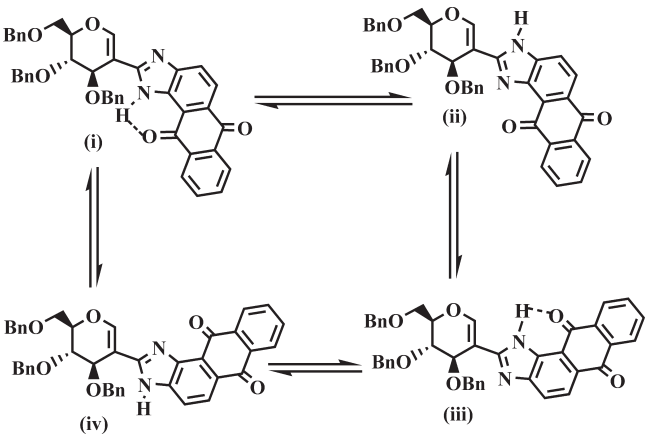


FIGURE 3. Four possible geometries of the compound **6i**.

The probable mechanistic pathway is illustrated in Scheme 3. $Ti(OBu)_4$-catalyzed generation of imine intermediate (**I**) from OAD (**1**) and 2-*C*-glycal aldehydes (**2**) is very fast because we have observed the appearance of a new intense yellow spot in the TLC with simultaneous disappearance of the substrates. Cyclization of the intermediate **I** to **II** and its subsequent dehydrogenation by the oxidant led to the desired product (**6**). $VO(acac)_2$ is a mild oxidant and we have found vanadium(V)[33] as the active species for this cyclization *cum* oxidation reactions. We have made two dilute solutions (1×10^{-5} M) of $VO(acac)_2$ in THF and kept them under pure oxygen. A weak magenta color slowly developed and one of the solutions became deep magenta colored immediately after addition of $CeCl_3$ (5 mol %). The normalized UV absorption spectra (Figure 2) of both solutions reveal that a new peak of vanadium(V) has appeared (372 nm) although intensity is extremely high for the solution containing $CeCl_3$. The active oxidant for this chemoselective reaction is probably the negatively charged vanadium(V) species, $VO_2(acac)_2^- \cdot VO(acac)_2^+$, and its generation is highly accelerated in the presence of $CeCl_3$. Although we believe that the role of $CeCl_3$ in this catalysis process is as O_2 supply to $VO(acac)_2$ to generate V(V), its involvement in the cyclization step cannot be avoided.[31] In our experiments we have also observed that the reaction cannot proceed under deoxygenated conditions, suggesting the active participation of O_2 for this catalytic process.

The structure of the chiral sugar-based benzimidazole (**6i**) is established by extensive NMR studies. The proton environment and C−C linkages in the chiral benzimidazole are deduced from one-dimensional NMR (^1H, ^{13}C, and DEPT-135) and 2D NMR (HSQC and COSY) spectra (Figures 2−6 in the Supporting Information). Strong interaction of the N-*H* with $C_{4'}$-*H* and $C_{4'}$-OCH_2Ph, and a relatively weak one with $C_{2'}$-*H* in NOESY spectrum (SI Figure 8) also suggests the preferred geometry (**i**) for compound **6i** among the four possible structures (**i**−**iv**, Figure 3). In the FT-IR experiments of compound **6i** we have found strong intramolecular hydrogen bonding between the N-*H* proton (hydrogen bond donor) of the imidazole ring with the neighboring quinone C_{11}=*O* group (hydrogen-bond acceptor). The presence of the intramolecular hydrogen bonding is also investigated by Peng and co-workers in 2-aryl-1*H*-anthra[1,2-*d*]imidazole-6,11-diones.[34] To establish the correct geometry we have undertaken a series of DFT calculations for optimization of all the stationary points using the B3LYP/6-31G** basis set as implemented in the Gaussian 03 program.[35] After extensive studies we have found structure **i** (Figure 3) as the most stable one having the lowest potential energy (−1369124.9 kcal/mol). However, the enyloxy group of the glycal moiety is not present in the aromatic plane of the imidazoanthraquinone skeleton. The dihedral angle of $C_3-C_4-C_8-C_9$ (panel a, Figure 4) is somewhat high (−24.6°). The theoretical results are in nice agreement with the experimental observation found in 2D NOESY. A similar type of geometry and energy optimized structure is also found for the epimer **6j** (panel b, Figure 4).

Design and synthesis of highly ordered low molecular mass self-aggregated organic materials (LMSOM)[4b,d] using chiral nanobuilding blocks[3] are important as the understanding of the nanoscale chirality has advanced significantly for their functional applications in the emerging field of nanoscience and nanotechnology.[36] As for example, it is found that chiral forms of silicon-based nonmetallic nanoware[36c] and CdS-penicillamine chiral quantum dot[36a,b]

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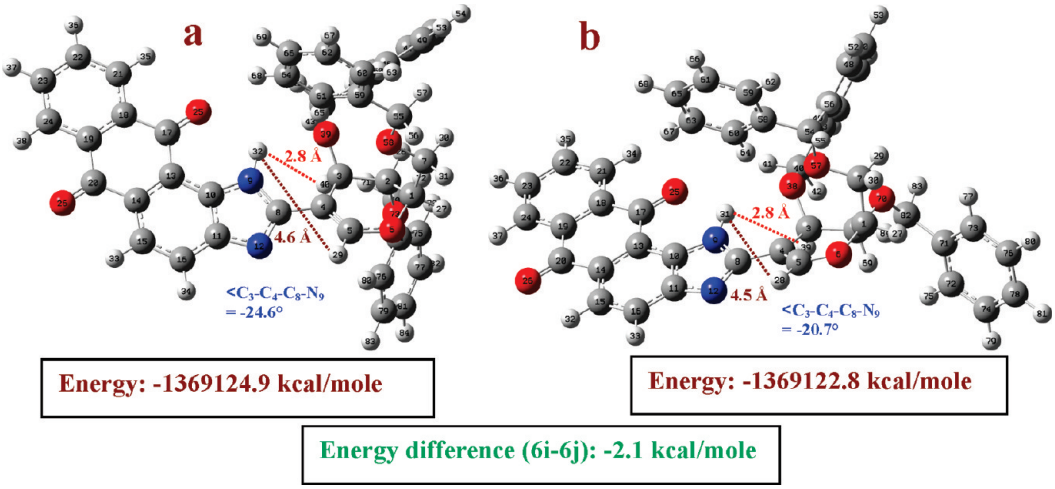

FIGURE 4. DFT optimized structure of compounds **6i** (a) and **6j** (b).

display interesting metallic conductivity. Supramolecular assemblies constructed by fluorescence active chiral organic compounds are more interesting for their potential applications as candidate materials in biological,[37] optical, and optoelectronic uses because the chirality in the self-assembly has a key role in mimicking the development of biological helical structures with specific function as well as controlling unique optoelectronic device applications. Optical and optoelectronic properties of the low molecular mass organic nanostructured materials are fundamentally different from those of inorganic and macrocyclic compounds due to the absence of the unfavorable intermolecular forces like magnetic and other interactions. The main operating forces in the LMSOM are the noncovalent types of interactions, e.g., hydrogen bonding, π-stacking, van der Waals forces, and charge transfer. Fabrication of organic nanostructured materials is documented in the literature.[3e,38] We disclose herein the preliminary observations that we have found in our experiments for construction of the novel self-aggregated architectures of well-defined shape and size from the chiral benzimidazoles and also their interesting photophysical properties. In the first instance, the aggregation behavior of the chiral benzimidazoles (**6**) is studied in polar aprotic solvents. As expected, compound **6i**, **6j**, and **6k** (Table 4) form highly ordered one-dimensional (1D) LMSOM by nanocrystallization. Although the analytically pure chiral benzimidazoles are liquid in nature, the solid organic materials are obtained in 1−2 days by a slow growth of the nanocrystals. Such a slow crystallization process can organize stacking with the right molecular orientation to grow along the axis of the untralong organic materials. Scanning electron microscope (SEM) imaging of the solid materials of (+)-2-(4*R*,5*S*-dibenzyloxy-6*R*-benzyloxymethyl-5,6-dihydro-4*H*-pyran-3-yl)-1*H*-anthra[1,2-*d*]imidazole-6,11-dione (**6j**, Table 4) reveals fabrication of ultralong fibrous bundles of about 200−300 nm diameter (panels a and b, Figure 5)

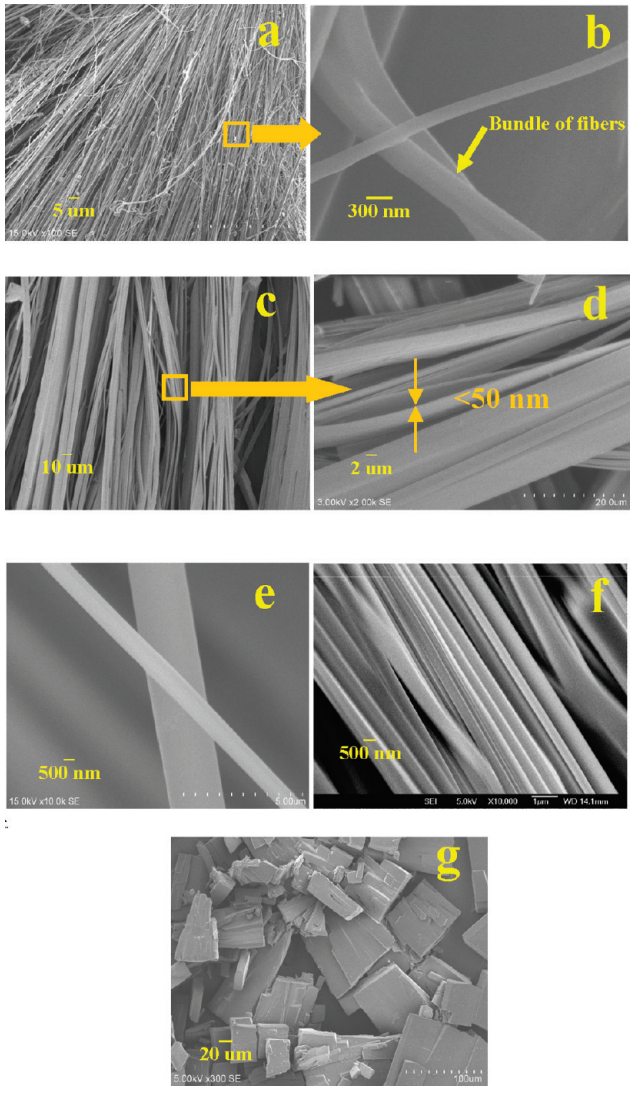

FIGURE 5. SEM image of the nanostructured materials of compound **6j**.

on crystallization in diethyl ether. It has also self-aggregated in ethyl acetate to flat sheets like highly ordered

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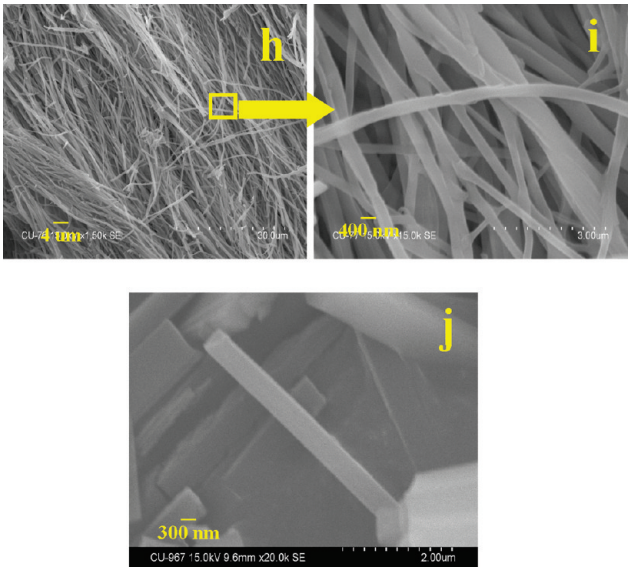

FIGURE 6. SEM image of the LMSOM of compounds **6i** and **6k**.

ultralong nanobelts[39] of about 1−2 μm width and 50 nm thickness (panels c−e). The extended side-way joining of two or more 1D nanobelts forms a stack-like architecture (panel f). In an attempt to make nanostructured materials of **6j** in cyclohexane, surprisingly we have found self-aggregated solid material of several micrometer widths (panel g, Figure 5). Probably the crystallization process of the nanobuilding blocks proceeds very fast in the apolar solvent like cyclohexane and thus unidirectional molecular packing is disturbed. The binding forces operating between the nanoscale building blocks for gluing processes become weaker, and as a result the broken macrostructured material is observed in the SEM image. As expected, it has also shown a little red shift in the UV absorbance spectrum (Figure 11, Supporting Information).

Although compound **6j** has produced a number of self-aggregated nanostructured materials, its methyl-protected analogue (+)-2-(4*R*,5*S*-dimethoxy-6*R*-methoxymethyl-5,6-dihydro-4*H*-pyran-3-yl)-1*H*-anthra[1,2-*d*]imidazole-6,11-dione (**6*l***, Table 4) does not form any such materials. However, its C-5 epimer (−)-2-(4*R*,5*R*-dibenzyloxy-6*R*-benzyloxymethyl-5,6-dihydro-4*H*-pyran-3-yl)-1*H*-anthra-[1,2-*d*]imidazole-6,11-dione (**6i**) forms fibrous LMSOM (panels h and i, Figure 6) in diethyl ether. Similarly, after several attempts we have generated only one rod-like nanostructured material (panel j) of chiral benzimidazole (+)-2-(4*R*,5*R*-dimethoxy-6*R*-methoxymethyl-5,6-dihydro-4*H*-pyran-3-yl)-1*H*-anthra[1,2-*d*]imidazole-6,11-dione (**6k**, Table 4) from its concentrated solution in the same solvent. The origin of this unique self-aggregation capability of the chiral benzimidazoles can be explained in terms of two structural features. First, the strong $\pi-\pi$ stacking interactions exerted by the rigid 1*H*-anthra[1,2-*d*]imidazole-6,11-dione aromatic segment must play an integral role to built direction-controlled LMSOM. The second factor to be considered is the outward orientation of the π-clouds in the rigid aromatic segment (Figure 4) bringing the molecules in close proximity where the $\pi-\pi$ interaction dominates in the molecular packing processes.

Photoluminescent organic materials have unique potential for high-tech applications as light emitting diodes,[40] flat panel devices,[41] biological probes,[42] and chemosensors.[43] As far as the application is concerned, the performance of the organic nanodevices depends on the aggregation pattern of the nanoscale building blocks in their self-assembled architectures. The compound **6i** has shown good UV absorbance (260 and 420 nm, panel a) and fluorescence emission (360 nm, panel b, Figure 7; excited at 260 nm) in methanol. The π-stacking-induced aggregation has become significant in the LMSOM because it exhibits a large red shift in UV absorption (305, 385, and 490 nm). It also exhibits a large red shift in fluorescence emission (425 nm; excited at 385 nm) with strong enhancement of the fluorescence intensity when self-aggregated. The steric crowdedness of the benzyl-protected galactal moiety present at C-2 forces the 1*H*-anthra-[1,2-*d*]imidazole-6,11-diones segment out of plane to the enyloxy group in the monomer state, reducing the possibility of conjugation. Geometrical optimization of the structure by DFT calculations (Figure 4) also shows a similar observation. When highly ordered self-aggregated organic materials are generated, the nanoscale building blocks of **6i** are greatly populated in the planar form through conformational transformation leading to swift increase of intensity along with the large bathochromic shift in the fluorescence decay and UV−vis absorbance. Further studies on the generation of the organic nanomaterials of the chiral benzimidazoles, development of their photoluminescence properties, practical applications of the ultralong organic nanostructured materials as channel material for high-tech nanodevices, and other related investigations are in progress in our laboratories.

In conclusion, we have developed an efficient combo catalyst $VO(acac)_2-CeCl_3$ for chemoselective cyclization *cum* oxidation of aldehyde with ortho aromatic diamines using molecular oxygen toward the synthesis of a new class of designed sugar-based chiral benzimidazoles. We have found vanadium(V) as an active component for the catalytic processes. This versatile approach provides direct access to chiral nanoscale building blocks toward the generation of a number of self-aggregated ultralong 1D-nanostructured organic materials. We have demonstrated the strong photophysical properties of the LMSOM caused by the restricted geometry in the more conjugated planar state relative to the

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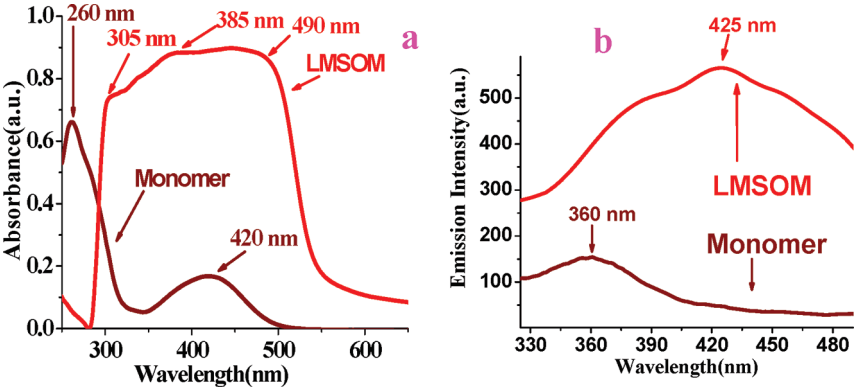

FIGURE 7. UV−vis (a) and fluorescence (b) spectra of **6i**.

out of planar geometry in the nonaggregated material as observed in the geometry optimization by the B3LYP/6-31G level of theoretical calculations. A more detailed investigation on the mechanism, the scope of the reaction, fabrication of LMSOM, operative noncovalent interactions among the nanobuilding blocks, and their photophysical properties is currently underway in our laboratory, and the results will be published soon.

Experimental Section

1. General Procedure for the Synthesis of Compound 6 by VO(acac)$_2$. A mixture of 2-*C*-formyl glycal **5** (1.0 mmol), OAD **1** (1.3 mmol), $VO(acac)_2$ (271 mg, 1.0 mmol), dichloromethane (5.0 mL), and anhydrous $MgSO_4$ (200 mg) was taken in a round-bottomed flask equipped with a calcium chloride guard tube or fitted with a pure oxygen balloon through a septum and stirred at 0 °C. Titanium(IV) butoxide was added dropwise (70 μL, 0.20 mmol), and the content was allowed to attain room temperature. The reaction was monitored by TLC [SiO_2 plate, run in ethyl acetate−petroleum ether (60−80), and developed by charring on a hot plate after spraying with 30% aqueous H_2SO_4]. The reaction was complete after 6−15 h. The post reaction mixture was filtered through a sintered funnel and the residue was extracted with dichloromethane (2 × 5 mL). The organic portion was washed with water (3 × 10 mL), dried on activated sodium sulfate, and concentrated in a rotary evaporator under reduced pressure at room temperature. The crude product was chromatographed on silica gel (60−120 mesh) and eluted with ethyl acetate−petroleum ether (60−80). Thus, the reaction of 2-*C*-formyl-3,4,6-tri-*O*-benzylglucal (**5a**, 446 mg, 1.0 mmol) with *o*-phenylenediamine (**1a**, 142 mg, 1.3 mmol) afforded (−)-2-(4*R*,5*R*-dibenzyloxy-6*R*-benzyloxymethyl-5,6-dihydro-4*H*-pyran-3-yl)-1*H*-benzimidazole (**6a**) after processing in an isolated yield of 77% (409 mg, 0.77 mmol). Compound **6a** and others (**6b**−**i**) were characterized by ^{1}H and ^{13}C NMR (NDC and DEPT), FT-IR, UV−vis absorption, optical rotation measurement, and mass spectroscopy and elemental analyses.

Compound 6a: yellow viscous liquid; $[\alpha]^{20}_D$ −10.5° (*c* 0.4, CH_3OH); UV/vis (MeOH) λ_{max} (log ε) 297 nm (4.36), 366 nm (3. 31); UV/vis (CH_3CN) λ_{max} (log ε) 298 nm (3.97), 366 nm (2.44); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.72 (1H, dd, J = 4.2, 10.8 Hz), 3.80 (1H, dd, J = 5.1, 10.5 Hz), 4.12 (1H, dd, J = 6.0, 10.5 Hz), 4.29−4.44 (2H, m), 4.49 (2H, s), 4.53 (2H, q, J = 5.0 Hz), 4.67 (2H, s), 7.03−7.32 (20H, m), 7.66 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 67.7, 70.5, 71.8, 72.6, 73.4, 73.5, 77.4, 103.8, 122.1, 127.8, 127.9, 128.0, 128.4, 128.5, 128.6, 128.9, 137.2, 137.6, 137.7, 149.3, 150.4; IR (neat, cm^{-1}) 1072, 1189, 1274, 1364, 1450, 1642, 2370, 2866, 3034, 3398; LC-Mass (*m*/*z*) 533.32 (M^+ + 1). Elemental Anal. calcd for $C_{34}H_{32}N_2O_4$: C 76.67, H 6.06, N 5.26. Found: C 76.59, H 6.04, N 5.31.

2. General Procedure for the Synthesis of Compound 6 by VO(acac)$_2$−CeCl$_3$ Combo Catalyst. A mixture of 2-*C*-formyl glycal **5** (1.0 mmol), OAD **1** (1.3 mmol), anhydrous cerium(III) chloride (7.3 mg, 0.05 mmol), $VO(acac)_2$ (80 mg, 0.30 mmol), THF (5.0 mL), and anhydrous $MgSO_4$ (200 mg) in a round-bottomed flask was stirred at 0 °C. Titanium(IV) butoxide was added dropwise (35 μL, 0.10 mmol), and the content was heated at 55 °C on a hot-water bath. The reaction was complete after 9−20 h. The post reaction mixture was filtered through a sintered funnel and the residue was extracted with dichloromethane (2 × 10 mL). The organic portion was washed with water (3 × 10 mL), dried on activated sodium sulfate, and concentrated in a rotary evaporator under reduced pressure at room temperature. The crude product was chromatographed on silica gel (60−120 mesh) and eluted with ethyl acetate−petroleum ether (60−80). Thus, the reaction of 2-*C*-formyl-3,4,6-tri-*O*-benzylglucal (**5a**, 444 mg, 1.0 mmol) with 1,2-diamminoanthraquinone (**1f**, 310 mg, 1.3 mmol) afforded (−)-2-(4*R*,5*R*-dibenzyloxy-6*R*-benzyloxymethyl-5,6-dihydro-4*H*-pyran-3-yl)-1*H*-anthra[1,2-*d*]imidazole-6,11-dione (**6i**) after processing in an isolated yield of 64% (423 mg, 0.64 mmol). The chiral benzimidazoles (**6f**−***I***) were characterized by ^{1}H and ^{13}C NMR (NDC and DEPT), FT-IR, and mass (EI-MS and HR-MS) spectral analyses.

Compound 6i: yellow liquid; melting point of the nanocrystal 106 °C; $[\alpha]^{20}_D$ −12.8° (*c* 1.00, CH_3OH); UV/vis (MeOH) λ_{max} (log ε) 260 nm (4.29), 420 nm (3.80); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.71 (1H, dd, J = 4.5 and 10.8 Hz, $C_{6'}$-CH_AH$_B$OBn), 3.81 (1H, dd, J = 5.7 and 10.8 Hz, $C_{6'}$-CH$_A$$H_B$OBn), 4.14 (1H, dd, J = 4.2 and 5.7 Hz, $C_{5'}$-*H*), 4.48 (3H, br s, $C_{6'}$-*H* and $C_{6'}$-CH_2OCH_2Ph), 4.59−4.73 (5H, m, $C_{4'}$-*H*, $C_{4'}$-OCH_2Ph and $C_{5'}$-OCH_2Ph), 7.17−7.27 (15H, m, 3 × $OCH_2C_6H_5$), 7.64−7.71 (2H, m, C_8-*H* and C_9-*H*), 7.78 (1H, s, $C_{2'}$-*H*), 7.87 (1H, d, J = 8.4 Hz, C_4-*H*), 8.07 (1H, d, J = 8.4 Hz, C_5-*H*), 8.13, 8.22 (1H each, m, C_7-*H* and C_{10}-*H*), 11.01 (1H, s, N-*H*) (please see Figure 1 in the SI for labeling of the atoms); ^{13}C NMR (75 MHz, $CDCl_3$) δ 67.6 ($C_{6'}$-CH_2OBn), 70.8 (OCH_2Ph), 70.9 ($C_{5'}$), 72.2 ($C_{4'}$), 72.3 (OCH_2Ph), 73.5 (OCH_2Ph), 77.0 ($C_{6'}$), 103.9 ($C_{3'}$), 117.4 (C_{11a}), 121.8 (C_5), 124.2 (C_4), 126.3 (C_{10}), 127.4 (C_7), 127.5 (C_{5a}), 127.8 (one of the pairs of $C_{2''}$ and $C_{6''}$ of OCH_2Ph), 127.8 (one of the $C_{4''}$ of OCH_2Ph), 127.9 (one of the pairs of $C_{2''}$ and $C_{6''}$ of OCH_2Ph), 128.0 (one of the $C_{4''}$ of OCH_2Ph), 128.0 (one of the $C_{4''}$ of OCH_2Ph), 128.4 (one of the pairs of $C_{2''}$ and $C_{6''}$ of OCH_2Ph), 128.4 (one of the pairs of $C_{3''}$ and $C_{5''}$ of OCH_2Ph), 128.5 (one of the pairs of $C_{3''}$ and $C_{5''}$ of OCH_2Ph), 128.5 (one of the pairs of $C_{3''}$ and $C_{5''}$ of OCH_2Ph), 132.7 (C_{11b}), 133.3 (C_{10a}), 133.5 (C_8), 134.0 (C_{6a}), 134.1 (C_9), 137.0 (one of the $C_{1''}$ OCH_2Ph), 137.4 (one of the $C_{1''}$ OCH_2Ph), 137.6 (one of the

$C_{1''}$ OCH_2Ph), 149.1 (C_{3a}), 150.9 ($C_{2'}$), 156.3 (C_2), 182.7 (C_{11}), 184.6 (C_6); IR (neat, cm^{-1}) 1088, 1194, 1290, 1398, 1513, 1638, 2106, 2921, 3430; HR-MS (m/z) for $C_{42}H_{35}N_2O_6$ (M + H) calcd 663.2495, found 663.2473.

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Supporting Information Available: General methods, experimental procedures, elucidation of structure by 2D NMR, spectroscopic data, and spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.