Enantioselective Vanadium Catalyzed Oxidative Coupling: Development and Mechanistic Insights

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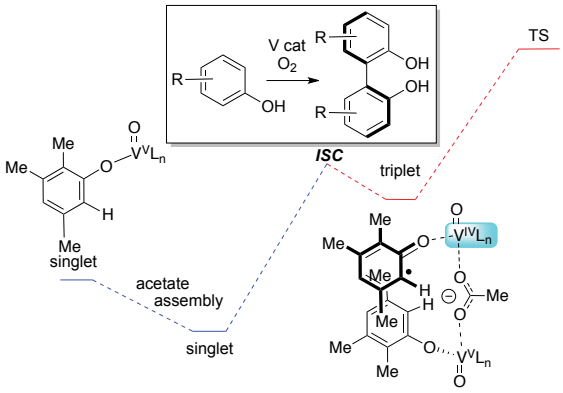
Supporting Information Placeholder



ABSTRACT: The evolution of a more reactive chiral vanadium catalyst for enantioselective oxidative coupling of phenols is reported ultimately resulting in a simple monomeric vanadium species combined with a Brønsted or Lewis acid additive. The resultant vanadium complex is found to effect the asymmetric oxidative *ortho—ortho* coupling of simple phenols and 2-hydroxycarbazoles with good to excellent levels of enantioselectivity. Experimental and quantum mechanical studies of the mechanism indicate that the additives aggregate the vanadium monomers. In addition, a singlet to triplet crossover is implicated prior to carbon-carbon bond formation. The two lowest energy diastereomeric transition states leading to the enantiomeric products differ substantially with the path to the minor enantiomer involving greater torsional strain between the two phenol moieties.

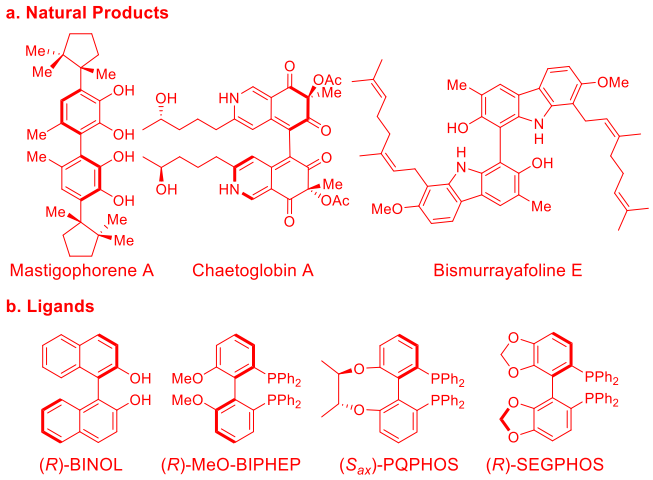
Introduction

Asymmetric oxidative catalysis offers a simple and atom-economic method to generate an enantioenriched biaryl motif, which is widely found in natural products[1] and catalysts (**Scheme 1**).[2] Naturally occurring dimeric scaffolds, connected through a chiral axis, feature intriguing structures as well as biological activities, such as agonism of neuritic streaming[1] or inhibition of cancer cell lines.[2] Furthermore, these axially chiral backbones have been widely utilized in asymmetric catalysts. BINOL has been proven to be effective in reduction, oxidation, and diverse asymmetric C-C bond forming reactions, which included the ene, Diels-Alder, aldol, allylation, alkynylation, cycloaddition, and Friedel-Crafts reactions etc.[2a] In addition, axially chiral bisphosphine ligands, which are derived from the biphenols, have been used in numerous reactions, including asymmetric hydrogenation and cycloaddition reaction.[2b-d]

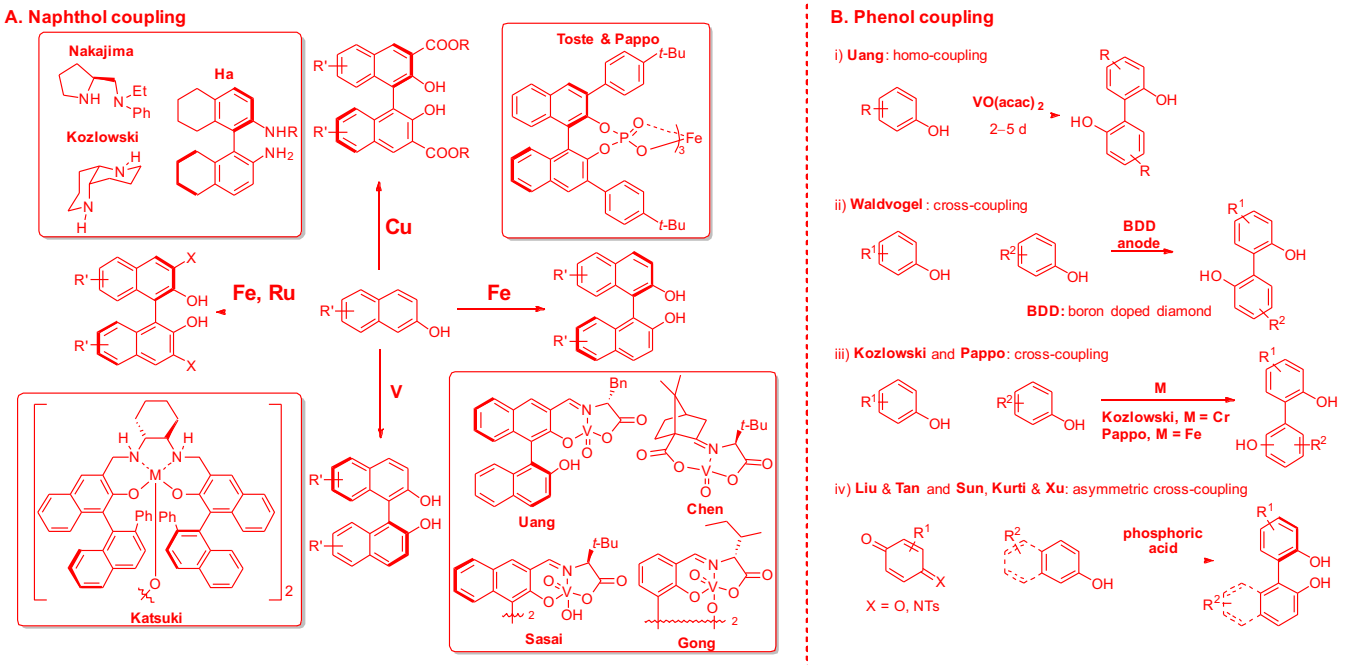
In the last three decades, a variety of transition metals have been proven to effect enantioselective oxidative couplings (**Scheme 2A**).

In 1999, Nakajima and coworkers reported that copper complexes with proline derivatives as a ligand allowed access to BINOL analogs.[3] We discovered that the 1,5-diaza-*cis*-decalin ligand afforded further improvement on both reactivity and enantioselectivity.[4] The unsymmetrical H_8–BINAM ligand has been utilized to construct a chiral axis by the Ha group in 2004.[5] For these catalysts, however, it was necessary yo have an additional coordinating group next to phenol to gain enantioselective control.

Scheme 1. Examples of a Stereogonic Axis in Natural Products and Catalysis



Scheme 2. Previous Approaches to Oxidative Coupling of Naphthols and Phenols



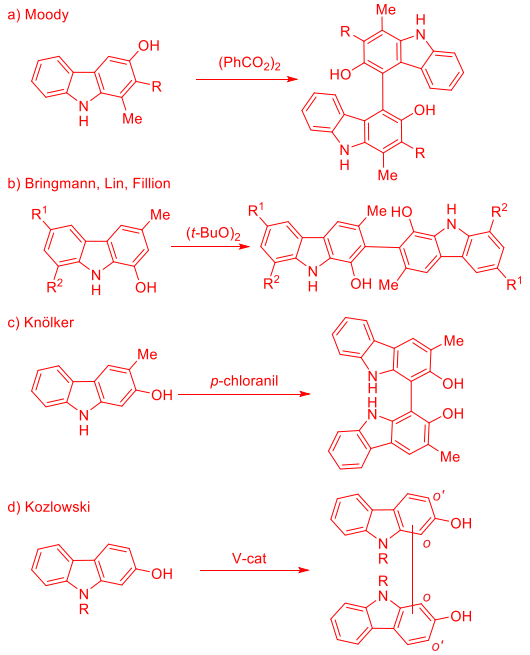
Vanadium also has been widely used as an asymmetric catalyst to couple BINOL derivatives. Monomeric vanadium complexes, by the Uang[6] and Chen groups,[7] or dimeric vanadium complexes, by the Gong[8] and Sasai groups,[9] afforded highly selective BINOL analogs. Later, Katsuki and coworkers disclosed that a Schiff base-iron complex was able to efficiently construct bisnaphthols, which are connected through a chiral axis.[10] Using an asymmetric phosphoric acid coordinated to iron, Toste and Pappo introduced the axial chiral bond in BINOL analogs in 2016.[11]

Compared to 2-naphthols, phenol couplings have been limited and less explored (**Scheme 2B**). Furthermore, no highly enantioselective oxidative phenol homocoupling was known prior to our initial report.[12] In 1999, Uang and coworkers reported oxidative phenol dimerization by means of vanadium catalyst (**Scheme 2B, I**).[13] Recently, we (Cr[14]) Pappo (Fe-catalyzed[15]) and Guo (Co[16]) disclosed metal catalysts for selective oxidative phenol cross-coupling to bisphenols that are not atropisomerically stable (**Scheme 2B, III**). Notably, the Liu and Kurti groups have reported highly enantioselective phenol couplings by utilizing preoxidized compounds, which imposes constraints on the product types that can be formed (**Scheme 2B, IV**).[17]

Hydroxycarbazoles have been found to be effective in oxidative coupling due to their electron-rich nature (**Scheme 3**). A variety of different oxidants have enabled the formation of the central bond. Benzoyl peroxide was utilized by Moody and coworkers to make biscarbazole in 1989.[18] Bringmann and other groups used *tert*-butyl peroxide to oxidatively introduce the C-C bond from 1-hydroxycarbazoles.[19] Later, Knölker reported that tetrachloro-*para*-benzoquinone produced an axial bond *ortho* to the hydroxyl group.[20] In 2015, the Kozlowski group revealed that the vanadium-catalyzed oxidative coupling with *N*-protected 2-hydroxycarbazole generated the *ortho-ortho'* adduct as the major product.[21]

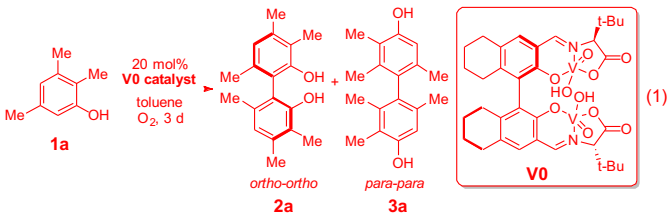
Recently, we reported that vanadium-catalyzed asymmetric oxidative coupling of phenols and hydroxycarbazoles afforded a chiral axis in good to excellent yield and selectivity.[12] Herein, we describe further understanding of the transformation via engineering of vanadium catalyst, expanded substrate scope, and mechanistic studies, and calculations.

Scheme 3. Oxidative Coupling of Hydroxycabazoles



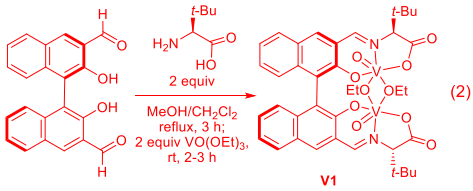
Results and Discussion

Catalyst Optimization. Inspired by an effective oxidative coupling with $VO(acac)_2$,[13] 2,3,5-trimethylphenol (**1a**) was examined as the substrate in initial studies (eq 1). Its success in asymmetric BINOL derivative syntheses indicates that vanadium catalysts are highly efficient at introducing a chiral axis. Encouragingly, our initial attempts coupling **1a** with dimeric vanadium catalyst **V0** provided only *ortho-ortho* **2a** and *para-para* **3a** products among the many potential outcomes (*ortho-para* coupling, different C-O couplings).



(1)

However, the outcome from trial to trial was found to vary considerably. Part of the irreproducibility arose from exactly how the catalyst was prepared as several protocols have been reported using different vanadium sources including $VO(SO_4)$[8,22] and $VO(Cl)_3$.[23] A base is sometimes used for ligand deprotonation prior to complexation and removal of inorganic salts is effected with an aqueous phase. For the phenol couplings, we discovered that the hydration state of the catalyst had a great influence on reactivity. For example, an inactive catalyst was produced when the complex was placed under high vacuum. We attributed this reduced reactivity to formation of a less potent, oxo-bridged species. Fortunately, using $VO(OEt)_3$ (eq 2) to generate the vanadium adduct as previously described for asymmetric homoallylic oxidation, provided reproducible results.[24] Using this procedure, product **2a** was obtained in 37% ee. Clearly, the **V1** catalyst can induce enantioselectivity, but it is hampered by poor reactivity with only 49% conversion of starting material **1a** after 3 days (Figure 1). Furthermore, the *para-para* isomer (**3a**, 21%) formed to similar extent as **2a** (28%).



(2)

To improve conversion and regioselectivity, it was necessary to modify the reaction conditions. We speculated that the phenoxide substrate accelerates the reaction rate. Using Et_3N as an additive, however, led to no product formation. Conversely, a protic acid additive, which was capable of catalyst activation by means of protonation, afforded both enhanced reactivity (91% conv, 75% isolated yield) and selectivity (60% ee) to produce *ortho-ortho* (**2a**) product (Figure 1).

To identify further means of activating the catalyst, an additive screen was undertaken (see Supporting Information). In line with the prior results, addition of water (2 equiv) resulted in a modest improvement. Even greater improvement in terms of reactivity and selectivity were seen with protic acids. Acetic acid proved optimal relative to stronger acids (TFA) which result in a loss of selectivity and weaker acids (alcohols and phenols) which maintain selectivity but compromise reactivity. The optimal conditions were 0.5 M in CH_2Cl_2 or 1,2-dichloroethane (DCE) with 6.25 equiv HOAc and **V1** which produced 75% of **2a** in 60% ee (Figure 1). To improve selectivity further, the framework of catalyst was modified. Altering the amino acid substituent (see Supporting Information) resulted in no improvement. The use of a scaffold with a greater dihedral angle between the upper and lower portions (**V2**, Figure 1) improved yields to 83% and enantioselectivity to 77% ee. Such a scaffold would disfavor the formation of strong μ-oxo-bridges between the two vanadium centers, which may account for the greater reactivity. Similar improvements were seen with derivatives of **V1** containing electron-withdrawing groups (6,6'-dibromo 64% yield, 54% ee; 6,6'-dinitro 49% yield, 78% ee). A more Lewis acidic and more oxidizing vanadium center seems advantageous. Even so, avenues for additional optimization of the biaryl scaffold were limited. The free acid positions were not found to be crucial since similar results were obtained with the methyl ester derived ligands. However, linking via the carboxylic acids was not effective with the original tetrahydronaphthol backbone using a variety of tether lengths (**V3**, 34% **2a**, 0% ee). We hypothesized that a large group is needed where the chiral axis had been to offer selective coupling. Thus, a *tert*-butyl substituted phenol was employed. With a linker length of six carbons being optimal (**V4**), a larger improvement in selectivity was seen (67% ee).

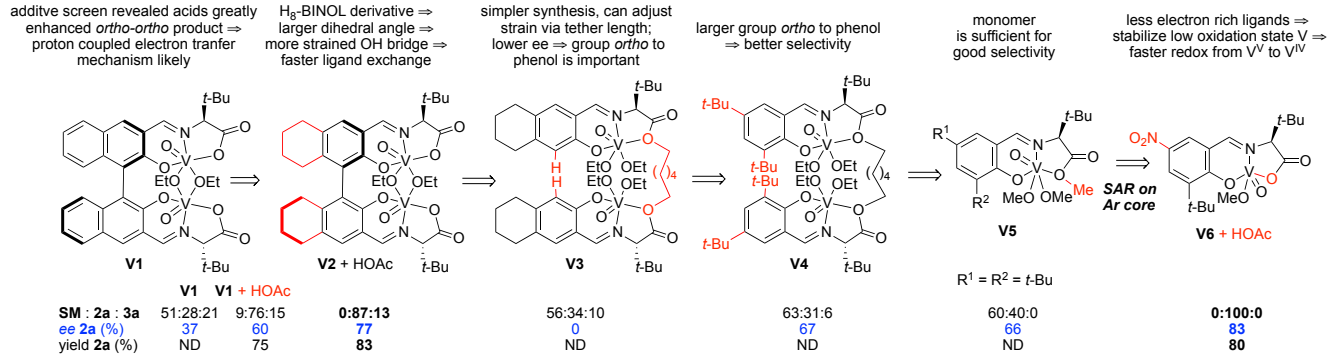
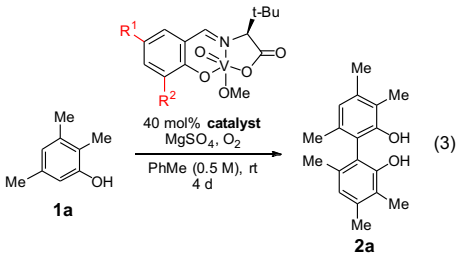


Figure 1. Catalyst evolution in the asymmetric phenol coupling (eq 1).

To interrogate whether a dimeric catalyst was really necessary, a trial with monomer **V5** was undertaken which revealed results similar to those of the dimer. Bulky groups, such as *tert*-butyl (**Table 1**, entry 1), SiR_3 (entry 6–8), or adamantyl (entry 10), at the R^2 position tend to provide better selectivity. A sterically more congested substituent, 1,1-dimethylbenzyl, gave higher selectivity (entry 12, 76% ee). However, the reactivity declined as R^2 became larger than TMS (entry 6–8).

Table 1. SAR of Monomeric Vanadium Catalyst (eq 3)



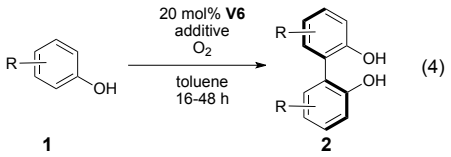
Entry	R^1	R^2	Conversion (%)[a]	*ee* (%)[b]
1	*t*-Bu	*t*-Bu	40	66
2	*t*-Bu	2-tolyl	78	49
3	*t*-Bu	2,6-xylyl	92	50
4	*t*-Bu	1-naphthyl	85	38
5	*t*-Bu	2-methoxy-1-naphthyl	81	57
6	*t*-Bu	$SiMe_3$	70	73
7	*t*-Bu	$SiEt_3$	58	75
8	*t*-Bu	Si^iPr_3	35	76
9	*t*-Bu	$SiPh_2{}^tBu$	13	60
10	*t*-Bu	adamantyl	24	66
11	*t*-Bu	CPh_3	15	56
12	*t*-Bu	CMe_2Ph	37	76
13	OMe	*t*-Bu	47	65
14	OAc	*t*-Bu	43	62
15	NO_2	*t*-Bu	86	75
16	NO_2	$SiEt_3$	100	75

[a]Determined from 1H NMR; isolated yield in parentheses. [b]Determined using CSP HPLC.

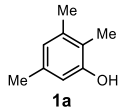
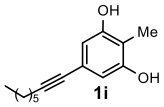
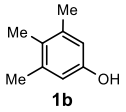
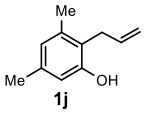
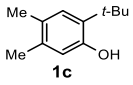
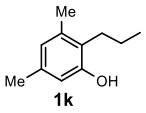
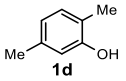
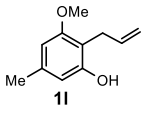
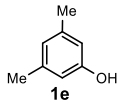
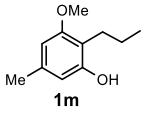
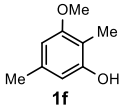
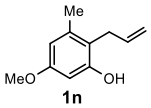
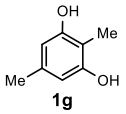
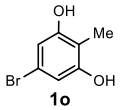
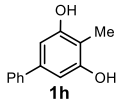
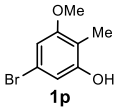
To tackle the low conversion issue, a more powerful oxidizing catalyst was engineered by destabilizing the higher oxidation state of the vanadium catalyst using electron withdrawing groups on the ligand. To our delight, a nitro group (entry 15) facilitated the reaction in accordance with this hypothesis (entry 13 vs 15). With the modified monomeric catalyst (**V6**) in the presence of HOAc, the *ortho-ortho* coupled product (**2a**) was obtained in 80% isolated yield as the only product with 83% ee (Figure 1).

Phenol Scope. A variety of phenols were examined with the optimized conditions (**Table 2**). The substituent *ortho* to the phenol possessed an important role relative to the enantioselectivity. Methyl was optimal, while smaller groups, such as a hydrogen, showed drastically decreased selectivity (entries 2, 5). Further, the larger *tert*-butyl group gave no selectivity (entry 3). 2,3,5-Trisubstituted phenols generally provided better results.

Table 2. Scope of Phenol Coupling (eq 4)[a]



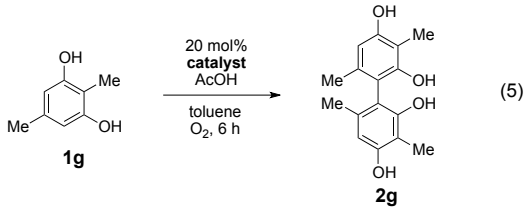
1 2

entry	substrate	additive[b]	T	yield (%)[c]	*ee* (%)[d]	entry	substrate	additive[b]	T	yield (%)[c]	*ee* (%)[d]
1	 **1a**	HOAc	rt	89(72)[e]	85(95)[e]	9	 **1i**	LiCl	0 °C	66	89
2	 **1b**	HOAc	rt	100[f]	10	10	 **1j**	HOAc	rt	56(99)[g]	77
3	 **1c**	HOAc	rt	100[f]	0	11	 **1k**	HOAc	rt	80(98)[g]	72
4	 **1d**	HOAc	rt	ND	60	12	 **1l**	HOAc	rt	44[f]	34
5	 **1e**	HOAc	rt	38[f]	38	13	 **1m**	HOAc	rt	100[f]	10
6	 **1f**	HOAc	rt	100[f]	50	14	 **1n**	HOAc	0 °C	78	40
		LiCl	0 °C	80(76)[e]	82(95)[e]						
7	 **1g**	HOAc	rt	89	63	15	 **1o**	HOAc	rt	24[f]	20
		LiCl	0 °C	81	86						
8	 **1h**	HOAc	0 °C	65	50	16	 **1p**	HOAc	rt	12[f]	47

[a]Reaction conditions: 20 mol% catalyst, x equiv additives, O_2, 0.5 M $PhCH_3$. [b]6.25 equiv HOAc, 0.4 equiv LiCl. [c]Isolated yield. [d] ee determined by chiral HPLC. [e]After trituration in parantheses. [f]Conversion. [g]Isolated yield based on recovered substrate

Dioxygenated substrates such as **1g** (eq 5) were examined next with the expectation that the more electron-rich systems would undergo oxidative coupling more readily. In line with this hypothesis, reaction of **1g** occurred quickly at room temperature (Table 3, entry 1) and the selectivity could be increased by lowering the temperature (entries 2-4). However, below 0 °C reaction rates were compromised.

Table 3. Oxidative Coupling of Dihydroxyarene 1g (eq 5)



(5)

Entry	Temperature (°C)	Conversion (%)[a]	*ee* (%)
1	23	72	50
2	0	53	63
3	−20	30	75
4	−40	15	85

As a result, additional additive screening was undertaken with this class of substrates (**Table 4**). Most additives resulted in lesser reactivity although cationic lithium species resulted in significantly higher reactivity (entries 10, 12, 17). LiCl (entry 5) afforded the highest enantioselectivity (entry 5, 85% ee), which did not appear to devolve solely from the chloride (c.f. entries 6-8). Using the LiCl additive with substrate **1f** gave a similar boost in selectivity (**Table 4**, entry 6, 82% ee). Unfortunately, LiCl did not provide equal levels of improvement for all substrates.

Table 4. Additive Screening with Dihydroxyarene 1g (eq 5)[a]

Entry	Additives	Conversion (%)[b]	*ee* (%)
1	-	70	52
2	$Sn(OTf)_2$	33	43
3	$Sc(OTf)_3$	43	67
4	$Yb(OTf)_3$	48	69
5	LiCl	46	85
6	NaCl	52	47
7	KCl	59	45
8	$MgCl_2$	28	78
9	LiF	46	46
10	LiBr	100	63
11	LiI	12	57
12	$LiClO_4$	94	73
13	LiOAc	43	18
14	Li_2CO_3	53	27
15	4Å MS	-	68
16	$MgSO_4$	50	70
17	LiCl + 12-crown-4	100	60

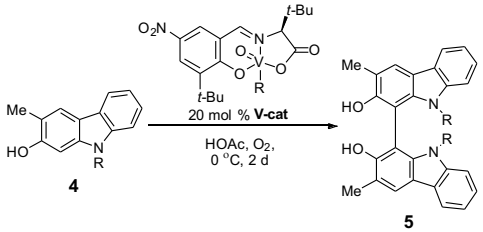
[a]Reaction conditions: 20 mol % **V6**, 40 mol % additive, $PhCH_3$, O_2, 0 °C, 6 h. [b]Conversion was determined by ^1H NMR.

Other substituents, such as allyl or propyl, *ortho* to the phenol, resulted in comparable selectivity (Table 2, entry 10, 11). However, the allyl or propyl group was no longer tolerated with either 3-methoxy or 5-methoxy substrates (entry 12–14) in contrast to 3-methoxy with 2-methyl substituent (entry 6). To examine the effects of substituents at 5-position, experiments were conducted with a phenyl (entry 8), alkynyl chain (entry 9), and electron-withdrawing groups (entry 15, 16). Notably, oxidative coupling of the phenol an bearing alkynyl chain afforded good selectivity (entry 9, 89% ee) in the presence of LiCl. As we expected, 5-bromo analogs caused slower oxidation with only 24% (**1o**) and 12% (**1p**) conversion after 48 h. Racemic biaryl products have much poorer solubility than enantiopure biaryls. Exploiting this difference, one trituration with hexanes was found to increase the enantiomeric excess of the filtrate substantially. For example, substrates **1a** and **1f** were enhanced to 95% ee following trituration.

Hydroxycarbazoles. The electron rich nature of hydroxycarbazoles allows access to dimeric compounds via oxidative coupling (Scheme 3). Accordingly, hydroxycarbazole **4** was examined in our asymmetric oxidative coupling (eq 6).[20] Our previous report demonstrated that the *N*-protecing group was essential for selective oxidation *ortho* to the hydroxyl group by excluding reaction with amine.[21]

With the nitrogen position protected with a benzyl substituent, promising levels of selectivity (70% ee) were observed (Table 5, entry 1). Examining related vanadium catalysts **V7** (R = F, entry 2) and **V8** (R = O*i*-Pr, entry 3) revealed that a larger alkoxy group on the vanadium center gave rise to higher selectivity (78% ee). However, even larger substituents on vanadium (R = O*t*-Bu, entry 4) did not afford further improvement. Finally, optimization of solvent (CH_2Cl_2, DCE, $CHCl_3$, toluene, dichlorobenzene) revealed that chlorobenzene (entry 5) provided the best result (91% yield, 87% ee).

Table 5. Oxidative Coupling of 2-Hydroxycarbazole (eq 6)[a]



(6)

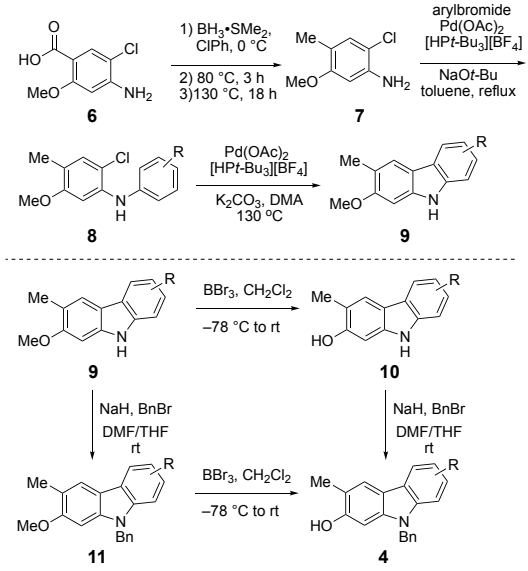
Entry	R	Catalyst	Solvent	Yield (%)	*ee* (%)
1	Bn (**4b**)	**V6** (R = OMe)	PhMe	78	70
2	Bn (**4b**)	**V7** (R = F)	PhMe	40	70
3	Bn (**4b**)	**V8** (R = O*i*-Pr)	PhMe	71	78
4	Bn (**4b**)	**V9** (R = O*t*-Bu)	PhMe	44	74
5	Bn (**4b**)	**V8** (R = O*i*-Pr)	PhCl	91	87
6	Me (**4c**)	**V8** (R = O*i*-Pr)	PhCl	82	71
7	allyl (**4d**)	**V8** (R = O*i*-Pr)	PhCl	71	76
8	*i*-Pr (**4e**)	**V8** (R = O*i*-Pr)	PhCl	58	42
9	2,4,6-Me_3Bn (**4f**)	**V8** (R = O*i*-Pr)	PhCl	27	37

[a]Reaction Conditions: 20 mol% catalyst, 6.5 equiv HOAc, O_2, 0.5 M solvent, 0 °C, 48 h.

With the optimal catalyst (**V8**), examination of the nitrogen substituent showed that either smaller (Me, entry 6, 71% ee) or larger groups (*i*-Pr; 2,4,6-trimethylbenzyl, entries 8-9) were detrimental. Moderate sized groups such as allyl (entry 7, 76% ee) and benzyl (entry 5, 87% ee) were superior.

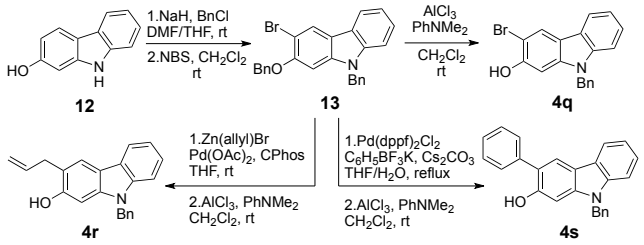
The synthetic routes to the 2-hydroxycarbazoles employed are outlined in Schemes 4–6. Most of the substituted carbazoles were prepared from commercially available aniline **6** (Scheme 4). The carboxylic acid was reduced exhaustively with BH_3•SMe_2, followed by a Buchwald–Hartwig amination using a wide range of aryl bromides, which allowed access to a variety of substituted precursors (**7**).[25] Cyclization was achieved in the presence of $Pd(OAc)_2$ and a monodentate trialkyl ligand to generate carbazole **9**.[25] To obtain nitrogen protected hydroxycarbazoles, BBr_3 demethylation[21] followed by selective *N*-benzylation (or vice versa) afforded 2-hydroxy-3-methylcarbazoles (**4**).[26]

Scheme 4. 2-Hydroxy-3-methylcarbazoles syntheses

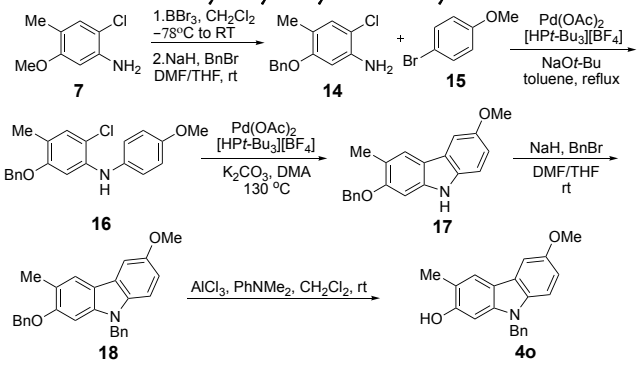


Substrates containing a different group adjacent to the phenol were prepared form the commercially available hydroxycarbazole **12** (Scheme 5). A one-pot benzylation of the oxygen and nitrogen was followed by a bromination, using NBS, to obtain **13**. Suzuki and Negishi[27] couplings introduced a phenyl and allyl groups, respectively, to the C-3 position. Thereafter, deprotection of the phenol with $AlCl_3$ afforded **4q**, **4r**, and **4s**.[28]

Scheme 5. 3-Substituted-2-hydroxycarbazole syntheses



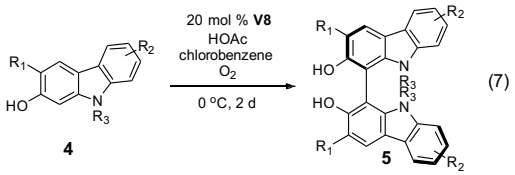
Scheme 6. 6-Methoxy-2-hydroxycarbazole synthesis

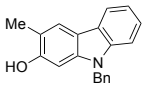
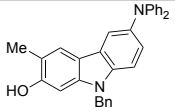
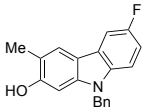
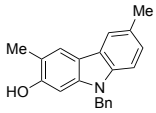
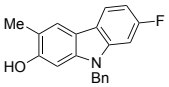
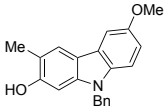
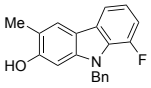
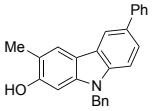
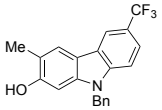
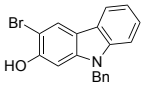
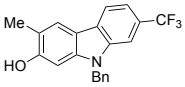
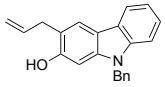
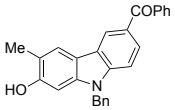
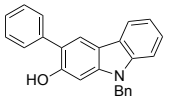
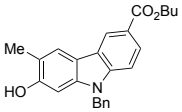


To investigate how introducing an electron donating group to the carbazole affected enantioselectivity, a substrate with a methoxy group at the C-6 position was synthesized. For substrates containing two methoxy substituents, selective deprotection of the oxygen at the C-2 position proved untenable. Thus, a demethylaton of **7** was undertaken with BBr_3 followed by a benzylation to yield the aniline **14**. Thereafter, a Buchwald Hartwig amination with aryl bromide **15** followed by cyclization in the presence of $Pd(OAc)_2$ and a monodentate trialkyl ligand generated carbazole **16**. Finally, N-benzylation followed by selective O-debenzylation with $AlCl_3$ afforded **4o**.

With these substrates in hand, the scope of the enantioselective douplign was investigated (Table 6). Electron-withdrawing substituents gave good to excellent selectivity (85–96% ee) along with moderate to good conversions (46–87% yield). Highly enantioenriched bishydroxycarbazoles were obtained with the fluoride substituent regardless of distal position (entry 2–4, 91–92% ee). More electron-deficient hydroxycarbazoles, 6-CF_3 (entry 5) and 7-CF_3 (entry 6), offered excellent selectivities (93% and 94% ee) with good yields. Use of an electron withdrawing carbonyl group (entry 7), however, gave rise to solubility issues. A mixed solvent system, which included hexafluoroisopropanol as a co-solvent, was needed. Accordingly, compromised conversion was observed along with slightly lower selectivity (85% ee). The ester substituted compound provided the most selective coupling result (entry 8, 96% ee). The diphenylamino group was an outlier with drastically lower selectivity (entry 9, 37% ee). Faster oxidative coupling reactions were observed with electron-donating substituents. For example, the 6-methoxyhydroxycarbazole coupling reaction was completed in 26 hours with moderate selectivity (entry 11, 74% ee). With a methyl or allyl group adjacent to the phenol, good enantioselectivites were observed (entry 1, 13). On the other hand, an electron-withdrawing bromide (entry 14) or an aryl group (entry 15) at this site compromised reactivity while retaining moderate levels of selectivity.

Table 6. Scope of 2-Hydroxycarbazole Coupling (eq 7) [a]



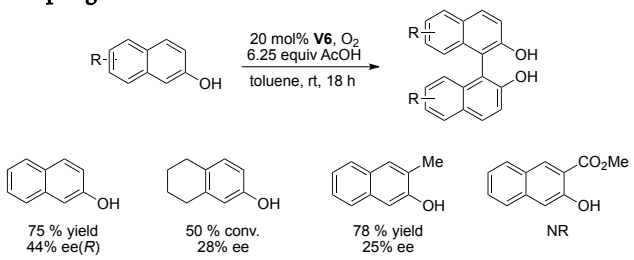
Entry	Substrate	Yield (%)[b]	*ee* (%)[c]	Entry	Substrate	Yield (%)[b]	*ee* (%)[c]
1	 **4a**	91	87	9	 **4m**	62	37
2	 **4f**	87	92	10	 **4n**	90(45)[f]	60(76)[f]
3	 **4g**	73	92	11[g]	 **4o**	82	74
4	 **4h**	80	91	12	 **4p**	70	82
5	 **4i**	70	93	13	 **4q**	17(30)[e]	72
6	 **4j**	60	94	14	 **4r**	75	83
7[d]	 **4k**	53(76)[e]	85	15	 **4s**	26(43)[e]	60
8	 **4l**	46(67)[e]	96				

[a]Reaction Conditions: 20 mol% catalyst, 6.5 equiv HOAc, O_2, 0.5 M chlorobenzene, 48 h. [b]Isolated yield. [c]ee determined by chiral HPLC. [d]HFIP/PhCl as a solvent. [e]Isolatted yield based on recovered substrate. [f]Reaction was conducted at −15 °C. [g]Reaction time was 26 h.

Mechanism. To determine whether the changes to the catalytic system, namely use of alkoxy derived monomeric vanadium catalysts with HOAc, would also be beneficial with the parent naphthol couplings, several substrates were screened (Scheme 7). However, the selectivities were uniformly low in line with prior reports with 2-naphthol using a valine analog of **V6**.[22b] Since the coupling selectivities are very different with the dimeric vanadium catalysts[22c-g] and the monomeric vanadium catalyst/Brønsted acid system used herein, a study of the mechanism was undertaken.

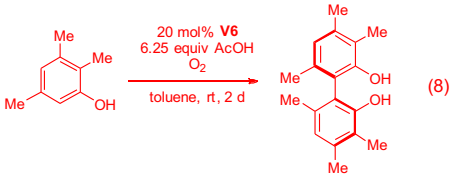
Scheme 7. Monomeric Vanadium Catalysts in Naphthol

Coupling



With 20 mol% of **V6**, the oxidative coupling of 2,3,5-trimethyl phenol was completed within 2 days at ambient temperature under oxygen (Table 7, entry 1). However, the addition of equimolar radical inhibitor TEMPO relative to catalyst, led to low conversion (35%, entry 2), which suggests a radical process. Under inert atmosphere, 9% and 26% conversions were detected in the presence of 20 and 50 mol% of **V6** catalyst (entry 3–4). Accordingly, vanadium(V) species were implicated as the active oxidant. Further, the stoichiometry is consistent with each vanadium (V) abstracting one electron [i.e. a V(V) to V(IV) redox couple].

Table 7. Control Experiments in Asymmetric Coupling (eq 8) [a]



entry	catalyst	condition[a]	conversion
1	20 mol% **V6**	control	100%
2	20 mol% **V6**	0.2 equiv TEMPO	35%
3	20 mol% **V6**	N_2 atmosphere	9% (3 days)
4	50 mol% **V6**	N_2 atmosphere	26% (3 days)

[a]Reaction Conditions: 6.25 equiv HOAc, toluene, O_2, rt, 2 d.

Based on these experiments, our initial proposed mechanism is outlined in Figure 3a. To reconcile the acceleration by acid, we speculated that additional catalyst activation would be achieved by protonation to produce **A**, or an analog thereof. Hydrogen atom abstraction was excluded by the absence of an isotope effect between HOAc and acetic acid-D_4 (Figure 4).[29] Rather, ligand exchange with phenol **1a** would generate intermediate **B**, which was observed by LCMS analysis. Subsequent single electron transfer to oxidize the phenol, would be followed by coupling (**C**). The control experiment in Table 7 (entry 2) supports such a radical coupling.

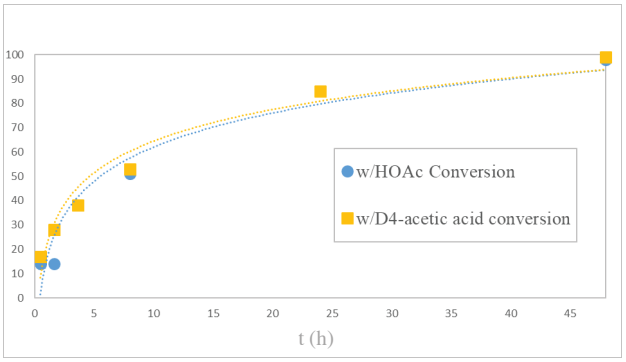


Figure 2. Reaction rates with CH_3COOH vs CD_3COOD.

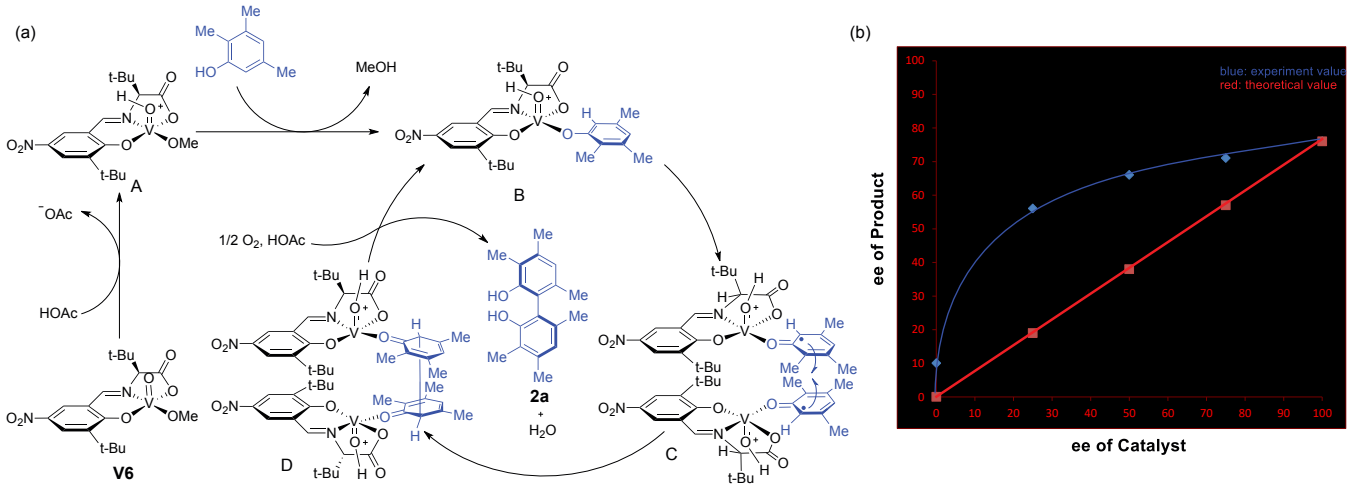
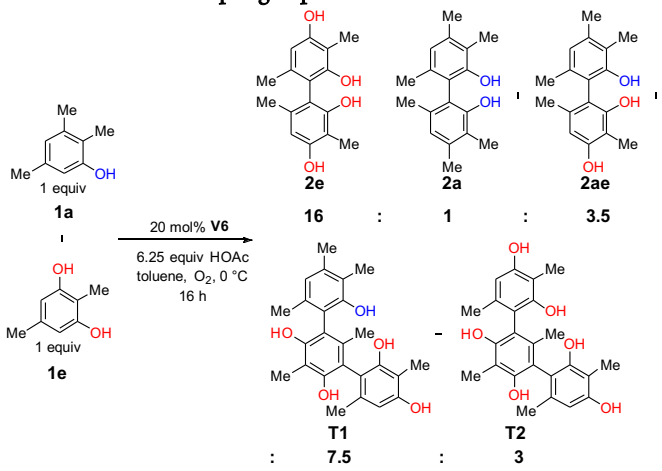


Figure 3. a) Initial mechanism. B) Nonlinear effect vs theoretical linear plot.

To further test this theory, we performed the cross-coupling experiment with **1a** and **1e** (Scheme 8). The major product was **2e**, which is derived from more readily oxidizable phenol **1e**. The overall product distribution is consistent with radical-radical mechanism where oxidizability dictates the rate of radical formation and a statistical distribution is observed.[8]

Scheme 8. Cross-Coupling Experiment with 1a and 1e



Bond formation via dimeric cluster **D** was supported by positive non-linear effect (Figure 3b). Subsequent tautomerization provides product **2a** while oxygen acts as the terminal oxidant to regenerate the vanadium(V).

The initial model depicted in Figure 3a engages the phenol after associative ligand exchange via the less hindered lone pair of **1a**. Subsequently, the *ortho* methyl group of the phenol points forward as shown in **B**. Dimerization of complex **B**, via **C**, by minimizing steric interactions provides the *P* (*aS*) stereoconfiguration. The stereochemistry was assessed experimentally by X-ray analysis of crystals of **2a** obtained from hexane and ethyl acetate (10:1). The absolute axial stereochemistry was found to be the *P* (*aS*) configuration (Figure 4) in accord with such a model.

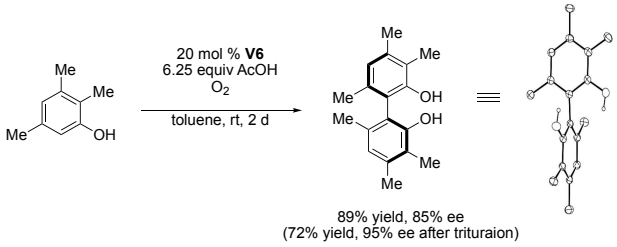


Figure 4. Absolute axial stereochemistry of dimerized phenol.

To further understand the origin of regio- and enantioselectivity and verify our proposed mechanism, a DFT study of the catalytic cycle was initiated using a truncated catalyst structure. Calculations were conducted with Gaussian09. Multiple pathways and conformational isomers were explored using UB3LYP/(6-31G(d); V, LANL2DZ. For anionic species, diffuse functions were explored, but resulted in no change. In addition, both singlet and triplet states were assessed. Additional single point calculations were done with UM06/(6-311+G(d,p); V, LANL2DZ;SMD, toluene.

Initial assessment of the pathway illustrated in Figure 3 revealed that protonated intermediate A was energetically unfavorable regardless of the site of protonation, the inclusion of counterions, or the use of solvation models. Thus, different roles for the acetic acid were surveyed. Ultimately, a pathway with energetics in line with the observed rates was found when acetate was used as a μ^2-bridging ligand (Figure 5). Notably, the same pathway without the bridging acetate was substantially less favorable ($\Delta H^{\ddagger}$ = 29.0 kcal/mol, $\Delta G^{\ddagger}$ = 42.2 kcal/mol; see Supporting Information).

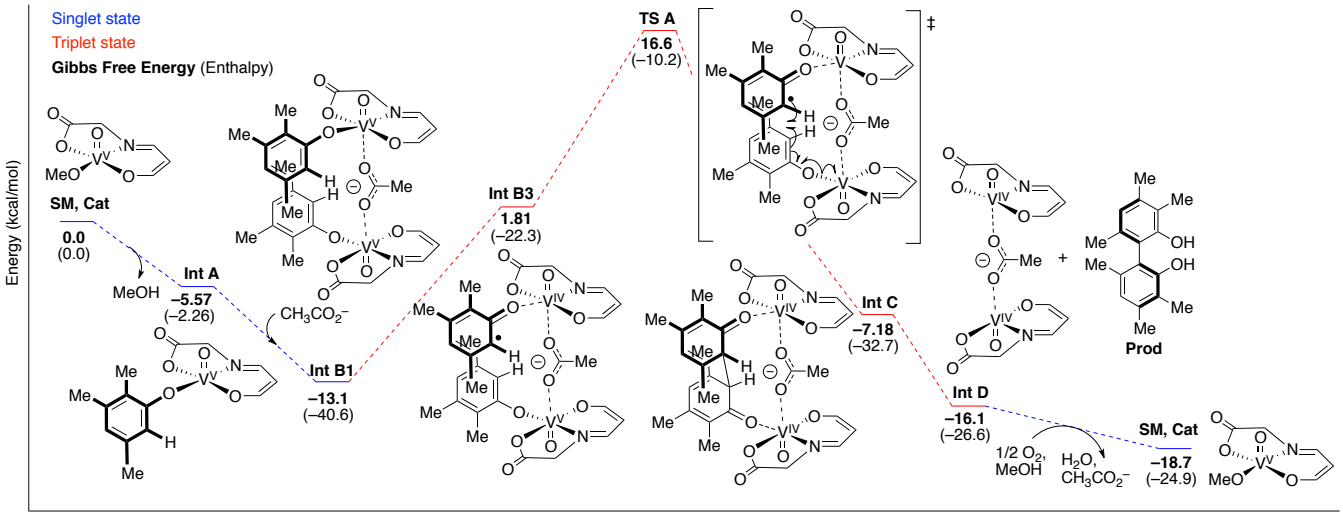


Figure 5. Reaction energy diagram representing alternative calculated pathway.

In this revised model (Figure 5), ligand exchange to generate the phenoxide adduct coordinated via the less hindered oxygen lone pair is again proposed to yield **IntA**. Assembly of two such adducts with an μ^2-acetate bridge to form **IntB1** is thermodynamically favorable by 7.5 kcal/mol. Singlet to triplet transition to form the diradical **IntB3** is uphill energetically. In going from **IntB1** to **IntB3**, one of the V–OAr bond distances increases from 1.784 Å to 2.155 Å, which is indicative of bond cleavage. Unsurprisingly, much of the spin density is concentrated on the reduced vanadium center, with the rest primarily delocalized around the phenol. This monoradical intermediate stands in contrast to the mechanisms typically proposed for these couplings involving two carbon-centered radicals (c.f. Figure 3). Notably, **IntB3** gives rise to a transition state **TS A** for C-C bond formation with a free energy of 16.6 kcal/mol which is substantially lower in energy than that from the singlet. In this transition state, the second vanadium center abstracts an electron from the other phenol, which results in C-C bond formation. Subsequent decoordination and tautomerization leads to the product. The overall process is driven by the favorable oxidation of the resultant V(IV) to V(V) by dioxygen.

To ascertain whether the singlet to triplet conversion was energetically feasible and/or rate-determining, an estimate of the Additional calculations (see Supporting Information) were undertaken to estimate the conical intersection. The UB3LYP energy of **IntB1** was calculated as if it were a triplet (**IntB1'**), and that of **IntB3** as if it were a singlet (**IntB3'**). Potential energy scans from **IntB1** to **IntB3'** and from **IntB1'** to **IntB3** were performed. The intersection of the two potential energy curves was marked as the approximate conical intersection (**MECP**, Figure 6). Since the relative UB3LYP energy (–32.4 kcal/mol) was markedly less than that of **TS A** (-12.9 kcal/mol), we conclude that the singlet-triplet transition was not rate-limiting. All told, the calculations support the C-C bond forming step as overall rate-limiting.

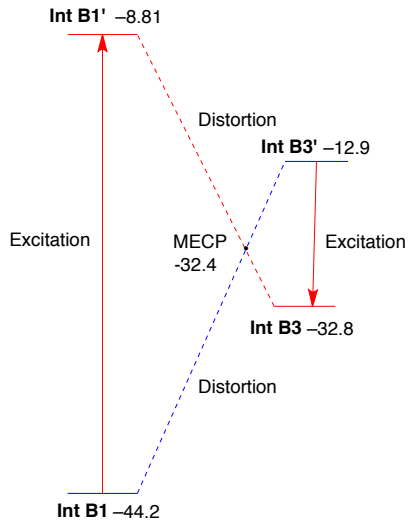


Figure 6. Estimate of singlet to triplet barrier (ΔE, kcal/mol; U3B3LYP/6-31G(D), V: LANL2DZ)

Of the two open sites on the dissociated phenol ring in IntB3, the greatest spin density is located at the para position (0.437) relative to the para position (0.231); on the other ring, the most negative spin density is on the ortho position (-0.017). However, when we modeled the ortho-para coupling, the transition state (see Supporting Information) leading to ortho–para coupled product was predicted to be 5.5 kcal/mol higher that that leading to ortho-ortho coupling, which explains why the ortho–para product is not observed and suggests that the coupling step is also regiodetermining. Indeed, distortion of the bridge in the *ortho–para* coupling transition state is readily apparent.

To model the enantioselectivity, we computed two diastereomeric transition structures incorporating the complete Schiff base ligand, which lead to formation of the S and R product enantiomers, respectively (Figure 7). The higher energy TS A(R) suffers from greater torsional strain along the forming C-C bond with a dihedral angle of 168.5° vs a closer-to-ideal of 177.5° for the lower energy TS A(S). This model predicts an enantiomeric excess of 84% in favor of the S-enantiomer, which agrees with the experimentally obtained value of 86% ee.

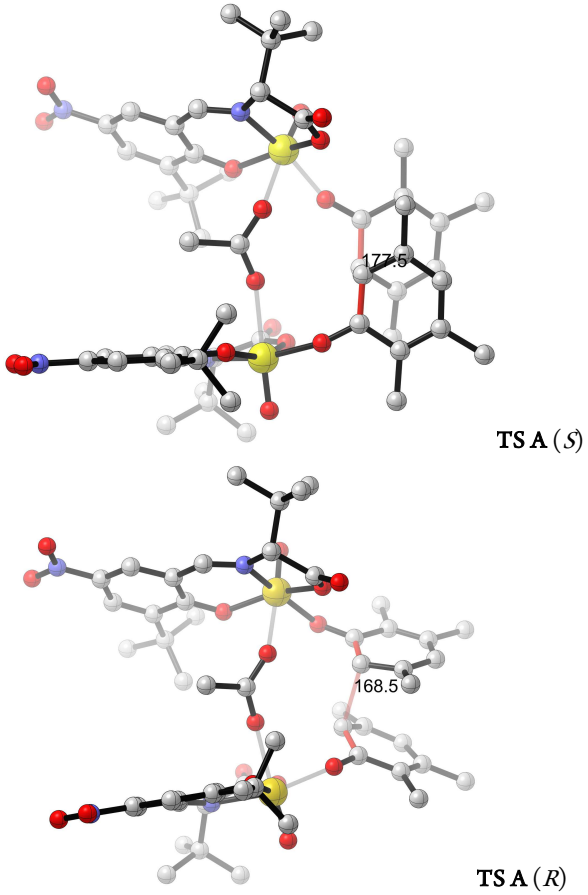


Figure 7. Diastereomeric transition states leading to enantiomeric products (Dihedral angles are for bonds highlighted in red. Hydrogen atoms not shown for clarity).

Concluding Remarks

Beginning from dimeric vanadium catalysts that had been previously reported as highly effective in coupling of 2-naphthols, a series of rational modifications were undertaken to identify a selective catalyst for coupling 2-phenols. Ultimately, the use of typically less reactive monomeric vanadium catalysts was found to be effective when combined with a Brønsted or Lewis acid additive, which provided considerable activation. The resultant vanadium catalyst system effected the asymmetric oxidative *ortho-ortho* coupling of a range of simple phenols and 2-hydroxycarbazoles with good to excellent levels of enantioselectivity. Experimental and DFT studies of the mechanism indicate that the additives serve to aggregate the vanadium monomers. In addition, a relatively facile singlet to triplet crossover is implicated prior to the carbon-carbon bond forming event. The resultant triplet intermediate gives rise to a transition state with character between an anion-radical coupling and a radical-radical coupling. The differences in energies between the transition states leading to the regiomeric (*ortho-ortho* vs *ortho-para*) and enantiomeric products (*R* vs *S*) correlate well with the observed selectivity. Overall, effective equivalents of dimeric vanadium catalysts can be assembled in situ from simple, easily made monomers, which may have implications for other vanadium catalyzed transformations.

Experimental

General Considerations: Unless otherwise noted, all non-aqueous reactions were carried out under an atmosphere of dry N_2 in dried glassware. When necessary, solvents and reagents were dried prior to use. THF was distilled from sodium benzophenone ketyl. CH_2Cl_2, $ClCH_2CH_2Cl$, and toluene were distilled from CaH_2. High throughput experiments were performed at the Penn/Merck High Throughput Experimentation Laboratory at the University of Pennsylvania. The screens were analyzed by HPLC by addition of an internal standard.

Analytical thin layer chromatography (TLC) was performed on EM Reagents 0.25 mm silica-gel 254-F plates. Visualization was accomplished with UV light. Chromatography was performed using a forced flow of the indicated solvent system on EM Reagents Silica Gel 60 (230-400 mesh). When necessary, the column was pre-washed with 1% Et_3N in the eluent system. ^1H NMR spectra were recorded on a 500 MHz spectrometer. Chemical shifts are reported in ppm from tetramethylsilane (0 ppm) or from the solvent resonance ($CDCl_3$ 7.26 ppm, DMSO-d_6 3.58 ppm, acetone-d_6 2.05 ppm, DMF-d_7 2.50 ppm, CD_3CN 1.94 ppm, CD_2Cl_2 5.32 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants, and number of protons. Decoupled ^{13}C NMR spectra were recorded at 125 MHz. IR spectra were taken on an FT-IR spectrometer using a thin film on NaCl plate. Accurate mass measurement analyses were conducted via time-of-flight mass analyzer GCMS with electron ionization (EI) or via time-of-flight mass analyzer LCMS with electrospray ionization (ESI). The signals were measured against an internal reference of perfluorotributylamine for EI-GCMS and leucine enkephalin for ESI-LCMS. The instrument was calibrated and measurements were made using neutral atomic masses; the mass of the electron removed or added to create the charged species is not taken into account. Low resolution LCMS data were obtained by use of a UPLC system with a SQD mass analyzer equipped with electrospray ionization. Circular dichroism and UV-vis spectroscopy measurements carried out at ambient temperature (23 °C). Solution spectra in methanol recorded in 10-mm quartz cuvettes and corrected by subtracting the spectrum of the pure solvent at the same temperature. A scan rate of 100 nm/min with a response time of 1 s and a bandwidth of 1 nm was used to measure the CD spectra, which were recorded in low sensitivity mode with 4 accumulations. Melting points are corrected. Enantiomeric excesses were determined using analytical HPLC with UV detection at 254 nm. Analytical Chiralpak columns (4.6 mm x 250 mm, 5 μm) from Daicel were used. Optical rotations were measured on a polarimeter with a sodium lamp.

(*S,S*)-Vanadium Catalyst V3. Under an inert atmosphere, 1-ethyl-3-(3-dimethyl-aminopropyl) carbodiimide (174 mg, 0.91 mmol) was added to a solution of hexanediol (50 μL, 0.43 mmol), Boc-protected *tert*-leucine[30] (200 mg, 0.86 mmol), 4-dimethylaminopyridine (11 mg, 0.09 mmol) in CH_2Cl_2 (0.75 mL) at 0 °C and was stirred for 10 min. The reaction mixture was stirred for a further 20 h at room temperature. The reaction mixture was diluted with CH_2Cl_2, washed with a satd NH_4Cl, and the aqueous layer was back extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated. The residue was chromatographed (10% EtOAc in hexane) to yield the *N*-Boc protected tethered amino acid as clear oil (200 mg) in 85% yield: ^1H NMR (300 MHz, $CDCl_3$) δ 5.10 (m, 2H), 4.15 (m, 4H), 4.09 (s, 2H), 1.66 (m, 4H), 1.44 (s, 18H), 1.39 (m, 4H), 0.97 (s, 18H).

To the the *N*-Boc protected tethered amino acid (200 mg) in 1,4-dioxane (1.0 mL) was added 4 *N* HCl in 1,4-dioxane (4.0 mL) followed by stirring for 3 h at room temperature. Removal of solvent afforded hexane-1,6-diyl (2*S*,2'*S*)-bis(2-amino-3,3-dimethylbutanoate)hydrochloric salt as a white solid (152 mg) in 99% yield.

Under an inert atmosphere, Et_3N (43 μL, 0.31 mmol) was added to a solution of hexane-1,6-diyl (2*S*,2'*S*)-bis(2-amino-3,3-dimethylbutanoate)hydrochloric salt (59 mg, 0.14 mmol) in ethanol (3.0 mL) and the mixture was stirred for 10 min. 3-Hydroxy-5,6,7,8-tetrahydronaphthalene-2-carbaldehyde[31] (50 mg, 0.28 mmol) dissolved in benzene (5.0 mL) was added to the reaction mixture. The mixture was then heated at reflux for 3 d. After evaporating the solvent, the triethylamine salt was removed via addition of diethyl ether and vacuum filtration. Removal of remaining solvent afforded the bis-Schiff base product as a yellow solid (72 mg) in 77% yield: ^1H NMR (300 MHz, $CDCl_3$) δ 12.88 (s, 2H), 8.19 (s, 2H), 6.95 (s, 2H), 6.68 (s, 2H), 4.10 (m, 4H), 3.62 (s, 2H), 1.77 (m, 16H), 1.62 (m, 4H), 1.36 (m, 4H), 1.02 (s, 18H).

The bis-Schiff base (72 mg, 0.11 mmol) was redissolved in EtOH (2.0 mL) and $VO(OEt)_3$ (19 μL, 0.11 mmol) was added dropwise. The resultant mixture was stirred for 3 h at room temperature. Removal of the solvent afforded **V3** as a dark blue solid (105 mg) in 99% yield.

(*S,S*)-Vanadium Catalyst V4. Following the above procedure using 3,5-bis-*tert*-butyl-2-hydroxybenzaldehyde, **V4** was obtained as

a dark blue solid (111 mg) in 99% yield. Bis-Schiff Base: ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.52 (s, 2H), 8.28 (s, 2H), 7.40 (s, 2H), 7.10 (s, 2H), 4.11 (m, 4H), 3.64 (s, 2H), 1.62 (m, 4H), 1.43 (s, 18H), 1.36 (m, 4H), 1.29 (s, 18H), 1.05 (s, 18H).

3-(*tert*-Butyl)-2-hydroxy-5-nitrobenzaldehyde. Dry formaldehyde (0.7 g, 23.3 mmol) was added in portions to a mixture of 4-*tert*-butylphenol (1.0 g, 6.66 mmol), Et_3N (2.6 mL, 18.8 mmol) and anhydrous $MgCl_2$ (2.0 g, 20.6 mmol) in THF (50 mL). The mixture was heated at reflux for 8 h, cooled to room temperature, acidified with 3 *N*HCl (70 mL), and extracted with Et_2O (30 mL x 3). The ether layer was washed with water (50 mL) and brine (50 mL) and dried using $MgSO_4$. Removal of solvent and chromatography yielded 3-(*tert*-butyl)-2-hydroxy-benzaldehyde as yellow oil (710 mg, 61% yield). Spectral data matched those reported in the literature.[32]

In a 100 mL round-bottom flask was placed 3-(*tert*-butyl)-2-hydroxy-benzaldehyde (710 mg, 4.0 mmol) in HOAc (12 mL). Nitric acid (4.0 mL, 96 mmol) was added dropwise at 0 °C and the mixture was stirred for 1 h at ambient temperature. The resulting mixture was poured into iced water (100 mL) with vigorous stirring. The orange precipitate formed was filtered through a sintered glass funnel, and then washed with water (10 mL). The product was recrystallized from ethanol to give 360 mg (65% yield) of the product as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.44 (s, 1H), 9.97 (s, 1H), 8.41 (s, 2H), 1.46 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.2, 165.8, 140.7, 140.1, 128.7, 127.0, 119.3, 35.4, 31.4; Spectral data matched that reported in the literature.[33]

(*S*)-Vanadium Catalyst V6. All glassware was flame dried. A mixture of L-*tert*-leucine (45 mg, 0.34 mmol) and 3-*tert*-butyl-5-nitro-2-hydroxybenzaldehyde (76 mg, 0.34 mmol) in MeOH:CH_2Cl_2 (2 mL, 1:1) was heated at reflux and monitored by TLC. The reaction mixture was cooled to room temperature and $VO(OEt)_3$ (69 mg, 0.34 mmol) was added followed by stirring for 3 h under Ar. Removal of solvent afforded the catalyst (147 mg, 99%) as a deep blue solid: HRMS (ESI-TOF) *m/z* = 433.1180 calcd for $C_{18}H_{26}N_2O_7V$ $[M+H]^+$, found 433.1179.

(*S*)-Vanadium Catalyst V8. 3-*tert*-Butyl-5-nitro-2-hydroxybenzaldehyde (300 mg, 1.34 mmol) and L-*tert*-leucine (176 mg, 1.34 mmol) in MeOH:CH_2Cl_2 (7.6 mL, 1:1) were added to an oven-dried round-bottom flask. The resultant mixture was heated at reflux for 3 h. After evaporation of organic solvents, the residual solid was redissolved in CH_2Cl_2 (6.7 mL). $VO(O\textit{i}\text{-}Pr)_3$ (0.32 mL, 1.34 mmol) was introduced to the mixture followed by stirring for 3 h under Ar. Removal of solvent afforded the catalyst (590 mg, 99%) as a deep blue solid: HRMS (ESI-TOF) *m/z* = 461.1493 calcd for $C_{20}H_{30}N_2O_7V$ $[M+H]^+$, found 461.1476.

Racemic coupling with VO(acac)$_2$. Substrate **1a** (30 mg, 0.22 mmol) and $VO(acac)_2$ (29 mg, 0.11 mmol) were dissolved in toluene (1 mL) at room temperature. Oxygen was added *via* an active purge. The resulting deep green solution was stirred for 3 d. The solution was concentrated and chromatographed (5% ethyl acetate in hexane) to yield racemic 3,3',4,4',6,6'-hexamethylbiphenyl-2,2'-diol (**2a**) as a pale-yellow solid (19 mg, 63%). Spectral data matched those reported in the literature.[34]

Asymmetric coupling with catalyst V6: Method A. To a microwave vial was added phenol (1.31 mmol), 20 mol% oxovanadium catalyst **V6** (0.27 mmol), and acetic acid (8.26 mmol). The vial was sealed and toluene (0.5 M) was added. Oxygen was added *via* an active purge. The deep blue reaction solution was stirred for 2 d at 25 °C and then, concentrated. The residue was chromatographed to afford the coupled product.

Asymmetric coupling with catalyst V6: Method B. To a microwave vial was added phenol (1.30 mmol), 20 mol% oxovanadium catalyst **V6** (0.27 mmol), and LiCl (0.52 mmol). The vial was sealed and toluene (0.5 M) was added. Oxygen was added *via an* active purge. The deep blue reaction solution was stirred for 12 h at 0 °C, and then concentrated. The residue was chromatographed to afford the coupled product.

(*S*)-3,3',4,4',6,6'-Hexamethyl-[1,1'-biphenyl]-2,2'-diol (2a). Following **Method A**, the product was obtained as a pale yellow solid (160 mg, 89%) in 83% ee. Crystallization from hexane and ethyl acetate (10:1) afforded white crystals with 95% ee. The absolute axial configuration was determined as *S* from the X-Ray crystal structure: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.74 (s, 2H), 4.74 (s, 2H), 2.29 (s, 6H), 2.17 (s, 6H), 1.92 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.7, 138.5, 135.0, 123.7, 120.3, 116.9, 19.9, 19.1, 11.8; IR (film) 3509, 3460, 2922, 2359, 1560, 1458, 1298, 1079 cm^{-1}; HRMS (ESI-TOF) *m/z* = 270.1620 calcd for $C_{18}H_{22}O_2$ $[M]^+$, found 270.1623. Mp 144.5-145.5 °C. $[\alpha]_D^{22}$ –52.39 (*c* 0.04, 86% ee, CH_2Cl_2); Chiral HPLC: Chiralpak IA column (1% *i*-PrOH/hexanes, 1 mL/min) $t_R(R)$ = 5.09 min, $t_R(S)$ = 6.11 min.

(*S*)-4,4',5,5',6,6'-Hexamethyl-[1,1'-biphenyl]-2,2'-diol (2b). Following **Method A**, using 20 mol% catalyst **V6**, the product was obtained as a white solid (176 mg, 100% conv.) in 10% ee. ^{1}H NMR (300 MHz, $CDCl_3$): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.92 (s, 6H), 2.16 (s, 6H), 2.31 (s, 6H), 4.46 (s, 2H), 6.75 (s, 2H). Spectral data matched that reported in the literature.[35] Chiral HPLC: Chiralpak AS column (1% *i*-PrOH/hexanes, 1 mL/min) $t_R(R)$ = 15.5 min; $t_R(S)$ = 19.0 min.

3,3'-Di-*tert*-butyl-5,5',6,6'-tetramethyl-[1,1'-biphenyl]-2,2'-diol (2c). Following **Method A**, using 20 mol% catalyst **V6**, the product was obtained as a white solid (230 mg, 100% conv.). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40 (s, 18H), 1.82 (s, 6H), 2.26 (s, 6H), 4.80 (s, 2H), 7.13 (s, 2H). Spectral data matched that reported in the literature.[36]

(*S*)-3,3',6,6'-Tetramethyl-[1,1'-biphenyl]-2,2'-diol (2d). Following **Method A**, using 40 mol% catalyst **V6**, the product was obtained as a white solid in 60% ee: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.96 (s, 6H), 2.26 (s, 6H), 4.72 (s, 2H), 6.83 (d, *J* = 7.6, 2H), 7.11 (d, *J* = 7.6, 2H). Spectral data match those reported in the literature.[37] Chiral HPLC: Chiralpak AD column (1% *i*-PrOH/hexanes, 1 mL/min) $t_R(R)$ = 6.3 min; $t_R(S)$ = 7.0 min.

(*S*)-4,4',6,6'-Tetramethyl-[1,1'-biphenyl]-2,2'-diol (2e). Following **Method A**, using 20 mol% catalyst **V6**, the product was obtained as a white solid in 38% ee. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.97 (s, 6H), 2.33 (s, 6H), 4.63 (s, 2H), 6.72 (s, 2H), 6.75 (s, 2H). Spectral data matched that reported in the literature.[38] Chiral HPLC: Chiralpak AS column (25% *i*-PrOH/hexanes, 1 mL/min)

$t_R(R)$ = 9.9 min; $t_R(S)$ = 11.9 min.

(*S*)-4,4'-Dimethoxy-3,3',6,6'-tetramethyl-[1,1'-biphenyl]-2,2'diol (2f). Following **Method B** at 0 °C for 18 h, the *ortho-ortho* product was obtained as a yellow solid (194 mg) in 80% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.46 (s, 2H), 4.80 (s, 2H), 3.86 (s, 6H), 2.12 (s, 6H), 1.97 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.7, 152.9, 136.3, 111.9, 109.9, 104.7, 55.5, 19.7, 8.4; IR (film) 3513, 2921, 1577, 1466, 1326, 1104, 819, 739 cm^{-1}; HRMS (ESI-TOF) *m/z* = 325.1416 calcd for $C_{18}H_{22}O_4Na$ $[M+Na]^+$, found 325.1414. $[\alpha]_D^{22}$ –19.68 (*c* 0.05, 82% ee, $CHCl_3$); Chiral HPLC: Chiralpak IA column (1% *i*-PrOH/hexanes, 1 mL/min) $t_R(R)$ = 7.99 min, $t_R(S)$ = 15.1 min.

(*S*)-3,3',6,6'-Tetramethyl-[1,1'-biphenyl]-2,2',4,4'-tetraol (2g). Following **Method B** at 0 °C for 12 h, the product was obtained as a white solid (144 mg) in 81% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.41 (s, 2H), 4.85 (s, 2H), 4.71 (s, 2H), 2.15 (s, 6H), 1.91 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.2, 153.5, 137.0, 111.7, 109.4, 108.1, 19.5, 8.5; IR (film) 3459, 2925, 1592, 1326, 1078 cm^{-1}; HRMS (ESI-TOF) *m/z* = 273.1127 calcd for $C_{16}H_{17}O_4$ $[M–H]^-$, found 273.1139. $[\alpha]_D^{22}$ –52.39 (*c* 0.04, 86% ee, CH_2Cl_2); Chiral HPLC: Chiralpak IA column (20% *i*-PrOH/hexanes, 1 mL/min) $t_R(S)$ = 4.95 min, $t_R(R)$ = 6.88 min.

4-Methyl-[1,1'-biphenyl]-3,5-diol (1h). Under an N_2 atmosphere, a mixture of 5-bromo-2-methylbenzene-1,3-diol (203 mg, 1.0 mmol), potassium phenyltrifluoroborate (200 mg, 1.1 mmol), $PdCl_2$(dppf)•CH_2Cl_2 (4.0 mg, 0.5 mol %), and Et_3N (0.4 mL, 3.0 mmol) in EtOH (4.0 mL) was stirred at 80 °C for 12 h. After completion as indicated by TLC, the reaction mixture was cooled to room temperature. After removal of the solvent, the residue was diluted with EtOAc (15 mL) and washed with water (15 mL). Removal of the solvent followed by chromatography (20% ethyl acetate in hexane) afforded the product as a yellow solid (110 mg) in 55% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.0 Hz, 2H), 7.41 (t, *J* = 7.0 Hz, 2H), 7.33 (t, *J* = 7.0 Hz, 1H), 6.65 (s, 2H), 4.84 (s, 2H), 2.18 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.9, 140.4, 140.1, 128.7, 127.4, 126.8, 109.4, 106.6, 7.8; IR (film) 3331, 2919, 1590, 1572, 1410, 1076, 848, 762, 694 cm^{-1}; HRMS (ESI-TOF) *m/z* = 201.0916 calcd for $C_{13}H_{13}O_2$ $[M+H]^+$, found 201.0914.

(*S*)-4',5"-Dimethyl-[1,1':2',1":2",1"'-quaterphenyl]-3',4",5',6"-tetraol (2h). Following **Method A** at 0 °C for 18 h, the product was obtained as a yellow solid (26 mg) in 65% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (t, *J* = 7.0 Hz, 2H), 7.02 (t, *J* = 8.0 Hz, 4H), 6.57 (d, *J* = 7.0 Hz, 4H), 6.31 (s, 2H), 5.32 (s, 2H), 4.87 (s, 2H), 2.23 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.0, 153.7, 141.9, 140.0, 128.5, 127.4, 126.5, 110.7, 109.6, 109.4, 8.5; IR (film) 3437, 2920, 1620, 1395, 1342, 1077, 790, 760, 738, 700 cm^{-1}; HRMS (ESI-TOF) *m/z* = 399.1596 calcd for $C_{26}H_{23}O_4$ $[M+H]^+$, found 399.1591; Chiral HPLC: Chiralpak IA column (50 % ee, 25% *i*-PrOH/hexanes, 1 mL/min) $t_R(S)$ = 14.27 min, $t_R(R)$ = 16.97 min.

2-Methyl-5-(oct-1-yn-1-yl)benzene-1,3-diol (1i). $Pd(PPh_3)_2Cl_2$ (561 mg, 0.80 mmol), CuI (152 mg, 0.80 mmol), and 1-octyne (1.2 mL, 8.0 mmol) were added to a flame-dried flask. A solution of 5-iodo-2-methylbenzene-1,3-diol[39] (1.0 g, 4.0 mmol) in DMF (13 mL) was transferred into the flask, followed by Et_2NH under Ar. The resultant mixture was stirred at 70°C for 22 h. After cooling to ambient temperature, the reaction mixture was treated with satd NH_4Cl (10 mL). The mixture was extracted with EtOAc (15 mL X 3) and washed with brine. The organic layer was dried over Na_2SO_4 and filtered. Removal of the solvent followed by chromatography (15% EtOAc in hexane) gave the desired product as a pale yellow solid (867 mg) in 93% yield: ^{1}H NMR (500 MHz, acetone-d_6) δ 8.20 (s, 2H), 6.44 (s, 2H), 2.86 (s, 3H), 2.35 (t, *J* = 7.0 Hz, 2H), 1.55 (m, 2H), 1.44 (m, 2H), 1.30 (m, 4H), 0.89 (t, *J* = 2.0 Hz, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 157.0, 122.4, 112.3, 110.5, 89.0, 81.7, 32.1, 28.6, 28.5, 22.5, 19.6, 14.3, 8.5; IR (film) 3435, 3053, 2931, 2857, 2232, 1772, 1735, 1618, 1583, 1322, 1080, 737 cm^{-1}; HRMS (ESI-TOF) *m/z* = 232.1463 calcd for $C_{15}H_{20}O_2$ $[M]^+$, found 232.1457.

(*S*)-3,3'-Dimethyl-6,6'-di(oct-1-yn-1-yl)-[1,1'-biphenyl]-2,2',4,4'-tetraol (2i). Following **Method B** at 0 °C for 18 h, the product was obtained as a yellow solid (19 mg) in 66% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (s, 2H), 5.01 (s, 2H), 4.84 (s, 2H), 2.16 (s, 6H), 2.16-2.15 (m, 4H), 1.34-1.20 (m, 10H), 1.18-1.12 (m, 6H), 0.87 (t, *J* = 8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.6, 153.5, 123.1, 115.3, 111.2, 110.9, 93.1, 78.3, 31.4, 28.4, 28.1, 22.5, 19.3, 14.1, 8.5; IR (film) 3443, 3304, 3054, 2930, 2306, 1606, 1584, 1395, 1265, 1077, 739 cm^{-1}; HRMS (ESI-TOF) *m/z* = 463.2848 calcd for $C_{30}H_{39}O_4$ $[M+H]^+$, found 463.2841; $[\alpha]_D^{22}$ –50.96 (*c* 0.05, 89% ee, $CHCl_3$); Chiral HPLC: Chiralpak IA column (20% *i*-PrOH/hexanes, 1 mL/min) $t_R(S)$ = 6.76 min, $t_R(R)$ = 16.0 min.

2-Allyl-3,5-dimethylphenol (1j). Allyl bromide (0.2 mL, 2.2 mmol) was added to a solution of 3,5-dimethylphenol (244 mg, 2.0 mmol) and potassium carbonate (304 mg, 2.2 mmol) in DMF (4.0 mL). The reaction mixture was stirred 16 h at room temperature, diluted with ether (15 mL), and quenched with water (10 mL). The organic layer was separated and the aqueous layer was extracted with ether (10 mL x 3). The combined organic layers were dried over Na_2SO_4. The resultant product was used without further purification for the next step.

To a solution of allyl aryl ether from above in CH_2Cl_2 (10 mL) was added BBr_3 (4.0 mL of 1.0 M solution in CH_2Cl_2, 4 mmol) dropwise at –50 °C. After stirring for 2 h at –50 °C, the solution was quenched with water (10 mL), extracted with dichloromethane (15 mL x 3), and dried over $MgSO_4$. The product was chromatographed (5% EtOAc/hexane) to give **1c** (292 mg) as a white solid in 90% yield for 2 steps: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.61 (s, 1H), 6.50 (s, 1H), 5.99- 5.91 (m, 1H), 5.05 (d, *J* = 10.5 Hz, 1H), 5.02 (d, *J* = 17 Hz, 1H), 4.73 (s, 1H), 3.39 (d, *J* = 4.5 Hz, 2H), 2.25 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.9, 137.8, 136.9, 135.8, 123.7, 120.6, 115.3, 114.1, 30.3, 20.9, 19.5; IR (film) 3466, 2921, 1623, 1584, 1458, 1308, 1207, 1138, 1110, 1039, 911, 837 cm^{-1}; HRMS (ESI-TOF) *m/z* = 161.0966 calcd for $C_{11}H_{13}O$ $[M–H]^-$, found 161.0972.

3,5-Dimethyl-2-propylphenol (1k). To a stirring solution of allylated phenol (400 mg, 2.4 mmol) in dry MeOH (4.0 mL) was added Pd/C (10 wt%, 40 mg). The reaction flask was evacuated and backfilled with H_2 (3 times). The reaction was stirred under H_2

atmosphere for 16 h. The reaction mixture was then filtered through Celite and concentrated. The product was chromatographed (5% EtOAc/hexane) to give the product (304 mg, 1.92 mmol) as a white solid in 79% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.59 (s, 1H), 6.46 (s, 1H), 4.57 (s, 1H), 2.56 (t, J = 8.0 Hz, 2H), 2.26 (s, 3H), 2.23 (s, 3H), 1.54 (sextet, J = 8.0 Hz, 2H), 1.00 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.4, 137.6, 136.0, 124.1, 123.6, 113.6, 28.1, 22.5, 20.8, 19.4, 14.4; IR (film) 3476, 2959, 1583, 1454, 1302, 1215, 1140, 1103, 1022, 949 cm^{-1}; HRMS (ESI-TOF) m/z = 163.1123 calcd for $C_{11}H_{15}O$ $[M–H]^-$, found 163.1117.

(*S*)-3,3'-Diallyl-4,4',6,6'-tetramethyl-[1,1'-biphenyl]-2,2'diol (2j). Following **Method A** at room temperature for 3 d, the *ortho-ortho* product was obtained as a white solid (36 mg) in 56% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.76 (s, 2H), 5.99-5.92 (m, 2H), 5.00-4.93 (m, 4H), 4.76 (s, 2H), 3.43 (d, J = 3.5 Hz, 4H), 2.30 (s, 6H), 1.93 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.8, 138.6, 136.0, 135.9, 124.2, 121.9, 117.2, 114.4, 30.6, 19.4, 19.2; IR (film) 3524, 3077, 2922, 1637, 1564, 1457, 1302, 1258, 1191, 1144, 1110, 1050, 995, 909, 851 cm^{-1}; HRMS (ESI-TOF) m/z = 323.2011 calcd for $C_{22}H_{27}O_2$ $[M+H]^+$, found 323.2020; $[\alpha]_D^{22}$ –21.88 (c 0.2, 77% ee, $CHCl_3$); Chiral HPLC: Chiralpak IA column (1% *i*-PrOH/hexanes, 1 mL/min) t_R(*R*) = 5.63 min, t_R(*S*) = 7.19 min.

(*S*)-4,4',6,6'-Tetramethyl-3,3'-dipropyl-[1,1'-biphenyl]-2,2'diol (2k). Following **Method A** at room temperature for 3 d, the *ortho-ortho* product was obtained as a white solid (52 mg) in 80% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.73 (s, 2H), 4.72 (s, 2H), 2.64-2.61 (m, 4H), 2.32 (s, 6H), 1.92 (s, 6H), 1.58-1.53 (m, 4H), 0.99-0.96 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.8, 138.0, 135.2, 125.2, 124.0, 117.1, 28.5, 22.4, 19.4, 19.2, 14.3; IR (film) 3524, 2959, 2871, 1616, 1563, 1453, 1394, 1296, 1260, 1205, 1146, 1103, 1039, 954, 850 cm^{-1}; HRMS (ESI-TOF) m/z = 327.2324 calcd for $C_{22}H_{31}O_2$ $[M+H]$+, found 327.2323; $[\alpha]_D^{22}$ –26.12 (c 0.2, 72% ee, $CHCl_3$); Chiral HPLC: Chiralpak IA column (1% *i*-PrOH/hexanes, 1 mL/min) t_R(*R*) = 4.79 min, t_R(*S*) = 6.24 min.

2-Chloro-5-methoxy-4-methylaniline (7) 4-Amino-5-chloro-2-methoxybenzoic acid (5.00 g, 24.8 mmol) was suspended in chlorobenzene (50 mL) and cooled to 0 °C. Neat BH_3•SMe_2 (7.1 mL, 74.4 mmol) was added with vigorous stirring. When effervescence ceased, the mixture was heated for 3 h at 80 °C and then for 18 h at 130 °C. The reaction was quenched by addition of aqueous Na_2CO_3 (aq) (1 M, 82 mL). The mixture was extracted with CH_2Cl_2 (50 mL X 3), dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure to give a yellow solid. Chromatography (9:1 = hexane/EtOAc) afforded the product as a white powder (2.76 g 65%): ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.90 (s, 1H), 6.40 (s, 1H), 5.05 (s, 2H), 3.68 (s, 3H), 1.96 (s, 3H). Spectra are in accord with those previously reported.[40]

General procedure C: Buchwald-Hartwig *C-N* coupling. A mixture of NaO*t*-Bu (2.8 g, 29.1 mmol), $Pd(OAc)_2$ (52 mg, 0.23 mmol), and $[HP(t\text{-}Bu)_3][BF_4]$ (85 mg, 0.29 mmol) was suspended in toluene (0.17 M). 2-Chloro-5-methoxy-4-methylaniline (1.0 g, 5.83 mmol) and an aryl bromide (5.94 mmol) were added. The reaction mixture was heated at reflux for 18 h. After the resultant mixture was cooled to ambient temperature, the mixture was quenched by addition of 2 M HCl (aq) (35 mL). The mixture was extracted with CH_2Cl_2 (30 mL X 3), dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure. Chromatography afforded the product.

General procedure D: palladium catalyzed cyclization (S-4). Chlorobiphenylaniline (1.89 mmol), K_2CO_3 (783 mg, 5.67 mmol), $Pd(OAc)_2$ (21 mg, 0.09 mmol), and $[HP(t\text{-}Bu)_3][BF_4]$ (55 mg, 0.19 mmol) were combined with DMA (7.6 mL) under an Ar atmosphere. After stirring at 130 °C for 18 h, the mixture was cooled and then quenched by addition of 2 M HCl (aq) (7 mL). The mixture was poured into excess amount of water and extracted with EtOAc (30 mL X 3). The combined organic layers were washed thoroughly with H_2O (2 mL X 5) and brine followed by drying over Na_2SO_4. After filtration and removal of solvent, the compounds was chromatographed.

General procedure E: demethylation. The 2-methoxycarbazole (1.62 mmol) was dissolved in CH_2Cl_2 (23 mL). After cooling to –78 °C, a solution of BBr_3 (1 M in dichloromethane, 3.24 mmol) was added dropwise. The resultant mixture was allowed to warm to room temperature and stirred until completion as judged by TLC (30 min – 18 h). The mixture was subsequently quenched with water (15 mL) under ice bath. The solution was then extracted with EtOAc (30 mL X 3), washed with brine and the combined organic layers were dried over Na_2SO_4. Removal of solvent was followed by chromatography.

General procedure F: protection of carbazole nitrogen. To a stirring solution of DMF (1.4 mL) and NaH (85 mg, 3.55 mmol) was added a solution of 2-hydroxycarbazole (1.42 mmol) in THF (14 mL) at 0 °C. After stirring for 30 minutes at room temperature, BnCl (1.6 mL, 1.56 mmol, 1.0 M in THF) was added to the solution. After stirring for 18 h at 10 °C, the solution was quenched with ice-water (15 mL), extracted with EtOAc (30 mL X 3). After washing the combined organic layers with water (2 mL X 5) and brine, the organic phase was dried with Na_2SO_4. Removal of solvent was followed by chromatography.

General procedure G: asymmetric oxidative 2-hydroxycarbazole coupling. To a microwave vial was added *N*-protected 2-hydroxycarbazole (0.42 mmol), catalyst **V8** (38 mg, 0.08 mmol) and HOAc (0.16 mL, 2.71 mmol). The vial was sealed with a septum and the chlorobenzene (0.84 mL) was added. After degassing and purging with O_2 three times, the vial was sealed with a microwave vial cap and was stirred at 0 °C for 48 h. Upon completion, the reaction mixture was then directly chromatographed using silica gel.

2-Chloro-5-methoxy-4-methyl-*N*-phenylaniline (8a). Following **General Procedure C** for 23 h, the product was obtained as brown oil (1.26 g) in 87% yield. R_f = 0.6 (EtOAc/Hexanes = 1/4): ^{1}H NMR (500 MHz, acetone-d_6) δ 7.30 (t, J = 6.3 Hz, 2H), 7.13-7.10 (m, 3H), 6.99 (s, 1H), 6.8 (s, 1H), 5.94 (s, 1H), 3.71 (s, 3H), 2.13 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 157.1, 143.3, 138.8, 130.7, 129.2, 120.9, 120.0, 118.2, 113.8, 101.3, 55.0, 14.5; IR (neat) 3400, 2925, 2850, 1512, 1200, 605 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{14}H_{15}ClNO$ $[M+H]^+$ 248.0842, found 248.0842.

2-Methoxy-3-methyl-9*H*-carbazole (9a). Following **General Procedure D** for 20 h, the product was obtained as a white solid (342 mg) in 86% yield. Spectral data were in agreement with those

reported.[41]

3-Methyl-9*H*-carbazol-2-ol (10a). Following **General Procedure E** for 23 h, the product was obtained as a white solid (342 mg) in 86% yield. Spectral data were in agreement with those reported.[41]

9-Benzyl-3-methyl-9*H*-carbazol-2-ol (4a). Following **General Procedure F** for 24 h, the product was obtained as an off-white powder (72 mg) in 52% yield. Spectral data were in agreement with those reported.[41]

3,9-Dimethyl-9*H*-carbazol-2-ol (4b). Following **General Procedure F** using a 1.0 M solution of MeI in THF (0.067 mL) for 2 h, the product was obtained as a brown solid (10 mg) in 23% yield. R_f = 0.4 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.29 (s, 1H), 7.94 (d, J = 7.5 Hz, 1H), 7.80 (s, 1H) 7.39 (d, J = 8.0 Hz, 1H), 7.30 (dt, J = 7.5, 1.0 Hz, 1H), 7.10 (dt, J = 8.0, 0.5 Hz, 1H), 6.89 (s, 1H), 3.76 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 155.9, 142.1, 141.8, 124.6, 124.0, 122.4, 119.7, 119.3, 117.6, 116.4, 109.1, 95.2, 29.2, 16.6; IR (neat) 3391, 2922, 2853, 1634, 1604, 815, 740, 719, 621 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{14}H_{14}NO$ $[M+H]^+$ 212.1075, Found 212.1083.

9-Allyl-3-methyl-9*H*-carbazol-2-ol (4c). Following **General Procedure F**, the product was obtained as a colorless solid (71 mg) in 43% yield. R_f = 0.47 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 7.7 Hz, 1H), 7.82 (s, 1H), 7.37 (td, J = 8.2, 1.1 Hz, 1H), 7.31 (d, J = 8.1 Hz, 1H), 7.20 (td, J = 7.8, 0.9 Hz, 1H), 6.79 (s, 1H), 6.00-5.93 (m, 1H), 5.16 (dd, J = 10.3, 1.3 Hz, 1H), 5.04 (dd, J = 17.1, 1.2 Hz, 1H), 4.85 (s, 1H), 4.81-4.80 (m, 2H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.3, 140.6, 132.4, 124.4, 123.2, 122.0, 119.5, 119.1, 117.0, 116.9, 115.9, 108.6, 95.1, 45.5, 16.2; IR (neat) 3350, 2918, 1633, 1604, 1495, 1461, 1326, 1251, 1183, 1141, 1120, 1022, 923, 808, 744, 721 cm^{-1}; HRMS (EI-TOF) calcd for $C_{16}H_{15}NO$ $[M]^+$ m/z = 237.1154; found 237.1152.

9-Isopropyl-3-methyl-9*H*-carbazol-2-ol (4d). Following **General Procedure F**, the product was obtained as a white solid (65 mg) in 39% yield. R_f = 0.43 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, J = 7.7 Hz, 1H), 7.81 (s, 1H), 7.45 (d, J = 8.3 Hz, 1H), 7.35 (td, J = 8.2, 1.2 Hz, 1H), 7.17 (td, J = 7.8, 0.8 Hz, 1H), 6.95 (s, 1H), 4.91-4.84 (m, 1H), 4.82 (s, 1H), 2.42 (s, 3H), 1.67 (d, J = 7.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.8, 139.7, 139.4, 124.0, 123.5, 121.9, 119.5, 118.6, 117.5, 115.4, 109.7, 96.4, 46.8, 20.8, 16.1; IR (neat) 3383, 2972, 2917, 2849, 1635, 1602, 1459, 1350, 1223, 1101, 996, 1879, 721 cm^{-1}; HRMS (EI-TOF) calcd for $C_{16}H_{17}NO$ $[M]^+$ m/z = 239.1310; found 239.1321.

3-Methyl-9-(2,4,6-trimethylbenzyl)-9*H*-carbazol-2-ol (4e). Following **General Procedure F** using 2,4,6-trimethylbenzylchloride (0.117 g, 0.70 mmol), the product was obtained as a white solid (92 mg) in 40% yield. R_f = 0.4 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, J = 7.7 Hz, 1H), 7.79 (s, 1H), 7.25 (td, J = 8.3, 1.2 Hz, 1H), 7.15 (td, J = 7.9, 0.8 Hz, 1H), 7.09 (d, J = 8.2 Hz, 1H), 6.89 (s, 2H), 6.50 (s, 1H), 5.34 (s, 2H), 4.69 (s, 1H), 2.38 (s, 3H), 2.30 (s, 3H), 2.18 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.0, 140.9, 140.8, 137.7, 137.6, 129.9, 129.6, 124.3, 123.3, 121.8, 119.3, 118.9, 117.1, 115.8, 109.2, 95.7, 43.3, 21.1, 20.5, 16.2; IR (neat) 3241, 2954, 1604, 1460, 1300, 1188, 742 cm^{-1}; HRMS (EI-TOF) calcd for $C_{23}H_{23}NO$ $[M]^+$ m/z = 329.1780; found 329.1798.

2-Chloro-*N*-(4-fluorophenyl)-5-methoxy-4-methylaniline (8f). Following **General Procedure C**, the product was obtained as brown oil (1.55 g) in 99% yield. R_f = 0.65 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 7.20-7.17 (m, 2H), 7.12 (s, 1H), 7.07-7.04 (m, 2H), 6.83 (s, 1H), 6.78 (s, 1H), 3.72 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 158.0 (d, J = 238 Hz), 157.2, 139.54 (d, J = 2.1 Hz), 139.5, 130.9 (d, J = 1.8 Hz), 121.0 (d, J = 8.2 Hz), 119.6, 115.7 (d, J = 22.0 Hz), 113.2, 100.5 (d J = 3.9 Hz), 55.1, 14.6; IR (neat) 3420, 2925, 1609, 1200, 602, cm^{-1}; HRMS (ESI-TOF) calcd for $C_{14}H_{14}ClFNO$ $[M+H]^+$ 266.0748, found 266.0743.

6-Fluoro-2-methoxy-3-methyl-9*H*-carbazole (9f). Following **General Procedure D**, the product was obtained as a yellow solid (104 mg) in 72% yield. R_f = 0.20 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 10.08 (s, 1H), 7.81 (s, 1H), 7.69 (dd, J = 9.3, 2.5 Hz, 1H), 7.40 (dd, J = 8.8, 4.4 Hz, 1H), 7.04 (td, J = 9.4, 2.4 Hz, 1H), 7.01 (s, 1H), 3.89 (s, 3H), 2.30 (3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 157.9, 157.3 (d, J = 233 Hz), 141.2, 136.3, 123.9 (d, J = 10.1 Hz), 121.4, 118.5, 115.7 (d, J = 3.8 Hz), 111.1, 111.0 (d, J = 15.1 Hz), 104.4 (d, J = 23.9 Hz), 92.6, 54.9, 16.0; IR (neat) 3395, 2910, 1486, 847, 822, 803, 783, cm^{-1}; HRMS (ESI-TOF) calcd for $C_{14}H_{13}FNO$ $[M+H]^+$ 230.0981, Found 230.0986.

6-Fluoro-3-methyl-9*H*-carbazol-2-ol (10f). Following **General Procedure E**, the product was obtained as a brown solid (166 mg) in 90% yield. R_f = 0.20 (EtOAc:Hexanes = 1:2): ^{1}H NMR (500 MHz, acetone-d_6) δ 9.94 (s, 1H), 8.34 (s, 1H), 7.78 (s, 1H), 7.66 (dd, J = 9.5, 2.6 Hz, 1H), 7.35 (dd, J = 8.8, 4.5 Hz, 1H), 7.01 (td, J = 9.0, 2.5 Hz, 1H), 6.97 (s, 1H), 2.35 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 157.0 (d, J = 233 Hz), 155.3, 141.3, 136.3, 124.2 (d, J = 10.1 Hz), 121.6, 117.2, 115.8 (d, J = 3.8 Hz), 110.9, 110.7 (d, J = 14.8 Hz), 104.4 (d, J = 23.9 Hz), 96.2, 15.8; IR (neat) 3406, 2919, 1485, 1406, 1257, 1146, 1013, 600 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{13}H_9NOF$ $[M-H]^+$ 214.0668, Found 214.0672.

9-Benzyl-6-fluoro-3-methyl-9*H*-carbazol-2-ol (4f). Following **General Procedure F**, the product was obtained as a yellow solid (193 mg) in 81% yield. R_f = 0.35 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.40 (s, 1H), 7.85 (s, 1H), 7.73 (dd, J = 9.0, 5.0 Hz, 1H), 7.41 (dd, J = 10.0, 5.0 Hz, 1H), 7.28-7.19 (m, 3H), 7.15-7.13 (m, 2H), 7.05 (td, J = 10.0, 1.0 Hz, 1H), 6.89 (s, 1H), 5.50 (s, 2H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 157.4 (d, J = 233 Hz), 155.6, 141.7, 137.9, 137.0, 128.6, 127.2, 126.5, 123.9, (d, J = 10.6 Hz), 122.0, 117.5, 115.3, 110.9 (d, J = 25.6 Hz), 109.3 (d, J = 9.3 Hz), 104.6 (d, J = 24.3 Hz), 94.9, 46.1, 15.7; IR (neat) 3301, 2922, 2851, 1633, 862, 828, 791, 729, 696, 626 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{20}H_{17}FNO$ $[M+H]^+$ 306.1494 Found: 306.1497.

2-Chloro-*N*-(3-fluorophenyl)-5-methoxy-4-methylaniline (8g). Following **General Procedure C**, the product was obtained as brown oil (826 mg) in 65% yield. R_f = 0.78 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 7.24 (dd, J = 15.0, 8.0 Hz, 1H), 7.18 (s, 1H), 7.11 (br s, 1H), 6.95 (s, 1H), 6.90 (dd, J = 8.0, 2.0 Hz,

1H), 6.80 (dt, *J* = 11.5, 2.5 Hz, 1H), 6.58 (td, *J* = 8.0, 2.5 Hz, 1H), 3.79 (s, 3H), 2.13 (s, 3H); ^{13}C NMR (125 MHz, acetone-*d*$_6$) δ 163.8 (d, *J* = 243 Hz), 156.9, 144.6 (d, *J* = 10.0 Hz), 137.1, 131.0, 130.6 (d, *J* = 10.0 Hz), 121.3, 114.2, 113.6 (d, *J* = 2.5 Hz), 108.0 (d, *J* = 21.3 Hz), 104.7 (d, *J* = 25.0 Hz), 101.3, 55.7, 15.4; IR (neat) 3405, 2920, 2851, 1604, 1582, 1518, 834, 815, 776, 767, 678, 615 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{14}H_{14}FClNO$ $[M+H]^+$ 266.0748, found 266.0740.

7-Fluoro-2-methoxy-3-methyl-9*H*-carbazole (9g). Following **General Procedure D**, the product was obtained as a yellow solid (60 mg) in 5% yield. R_f = 0.10 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-*d*$_6$) δ 10.18 (s, 1H), 7.92 (dd, *J* = 8.6, 5.5 Hz, 1H), 7.78 (s, 1H), 7.15 (dd, *J* = 10.0, 2.4 Hz, 1H), 7.03 (s, 1H), 6.90-6.86 (m, 1H), 3.89 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (125 MHz, acetone-*d*$_6$) δ 158.7 (d, *J* = 245 Hz), 158.5, 143.2 (d, *J* = 11.0 Hz), 140.6, 125.4 (d, *J* = 8.2 Hz), 124.0 (d, *J* = 2.9 Hz), 120.0, 114.0, 112.3, 107.6 (d, *J* = 3.5 Hz), 105.0 (d, *J* = 19.1 Hz), 93.5, 55.8, 16.8; IR (neat) 3396, 2921, 1611, 841, 808, 742 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{14}H_{11}FNO$ $[M-H]^-$ 228.0825, Found 228.0822.

7-Fluoro-3-methyl-9*H*-carbazol-2-ol (10g). Following **General Procedure E**, the product was obtained as a brown solid (69 mg) in 99% yield. R_f = 0.20 (EtOAc:Hexanes = 1:2): ^{1}H NMR (500 MHz, acetone-*d*$_6$) δ 10.06 (s, 1H), 8.26, (s, 1H), 7.89 (dd, *J* = 8.5, 5.5 Hz, 1H), 7.74 (s, 1H), 7.11 (dd, *J* = 10.5, 2.5 Hz, 1H), 6.96 (s, 1H), 6.88-6.84 (m, 1H) 2.33 (s, 3H); ^{13}C NMR (125 MHz, acetone-*d*$_6$) δ 161.0 (d, *J* = 235 Hz), 154.6, 140.6 (d, *J* = 14.8 Hz), 140.6, 121.2, 120.3, 119.7 (d, *J* = 10.5 Hz), 117.4, 115.7, 106.2 (d, *J* = 24.1 Hz), 97.0 (d, *J* = 26.3 Hz), 96.5, 15.9; IR (neat) 3406, 2920, 1486, 1293, 834, 820, 810, 781, 600, cm^{-1}; HRMS (ESI-TOF) calcd for $C_{13}H_9FNO$ $[M-H]^-$ 214.0668, Found: 214.0669.

9-Benzyl-7-fluoro-3-methyl-9*H*-carbazol-2-ol (4g). Following **General Procedure F**, the product was obtained as a yellow solid (57 mg) in 83% yield. R_f = 0.17 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-*d*$_6$) δ 8.38 (s, 1H), 7.84 (s, 1H), 7.28-7.19 (m, 5H), 7.14 (d, *J* = 7.0 Hz, 2H), 6.91 (s, 1H), 6.84 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H), 5.50 (s, 2H), 2.33 (s, 3H); ^{13}C NMR (125 MHz, acetone-*d*$_6$) δ 157.6 (d, *J* = 245 Hz), 155.0, 143.0, 140.3, 137.5, 128.5, 127.2, 126.4, 124.5 (d, *J* = 8.3 Hz), 123.7 (d, *J* = 3.0 Hz), 117.9, 112.8, 111.0, (d, *J* = 21.0 Hz), 104.9, 104.4 (d, *J* = 19.3 Hz), 94.3, 46.2, 15.5; IR (neat) 3456, 3370, 2918, 1470, 883, 776, 741, 715, 702, 693 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{20}H_{15}FNO$ $[M-H]^-$ 304.0876 Found: 304.0875.

2-Chloro-*N*-(2-fluorophenyl)-5-methoxy-4-methylaniline (8h). Following **General Procedure C** for 20 h, the product was obtained as brown oil (398 mg) in 64% yield. Spectral data were in agreement with those reported.[42]

1-Fluoro-7-methoxy-6-methyl-9*H*-carbazole (9h). Following **General Procedure D** for 20 h, the product was obtained as a light brown solid (313 mg) in 91% yield. Spectral data were in agreement with those reported.[42]

8-Fluoro-3-methyl-9*H*-carbazol-2-ol (10h). Following **General Procedure E**, the product was obtained as a brown solid (200 mg) in 69% yield. R_f = 0.38 (EtOAc:Hexanes = 1:2): ^{1}H NMR (500 MHz, acetone-*d*$_6$) δ 10.28 (br s, 1H), 8.43 (s, 1H), 7.80 (s, 1H), 7.75-7.74 (m, 1H), 7.06-7.03 (m, 3H), 2.37 (s, 3H); ^{13}C NMR (125 MHz, acetone-*d*$_6$) δ 156.3, 149.8 (d, *J* = 240.5 Hz), 141.2, 128.3 (d, *J* = 6.0 Hz), 128.1, 122.4 (d, *J* = 4.0 Hz), 119.6 (d, *J* = 5.9 Hz), 118.6, 116.8 (d, *J* = 2.6 Hz), 115.6, 109.6 (d, *J* = 16.6 Hz), 97.4, 16.7; IR (neat) 3540, 3404, 2911, 1623, 1576, 1475, 1450, 1429, 1299, 1290, 1262, 1237, 1219, 1200, 1174, 1157, 1137, 1057, 1050, 833 cm^{-1}; HRMS (EI-TOF) calcd for $C_{13}H_{10}FNO$ $[M]^+$ m/z = 215.0746, found 215.0758.

9-Benzyl-8-fluoro-3-methyl-9*H*-carbazol-2-ol (4h). Following **General Procedure F**, the product was obtained as a yellow solid (55 mg) in 28% yield. R_f = 0.65 (EtOAc:Hexanes = 1:2): ^{1}H NMR (500 MHz, acetone-*d*$_6$) δ 8.49 (br s, 1H), 7.86 (s, 1H), 7.81 (d, *J* = 7.5 Hz, 1H), 7.27 (t, *J* = 7.0 Hz, 2H), 7.22 (t, *J* = 7.2 Hz, 1H), 7.15 (d, *J* = 7.2 Hz, 2H), 7.11-7.02 (m, 2H), 6.93 (s, 1H), 5.65 (s, 2H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, acetone-*d*$_6$) δ 156.5, 150.2 (d, *J* = 241.5 Hz), 142.1, 139.4, 129.5, 129.4, 128.3 (d, *J* = 5.0 Hz), 128.0, 127.1, 122.6, 120.1 (d, *J* = 6.3 Hz), 119.0, 116.6, 115.9 (d, *J* = 3.8 Hz), 110.8 (d, *J* = 18.9 Hz), 95.9, 49.0, 16.6; IR (neat) 3310, 2918, 1577, 1472, 1454, 1423, 1347, 1296, 1235, 1219, 1186, 1137, 1105, 1058, 1000, 819 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{20}H_{17}FNO$ $[M+H]^+$ *m/z* = 306.1294, found 306.1314.

2-Chloro-5-methoxy-4-methyl-*N*-(4-(trifluoromethyl)phenyl)aniline (8i). Following **General Procedure C** using $Pd_2(dba)_3$ as the catalyst at room temperature for 10 min, the product was obtained as a white solid (252 mg) in 45% yield. R_f = 0.57 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.5 Hz, 2H), 7.18 (s, 1H), 7.10 (d, *J* = 8.5 Hz, 2H), 6.89 (s, 1H), 6.08 (br s, 1H), 3.78 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.0, 146.3, 136.4, 131.2, 126.9, 124.6 (q, *J* = 271 Hz), 122.6 (q, *J* = 32.7 Hz), 122.5, 116.4, 115.5, 102.6, 55.7, 15.5; IR (neat) 3400, 2925, 1604, 1525, 1509, 1481, 1450, 1395, 1323, 1289, 1244, 1201, 1186, 1159, 1103, 1066, 990, 946, 873 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{15}H_{14}ClF_3NO$ $[M+H]^+$ *m/z* = 316.0716, found 316.0742.

2-methoxy-3-methyl-6-(trifluoromethyl)-9*H*-carbazole (9i) Following **General Procedure D** for 48 h, the product was obtained as a light brown solid (94 mg) in 84% yield. R_f = 0.44 (EtOAc:Hexanes = 1:2): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.87 (br s, 1H), 7.81 (s, 1H), 7.55 (d, *J* = 8.5 Hz, 1H), 7.30 (d, *J* = 8.5 Hz, 1H), 6.72 (s, 1H), 3.87 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.2, 140.7, 139.8, 125.5 (q, *J* = 271 Hz), 123.2, 121.8, 121.7 (q, *J* = 31.8 Hz), 121.0, 120.5, 116.8, 115.6, 110.3, 92.5, 55.6, 16.8; IR (neat) 3360, 2915, 1614, 1458, 1334, 1297, 1261, 1230, 1197, 1164, 1145, 1112, 1095, 1051, 1039, 1015, 978, 880, 819 cm^{-1}; HRMS (EI-TOF) calcd for $C_{15}H_{12}F_3NO$ $[M]^+$ *m/z* = 279.0871, found 279.0877.

3-Methyl-6-(trifluoromethyl)-9*H*-carbazol-2-ol (10i). Following **General Procedure E**, the product was obtained as a light tan solid (98 mg) in 71% yield. R_f = 0.29 (EtOAc:Hexanes = 1:1): ^{1}H NMR (500 MHz, acetone-*d*$_6$) δ 10.36 (br s, 1H), 8.44 (s, 1H), 8.31 (s, 1H), 7.95 (s, 1H), 7.57-7.53 (m, 2H), 7.04 (s, 1H), 2.37 (s, 3H); ^{13}C NMR (125 MHz, acetone-*d*$_6$) δ 156.5, 142.5, 141.7, 126.7 (q, *J* = 270 Hz), 124.2, 122.7, 121.1 (q, *J* = 3.8 Hz), 121.0 (q, *J* = 31.4

Hz), 119.0, 117.1 (q, J = 3.8 Hz), 116.3, 111.4, 97.3, 16.7; IR (neat) 3412, 3270, 2925, 1641, 1616, 1414, 1330, 1298, 1255, 1225, 1210, 1194, 1169, 1156, 1137, 1108, 1052, 1015, 883 cm^{-1}; HRMS (EI-TOF) calcd for $C_{14}H_{10}F_3NO$ $[M]^+$ m/z = 265.0714, found 265.0714.

9-Benzyl-3-methyl-6-(trifluoromethyl)-9*H*-carbazol-2-ol (4i). Following **General Procedure F**, the product was obtained as a white powder (24 mg) in 29% yield. R_f = 0.50 (EtOAc:Hexanes = 1:2): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.52 (s, 1H), 8.37 (s, 1H), 8.01 (s, 1H), 7.64-7.58 (m, 2H), 7.30-7.24 (m, 3H), 7.17 (d, J = 7.0 Hz, 2H), 6.97 (s, 1H), 5.58 (s, 2H), 2.37 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 156.7, 143.0, 142.4, 138.3, 129.5, 128.2, 127.4, 126.6 (q, J = 270 Hz), 124.0, 123.0, 121.4 (q, J = 3.6 Hz), 121.3 (q, J = 31.7 Hz), 119.4, 117.2 (q, J = 4.3 Hz), 116.0, 109.8, 96.1, 47.0, 16.6; IR (neat) 3350, 2923, 1613, 1453, 1371, 1330, 1301, 1260, 1213, 1175, 1158, 1141, 1103, 1068, 1044, 1013, 963, 882 cm^{-1}; HRMS (EI-TOF) calcd for $C_{21}H_{16}F_3NO$ $[M]^+$ m/z = 355.1184, found 355.1175.

2-Chloro-5-methoxy-4-methyl-*N*-(3-(trifluoromethyl)phenyl)aniline (8j). Following **General Procedure C** using $Pd_2(dba)_3$ as the catalyst at room temperature for 10 min, the product was obtained as a yellow oil (677 mg) in 92% yield. R_f = 0.69 (EtOAc:Hexanes = 1:5): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.36 (m, 2H), 7.23-7.19 (m, 2 H), 7.15 (s, 1H), 6.81 (s, 1H), 6.03 (s, 1H), 3.74 (s, 3H), 2.16 (s, 3H); IR (neat) 3405, 2940, 1607, 1598, 1518, 1496, 1466, 1447, 1434, 1398, 1332, 1320, 1236, 1200, 1162, 1120, 1098, 1069, 1000, 875, 789, 697 cm^{-1}; HRMS (ESI-TOF) m/z = 315.0638 calcd for $C_{15}H_{13}ClF_3NO$ $[M]^+$, found 315.0627.

2-Methoxy-3-methyl-7-(trifluoromethyl)-9*H*-carbazole (9j). Following **General Procedure D** for 24 h, the product was obtained as a light tan solid (295 mg) in 67% yield. R_f = 0.10 (EtOAc:Hexanes = 1:6): ^{1}H NMR (500 MHz, acetone-d_6) δ 10.43 (br s, 1H), 8.13 (d, J = 8.2 Hz, 1H), 7.91 (s, 1H), 7.77 (s, 1H), 7.41 (d, J = 8.1 Hz, 1H), 7.10 (s, 1H), 3.93 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 159.6, 142.3, 139.9, 127.2, 126.5 (q, J = 269 Hz), 125.8 (q, J = 31.0 Hz), 122.7, 120.5, 120.4, 116.1 (q, J = 4.0 Hz), 116.0, 108.6, (q, J = 4.0 Hz), 93.7, 56.0, 17.0; IR (neat) 3395, 2935, 1630, 1478, 1448, 1332, 1323, 1293, 1217, 1197, 1163, 1146, 1114, 1070, 1057, 1035, 1002, 920, 874, 821, 791, 666 cm^{-1}; HRMS (ESI-TOF) m/z = 279.0871 calcd for $C_{15}H_{12}F_3NO$ $[M]^+$, found 279.0866

3-Methyl-7-(trifluoromethyl)-9*H*-carbazol-2-ol (10j). Following **General Procedure E**, the product was obtained as a tan solid (144 mg) in 68% yield. R_f = 0.15 (EtOAc:Hexanes = 1:5): ^{1}H NMR (500 MHz, acetone-d_6) δ 10.31 (br s, 1H), 8.52 (s, 1H), 8.11 (d, J = 8.1 Hz), 7.89 (s, 1H), 7.73 (s, 1H), 7.40 (d, J = 8.0 Hz, 1H), 7.03, (s, 1H), 2.36 (s, 3H); IR (neat) 3505, 3380, 2920, 1635, 1620, 1473, 1451, 1433, 1351, 1322, 1302, 1285, 1217, 1161, 1115, 1056, 1010 917, 873, 843, 822, 727, 669 cm^{-1}; HRMS (ESI-TOF) m/z = 265.0714 calcd for $C_{14}H_{10}F_3NO$ $[M]^+$, found 265.0726.

9-Benzyl-3-methyl-7-(trifluoromethyl)-9*H*-carbazol-2-ol (4j). Following **General Procedure F**, the product was obtained as a white solid (77 mg) in 58% yield. R_f = 0.28 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.60 (s, 1H), 8.18 (d, J = 8.2 Hz, 1H), 7.96 (s, 1H), 7.83 (s, 1H), 7.45 (d, J = 8.1 Hz, 1H), 7.30-7.24 (m, 3H), 7.16 (d, J = 7.1 Hz, 2H), 6.96 (s, 1H), 5.63 (s, 2H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 156.3, 142.0, 139.8, 137.5, 128.7, 127.3, 126.5, 126.2, 125.5 (q, J = 269 Hz), 125.1 (q, J = 31.0 Hz), 122.4, 119.4, 118.5, 115.3 (q, J = 4.0 Hz), 114.7, 105.8 (q, J = 4.0 Hz), 95.1, 46.1, 15.7; IR (neat) 3345(w), 2915, 1640, 1453, 1370, 1317, 1296, 1262, 1248, 1214, 1168, 1142, 1132, 1116, 1063, 1042, 1011, 887, 858, 821, 702, 665, 653 cm^{-1}; HRMS (ESI-TOF) m/z = 356.1262 calcd for $C_{21}H_{17}F_3NO$ $[M+H]^+$, found 356.1247.

(4-((2-Chloro-5-methoxy-4-methylphenyl)amino)phenyl)(phenyl)methanone (8k). Following **General Procedure C** using $Pd_2(dba)_3$ (4 mol %) as a catalyst at room temperature for 20 min, the product was obtained as a brown solid (497 mg) in 81% yield. R_f = 0.44 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, J = 8.5 Hz, 2H), 7.77 (d, J = 7.0 Hz, 2H), 7.55 (t, J = 7.5 Hz, 1H), 7.46 (t, J = 8.0 Hz, 2H), 7.16 (s, 1H), 7.05 (d, J = 6.5 Hz, 2H), 6.92 (s, 1H), 6.31 (s, 1H), 3.76 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.2, 156.8, 147.5, 138.5, 135.7, 132.6, 131.7, 131.1, 129.6, 129.3, 128.2, 122.9, 116.0, 115.1, 103.3, 55.7, 15.6; IR (neat) 3360, 3000, 2949, 1584, 1574, 1516, 1500, 1480, 1465, 1443, 1394, 1309, 1282, 1249, 1201, 1174, 1165, 1143, 837 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{21}H_{19}ClNO_2$ $[M+H]^+$ m/z = 352.1104, found 352.1100.

(7-Methoxy-6-methyl-9*H*-carbazol-3-yl)(phenyl)methanone (9k). Following **General Procedure D** for 23 h, the product was obtained as a brown solid (288 mg) in 65% yield. R_f = 0.19 (EtOAc:Hexanes = 1:2): ^{1}H NMR (500 MHz, DMF-d_7) δ 11.55 (br s, 1H), 8.53 (s, 1H), 7.99 (s, 1H), 7.84 (d, J = 8.4 Hz, 3H), 7.70 (t, J = 7.4 Hz, 1H), 7.63-7.60 (m, 3H), 7.15 (s, 1H), 3.96 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (125 MHz, DMF-d_7) δ 196.0, 158.2, 143.1, 141.2, 139.6, 131.9, 129.8, 128.6, 128.5, 126.6, 123.1, 122.7, 121.9, 119.4, 116.1, 110.6, 93.4, 55.5, 16.3; IR (neat) 3300, 2910, 1629, 1599, 1565, 1473, 1332, 1312, 1282, 1247, 1195, 1147, 1131, 1036, 1001, 876, 825 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{21}H_{18}NO_2$ $[M+H]^+$ m/z = 316.1338, found 316.1347.

(9-Benzyl-7-methoxy-6-methyl-9*H*-carbazol-3-yl)(phenyl)methanone (11k). Following **General Procedure F** at room temperature for 22 h, the product was obtained as a pale yellow solid (206 mg) in 80% yield. R_f = 0.80 (EtOAc:Hexanes = 1:1): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.51 (s, 1H), 7.97 (s, 1H), 7.84 (dd, J = 8.6, 1.6 Hz, 1H), 7.81 (dd, J = 8.1, 1.5 Hz, 2H), 7.64-7.54 (m, 4H), 7.31-7.24 (m, 6H), 5.72 (s, 2H), 3.91 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 196.2, 159.1, 143.7, 142.4, 140.1, 138.4, 132.3, 130.4, 129.6, 129.5, 129.0, 128.2, 127.6, 127.3, 123.6, 123.1, 122.6, 120.6, 116.5, 109.6, 92.6, 56.0, 47.0, 16.8; IR (neat) 2925, 1649, 1630, 1600, 1452, 1356, 1310, 1283, 1254, 1194, 1174, 1161, 1140, 877 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{28}H_{24}NO_2$ $[M+H]^+$ m/z = 406.1807, found 406.1792.

(9-Benzyl-7-hydroxy-6-methyl-9*H*-carbazol-3-yl)(phenyl)methanone (4k). Following **General Procedure E** at room temperature for 45 min, the product was obtained as an off-white powder (97 mg) in quantitative yield. R_f = 0.34 (EtOAc:Hexanes = 1:2): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.48 (d, J = 3.9 Hz, 2H), 7.94 (s, 1H), 7.84 (dd, J = 8.5, 1.6 Hz, 1H), 7.81

(d, J = 7.0 Hz, 2H), 7.65 (t, J = 7.5 Hz, 1H), 7.61-7.55 (m, 3H), 7.32-7.25 (m, 3H), 7.21 (d, J = 7.0 Hz, 2 H), 6.98 (s, 1H), 5.61 (s, 2H), 2.35 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 196.2, 156.5, 144.0, 142.3, 140.2, 138.3, 132.3, 130.4, 129.6, 129.5, 129.1, 128.3, 127.5, 127.4, 123.8, 122.98, 122.97, 119.3, 116.6, 109.2, 96.3, 47.1, 16.6; IR (neat) 3381, 2924, 2854, 1649, 1597, 1449, 1414, 1318, 1281, 1251, 1183, 1136, 1072, 1028, 1002, 948 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{27}H_{22}NO_2$ $[M+H]^+$ m/z = 392.1651, found 392.1664.

4-((2-Chloro-5-methoxy-4-methylphenyl)amino)benzonitrile (8l). Following **General Procedure C** using $Pd_2(dba)_3$ as a catalyst at room temperature for 10 min, the product was obtained as a yellow powder (412 mg) in 86% yield. R_f = 0.41 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, J = 8.5 Hz, 2H), 7.17 (s, 1H), 6.99 (d, J = 8.5 Hz, 2H), 6.83 (s, 1H), 6.11 (br s, 1H), 3.77 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.0, 147.5, 135.1, 133.9, 131.3, 124.0, 119.7, 116.9, 115.8, 104.1, 102.6, 55.8, 15.7; IR (neat) 3402, 2925, 2217, 1599, 1506, 1469, 1455, 1441, 1396, 1372, 1333, 1299, 1283, 1251, 1202, 1169, 985, 868, 815 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{15}H_{13}ClN_2O$ $[M]^+$ m/z = 272.0716, found 272.0706.

7-Methoxy-6-methyl-9*H*-carbazole-3-carbonitrile (9l). Following **General Procedure D** for 48 h, the product was obtained as a light brown powder (249 mg) in 78% yield. R_f = 0.33 (EtOAc:Hexanes = 1:2): ^{1}H NMR (500 MHz, acetone-d_6) δ 10.62 (br s, 1H), 8.38 (s, 1H), 7.93 (s, 1H), 7.57 (s, 2H), 7.09 (s, 1H), 3.92 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 159.3, 142.5, 141.4, 127.8, 124.6, 124.4, 122.4, 121.2, 120.8, 115.7, 112.2, 102.2, 93.7, 55.8, 16.8; IR (neat) 3311, 2910, 2217, 1609, 1466, 1444, 1323, 1297, 1272, 1234, 1200, 1160, 1136, 1118, 1039, 1003, 862, 806 cm^{-1}; HRMS (EI-TOF) calcd for $C_{15}H_{12}N_2O$ $[M]^+$ m/z = 236.0950, found 236.0964.

9-Benzyl-7-methoxy-6-methyl-9*H*-carbazole-3-carbonitrile (11l). Following **General Procedure F** at room temperature for 22 h, the product was obtained as a yellow solid (249 mg) in 90% yield. R_f = 0.63 (EtOAc:Hexanes = 1:2): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.46 (s, 1H), 8.02 (s, 1H), 7.64-7.60 (m, 2H), 7.30-7.20 (m, 6H), 5.72 (s, 2H), 3.92 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 159.6, 142.9, 142.4, 138.1, 129.6, 128.3, 128.0, 127.6, 124.7, 124.3, 122.8, 121.1, 121.0, 115.5, 110.8, 102.5, 92.7, 56.1, 47.0, 16.8; IR (neat) 2923, 2852, 2211, 1632, 1602, 1487, 1469, 1455, 1352, 1326, 1255, 1198, 1171, 1141, 1051, 1039, 873 cm^{-1}; HRMS (EI-TOF) calcd for $C_{22}H_{18}N_2O$ $[M]^+$ m/z = 326.1419, found 326.1436.

9-Benzyl-7-methoxy-6-methyl-9H-carbazole-3-carboxylic acid (19). To a solution of **11l** (90 mg, 0.28 mmol) in EtOH (1.0 mL) and H_2O (0.5 mL) was added NaOH (276 mg, 6.89 mmol). The reaction mixture was refluxed overnight and then cooled to room temperature. EtOH was removed under reduced pressure, and the resultant aqueous mixture was acidified at 0 °C with 2 M HCl (3.5 mL). The resultant insoluble solid was filtered, washed with water (20 mL X 2), and dried to give the product as a white solid (95 mg) in quantitative yield. R_f = 0.20 (EtOAc:Hexanes = 1:2): ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.50 (br s, 1H), 8.64 (d, J = 1.0 Hz, 1H), 8.01 (s, 1H), 7.92 (dd, J = 8.5, 1.5 Hz, 1H), 7.56 (d, J = 9.0 Hz, 1H), 7.29-7.18 (m, 6H), 5.69 (s, 2H), 3.87 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 168.0, 157.5, 142.3, 140.9, 137.4, 128.5, 127.2, 126.7, 125.4, 122.2, 121.6, 121.3, 121.2, 118.9, 114.8, 108.8, 92.1, 55.6, 45.7, 16.4; IR (neat) 3350, 2924, 1605, 1556, 1495, 1446, 1391, 1351, 1324, 1254, 1192, 1161, 1133, 1054, 1037, 884 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{22}H_{20}NO_3$ $[M+H]^+$ m/z = 346.1443, found 346.1460.

Butyl 9-benzyl-7-hydroxy-6-methyl-9*H*-carbazole-3-carboxylate (4l). To a solution of **19** (267 mg, 0.77 mmol) in CH_2Cl_2 (11 mL) at –78 °C, a solution of BBr_3 (1 M in CH_2Cl_2, 1.5 mL, 1.54 mmol) was added dropwise. The resultant mixture was allowed to warm to room temperature and stirred for 40 min. The mixture was subsequently quenched with water (15 mL) with cooling in an ice bath. The solution was extracted with EtOAc (30 mL X 3), washed with brine, and the combined organic layers were dried over Na_2SO_4. Removal of solvent yielded the product (234 mg). No further purification was necessary.

A microwave vial was charged with above product (103 mg, 0.31 mmol), *n*-BuOH (3.9 mL), and two drops of concentrated H_2SO_4. After stirring at at 100 °C for 22 h, the solvent was removed and the resultant residue was basified with satd $NaHCO_3$ (aq) to a pH of 8. The mixture was extracted with EtOAc (10 mL X 3) and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. Chromatography (hexane:ethyl acetate = 10:1) afforded the product as a tan amorphous solid (59 mg) in 49% yield. R_f = 0.47 (EtOAc:Hexanes = 1:2): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.70 (d, J = 1.4 Hz, 1H), 8.44 (s, 1H), 8.01 (dd, J = 8.6, 1.7 Hz, 1H), 7.96 (s, 1H), 7.52 (d, J = 8.5 Hz, 1H), 7.29-7.23 (m, 3H), 7.17 (d, J = 7.1 Hz, 2H), 6.95 (s, 1H), 5.56 (s, 2H), 4.34 (t, J = 6.5 Hz, 2H), 2.38 (s, 3H), 1.81-1.76 (m, 2H), 1.56-1.48 (m, 2H), 1.00 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 167.5, 156.4, 144.1, 142.2, 138.3, 129.5, 128.2, 127.4, 126.3, 124.0, 122.8, 122.1, 121.8, 119.2, 116.5, 109.1, 96.2, 64.7, 47.0, 31.8, 20.0, 16.6, 14.1; IR (neat) 3351, 2955, 2930, 1674, 1633, 1602, 1450, 1388, 1353, 1297, 1281, 1241, 1178, 1134, 1100, 1020, 997, 972, 768 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{25}H_{26}NO_3$ $[M+H]^+$ m/z = 388.1913, found 388.1911.

***N*^{4}-(2-Chloro-5-methoxy-4-methylphenyl)-*N*^{4},*N*^{4}-diphenylbenzene-1,4-diamine (8m).** Following **General Procedure C** for 18 h, the product was obtained as a pale brown solid (720 mg) in 87% yield. R_f = 0.40 (EtOAc:Hexanes = 1:9): ^{1}H NMR (500 MHz, acetone-d_6) δ 7.26 (t, J = 7.4 Hz, 4H), 7.16 (d, J = 8.7 Hz, 2H), 7.13 (s, 1H), 7.03 (d, J = 7.7 Hz, 6H), 6.98 (t, J = 7.4 Hz, 2H), 6.90 (s, 1H), 6.83 (br s, 1H), 3.75 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 157.9, 149.0, 142.1, 140.1, 139.8, 131.6, 130.0, 127.4, 126.7, 124.1, 123.9, 123.3, 123.2, 123.0, 120.52, 120.49, 114.2, 101.8, 55.9, 15.4; IR (neat) 3401, 3036, 2926, 1586, 1506, 1463, 1395, 1313, 1246, 1200, 1186, 995, 876, 819 cm^{-1}; HRMS (EI-TOF) calcd for $C_{26}H_{23}ClN_2O$ $[M]^+$ m/z = 414.1499; found 414.1508.

7-Methoxy-6-methyl-*N*, *N*′-diphenyl-9*H*-carbazol-3-amine (9m). Following **General Procedure D** for 24 h, the product was obtained as a colorless solid (529 mg) in 70% yield. R_f = 0.25 (EtOAc:Hexanes = 3:7): ^{1}H NMR (500 MHz, acetone-d_6) δ 10.11

(br s, 1H), 7.75 (d, *J* = 1.9 Hz, 1H), 7.73 (s,1H), 7.43 (d, *J* = 8.5 Hz, 1H), 7.23 (t, *J* = 8.0 Hz, 4H), 7.07 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.04 (d, *J* = 8.7 Hz, 5H), 6.93 (t, *J* = 7.3 Hz, 2H), 3.90 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 158.5, 149.8, 141.6, 141.4, 140.1, 138.3, 138.1, 129.9, 125.4, 125.3, 124.7, 123.2, 122.2, 119.3, 118.7, 116.7, 112.4, 112.3, 93.50, 93.45, 55.8, 16.8; IR (neat) 3403, 3042, 2908, 1584, 1484, 1433, 1310, 1275, 1228, 1200, 1037 cm^{-1}; HRMS (EI-TOF) calcd for $C_{26}H_{22}N_2O$ [M]$^+$ *m/z* = 378.1732; found 378.1732.

9-Benzyl-7-methoxy-6-methyl-*N,N'*-diphenyl-9*H*-carbazol-3-amine (11m). Following **General Procedure F** at room temperature for 2 h, the product was obtained as a colorless solid (222 mg) in 95% yield. R_f = 0.46 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 7.79 (dd, *J* = 7.8, 2.1 Hz, 2H), 7.44 (d, *J* = 8.6 Hz, 1H), 7.31-7.20 (m, 9H), 7.15 (s, 1H), 7.10 (dd, *J* = 8.6, 2.1 Hz, 1H), 7.03 (dd, *J* = 8.7, 1.0 Hz, 4H), 6.93 (t, *J* = 7.4 Hz, 2H), 5.62 (s, 2H), 3.89 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 158.8, 149.7, 142.3, 140.5, 138.9, 138.7, 129.9, 129.5, 128.2, 127.7, 125.1, 124.6, 123.3, 122.5, 122.3, 119.5, 118.7, 116.2, 110.8, 92.2, 56.0, 47.0, 16.7; IR (neat) 3021, 2912, 1632, 1585, 1490, 1470, 1423, 1354, 1317, 1254, 1193, 1037, 805, 736 cm^{-1}; HRMS (EI-TOF) calcd for $C_{33}H_{28}N_2O$ [M]$^+$ *m/z* = 468.2202; found 468.2215.

9-Benzyl-6-(diphenylamino)-3-methyl-9*H*-carbazol-2-ol (4m). Following **General Procedure E** at room temperature for 1.5 h, the product was obtained as a white solid (105 mg) in 93% yield. R_f = 0.30 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (br s, 1H), 7.67 (s, 1H), 7.29-7.07 (m, 15H), 6.92 (s, 2H), 6.71 (s, 1H), 5.36 (s, 2H), 4.76 (s, 1H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 155.2, 148.8, 141.2, 139.4, 137.93, 137.90, 128.9, 128.5, 127.1, 126.6, 124.3, 123.6, 122.3, 121.8, 121.3, 117.6, 117.3, 115.4, 109.5, 94.8, 46.1, 15.6; IR (neat) 3421, 2923, 1632, 1585, 1490, 1393, 1367, 1355, 1310, 648 cm^{-1}; HRMS (EI-TOF) calcd for $C_{32}H_{26}N_2O$ [M]$^+$ *m/z* 454.2045; found 454.2072.

2-Chloro-5-methoxy-4-methyl-*N*-(*p*-tolyl)aniline (8n). Following **General Procedure C** for 20 h, the product was obtained as yellow oil (443 mg) in 73% yield. R_f = 0.75 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 7.12 (d, *J* = 8.0, 2H), 7.08 (s, 1H), 7.04 (d, *J* = 8.5, 2H), 6.72 (s, 1H), 6.72 (s, 1H), 5.88 (br s, 1H), 3.96 (s, 3H), 2.32 (s, 3H), 2.12 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 2 rotamers; IR (neat) 3420, 2921, 1589, 606 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{15}H_{17}ClNO$ [M+H]$^+$ 262.0999, found 262.1003.

2-Methoxy-3,6-dimethyl-9*H*-carbazole (9n). Following **General Procedure D**, the product was obtained as a brown solid (1.39 g) in 83% yield. R_f = 0.30 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 7.79 (s, 1H), 7.74 (s, 2H), 7.25 (d, *J* = 8.0 Hz, 1H), 7.12 (d, *J* = 7.0 Hz, 1H), 6.84 (s, 1H), 3.91 (s, 3H), 2.56 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 157.3, 140.3, 138.2, 127.5, 125.0, 123.5, 121.0, 118.9, 117.9, 115.8, 110.1, 92.6, 54.8, 20.6, 15.0; IR (neat) 3390, 2920, 1634, 1615, 818, 746 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{15}H_{16}NO$ [M+H]$^+$ 226.1232, found 226.1229.

3,6-Dimethyl-9*H*-carbazol-2-ol (10n). Following **General Procedure E**, the product was obtained as a brown solid (510 mg) in 94% yield. R_f = 0.24 (EtOAc:Hexanes = 1:2): ^{1}H NMR (500 MHz, acetone-d_6) δ 9.75 (s, 1H), 8.15 (s, 1H), 7.74 (s, 1H), 7.72 (d, *J* = 0.6 Hz, 1H), 7.26 (d, *J* = 8.2 Hz, 1H), 7.06 (dd, *J* = 8.2, 1.3 Hz, 1H), 6.93 (s, 1H), 2.44 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 155.5, 141.3, 139.1, 128.2, 125.8, 124.6, 122.1, 119.7, 117.4, 116.9, 110.9, 97.1, 21.5, 16.8; IR (neat) 3398, 2921, 1603, 826, 744, 719, 640 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{14}H_{14}NO$ [M+H]$^+$ 212.1075, Found 212.1080.

9-Benzyl-3,6-dimethyl-9*H*-carbazol-2-ol (4n). Following **General Procedure F**, the product was obtained as a yellow solid (81 mg) in 53% yield. R_f = 0.40 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.22 (s, 1H), 7.80 (s, 1H), 7.79 (s, 1H), 7.30 (d, *J* = 8.3 Hz, 1H), 7.27-7.21 (m, 3H), 7.14 (d, *J* = 7.0 Hz, 2H), 7.10 (dd, *J* = 8.3, 1.1 Hz, 1H), 6.86 (s, 1H), 5.46 (s, 2H), 2.46 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 154.8, 140.9, 138.9, 138.2, 128.5, 127.8, 127.1, 126.5, 125.1, 123.5, 121.5, 119.0, 116.8, 115.6, 108.3, 94.8, 45.9, 20.5, 15.7. IR (neat) 3421, 2919, 2852, 1494, 863, 796, 735, 697 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{21}H_{20}NO$ [M+H]$^+$ 302.1545, Found: 302.1545.

5-Amino-4-chloro-2-methylphenol (S-2). Following **General Procedure E**, the product was obtained as a light tan solid (244 mg) in 49% yield. R_f = 0.22 (EtOAc:Hexanes = 1:5): ^{1}H NMR (500 MHz, CD_3CN) δ 6.97 (s, 1H), 6.25 (s, 1H), 4.50 (s, 1H), 3.82 (br s, 2H), 2.12 (s, 3H); ^{13}C NMR (125 MHz, CD_3CN) δ 155.4, 143.5, 131.4, 115.8, 110.0, 103.3, 15.2; IR (neat) 3405, 3416, 3195 (w), 2923, 1618, 1515, 1413, 1378, 1311, 1274, 1197, 1164, 988, 847, 723, 630, 460 cm^{-1}; HRMS (ESI-TOF) *m/z* = 158.0373 calcd for C_7H_9ClNO [M+H]$^+$, found 158.0380.

5-(Benzyloxy)-2-chloro-4-methylaniline (14). Following **General Procedure F** using 1 equiv NaH, 1 equiv BnBr, 2.4 mL DMF and 24 mL THF on a 2.41 mmol scale with **S-2**, the product was obtained as a light tan solid (372 mg) in 62% yield. R_f = 0.40 (EtOAc:Hexanes = 1:5): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43-7.31 (m, 5H), 7.01 (s, 1H), 6.34 (s, 1H), 5.01 (s, 2H), 3.88 (s, 2H), 2.15 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.3, 141.2, 137.2, 130.6, 128.5, 127.8, 127.0, 118.3, 110.4, 100.4, 70.1, 15.3; IR (neat) 3465, 3390, 2945, 1619, 1506, 1454, 1413, 1380, 1282, 1265, 1215, 1201, 1169. 1079, 1045, 1028, 988, 875, 819, 801, 734, 695, 651 cm^{-1}; HRMS (ESI-TOF) *m/z* = 248.0842 calcd for $C_{14}H_{15}ClNO$ [M+H]$^+$, found 248.0839.

5-(Benzyloxy)-2-chloro-*N*-(4-methoxyphenyl)-4-methylaniline (16). Following **General Procedure C**, the product was obtained as red oil (316 mg) in 68% yield. R_f = 0.80 (EtOAc:Hexanes = 1:5): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.31 (m, 5H), 7.09 (s, 1H), 6.97 (dd, *J* = 6.7, 2.2 Hz, 2H), 6.84 (dd, *J* = 5.7, 3.5 Hz, 2H), 6.55 (s, 1H), 5.79 (s, 1H), 4.92 (s, 2H), 3.82 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 157.3, 157.0, 141.8, 138.8, 136.5, 132.1, 129.8, 129.0, 128.5, 124.0, 119.6, 115.9, 112.9, 101.4, 71.0, 56.3, 16.1; IR (neat) 3400, 2940, 1611, 1578, 1508, 1489, 1454, 1416, 1399, 1375, 1287, 1242, 1164, 1032, 1002, 841, 820, 775, 735, 696, 655, 600 cm^{-1}; HRMS (ESI-TOF) *m/z* = 354.1261 calcd for $C_{21}H_{21}ClNO_2$ [M+H]$^+$, found 354.1268.

2-(Benzyloxy)-6-methoxy-3-methyl-9*H*-carbazole (17). Following **General Procedure D**, the product was obtained as a light

tan solid (161 mg) in 80% yield. R_f = 0.23 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 9.86 (br s, 1H), 7.83 (s, 1H), 7.55-7.53 (m, 3H), 7.41 (td, J = 5.8, 1.6 Hz, 2H), 7.34-7.31 (m, 2H), 7.07 (s, 1H), 6.91 (dd, J = 8.7, 2.5 Hz, 1H), 5.19 (s, 2H), 3.86 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 157.3, 154.7, 141.5, 138.8, 135.7, 129.3, 128.5, 128.1, 124.7, 122.1, 119.0, 117.3, 113.8, 111.9, 103.2, 95.0, 70.6, 56.1, 17.1; IR (neat) 3385, 2910, 1648, 1486, 1472, 1450, 1429, 1298, 1276, 1217, 1203, 1179, 1170, 1135, 1113, 1026, 839, 837, 813, 743, 699, 468 cm^{-1}; HRMS (ESI-TOF) m/z = 317.1416 calcd for $C_{21}H_{19}NO_2$ $[M]^+$, found 317.1430.

9-Benzyl-2-(benzyloxy)-6-methoxy-3-methyl-9*H*-carbazole (18). Following **General Procedure F** using 1.1 equiv NaH, 1.1 equiv BnBr, 0.51 mL DMF and 5.1 mL THF on a 0.51 mmol scale, the product was obtained as a light tan solid (129 mg) in 62% yield. R_f = 0.65 (EtOAc:Hexanes = 1:5): ^{1}H NMR (500 MHz, acetone-d_6) δ 7.88 (s, 1H), 7.60 (d, J = 2.5 Hz, 1H), 7.52 (d, J = 7.5 Hz, 2H), 7.39 (t, J = 7.2 Hz, 2H), 7.33-7.31 (m, 2H), 7.24-7.20 (m, 4H), 7.16 (dd, J = 8.2 Hz, 1.5 Hz, 2H), 6.93 (dd, J = 8.8, 2.5 Hz, 1H), 5.86 (s, 2H), 5.21 (s, 2H), 3.86 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 157.5, 155.0, 142.0, 139.1, 138.7, 136.3, 129.4, 129.3, 128.5, 128.3, 128.0, 127.6, 124.5, 122.4, 119.2, 116.8, 113.7, 110.5, 103.5, 93.7, 70.7, 56.1, 46.9, 17.0; IR (neat) 2910, 1645, 1494, 1474, 1464, 1454, 1441, 1431, 1305, 1252, 1234, 1226, 1202, 1181, 1141, 1053, 1027, 807, 793, 778, 732, 698 cm^{-1}; HRMS (ESI-TOF) m/z = 408.1964 calcd for $C_{28}H_{26}NO_2$ $[M+H]^+$, found 408.1960.

9-Benzyl-6-methoxy-3-methyl-9*H*-carbazol-2-ol (4o). Mono debenzylation of **18** following the procedure for **4h** afforded a tan solid (39 mg) in 58% yield. R_f = 0.17 (EtOAc:Hexanes = 1:5): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.29 (s, 1H), 7.83 (s, 1H), 7.59 (dd, J = 2.4 Hz, 1H), 7.31 (d, J = 8.8 Hz, 1H), 7.25-7.20 (m, 3H), 7.13 (d, J = 7.1 Hz, 2H), 6.92 (dd, J = 8.8, 2.5 Hz, 1H), 6.86 (s, 1H), 5.44 (s, 2H), 3.86 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 156.0, 155.0, 142.3, 139.2, 136.5, 129.5, 128.1, 127.5, 124.8, 122.7, 117.7, 116.8, 113.4, 110.2, 103.6, 95.8, 56.2, 47.0, 16.7; IR (neat) 3375, 2910, 1633, 1474, 1453, 1433, 1298, 1275, 1253, 1233, 1219, 1202, 1182, 1170, 1140, 1046, 1014, 823, 803, 732, 700, 632 cm^{-1}; HRMS (ESI-TOF) m/z = 318.1494 calcd for $C_{21}H_{20}NO_2$ $[M+H]^+$, found 318.1492.

***N*-(2-Chloro-5-methoxy-4-methylphenyl)-[1,1'-biphenyl]-4-amine (8p).** Following **General Procedure C**, the product was obtained as a white solid (412 mg) in 73% yield. R_f = 0.75 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, J = 8.0 Hz, 2H), 7.57 (d, J = 9.0 Hz, 2H), 7.45 (t, J = 7.5 Hz, 2H), 7.33 (t, J = 7.5 Hz, 1H), 7.21 (d, J = 8.5 Hz, 2H), 7.15 (s, 1H), 6.89 (s, 1H), 6.03(br s, 1H), 3.76 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.0, 141.9, 140.8, 138.1, 134.8, 131.0, 128.9, 128.2, 126.9, 126.2, 120.2, 119.1, 113.4, 100.4, 55.7, 15.4; IR (neat) 3400, 2921, 1589, 1523, 1486, 1450, 1412, 1374, 1248, 1232, 992, 822 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{20}H_{19}ClNO$ $[M+H]^+$ m/z = 324.1155, found 324.1176.

2-Methoxy-3-methyl-6-phenyl-9*H*-carbazole (9p). Following **General Procedure D**, the product was obtained as a brown solid (143 mg) in 83% yield. R_f = 0.25 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.86 (s, 1H), 7.74 (d, J = 7.0 Hz, 2H), 7.64 (br s, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.50 (t, J = 7.5 Hz, 2H), 7.37 (t, J = 7.5 Hz, 1H), 7.29 (d, J = 8.0 Hz, 1H), 6.68 (s, 1H), 3.84 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.7, 142.4, 139.9, 138.9, 132.9, 128.8, 127.4, 126.5, 124.1, 123.8, 121.6, 119.5, 117.9, 116.3, 110.6, 92.7, 55.5, 16.8; IR (neat) 3390, 2925, 1621, 1481, 1323, 1284, 1226, 1195, 1171, 1034, 881, 752 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{20}H_{18}NO$ $[M+H]^+$ m/z = 288.1388, found 288.1387.

3-Methyl-6-phenyl-9*H*-carbazol-2-ol (10p), Following **General Procedure E**, the product was obtained as a dark brown solid (103 mg) in 76% yield. R_f = 0.21 (EtOAc:Hexanes = 1:2): ^{1}H NMR (500 MHz, CD_3CN) δ 8.74 (br s, 1H), 7.88 (d, J = 1.5 Hz, 1H), 7.52 (s, 1H), 7.39 (dd, J = 8.0, 1.0 Hz, 2H), 7.23 (dd, J = 8.0, 1.5 Hz, 1H), 7.15-7.12 (m, 3H), 6.99 (td, J = 8.0, 1.0 Hz, 1H), 6.67 (br s, 1H), 6.59 (s, 1H), 2.00 (s, 3H); ^{13}C NMR (125 MHz, CD_3CN) δ 155.5, 143.1, 141.2, 140.3, 132.9, 129.8, 127.9, 127.3, 124.9, 124.2, 122.6, 118.4, 118.1, 117.2, 111.7, 97.3, 16.7; IR (neat) 3409, 2923, 1635, 1480, 1398, 1264, 1175, 1122, 1009, 879, 764 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{19}H_{16}NO$ $[M+H]^+$ m/z = 274.1232, found 274.1245.

9-Benzyl-3-methyl-6-phenyl-9*H*-carbazol-2-ol (4p). Following **General Procedure F**, the product was obtained as a white powder (71 mg) in 52% yield. R_f = 0.45 (EtOAc:Hexanes = 1:2): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, J = 1.5 Hz, 1H), 7.89 (s, 1H), 7.70 (dd, J = 8.5, 1.5 Hz, 2H), 7.59 (dd, J = 8.5, 1.5 Hz, 1H), 7.47 (t, J = 8.0 Hz, 2H), 7.36-7.32 (m, 2H), 7.30-7.24 (m, 3H), 7.16 (d, J = 8.0 Hz, 2H), 6.76 (s, 1H), 5.43 (s, 2H), 4.81 (s, 1H), 2.43 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.5, 142.3, 141.2, 140.3, 137.2, 132.8, 128.9, 128.8, 127.6, 127.4, 126.5, 126.4, 124.0, 123.8, 122.1, 118.1, 117.1, 116.4, 108.8, 95.3, 46.8, 16.2; IR (neat) 3305, 2920, 1634, 1607, 1482, 1466, 1454, 1368, 1348, 1300, 1249, 1219, 1174, 1139, 998, 871 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{26}H_{22}NO$ $[M+H]^+$ m/z = 364.1701, found 364.1692.

9-Benzyl-2-(benzyloxy)-9*H*-carbazole (S-3). To a stirring solution of DMF (20 mL) and NaH concentrated to a volume of 25 mL and EtOAc was added. The resultant precipitate was filtered and (784 mg, 32.7 mmol) was added a solution of 2-hydroxycarbazole (2.00 g, 10.9 mmol) in THF (75 mL). After stirring 30 min at room temperature, BnBr (4.50 mL, 38.5 mmol) was added to the solution. After stirring 3 h, the solution was quenched with H_2O (100 mL), extracted with CH_2Cl_2 (3 X 100 mL), washed with brine (100 mL), and dried with $MgSO_4$. EtOAc was then added to the filtrate and the precipate was collected to afford a white powder (3.85 g) in 97% yield. R_f = 0.5 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, CD_2Cl_2) δ 8.02 (d, J = 7.6 Hz, 1H), 7.99 (d, J = 8.5 Hz, 1H), 7.45 (d, J = 7.1 Hz, 2H), 7.38 (td, J = 8.6, 1.0 Hz, 2H), 7.36-7.31 (m, 3H), 7.24 (m, 4H), 7.13 (d, J = 6.7 Hz, 2H), 6.95-6.92 (m, 2H), 5.45 (s, 2H) 5.12 (s, 2H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 159.0 142.6, 141.4, 137.87, 137.85, 129.3, 129.0, 128.5, 128.2, 128.0, 127.1, 125.2, 123.7, 121.6, 120.0, 119.9, 117.6, 109.3, 108.9, 95.2, 71.0, 47.1; IR (neat) 3020, 1626, 1598, 1495, 1460, 1451, 1437, 1359, 1328, 1246, 1179, 1120, 1009, 993, 944, 820, 804, 735, 726, 719, 695 cm^{-1}; HRMS (ESI-TOF) m/z = 363.1623 calcd for $C_{26}H_{21}NO$ $[M]^+$, found 363.1612.

9-Benzyl-2-(benzyloxy)-3-bromo-9*H*-carbazole (13). To a stirring solution of 9-benzyl-2-(benzyloxy)-9*H*-carbazole (1.45 g,

3.99 mmol) and CH_2Cl_2 (40 mL) was added *N*-bromosuccinimide (729 mg, 4.11 mmol). After stirring 30 min at room temperature, the mixture was quenched with ice-cold water, extracted with EtOAc, washed (3 X 20 mL) with brine (30 mL), and dried with $MgSO_4$. After filtration and concentration, trituration with acetone (3 X 10 mL) afforded a white solid (1.46 g) in 83% yield. R_f = 0.43 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.98 (d, *J* = 7.7 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 2H), 7.35 (m, 5H), 7.24 (m, 4H), 7.08 (dd, *J* = 5.2, 1.7 Hz, 2H), 6.87 (s, 1H), 5.42 (s, 2H), 5.16 (s, 2H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 154.2, 141.31, 141.29, 137.4, 137.2, 129.4, 129.1, 128.5, 128.1, 127.9, 127.0, 125.8, 125.1, 122.7, 120.3, 120.2, 118.4, 109.5, 104.4, 95.2, 71.8, 47.1; IR (neat) 3015, 1597, 1469, 1445, 1433, 1356, 1307, 1273, 1249, 1182, 1151, 1121, 1024, 996, 748, 736, 724, 715, 695, 673, 616 cm^{-1}; HRMS (ESI-TOF) *m/z* = 441.0278 calcd for $C_{26}H_{20}BrNO$ $[M]^+$, found 441.0267.

9-Benzyl-3-bromo-9*H*-carbazol-2-ol (4q). To a stirring solution of 9-benzyl-2-(benzyloxy)-3-bromo-9*H*-carbazole (1.20 g, 2.72 mmol) in CH_2Cl_2 (30.0 mL) was added *N,N*-dimethylaniline (3.40 mL, 27.2 mmol) followed by the slow addition of $AlCl_3$ (2.18 g, 16.32 mmol). After stirring 10 min at room temperature, the solution was cooled to 0 ^{0}C and quenched with H_2O (30 mL). The solution was extracted with EtOAc (3 X 30 mL), washed with brine (30 mL), and dried with $MgSO_4$. Removal of solvent and chromatography (5:1 Hex/EtOAc) afforded a white solid (382 mg) in 40% yield. R_f = 0.27 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.72 (br s, 1H), 8.29 (s, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.47 (d, *J* = 8.2 Hz, 1H), 7.36 (td, *J* = 8.3, 1.1 Hz, 1H), 7.28-7.18 (m, 4H), 7.16(d, *J* = 7.1 Hz, 2H), 7.10 (s, 1H), 5.52 (s, 2H); ^{13}C NMR (125 MHz, acetone-d_6) δ 153.4, 142.2, 142.0, 138.5, 129.6, 128.3, 127.5, 126.0, 125.1, 123.3, 120.53, 120.45, 118.5, 110.0, 102.9, 97.3, 47.0; IR (neat) 3410 (w), 2925, 1601, 1475, 1451, 1380, 1360, 1337, 1318, 1262, 1216, 1157, 1120, 1079, 1059, 1020, 946, 883, 824, 738, 717, 696 cm^{-1}; HRMS (ESI-TOF) *m/z* = 351.0259 calcd for $C_{19}H_{14}BrNO$ $[M]^+$, found 351.0283.

3-Allyl-9-benzyl-2-(benzyloxy)-9*H*-carbazole (S-4). To a flask charged with 9-benzyl-2-(benzyloxy)-3-bromo-9*H*-carbazole (300 mg, 0.680 mmol), $Pd(OAc)_2$ (7.60 mg, 0.034 mmol), and CPhos (24 mg, 0.068 mmol), was added THF (0.7 mL) followed by allyl zinc bromide[43] (1.85 mL, 1.02 mmol). After stirring 18 h under Ar atmosphere, the solution was quenched with H_2O (10 mL), extracted with EtOAc (3 X 20 mL), washed with brine (20 mL), and dried with $MgSO_4$. Removal of solvent and chromatography (10:1 Hex/EtOAc) afforded a white solid (183 mg) in 67% yield. R_f = 0.6 (EtOAc:Hexanes = 1:5): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.04 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.92 (d, *J* = 7.7 Hz, 1H), 7.52 (dt, *J* = 7.5, 0.5 Hz, 2H), 7.46 (d, *J* = 8.5 Hz, 1H), 7.39 (td, *J* = 7.5, 1.5 Hz, 2H), 7.32-7.25 (m, 6H), 7.19 (dd, *J* = 8.3, 1.5 Hz, 2H), 7.14 (td, *J* = 7.0, 0.5 Hz, 1H), 6.14-6.09 (m, 1H), 5.62 (s, 2H), 5.23 (s, 2H), 5.10 (dd, *J* = 17.1, 3.8 Hz, 1H), 5.01 (dd, *J* = 11.3, 2.4 Hz, 1H), 3.57 (d, *J* = 6.6 Hz, 2H); ^{13}C NMR (125 MHz, acetone-d_6) δ 157.1, 141.7, 141.5, 139.0, 138.9, 138.6, 129.5, 129.4, 128.6, 128.4, 128.2, 127.7, 125.1, 124.1, 122.1, 121.9, 120.2, 120.0, 117.03, 115.4, 110.0, 94.1, 71.0, 46.9, 35.7; IR (neat) 3010, 1602, 1495, 1480, 1462, 1448, 1355, 1328, 1254, 1175, 1156, 1145, 1122, 1056, 1028, 910, 807, 740, 731, 719, 694 cm^{-1}; HRMS (ESI-TOF) *m/z* = 403.1936 calcd for $C_{29}H_{25}NO$ $[M]^+$, found 403.1939.

3-Allyl-9-benzyl-9*H*-carbazol-2-ol (4r). Mono debenzylation of **S-9** following the procedure for **4q** afforded a white solid (22 mg) in 63% yield. R_f = 0.23 (EtOAc:Hexanes = 1:5): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.35 (s, 1H), 8.01 (dd, *J* = 7.6, 0.7 Hz, 1H), 7.85 (s, 1H), 7.45 (d, *J* = 8.2 Hz, 1H), 7.31-7.21 (m, 4H), 7.18-7.12 (m, 3H), 6.91 (s, 1H), 6.15-6.07 (m, 1H), 5.51 (s, 2H), 5.11 (dd, *J* = 19.1, 2.1 Hz, 1H), 5.01 (dd, *J* = 10.1, 1.3 Hz, 1H), 3.53 (d, *J* = 6.6 Hz, 2H); ^{13}C NMR (125 MHz, acetone-d_6) δ 155.4, 141.8, 141.6, 138.98, 138.97, 129.5, 128.2, 127.5, 125.0, 124.3, 122.0, 120.6, 120.0, 119.9, 116.9, 115.2, 109.6, 96.0, 46.9, 35.4; IR (neat) 3300 (w), 2995, 1636, 1604, 1495, 1467, 1450, 1441, 1348, 1319, 1247, 1178, 1139, 1122, 959, 914, 823, 741, 729, 709, 697, 603 cm^{-1}; HRMS (ESI-TOF) *m/z* = 313.1467 calcd for $C_{22}H_{19}NO$ $[M]^+$, found 313.1466.

9-Benzyl-2-(benzyloxy)-3-phenyl-9*H*-carbazole (S-5). 9-Benzyl-2-(benzyloxy)-3-bromo-9*H*-carbazole (300 mg, 0.680 mmol), potassium phenyl trifluoroborate (188 mg, 1.02 mmol), $Pd(dppf)Cl_2$ (28 mg, 0.0340 mmol), and cesium carbonate (775 mg, 2.38 mmol) were treated with a 2:1 mixture of THF and H_2O (30 mL). After stirring 18 h at 70 ^{0}C, the solution was cooled to room temperature and diluted with H_2O (20 mL). The solution was then extracted with EtOAc (3 X 30 mL), washed with brine (30 mL), and dried with $MgSO_4$. Removal of solvent and chromatography (5:1 = Hex/EtOAc) afforded a white solid (257 mg) in 88% yield. R_f = 0.52 (EtOAc:Hexanes = 1:5): ^{1}H NMR (500 MHz, CD_2Cl_2) δ 8.12 (s, 1H), 8.10 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 7.5 Hz, 2H), 7.50 (t, *J* = 7.5 Hz, 2H), 7.41-7.28 (m, 12H), 7.19 (d, *J* = 6.0 Hz, 2H), 7.04 (s, 1H), 5.49 (s, 2H), 5.15 (s, 2H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 155.8, 141.7, 141.3, 140.1, 137.8, 137.7, 130.6, 129.3, 129.0, 128.5, 128.3, 128.1, 127.7, 127.1, 127.0, 125.3, 124.8, 123.8, 123.0, 120.1, 120.0, 117.3, 109.4, 94.2, 71.3, 47.1; IR (neat) 2940, 1601, 1456, 1448, 1430, 1351, 1314, 1262, 1225, 1210, 1179, 1125, 1028, 1021, 809, 764, 737, 732, 701, 692, 662 cm^{-1}; HRMS (ESI-TOF) *m/z* = 440.2014 calcd for $C_{32}H_{26}NO$ $[M+H]^+$, found 440.2003.

9-Benzyl-3-phenyl-9*H*-carbazol-2-ol (4s). Mono debenzylation of **S-10** following the procedure for **4q** afforded a white solid (25 mg) in 71% yield. R_f = 0.24 (EtOAc:Hexanes = 1:5): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.39 (br s, 1H), 8.10 (d, *J* = 7.7 Hz, 1H), 8.06 (s, 1H), 7.66 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.51 (d, *J* = 8.2 Hz, 1H), 7.42 (t, *J* = 5.8 Hz, 2H), 7.36-7.30 (m, 4H), 7.29 (dd, *J* = 6.0, 1.7 Hz, 1H), 7.22 (dd, *J* = 8.5, 1.4 Hz, 2H), 7.18 (td, *J* = 7.8, 0.8 Hz, 1H), 7.03 (s, 1H), 5.58, (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.0, 142.0, 141.2, 138.0, 137.2, 129.8, 129.6, 129.0, 127.8, 127.7, 126.7, 125.0, 123.5, 121.9, 121.6, 119.74, 119.65, 117.4, 109.0, 95.6, 46.9 cm^{-1}; IR (neat) 3495 (w), 2910, 1633, 1603, 1490, 1477, 1453, 1431, 1353, 1324, 1291, 1263, 1218, 1167, 1122, 950, 822, 744, 723, 700, 660, 608 cm^{-1}; HRMS (ESI-TOF) *m/z* = 350.1545 calcd for $C_{25}H_{20}NO$ $[M+H]^+$, found 350.1556.

9,9'-Dibenzyl-3,3'-dimethyl-9H,9'H-[1,1'-bicarbazole]-2,2'-diol (5a). Following **General Procedure G**, the product was obtained as a yellow solid (109 mg) in 91% yield. R_f = 0.65 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.06 (d, *J* = 8.0 Hz, 2H), 7.94 (s, 2H), 7.23 (td, *J* = 8.2, 1.2 Hz, 2H), 7.17

(t, J= 7.2 Hz, 2H), 7.08 (d, J= 8.1 Hz, 2H), 6.85-6.82 (m, 8H), 6.46-6.44 (m, 4H), 4.83 (d, J= 17.3 Hz, 2H), 4.61 (d, J= 17.3 Hz, 2H), 2.21 (s, 6H); ^{13}C NMR (125 MHz, acetone-d_6) δ 153.6, 141.7, 139.0, 138.0, 127.5, 126.0, 125.4, 123.9, 123.1, 122.0, 119.0, 118.6, 117.5, 116.8, 109.0, 101.0, 46.5, 16.2; IR (neat) 3513, 2923, 1603, 736, 706 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{40}H_{31}N_2O_2$ [M-H]$^-$ 571.2386, found 571.2380; $[\alpha]_D^{22}$ +164 (c 0.35, 87% ee, CH_2Cl_2); Chiral HPLC: Chiralpak IA column (10% i-PrOH/hexanes, 1 mL/min) t_R(1) = 8.12 min, t_R(2) = 11.8 min.

3,3',9,9'-Tetramethyl-9*H*,9'*H*-[1,1'-bicarbazole]-2,2'-diol (5b). Following **General Procedure G**, the product was obtained as a yellow solid (9.0 mg) in 82% yield. R_f = 0.63 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.03 (dd, J = 7.8, 0.8 Hz, 2H), 8.00 (d, J= 1.0 Hz, 2H), 7.31-7.30 (m, 4H), 7.25 (s, 2H), 7.16 (ddd, J= 2.9, 5.2, 7.9 Hz, 2H), 3.45 (s, 6H), 2.45 (s, 6H); ^{13}C NMR (125 MHz, acetone-d_6) δ 153.9, 141.7, 139.8, 123.9, 122.9, 122.1, 118.8, 118.6, 117.0, 116.3, 108.4, 101.7, 29.3, 16.3; IR (neat) 3509, 2924, 2854, 1626, 1603, 882, 768, 737 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{28}H_{25}N_2O_2$ [M+H]$^+$ 421.1916, found: 421.1928. $[\alpha]_D^{22}$ +180 (c 0.43, 60% ee, CH_2Cl_2); CSP HPLC (Chiralpak AD, 1.0 mL/min, 90:10 hexanes:i-PrOH): t_R(1) = 16.6 min, t_R(2) = 20.9 min.

9,9'-Diallyl-3,3'-dimethyl-9*H*,9'*H*-[1,1'-bicarbazole]-2,2'-diol (5c). Following **General Procedure G**, the product was obtained as pale yellow oil (5.7 mg) in 71% yield. R_f = 0.48 (EtOAc:Hexanes = 1:9): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, J= 7.7 Hz, 2H), 8.03 (s, 2H), 7.36 (td, J= 8.2, 1.0 Hz, 2H), 7.25 (t, J= 7.6 Hz, 2H), 7.20 (d, J= 8.2 Hz, 2H), 5.40-5.33 (m, 2H), 5.17 (br s, 2H), 4.74 (dd, J = 10.4, 1.2 Hz, 2H), 4.41 (dd, J= 17.2, 1.2 Hz, 2H), 4.25-4.15 (m, 4H), 2.46 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.4, 141.2, 138.2, 132.5, 124.8, 123.6, 122.9, 119.7, 119.2, 117.6, 117.4, 115.8, 109.3, 98.3, 46.0, 16.8; IR (neat) 3510, 2919, 1603, 1477, 1459, 1355, 1235, 1184, 1072, 737cm^{-1}; HRMS (ESI-TOF) calcd for $C_{32}H_{29}N_2O_2$ [M+H]$^+$ m/z = 473.2229; found 473.2236; $[\alpha]_D^{22}$ +177 (c 0.28, 76% ee, CH_2Cl_2); Chiral HPLC: Chiralpak IA column (10% i-PrOH/hexanes, 1 mL/min) t_R(1) = 11.5 min, t_R(2) = 21.1 min.

9,9'-Diisopropyl-3,3'-dimethyl-9*H*,9'*H*-[1,1'-bicarbazole]-2,2'-diol (5d). Following **General Procedure G**, the product was obtained as pale yellow oil (3.5 mg) in 58% yield. R_f = 0.60 (EtOAc:Hexanes = 1:9): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, J = 7.7 Hz, 2H), 8.00 (s, 2H), 7.52 (d, J= 8.2 Hz, 2H), 7.33 (td, J= 8.3, 1.2 Hz, 2H), 7.23 (t, J= 7.7 Hz, 2H), 5.16 (s, 2H), 4.62-4.54 (m, 2H), 2.45 (s, 6H), 1.38 (d, J= 7.0 Hz, 6H), 1.18 (d, J= 7.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.0, 139.1, 137.5, 124.2, 124.1, 123.2, 119.4, 119.2, 117.5, 117.2, 112.6, 99.2, 46.8, 20.9, 20.7, 16.7; IR (neat) 3510, 2918, 2832, 1601, 1459, 1395, 1183, 1133, 1066, 738 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{32}H_{33}N_2O_2$ [M+H]$^+$ m/z = 477.2542; found 477.2522; $[\alpha]_D^{22}$ +18 (c 0.15, 42% ee, CH_2Cl_2); Chiral HPLC: Chiralpak IA column (10% i-PrOH/hexanes, 1 mL/min) t_R(1) = 7.46 min, t_R(2) = 11.0 min.

3,3'-Dimethyl-9,9'-bis(2,4,6-trimethylbenzyl)-9*H*,9'*H*-[1,1'-bicarbazole]-2,2'-diol (5e). Following **General Procedure G**, the product was obtained as yellow oil (4.0 mg) in 37% yield. R_f = 0.50 (EtOAc:Hexanes = 1:9): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, J = 7.7 Hz, 2H), 7.94 (s, 2H), 7.12 (t, J= 7.8 Hz, 2H), 7.03 (td, J= 8.4, 1.2 Hz, 2H), 6.70 (s, 2H), 6.64 (s, 2H), 6.48 (d, J= 8.5 Hz, 2H), 5.30 (br s, 2H), 4.91 (d, J= 15.3 Hz, 2H), 4.75 (d, J= 15.3 Hz, 2H), 2.37 (s, 6H), 2.19 (s, 6H), 1.82 (s, 6H), 1.64 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.3, 141.4, 139.4, 137.2, 136.7, 130.0, 129.8, 129.22, 129. 124.6, 123.6, 123.4, 119.4, 119.0, 117.9, 117.5, 110.6, 100.2, 44.7, 20.9, 20.1, 19.6, 16.7; IR (neat) 3509, 2920, 1603, 1456, 1180, 1135, 1076, 1041, 851, 743m^{-1}; HRMS (EI-TOF) calcd for $C_{46}H_{43}N_2O_2$ [M-H]$^-$ m/z= 655.3325; found 655.3322; $[\alpha]_D^{22}$ +182 (c 0.18, 37% ee, CH_2Cl_2); Chiral HPLC: Chiralpak IA column (5% i-PrOH/hexanes, 1 mL/min) t_R(1) = 5.09 min, t_R(2) = 14.9 min.

9,9'-Dibenzyl-6,6'-difluoro-3,3'-dimethyl-9*H*,9'*H*-[1,1'-bicarbazole]-2,2'-diol (5f). Following **General Procedure G**, the product was obtained as a yellow solid (26 mg) in 87% yield. R_f = 0.58 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 7.94 (s, 2H), 7.78 (dd, J= 9.0, 2.5 Hz, 2H), 7.06 -6.98 (m, 6H), 6.86-6.84 (m, 6H), 6.47-6.45 (m, 4H), 4.82 (d, J= 17.3 Hz, 2H), 4.60 (d, J= 17.3 Hz, 2H), 2.21 (s, 6H); ^{13}C NMR (125 MHz, acetone-d_6) δ 158.5 (d, J= 233 Hz), 155.3, 140.9, 139.0, 138.8, 128.5, 127.1, 126.2, 124.6 (d, J= 8.8 Hz), 123.4, 118.7, 117.4 (d, J= 3.8 Hz), 112.1 (d, J = 26.4 Hz), 110.7 (d, J= 10.1 Hz), 105.2 (d, J= 23.9 Hz), 101.9, 47.7, 17.1; IR (neat) 3515, 2923, 1627, 856, 796, 781, 703 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{40}H_{31}F_2N_2O_2$ [M+H]$^+$ 609.2354, found 609.2368; $[\alpha]_D^{22}$ +183 (c 0.40, 92% ee, CH_2Cl_2); Chiral HPLC: Chiralpak IA column (10% i-PrOH/hexanes, 1 mL/min) t_R(1) = 9.52 min, t_R(2) = 10.4 min.

9,9'-Dibenzyl-7,7'-difluoro-3,3'-dimethyl-9*H*,9'*H*-[1,1'-bicarbazole]-2,2'-diol (5g). Following **General Procedure G**, the product was obtained as a yellow solid (17.8 mg) in 93% yield. R_f = 0.60 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 7.95 (s, 2H), 7.21 (td, J= 8.1, 5.5 Hz, 2H), 7.06 (s, 2H), 6.91 (d, J= 8.1 Hz, 2H), 6.89 (d, J= 8.1 Hz, 2H), 6.84-6.82 (m, 6H), 6.45-6.43 (m, 4H), 4.85 (d, J= 17.9 Hz, 2H), 4.60 (d, J= 17.4 Hz, 2H), 2.21 (s, 6H); ^{13}C NMR (125 MHz, acetone-d_6) δ 157.7 (d, J= 243 Hz), 153.9, 144.1 (d, J= 10.6 Hz), 138.7, 137.5, 127.5, 126.1, 125.2, 124.6 (d, J= 20.1 Hz), 124.4 (d, J= 20.1 Hz), 118.4, 114.1, 110.8, 105.3, 104.7 (d, J= 18.7 Hz), 101.0, 47.0, 16.2; IR (neat) 3519, 2925, 1601, 965, 709 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{40}H_{29}F_2N_2O_2$ [M-H]$^-$ 607.2197, found 607.2191, $[\alpha]_D^{22}$ +157 (c 0.35, 92% ee, CH_2Cl_2); Chiral HPLC: Chiralpak IA column (5% i-PrOH/hexanes, 1 mL/min) t_R(1) = 6.80 min, t_R(2) = 7.61 min.

9,9'-Dibenzyl-8,8'-difluoro-3,3'-dimethyl-9*H*,9'*H*-[1,1'-bicarbazole]-2,2'-diol (5h). Following **General Procedure G**, the product was obtained as yellow oil (12 mg) in 80% yield. R_f = 0.65 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 7.97 (s, 2H), 7.90 (d, J= 5.0 Hz, 2H), 7.16-7.12 (m, 2H), 7.00-6.96 (m, 4H), 6.87-6.83 (m, 6H), 6.38 (d, J= 5.0 Hz, 4H), 4.95 (d, J= 15.0 Hz, 2H), 4.81 (d, J= 15.0 Hz, 2H), 2.19 (s, 6H); ^{13}C NMR (125 MHz, acetone-d_6) δ 155.2, 150.2 (d, J= 243 Hz), 140.2, 139.9, 129.5 (d, J = 7.5 Hz), 128.3, 128.1 (d, J= 5.0 Hz), 126.8, 125.6, 123.1, 120.4 (d, J = 6.3 Hz), 119.5, 117.8, 115.6 (d, J= 2.5 Hz), 111.1 (d, J= 18.9 Hz), 102.0, 49.5, 17.1; IR (neat) 3516, 2920, 1630, 1613, 1579,

1497, 1450, 1414, 1380, 1348, 1239, 1216, 1192, 1178, 1160, 1141, 1124, 1062, 987 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{40}H_{31}F_2N_2O_2$ $[M+H]^+$ *m/z* = 609.2354, found 609.2370; $[\alpha]_D^{22}$ +211 (*c* 0.25, 91% ee, CH_2Cl_2); Chiral HPLC: Chiralpak IA column (10% *i*-PrOH/hexanes, 1 mL/min) t_R(*1*) = 8.29 min, t_R(*2*) = 9.39 min.

9,9'-Dibenzyl-3,3'-dimethyl-6,6'-bis(trifluoromethyl)-9*H*,9'*H*-[1,1'-bicarbazole]-2,2'-diol (5i). Following **General Procedure G**, the product was obtained as light yellow oil (12 mg) in 70% yield. R_f = 0.53 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.43 (s, 2H), 8.12 (s, 2H), 7.54 (d, *J* = 8.5 Hz, 2H), 7.25 (d, *J* = 8.5 Hz, 2H), 7.23 (s, 2H), 6.86-6.83 (m, 6H), 6.45-6.43 (m, 4H), 4.89 (d, *J* = 17.4 Hz, 2H), 4.68 (d, *J* = 17.4 Hz, 2H), 2.23 (s, 6H); ^{13}C NMR (125 MHz, acetone-d_6) δ 155.6, 144.0, 140.7, 138.2, 128.5, 127.1, 126.6 (q, *J* = 270 Hz), 126.0, 123.8, 123.5, 121.6 (q, *J* = 31.4 Hz), 121.5 (q, *J* = 2.5 Hz), 119.0, 117.2, 117.0 (q, *J* = 3.8 Hz), 110.3, 102.2, 47.7, 17.1; IR (neat) 3525, 2925, 1609, 1451, 1411, 1365, 1346, 1325, 1300, 1262, 1186, 1163, 1148, 1113, 1080, 1069, 1051, 1034, 1005 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{42}H_{31}F_6N_2O_2$ $[M+H]^+$ *m/z* = 709.2292, found 709.2290; $[\alpha]_D^{22}$ +175 (*c* 0.6, 93% ee, CH_2Cl_2); Chiralpak IA column (10% *i*-PrOH/hexanes, 1 mL/min) t_R(*1*) = 8.61 min, t_R(*2*) = 9.89 min.

9,9'-Dibenzyl-3,3'-dimethyl-7,7'-bis(trifluoromethyl)-9*H*,9'*H*-[1,1'-bicarbazole]-2,2'-diol (5j). Following **General Procedure G**, the product was obtained as yellow oil (15 mg) in 60% yield. R_f = 0.55 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.25 (d, *J* = 8.2 Hz, 2H), 8.07 (s, 2H), 7.48 (d, *J* = 8.3 Hz, 2H), 7.42 (s, 2H), 7.29 (s, 2H), 6.86-6.79 (m, 6H), 6.44 (d, *J* = 7.0 Hz, 4H), 4.93 (d, *J* = 17.5 Hz, 2H), 4.73 (d, *J* = 17.5 Hz, 2H), 2.24 (s, 6H); ^{13}C NMR (125 MHz, acetone-d_6) δ 156.0, 141.6, 141.2, 138.3, 128.5, 127.1, 126.9, 126.3 (q, *J* = 271.1 Hz), 126.1 (q, *J* = 31.2 Hz), 126.0, 123.7, 120.0, 119.8, 116.8, 116.5 (q, *J* = 3.6 Hz), 107.0 (q, *J* = 4.1 Hz), 102.0, 47.7, 17.1; IR (neat) 3519, 2925, 1629, 1574, 1451, 1351, 1321, 1294, 1280, 1264, 1232, 1164, 1135, 1118, 1061, 1005, 910 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{42}H_{31}F_6N_2O_2$ $[M+H]^+$ *m/z* = 709.2290, found 709.2270; $[\alpha]_D^{22}$ +254 (*c* 0.42, 94% ee, CH_2Cl_2); Chiral HPLC: Chiralpak IA column (5% *i*-PrOH/hexanes, 1 mL/min) t_R(*1*) = 6.42 min, t_R(*2*) = 21.8 min.

(9,9'-Dibenzyl-2,2'-dihydroxy-3,3'-dimethyl-9*H*,9'*H*-[1,1'-bicarbazole]-6,6'-diyl)bis(phenylmethanone) (5k). Following **General Procedure G** with chlorobenzene/HFIP(1:1, 0.5 M) as a solvent, the product was obtained as an off-white solid (9.1 mg) in 76% yield based on recovered starting material. R_f = 0.50 (EtOAc:Hexanes = 1:2): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.56 (d, *J* = 1.0 Hz, 2H), 8.03 (s, 2H), 7.85 (d, *J* = 8.0 Hz, 4H), 7.79 (dd, *J* = 8.5, 1.5 Hz, 2H), 7.67 (d, *J* = 7.5 Hz, 2H), 7.60 (t, *J* = 7.5 Hz, 4H), 7.25 (br s, 2H), 7.22 (d, *J* = 8.5 Hz, 2H), 6.89-6.86 (m, 6H), 6.50-6.48 (m, 4H), 4.94 (d, *J* = 15.0 Hz, 2H), 4.70 (d, *J* = 15.0 Hz, 2H), 2.23 (s, 6H); ^{13}C NMR (125 MHz, acetone-d_6) δ 196.2, 155.4, 145.0, 140.7, 140.1, 138.2, 132.4, 130.4, 129.8, 129.1, 128.5, 127.4, 127.2, 126.1, 123.6, 123.4, 122.6, 119.7, 117.8, 109.6, 102.4, 47.8, 17.1; IR (neat) 3500, 2923, 2853, 1645, 1596, 1569, 1494, 1449, 1412, 1365, 1346, 1318, 1286, 1250, 1184, 1134, 1072, 1003, 948 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{54}H_{41}N_2O_4$ $[M+H]^+$ *m/z* = 781.3066, found 781.3054; $[\alpha]_D^{22}$ +55 (*c* 0.15, 85% ee, CH_2Cl_2); Chiral HPLC: Chiralpak IA column (20% *i*-PrOH/hexanes, 1 mL/min) t_R(*1*) = 29.8 min, t_R(*2*) = 39.8 min.

Dibutyl 9,9'-dibenzyl-2,2'-dihydroxy-3,3'-dimethyl-9*H*,9'*H*-[1,1'-bicarbazole]-6,6'-dicarboxylate (5l). Following **General Procedure G**, the product was obtained as light yellow oil (16 mg) in 67% yield based on recovered starting material. R_f = 0.41 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.75 (d, *J* = 1.5 Hz, 2H), 8.08 (s, 2H), 7.95 (dd, *J* = 8.6, 1.7 Hz, 2H), 7.15 (d, *J* = 8.9 Hz, 2H), 7.14 (s, 2H), 6.84-6.82 (m, 6H), 6.43-6.41 (m, 4H), 4.87 (d, *J* = 17.3 Hz, 2H), 4.65 (d, *J* = 17.3 Hz, 2H), 4.39-4.34 (m, 4H), 2.23 (s, 6H), 1.84-1.78 (m, 4H), 1.59-1.51 (m, 4H), 1.02 (t, *J* = 7.4 Hz, 6H); ^{13}C NMR (125 MHz, acetone-d_6) δ 167.6, 155.3, 145.2, 140.6, 138.2, 128.5, 127.1, 126.4, 126.1, 123.8, 123.3, 122.4, 121.5, 119.7, 117.7, 109.6, 102.4, 64.8, 47.8, 31.8, 20.0, 17.1, 14.1; IR (neat) 3395, 2958, 2926, 1697, 1603, 1577, 1495, 1451, 1412, 1382, 1364, 1348, 1287, 1240, 1182, 1132, 1102, 1071, 1004, 972 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{50}H_{49}N_2O_6$ $[M+H]^+$ *m/z* = 773.3591, found 773.3585; $[\alpha]_D^{22}$ +100 (*c* 0.30, 96% ee, CH_2Cl_2); Chiral HPLC: Chiralpak IA column (20% *i*-PrOH/hexanes, 1 mL/min) t_R(*1*) = 9.80 min, t_R(*2*) = 19.9 min.

9,9'-Dibenzyl-6,6'-bis(diphenylamino)-3,3'-dimethyl-9*H*,9'*H*-[1,1'-bicarbazole]-2,2'-diol (5m). Following **General Procedure G**, the product was obtained as a colorless solid (8.0 mg) in 62% yield. R_f = 0.58 (EtOAc:Hexanes = 1:9): ^{1}H NMR (500 MHz, acetone-d_6) δ 7.85 (s, 2H), 7.83 (d, *J* = 2.0 Hz, 2H), 7.27 (t, *J* = 8.6 Hz, 8H), 7.09-7.03 (m, 12H), 7.00 (s, 2H), 6.96 (t, *J* = 7.4 Hz, 4H), 6.91-6.88 (m, 6H), 6.54 d, (*J* = 6.6 Hz, 4H), 4.87 (d, *J* = 17.2 Hz, 2H), 4.61 (d, *J* = 17.2 Hz, 2H), 2.19 (s, 6H); ^{13}C NMR (125 MHz, acetone-d_6) δ 154.9, 149.7, 140.6, 140.5, 140.0, 138.9, 129.9, 128.5, 127.1, 126.3, 125.1, 124.7, 123.2, 122.3, 121.8, 118.6, 118.2, 117.5, 110.9, 101.8, 47.8, 17.1; IR (neat) 3526, 3032, 2919, 1635, 1585, 1490, 1454, 1326, 1285, 1257, 1217, 1164, 1132, 1028, 998, 804, 752 cm^{-1}; HRMS (EI-TOF) calcd for $C_{64}H_{50}N_4O_2Na$ $[M+Na]^+$ *m/z* 929.3831; found 929.3810; $[\alpha]_D^{22}$ +31 (*c* 0.35, 37% ee, CH_2Cl_2); Chiral HPLC: Chiralpak IA column (5% *i*-PrOH/hexanes, 1 mL/min) t_R(*1*) = 6.95 min, t_R(*2*) = 8.19 min.

9,9'-Dibenzyl-3,3',6,6'-tetramethyl-9*H*,9'*H*-[1,1'-bicarbazole]-2,2'-diol (5n). Following **General Procedure G**, the product was obtained as a yellow solid (13 mg) in 93% yield. R_f = 0.74 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 7.89 (s, 2H), 7.84 (s, 2H), 7.06 (dd, J = 1.8, 7.5, 2H), 6.97 (d, J = 8.0, 2H), 6.86-6.82 (m, 6H), 6.71 (s, 2H), 6.45 (s, 2H), 6.46-6.42 (m, 2H), 4.77 (d, J = 17.1, 2H), 4.58 (d, J = 17.1, 2H), 2.49 (s, 6H), 2.19 (s, 6H); ^{13}C NMR (125 MHz, acetone-d_6) δ 140.0, 139.2, 138.3, 128.1, 127.3, 126.1, 125.4, 125.2, 123.3, 121.9, 118.6, 117.2, 116.7, 108.9, 108.8, 100.9, 46.6, 20.5, 16.2; IR (neat) 3503, 2920, 1608, 793, 733, 701 cm^{-1}; HRMS(ESI-TOF) calcd for $C_{42}H_{37}N_2O_2$ $[M+H]^+$ 601.2855, found 601.2849 $[\alpha]_D^{22}$ +180 (*c* 0.43, 60% ee, CH_2Cl_2); Chiral HPLC: Chiralpak IA column (10% *i*-PrOH/hexanes, 1 mL/min): t_R(*1*) = 8.97 min, t_R(*2*) = 13.3 min.

9,9'-Dibenzyl-6,6'-dimethoxy-3,3'-dimethyl-9H,9'H-[1,1'-bicarbazole]-2,2'-diol (5o). Following **General Procedure G** for 26 h, the product was obtained as a light brown powder (10.6 mg) in 82% yield. R_f = 0.33 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 7.91 (s, 2H), 7.63 (d, *J* = 2.5 Hz, 2H), 6.98 (d, *J*

= 8.8 Hz, 2H), 6.88-6.83 (m, 8H), 6.81 (s, 2H), 6.46 (d, *J* = 7.8 Hz, 4H), 4.78 (d, *J* = 17.2 Hz, 2H), 4.56 (d, *J* = 17.2 Hz, 2H), 3.90 (s, 6H), 2.20 (s, 6H); ^{13}C NMR (125 MHz, acetone-d_6) δ 155.1, 154.5, 140.4, 139.2, 137.4, 128.4, 126.9, 126.3, 124.4, 123.0, 117.9, 117.6, 113.5, 110.6, 102.9, 101,7, 56.1, 47.5, 17.1; IR (neat) 3500, 2925, 1627, 1482, 1450, 1433, 1409, 1349, 1298, 1229, 1191, 1181, 1159, 1145, 1073, 1055, 1027, 1004 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{42}H_{37}N_2O_4$ $[M+H]^+$ *m/z* = 633.2753, found 633.2766. $[\alpha]_D^{22}$ +142 (*c* 0.45, 74% ee, CH_2Cl_2); Chiral HPLC: Chiralpak IA column (15% *i*-PrOH/hexanes, 1 mL/min) t_R(*1*) = 12.6 min, t_R(*2*) = 14.1 min.

9,9'-Dibenzyl-3,3'-dimethyl-6,6'-diphenyl-9*H*,9'*H*-[1,1'-bicarbazole]-2,2'-diol (5p). Following **General Procedure G**, the product was obtained as a yellow solid (23 mg) in 70% yield. R_f = 0.64 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, *J* = 1.5 Hz, 2H), 8.04 (s, 2H), 7.77 (d, *J* = 7.0 Hz, 4H), 7.61 (dd, *J* = 8.5, 2.0 Hz, 2H), 7.52 (t, *J* = 7.5 Hz, 4H), 7.34 (t, *J* = 7.0 Hz, 2H), 7.18 (d, *J* = 8.5 Hz, 2H), 6.94 (t, *J* = 7.0 Hz, 2H), 6.89 (t, *J* = 7.0 Hz, 4H), 6.31 (d, *J* = 7.0 Hz, 4H), 4.78 (s, 2H), 4.74 (d, *J* = 17.0 Hz, 2H), 4.69 (d, *J* = 17.0 Hz, 2H), 2.22 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.7, 142.2, 141.4, 138.7, 137.3, 133.3, 128.9, 128.0, 127.4, 126.8, 126.6, 125.1, 124.4, 123.4, 123.3, 118.0, 117.8, 117.7, 109.3, 99.2, 47.0, 16.6; IR (neat) 3502, 2921, 1603, 1468, 1450, 1406, 1361, 1347, 1290, 1251, 1178, 1135, 1076, 1003, 964, 878 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{52}H_{41}N_2O_2$ $[M+H]^+$ *m/z* = 725.3168, found 725.3168. $[\alpha]_D^{22}$ +82 (*c* 0.25, 82% ee, CH_2Cl_2); Chiral HPLC: Chiralpak IA column (10% *i*-PrOH/hexanes, 1 mL/min) t_R(*1*) = 14.6 min, t_R(*2*) = 27.1 min.

9,9'-Dibenzyl-3,3'-dibromo-9*H*,9'*H*-[1,1'-bicarbazole]-2,2'-diol (5q). Following **General Procedure G**, the product was obtained as yellow oil (12.0 mg) in 30% yield based on recovered starting material. R_f = 0.63 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.37 (s, 2H), 8.14 (d, *J* = 7.4 Hz, 2H), 7.56 (s, 2H), 7.31 (td, *J* = 8.3, 1.2 Hz, 2H), 7.23 (td, *J* = 7.8, 0.8 Hz, 2H), 7.13 (d, *J* = 8.2 Hz, 2H), 6.87-6.82 (m, 6H), 6.48 (dd, *J* = 8.1, 1.9 Hz, 4H), 4.90 (d, *J* = 17.3 Hz, 2H), 4.63 (d, *J* = 17.4 Hz, 2H); ^{13}C NMR (125 MHz, acetone-d_6) δ 152.1, 143.0, 140.6, 138.4, 128.6, 127.3, 126.2, 126.1, 125.1, 123.1, 120.7, 120.1, 119.5, 110.3, 104.7, 103.6, 47.8; IR (neat) 3503, 2924, 2853, 1591, 1473, 1446, 1412, 1340, 1319, 1259, 1205, 1184, 1123, 1027, 960, 777, 746, 730 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{38}H_{27}Br_2N_2O_2$ $[M+H]^+$ *m/z* = 701.0439, found 701.0462; $[\alpha]_D^{22}$ +58 (*c* 0.25, 72% ee, CH_2Cl_2); Chiral HPLC: Chiralpak IA column (20% *i*-PrOH/hexanes, 1 mL/min) t_R(*1*) = 12.0 min, t_R(*2*) = 19.6 min.

3,3'-Diallyl-9,9'-dibenzyl-9*H*,9'*H*-[1,1'-bicarbazole]-2,2'-diol (5r). Following **General Procedure G**, the product was obtained as a yellow powder (9.0 mg) in 75% yield. R_f = 0.72 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.07 (d, *J* = 7.5 Hz, 2H), 7.94 (s, 2H), 7.23 (dt, *J* = 8.3, 1.3 Hz, 2H), 7.18 (dt, *J* = 7.8, 1.0 Hz, 2H), 7.06 (d, *J* = 8.0 Hz, 2H), 7.00 (br s, 2H), 6.83-6.81 (m, 6H), 6.48-6.46 (m, 4H), 6.00-5.93 (m, 2H), 5.11 (dq, *J* = 17.1, 1.6 Hz, 2H), 4.98 (dq, *J* = 10.0, 1.2 Hz, 2H), 4.88 (d, *J* = 17.2 Hz, 2H), 4.58 (d, *J* = 17.2 Hz, 2H), 3.42-3.33 (m, 4H); ^{13}C NMR (125 MHz, acetone-d_6) δ 154.1, 142.5, 140.0, 138.8, 138.6, 128.4, 126.9, 126.2, 125.0, 124.1, 122.3, 120.8, 120.0, 119.5, 118.0, 115.3, 110.1, 101.9, 47.4, 35.7; IR (neat) 3513, 2923, 1603, 1477, 1449, 1417, 1348, 1244, 1180, 1124, 919 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{44}H_{36}N_2O_2Na$ $[M+Na]^+$ *m/z* = 647.2674, found 647.2659; $[\alpha]_D^{22}$ +268 (*c* 0.10, 83% ee, CH_2Cl_2); Chiral HPLC: Chiralpak IA column (10% *i*-PrOH/hexanes, 1 mL/min) t_R(*1*) = 9.72 min, t_R(*2*) = 11.0 min.

9,9'-Dibenzyl-3,3'-diphenyl-9*H*,9'*H*-[1,1'-bicarbazole]-2,2'-diol (5s). Following **General Procedure G**, the product was obtained as orange oil (12 mg) in 43% based on recovery of starting material yield. R_f = 0.62 (EtOAc:Hexanes = 1:4): ^{1}H NMR (500 MHz, acetone-d_6) δ 8.16 (d, *J* = 10.0 Hz, 2H), 8.14 (s, 2H), 7.40 (d, *J* = 10.0 Hz, 4H), 7.35 (d, *J* = 10.0 Hz, 4H), 7.29-7.20 (m, 8H), 7.09 (d, *J* = 5.0 Hz, 2H), 6.88-6.86 (m, 6H), 6.63-6.61 (m, 4H), 5.10 (d, *J* = 20.0 Hz, 2H), 4.74 (d, *J* = 20.0 Hz, 2H); ^{13}C NMR (125 MHz, acetone-d_6) δ 153.3, 142.7, 140.7, 140.3, 138.8, 130.6, 128.69, 128.65, 127.1, 127.0, 126.3, 125.3, 124.3, 123.4, 123.3, 120.3, 119.8, 118.5, 110.3, 102.8, 47.5; IR (neat) 3506, 2923, 1625, 1603, 1495, 1474, 1448, 1434, 1411, 1347, 1320, 1264, 1228, 1203, 1182, 1152, 1125, 958 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{50}H_{37}N_2O_2$ $[M+H]^+$ *m/z* = 697.2855, found 697.2839. $[\alpha]_D^{22}$ +39 (*c* 0.25, 60% ee, CH_2Cl_2); Chiral HPLC: Chiralpak IA column (10% *i*-PrOH/hexanes, 1 mL/min) t_R(*1*) = 10.4 min, t_R(*2*) = 15.7 min.

Procedure Control Experiments

Radical Inhibitor: To a microwave vial was added 1.0 equiv of **1a**, 20 mol % of **V6**, 6.25 equiv of acetic acid, and 0.2 equiv of TEMPO. The vials were sealed and toluene (0.5 M) was added. Oxygen was added *via an* active purge. The deep blue reaction solution was stirred at room temperature. The reaction conversion was determined by ^{1}H NMR.

Catalyst Stoichiometry: In microwave vials were added **1a** (1.0 equiv), acetic acid (6.25 equiv), and 20 mol % of **V6** or 50 mol % of **V6** in a separate vial. The vials were sealed and toluene (0.5 M) was added. Argon was added *via an* active purge. The deep blue reaction solution was stirred at an ambient temperature. The reaction conversions were determined by ^{1}H NMR.

Procedure for Deuterium Isotope Effects Experiment. In microwave vials were added **1a** (50 mg, 0.37 mmol), **V6** (32 mg, 0.07 mmol), 4,4'-di-*tert*-butylbiphenyl (24 mg, 0.09 mmol), and acetic acid (0.13 mL, 2.23 mmol) or acetic acid-d_4 (0.13 mL, 2.23 mmol) in a separate vial. The vials were sealed and toluene (0.73 mL) was added. Oxygen was added *via an* active purge. The deep blue reaction solution was stirred at 0 °C. The reaction conversions and yields were determined by ^{1}H NMR.

Computational Studies. Optimizations of intermediates and transition states were performed using Gaussian 09[44] software with spin-unrestricted DFT at the UB3LYP[45]/(6-31G(d), V: LANL2DZ[46]) level in the gas phase. For all species, vibrational frequencies were also computed at the specified level of theory to obtain thermal Gibbs Free Energy corrections (at 298 K) and to characterize the stationary points as transition states (one and only one imaginary frequency) or relative minima (zero imaginary frequencies). Single point energy calculations were performed on optimized geometries in toluene solvent using the SMD[47]-solvation model with UM06[48] functional and LANL2DZ basis set for vanadium and 6-311+G(d,p) basis set for all other atoms. Obtained single-point energies were converted to the enthalpies and Gibbs

free energies using corrections from gas-phase frequency analysis. Extensive conformational analysis of the transition states was performed manually. Distortion-interaction analysis[49] of the coupling step was performed at UB3LYP/6-31g(d), V: LANL2DZ using gas-phase geometries.

ASSOCIATED CONTENT

Supporting Information. Mechanistic experimental results, NRM spectra, and computational data. This material is available free of charge via the Internet at http://pubs.acs.org.

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REFERENCES

(1) (a) Fukuyama, Y.; Asakawa, Y. Novel Neurotrophic Isocuparane-Type Sesquiterpene Dimers, Mastigophorenes A, B, C and D, Isolated from the Liverwort Mastigophora Diclados. *J. Chem. Soc. [Perkin 1]* **1991**, *0* (11), 2737–2741. (b) Degnan, A. P.; Meyers, A. I. Total Syntheses of (−)-Herbertenediol, (−)-Mastigophorene A, and (−)-Mastigophorene B. Combined Utility of Chiral Bicyclic Lactams and Chiral Aryl Oxazolines. *J. Am. Chem. Soc.* **1999**, *121*, 2762–2769. (c) Narayan, S.; Roush, W. R. Studies Toward the Total Synthesis of Angelmicin B (Hibarimicin B): Synthesis of a Model CD–D′ Arylnaphthoquinone. *Org. Lett.* **2004**, *6*, 3789–3792. (d) Kenar, J. A. Reaction Chemistry of Gossypol and Its Derivatives. *J. Am. Oil Chem. Soc.* **2006**, *83*, 269–302. (e) Buter, J.; Heijnen, D.; Vila, C.; Hornillos, V.; Otten, E.; Giannerini, M.; Minnaard, A. J.; Feringa, B. L. Palladium-Catalyzed, Tert-Butyllithium-Mediated Dimerization of Aryl Halides and Its Application in the Atropselective Total Synthesis of Mastigophorene A. *Angew. Chem. Int. Ed.* **2016**, *55*, 3620–3624. (f) Ming Ge, H.; Yun Zhang, W.; Ding, G.; Saparpakorn, P.; Chun Song, Y.; Hannongbua, S.; Xiang Tan, R. Chaetoglobins A and B, Two Unusual Alkaloids from Endophytic Chaetomium Globosum Culture. *Chem. Commun.* **2008**, 5978-5980. (g) Nutan, M. T.; Hasan, C.; Rashid, M. Bismurrayafoline E: A New Dimeric Carbazole Alkaloid from Murraya Koenigii. *Fitoterapia* **1999**, *70*, 130–133. (h) Tachibana, Y.; Kikuzaki, H.; Lajis, N. H.; Nakatani, N. Comparison of Antioxidative Properties of Carbazole Alkaloids from Murraya Koenigii Leaves. *J. Agric. Food Chem.* **2003**, *51*, 6461–6467.

(2) (a) Brunel, J. M. BINOL: A Versatile Chiral Reagent. *Chem. Rev.* **2005**, *105*, 857–898. (b) Qiu, L.; Kwong, F. Y.; Wu, J.; Lam, W. H.; Chan, S.; Yu, W.-Y.; Li, Y.-M.; Guo, R.; Zhou, Z.; Chan, A. S. C. A New Class of Versatile Chiral-Bridged Atropisomeric Diphosphine Ligands: Remarkably Efficient Ligand Syntheses and Their Applications in Highly Enantioselective Hydrogenation Reactions. *J. Am. Chem. Soc.* **2006**, *128*, 5955–5965. (c) Melhado, A. D.; Luparia, M.; Toste, F. D. Au(I)-Catalyzed Enantioselective 1,3-Dipolar Cycloadditions of Münchnones with Electron-Deficient Alkenes. *J. Am. Chem. Soc.* **2007**, *129*, 12638–12639. (d) Heiser, B.; Broger, E. A.; Crameri, Y. New Efficient Methods for the Synthesis and In-Situ Preparation of Ruthenium(II) Complexes of Atropisomeric Diphosphines and Their Application in Asymmetric Catalytic Hydrogenations. *Tetrahedron Asymmetry* **1991**, *2*, 51–62.

(3) (a) Nakajima, M.; Miyoshi, I.; Kanayama, K.; Hashimoto, S.; Noji, M.; Koga, K. Enantioselective Synthesis of Binaphthol Derivatives by Oxidative Coupling of Naphthol Derivatives Catalyzed by Chiral Diamine·Copper Complexes. *J. Org. Chem.* **1999**, *64*, 2264–2271. (b) Kim, H. Y.; Takizawa, S.; Sasai, H.; Oh, K. Reversal of Enantioselectivity Approach to BINOLs via Single and Dual 2-Naphthol Activation Modes. *Org. Lett.* **2017**, *19* (14), 3867–3870.
(4) Li, X.; Yang, J.; Kozlowski, M. C. Enantioselective Oxidative Biaryl Coupling Reactions Catalyzed by 1,5-Diazadecalin Metal Complexes. *Org. Lett.* **2001**, *3*, 1137–1140.
(5) Kim, K. H.; Lee, D.-W.; Lee, Y.-S.; Ko, D.-H.; Ha, D.-C. Enantioselective Oxidative Coupling of Methyl 3-Hydroxy-2-Naphthoate Using Mono-N-Alkylated Octahydrobinaphthyl-2,2′-Diamine Ligand. *Tetrahedron* **2004**, *60*, 9037–9042.
(6) Chu, C.-Y.; Uang, B.-J. Catalytic Enantioselective Coupling of 2-Naphthols by New Chiral Oxovanadium Complexes Bearing a Self Accelerating Functional Group. *Tetrahedron Asymmetry* **2003**, *14*, 53–55.
(7) Barhate, N. B.; Chen, C.-T. Catalytic Asymmetric Oxidative Couplings of 2-Naphthols by Tridentate N-Ketopinidene-Based Vanadyl Dicarboxylates. *Org. Lett.* **2002**, *4*, 2529–2532.
(8) Guo, Q.-X.; Wu, Z.-J.; Luo, Z.-B.; Liu, Q.-Z.; Ye, J.-L.; Luo, S.-W.; Cun, L.-F.; Gong, L.-Z. Highly Enantioselective Oxidative Couplings of 2-Naphthols Catalyzed by Chiral Bimetallic Oxovanadium Complexes with Either Oxygen or Air as Oxidant. *J. Am. Chem. Soc.* **2007**, *129*, 13927–13938.
(9) (a) Takizawa, S.; Katayama, T.; Somei, H.; Asano, Y.; Yoshida, T.; Kameyama, C.; Rajesh, D.; Onitsuka, K.; Suzuki, T.; Mikami, M.; Yamataka, H.; Jayaprakash, D.; Sasai, H. Dual Activation in Oxidative Coupling of 2-Naphthols Catalyzed by Chiral Dinuclear Vanadium Complexes. *Tetrahedron* **2008**, *64*, 3361–3371. (b) Kim, H. Y.; Takizawa, S.; Sasai, H.; Oh, K. Reversal of Enantioselectivity Approach to BINOLs via Single and Dual 2-Naphthol Activation Modes. *Org. Lett.* **2017**, *19* (14), 3867–3870.
(10) Egami, H.; Katsuki, T. Iron-Catalyzed Asymmetric Aerobic Oxidation: Oxidative Coupling of 2-Naphthols. *J. Am. Chem. Soc.* **2009**, *131*, 6082–6083.
(11) Narute, S.; Parnes, R.; Toste, F. D.; Pappo, D. Enantioselective Oxidative Homocoupling and Cross-Coupling of 2-Naphthols Catalyzed by Chiral Iron Phosphate Complexes. *J. Am. Chem. Soc.* **2016**, *138*, 16553–16560.
(12) Kang, H.; Lee, Y. E.; Reddy, P. V. G.; Dey, S.; Allen, S. E.; Niederer, K. A.; Sung, P.; Hewitt, K.; Torruellas, C.; Herling, M. R.; Kozlowski, M. C. Asymmetric Oxidative Coupling of Phenols and Hydroxycarbazoles. *Org. Lett.* **2017**, *19*, 5505–5508.
(13) Hwang, D.-R.; Chen, C.-P.; Uang, B.-J. Aerobic Catalytic Oxidative Coupling of 2-Naphthols and Phenols by $VO(acac)_2$. *Chem. Commun.* **1999**, 1207–1208.
(14) Lee, Y. E.; Cao, T.; Torruellas, C.; Kozlowski, M. C. Selective Oxidative Homo- and Cross-Coupling of Phenols with Aerobic Catalysts. *J. Am. Chem. Soc.* **2014**, *136*, 6782–6785.
(15) Libman, A.; Shalit, H.; Vainer, Y.; Narute, S.; Kozuch, S.; Pappo, D. Synthetic and Predictive Approach to Unsymmetrical Biphenols by Iron-Catalyzed Chelated Radical–Anion Oxidative Coupling. *J. Am. Chem. Soc.* **2015**, *137*, 11453–11460.
(16) Jiang, Q.; Sheng, W.; Tian, M.; Tang, J.; Guo, C. Cobalt(II)-Porphyrin-Catalyzed Aerobic Oxidation: Oxidative Coupling of Phenols. *Eur. J. Org. Chem.* **2013**, 1861–1866.
(17) (a) Chen, Y.-H.; Cheng, D.-J.; Zhang, J.; Wang, Y.; Liu, X.-Y.; Tan, B. Atroposelective Synthesis of Axially Chiral Biaryldiols via Organocatalytic Arylation of 2-Naphthols. *J. Am. Chem. Soc.* **2015**, *137*, 15062–15065. (b) Wang, J.-Z.; Zhou, J.; Xu, C.; Sun, H.; Kürti, L.; Xu, Q.-L. Symmetry in Cascade Chirality-Transfer Processes: A Catalytic Atroposelective Direct Arylation Approach to BINOL Derivatives. *J. Am. Chem. Soc.* **2016**, *138*, 5202–5205.
(18) Moody, C. J.; Shah, P. Diels-Alder Reactivity of Pyrano[3,4-b]Indol-3-Ones. Part 4. Synthesis of the Carbazole Alkaloids Carbazomycin A and B and Hyellazole. *J. Chem. Soc. [Perkin 1]* **1989**, 2463–2471.
(19) (a) Bringmann, G.; Ledermann, A.; Stahl, M.; Gulden, K. Bismurrayaquinone A: Synthesis, Chromatographic Enantiomer Resolution, and Stereoanalysis by Computational and Experimental CD Investigations. *Tetrahedron* **1995**, *51*, 9353–9360. (b) Lin, G.; Zhang, A. Synthesis of Optically Pure Clausenamine-A and Its Demethoxylated Analogs. *Tetrahedron* **2000**, *56*, 7163–7171. (c) Fillion, H.; Bouaziz, Z.; Nebois, P.; Poumaroux, A. Carbazole-1,4-Diones: Syntheses and Properties. *HETEROCYCLES* **2000**, *52*, 977–1000.
(20) Knölker, H.-J.; Goesmann, H.; Hofmann, C. Transition Metal Complexes in Organic Synthesis, Part 31.1 A Novel Molybdenum-Mediated Synthesis of Carbazole Derivatives: Application to the Total Synthesis of Mukonal and 1,1'-Bis(2-Hydroxy-3-Methylcarbazole). *Synlett* **1996**, *1996*, 737–740.
(21) Liu, L.; Carroll, P. J.; Kozlowski, M. C. Vanadium-Catalyzed Regioselective Oxidative Coupling of 2-Hydroxycarbazoles. *Org. Lett.* **2015**, *17*, 508–511.

(22) (a) Chu, C.-Y.; Hwang, D.-R.; Wang, S.-K.; Uang, B.-J. Chiral Oxovanadium Complex Catalyzed Enantioselective Oxidative Coupling of 2-Naphthols. *Chem. Commun.* **2001**, 980–981. (b) Hon, S.-W.; Li, C.-H.; Kuo, J.-H.; Barhate, N. B.; Liu, Y.-H.; Wang, Y.; Chen, C.-T. Catalytic Asymmetric Coupling of 2-Naphthols by Chiral Tridentate Oxovanadium(IV) Complexes. *Org. Lett.* **2001**, *3*, 869–872. (c) Luo, Z.; Liu, Q.; Gong, L.; Cui, X.; Mi, A.; Jiang, Y. The Rational Design of Novel Chiral Oxovanadium(IV) Complexes for Highly Enantioselective Oxidative Coupling of 2-Naphthols. *Chem. Commun.* **2002**, 914–915. (d) Somei, H.; Asano, Y.; Yoshida, T.; Takizawa, S.; Yamataka, H.; Sasai, H. Dual Activation in a Homolytic Coupling Reaction Promoted by an Enantioselective Dinuclear Vanadium(IV) Catalyst. *Tetrahedron Lett.* **2004**, *45*, 1841–1844.
(23) (a) Takizawa, S.; Katayama, T.; Kameyama, C.; Onitsuka, K.; Suzuki, T.; Yanagida, T.; Kawai, T.; Sasai, H. Chiral Dinuclear Vanadium(V) Catalysts for Oxidative Coupling of 2-Naphthols. *Chem. Commun.* **2008**, *0* (15), 1810–1812. (b) Takizawa, S.; Katayama, T.; Sasai, H. Dinuclear Chiral Vanadium Catalysts for Oxidative Coupling of 2-Naphtholsvia a Dual Activation Mechanism. *Chem. Commun.* **2008**, *0*(35), 4113–4122. (c) Takizawa, S.; Kodera, J.; Yoshida, Y.; Sako, M.; Breukers, S.; Enders, D.; Sasai, H. Enantioselective Oxidative-Coupling of Polycyclic Phenols. *Tetrahedron* **2014**, *70*, 1786–1793. (d) Sako, M.; Takeuchi, Y.; Tsujihara, T.; Kodera, J.; Kawano, T.; Takizawa, S.; Sasai, H. Efficient Enantioselective Synthesis of Oxahelicenes Using Redox/Acid Cooperative Catalysts. *J. Am. Chem. Soc.* **2016**, *138*, 11481–11484.
(24) Hartung, J.; Drees, S.; Greb, M.; Schmidt, P.; Svoboda, I.; Fuess, H.; Murso, A.; Stalke, D. (Schiff-Base)Vanadium(V) Complex-Catalyzed Oxidations of Substituted Bis(Homoallylic) Alcohols – Stereoselective Synthesis of Functionalized Tetrahydrofurans. *Eur. J. Org. Chem.* **2003**, 2388–2408.

(25) Bedford, R. B.; Betham, M. N-H Carbazole Synthesis from 2-Chloroanilines via Consecutive Amination and C−H Activation. *J. Org. Chem.* **2006**, *71*, 9403–9410.
(26) Albanese, D.; Landini, D.; Penso, M.; Spanò, G.; Trebicka, A. Chemoselective N-Alkylation of 2-Hydroxycarbazole as a Model for the Synthesis of N-Substituted Pyrrole Derivatives Containing Acidic Functions. *Tetrahedron* **1995**, *51*, 5681–5688.
(27) Duggan, K. A. Preparation of biphenyl propanamide compounds for the treatment of hypertension and/or fibrosis. *PCT Int. Appl.* WO 2015039172 A1, Mar. 26, 2015.
(28) Akiyama, T.; Hirofuji, H.; Ozaki, S. $AlCl_3$-N,N-Dimethylaniline: A New Benzyl and Allyl Ether Cleavage Reagent. *Tetrahedron Lett.* **1991**, *32*, 1321–1324.
(29) Wiberg, K. B. The Deuterium Isotope Effect. *Chem. Rev.* **1955**, *55*, 713–743.
(30) Vernall, A. J.; Ballet, S.; Abell, A. D. Cross-Metathesis and Ring-Closing Metathesis Reactions of Amino Acid-Based Substrates. *Tetrahedron* **2008**, *64*, 3980–3997.
(31) Jin, Z.; Yang, R.; Du, Y.; Tiwari, B.; Ganguly, R.; Chi, Y. R. Enantioselective Intramolecular Formal [2 + 4] Annulation of Acrylates and α,β-Unsaturated Imines Catalyzed by Amino Acid Derived Phosphines. *Org. Lett.* **2012**, *14*, 3226–3229.
(32) Gisch, N.; Balzarini, J.; Meier, C. Enzymatically Activated Cyclo Sal-D4T-Monophosphates: The Third Generation of Cyclo Sal-Pronucleotides. *J. Med. Chem.* **2007**, *50*, 1658–1667.
(33) Chen, C.-T.; Kao, J.-Q.; Salunke, S. B.; Lin, Y.-H. Enantioselective Aerobic Oxidation of α-Hydroxy-Ketones Catalyzed by Oxidovanadium(V) Methoxides Bearing Chiral, N -Salicylidene- Tert -Butylglycinates. *Org. Lett.* **2011**, *13*, 26–29.
(34) Armstrong, D. R.; Cameron, C.; Nonhebel, D. C.; Perkins, P. G. Oxidative Coupling of Phenols. Part 9. The Role of Steric Effects in the Oxidation of Methyl-Substituted Phenols. *J. Chem. Soc. Perkin Trans. 2* **1983**, 581–585.
(35) Henschke, J. P.; Burk, M. J.; Malan, C. G.; Herzberg, D.; Peterson, J. A.; Wildsmith, A. J.; Cobley, C. J.; Casy, G. Synthesis and Applications of HexaPHEMP, a Novel Biaryl Diphosphine Ligand. Adv. Synth. Catal. 2003, 345, 300–307.
(36) Malkowsky, I. M.; Rommel, C. E.; Fröhlich, R.; Griesbach, U.; Pütter, H.; Waldvogel, S. R. Novel Template-Directed Anodic Phenol-Coupling Reaction. *Chem. Eur. J.* **2006**, *12*, 7482–7488.
(37) Shapiro, R. Process for preparing 3,3',6,6'-tetraalkyl-2,2'-biphenols and 3,3',6,6'-tetraalkyl-5,5'-dihalo-2,2'-biphenols. US Patent 6,489,517 B1, Dec. 3, 2002.
(38) Tanaka, K.; Moriyama, A.; Toda, F. New Preparative Method for Optically Active 2,2′- and 4,4′-Dihydroxybiphenyl Derivatives. A New Chiral Host Compound 4,4′-Dihydroxy-2,2′,3,3′,6,6′-Hexamethylbiphenyl. *J. Chem. Soc. [Perkin 1]* **1996**, 603–604.
(39) Duggan, K. A. Preparation of biphenyl propanamide compounds for the treatment of hypertension and/or fibrosis. PCT Int. Appl. WO 2015039172 A1, Mar. 26, 2015.
(40) Bedford, R. B.; Betham, M. N-H Carbazole Synthesis from 2-Chloroanilines via Consecutive Amination and C−H Activation. *J. Org. Chem.* **2006**, *71*, 9403–9410.
(41) Dai, J.; Ma, D.; Fu, C.; Ma, S. Gram Scale Total Synthesis of 2-Hydroxy-3-Methylcarbazole, Pyrano[3,2-a]Carbazole and Prenylcarbazole Alkaloids. *Eur. J. Org. Chem.* **2015**, 5655–5662.
(42) Bedford, R. B.; Betham, M.; Charmant, J. P. H.; Weeks, A. L. Intramolecular Direct Arylation in the Synthesis of Fluorinated Carbazoles. *Tetrahedron* **2008**, *64*, 6038–6050.
(43) Yang, Y.; Mustard, T. J. L.; Cheong, P. H.-Y.; Buchwald, S. L. Palladium-Catalyzed Completely Linear-Selective Negishi Cross-Coupling of Allylzinc Halides with Aryl and Vinyl Electrophiles. *Angew. Chem. Int. Ed.* **2013**, *52*, 14098–14102.
(44) Gaussian 09, Revision D.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2013.
(45) (a) Lee, C.; Yang, W.; Parr, R. G. Development of the Colle-Salvetti Correlation-Energy Formula into a Functional of the Electron Density. *Phys. Rev. B* **1988**, *37*, 785–789. (b) Becke, A. D. A New Mixing of Hartree–Fock and Local Density-functional Theories. *J. Chem. Phys.* **1993**, *98*, 1372–1377. (c) Becke, A. D. Density-functional Thermochemistry. III. The Role of Exact Exchange. *J. Chem. Phys.* **1993**, *98*, 5648–5652.
(46) Hay, P. J.; Wadt, W. R. Ab Initio Effective Core Potentials for Molecular Calculations. Potentials for the Transition Metal Atoms Sc to Hg. *J. Chem. Phys.* **1985**, *82*, 270–283.
(47) Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. Universal Solvation Model Based on Solute Electron Density and on a Continuum Model of the Solvent Defined by the Bulk Dielectric Constant and Atomic Surface Tensions. *J. Phys. Chem. B* **2009**, *113*, 6378–6396.
(48) Zhao, Y.; Truhlar, D. G. The M06 Suite of Density Functionals for Main Group Thermochemistry, Thermochemical Kinetics, Noncovalent Interactions, Excited States, and Transition Elements: Two New Functionals and Systematic Testing of Four M06-Class Functionals and 12 Other Functionals. *Theor. Chem. Acc.* **2008**, *120*, 215–241.
(49) Bickelhaupt, F. M.; Houk, K. N. Analyzing Reaction Rates with the Distortion/Interaction-Activation Strain Model. *Angew. Chem. Int. Ed.* **2017**, *56*, 10070–10086.