Enantioselective Allylation of Indoles: A Surprising Diastereoselectivity

Patrick Ullrich[†]

Julie Schmauck[‡]

Marcus Brauns[†]

Marvin Mantel[†]

Martin Breugst[‡*]

Jörg Pietruszka[†,§*]

[†] Institut für Bioorganische Chemie (IBOC), Heinrich-Heine-Universität Düsseldorf im Forschungszentrum Jülich, Stetternicher Forst, Geb. 15.8, 52426 Jülich, Germany

[‡] Department für Chemie, Universität zu Köln, Greinstraße 4, 50939 Köln, Germany

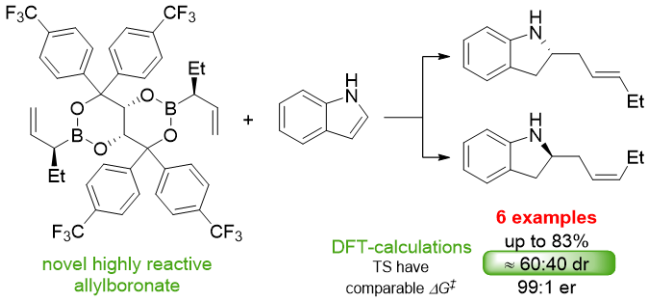
[§] Institut für Bio- und Geowissenschaften (IBG-1: Bioorganische Chemie), Forschungszentrum Jülich, 52428 Jülich, Germany

mbreugst@uni-koeln.de

j.pietruszka@fz-juelich.de

Dedicated to the memory of Dieter Enders

Graphical Abstract



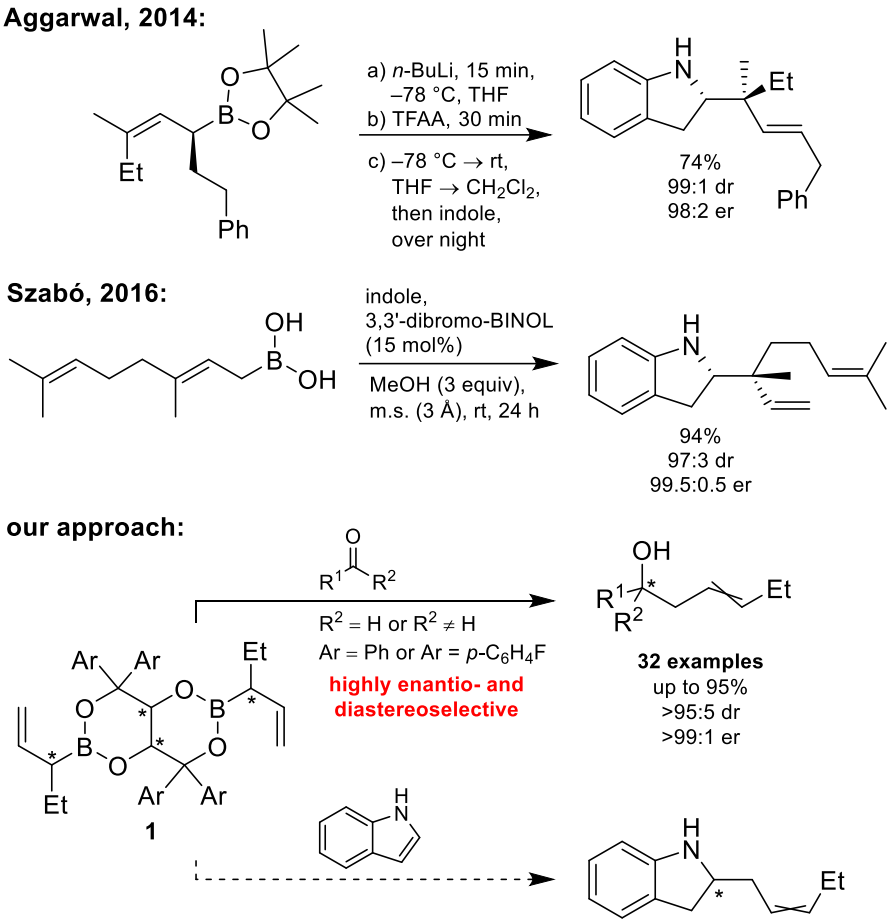
Abstract

Herein we show a novel approach towards the allylation of indoles. Thereby we explore a class of bench-stable allylboronates and fine-tune their reactivity. The allylations of different substituted indoles proceed with negligible diastereo- and excellent enantioselectivities. This surprising selectivity (up to 99:1 er, up to ≈ 60:40 dr) is rationalized by DFT-calculations.

Introduction

Since first evidence for the extraordinary high stereoinduction of boronates in allylation reactions was presented in 1978,[1] this class of compounds has emerged as an indispensable tool in synthetic organic chemistry.[2-7] Thus asymmetric allylation reactions have been investigated intensively in the last decades; research is mostly concentrating on the stereoselective synthesis of homoallylic alcohols descending from aldehydes and ketones.[2, 8-9] However, addressing less reactive electrophiles remains a challenging task, even though nitrogen-containing substrates such as indoles represent an important class of compounds in many biologically active pharmaceuticals and natural products, by implication a reliable portfolio for their selective derivatisation is crucial.[10-14] Underlining the demanding nature of this synthetic issue, to the best of our knowledge, only two examples for the enantioselective allylation of indoles have been reported so far. Namely, the groups of Aggarwal and Szabó demonstrated elegant allylborations of indoles, providing high dia- and enantioselectivity.[15-16] On behalf of further improving the access to the corresponding homoallylic amines, we now sought out to employ bench-stable boron-based reagent **1** recently developed in our group. Easily used for the fully stereodivergent allylation of aldehydes and ketones to the corresponding *Z*- and *E*-configured homoallylic alcohols in high yields and with excellent stereoselectivities (scheme 1),[17-18] application to the allylation of indoles seemed a promising endeavour.

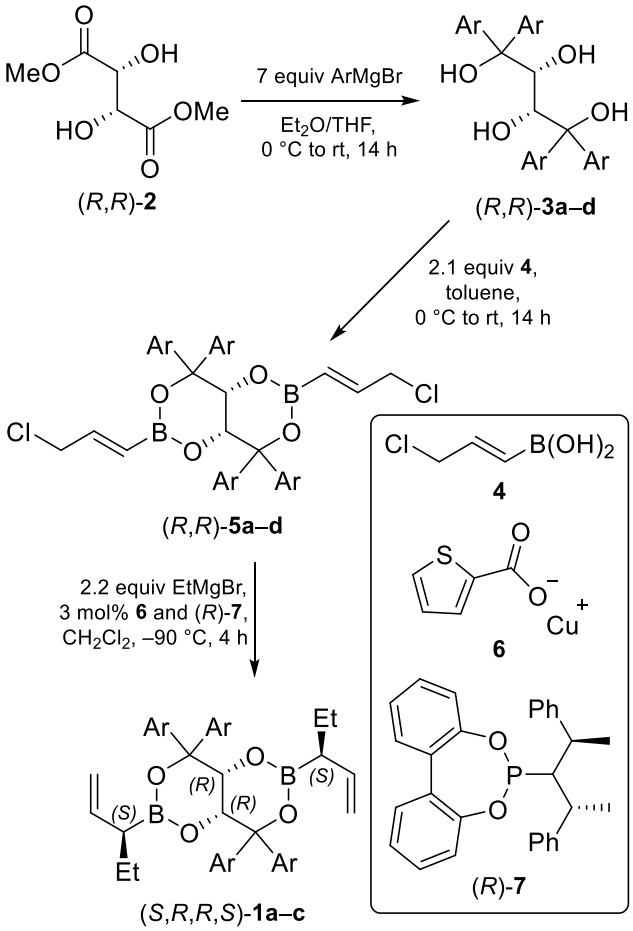
Scheme 1. Previously reported enantioselective allylborations of indole by Aggarwal and Szabó[15-16] and the outline of our attempt based on the highly enantioselective stereodivergent allylation of aldehydes and ketones utilizing bench-stable boronate **1**.[17-18]

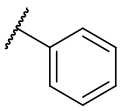
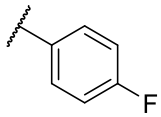
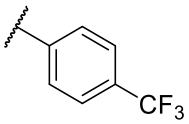
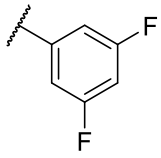


Results and Discussion

We initially started our research with reported allylboronates **1a–b**, attempting to allylate indole in a similar fashion to aldehydes and ketones. Unfortunately, both reported bench-stable reagents **1a**–**b** were not capable of converting indole completely within an adequate period, thus making modifications of reagent **1** mandatory. Prior studies had revealed that introduction of electron donating or withdrawing groups in *para*-position of the aromatic moieties modulate the reagents' reactivity; implementation of the latter led to an increased rate of the intended conversions.[18] We anticipated to extend this trend by introducing additional electron withdrawal and designed boronates **1c–d** bearing either a *para*-trifluoromethyl or two *meta*-fluoride groups (scheme 2). Starting our attempt by the reagent's synthesis in analogy to known procedures with the addition of the corresponding *Grignard*-reagents to dimethyl tartrate **2**,[19] followed by the condensation of the resulting tetraols **3a–d** with boronic acid **4**. Vinylboronic acids **5a–c** then underwent a stereoselective allylic substitution reaction using copper(I) thiophene-2-carboxylate (**6**) and phosphoramidite ligand **7**;[20-21] affording the bench-stable boronates **1a–c** in three steps with good overall yields (61–74%) and in high regio- and stereoselectivities (>95:5). Their configuration can be stipulated on the one hand by the choice of L- or D-tartrate **2** as starting material of the sequence and by the selection of the phosphoramidite ligand **7** in the last synthetic step shown in scheme 2. Unfortunately, compound **1d** could not be isolated under standard conditions likely due to its fast hydrolysis during the work-up procedure.

Scheme 2. Three-step syntheses of allylboronates **1a–c**. [a] one single regio- and stereoisomer was detected in NMR (>95:5 dr), [b] instead of (*R*)-**7** the (*S*)-enantiomer was used, [c] no product could be isolated though ^{1}H NMR reaction control showed full conversion



entry	residue	compound	yield
1		(*R*,*R*)-**3a**	66%
2		(*R*,*R*)-**5a**	96%
3		(*S*,*R*,*R*,*S*)-**1a**	98%[a]
4		(*R*,*R*)-**3b**	85%
5		(*R*,*R*)-**5b**	94%
6		(*S*,*R*,*R*,*S*)-**1b**	92%[a]
7		(*R*,*R*)-**3c**	66%
8		(*R*,*R*)-**5c**	93%
9		(*S*,*R*,*R*,*S*)-**1c**	99%[a]
10		(*R*,*R*,*R*,*R*)-**1c**	97%[a,b]
11		(*R*,*R*)-**3d**	68%
12		(*R*,*R*)-**5d**	89%
13		(*S*,*R*,*R*,*S*)-**1d**	–[c]

Next, ^{1}H NMR kinetics were employed to illustrate the reactivity trend of compounds **1a–c** by monitoring the formation of homoallyl amines **9a** over time (figure 1). As intended, the novel boronate **1c** converted indole **8a** much more rapidly – sixteen times faster than boronate **1a** and four times faster than fluorine-derivate **1b** – to the corresponding products **9a**. The tautomerisation of indole **8a** into its imine form seems to be crucial for the reaction's progress, as indicated by pseudo-zero order kinetics.

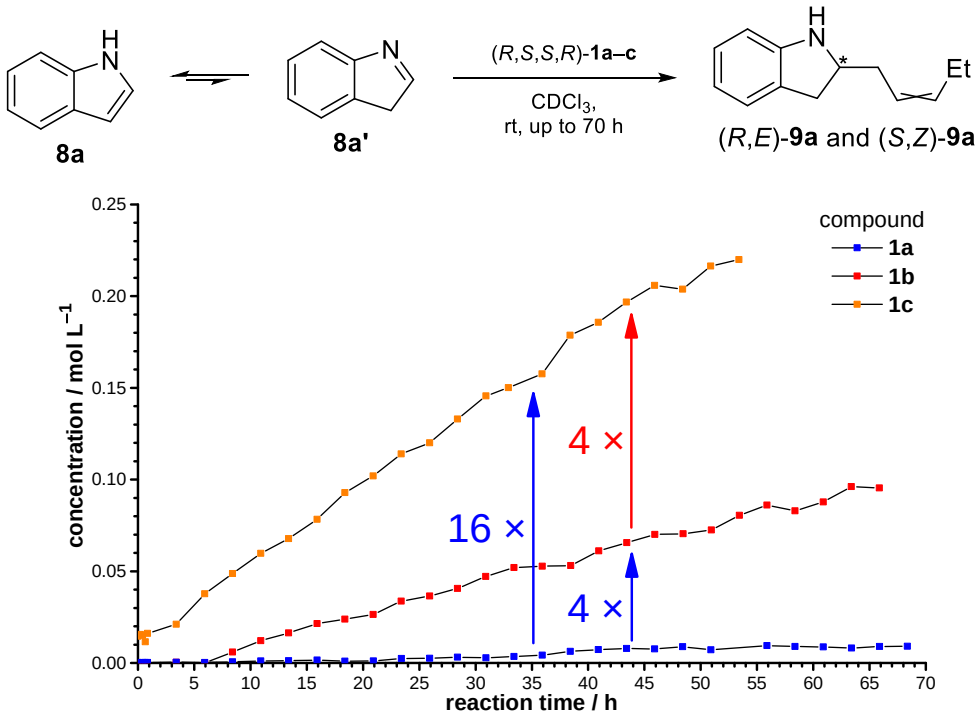
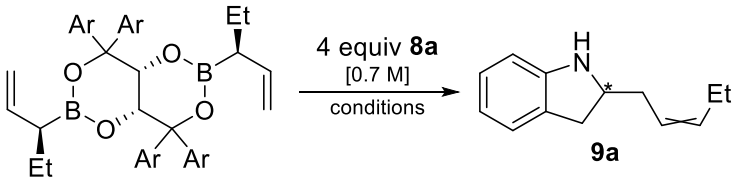


Figure 1. Model reaction for ^{1}H-NMR kinetics and the progress of product formation over time.

Having achieved satisfying reactivity, our attention was drawn towards the stereoselectivity of the allylation of indole **8a**. As with its analogues **1a–b** all four stereoisomers of compound **1c** are easily accessible (scheme 2). Unfortunately, the extraordinary high stereoinduction generated by compound **1a–b** in the reaction with aldehydes[17] and ketones[18] could not be fully maintained when switching to indole **8a** as an electrophile. Hence, we investigated the variation of several reaction parameters for the allylation of indole **8a** – such as addition of *Lewis* acids, solvent and temperature to improve the observed diastereoselectivities and the isolated yields. The rational for the addition of external *Lewis* acids was the hope for a faster tautomerisation of indole into its imine form and thereby a faster reaction. At the same time this could be used as a handle for an additional induction of stereoselectivity when chiral *Lewis* acids would be

used. The beneficial influence of acid addition was prior reported.[22-26] We also examined the addition of iodine as a halogen-bond donor.[27-28] The reaction proceeds optimal when refluxing dichloromethane is used as a solvent without any additional *Lewis* acid present (scheme 3).

Scheme 3. Temperature, solvent and *Lewis* acid screening for the allylation of indole with boronates **1c**. Reaction conditions: 0.15 mmol **1c**, 0.60 mmol **8a** were stirred until total conversion of **1c**, monitored by ^{1}H NMR. [a] determined by ^{1}H-NMR, [b] determined by HPLC, [c] 0.1 mol% of the additional reagent and only 2.1 eq. of **8a** were used.



Ar = *p*-$CF_3C_6H_4$

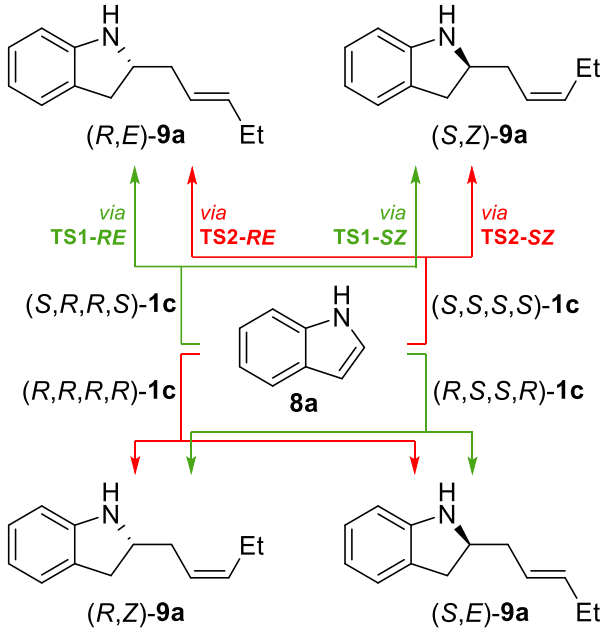
(*S*,*R*,*R*,*S*)-**1c**

entry	T / °C	solvent	additive	t / d	yield	dr[a] (*E*:*Z*)	er[b] (*S*:*R*) of *E*	er[b] (*S*:*R*) of *Z*
1[c]	24	CH_2Cl_2	HCl in Et_2O	5	32%	49:51	n.d.	n.d.
2[c]	24	CH_2Cl_2	$AlCl_3$	5	31%	61:39	n.d.	n.d.
3[c]	24	CH_2Cl_2	$Sc(OTf)_3$	5	15%	48:52	n.d.	n.d.
4[c]	24	CH_2Cl_2	$Ti(^iPrO)_4$	2	decomposition of **1c**			
5[c]	24	CH_2Cl_2	$ZnCl_2$	2	decomposition of **1c**			
6[c]	24	CH_2Cl_2	$Cu(OTf)_2$	5	36%	59:41	n.d.	n.d.
7[c]	24	CH_2Cl_2	I_2	5	23%	50:50	n.d.	n.d.
8	24	CH_2Cl_2	–	5	62%	63:37	2:98	97:3
9	30	CH_2Cl_2	–	4	42%	56:44	2:98	99:1
10	40	CH_2Cl_2	–	2	80%	48:52	1:99	98:2
11	40	*n*-pentane	–	4	38%	48:52	6:94	97:3
12	40	toluene	–	4	30%	43:57	6:94	97:3
13	40	THF	–	3	11%	41:59	11:89	91:9
14	40	EtOAc	–	3	12%	40:60	14:86	89:11
15	40	$CHCl_3$	–	3	42%	47:53	3:97	98:2
16	40	DCE	–	4	35%	43:57	6:94	97:3
17	40	^{t}BuOH	–	3	29%	44:56	10:90	93:7
18	40	CH_3CN	–	3	41%	45:55	4:96	97:3
19	40	CH_3NO_2	–	4	46%	43:57	6:94	96:4
20	40	HFIP	–	3	51%	54:46	6:94	97:3

Thus, the use of every stereoisomer of boronate **1c** leads to a diastereomeric mixture of homoallyl amines **9a** (scheme 4). For example, both boronates (*S*,*R*,*R*,*S*)-**1c** and (*S,S,S,S*)-**1c** deliver a 1:1-diastereomeric mixture of homoallylic amines (*R*,*E*)-**9a** and

(*S*,*Z*)-**9a**, albeit still excellent enantioselectivity for each diastereomer is given (up to 1:99 er). Similarly, employment of (*R*,*S*,*S*,*R*)-**1c** and (*R*,*R*,*R*,*R*)-**1c** leads to the enantiomeric products. The absolute configuration of all products **9a** was determined by reduction of the isolated double bond after separating the diastereomers and comparing the optical rotational values to literature value.[29-31]

Scheme 4. Stereochemical outcome of the allylation of indole with boronates **1c**. Reaction conditions: 0.15 mmol **1c**, 0.60 mmol **8a** were stirred in dry CH_2Cl_2 for 40 h at 40 °C. [a] determined by ^{1}H-NMR, [b] determined by HPLC.

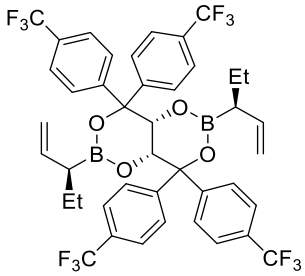
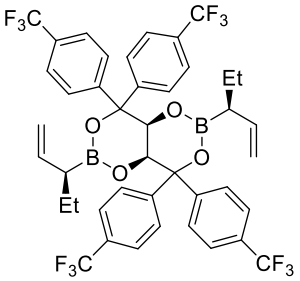


entry	boronate	yield	dr[a] (*E*:*Z*)	er[b] (*S*:*R*) of *E*	er[b] (*S*:*R*) of *Z*
1	(*S*,*R*,*R*,*S*)-**1c**	80%	48:52	1:99	98:2
2	(*R*,*S*,*S*,*R*)-**1c**	59%	62:38	97:3	2:98
3	(*R*,*R*,*R*,*R*)-**1c**	76%	58:42	90:10	6:94
4	(*S*,*S*,*S*,*S*)-**1c**	83%	61:39	5:95	88:12

To get a better understanding of the observed diastereoselectivity, density functional theory calculations were performed employing M06-2X-D3/def2-TZVPP/IEFPCM (CH_2Cl_2)//M06-L-D3/6-31+G(d,p). More precisely, we studied the allylation reactions of indole using allylboronates (*S,R,R,S*)-**1c** and (*S,S,S,S*)-**1c** leading to the product complexes via transition states **TS1** and **TS2** (table 1). The results of these calculations are summarized in table 1 and selected structures are depicted in figure 2.

In line with experimental observations, the equilibrium between 1*H*- and 3*H*-indole lies completely on the side of the 1*H*-tautomer **8a** (ΔG = + 48 kJ mol^{-1}) and only very small concentrations of the reactive 3*H*-tautormer are present in solution. As tautomerization reactions typically proceed quickly, even very small concentrations are sufficient for the subsequent allylation reactions according to the Curtin-Hammett principle. The reaction free energies for the allylation step are all highly exergonic with –82 kJ mol^{-1} < ΔG < –66 kJ mol^{-1} (see the Supporting Information for details) and indicate that the stereochemistry for this reaction is dictated by kinetic control (i.e., relative activation free energies). In comparison to the related allylation reactions involving aldehydes[17] or ketones,[18] the allylation of indoles is thermodynamically less favorable. This furthermore indicates the lower reactivity of the latter compared to carbonyl derivatives. As shown in table 1, the activation free energies for both (*S*,*R*,*R*,*S*)-**1c** and (*S*,*S*,*S*,*S*)-**1c** leading to the four different stereoisomers vary to a much larger extent (+81 < $\Delta G^{‡}$ < +135 kJ mol^{-1}).

Table 1. Calculated activation barriers for the reactions of (*S,R,R,S*)-**1c** and (*S,S,S,S*)-**1c** with indole [kJ mol^{-1}].

Boronate	$\Delta G^{‡}$(***RE***)	$\Delta G^{‡}$(***RZ***)	$\Delta G^{‡}$(***SE***)	$\Delta G^{‡}$(***SZ***)
 (*S*,*R*,*R*,*S*)-**1c**	+99 (**TS1-*RE***)	+140 (**TS1-*RZ***)	+130 (**TS1-*SE***)	+97 (**TS1-*SZ***)
 (*S*,*S*,*S*,*S*)-**1c**	+95 (**TS2-*RE***)	+119 (**TS2-*RZ***)	+113 (**TS2-*SE***)	+85 (**TS2-*SZ***)

For the allylboronate (*S*,*R*,*R*,*S*)-**1c**, the lowest barrier was calculated for the reactions leading to (*R*,*E*)-**9a** and (*S*,*Z*)-**9a** via **TS1-*RE*** and **TS1-*SZ***. In these transition states, the six-membered ring adopts a chair conformation while for the higher-energy transition states (**TS1-*RZ***, **TS1-*SE***) a boat conformation is preferred (figure 2). Due to the

fixed geometry of the imine no chair-like transition states are geometrically feasible for these orientations. Interestingly, the ethyl group is located in the equatorial position for **TS1-*RE***, while the axial position is preferred for **TS1-*SZ***. Both transition states have almost identical activation energy (+99 vs +97 kJ mol^{-1}) which fits to the observation of almost no diastereoselectivity (48:52, scheme 3). This indicates that the less favored axial position of the ethyl group within **TS1-*SZ*** in combination with an unfavorable *syn*-pentane-type interaction within the six-membered transition state (indole ↔ ethyl) is counterbalanced by a smaller steric repulsion with the aryl group of the bisboronate backbone compared to the equatorial orientation in **TS1-*RE***. Obviously, the contribution from the unfavorable steric interactions is much smaller in **TS1-*SZ*** compared to **TS1-*RE***.The calculated barrier also nicely agrees with the experimental conditions (40 h at 40 °C). In line with the experimental data, the high enantioselectivity for both the *E*- and *Z*- configured products is also reflected in the computational data (e.g., 92 vs 125 kJ mol^{-1} for **TS1-*RE*** and **TS1-*SE***).

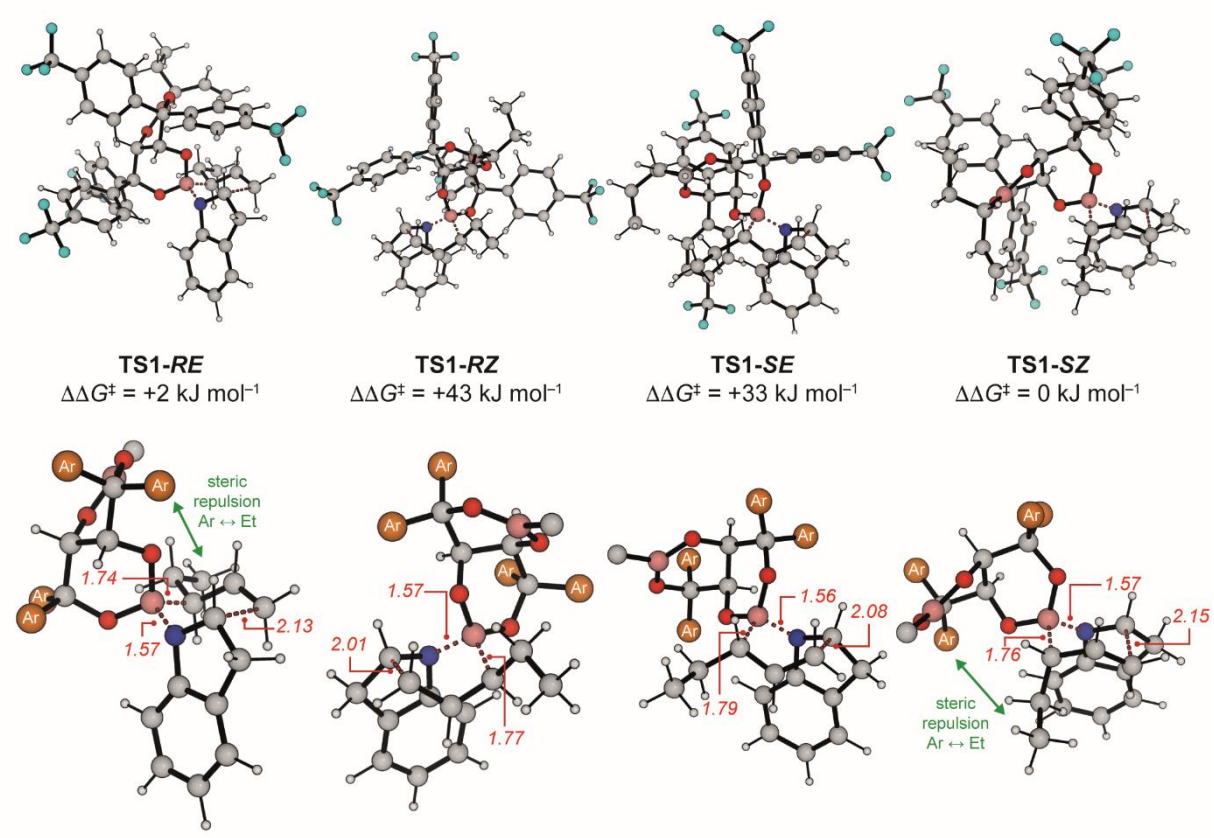


Figure 2. Calculated transition states **TS1** for the reaction of allylboronate (*S*,*R*,*R*,*S*)-**1c** with indole: complete structures (top) and simplified structures highlighting the chair- and boat-like structures (bottom) with selected bond lengths (in Å).

For the isomeric allylboronate (*S,S,S,S*)-**1c**, the calculations predict a kinetic preference for the formation of (*S*,*Z*)-**9a** followed by the formation of (*R*,*E*)-**9a**. Again, these transition states adopt chair-like conformation and the energetically less favored transition states (**TS2-*RZ***, **TS2-*SE***) are in boat-like conformations (figure 3). The explanation for the relative activation energies is similar to that discussed for the diastereometic allylboronate (*S*,*R*,*R*,*S*)-**1c**. The axial orientation of the ethyl group as well as the syn-pentane interaction present in **TS2-*SZ*** are counterbalanced by the smaller steric repulsion caused by the aryl substituents in the backbone. While the enantioselectivity within each diastereomer (*RE* vs. *SE* and *RZ* vs. *SZ*) is nicely paralleled in the computational investigations, the DFT calculations incorrectly predicts a moderate kinetic preference of the *Z*-alkene over the *E*-alkene. Besides chair- and boat-like conformations, we have also considered other orientations, which also included “open” transition states without a direct interaction between the indole nitrogen and the boron atoms. Furthermore, different functionals (e.g., B3LYP-D3BJ, M06-L, TPSS-D3BJ, ωB97X-D) have also been tested and resulted in comparable results (see the Supporting Information for more details). However, the experimentally observed diastereoselectivity slightly varied during the optimization of the synthetic procedure (see the Supporting Information). This indicates that the actual energy difference between the transition states is relatively small. Small changes that are very difficult to model computationally (e.g. specific interactions with the solvent) could easily affect the experimental outcome.

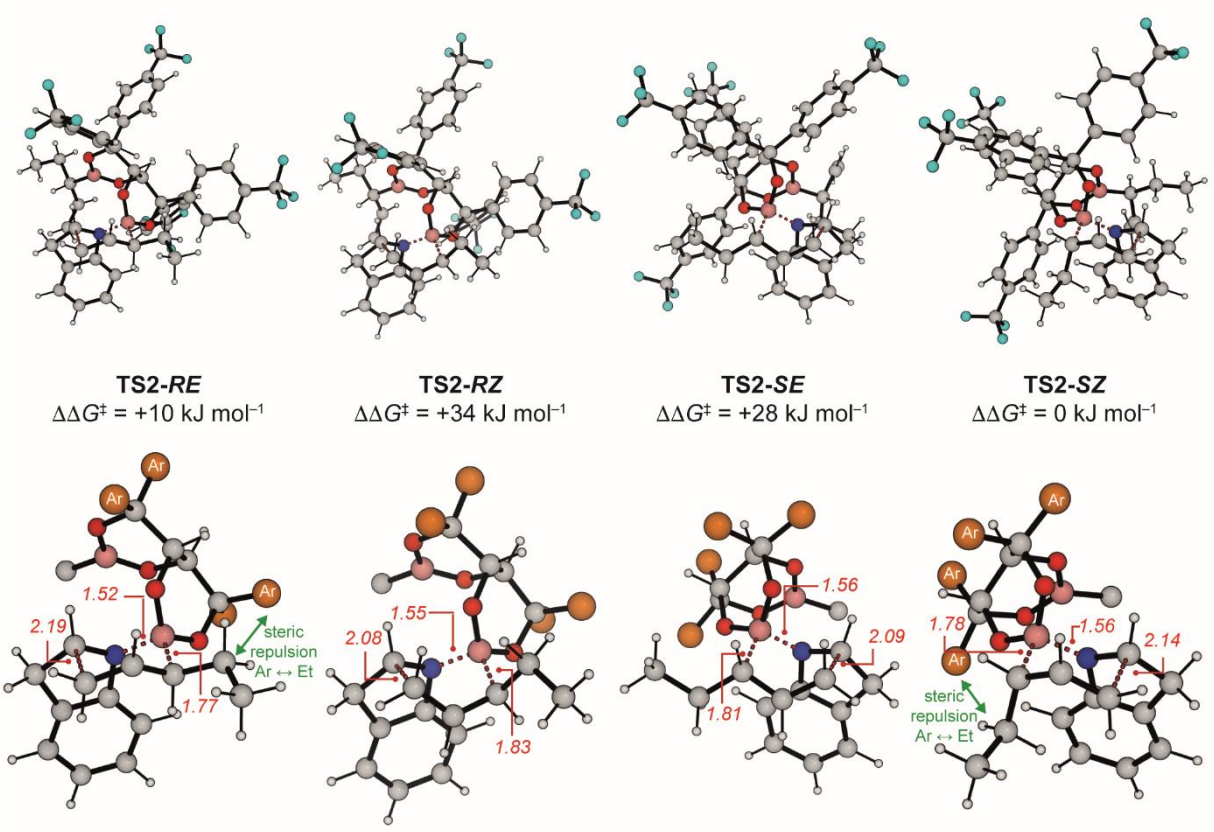
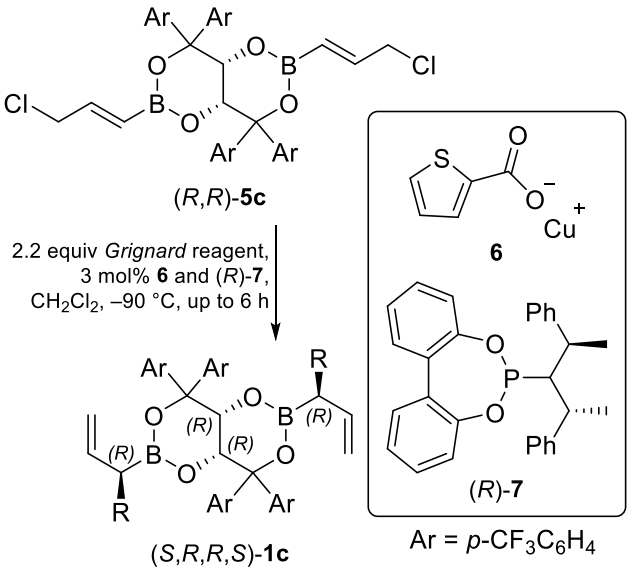


Figure 3. Calculated transition states **TS2** for the reaction of allylboronate (*S,S,S,S*)-**1c** with indole: complete structures (top) and simplified structures highlighting the chair- and boat-like structures (bottom) with selected bond lengths (in Å).

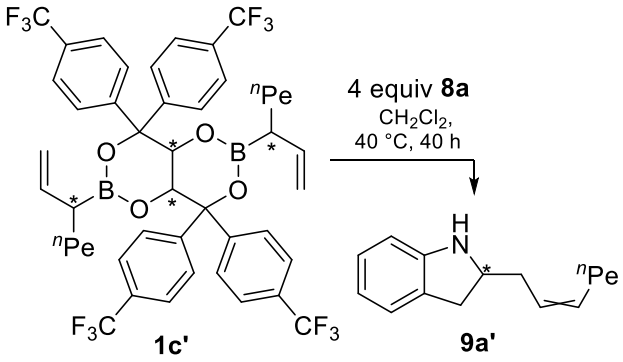
After understanding the stereochemical outcome of the allylation of indole, we investigated the scope of the cuprate catalyzed S_N2' reaction towards a broader spectrum of α-chiral boronates **1c** bearing other substituents than ethyl. The shown method (scheme 5) provides excellent results for different primary alkyl residues,[20] yet appears to be unsuitable for the sufficient installation of further residues to bisboronate **5c** as it has been reported in literature previously.[17] For *n*-pentyl α-substitued boronates **1c'** the allylation of compound **8a** was performed analoguosly to the previously shown cases and the results are depicted in scheme 6. Both diastereo- and enantioselectivity of the reaction are less pronounced than those of the ethyl substitued reagents **1c**.

Scheme 5. Copper-catalysed allylic substitutions of allyl chloride **5c** with different commercially available *Grignard* reagents.



entry	*Grignard* reagent		yield
1	BrMg	925-90-6	quant.
2	BrMg	693-25-4	quant.
3	BrMg	480438-44-6	–[a]
4	ClMg–Si	13170-43-9	–[a]
5	ClMg	2622-05-1	–[a]
6	BrMg	1826-67-1	–[a]
7	BrMg–Ph	100-58-3	–[a]
8	ClMg Ph	6921-34-2	–[a]
9	ClMg Ph	90878-19-6	–[a]

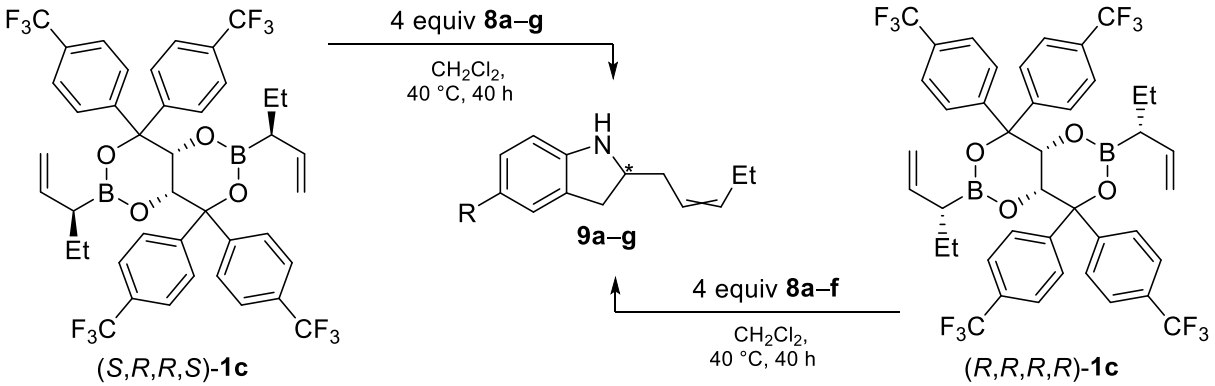
Scheme 6. Allylation of indole with *n*-pentyl α-substitued boronates **1c'**. Reaction conditions: 0.15 mmol (*S*,*R*,*R*,*S*)- or (*R*,*R*,*R*,*R*)-**1c'**, 0.60 mmol. **8a** were stirred in dry CH_2Cl_2 for 40 h at 40 °C. [a] determined by ^{1}H-NMR, [b] determined by HPLC



entry	compound	yield	dr[a] (*E*:*Z*)	er[b] (*S*:*R*) of *E*	er[b] (*S*:*R*) of *Z*
1	(*S*,*R*,*R*,*S*)-**1c'**	45%	67:33	7:93	80:20
2	(*R*,*R*,*R*,*R*)-**1c'**	45%	45:55	67:33	12:88

Lastly, we studied the influence of the electrophile's nature on the reaction. Therefore, differently 5-substituted indoles **8b–g** were converted into the corresponding homoallyl amines as shown before (scheme 7). We presumed that an electron rich indole would undergo allylation faster due to the increased nucleophilicity of the nitrogen. All compounds **9b–e** could be isolated in moderate yields (40–53%) when boronate (*S*,*R*,*R*,*S*)-**1c** was used. The enantioselectivities are without exceptions very good to excellent (96:4–99:1 er) while again diastereomeric ratios near 50:50 were observed. Substrates **8f–g** could not be converted in reasonable yields; which might be attributed to the strong electron withdrawing character of the substituents. Comparing these to the products resulting from an allylation with the diastereomeric reagent (*R*,*R*,*R*,*R*)-**1c**, only low yields with worse enantioselectivities could be obtained. Nonetheless, all four possible products can be addressed by converting indoles of different electronic character with either (*S*,*R*,*R*,*S*)-**1c** or its enantiomer in excellent enantioselectivity; upfront diastereomeric mixtures could be readily separated. It should be noted that due to its negligible diastereoselectivity, the conversion of **1c** with 3-substituted indoles such as the natural product skatole led to a complex mixture of multiple, inseperable stereoisomers in average yields (38%).

Scheme 7. Allylation of indoles with different functional groups. Reaction conditions: 0.15 mmol (*S*,*R*,*R*,*S*)- or (*R*,*R*,*R*,*R*)-**1c**, 0.60 mmol. **8a–g** were stirred in dry CH_2Cl_2 for 40 h at 40 °C. [a] determined by ^{1}H-NMR, [b] determined by HPLC



entry	compound		yield	dr[a] (*E*:*Z*)	er[b] (*S*:*R*) of *E*	er[b] (*S*:*R*) of *Z*
1	**9a**	H	80%	48:52	1:99	98:2
2	**9b**	Me	40%	47:53[b]	3:97	96:4
3	**9c**	OMe	53%	46:54	3:97	96:4
4	**9d**	F	46%	48:52	1:99	96:4
5	**9e**	Br	43%	49:51	2:98	98:2
6	**9f**	CO_2Me	traces	49:51	2:98	98:2
7	**9g**	NO_2	no conversion after 12 d			

entry	compound		yield	dr[a] (*E*:*Z*)	er[b] (*S*:*R*) of *E*	er[b] (*S*:*R*) of *Z*
8	**9a**	H	76%	58:42	90:10	6:94
9	**9b**	Me	43%	36:64[b]	91:9	8:92
10	**9c**	OMe	30%	34:66	92:8	7:93
11	**9d**	F	47%	44:56	83:17	8:92
12	**9e**	Br	35%	46:54	92:8	9:91
13	**9f**	CO_2Me	traces	50:50	89:11	14:86

Conclusion

We have illustrated a straightforward approach towards the allylation of indoles. To this end, the highly potent, bench-stable allylboronate **1c** was established. Though the allylboration of differently substituted indoles **8a–g** proceeds only with negligible diastereoselectivity, excellent enantioselectivities for all four possible homoallylic amines (up to er 99:1) can be observed using only one diastereomeric form of the allylation reagent **1c**. The separation of diastereomeric mixtures is readily achievable.

DFT calculations furthermore provide insights into the geometries and relative activation free energies of the relevant transition states. While the diastereoselectivity for the (*S*,*S*,*S*,*S*)-**1c** was problematic probably due to specific interactions with the solvent molecules, the more stable chair-like transition states are responsible for the stereochemical outcome for the isomeric (*S*,*R*,*R*,*S*)-**1c**. For both allylboronates, the experimentally observed enantioselectivity could also be rationalized by chair-like transition states.

Based on the relatively broad functional group tolerance, albeit limited to non-electron-withdrawing moieties, accompanied by high enantioselectivities, an air- and moisture-insensitive allylation reagent was found with which natural products or intermediates *en route* bearing an indole motif can be functionalised conveniently.

Experimental Section

General Information

If not otherwise mentioned all chemicals were obtained from commercial sources and used without any further purification. The solvents CH_2Cl_2, Et_2O, THF and toluene were purchased from commercial sources and dried using a *MB-SPS-800* solvent purification system. Furthermore all reactions were performed under inert conditions (N_2- or Ar-atmosphere) utilizing *Schlenk*-technique. The TLC-foil *Polygram SilG/UV$_{254}$* by *Macherey-Nagel* was used as stationary phase in thin layer chromatography. TLC-plates were stained using either a $KMnO_4$-solution or an I_2-chamber. Most products were isolated using preparative column chromatography. The silica gel (0.040 mm to 0.063 mm) was provided by *Merck*; as mobile phase mixtures of petrol ether and ethyl acetate or *n*-pentane and diethyl ether were used. For determination of the enantiomeric excess the *Dionex UltiMate 3000 Column Compartment* by *Thermo Fisher Scientific* was utilized. More detailed information on the employed solvent mixtures as well as on the used columns are mentioned in the corresponding *Supporting Information* section. For the separation of diastereomeric homoallylamines a preparative *Dionex* HPLC by *Thermo Fisher Scientific* with a *Chiracel-IC* column was used. Melting points were determined using a *Büchi Melting Point B-540*. The specific rotation of optically active, enantiomerically pure compounds was measured using a *JASCO P-2000* polarimeter. All shown NMR-spectra are recorded on a *Bruker Avance DRX 600*. The samples have been solved in deuterated chloroform or dichloromethane. All spectra have been referred to the solvent peak or the internal standard tetramethylsilane. IR spectra were measured using a *PerkinElmer SpectrumTwo* spectrometer with attenuated total reflection. High resolution ESI mass spectra were recorded on a *Finnigen Model MAT LC-Q* by the *Zentralinstitut für Engineering, Elektronik und Analytik (ZEA-3)* at the *Forschungszentrum Jülich* or on a *MDS SCIEXQ Model Trap 4000* by the *HHU Center of Molecular and Structural Analytics (HHUCeMSA)* at the *Heinrich-Heine-Universität Düsseldorf*. For detailed information on the characterisation of the obtained products and the enantiomeric analysis see the corresponding *Supporting Information.*

Synthesis of the Boronates 1a–c

The boronates **1a–c** were synthesised according to the three step sequence published by *Brauns et al.* with slight adaptations.[17-18]

General procedure for the synthesis of tetraols 3a–d

Vacuum dried magnesium (0.1 mol, 7 equiv) is overlayed with dry Et_2O (0.1 M), after which a solution of the aryl bromide (0.1 mol, 7 equiv) in dry THF (0.1 M) is slowly added. Meanwhile the reaction is kept at rt with a water bath and stirred for 2 h at rt. The dimethyl tartrate (14 mmol, 1 equiv) is solved in dry THF (0.5 M) and slowly added to the *Grignard* reagent within 30 min. The reaction is stirred over night at rt. Subsequently, the reaction was quenched by the addition of sat. aq. NH_4Cl-solution, to remove the precipitate 1 M HCl is cautiously dripped into the reaction until solids vanished. After phase separation, the aq. phase was extracted three times with ethyl acetate. The combined organic layers were dried over $MgSO_4$ and the solvent is removed under reduced pressure. The crude product is purified either *via* column chromatography or by recrystallization.

(2*R*,3*R*)-1,1,4,4-Tetraphenylbutan-1,2,3,4-tetraol [(*R,R*)-3a]

Yield: 78%, 8.3 g (19 mmol); white solid. R_f (PE:EE 80:20): 0.03. Mp: 147.7–149.2 °C. $[\alpha]_D^{20}$ +157 (*c* 1.0, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.77 (d, *J* = 4.4 Hz, 2 H), 4.43 (d, *J* = 3.5 Hz, 2 H), 4.63 (s, 2 H), 7.13–7.37 (m, 20 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 72.1, 81.7, 124.9, 126.0, 127.2, 127.3, 128.4, 128.6, 143.8, 144.1 ppm. IR (ATR): $\tilde{\nu}$ 3391, 1493, 1449, 1061, 905, 733, 698, 603 cm^{-1}. The analytics are in alignment with the literature.[17]

(2*R*,3*R*)-1,1,4,4-Tetra(4-fluorophenyl)butan-1,2,3,4-tetraol [(*R,R*)-3b]

Yield: 85%, 2.1 g (4.2 mmol); white solid. R_f (PE:EE 80:20): 0.25. Mp: 128.1–132.2 °C. $[\alpha]_D^{20}$ +128 (*c* 1.1, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.95 (d, *J* = 4.1 Hz, 2 H), 4.30 (d, *J* = 3.9 Hz, 2 H), 4.56 (s, 2 H), 6.94 (t, *J* = 8.7 Hz, 4 H), 7.04 (t, *J* = 8.7 Hz, 4 H), 7.19 (dd, *J* = 5.1, 8.5 Hz, 4 H), 7.25 (dd, *J* = 4.9, 8.5 Hz, 4 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 72.0, 81.2, 115.3 (d, *J* = 21.4 Hz), 115.6 (d, *J* = 21.4 Hz), 126.7 (d, *J* = 8.0 Hz), 128.0 (d, *J* = 8.0 Hz), 139.3 (d, *J* = 3.3 Hz), 139.6 (d, *J* = 3.2 Hz), 161.9 (d, *J* = 247.2 Hz) ppm. IR (ATR): $\tilde{\nu}$ 3411, 1602, 1506, 1415, 1226, 1160, 1073, 1015, 986, 907, 831, 730, 650, 601, 590, 561, 590 cm^{-1}. The analytics are in alignment with the literature.[18]

(2*R*,3*R*)-1,1,4,4-Tetra[4-(trifluoromethyl)phenyl]butan-1,2,3,4-tetraol [(*R,R*)-3c]

Yield: 66%, 6.2 g (8.9 mmol); pale yellow solid. R_f (PE:EE 80:20): 0.22. Mp: 104.6 °C. $[\alpha]_D^{20}$ +83 (*c* 1.1, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.86 (d, *J* = 4.4 Hz, 2 H), 4.45 (d, *J* = 4.3 Hz, 2 H), 4.65 (s, 2 H), 7.37–7.45 (m, 8 H), 7.54 (d, *J* = 8.3 Hz, 4 H), 7.65

(d, *J* = 8.2 Hz, 4 H) ppm. $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): *δ* 72.0, 81.6, 123.9 (d, *J* = 272.2 Hz), 125.5, 125.8 (q, *J* = 3.5 Hz), 126.1 (q, *J* = 3.4 Hz), 126.6, 130.3 (q, *J* = 32.8 Hz), 146.6, 146.8 ppm. IR (ATR): $\tilde{\nu}$ 3417, 1618, 1415, 1321, 1164, 1119, 1067, 1017, 989, 909, 834, 773, 734, 710, 678, 630, 610 cm^{-1}. HRMS: *m/z* $[M - H]^-$ calcd. 697.1248 for $C_{32}H_{21}F_{12}O_4$; found 697.1234.

(2*R*,3*R*)-1,1,4,4-Tetra(3,5-difluorophenyl)butan-1,2,3,4-tetraol [(*R,R*)-3d]

Yield: 58%, 3.2 g (5.6 mmol); pale yellow solid. R_f (PE:EE 80:20): 0.16. Mp: 133.2 °C. $[\alpha]_D^{20}$ +152 (*c* 1.0, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): *δ* 3.58 (d, *J* = 5.0 Hz, 2 H), 4.32 (d, *J* = 4.9 Hz, 2 H), 4.62 (s, 2 H), 6.62–6.90 (m, 12 H) ppm. $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): *δ* 71.7, 80.8, 103.6 (t, *J* = 25.3 Hz), 104.0 (t, *J* = 25.1 Hz), 108.2 (d, *J* = 26.5 Hz), 109.0–109.5 (m), 146.2–146.4 (m), 163.1 (dd, *J* = 249.5 Hz, 12.6 Hz), 163.4 (dd, *J* = 251.2 Hz, 12.7 Hz) ppm. IR (ATR): $\tilde{\nu}$ 3412, 1620, 1597, 1438, 1304, 1118, 980, 909, 850, 788, 768, 734, 705, 512 cm^{-1}. HRMS: *m/z* $[M - H]^-$ calcd. 569.0999 for $C_{28}H_{17}F_8O_4$; found 569.0992.

General procedure for the synthesis of allyl chlorides 5a–d

Tetraol **3** (2.9 mmol,1 equiv) and ground molecular sieves (3 Å, 0.5 g per mmol tetraol) are stirred in dry toluene (40 mM). (*E*)-(3-Chloroprop-1-en-1-yl)boronic acid (6 mmol, 2.05 equiv) is added to the suspension. The reaction is stirred at 0 °C for 1 h and afterwards over night at rt. The solvent is removed under reduced pressure and the crude product is purified by column chromatography.

(4a*R*,8a*R*,1'*E*,1''*E*)-2,6-Di(3-chloroprop-1-en-1-yl)-4,4,8,8-tetraphenyltetrahydro[1,3,2]dioxaborinino[5,4-d][1,3,2]dioxaborinin [(*R,R*)-5a]

Yield: 96%, 2.9 g (4.9 mmol); white solid. R_f (*n*-pentane:Et_2O 90:10): 0.30. Mp: 164.3–168.0 °C. $[\alpha]_D^{20}$ +28 (*c* 1.2, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): *δ* 4.08 (d, *J* = 5.9 Hz, 4 H), 4.82 (s, 2 H), 5.77 (dd, *J* = 1.7 Hz, 17.6 Hz, 2 H), 7.15–7.44 (m, 21 H) ppm. $^{13}C\{^{1}H\}$ NMR (151 MHz, CDCl3): *δ* 46.3, 69.2, 80.9, 125.0, 126.3, 127.3, 128.0, 128.1, 129.1, 142.2, 143.5, 145.7 ppm. IR (ATR): $\tilde{\nu}$ 3063, 3021, 1958, 1711, 1640, 1493, 1450, 1386, 1328, 1266, 1219, 993, 822, 749, 697, 624 cm^{-1}. The analytics are in alignment with the literature.[17]

(4a*R*,8a*R*,1'*E*,1''*E*)-2,6-Di(3-chloroprop-1-en-1-yl)-4,4,8,8-tetrakis(4-fluorophenyl)tetrahydro[1,3,2]dioxaborinino[5,4-d][1,3,2]dioxaborinin [(*R,R*)-5b]

Yield: 97%, 2.0 g (3.0 mmol); white solid. R_f (*n*-pentane:Et_2O 90:10): 0.36. Mp: 99.7–102.3 °C. $[\alpha]_D^{20}$ +38 (*c* 1.0, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 4.11 (dd, *J* = 1.5 Hz, 5.9 Hz, 4 H), 4.71 (s, 2 H), 5.78 (d, *J* = 17.5 Hz, 2 H), 6.63 (dt, *J* = 5.9 Hz, 17.5 Hz, 2 H), 6.98 (t, *J* = 8.7 Hz, 4 H), 7.08 (t, *J* = 8.5 Hz, 4 H), 7.19–7.24 (m, 4 H), 7.34–7.40 (m, 4 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 46.1, 69.0, 80.4, 115.1 (d, *J* = 21.5 Hz), 116.3 (d, *J* = 21.5 Hz), 125.0, 126.7 (d, *J* = 8.1 Hz), 128.1 (d, *J* = 7.9 Hz), 137.6 (d, *J* = 3.2 Hz), 139.0 (d, *J* = 3.3 Hz), 146.3, 162.1 (d, *J* = 246.7 Hz), 162.4 (d, *J* = 248.6 Hz) ppm. IR (ATR): $\tilde{\nu}$ 1713, 1640, 1603, 1506, 1363, 1328, 1266, 1219, 1160, 992, 832, 739, 702, 585, 567 cm^{-1}. The analytics are in alignment with the literature.[18]

(4a*R*,8a*R*,1'*E*,1''*E*)-2,6-Di(3-chloroprop-1-en-1-yl)-4,4,8,8-tetrakis[4-(trifluoromethyl)phenyl]tetrahydro[1,3,2]dioxaborinino[5,4-d][1,3,2]dioxaborinin [(*R,R*)-5c]

Yield: 93%, 2.2 g (2.5 mmol); white solid. R_f (*n*-pentane:Et_2O 90:10): 0.26. Mp: 108.1–109.5 °C. $[\alpha]_D^{20}$ +48 (*c* 1.1, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 4.12 (dd, *J* = 1.4 Hz, 5.9 Hz, 4 H), 4.87 (s, 2 H), 5.79 (dd, *J* = 1.5 Hz, 17.5 Hz, 2 H), 6.64 (dt, *J* = 5.8 Hz, 17.5 Hz, 2 H), 7.43 (d, *J* = 8.2 Hz, 4 H), 7.53–7.60 (m, 8 H), 7.70 (d, *J* = 8.3 Hz, 4 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 45.8, 68.7, 80.4, 124.1, 125.2, 125.3 (d, *J* = 3.6 Hz), 126.4, 126.5 (d, *J* = 3.6 Hz), 127.7, 130.0 (q, *J* = 32.6 Hz), 131.0 (q, *J* = 33.0 Hz), 145.4 (d, *J* = 206.1 Hz), 146.8 ppm. IR (ATR): $\tilde{\nu}$ 1641, 1616, 1461, 1321, 1220, 1209, 1166, 1122, 1069, 1017, 992, 908, 851, 821, 773, 733, 649, 597 cm^{-1}. HRMS: *m/z* $[M + NH_4]^+$ calcd. 884.1541 for $C_{38}H_{30}B_2Cl_2F_{12}NO_4$; found 884.1537.

(4a*R*,8a*R*,1'*E*,1''*E*)-2,6-Di(3-chloroprop-1-en-1-yl)-4,4,8,8-tetrakis(3,5-difluorophenyl)tetrahydro[1,3,2]dioxaborinino[5,4-d][1,3,2]dioxaborinin [(*R,R*)-5d]

Yield: 43%, 0.33 g (0.45 mmol); white solid. R_f (*n*-pentane:Et_2O 90:10): 0.29. $[\alpha]_D^{20}$ +15 (*c* 1.0, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 4.13 (dd, *J* = 1.5 Hz, 5.8 Hz, 4 H), 4.69 (s, 2 H), 5.77 (dd, *J* = 1.5 Hz, 17.5 Hz, 2 H), 6.63 (dt, *J* = 5.8 Hz, 17.5 Hz, 2 H), 6.73 (tt, *J* = 2.4 Hz, 8.6 Hz, 2 H), 6.82 (dd, *J* = 2.2 Hz, 8.1 Hz 4 H), 6.87 (tt, *J* = 2.3 Hz, 8.4 Hz, 2 H), 6.95 (dd, *J* = 2.2 Hz, 8.3 Hz, 4 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 45.8, 68.6, 79.8, 103.49 (t, *J* = 25.2 Hz), 104.7 (t, *J* = 25.1 Hz), 108.1 (dd, *J* = 5.2 Hz, 27.6 Hz), 109.1 (dd, *J* = 5.8 Hz, 27.0 Hz), 144.4 (t, *J* = 8.9 Hz), 145.8 (t, *J* = 7.6 Hz), 147.3, 162.9 (dd, *J* = 12.8 Hz, 248.8 Hz), 163.6 (dd, *J* = 12.6 Hz, 252.2 Hz) ppm. IR (ATR): $\tilde{\nu}$ 1641, 1611, 1588, 1487, 1446, 1381, 1358, 1327, 1266, 1251, 1221, 1173,

1146, 1070, 989, 885, 862, 807, 774, 716, 681 cm^{-1}. HRMS: *m/z* $[M - C_3H_4BCl]^+$ calcd. 653.0943 for $C_{31}H_{19}BClF_8O_4$; found 653.0943.

General procedure for the synthesis of allyl boronates 1a–c

Allyl chloride **5** (0.3 mmol, 1 equiv), copper(I) thiophene-2-carboxylate (9 µmol, 3 mol%) and either the (*S*)- or the (*R*)-enantiomer of *N*,*N*-bis(1-phenylethyl)dibenzo-[d,f][1,3,2]dioxaphosphepin-6-amine (9 µmol, 3 mol%) are dissolved in dry CH_2Cl_2 (20 mM). The solution is cooled to –90 °C and an ethyl magnesium chloride solution (0.65 mmol, 2.2 equiv, 3 M in Et_2O diluted to 0.5 M with CH_2Cl_2) is added using a syringe pump within 1 h at –90 °C. The solution is stirred for additional 2 h at –90 °C. Subsequently, quenching is conducted by addition of sat. aq. NH_4Cl-solution. After separation of the organic and aqueous layer, the latter is extracted three times with CH_2Cl_2. The combined organic layers are dried over $MgSO_4$ and the solvent is removed under reduced pressure. The product is purified by column chromatography.

(4a*R*,8a*R*,3'*S*,3''*S*)-2,6-Di(pent-1-en-3-yl)-4,4,8,8-tetraphenyltetrahydro[1,3,2]dioxaborinino[5,4-d][1,3,2]dioxaborinine [(*S,R,R,S*)-1a]

Yield: quant., 0.98 g (1.7 mmol); white solid. R_f (*n*-pentane:Et_2O 90:10): 0.68. Mp: 158.3–159.4 °C. $[\alpha]_D^{20}$ +13 (*c* 0.9, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 0.87 (t, *J* = 7.4 Hz, 6 H), 1.42 (ddq, *J* = 7.5 Hz, 14.9 Hz, 2 H), 1.61 (ddq, *J* = 7.0 Hz, 14.0 Hz, 2 H), 1.79 (ddd, *J* = 7.9 Hz, 2 H), 4.76 (s, 2 H), 4.91–5.00 (m, 4 H), 5.82 (dt, *J* = 9.5 Hz, 17.4 Hz, 2 H), 7.11–7.40 (m, 22 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 13.8, 23.1, 35.7, 69.1, 80.5, 113.4, 125.2, 126.4, 127.0, 127.8, 127.9, 129.0, 140.4, 142.4, 143.8 ppm. IR (ATR): $\tilde{\nu}$ 2958, 1493, 1386, 1280, 1185, 1034, 1002, 901, 838, 747, 694, 651, 624 cm^{-1}. The analytics are in alignment with the literature.[17]

(4a*R*,8a*R*,3'*S*,3''*S*)-2,6-Di(pent-1-en-3-yl)-4,4,8,8-tetrakis(4-fluorophenyl)tetrahydro[1,3,2]dioxaborinino[5,4-d][1,3,2]dioxaborinine [(*S,R,R,S*)-1b]

Yield: quant., 0.80 g (1.2 mmol); white solid. R_f (*n*-pentane:Et_2O 90:10): 0.79. Mp: 150.8–155.3 °C. $[\alpha]_D^{20}$ +12 (*c* 0.8, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 0.87 (t, *J* = 7.4 Hz, 6 H), 1.36–1.46 (m, 2 H), 1.53–1.63 (m, 2 H), 1.75–1.83 (m, 2 H), 4.64 (s, 2 H), 4.92–5.01 (m, 4 H), 5.78 (ddd, *J* = 8.8 Hz, 10.3 Hz, 17.1 Hz, 2 H), 6.94 (t, *J* = 8.7 Hz, 4 H), 7.07 (t, *J* = 8.6 Hz, 4 H), 7.23 (dd, *J* = 5.2 Hz, 8.8 Hz, 4 H), 7.32 (dd, *J* = 5.3 Hz, 8.9 Hz, 4 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 13.6, 22.9, 35.4, 68.8, 79.8, 113.7,.114.6 (d, *J* = 21.5 Hz), 116.0 (d, *J* = 21.5 Hz), 126.7 (d, *J* = 8.0 Hz), 128.1 (d, *J* = 7.9 Hz), 137.7 (d, *J* = 3.3 Hz), 139.1 (d, *J* = 3.3 Hz), 139.9, 161.9 (d, *J* = 246.1 Hz),

162.2 (d, *J* = 248.3 Hz) ppm. IR (ATR): $\tilde{\nu}$ 2959, 1604, 1507, 1385, 1279, 1229, 1197, 1160, 1015, 999, 903, 831, 765, 739, 675, 587, 568 cm^{-1}. The analytics are in alignment with the literature.[18]

(4a*R*,8a*R*,3'*S*,3''*S*)-2,6-Di(pent-1-en-3-yl)-4,4,8,8-tetrakis[4-(trifluoromethyl)phenyl]tetrahydro[1,3,2]dioxaborinino[5,4-d][1,3,2]dioxaborinine [(*S,R,R,S*)-1c]

Yield: 96%, 1.0 g (1.2 mmol); white solid. R_f (*n*-pentane:Et_2O 90:10): 0.90. Mp: 167.2–170.8 °C. $[\alpha]_D^{20}$ +6 (*c* 1.2, $CHCl_3$). $[\alpha]_D^{20}$ of enantiomer –4 (*c* 1.0, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.86 (t, *J* = 7.4 Hz, 6 H), 1.40 (dq, *J* = 6.8 Hz, 13.6 Hz, 2 H), 1.52–1.60 (m, 4 H), 1.81 (q, *J* = 7.7 Hz, 2 H), 4.78 (s, 2 H), 4.97 (s, 2 H), 4.99 (d, *J* = 8.4 Hz, 2 H), 5.75 (dt, *J* = 9.6 Hz, 17.0 Hz, 2 H), 7.43 (d, *J* = 8.1 Hz, 4 H), 7.49–7.56 (m, 8 H), 7.69 (d, *J* = 8.2 Hz, 4 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 13.7, 23.0, 35.4, 68.6, 80.2, 114.2, 122.9, 123.2, 124.7, 125.2 (q, *J* = 3.3 Hz), 125.5, 126.5 (m), 130.0 (q, *J* = 32.7 Hz), 131.1 (q, *J* = 32.6 Hz), 139.5, 145.8 (d, *J* = 210.4 Hz) ppm. IR (ATR): $\tilde{\nu}$ 2962, 1619, 1417, 1387, 1324, 1284, 1168, 1127, 1071, 1018, 906, 841, 768, 720 cm^{-1}. HRMS (ESI-TOF): m/z $[M + NH_4]^+$ calcd. 872.2946 for $C_{42}H_{40}B_2F_{12}NO_4$; found 872.2948.

(4a*R*,8a*R*,3'*R*,3''*R*)-2,6-Di(pent-1-en-3-yl)-4,4,8,8-tetrakis[4-(trifluoromethyl)phenyl]tetrahydro[1,3,2]dioxaborinino[5,4-d][1,3,2]dioxaborinine [(*R,R,R,R*)-1c]

Yield: quant., 0.68 g (0.80 mmol); white solid. R_f (*n*-pentane:Et_2O 90:10): 0.84. Mp: 189.2–191.3 °C. $[\alpha]_D^{20}$ –32 (*c* 0.9, $CHCl_3$). $[\alpha]_D^{20}$ of enantiomer –9 (*c* 1.1, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.86 (t, *J* = 7.3 Hz, 6 H), 1.44 (dq, *J* = 7.3 Hz, 14.4 Hz, 2 H), 1.59 (dq, *J* = 7.1 Hz, 14.0 H, 2 H), 1.79 (q, *J* = 7.8 Hz, 2 H), 4.77 (s, 2 H), 4.96 (d, *J* = 4.6 Hz, 2 H), 4.98 (s, 2 H), 5.78 (dt, *J* = 9.1 Hz, 18.1 Hz, 2 H), 7.41 (d, *J* = 8.1 Hz, 4 H), 7.49–7.57 (m, 8 H), 7.69 (d, *J* = 8.1 Hz, 4 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 13.8, 23.0, 27.1, 68.6, 80.2, 114.1, 123.8, 125.2 (d, *J* = 3.83 Hz), 125.4, 126.5 (d, *J* = 3.83 Hz), 129.8 (d, *J* = 32.5 Hz), 130.9 (d, *J* = 32.8 Hz), 139.5, 145.7 (q, *J* = 205.6 Hz) ppm. IR (ATR): $\tilde{\nu}$ 2961, 1619, 1417, 1324, 1284, 1169, 1128, 1071, 1018, 906, 850 cm^{-1}. HRMS (ESI-TOF): m/z $[M + NH_4]^+$ calcd. 872.2946 for $C_{42}H_{40}B_2F_{12}NO_4$; found 872.2946.

General procedure for the synthesis of allyl boronates 1c'

Allyl chloride **5** (0.3 mmol, 1 equiv), copper(I) thiophene-2-carboxylate (9 µmol, 3 mol%) and either the (*S*)- or the (*R*)-enantiomer of *N*,*N*-bis(1-phenylethyl)dibenzo-[d,f][1,3,2]dioxaphosphepin-6-amine (9 µmol, 3 mol%) are dissolved in dry CH_2Cl_2

(20 mM). The solution is cooled to –90 °C and a pentyl magnesium bromide solution (0.65 mmol, 2.2 equiv, 2 M in Et_2O diluted to 0.5 M with CH_2Cl_2) is added using a syringe pump within 1 h at –90 °C. The solution is stirred for additional 2 h at –90 °C. Subsequently, quenching is conducted by addition of sat. aq. NH_4Cl-solution. After separation of the organic and aqueous layer, the latter is extracted three times with CH_2Cl_2. The combined organic layers are dried over $MgSO_4$ and the solvent is removed under reduced pressure. The product is purified by column chromatography.

(4a*R*,8a*R*,3'*S*,3''*S*)-2,6-Di(oct-1-en-3-yl)-4,4,8,8-tetrakis[4-(trifluoromethyl)phenyl]tetrahydro[1,3,2]dioxaborinino[5,4-d][1,3,2]dioxaborinine [(*R*,*S*,*S*,*R*)-1c']

Yield: quant., 0.28 g (0.30 mmol); white foam. R_f (*n*-pentane:Et_2O 90:10): 0.89. Mp: 182.2–186.1 °C. $[\alpha]_D^{20}$ +32 (*c* 1.1, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.86 (t, *J* = 7.2 Hz, 6 H), 1.13–1.52 (m, 12 H), 1.91 (q, *J* = 7.8 Hz, 2 H), 4.79 (s, 2 H), 4.94–5.04 (m, 4 H), 5.79 (dt, *J* = 9.5 Hz, 16.9 Hz, 2 H), 7.44 (d, *J* = 8.0 Hz, 4 H), 7.49–7.58 (m, 8 H), 7.70 (d, *J* = 8.2 Hz, 4 H) ppm. ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 14.1, 22.6, 28.7, 29.7, 32.0, 68.4, 80.0, 113.8, 125.1 (d, *J* = 3.74 Hz), 125.3, 126.3 (m), 126.4, 129.8 (d, *J* = 32.50 Hz), 130.9 (d, *J* = 32.88 Hz), 139.7, 145.7 (d, *J* = 199.63 Hz) ppm. IR (ATR): $\tilde{\nu}$ 2957, 2923, 2854, 1420, 1325, 1289, 1170, 1129, 1071, 1017, 840, 762 cm^{-1}. HRMS (ESI-TOF): m/z $[M + NH_4]^+$ calcd. 956.3885 for $C_{48}H_{52}B_2F_{12}NO_4$; found 956.3888.

(4a*R*,8a*R*,3'*R*,3''*R*)-2,6-Di(oct-1-en-3-yl)-4,4,8,8-tetrakis[4-(trifluoromethyl)phenyl]tetrahydro[1,3,2]dioxaborinino[5,4-d][1,3,2]dioxaborinine [(*R*,*R*,*R*,*R*)-1c']

Yield: quant., 0.28 g (0.30 mmol); white foam. R_f (*n*-pentane:Et_2O 90:10): 0.88. Mp: 195.0–196.8 °C. $[\alpha]_D^{20}$ –81 (*c* 1.5, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.84 (t, *J* = 7.0 Hz, 6 H), 1.13–1.32 (m, 8 H), 1.34–1.43 (m, 2 H), 1.45–1.52 (m, 2 H), 1.87 (q, *J* = 7.8 Hz, 2 H), 4.77 (d, *J* = 4.7 Hz, 2 H), 4.95 (s, 2 H), 4.98 (d, *J* = 6.5 Hz, 2 H), 5.78 (dt, *J* = 10.9 Hz, 16.9 Hz, 2 H), 7.42 (d, *J* = 8.3 Hz, 4 H), 7.49–7.57 (m, 8 H), 7.67–7.72 (m, 4 H) ppm. ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 14.1, 22.5, 28.8, 29.7, 31.9, 68.4, 80.0, 113.8, 124.5, 125.1 (d, *J* = 3.29 Hz), 125.3 (d, *J* = 3.30 Hz), 126.4, 129.8 (d, *J* = 32.61 Hz), 130.9 (d, *J* = 33.31 Hz), 139.6, 145.7 (d, *J* = 199.56 Hz) ppm. IR (ATR): $\tilde{\nu}$ 2957, 2929, 2854, 1414, 1325, 1284, 1169, 1128, 1071, 1018, 849, 648 cm^{-1}. HRMS (ESI-TOF): m/z $[M + NH_4]^+$ calcd. 956.3885 for $C_{48}H_{52}B_2F_{12}NO_4$; found 956.3909.

Allylation of Indoles

General Procedure for the racemic allylation of indoles

An equimolar amount of the four stereoisomers of the allyl boronate **1c** (0.14 mmol, 1 equiv) and the indole of choice **8** [0.6 mmol, 4.4 equiv are dissolved in dry CH_2Cl_2 (0.5 M)]. The reaction is overlayed with Argon and stirred for 40 h at 40 °C. After completion the reaction is quenched with sat. aq. $NaHCO_3$-solution. After phase separation, the aq. layer is extracted three times with CH_2Cl_2 and the combined organic layers are dried over $MgSO_4$. The solvent is removed under reduced pressure and the crude product is purified *via* column chromatography.

General Procedure for the stereoselective allylation of indoles (9a–e)

Allyl boronate (*S*,*R*,*R*,*S*)-**1c** (0.14 mmol, 1 equiv) and the indole of choice **8** [0.6 mmol, 4.4 equiv are dissolved in dry CH_2Cl_2 (0.5 M)]. The reaction is overlayed with Argon and stirred for 40 h at 40 °C. After completion the reaction is quenched with sat. aq. $NaHCO_3$-solution. After phase separation, the aq. layer is extracted three times with CH_2Cl_2 and the combined organic layers are dried with $MgSO_4$. The solvent is removed under reduced pressure and the crude product purified *via* column chromatography. For analytics, the resulting diastereomeric mixtures are separated by preparative HPLC since traditional column chromatography is not successful.

2-(Pent-2-en-1-yl)indoline (9a)

Yield: 80%, 42 mg (0.22 mmol); colourless oil. R_f (*n*-pentane:Et_2O 90:10): 0.38. HPLC (Chiracel OD-H, 250 × 4.6 mm, 25 °C, 5 µL, 0.5 mL min^{-1}, UV 245 nm, *n*-heptane:*i*-propanol 99:1): R_t (*R*,*E*) 15.0 min, R_t (*R*,*Z*) 16.6 min, R_t (*S*,*E*) 17.7 min, R_t (*S*,*Z*) 21.1 min.

(*R*,*E*)-2-(Pent-2-en-1-yl)indoline [(*R*,*E*)-9a]

95:5 dr; 5:95 er; $[\alpha]_D^{20}$ +44 (*c* 0.7, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.99 (t, *J* = 7.5 Hz, 3 H), 2.01–2.08 (m, 2 H), 2.24–2.29 (m, 2 H), 2.73 (dd, *J* = 6.9 Hz, 15.5 Hz, 1 H), 3.13 (dd, *J* = 8.6 Hz, 15.6 Hz, 1 H), 3.82–3.89 (m, 1 H), 5.41 (dq, *J* = 6.8 Hz, 15.2 Hz, 1 H), 5.58 (dt, *J* = 6.2 Hz, 15.3 Hz, 1 H), 6.64 (d, *J* = 7.8 Hz, 1 H), 6.71 (t, *J* = 7.4 Hz, 1 H), 7.02 (t, *J* = 7.5 Hz, 1 H), 7.08 (d, *J* = 7.5 Hz, 1 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 14.0, 25.8, 35.7, 39.7, 59.3, 109.8, 119.0, 124.9, 125.3, 127.4, 129.0, 135.6, 150.3 ppm. IR (ATR): $\tilde{\nu}$ 3371, 2962, 2934, 2849, 1726, 1613, 1488, 1471,

1397, 1318, 1255, 966, 751, 705 cm^{-1}. HRMS: *m/z* $[M + H]^+$ calcd. 188.1434 for $C_{13}H_{18}N$; found 188.1433.

(*S*,*Z*)-2-(Pent-2-en-1-yl)indoline [(*S*,*Z*)-9a]

6:94 dr; 95:5 er; $[\alpha]_D^{20}$ –22 (*c* 0.8, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): *δ* 0.97 (t, *J* = 7.5 Hz, 3 H), 2.01–2.07 (m, 2 H), 2.24–2.30 (m, 1 H), 2.37–2.43 (m, 1 H), 2.73 (dd, *J* = 6.8 Hz, 15.5 Hz, 1 H), 3.14 (dd, *J* = 8.6 Hz, 15.5 Hz, 1 H), 3.83–3.89 (m, 1 H), 5.38 (dq, *J* = 8.1 Hz, 9.5 Hz, 1 H), 5.56 (dt, *J* = 7.2 Hz, 10.8 Hz, 1 H), 6.63 (d, *J* = 7.8 Hz, 1 H), 6.71 (t, *J* = 6.8 Hz, 1 H), 7.02 (t, *J* = 7.2 Hz, 1 H), 7.09 (d, *J* = 7.2 Hz, 1 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): *δ* 14.4, 20.9, 34.1, 35.8, 59.5, 109.7, 119.1, 125.0, 125.0, 127.5, 128.9, 134.9, 150.2 ppm. IR (ATR): $\tilde{\nu}$ 3376, 2961, 2934, 2866, 1732, 1610, 1485, 1465, 1403, 1289, 1247, 1017, 746, 705 cm^{-1}. HRMS: *m/z* $[M + H]^+$ calcd. 188.1434 for $C_{13}H_{18}N$; found 188.1434.

5-Methyl-2-(pent-2-en-1-yl)indoline (9b)

Yield: 40%, 29 mg (0.14 mmol); colourless oil. R_f (*n*-pentane:Et_2O 90:10): 0.37. HPLC (Chiracel OD-H, 250 × 4.6 mm, 25 °C, 5 µL, 0.5 mL min^{-1}, UV 248 nm, *n*-heptane:*i*-propanol 99:1): R_t (*R*,*E*) 13.0 min, R_t (*S*,*E*) 14.2 min, R_t (*R*,*Z*) 16.2 min, R_t (*S*,*Z*) 19.6 min.

(*R*,*E*)-5-Methyl-2-(pent-2-en-1-yl)indoline [(*R*,*E*)-9b]

>99:1 dr; 6:94 er; $[\alpha]_D^{20}$ +51 (*c* 1.0, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): *δ* 0.99 (t, *J* = 7.5 Hz, 3 H), 2.01–2.07 (m, 2 H), 2.21–2.29 (m, 5 H), 2.69 (dd, *J* = 6.9 Hz, 15.6 Hz, 1 H), 3.09 (dd, *J* = 8.5 Hz, 15.6 Hz, 1 H), 3.78–3.88 (m, 2 H), 5.41 (dq, *J* = 6.9 Hz, 15.4 Hz, 1 H), 5.57 (dt, *J* = 6.1 Hz, 15.4 Hz, 1 H), 6.56 (d, *J* = 7.8 Hz, 2 H), 6.83 (d, *J* = 7.7 Hz, 1 H), 6.91 (s, 1 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): *δ* 14.0, 21.0, 26.0, 35.8, 39.6, 59.6, 109.8, 125.4, 125.7, 127.7, 128.5, 129.3, 135.5, 147.8 ppm. IR (ATR): $\tilde{\nu}$ 3365, 3013, 2962, 2923, 1618, 1495, 1250, 972, 807 cm^{-1}. HRMS: *m/z* $[M + H]^+$ calcd. 202.1590 for $C_{14}H_{20}N$; found 202.1590.

(*S*,*Z*)-5-Methyl-2-(pent-2-en-1-yl)indoline [(*S*,*Z*)-9b]

>1:99 dr; >99:1 er; $[\alpha]_D^{20}$ –33 (*c* 0.7, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): *δ* 0.96 (t, *J* = 7.5 Hz, 3 H), 2.00–2.08 (m, 2 H), 2.22–2.29 (m, 4 H), 2.36–2.43 (m, 1 H), 2.69 (dd, *J* = 6.8 Hz, 15.5 Hz, 1 H), 3.11 (dd, *J* = 8.5 Hz, 15.5 Hz, 1 H), 3.81–3.87 (m, 2 H), 5.38 (dq, *J* = 8.2 Hz, 10.6 Hz, 1 H), 5.55 (dt, *J* = 7.3 Hz, 10.7 Hz, 1 H), 6.56 (d, *J* = 7.8 Hz, 2 H), 6.83 (d, *J* = 7.4 Hz, 1 H), 6.92 (s, 1 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): *δ*

14.4, 20.9, 21.0, 34.0, 35.8, 59.8, 109.8, 125.0, 125.8, 127.8, 128.6, 129.3, 134.8, 147.6 ppm. IR (ATR): $\tilde{\nu}$ 3365, 3008, 2962, 2928, 2871, 1618, 1493, 1250, 807 cm^{-1}. HRMS: *m/z* $[M + H]^+$ calcd. 202.1590 for $C_{14}H_{20}N$; found 202.1590.

5-Methoxy-2-(pent-2-en-1-yl)indoline (9c)

Yield: 53%, 32 mg (0.15 mmol); colourless oil. R_f (*n*-pentane:Et_2O 90:10): 0.15. HPLC (Chiracel OD-H, 250 × 4.6 mm, 25 °C, 5 µL, 0.5 mL min^{-1}, UV 244 nm, *n*-heptane:*i*-propanol 99:1): R_t (*R*,*E*) 20.9 min, R_t (*S*,*E*) 21.3 min, R_t (*R*,*Z*) 36.1 min, R_t (*S*,*Z*) 49.9 min.

(*R*,*E*)-5-Methoxy-2-(pent-2-en-1-yl)indoline [(*R*,*E*)-9c]

>99:1 dr; 4:96 er; $[\alpha]_D^{20}$ +38 (*c* 1.0, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 0.99 (t, *J* = 7.5 Hz, 3 H), 2.01–2.07 (m, 2 H), 2.26–2.30 (m, 2 H), 2.71 (dd, *J* = 7.0 Hz, 15.7 Hz, 1 H), 3.11 (dd, *J* = 8.5 Hz, 15.7 Hz, 1 H), 3.74 (s, 3 H), 3.81–3.88 (m, 2 H), 5.40 (dq, *J* = 7.0 Hz, 15.2 Hz, 1 H), 5.57 (dt, *J* = 6.3 Hz, 15.0 Hz, 1 H), 6.57–6.63 (m, 2 H), 6.70–6.73 (m, 1 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 14.0, 25.8, 36.2, 39.5, 56.1, 59.9, 110.7, 111.9, 112.4, 125.3, 130.9, 135.6, 143.6, 154.0 ppm. IR (ATR): $\tilde{\nu}$ 3365, 2962, 2928, 2877, 2843, 1720, 1624, 1590, 1490, 1459, 1442, 1289, 1216, 1142, 1034, 972, 807 cm^{-1}. HRMS: *m/z* $[M + H]^+$ calcd. 218.1539 for $C_{14}H_{20}ON$; found 218.1539.

(*S*,*Z*)-5-Methoxy-2-(pent-2-en-1-yl)indoline [(*S*,*Z*)-9c]

7:93 dr; >99:1 er; $[\alpha]_D^{20}$ –3 (*c* 0.7, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 0.96 (t, *J* = 7.5 Hz, 3 H), 2.01–2.07 (m, 2 H), 2.26–2.32 (m, 1 H), 2.39–2.45 (m, 1 H), 2.72 (dd, *J* = 6.9 Hz, 15.6 Hz, 1 H), 3.13 (dd, *J* = 8.4 Hz, 15.7 Hz, 1 H), 3.75 (s, 3 H), 3.83–3.90 (m, 2 H), 5.37 (dq, *J* = 7.7 Hz, 9.9 Hz, 1 H), 5.55 (dt, *J* = 7.2 Hz, 11.1 Hz, 1 H), 6.59–6.64 (m, 2 H), 6.72–6.74 (m, 1 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 14.4, 20.9, 33.8, 36.2, 56.1, 60.1, 111.0, 111.9, 112.4, 124.8, 131.0, 134.9, 143.1, 154.3 ppm. IR (ATR): $\tilde{\nu}$ 3371, 2959, 2928, 2877, 1732, 1596, 1491, 1454, 1374, 1284, 1233, 1136, 1040 cm^{-1}. HRMS: *m/z* $[M + H]^+$ calcd. 218.1539 for $C_{14}H_{20}ON$; found 218.1539.

5-Fluoro-2-(pent-2-en-1-yl)indoline (9d)

Yield: 46%, 26 mg (0.13 mmol); colourless oil. R_f (*n*-pentane:Et_2O 95:5): 0.10. HPLC (Chiracel OD-H, 250 × 4.6 mm, 25 °C, 5 µL, 0.5 mL min^{-1}, UV 241 nm, *n*-heptane:*i*-propanol 99.8:0.2): R_t (*R*,*E*) 19.3 min, R_t (*S*,*E*) 20.6 min, R_t (*R*,*Z*) 28.9 min, R_t (*S*,*Z*) 40.0 min.

(*R*,*E*)-5-Fluoro-2-(pent-2-en-1-yl)indoline [(*R*,*E*)-9d]

97:3 dr; 3:97 er; $[\alpha]_D^{20}$ +19 (*c* 0.4, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 0.99 (t, *J* = 7.5 Hz, 3 H), 2.00–2.07 (m, 2 H), 2.19–2.29 (m, 2 H), 2.69 (dd, *J* = 7.0 Hz, 15.8 Hz, 1 H), 3.10 (dd, *J* = 8.6 Hz, 15.8 Hz, 1 H), 3.73–3.87 (m, 2 H), 5.39 (dq, *J* = 6.9 Hz, 15.1 Hz, 1 H), 5.56 (dt, *J* = 6.3 Hz, 15.3 Hz, 1 H), 6.47–6.51 (m, 1 H), 6.66–6.71 (m, 1 H), 6.77–6.81 (m, 1 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 14.0, 25.8, 36.0, 39.7, 59.9, 109.4 (d, *J* = 8.3 Hz), 112.3 (d, *J* = 23.8 Hz), 113.2 (d, *J* = 23.2 Hz), 125.2, 130.5 (d, *J* = 8.3 Hz), 135.6, 146.8, 157.1 (d, *J* = 234.9 Hz) ppm. IR (ATR): $\tilde{\nu}$ 3371, 2962, 2928, 1720, 1489, 1448, 1284, 1233, 1122, 972, 807 cm^{-1}. HRMS: *m/z* $[M + H]^+$ calcd. 206.1340 for $C_{13}H_{17}NF$; found 206.1339.

(*S*,*Z*)-5-Fluoro-2-(pent-2-en-1-yl)indoline [(*S*,*Z*)-9d]

4:96 dr; 95:5 er; $[\alpha]_D^{20}$ –7 (*c* 0.4, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 0.96 (t, *J* = 7.5 Hz, 3 H), 1.99–2.07 (m, 2 H), 2.20–2.27 (m, 1 H), 2.32–2.40 (m, 1 H), 2.69 (dd, *J* = 6.9 Hz, 15.8 Hz, 1 H), 3.11 (dd, *J* = 8.5 Hz, 15.8 Hz, 1 H), 3.69–3.88 (m, 2 H), 5.38 (dq, *J* = 8.2 Hz, 9.0 Hz, 1 H), 5.56 (dt, *J* = 7.2 Hz, 10.9 Hz, 1 H), 6.45–6.51 (m, 1 H), 6.66–6.73 (m, 1 H), 6.77–6.82 (m, 1 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 14.4, 20.9, 34.1, 36.1, 60.1, 109.3 (d, *J* = 8.3 Hz), 112.3 (d, *J* = 23.7 Hz), 113.3 (d, *J* = 23.2 Hz), 124.9, 130.4 (d, *J* = 8.0 Hz), 134.9, 146.8, 157.1 (d, *J* = 234.9 Hz) ppm. IR (ATR): $\tilde{\nu}$ 3376, 2962, 2928, 1726, 1488, 1448, 1289, 1233, 1125, 938, 864, 807, 751 cm^{-1}. HRMS: *m/z* $[M + H]^+$ calcd. 206.1340 for $C_{13}H_{17}NF$; found 206.1339.

5-Bromo-2-(pent-2-en-1-yl)indoline (9e)

Yield: 43%, 25 mg (0.09 mmol); colourless oil. R_f (*n*-pentane:Et_2O 90:10): 0.40. HPLC (Chiracel OD-H, 250 × 4.6 mm, 15 °C, 5 µL, 0.5 mL min^{-1}, UV 254 nm, *n*-heptane:*i*-propanol 99.8:0.2): R_t (*R*,*E*) 23.7 min, R_t (*S*,*E*) 25.5 min, R_t (*R*,*Z*) 49.4 min, R_t (*S*,*Z*) 76.7 min.

(*R*,*E*)-5-Bromo-2-(pent-2-en-1-yl)indoline [(*R*,*E*)-9e]

>99:1 dr; 4:96 er; $[\alpha]_D^{20}$ +52 (*c* 0.7, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 0.98 (t, *J* = 7.5 Hz, 3 H), 2.00–2.08 (m, 2 H), 2.22–2.29 (m, 2 H), 2.72 (dd, *J* = 6.7 Hz, 15.9 Hz, 1 H), 3.11 (dd, *J* = 8.6 Hz, 15.8 Hz, 1 H), 3.83–3.91 (m, 1 H), 5.38 (dq, *J* = 6.4 Hz, 15.3 Hz, 1 H), 5.57 (dt, *J* = 6.3 Hz, 15.3 Hz, 1 H), 6.52 (d, *J* = 8.2 Hz, 2 H), 7.10 (d, *J* = 8.2 Hz, 1 H), 7.17 (s, 1 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 13.9, 25.8, 35.5, 39.5, 59.7, 110.8, 111.1, 124.9, 127.9, 130.1, 131.5, 135.9, 149.0 ppm. IR (ATR): $\tilde{\nu}$ 3382, 2961, 2928, 2843, 1601, 1479, 1420, 1248, 1057, 969, 881, 805 cm^{-1}. HRMS:

m/z $[M + H]^+$ calcd. 266.0539 and 268.0518 for $C_{13}H_{17}NBr$; found 266.0539 and 268.0519.

(*S*,*Z*)-5-Bromo-2-(pent-2-en-1-yl)indoline [(*S*,*Z*)-9e]

>1:99 dr; 97:3 er; $[\alpha]_D^{20}$ –41 (*c* 0.9, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): *δ* 0.96 (t, *J* = 7.5 Hz, 3 H), 1.99–2.06 (m, 2 H), 2.21–2.27 (m, 1 H), 2.34–2.40 (m, 1 H), 2.71 (dd, *J* = 6.5 Hz, 15.8 Hz, 1 H), 3.12 (dd, *J* = 8.6 Hz, 15.8 Hz, 1 H), 3.83–3.90 (m, 1 H), 5.34 (dq, *J* = 6.8 Hz, 10.4 Hz, 1 H), 5.56 (dt, *J* = 7.0 Hz, 10.7 Hz, 1 H), 6.49 (d, *J* = 8.2 Hz, 2 H), 7.10 (d, *J* = 8.2 Hz, 1 H), 7.17 (s, 1 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): *δ* 14.4, 20.9, 34.0, 35.6, 59.8, 110.6, 110.9, 124.6, 127.9, 130.1, 131.4, 135.2, 149.2 ppm. IR (ATR): $\tilde{\nu}$ 3382, 2968, 2934, 1607, 1475, 1420, 1250, 807 cm^{-1}. HRMS: *m/z* $[M + H]^+$ calcd. 266.0539 and 268.0518 for $C_{13}H_{17}NBr$; found 266.0539 and 268.0519.

2-(Oct-2-en-1-yl)indoline (9a')

Yield: 45%, 29 mg (0.13 mmol); colourless oil. R_f (*n*-pentane:Et_2O 90:10): 0.30. HPLC (Chiracel OD-H, 250 × 4.6 mm, 25 °C, 5 µL, 0.5 mL min^{-1}, UV 300 nm, *n*-heptane:*i*-propanol 99.8:0.2): R_t (*R*,*E*) 22.4 min, R_t (*S*,*E*) 25.4 min, R_t (*R*,*Z*) 27.7 min, R_t (*S*,*Z*) 33.3 min

(*R*,*E*)-2-(Oct-2-en-1-yl)indoline [(*R*,*E*)-9a']

>95:5 dr; 7:93 er; $[\alpha]_D^{20}$ +79 (*c* 1.0, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): *δ* 0.90 (t, *J* = 7.1 Hz, 3 H), 1.41–1.24 (m, 6 H), 2.00–2.04 (m, 2 H), 2.24–2.26 (m, 2 H), 2.71 (dd, *J* = 6.9 Hz, 15.5 Hz, 1 H), 3.12 (dd, *J* = 8.7 Hz, 15.6 Hz, 1 H), 3.83 (dt, *J* = 7.3 Hz, 14.5 Hz, 1 H), 3.91 (brs, 1 H), 5.41 (dq, *J* = 7.3 Hz, 15.4 Hz, 1 H), 5.52 (dt, *J* = 7.3 Hz, 15.4 Hz, 1 H), 6.60 (d, *J* = 7.7 Hz, 1 H), 6.68 (t, *J* = 7.3 Hz, 1 H), 7.00 (t, *J* = 7.6 Hz, 1 H), 7.07 (d, *J* = 7.2 Hz, 1 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): *δ* 14.1, 22.6, 29.2, 31.4, 32.6, 35.6, 39.8, 59.1, 109.2, 118.5, 124.8, 126.3, 127.2, 128.6, 133.9, 150.7 ppm. IR (ATR): $\tilde{\nu}$ 2957, 2926, 2857, 1721, 1610, 1485, 1466, 1408, 1268, 1248, 1117, 1102, 1019, 971, 745, 731 cm^{-1}. HRMS: *m/z* $[M + H]^+$ calcd. 230.1903 for $C_{16}H_{24}N$; found 230.1905.

(*S*,*Z*)-2-(Oct-2-en-1-yl)indoline [(*S*,*Z*)-9a']

>5:95 dr; 80:20 er; $[\alpha]_D^{20}$ –49 (*c* 0.9, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): *δ* 0.89 (t, *J* = 7.5 Hz, 3 H), 1.23–1.38 (m, 6 H), 1.99–2.04 (m, 2 H), 2.19–2.30 (m, 1 H), 2.33–2.42 (m, 1 H), 2.72 (dd, *J* = 6.8 Hz, 15.5 Hz, 1 H), 3.13 (dd, *J* = 8.8 Hz, 15.6 Hz, 1 H), 3.80–3.88 (m, 1 H), 3.91 (brs, 1 H), 5.41 (dq, *J* = 8.3 Hz, 9.4 Hz, 1 H), 5.53 (dt, *J* = 7.0 Hz,

11.1 Hz, 1 H), 6.59 (d, *J* = 7.3 Hz, 1 H), 6.68 (t, *J* = 7.4 Hz, 1 H), 7.00 (t, *J* = 7.6 Hz, 1 H), 7.07 (d, *J* = 7.3 Hz, 1 H) ppm.$^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): δ 14.1, 23.0, 24.0, 29.2, 31.4, 32.6, 35.7, 40.0, 59.1, 109.2, 118.5, 124.8, 126.3, 127.2, 128.6, 133.9, 150.7 ppm. IR (ATR): $\tilde{\nu}$ 2957, 2926, 2856, 1721, 1610, 1485, 1866, 1269, 1247, 1103, 1019, 746 cm^{-1}. HRMS: *m/z* $[M + H]^+$ calcd. 230.1903 for $C_{16}H_{24}N$; found 230.1904.

Computational Details

The conformational space for each structure was explored using the OPLS-2005 force field[32] and a modified Monte Carlo search algorithm implemented in MacroModel.[33] An energy cut-off of 84 kJ mol^{-1} was employed for the conformational analysis, and structures with heavy-atom root-mean-square deviations (RMSD) up to 2.5 Å after the initial force field optimizations were considered to be the same conformer. The remaining structures were subsequently optimized with the dispersion-corrected M06-L functional[34] with Grimme's dispersion correction D3 (zero-damping)[35] and the double-ζ basis set 6-31+G(d,p). Vibrational analysis verified that each structure was a minimum or transition state. Thermal corrections were obtained from unscaled harmonic vibrational frequencies at the same level of theory for a standard state of 1 mol L^{-1} and 298.15 K. Entropic contributions to free energies were obtained from partition functions evaluated with Grimme's quasi-harmonic approximation.[36] This method employs the free-rotor approximation for all frequencies below 100 cm^{-1}, the rigid-rotor-harmonic-oscillator (RRHO) approximation for all frequencies above 100 cm^{-1}, and a damping function to interpolate between the two expressions. Similar results were obtained from partition functions evaluated with Cramer's and Truhlar's quasiharmonic approximation.[37] This method uses the same approximations as the usual harmonic oscillator approximation, except that all vibrational frequencies lower than 100 cm^{-1} are set equal to 100 cm^{-1}. Electronic energies were subsequently obtained from single point calculations of the M06-L-D3 geometries employing the meta-hybrid M06-2X functional,[38] Grimme's dispersion-correction D3 (zero-damping), the triple-ζ basis set def2-TZVPP,[39] and the integral equation formalism polarizable continuum model (IEFPCM)[40] for dichloromethane.[41] An ultrafine grid was used throughout this study for numerical integration of the density. All density functional theory calculations were performed with Gaussian 16.[42]

Associated Content

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.____.

Copies of all ^{1}H and ^{13}C spectral data

HPLC chromatograms

Computational details including all coordinates

Author Information

Corresponding Author

*eMail: mbreugst@uni-koeln.de, j.pietruszka@fz-juelich.de

ORCID

Patrick Ullrich: 0000-0001-5289-1528

Julie Schmauck:

Marcus Brauns:

Marvin Mantel: 0000-0002-3541-3388

Martin Breugst: 0000-0003-0950-8858

Jörg Pietruszka: 0000-0002-9819-889X

Present Address

Institut für Bio- und Geowissenschaften, (IBG-1: Bioorganische Chemie), Forschungszentrum Jülich, 52428 Jülich, Germany

Notes

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