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Enantioselective synthesis of butadien-2-ylcarbinols via (silylmethyl)allenic alcohols from chromium-catalyzed additions to aldehydes utilizing chiral carbazole ligands

María Durán-Galván, Shilpa A. Worlikar, Brian T. Connell *

Department of Chemistry, Texas A&M University, PO Box 30012, College Station, TX 77842-3012, US

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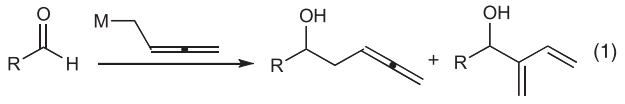
ABSTRACT

The synthesis of chiral, nonracemic butadienylcarbinols by employing intermediate (trimethylsilyl) methylallenic alcohols is described. Allenic alcohols are obtained by treatment of aldehydes with (4-bromobut-2-ynyl)trimethylsilane in the presence of a catalytic amount of $CrCl_3$ or $CrCl_2$. Several new tridentate bis(oxazolinyl)carbazole ligands were synthesized and evaluated as the source of chirality. The synthesis of chiral allenic alcohols can be achieved in good yields (58–88%) and enantioselectivities (55–78% ee). Allenic alcohols may be treated with TBAF or 2 M HCl to provide the desired dienes in 43–86% yields. Alternatively, the (trimethylsilyl)methyl allenic alcohols afford iodobutadienyl carbinols when treated with *N*-iodosuccinimide.

1. Introduction

1,3-Butadien-2-ylcarbinols are highly functionalized molecules that are attractive to organic chemists due to their versatility as building blocks in organic synthesis.[1] As a result, a number of methodologies have been developed for the synthesis of these molecules. Early protocols include addition of Grignard[2] and lithium[3] reagents to aldehydes or epoxides. The majority of these methods gave low regioselectivity, providing mixtures of 1,3-butadien-2-ylcarbinols and allenic alcohols (Eq. 1). Therefore, methodologies involving the use of different organometallic reagents, such as tin,[4] boron,[5] and silicon[1d,e] compounds were developed to overcome regioselectivity problems. These methods have achieved modest to high enantioselectivities.



(1)

Unfortunately, these procedures require the preparation of non-readily available organometallic starting materials as well as the use of considerable amounts of toxic reagents. Recently, new approaches have emerged to avoid these drawbacks.[1a,6] For instance, Chan developed an indium-mediated coupling in aqueous media where the active organoindium intermediate is formed in situ.[6d] In other approaches, Alcaraz reported the homologation of chiral epoxy bromides while Diver developed an alkyne-ethylene cross-metathesis protocol to provide the corresponding 1,3-butadien-2-ylcarbinols.[6b,e] More recently, Yamamoto et al. reported an enantioselective protocol, which allows the formation of 1,3-butadien-2-ylcarbinols with high enantioselectivity and moderate yields by directly coupling aldehydes with 4-bromobuta-1,2-diene.[6f]

Although the methods recently developed have overcome many of the limitations presented by early approaches, only a few enantioselective synthetic procedures are known and which present various drawbacks including limited functional group tolerance or low reactivity that results in modest yields. Hence, there is an interest in developing an alternate method for the synthesis of 1,3-butadien-2-ylcarbinols. (Allenylmethyl)silanes are powerful synthetic reagents capable of reacting with a wide variety of electrophiles to afford 1,3-dienyl-2-yl compounds.[4d,7] It is known that (trimethylsilyl) methyl allenic alcohols provide the corresponding 1,3-butadien-2-ylcarbinols by treatment with hydrofluoric acid.[4d] Therefore, we focused on the synthesis of these chiral (silylmethyl)allenic alcohols, which could be directly converted to the desired dienes (Eq. 2).

* Corresponding author. Tel.: +1 979 845 5746; fax: +1 979 458 2969; e-mail address: connell@chem.tamu.edu (B.T. Connell).

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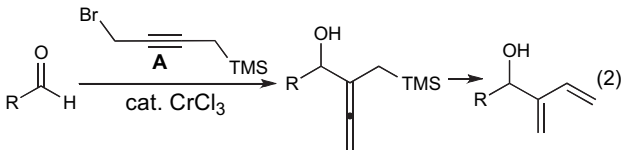


A Cr/Mn redox system catalyzes the enantioselective allenylation of aldehydes with propargyl bromides or 4-bromobuta-1,2-diene (Eq. 3).[8] The asymmetric allenylation utilizing tridentate bis (oxazoline) carbazole ligands **1** (Fig. 1) developed by Nakada et al. is among these reports. These carbazole ligands attracted our attention because they proved to be an excellent source of chirality for these asymmetric Nozaki–Hiyama type reactions.[8a,9]

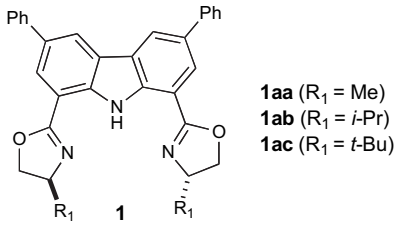
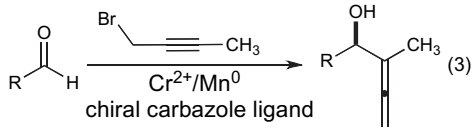


Figure 1. Tridentate bis(oxazoline)carbazoles.

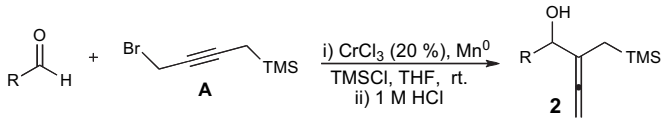
We envisioned that the chiral (trimethylsilyl)methyl allenic alcohols can be prepared by the chromium-catalyzed allenylation of aldehydes with (4-bromobut-2-ynyl)trimethylsilane (**A**) utilizing the bis-oxazoline carbazole ligands. Herein, we describe the racemic and enantioselective synthesis of (trimethylsilyl)methyl allenic alcohols and its transformation to 1,3-butadien-2-ylcarbinols.[10]

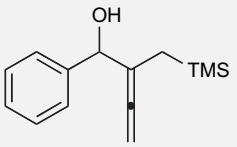
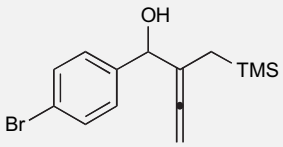
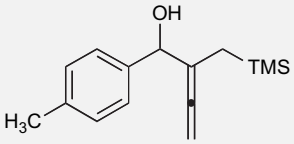
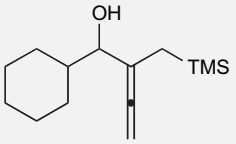
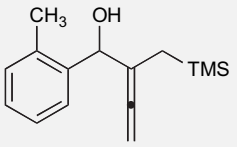
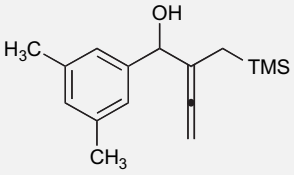
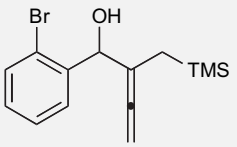
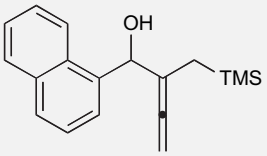
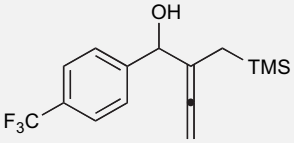
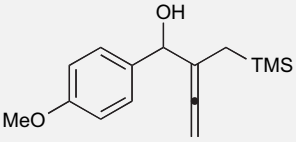


2. Results and discussion

The propargylic bromide (4-bromobut-2-ynyl) trimethylsilane (**A**) was prepared from but-2-yn-1-ol by a known procedure.[11] Benzaldehyde was combined with **A** in the presence of a catalytic amount of $CrCl_3$, 2 equiv Mn^0 and 1.1 equiv TMSCl in THF. The desired allenic alcohol **2a** was formed in 75% yield after 16 h with excellent regioselectivity (Table 1, entry 1). The corresponding propargylic

Table 1
Scope of the chromium-catalyzed allenylation reaction[a]



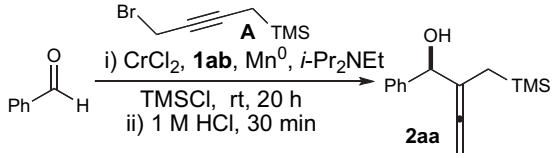
Entry	Product		Yield[b] (%)	Entry	Product		Yield[b] (%)
1		**2a**	75	6		**2f**	56
2		**2b**	70	7[d]		**2g**	81
3[c]		**2c**	54	8		**2i**	59
4		**2d**	77	9[c]		**2j**	60
5		**2e**	83	10[e]		**2k**	56

[a] Reaction conditions: (4-bromobut-2-ynyl)trimethylsilane (**A**) (1.1 equiv), $CrCl_3$ (20 mol %), Mn^0 (2 equiv), TMSCl (1.1 equiv), THF, 16 h; 2 mL of 1 M HCl.
[b] Isolated yields.
[c] Reaction time: 48 h.
[d] Reaction time: 12 h.
[e] $CrCl_2$ (10 mol %).

alcohol was not observed. To explore the scope of the reaction, various aldehydes were examined as substrates. Aromatic aldehydes containing *para* substituents are excellent substrates for this reaction and afford the corresponding product in good yields (entry 2). However, more sterically hindered aldehydes required a longer reaction time, but the desired product was obtained in good yield after 48 h (entries 3 and 9). Allenic alcohol **2d** was obtained after only 16 h despite the presence of an *o*-bromo substituent (entry 4). The formation of allenic alcohols proceeds rapidly with good yields with aromatic aldehydes containing electron-withdrawing substituents (entries 4–6) and aliphatic aldehydes (entry 7). When *meta* substituted aldehydes are used, the product is obtained with 59% yield (entry 8). In the case of *p*-methoxybenzaldeyde only, the desired product is obtained when $CrCl_2$ is utilized for the allenylation reaction (entry 10).

Encouraged by these results, we directed our attention to the development of a method for the asymmetric synthesis of (trimethylsilyl)methyl allenic alcohols. We chose to examine the effect of ligand **1ab** under various conditions.[10] When **1ab** was utilized in THF (Table 2, entry 1), the desired alcohol **2aa** was obtained after 20 h in 31% ee. The %ee increased to 46% when $CrCl_2$ was used (entry 2). To optimize the reaction conditions, different solvents were explored (entries 3–6). No product was observed when 1,2-dimethoxyethane was used, while DMF and EtCN[8a] afforded the desired product with poor to moderate enantiomeric excess (entries 4 and 5). MeCN became the solvent of choice, increasing the %ee to 73%. Next, the effect of catalyst loading was studied (entries 7 and 8). Decreasing the loading of $CrCl_2$ and ligand to 5 mol % had virtually no effect on the %ee (entries 6 and 7) but when the loading was further reduced to 2.5 mol % the %ee decreased considerably (entry 8). A slight increase in the %ee was observed with 5 mol % of the catalyst and 2 equiv Mn^0 (entry 9). Under these conditions, the starting material was completely consumed after 36 h (entry 10). Additional Mn^0 (5 equiv) reduced the %ee (entry 11).[12]

Table 2
Optimization of enantioselective reaction conditions[a]

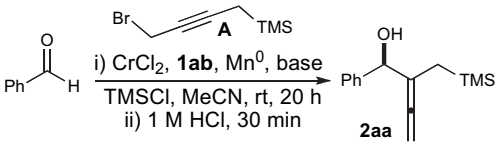


Entry	$CrCl_2$ (%)	Mn^0(equiv)	Solvent	Yield (%)	ee[b] (%)
1	10% $CrCl_3$	1.5	THF	99	31
2	10	1.5	THF	99	46
3	10	1.5	DME	0	0
4	10	1.5	DMF	74	8
5	10	1.5	EtCN	95	48
6	10	1.5	CH_3CN	99	73
7	5	1.5	CH_3CN	—	72
8	2.5	1.5	CH_3CN	—	51
9	5	2	CH_3CN	91	75
10[c]	5	2	CH_3CN	99	78
11	5	5	CH_3CN	—	21

[a] Reaction conditions: (4-bromobut-2-ynyl)trimethylsilane (**A**) (1.5 equiv), ligand **1ab** (5 mol %), TMSCl (1.1 equiv), *i*-Pr_2NEt (0.3 equiv), 20 h; 2 mL of 1 M HCl.
[b] Enantiomeric excess determined by chiral HPLC.
[c] Reaction time: 36 h.

The reaction rate is not dependent on the base employed. On the other hand, the %ee is higher when *i*-Pr_2NEt, 2,6-lutidine or pyridine is used (Table 3, entries 1–3) compared to bases with more steric hindrance, such as 2,6-di-*tert*-butylpyridine, DBU or DABCO (entries 5, 9, and 10).

Table 3
Screening of bases[a]

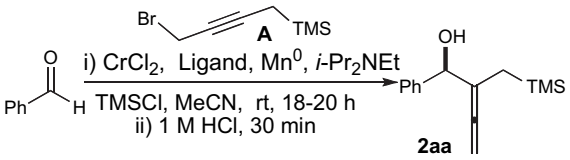


Entry	Base	Conversion (%)	ee[b] (%)
1	*i*-Pr_2Et	91	78
2	2,6-Lutidine	97	74
3	Pyridine	99	68
4	4-*tert*-Bupyridine	85	26
5	2,6-di-*tert*-Bupyridine	99	40
6	2-Chloropyridine	86	52
7	2-Bromopyridine	95	52
8	1,8-Bis(dimethyl amino)naphthalene	99	45
9	DBU	99	29
10[c]	DABCO	98	24
11	K_2CO_3	95	11

[a] Reaction conditions: (4-bromobut-2-ynyl)trimethylsilane (**A**) (1.5 equiv), $CrCl_2$ (5 mol %), ligand **1ab** (5 mol %), Mn^0 (2 equiv), TMSCl (1.1 equiv), *i*-Pr_2NEt (0.3 equiv), 20 h 2 mL of 1 M HCl.
[b] Enantiomeric excess and conversion determined by chiral HPLC.

After the reaction conditions were optimized with respect to solvent, catalyst loading, Mn^0 and base, different carbazole ligands were explored. Ligands **1aa**–**ac** were synthesized by known procedures (Fig. 1).[9b,13] It was observed that the substituent R^1 plays an important role in the %ee of the reaction. Smaller R^1 substituents, such as Me or *i*-Pr afforded the product with higher %ee values (Table 4, entries 1 and 2), while the bulkier *t*-Bu-substituted ligand decreased the %ee and considerably slowed the reaction rate (entry 3).

Table 4
Initial screening of carbazole ligands[a]

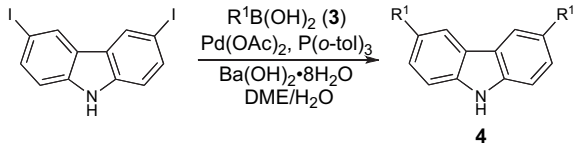


Entry	Ligand	Conversion (%)	ee[b] (%)
1	**1aa** (R_1=Me)	92	74
2	**1ab** (R_1=*i*-Pr)	91	78
3[c]	**1ac** (R_1=*t*-Bu)	86	20

[a] Reaction conditions: (4-bromobut-2-ynyl)trimethylsilane (**A**) (1.5 equiv), $CrCl_2$ (5 mol %), ligand (5 mol %), Mn^0 (2 equiv), TMSCl (1.1 equiv), *i*-Pr_2NEt (0.3 equiv), 20 h; 2 mL of 1 M HCl.
[b] Enantiomeric excess and conversion determined by chiral HPLC.
[c] Reaction time: 4 days.

With the results of Table 4 in hand, we felt that a more thorough investigation of the effects of carbazole ligand substitution on reaction yield and enantioselectivity was warranted. Unfortunately, the known methods of synthesizing substituted carbazoles cannot be broadly applied to a range of analogues of ligand **1**, therefore modified synthetic routes to these molecules were explored. Our strategy for a more general synthesis of ligands **1** can be described as a cross-coupling of dihalocarbazoles with boronic acids, followed by halogenation, carbonylative amidation, and cyclization.[13] 3,6-Disubstituted carbazoles **4a**–**c**, **4e**, and **4f** were prepared by Suzuki coupling of 3,6-diiodo-9*H*-carbazole with the corresponding boronic acid **3** using $Pd(OAc)_2$ catalyst, P(*o*-tol)$_3$ ligand, and $Ba(OH)_2 \cdot 8H_2O$ base in DME/H_2O (Table 5). Known carbazoles **4a**, **4b**, and **4f** were obtained with excellent yield.[9b,14] While carbazole **4c** was obtained with moderate yield, carbazole **4d** was not obtained under these conditions. However, when $Pd(PPh_3)_4$ was used as

Table 5
Suzuki coupling of 3,6-diiodo-9*H*-carbazole with boronic acids **3**[a]



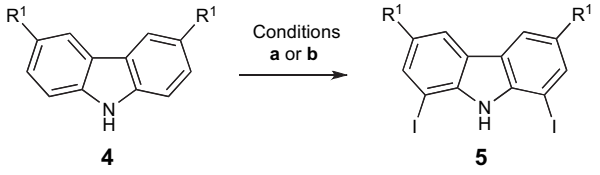
Entry	Boronic acid	Product	Yield[b] (%)
1	**3a** (R^1=Ph)	**4a**	84
2	**3b** (R^1=α-Naphthyl)	**4b**	79
3	**3c** (R^1=β-Naphthyl)	**4c**	23
4[c]	**3d** (R^1=9-Anthracenyl)	**4d**	<10
5	**3e** (R^1=2,6-Dimethylphenyl)	**4e**	96
6	**3f** (4-Methoxyphenyl)	**4f**	91

[a] $R^1B(OH)_2$ **3** (3.0 equiv), $Pd(OAc)_2$ (5 mol %), P(*o*-tol)$_3$ (10 mol %), $Ba(OH)_2\cdot 8H_2O$ (3.0 equiv), DME/H_2O, 80 °C, 8 h.
[b] Isolated yields.
[c] $R^1B(OH)_2$ (3.0 equiv), $Pd(PPh_3)_4$ (10 mol %), satd $NaHCO_3$, PhMe, EtOH, reflux, overnight.

catalyst, carbazole **4d** was obtained albeit with poor yield (Table 5, entry 4). Although TLC indicated completion of the reaction and a peak for the desired product was observed in the mass spectrum, we believe the limited solubility of carbazole **4d** lead to problems in purification and an ultimately low yield.

Next, substituted carbazoles **4** were halogenated to complete the preparation of the carbonylative amidation substrates (Table 6). Carbazole **5a** was obtained by the known procedure.[9b] Iodination of carbazole **4b** with benzyltrimethylammonium dichloroiodide (BTMA·ICl_2) afforded 3,6-di-α-naphtyl carbazole **5b** in 40% yield (Table 6, entry 2). Carbazole **5c** was obtained in 80% crude yield after iodination with a KI/KIO_4 mixture. Unfortunately, the yield decreases considerably after recrystallization from PhMe and the pure compound is obtained in only 18% yield (Table 6, entry 3). Carbazole **4d**, with bulky anthracenyl groups as 3,6-substituents, failed to give the desired halogenated carbazole. Although TLC indicated the formation of a new product, this compound was highly insoluble and could not be readily purified. Carbazoles **4e** and **4f** failed to give the desired iodinated product upon attempted iodination with either BTMA·ICl_2 or KI/KIO_4 as iodinating reagents.

Table 6
Iodination of 3,6-disubstituted carbazoles **4**



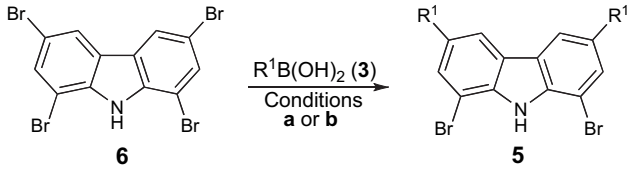
Entry	Carbazole	Conditions	Product	Yield[c] (%)
1	**4a** (R^1=Ph)	[a]	**5a**	38
2	**4b** (R^1=α-Naphthyl)	[b]	**5b**	40
3	**4c** (R^1=β-Naphthyl)	[a]	**5c**	18

[a] KI, KIO_4,·$2H_2O$, AcOH, H_2SO_4, H_2O, 5 h.
[b] $BnMe_3N\cdot ICl_2$ (2.2 equiv), AcOH, H_2SO_4, 60 °C, overnight.
[c] Isolated yields.

An alternative route was considered to obtain the desired 1,8-dihalocarbazoles, which were unattainable by the previous method. It was envisioned that 1,3,6,8-tetrabromo-9*H*-carbazole **6**[15] could be functionalized to afford the desired carbazoles **5d**–**e** (Table 7).

However, when **6** was combined with boronic acid **3d** under Suzuki coupling conditions, the desired 3,6–di(anthracen-9-yl)-1,8-dibromo-9*H*-carbazole **5d** was not obtained (entry 1). As observed previously for iodination, TLC suggested the formation of a coupled product but it was not isolated it due to extreme

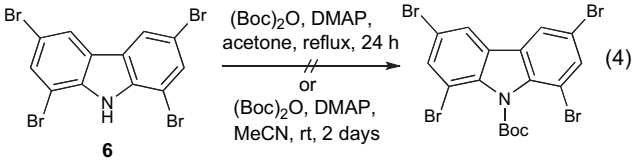
Table 7
Alternative route to obtain 1,8-dihalo-9*H*-carbazoles



Entry	Boronic acid	Conditions	Product	Yield[c] (%)
1	**3d** (R^1=9-Anthracenyl)	[a]	**5d**	0
2	**3e** (R^1=2,6-Dimethylphenyl)	[a,b]	**5e**	0
3	**3f** (4-Methoxyphenyl)	[a]	**5f**	40

[a] $Pd(PPh_3)_4$ (10 mol %), satd $NaHCO_3$, PhMe, EtOH, reflux, 5 h.
[b] $Pd(OAc)_2$ (5 mol %), P(*o*-tol)$_3$(10 mol %), $Ba(OH)_2\cdot 8H_2O$ (3.0 equiv), DME/H_2O, 80 °C, 8 h.
[c] Isolated yields.

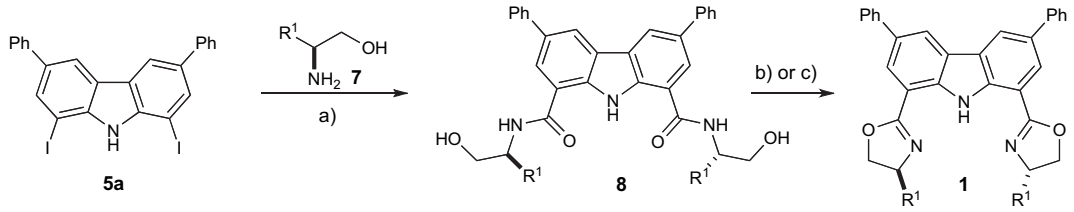
solubility problems. Sterically hindered boronic acid **3e** failed to give the desired carbazole **5e** upon coupling with 1,3,6,8-tetrabromo-9*H*-carbazole using either $Pd(OAc)_2$ or $Pd(PPh_3)_4$ catalysts. The bulky nature of boronic acid **3e** renders the oxidative addition of Pd to the C–Br bond difficult.[16] The electron-rich boronic acid **3f** gave the desired carbazole **5h** in 40% yield upon Suzuki coupling with 1,3,6,8-tetrabromo-9*H*-carbazole using $Pd(PPh_3)_4$ as the catalyst. With a view to improve the solubility of the product obtained by coupling **6** with boronic acid **3d**, we tried to introduce polar groups in the molecule before the Suzuki–Miyaura coupling step (Eq. 4). All attempts to protect the amino group of 1,3,6,8-tetrabromo-9*H*-carbazole with the Boc group failed, likely due to the steric hindrance surrounding the amine.



After obtaining the desired 1,8-dihalo precursors **5**, we carried out Pd-catalyzed carbonylative amidation with amino alcohols **7** derived by reduction of the corresponding chiral amino acids.[17] The bisamides were partially purified by passing through a short silica plug followed by immediate subjection to dehydrative cyclization. First, we focused on the variation of the substituent on the oxazoline group. Bisamide **8aa** was obtained from the $Pd(PPh_3)_4$ catalyzed coupling of carbazole **5a** and amino alcohol **7a** in the presence of Et_3N and under a CO atmosphere (Table 8). The desired ligand **1aa** was not obtained in good yields when subjected to $BF_3\cdot OEt_2$ induced cyclization, but it was isolated in 48% yield after two steps and high purity when subjected to $MeSO_2Cl$ cyclization followed by refluxing in 5% alcoholic KOH (Table 8, entry 1). Bisamides **8ad** and **8ae** provided 27% and 25% yields of the corresponding bis(oxazolinyl)carbazole, respectively (entries 2 and 3) after $BF_3\cdot OEt_2$ induced cyclization. Carbonylative amidation of **5a** with amino alcohol **7f**[18] provided bisamide **8af**, which failed to give the desired ligand **1af** when subjected to $BF_3\cdot OEt_2$ cyclization. $MeSO_2Cl$ cyclization of **8af** gave the desired ligand **1af** in 61% yield from **5a** (entry 4).

Next, we turned our attention to the synthesis of ligands **1** with different substituents in the carbazole nucleus. For this purpose, halogenated carbazoles **5** were subjected to carbonylative amidation with amino alcohol **7b**. Bisamides **8bb** and **8cb** gave the corresponding ligands by $BF_3\cdot OEt_2$ cyclization in 35% and 25% yields, respectively, starting with the corresponding 1,8-diiodo-9*H*-carbazoles **5b** and **5c** (Table 9, entries 1 and 2). Bisamide **8fb** failed to give the desired ligand when subjected to $BF_3\cdot OEt_2$ cyclization, but

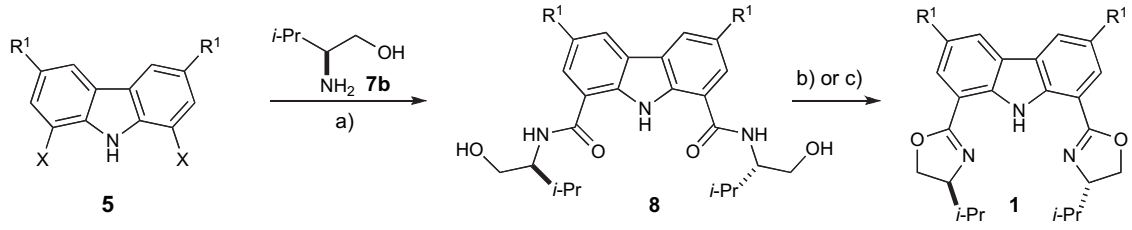
Table 8
Synthesis of bis(oxazolinyl)carbazoles from **5a**[a]



Entry	Amino alcohols	Bisamide	Cyclization method	Product	Yield[d] (%)
1	**7a** (R^1=Me)	**8aa**	[c]	**1aa**	48
2[e]	**7d**(R^1=Ph)	**8ad**	[b]	**1ad**	27
3	**7e**(R^1=Bn)	**8ae**	[b]	**1ae**	25
4[e]	**7f**(R^1=(*R*)-1-Methoxyethyl)	**8af**	[c]	**1af**	61

[a] Amino alcohol **7** (2.5 equiv) CO (1 atm), $Pd(PPh_3)_4$ (20 mol %), NEt_3 (4.0 equiv), DMF, 60 °C, 8 h.
[b] $BF_3{\cdot}Et_2O$, 120 °C, 6 h.
[c] (i) $MeSO_2Cl$ (2.5 equiv), NEt_3 (2.0 equiv), CH_2Cl_2, 0 °C to rt, 12 h. (ii) 5% alc KOH, reflux, 4 h.
[d] Isolated yields.
[e] The absolute configuration is as indicated, except for compounds containing amino alcohols **7d** or **7f**, for which the absolute configuration is (*R*).

Table 9
Synthesis of bis(oxazolinyl)carbazoles by coupling with **7b**[a]



Entry	Carbazole	R^1	X	Bisamide	Cyclization method	Product	Yield[d] (%)
1	**5b**	α-Naphthyl	I	**8bb**	[b]	**1bb**	35
2	**5c**	β-Naphthyl	I	**8cb**	[b]	**1cb**	25
3	**5f**	4-Methoxyphenyl	Br	**8fb**	[c]	**1fb**	55
4	**5g**	*tert*-Butyl	Br	**8gb**	[b]	**1gb**	26
5	**5g**	*tert*-Butyl	Br	**8gb**	[c]	**1gb**	51

[a] Amino alcohol **7** (2.5 equiv) CO (1 atm), $Pd(PPh_3)_4$ (20 mol %), NEt_3 (4.0 equiv), DMF, 60 °C, 8 h.
[b] $BF_3{\cdot}Et_2O$, 120 °C, 6 h.
[c] (i) $MeSO_2Cl$ (2.5 equiv), NEt_3 (2.0 equiv), CH_2Cl_2, 0 °C to rt, 12 h. (ii) 5% alc KOH, reflux, 4 h.
[d] Isolated yields.

provided a 55% yield of **1fb** when subjected to $MeSO_2Cl$ cyclization (entry 3). 1,8-Dibromo-3,6-di-*tert*-butyl-9*H*-carbazole (**5g**)[19] was prepared by the literature method. When bisamide **8gb** was subjected to $BF_3{\cdot}OEt_2$ cyclization, ligand **1gb** was isolated with poor yield (entry 5). The yield improved to 51% when $MeSO_2Cl$ was used for the dehydrative oxazoline formation (entry 6).

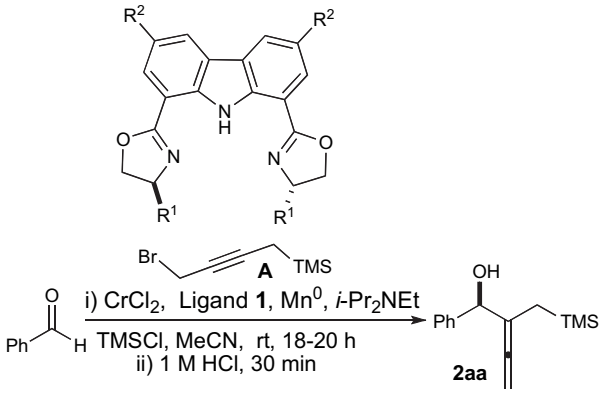
Due to solubility-related difficulties with the purification of diiodo-9*H*-carbazole **5d**, we subjected the unpurified Suzuki-coupled product to Pd-catalyzed carbonylative amidation and then, separately, $BF_3{\cdot}OEt_2$ and $MeSO_2Cl$ induced cyclization. No desired ligand was obtained in either case. Additionally, no desired ligand was isolated upon subjecting unpurified 9*H*-carbazole **4d** to iodination followed by carbonylative amidation and cyclization.

Having obtained several additional bis(oxazolinyl)carbazoles **1** with varying substitution patterns (Tables 8 and 9), we now elected to examine their efficacy in promoting the asymmetric allenylation reaction. Following the same trends as shown in Table 4, the presence of a small R^1 substituent such as a benzyl group afforded the **2aa** with higher enantiomeric excess than when a phenyl group was used (Table 10, entries 1 and 2). The %ee of the product decreased slightly with R^1=(*R*)-1-methoxyethyl, which is not as bulky as a Ph or a *t*-Bu group (entry 3). Phenyl was the best substituent at the R^2 position, other aliphatic or aromatic R^2 substituents, including *t*-Bu, α-naphthyl, and β-naphthyl, did not increase the %ee observed (entries 4–6).

Interestingly, a decrease in the temperature of the reaction from rt to 10 °C results in a slight decrease in the %ee observed from 75% ee to 70% ee (Table 11, entries 1 and 2). However, %ee was drastically reduced to 30% ee when the reaction temperature was further lowered to 0 °C. The same effect was also observed when ligand **1ab** was utilized for the reaction. When allenic alcohol **2aa** is resubmitted to the reaction conditions at 0 °C a decrease in the ee value from 72% to 62% ee occurs. These results implicate that a racemization process is occurring under the lower temperature reaction conditions. When **2aa** is resubmitted to the reaction conditions at rt, no racemization is observed.

After optimizing the reaction conditions, the scope of the asymmetric reaction was examined by studying a variety of aldehydes as electrophiles (Table 12). *para*-Substituted or unsubstituted aromatic aldehydes are excellent substrates and afforded the desired product in high yields and good enantioselectivities (Table 12, entries 1 and 2). When more sterically hindered *o*-methyl benzaldehyde was used, the reaction is slower and the ee dropped to 59% ee (entry 3). Electron deficient aldehydes gave the desired product with good ee values (entries 4–6). As is the case with no chiral ligands present, aliphatic aldehydes undergo reaction more quickly than aromatic aldehydes. The products derived from addition to aliphatic aldehydes afford the corresponding allenes in good yields and modest enantioselectivities. The absolute configuration of all products in Table 12 was established

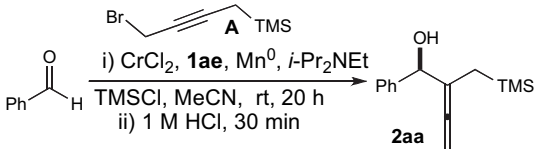
Table 10
Effect of ligand substituents on enantiomeric excess[a]



Entry	Ligand	Conversion (%)	ee[b] (%)
1	**1ad** (R_1=Ph, R_2=Ph)	99	31
2	**1ae** (R_1=Bn, R_2=Ph)	68	75
3	**1af** (R_1=(*R*)-1-Methoxyethyl, R_2=Ph)	32	68
4	**1bb** (R_1=*i*-Pr, R_2=α-naphthyl)	99	57
5[c]	**1cb**(R_1=*i*-Pr,R_2=β-Naphthyl)	99	21
6	**1gb** (R_1=*i*-Pr, R_2=*t*-Bu)	86	20

[a] Reaction conditions: (4-bromobut-2-ynyl)trimethylsilane (**A**) (1.5 equiv), $CrCl_2$ (5 mol %), ligand (5 mol %), Mn^0 (2 equiv), TMSCl (1.1 equiv), *i*-Pr_2NEt (0.3 equiv), 20 h; 2 mL of 1 M HCl.
[b] Enantiomeric excess and conversion determined by chiral HPLC.
[c] $CrCl_2$ (3 mol %), **1cb** (3 mol %).

Table 11
Effect of temperature on enantiomeric excess[a]



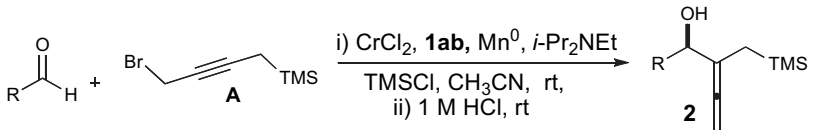
Entry	Temperature (°C)	ee[b] (%)
1	rt	75
2	10	70
3	0	30

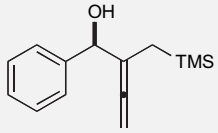
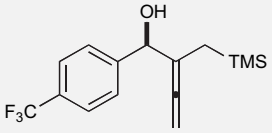
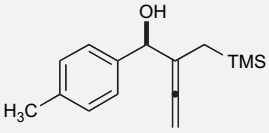
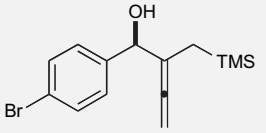
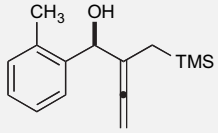
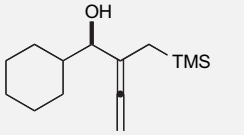
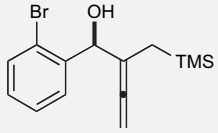
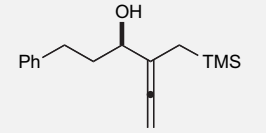
[a] Reaction conditions: (4-bromobut-2-ynyl)trimethylsilane (**A**) (1.5 equiv), $CrCl_2$ (5 mol %), ligand **1ae** (5 mol %), Mn^0 (2 equiv), TMSCl (1.1 equiv), *i*-Pr_2NEt (0.3 equiv), 20 h; 2 mL of 1 M HCl.
[b] Enantiomeric excess determined by chiral HPLC.

after conversion of the (trimethylsilyl)methyl allenic alcohols to the corresponding diene and comparison of the sign of optical rotation to the known compounds.[4d]

Having the (trimethylsilyl)methyl allenic alcohols in hand, we explored the synthesis of 1,3-butadien-2-ylcarbinols. It is known that treatment of (trimethylsilyl)methyl allenic alcohols with a mixture of hydrofluoric acid and hydrochloric acid affords the desired diene.[4d] In search of milder reaction conditions that would allow the use of this methodology in sensitive substrates, we explored the use of various fluoride sources. We found TBAF can be utilized for the clean desilylation of the (silylmethyl)allenic alcohols to afford the corresponding dienes. When **2aa** was treated with TBAF in THF for 36 h, diene **9a** was obtained in 54% yield (Table 13, entry 1). These reaction

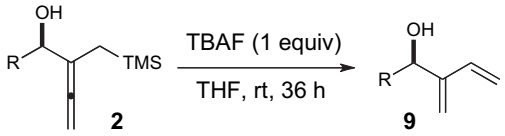
Table 12
Scope of the asymmetric chromium-catalyzed allenylation reaction[a]



Entry	Product		Yield[b] (%)	ee[c] (%)	Entry	Product		Yield[b] (%)	ee[c] (%)
1		**2aa**	88	78	5		**2ee**	88	72
2		**2bb**	75	70	6		**2ff**	60	74
3[d]		**2cc**	77	59	7[e]		**2gg**	67	68
4		**2dd**	82	68	8[e]		**2hh**	58	55

[a] Reaction conditions: (4-bromobut-2-ynyl)trimethylsilane (**A**) (1.5 equiv), $CrCl_2$(5 mol %), **1ab** (5 mol %), Mn^0 (2 equiv), TMSCl (1.1 equiv), *i*-Pr_2NEt (0.3 equiv), 48 h; 2 ml of 1 M HCl.
[b] Isolated yields.
[c] Enantiomeric excess determined by chiral HPLC.
[d] (4-Bromobut-2-ynyl)trimethylsilane (3 equiv), 50 h.
[e] Reaction time: 36 h.

Table 13
Conversion of allenic alcohols to 1,3-butadien-2-ylcarbinols[a]



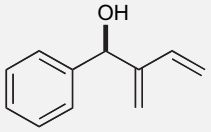
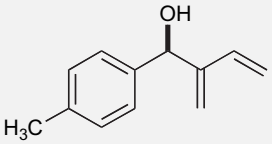
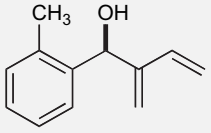
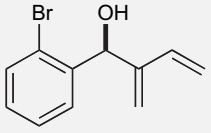
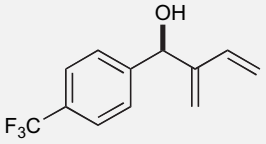
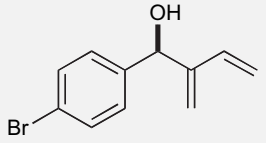
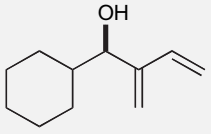
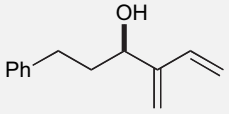
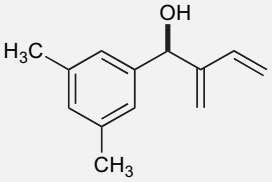
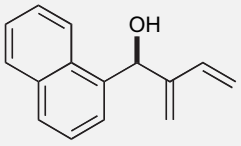
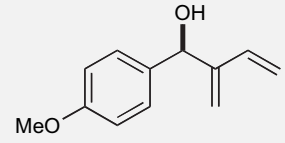
Entry	Product		Yield[b] (%)
1		**9a**	54
2		**9b**	86
3		**9c**	79
4		**9d**	82
5		**9e**	59
6		**9f**	72
7		**9g**	84
8		**9h**	43
9		**9i**	81
10		**9j**	74

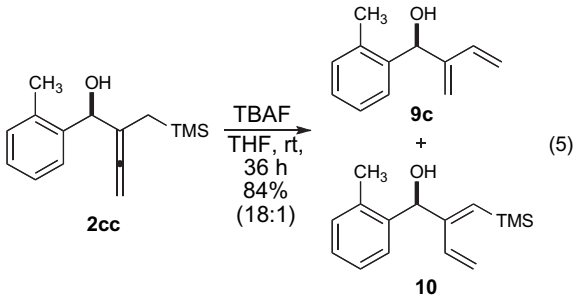
Table 13 (*continued*)

Entry	Product		Yield[b] (%)
11		**9k**	75

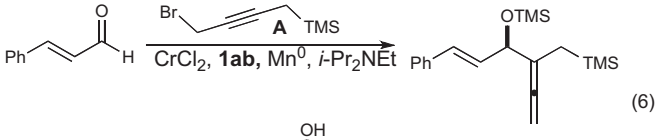
[a] Reaction conditions: TBAF (1 equiv), THF, rt, 36 h.
[b] Isolated yields.

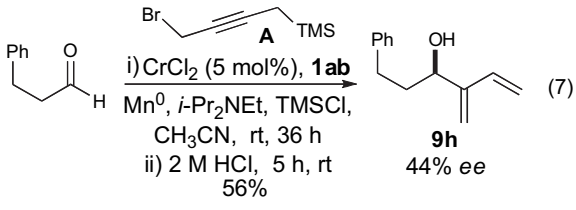
conditions were tolerant of several functional groups and the (silylmethyl)allenic alcohols synthesized were successfully transformed to 1,3-butadien-2-ylcarbinols in good to excellent yields.

For most of the substrates, no regioselectivity issues were encountered and racemization was avoided. However, for the synthesis of compound **9c**, byproduct vinylsilane **10** was obtained, albeit in less than 5% yield (Eq. 5). The vinylsilane was also observed as a very minor byproduct in the synthesis of compounds **9a**, **9b**, and **9d** (Table 13, entries 1, 2, and 4). The α,β-unsaturated aldehyde cinnamaldehyde affords TMS-protected allenic alcohols (Eq. 6). Bisdesilylation with TBAF in THF affords the desired adduct **9l** in 35% yield.

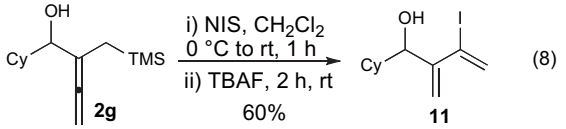


The synthesis of 1,3-butadien-2-ylcarbinols can be achieved under basic conditions (TBAF) but also under acidic conditions. When aliphatic allenic alcohols are treated with HCl, desilylation occurs and the corresponding dienes are obtained. The formation of 1,3-butadien-2-ylcarbinol **9h** from 3-phenylpropionaldehyde in one pot is illustrated in Eq. 7. After the aldehyde was treated with **A** under our reaction conditions, 2 M HCl was added to the reaction mixture and **9h** was obtained after 5 h in 56% yield.



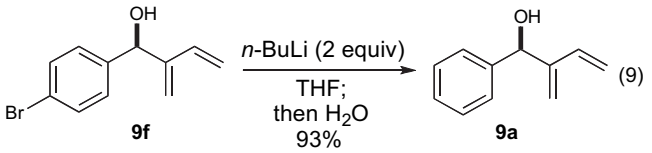


To illustrate the versatility of (trimethylsilyl)methyl allenic alcohols, **2g** was treated with NIS to give the iodinated adduct **11** in 60% yield (Eq. 8). During this process, the alcohol was protected in situ and a 1:1 mixture of the free alcohol and the silyl ether was obtained.[4d] TBAF was added after 1 h and the free alcohol **11** was obtained in 60% yield. The synthesis of 2-iodo-1,3-dienes can also be accomplished by treatment with I_2.[7c] Furthermore, (trimethylsilyl)methyl allenic alcohols may also be reacted with other electrophiles including Br_2[4d] and Selectfluor[7e] to afford the corresponding halogenated derivatives.



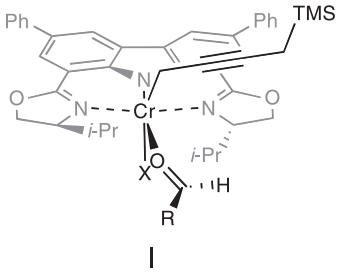
(8)

The absolute configuration of the chiral alcohols was assigned by comparing the optical rotations of known compounds **9a**, **9g**, and **9h** with the values reported in the literature.[1d,5a] The absolute configuration of **9f** was established by debromination to afford **9a** and comparison with the known compound (Eq. 9).



(9)

A plausible transition state that rationalizes the observed stereochemical outcome is depicted in Figure 2. The propargyl moiety is in the apical, less hindered position, avoiding steric interactions with the oxazoline substituents. The aldehyde coordinates to chromium with a trans geometry and occupies the less encumbered equatorial position. Addition to the aldehyde takes place from the *Si*-face, affording the *R*-alcohol. This is comparable with the observations made by Nakada and Inoue.[8a] Nonetheless, as previously discussed,[8a,d] the formation of a dinuclear complex or an intermolecular mechanism cannot be ruled out at this time.[20]



I

Figure 2. Proposed transition state.

3. Conclusion

In summary, we have executed asymmetric syntheses of (trimethylsilyl)methylallenic alcohols and shown their further transformation into 1,3-butadien-2-ylcarbinols. Several analogues of the bis(oxazoline) carbazole ligand **1** were synthesized. An alternative route was also developed via the intermediate 3,6-disubstituted-1,8-dibromo-9*H*-carbazoles **5d**–**f**, which are produced in one step by selective cross-coupling of tetrabromide **6**. This route is especially useful for synthesis of analogues of ligand **1** with electron-rich aryl substituents at the 3,6-positions of the carbazole nucleus, which could not be obtained by previous methods. After Pd-catalyzed carbonylative amidation of the substituted 1,8-dihalocarbazoles, the desired ligands are obtained by dehydrative oxazoline formation induced by either $BF_3 \cdot OEt_2$ or $MeSO_2Cl$.

Bis(oxazoline) carbazoles are reasonable ligands for this chromium-catalyzed addition reaction, affording chiral alcohols in generally good yields and enantioselectivities. These versatile adducts can be converted to 1,3-butadien-2-ylcarbinols by desilylation using TBAF or iodinated for further functionalization. Aliphatic aldehydes can also be converted to 1,3-butadien-2-ylcarbinols in one pot under acidic conditions.

4. Experimental section

4.1. General information

All reactions were performed under an argon atmosphere in oven-dried glassware with magnetic stirring. Acetonitrile, propionitrile, DME, TMSCl, and DIPEA were distilled from CaH_2 before use. THF was dried with a solvent purification system. Liquid aldehydes were distilled under reduced pressure and stored refrigerated. Carbazole ligands **1aa**–**ac** were prepared according to previously reported procedures.[9,13] Other commercially available reagents were used as received. Reactions were monitored by analytical thin layer chromatography using 0.25 mm glass-backed silica gel plates. Flash column chromatography was performed using silica gel (230–400 mesh). Visualization was accomplished by UV light and potassium permanganate or *p*-anisaldehyde stains.

^{1}H NMR spectra were recorded at 300 MHz and referenced to $CDCl_3$ (δ 7.27). ^{1}H NMR coupling constants (J) are reported in hertz (Hz) and multiplicities are indicated by: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dt (doublet of triplets), td (triplet of doublets) br (broad), dd (doublet of doublets). Proton-decoupled ^{13}C NMR spectra were recorded at 75 MHz and reported relative to $CDCl_3$ (δ 77). Infrared Spectra were obtained as thin film on NaCl plates. High performance liquid chromatography was performed on a system equipped with a wavelength detector and chiral stationary columns (0.46×25 cm).

4.2. General method for the preparation of allenic alcohols

Inside a nitrogen atmosphere drybox, a mixture of $CrCl_3$ (10 mg, 0.06 mmol) and Mn powder (325 mesh, 33 mg, 0.6 mmol) were added to a 2-dram vial. Then, the vial was capped with a Teflon lid and it was removed from the drybox. THF (2 mL) was added via syringe and a purple suspension resulted. This was followed by addition of (4-bromo-2-butyn-1-yl)trimethylsilane **A** (88 mg, 0.33 mmol), the aldehyde (0.3 mmol) and TMSCl (42 μL, 0.33 mmol). The mixture was stirred at rt until the reaction was completed as judged by TLC. HCl (1 M) was added to the gray solution and it was stirred until the alcohol is completely deprotected as judged by TLC. The mixture was then extracted with EtOAc. The mixed organic phases were washed with brine, dried with $MgSO_4$, and concentrated under reduced pressure to give dark yellow oil. The residue was purified by flash chromatography using EtOAc/hexanes (1:50 to 1:9) as eluent.

*4.2.1. 1-(3,5-Dimethylphenyl)-2-((trimethylsilyl)methyl)buta-2,3-dien-1-ol (**2i**).* Obtained as a yellow oil (47 mg, 0.18 mmol, 59%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.98 (s, 2H), 6.94 (s, 1H), 5.03 (q, J=3.0 Hz, 2H), 4.90 (m, 1H), 2.33 (s, 6H), 2.21 (d, J=4.8 Hz 1H), 1.30–1.22 (dt, J=15, 2.30 Hz 1H), 1.04–0.96 (dt, J=14.8, 2.8 Hz, 1H), 0.02 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.6, 142.9, 139.0, 130.7, 126.0, 106.3, 81.0, 75.9, 22.4, 18.0, 0.5; IR (thin film) 3417,

2953, 1953, 1248 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{24}OSi$ (M+H) 261.1675, found 261.1668.

*4.2.2. 1-(Naphthalen-2-yl)-2-((trimethylsilyl)methyl)buta-2,3-dien-1-ol (**2j**).* Obtained as a light yellow oil (51 mg, 0.18 mmol, 60%). ^1H NMR ($CDCl_3$, 300 MHz) δ 8.24(d, J=8.3 Hz, 1H), 7.88 (d, J=8.3 Hz, 1H), 7.82 (d, J=8.3 Hz, 1H), 7.64 (d, J=6.2 Hz, 1H), 7.51 (m, 3H), 5.78 (m, 1H), 5.01 (q, J=2.8, 2.8 Hz, 2H), 2.31 (d, J=4.5 Hz 1H), 1.43–1.36 (dt, J=15.1, 2.9 Hz, 1H), 1.13–1.05 (dt, J=15.1, 2.9 Hz, 1H), 0.0 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.0, 137.1, 134.2, 131.6, 128.9, 128.8, 126.3, 125.8, 125.4, 125.1, 124.2, 104.8, 79.6, 73.0, 17.0, −0.8. IR (thin film) 3386, 3061, 2953, 1952, 1248, 1056 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{22}OSi$ (M+Li) 289.1600, found 289.1594.

*4.2.3. 1-(4-Methoxyphenyl)-2-((trimethylsilyl)methyl)buta-2,3-dien-1-ol (**2k**).* Obtained as yellow oil (30 mg, 0.11 mmol, 56%). ^1H NMR ($CDCl_3$, 300 MHz) δ 7.32–7.28(d, J=8.8 Hz, 2H), 6.91–6.87 (d, J=8.8 Hz, 2H), 5.01 (q, J=2.8 Hz, 2H), 4.94 (m, 1H), 3.82 (s, 3H), 2.23 (br s, 1H), 1.31–1.23 (dt, J=15.0, 2.9 Hz, 1H), 1.06–0.98 (dt, J=15.0, 2.9 Hz, 1H), 0.02 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.6, 159.5, 134.3, 128.5, 113.9, 105.6, 80.1, 74.6, 55.5, 17.3, −0.8; IR (thin film) 3428, 2954, 1953, 1248, 1118 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{22}O_2Si$ (M+ Li) 269.1549, found 269.1543.

4.3. General method for the preparation of enantioenriched allenic alcohols

Inside a nitrogen atmosphere drybox, a mixture of $CrCl_2$ (1.2 mg, 0.01 mmol), Mn powder (325 mesh, 22 mg, 0.4 mmol), and carbazole ligand **1ab** (5.5 mg, 0.01 mmol) were added to a 2-dram vial. Then, the vial was capped with a Teflon lid and it was removed from the drybox. Freshly distilled CH_3CN (2 mL) was added via syringe and a yellow suspension resulted. This was followed by addition of i-Pr_2NEt (10 μL, 0.06 mmol) and the mixture was stirred for 5 min. After this time, (4-bromo-2-butyn-1-yl) trimethylsilane (61 mg, 0.3 mmol) was added and the solution was allowed to stir for 30 min. Next, the aldehyde (0.2 mmol) and TMSCl (28 μL, 0.22 mmol) were successively added at 0 °C. The mixture was stirred at rt for 48 h or until the reaction was completed as judged by TLC. HCl (1 M) was added and the obtained green solution was stirred until the alcohol is completely deprotected as judged by TLC. The mixture was then extracted with EtOAc. The mixed organic phases were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to give a dark orange oil. The residue was purified by flash chromatography using EtOAc/hexanes (1:50 to 1:9) as eluent.

*4.3.1. (R)-1-Phenyl-2-((trimethylsilyl)methyl)buta-2,3-dien-1-ol (**2aa**)[10].* Obtained as a clear oil (40 mg, 0.17 mmol, 88%, 78% ee) ^1H NMR ($CDCl_3$, 300 MHz) δ 7.36–7.27(m, 5H), 4.98 (m, 3H), 2.23 (d, J=4.5 Hz 1H), 1.30–1.23 (dt, J=15.3, 2.4 Hz, 1H), 1.07–0.94 (dt, J=14.2, 2.6 Hz, 1H), 0.0 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.7, 141.9, 128.3, 127.8, 127.0, 105.1, 79.7, 74.9, 16.8, −1.1; IR (thin film) 3387, 3029, 2954, 1952, 1247 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{20}OSi$ (M−OH) 215.1251, found 215.1252. Enantiomeric excess determined by HPLC (250 nm) using a ChiralPAK AD-H column (hexanes/isopropanol=98:2, flow rate=0.6 ml/min) retention time=14.3 min (major), 13.0 (minor). $[\alpha]_D^{23}$ −107.2 (c 1.0, $CHCl_3$).

*4.3.2. (R)-1-p-Tolyl-2-((trimethylsilyl)methyl)buta-2,3-dien-1-ol (**2bb**).* Obtained as a clear oil (27 mg, 0.17 mmol, 75%, 70% ee) ^1H NMR ($CDCl_3$, 300 MHz) δ 7.29–7.24 (d, J=8.0 Hz, 2H), 7.19–7.14 (d, J=8.0 Hz, 2H), 5.01 (q, J=2.8 Hz, 2H), 4.94 (m, 1H), 2.36 (s, 3H), 2.23 (d, J=4.5 Hz 1H), 1.30–1.23 (dt, J=2.7, 15.0 Hz, 1H), 1.05–0.97 (dt, J=2.8, 15.0 Hz, 1H), 0.0 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.6, 139.0, 137.5, 129.0, 126.9, 105.2, 79.7, 74.7, 21.2, 17.0, −1.0; IR (thin film) 3408, 2953, 1953, 1247 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{22}OSi$ (M+Li) 253.1600, found 253.1596. Enantiomeric excess determined by HPLC (250 nm) using a ChiralPAK AD-H column (hexanes/isopropanol=98:2, flow rate=0.6 ml/min) retention time=17.8 min (major), 14.0 (minor). $[\alpha]_D^{18}$ −106.7 (c 1.0, $CHCl_3$).

*4.3.3. (R)-1-o-tolyl-2-((trimethylsilyl)methyl)buta-2,3-dien-1-ol (**2cc**).* Obtained as a clear oil (38 mg, 0.15 mmol, 77%, 59% ee) ^1H NMR ($CDCl_3$, 300 MHz) δ 7.41 (m, 1H), 7.18 (m, 3H), 5.24 (m, 1H), 4.94 (q, J=3.0 Hz, 2H), 2.37 (s, 3H), 2.07 (d, J=4.8 Hz 1H), 1.36–1.28 (dt, J=2.9, 15.1 Hz, 1H), 1.06–0.99 (dt, J=2.9, 15.1 Hz, 1H), 0.02 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.4, 139.5, 136.3, 130.5, 127.6, 126.7, 125.9, 104.1, 79.2, 72.1, 19.3, 16.5, −1.1 IR (thin film) 3358, 2953, 1955, 1247 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{22}OSi$ (M+Li) 253.1600, found 253.1597. Enantiomeric excess determined by HPLC (210 nm) using a ChiralPAK AD-H column (hexanes/isopropanol=98:2, flow rate=0.6 ml/min) retention time 12.8 min (major), 11.3 (minor). $[\alpha]_D^{19}$ −49.3 (c 1.0, $CHCl_3$).

*4.3.4. (S)-1-(2-Bromophenyl)-2-((trimethylsilyl)methyl)buta-2,3-dien-1-ol (**2dd**).* Obtained as a yellow oil (44 mg, 0.14 mmol, 72%, 68% ee) ^1H NMR ($CDCl_3$, 300 MHz) δ 7.52–7.44 (m, 2H), 7.33 (td, J=1.57, 7.67 Hz, 1H), 7.33 (td, J=1.92, 7.67 Hz, 1H), 5.42 (m, 1H), 4.94 (q, J=3.09 Hz, 2H), 2.29 (d, J=6.95 Hz 1H), 1.39–1.33 (dt, J=2.8, 15.0 Hz, 1H), 1.16–1.08 (dt, J=2.6, 15.0 Hz, 1H), 0.0 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.4, 141.0, 132.8, 129.1, 128.8, 127.6, 123.7, 104.16, 79.7, 73.7, 16.8, −1.1; IR (thin film) 3384, 2953, 1953 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{19}BrOSi$ (M−OH) 293.0356, found 293.0348; Enantiomeric excess determined by HPLC (250 nm) using a ChiralPAK AD-H column (hexanes/isopropanol=98:2, flow rate=0.6 ml/min) retention time=15.5 min (major), 13.9 (minor). $[\alpha]_D^{23}$ −74.5 (c 1.0, $CHCl_3$).

*4.3.5. (R)-1-(4-(Trifluoromethyl)phenyl)-2-((trimethylsilyl)methyl)-buta-2,3-dien-1-ol (**2ee**).* Obtained as a yellow oil (53 mg, 0.17 mmol, 88%, 72% ee) ^1H NMR ($CDCl_3$, 300 MHz) δ 7.64–7.58 (d, J=8.4 Hz, 2H), 7.52–7.46 (d, J=8.4 Hz, 2H), 5.06 (m, 1H), 5.00 (q, J=2.8, 2.9 Hz, 2H), 2.31 (d, J=4.75 Hz, 1H), 1.29–1.21 (dt, J=2.9, 15.1 Hz, 1H), 1.06–0.98 (dt, J=2.9, 15.1 Hz, 1H), 0.02 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.9, 146.06, 127.28, 125.22 (q, J=3.72, 3.76 Hz), 104.69, 79.94, 74.63, 16.46, −1.15; IR (thin film) 3307, 2956, 2895, 1951, 1326, 1249 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{19}F_3OSi$ (M+Li) 307.1317, found 307.1320; Enantiomeric excess determined by HPLC (250 nm) using a ChiralPAK AD-H column (hexanes/isopropanol=98:2, flow rate=0.6 ml/min) retention time=13.55 min (major), 10.17 (minor). $[\alpha]_D^{23}$ −101.9 (c 1.0, $CHCl_3$).

*4.3.6. (R)-1-(4-Bromophenyl)-2-((trimethylsilyl)methyl)buta-2,3-dien-1-ol (**2ff**).* Obtained as a clear oil (37 mg, 0.12 mmol, 60%, 74% ee) ^1H NMR ($CDCl_3$, 300 MHz) δ 7.48–7.44 (d, J=8.559 Hz, 2H), 7.25–7.21 (d, J=8.37 Hz, 2H), 4.98 (q, J=3.2 Hz, 2H), 4.94 (m, 1H), 2.21 (d, J=4.4 Hz 1H), 1.28–1.20 (dt, J=2.7, 15.1 Hz, 1H), 1.04–0.96 (dt, J=2.8, 15.0 Hz, 1H), −0.03 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) 204.6, 141.0, 131.3, 128.8, 121.6, 104.9, 80.1, 74.4, 16.6, −0.9 δ; IR (thin film) 3422, 2953, 1952, 1247 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{19}BrOSi$ (M−H) 309.0310, found 309.0314. Enantiomeric excess determined by HPLC (250 nm) using a ChiralPAK AD-H column (hexanes/isopropanol=98:2, flow rate=0.6 ml/min) retention time=18.4 min (major), 14.6 (minor). $[\alpha]_D^{20}$ −69.8 (c 1.0, $CHCl_3$).

*4.3.7. (R)-1-Cyclohexyl-2-((trimethylsilyl)methyl)buta-2,3-dien-1-ol (**2gg**).* Obtained as a light yellow oil (32 mg, 0.14 mmol, 67%, 68% ee) ^1H NMR ($CDCl_3$, 300 MHz) δ 4.80 (q, J=2.8 Hz, 2H), 3.67 (m, 1H), 1.79–0.81 (m, 13H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.4, 104.5, 79.4, 77.6, 42.3, 31.1, 28.1, 27.5, 27.4, 27.1, 17.7, 0.05; IR (thin film) 3415, 2925, 2852, 1952, 1247 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{26}OSi$

(M−OH) 221.1720, found 221.1725. Enantiomeric excess determined by HPLC (250 nm) using a ChiralPAK AD-H column (hexanes/isopropanol=98:2, flow rate=0.6 ml/min) retention time=8.14 min (major), 8.7 (minor). $[\alpha]_D^{20}$ −15.7 (*c* 1.0, $CHCl_3$).

*4.3.8. (R)-1-Phenyl-4-((trimethylsilyl)methyl)hexa-4,5-dien-3-ol (**2hh**).* Obtained as a yellow oil (30 mg, 0.11 mmol, 58%, 55% ee) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.28−7.13 (m, 5H), 4.83 (q, *J*=2.7, 2.6 Hz, 2H), 3.89 (m, 1H), 2.8−2.57 (m, 2H), 2.00−1.87 (m, 1H), 1.84−1.7 (m, 1H), 1.57 (br s, 1H), 1.42−1.34 (dt, *J*=2.8, 14.9 Hz, 1H), 1.24−1.15 (dt, *J*=2.9, 15.9 Hz, 1H), 0.0 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.8, 142.36, 128.7, 128.62, 216.0, 104.8, 79.0, 72.2, 37.4, 32.1, 17.1, −0.8; IR (thin film) 3362, 2951, 1951, 1247 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{24}OSi$ (M+Li) 267.1756, found 267.1759. Enantiomeric excess determined by HPLC (250 nm) using a ChiralPAK AD-H column (hexanes/isopropanol=98:2, flow rate=0.6 ml/min) retention time=15.8 min (major), 14.38 (minor). $[\alpha]_D^{20}$ −5.6 (*c* 1.0, $CHCl_3$).

4.4. General method for the preparation of 1,3-butadien-2-ylcarbinols from allenic alcohols

Allene (0.11 mmol) was dissolved in dry THF (1.5 mL). TBAF (1 M in THF, 0.1 mL, 0.1 mmol) was added and the solution was stirred at rt for 36 h. After this time, a saturated solution of NH_4Cl (3 mL) was added and the mixture was extracted with three portions of EtOAc. The combined organic fractions were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by preparative TLC using (1:6) EtOAc/hexanes.

*4.4.1. 1-(3,5-Dimethylphenyl)-2-methylenebut-3-en-1-ol (**9i**).* Allene **2i** (25 mg, 0.09 mmol), 1 M TBAF in THF (0.09 mL, 0.09 mmol). Compound was obtained as yellow oil (19 mg, 0.07 mmol, 81%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.01 (s, 2H), 6.94 (s, 1H) 6.32 (dd, *J*=11.4, 17.7 Hz, 1H), 5.45 (s, 1H), 5.41 (s, 1H), 5.35 (s, 1H), 5.24 (d, *J*=18.09 Hz, 1H), 5.05 (d, *J*=11.3 Hz, 1H), 2.32 (s, 1H), 1.94 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.3, 141.8, 138.0, 135.9, 129.5, 124.6, 115.3, 73.9, 21.3; IR (thin film) 3356, 3009, 2918, 1608 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{16}O$ (M+Li) 195.1361, found 195.1348.

*4.4.2. 2-Methylene-1-(naphthalen-1-yl)but-3-en-1-ol (**9j**)*[6f]. Allene **9j** (25 mg, 0.09 mmol), 1 M TBAF in THF (0.16 mL, 0.16 mmol). The title compound was obtained as yellow oil (28 mg, 0.13 mmol, 74%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.13 (d, *J*=9.0, 1H), 7.89 (d, *J*=7.3, 1H), 7.83 (d, *J*=8.4, 1H), 7.63 (d, *J*=8.4, 1H), 7.58−7.44 (m, 3H), 6.47 (dd, *J*=11.1, 18.2 Hz, 1H), 6.27 (s, 1H), 5.43 (s, 1H), 5.35 (s, 1H), 5.24 (d, *J*=19.0 Hz, 1H), 5.10 (d, *J*=11.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.3, 137.1, 136.4, 133.8, 131.0, 128.6, 126.3, 125.6, 125.5, 125.3, 124.4, 123.4, 117.3, 115.1, 69.6; HRMS (ESI) calcd for $C_{15}H_{14}O$ (M+Li) 217.1205, found 217.1244.

*4.4.3. 1-(4-Methoxyphenyl)-2-methylenebut-3-en-1-ol (**9k**)*[6f]. Allene **9k** (30 mg, 0.11 mmol), 1 M TBAF in THF (0.11 mL, 0.11 mmol). Title compound was obtained as yellow oil (16 mg, 0.082 mmol, 75%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.32 (d, *J*=8.9 Hz, 2H), 6.89 (d, *J*=8.9 Hz, 2H), 6.32 (dd, *J*=11.9, 18.4 Hz, 1H), 5.46 (s, 1H), 5.44 (s, 1H), 5.34 (s, 1H), 5.19 (d, *J*=18.1 Hz, 1H), 5.04 (d, *J*=11.5 Hz, 1H), 3.81 (s, 3H), 1.93 (d, *J*=4.0, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 147.6, 135.9, 134.2, 123.2, 115.4, 115.3, 113.9, 73.4, 55.3; IR (thin film) 3417, 3005, 2959, 1824, 1611, 1511, 1249, cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{14}O_2$ (M+Li) 197.1154, found 197.1154.

*4.4.4. 1-o-Tolyl-2-((trimethylsilyl)methylene)but-3-en-1-ol (**10**).* ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.31−7.27 (m, 1H), 7.09−7.00 (m, 3H), 5.56 (d, *J*=2.9 Hz, 1H), 5.37 (s, 1H), 5.20 (d, *J*=2.9 Hz, 1H), 4.93−5.15 (m, 2H), 2.37 (s, 3H), 1.76 (d, *J*=3.8, 1H), −0.13 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.7, 140.6, 136.6, 131.1, 128.4, 128.1, 128.0, 127.5, 126.8, 113.4, 72.2, 20.1, 0.0; IR (thin film) 3374, 2956, 1620, 1486, 1248 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{22}OSi$ (M+Na) 269.1338, found 269.1334.

4.5. 1-Cyclohexyl-3-iodo-2-methylenebut-3-en-1-ol (11)

Allenic alcohol **2g** (20 mg, 0.08 mmol) was dissolved in dry CH_2Cl_2 (1 mL). Then, at 0 °C, a solution of NIS (40 mg, 0.17 mmol) in CH_2Cl_2 (0.5 mL) was added via cannula. The pink solution was stirred at rt for 1 h. After this time, 0.16 mL of a TBAF (1 M in THF, 0.16 mmol) was added via syringe and the mixture was stirred for 2 h. After this time, a saturated solution of NH_4Cl was added and the mixture was extracted with three portions of EtOAc. The combined organic phases were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash chromatography using EtOAc/hexanes 1:6 as eluent. The title compound was obtained as a yellow oil (35 mg, 0.12 mmol, 60% yield). ^{1}H NMR δ 6.3 (d, *J*=1.7H), 5.91 (d, *J*=1.5H), 5.42 (s, 1H), 5.30 (s, 1H), 4.28 (t, *J*=4.8, 1H) 1.73−1.63 (m, 3H), 1.56 (m, 2H), 1.23−0.89 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.8, 127.8, 118.9, 107.3, 76.3, 41.5, 30.1, 27.7, 26.36, 26.33, 26.0; IR (thin film) 3437, 2926, 2852, 1723, 1260 cm^{-1}; HRMS (ESI) calcd for $C_{11}H_{17}IO$ (M−I) 265.1274, found 265.1274.

4.6. Preparation of (*S*)-2-methylene-1-phenylbut-3-en-1-ol (9a) from (*S*)-1-(4-bromophenyl)-2-methylenebut-3-en-1-ol (9f)

Compound **9f** (16 mg, 0.067 mmol) was dissolved in THF (2 mL) and cooled to −78 °C. Then *n*-BuLi (0.53 mL of 2.5 M solution, 0.13 mmol) was added dropwise and the mixture was stirred for 15 min. Water (0.5 mL) was added dropwise and stirred for 5 min. The mixture was diluted with ethyl acetate, washed with brine, dried over Mg_2SO_4, and concentrated under reduced pressure. The residue was filtered through a short plug of silica. Compound **9a** was obtained as a yellow oil (11 mg, 0.06 mmol, 93% yield, 69% ee). $[\alpha]_D^{19}$ −32.4 (*c* 1.0, $CHCl_3$).

4.7. Representative procedure for the synthesis of carbazoles 4. 3,6-Di(naphthalen-2-yl)-9*H*-carbazole (4c)

Prepared by modification of the procedure reported by Nakada et al.[9b] 3,6-diiodocarbazole (2.00 g, 4.84 mmol), 2-naphthylboronic acid (2.5 g, 14.5 mmol), and $Ba(OH)_2 \cdot 8H_2O$ (4.5 g, 14.5 mmol) were dissolved in a 6:1 mixture of DME/H_2O (60 mL). A solution of Pd$(OAc)_2$ (54.3 mg, 0.24 mmol) and P(*o*-tol)$_3$ (148 mg, 0.48 mmol) in DME (5 ml) was then added via cannula. The mixture was stirred at 80 °C for 18 h and then cooled to rt. The precipitate was removed by filtration and the filtrate was extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography (30% CH_2Cl_2 in hexanes as eluent) and then recrystallized from toluene. The product was obtained in 23% yield as a white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.53 (s, 2H), 8.19 (s, 3H), 8.01−7.83 (m, 10H), 7.61−7.47 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.7, 139.5, 134.1, 133.2, 132.5, 128.6, 128.3, 127.9, 126.4, 126.3, 126.1, 125.9, 125.8, 124.3, 119.5, 111.3; HRMS (MALDI) calcd for $C_{32}H_{22}N$ (M+H) 420.1752, found 420.1708.

*4.7.1. 3,6-di(2,6-Methylphenyl-1-yl)-9H-carbazole (**4e**).* 3,6-Diiodocarbazole (0.10 g, 0.25 mmol), 2,6-dimethylbenzeneboronic acid (0.112 g, 0.75 mmol), $Ba(OH)_2 \cdot 8H_2O$ (0.236 g, 0.75 mmol), Pd$(OAc)_2$ (2.8 mg, 0.012 mmol), and P(*o*-tol)$_3$ (7.6 mg, 0.025 mmol). After flash chromatography purification (3:1 hexanes/CH_2Cl_2), the product was obtained in 96% yield. The pure compound was characterized by ^{1}H and ^{13}C NMR. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.10 (s, 1H), 7.84 (2, 2H), 7.53 (d, *J*=8.4 Hz, 2H), 7.27−7.16 (m, 8H), 2.13, (s,

12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.5, 138.6, 136.8, 132.3, 127.3, 127.2, 126.9, 123.5, 120.6, 110.5, 21.1.

4.8. Procedure for the synthesis of carbazole 4d

Prepared by slight modification of a procedure reported by Routier et al.[14a] A solution of 3,6-diiodocarbazole (0.419 g, 1.0 mmol) and 9-anthracenylboronic acid **3d** (2.5 equiv) in a mixture of toluene (21 mL), ethanol (13 mL), and saturated aq $NaHCO_3$ solution (8.4 ml) was degassed by bubbling Ar for 20 min. $Pd(PPh_3)_4$ (10 mol %) was added and the mixture was immediately transferred to a preheated oil bath and refluxed overnight. After hydrolysis (20 mL H_2O) the mixture was extracted with EtOAc (2×20 ml), washed with brine (20 ml) and dried over $MgSO_4$. The organic layer was then concentrated under reduced pressure to yield the desired product.

4.9. 1,8-Diiodo-3,6-di(naphthalen-1-yl)-9*H*-carbazole (5b)

Prepared by a modification of previously reported procedures.[13,21] $BnMe_3NCl_2I$ was added to a suspension of **4b** in a mixture of AcOH (33 mL) and H_2SO_4 (1 mL). The mixture was stirred at 60 °C until the reaction was completed as judged by TLC. The mixture was cooled to rt and poured into 60 mL of water. The precipitate was filtered and partitioned between EtOAc (33 mL) and a saturated solution of $NaHCO_3$ (10 mL). The organic layer was washed with a saturated solution of $Na_2S_2O_3$ (20 mL) and brine (40 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Flash chromatography (ethyl acetate/hexanes, 1:50) afforded title compound, more than 90% pure, in 40% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.32 (s, 1H), 8.11 (s, 2H), 7.99 (d, J=1.4 Hz, 2H), 7.94–7.85 (m, 7H), 7.57–7.40 (m, 7H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.3, 139.0, 136.9, 136.8, 134.7, 133.7, 131.8, 128.3, 127.8, 127.4, 127.1, 126.2, 125.8, 125.3, 124.0, 122.3; IR 3430, 3054, 2924, 1722, 1508; HRMS (MALDI) calcd for $C_{32}H_{19}I_2N$ (M−I) 544.0557, found 544.0573.

4.10. 1,8-Dibromo-3,6-bis(4-methoxyphenyl)-9*H*-carbazole (5f)

Prepared by slight modification of a procedure reported by Routier et al.[14a] A solution of 1,3,6,8-tetrabromocarbazole **6** (0.240 g, 0.5 mmol) and 4-methoxyphenylboronic acid (2.2 equiv) in a mixture of toluene (10.5 mL), ethanol (6.5 mL), and saturated aq $NaHCO_3$ solution (4.2 ml) was degassed by bubbling Ar for 20 min. $Pd(PPh_3)_4$ (10 mol %) was added and the mixture was immediately transferred to a preheated oil bath and refluxed for 5 h. After hydrolysis (20 mL H_2O) the mixture was extracted with EtOAc (2×20 ml), washed with brine (20 ml) and dried over $MgSO_4$. The organic layer was then concentrated under reduced pressure to yield the desired product, which was purified by column chromatography on silica gel (25:1 hexanes/EtOAc) to afford 40% of the product as a white solid. Mp 195–197 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.50 (s, 1H), 8.42 (d, J=1.5 Hz, 2H), 7.65 (d, J=4.3 Hz, 4H), 7.45 (d, J=1.5 Hz, 2H), 7.06 (d, J=8.4 Hz, 4H), 3.80 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5, 137.4, 129.9, 129.8, 128.7, 127.9, 125.2, 122.2, 114.8, 112.6, 55.6; HRMS calcd for $C_{26}H_{20}Br_2NO_2$: 535.9855 $[M+H]^+$, found 535.9858.

4.11. (2*R*,3*R*)-2-Amino-3-methoxybutan-1-ol (7f)

A modification of the procedure reported by Hsiao and Hegedus was used.[17a] Lithium aluminum hydride (480 mg, 12 mmol) was suspended in THF (30 ml) at 0 °C. Then L-threonine methyl ether (399 mg, 3 mmol) was added slowly in small portions. The reaction mixture was heated at reflux overnight and then cooled to rt. A saturated aq solution of K_2CO_3 was added slowly. Filtration and evaporation of the solvent under reduced pressure afforded the crude product. The residue was purified by flash chromatography (1:10 MeOH/CH_2Cl_2 followed by MeOH) to give the pure compound in 55% yield as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.56 (dd, J=4.2, 10.8 Hz, 1H), 3.43 (dd, J=6.3, 10.8 Hz, 1H), 3.28 (s, 3H), 3.19 (t, J=6.3 Hz, 1H), 2.7 (br s, 1H), 1.08(d, J=6.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 63.2, 57.3, 56.4, 29.6, 15.2; IR 3362, 2929, 1582, 1462; HRMS calcd for $C_5H_{14}NO_2$: 120.1025 $[M+H]^+$, found 120.1022.

4.12. General procedure for synthesis of bis(oxazoline) carbazole ligand 1 from 1,8-dihalocarbazole (5) via Pd-catalyzed carbonylative amidation followed by $BF_3\cdot OEt_2$ induced cyclization

A modified procedure reported by Nakada and Inoue was used.[13] To a solution of 0.5 mmol of the 1,8-diiodocarbazole and Pd $(PPh_3)_4$ (20 mol %) in 5 mL of dry, degassed DMF was added the corresponding amino alcohol (2.6 equiv) and Et_3N (4 equiv) via a syringe. CO gas was then bubbled through the reaction mixture and a balloon of CO placed over the reaction flask. The reaction mixture was stirred at 60 °C for 8 h. After the mixture was cooled down it was diluted with CH_2Cl_2, washed with brine and 1 M $CuSO_4$ several times. The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure to give the desired bisamide. The bisamide was partially purified by passing through a short silica bed and eluting with DCM and methanol. The eluent was concentrated under rotovap, dried under vacuum, and the bisamide thus obtained was suspended in 15% w/v of $BF_3\cdot Et_2O$. The resulting suspension was stirred at 120 °C for 6 h. The reaction mixture was cooled to rt and poured into ice cold 2 M NaOH (5 mL), extracted with CH_2Cl_2, washed with a saturated aq solution of $NaHCO_3$, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography to afford the desired ligand.

*4.12.1. (4R,4′R)-2,2′-(3,6-Diphenyl-9H-carbazole-1,8-diyl)bis(4-phenyl-4,5-dihydrooxazole) (**1ad**).* Purification by flash chromatography (1:1 hexanes/CH_2Cl_2) afforded 27% of the product as a bright yellow solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 11.91 (br s, 1H), 8.51 (d, J=1.2 Hz, 2H), 8.29 (d, J=1.7 Hz, 2H), 7.8 (d, J=8.7 Hz, 4H), 7.53 (d, J=7.4 Hz, 4H), 7.45–7.28 (m, 12H), 5.55 (t, J=9.4 Hz, 2H), 4.90 (t, J=9.2 Hz, 2H), 4.36 (t, J=8.7 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.9, 142.6, 141.5, 139.1, 132.7, 129.1, 128.8, 127.5, 127.0, 126.9, 125.5, 124.5, 122.4, 110.7, 74.0, 70.1; IR (thin film) 3354, 3060, 2962, 1949, 1719, 1646, 1479; HRMS (MALDI) calcd for $C_{42}H_{32}N_3O_2$ (M+H) 610.2495, found 609.9933; $[\alpha]_D^{18}$ −135.6 (*c* 1.0, $CHCl_3$).

*4.12.2. (4S,4′S)-2,2′-(3,6-Diphenyl-9H-carbazole-1,8-diyl)bis(4-benzyl-4,5-dihydrooxazole) (**1ae**).* Purification by flash chromatography (1:1 hexanes/CH_2Cl_2) afforded 25% of the product as a bright yellow solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 11.91 (br s, 1H), 8.4 (d, J=1.8 Hz, 2H), 8.12 (d, J=1.7 Hz, 2H), 7.68 (d, J=8.0 Hz, 4H), 7.41 (d, J=7.1 Hz, 4H), 7.25 (m, 12H), 4.7 (m, 2H), 4.4 (t, J=8.8 Hz, 2H), 4.12 (t, J=8.0 Hz, 2H), 3.22 (dd, J=5.5, 5.2 Hz, 2H), 2.82 (dd, J=8.3, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.0, 141.3, 138.8, 138.0, 132.5, 129.4, 128.8, 128.5, 127.3, 126.7, 126.4, 125.3, 124.2, 122.0, 110.7, 71.3, 67.8, 42.0; IR (thin film) 3345, 2897, 1646, 1620, 1478, 1266; HRMS (MALDI) calcd for $C_{44}H_{36}N_3O_2$ (M+H) 638.2802, found 638.2807; $[\alpha]_D^{18}$ +51.34 (*c* 1.0, $CHCl_3$).

*4.12.3. (4S,4′S)-2,2′-(3,6-Di(naphthalen-1-yl)-9H-carbazole-1,8-diyl)-bis(4-isopropyl-4,5-dihydrooxazole) (**1bb**).* Purification by flash chromatography (4:1 hexanes/CH_2Cl_2) afforded 35% of the product as a yellow solid. Mp 139–141 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.20 (s, 1H), 8.31 (d, J=1.5 Hz, 2H), 8.10 (d, J=1.5 Hz, 2H), 7.85–7.97 (m, 6H), 7.39–7.55 (m, 8H), 4.47–4.52 (m, 2H), 4.47–4.52 (m, 2H), 4.18–4.29 (m, 4H), 1.91–1.95 (m, 2H), 1.20 (d, J=6.6 Hz, 6H), 1.06 (d, J=6.3 Hz, 6H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 162.6, 140.4, 138.9, 134.0, 132.3, 131.7, 128.4, 128.1, 127.7, 127.6, 126.3, 126.2, 125.9, 125.5, 125.0, 123.7, 110.6, 73.1, 70.1, 33.7, 19.4, 18.9; IR (thin film)

3430, 1719, 1508; HRMS calcd for $C_{44}H_{40}N_3O_2$ $[M+H]^+$ 642.3114, found 642.3123; $[\alpha]_D^{18}$ +30.01 (*c* 1.0, $CHCl_3$).

*4.12.4. (4S,4′S)-2,2′-(3,6−di(Naphthalen-2-yl)-9H-carbazole-1,8-diyl)bis(4-isopropyl-4,5-dihydrooxazole) (**1cb**).* Prepared by a modification of previously reported procedures.[13,21] Compound **4c** (470 mg, 1.12 mmol) was suspended in a mixture of AcOH, H_2O, and H_2SO_4 (1:0.2:0.03). After addition of I_2 (142 mg, 1.12 mmol) and $HIO_4 \cdot 2H_2O$ (127 mg, 0.56 mmol), the pink suspension was stirred at 80 °C for 5 h. The mixture was then cooled down to rt and poured into water. The solid was filtrated and dried under reduced pressure (600 mg, 0.89 mmol, 80% crude yield). After recrystallization from toluene pure 1,8-diiodo-3,6-di(naphthalen-2-yl)-9*H*-carbazole was obtained as a pink solid (130 mg, 0.2 mmol, 18% yield). Next, the procedure described above for the synthesis of bis-oxazoline carbazoles was followed. Purification by flash chromatography (50−80% CH_2Cl_2 in hexanes) afforded the title compound as a yellow solid, more than 90% pure (32 mg, 0.05 mmol, 25% yield). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.65 (s, 2H), 8.35 (m, 2H), 8.22 (m, 2H), 7.99−7.88 (m, 8H), 7.58−7.46 (m, 4H), 4.54 (m, 2H), 4.28 (m, 4H), 1.95 (m, 2H), 1.22 (d, *J*=6.2 Hz, 6H), 1.08 (d, *J*=6.4 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.4, 138.9, 138.7, 133.8, 132.37, 132.33, 128.4, 128.1, 127.6, 126.2, 125.9, 125.7, 125.6, 125.5, 124.3, 122.1, 110.9, 72.9, 70.0, 33.4, 19.2, 18.6; IR (thin film) 3053, 2959, 1649, 1601, 1486, 1436; LRMS (APCI) calcd for $C_{44}H_{40}N_3O_2$ (M+H) 642.31, found 642.54; $[\alpha]_D^{18}$ +55.6 (*c* 1.0, $CHCl_3$).

*4.12.5. (4S,4′S)-2,2′-(3,6-Di-tert-butyl-9H-carbazole-1,8-diyl)bis(4-isopropyl-4,5-dihydrooxazole) (**1gb**).* Purification by flash chromatography (3:1 hexanes/CH_2Cl_2) afforded 26% of the product as a yellow solid. Mp 178−180 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.80 (s, 1H), 8.30 (d, *J*=1.5 Hz, 2H), 8.03 (d, *J*=1.8 Hz, 2H), 4.47−4.56 (m, 2H), 4.19−4.30 (m, 4H), 1.90−1.97 (m, 2H), 1.54 (s, 18H), 1.20 (d, *J*=6.6 Hz, 6H), 1.07 (d, *J*=6.6 Hz, 6H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 162.7, 141.5, 137.6, 123.4, 123.2, 119.7, 109.7, 72.9, 69.8, 34.8, 33.4, 32.1, 19.2, 18.7; IR 3355, 2959, 1649, 1488, 1283; HRMS calcd for $C_{32}H_{44}N_3O_2$ $[M+H]^+$ 502.3434, found 502.3427; $[\alpha]_D^{18}$ +64.0 (*c* 1.0, $CHCl_3$).

4.13. General procedure for synthesis of bis(oxazoline) carbazole ligand 1 from 1,8-dihalocarbazole (6) via Pd-catalyzed carbonylative amidation followed by CH_3SO_2Cl induced cyclization

Modified procedures from the literature were used.[13,22] To a solution of 0.5 mmol of the 1,8-diiodocarbazole and $Pd(PPh_3)_4$ (20 mol %) in 5 ml of dry, degassed DMF was added the corresponding amino alcohol (2.6 equiv) and Et_3N (4 equiv) via a syringe. CO gas was then bubbled through the reaction mixture and a balloon of CO placed over the reaction flask. The reaction mixture was stirred at 60 °C for 8 h. After the mixture was cooled down it was diluted with CH_2Cl_2, washed with brine and 1 M aq $CuSO_4$ several times. The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure to give the desired bisamide. The bisamide was partially purified by passing through a short silica bed and eluting with CH_2Cl_2 and methanol. The eluent was concentrated under rotovap, dried under vacuum, and the bisamide thus obtained was dissolved in 3 mL CH_2Cl_2. NEt_3 (2 equiv) was added and the solution was cooled to 0 °C. $MeSO_2Cl$ (2.5 equiv) was added and the reaction mixture was allowed to warm to rt and stirred overnight. It was then poured into saturated aq NH_4Cl, the organic layer was separated and the aqueous layer extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was treated with 5% methanolic KOH soln (3 mL) and heated under reflux for 3 h. The solvent was evaporated, residue poured into H_2O, and extracted with CH_2Cl_2. The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure to obtain desired product, which was purified by column chromatography.

*4.13.1. (4S,4′S)-2,2′-(3,6-Diphenyl-9H-carbazole-1,8-diyl)bis(4-methyl-4,5-dihydrooxazole) (**1aa**)[9b].* Purification by column chromatography (1:1 hexanes/CH_2Cl_2) and recrystallization (from hexanes/EtOAc) afforded 48% of the product as a yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.00 (s, 1H), 8.48 (d, *J*=1.8 Hz, 2H), 8.22 (d, *J*=1.8 Hz, 2H), 7.77−7.80 (m, 4H), 7.49−7.54 (m, 4H), 7.36−7.41 (m, 2H), 4.61−4.70 (m, 4H), 4.05−4.09 (m, 2H), 1.55 (d, *J*=6.3 Hz, 6H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 162.6, 141.4, 138.8, 132.5, 128.8, 127.3, 126.7, 125.2, 124.2, 121.9, 110.7, 73.6, 62.3, 21.7.

*4.13.2. (4R,4′R)-2,2′-(3,6-Diphenyl-9H-carbazole-1,8-diyl)bis(4-((R)-1-methoxyethyl)-4,5-dihydrooxazole) (**1af**).* Purification by column chromatography (1−3% MeOH in CH_2Cl_2) afforded 61% of the product as a yellow solid. Mp 147−148 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.43 (d, *J*=1.5 Hz, 2H), 8.18 (d, *J*=1.8 Hz, 2H), 7.71−7.74 (m, 4H), 7.42−7.47 (m, 4H), 7.29−7.35 (m, 2H), 4.64−4.66 (m, 2H), 4.43−4.46 (m, 4H), 3.68−3.71 (m, 2H), 3.44 (s, 6H), 1.31 (d, *J*=6.3 Hz, 6H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 163.8, 141.5, 139.1, 132.7, 129.0, 127.5, 126.9, 125.6, 124.4, 122.2, 110.8, 77.8, 70.4, 68.1, 57.3, 14.7; HRMS calcd for $C_{36}H_{36}N_3O_4$ $[M+H]^+$ 574.2706, found 574.2704; $[\alpha]_D^{23}$ +35.3 (*c* 1.0, $CHCl_3$).

*4.13.3. (4S,4′S)-2,2′-(3,6-Bis(4-methoxyphenyl)-9H-carbazole-1,8-diyl)bis(4-isopropyl-4,5-dihydrooxazole) (**1fb**).* Purification by column chromatography (2% Et_3N in CH_2Cl_2 then 1% MeOH in CH_2Cl_2) and recrystallization (from hexanes/EtOAc; a few drops of petroleum ether induced crystallization) to afford 55% of the product as a white solid, mp 163−165 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.64 (d, *J*=1.5 Hz, 2H), 8.57 (s, 1H), 8.00 (d, *J*=1.5 Hz, 2H), 7.49−7.53 (m, 4H), 6.96−7.00 (m, 4H), 4.40−4.41 (m, 2H), 4.10−4.14 (m, 4H), 3.81 (s, 6H), 1.83−1.85 (m, 2H), 1.01 (d, *J*=6.9 Hz, 6H), 0.90 (d, *J*=6.9 Hz, 6H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 164.1, 159.5, 139.5, 130.4, 129.4, 126.4, 125.0, 124.0, 120.7, 120.2, 114.9, 72.8, 70.3, 55.6, 33.1, 19.2, 18.3; IR 3474, 2959, 1770, 1647, 1515; HRMS calcd for $C_{38}H_{40}N_3O_4$ $[M+H]^+$ 602.3013, found 602.3023; $[\alpha]_D^{23}$ +105.4 (*c* 1.0, $CHCl_3$).

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.07.065.

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