Asymmetric stereodivergent catalysis achieved by means of a switchable asymmetric catalyst built on supramolecular helices

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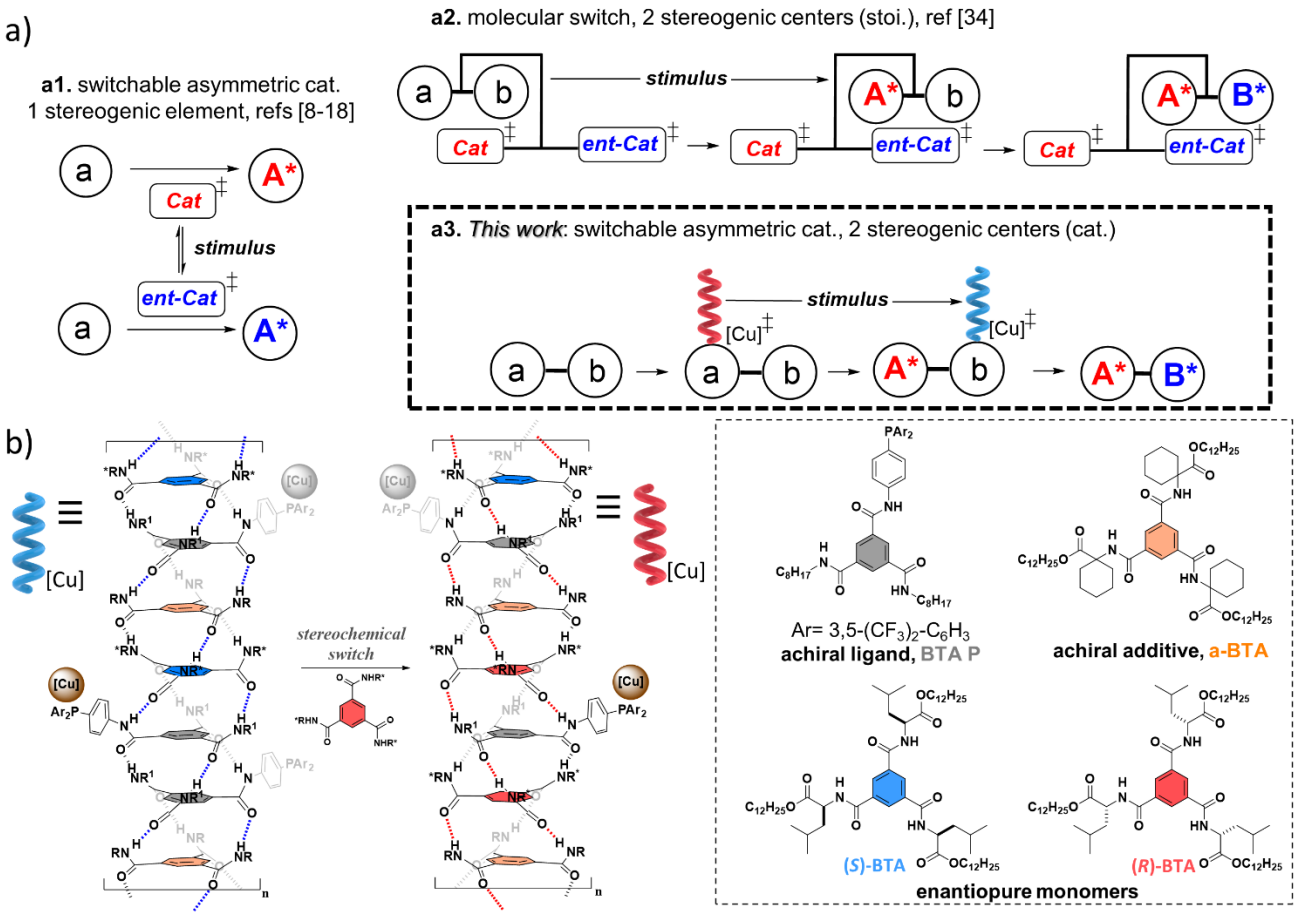
Abstract: Despite recent developments on the design of dynamic catalysts, none of them have been exploited for the in-situ control of multiple stereogenic centers in a single molecular scaffold. We report herein that it is possible to select one major amongst four possible stereoisomers of an amino alcohol by means of a switchable asymmetric catalyst built on supramolecular helices. Hydrogen-bonded assemblies between a benzene-1,3,5-tricarboxamide (BTA) achiral phosphine ligand coordinated to copper and an enantiopure BTA monomer are engaged in a concomitant copper-hydride catalyzed hydrosilylation and hydroamination process, yielding mainly one of the possible stereoisomers in good yield. The nature of the product stereoisomer is related to the handedness of the helices and can thus be directed in a predictable way by the nature of the major enantiopure BTA present in the assemblies. Accordingly, a sequential reaction, during which the handedness of the supramolecular helices is switched in between the hydrosilylation and hydroamination steps, mainly yields the diastereoisomer that cannot be obtained in the aforementioned concomitant process. The strategy allows all stereoisomers to be obtained with similar selectivities. This work paves the way for the development of supramolecular helical catalysts as a platform to readily access molecules embedding several stereogenic centers.

Introduction

The combination of molecular switches or non-covalent interactions with catalytic units within the same (macro)molecular scaffold led to the advent of dynamic catalysts for the temporal control of catalytic reactions.[1–6] Amongst this emerging area, selecting the configuration of the generated stereogenic element in a predictable manner is a current challenge that has been achieved by a limited number of reconfigurable catalysts.[7] In the most-employed strategies, the intrinsically achiral catalytic unit is connected to a molecular,[8–13] macromolecular,[14,15] or supramolecular chiroptical switch,[16–18] leading to pseudo-enantiomeric states upon activation of the switch[19] by a suitable stimulus (Scheme 1a1). These switchable asymmetric catalysts have been exclusively employed for the generation of chiral molecules having opposite configurations, i.e. enantiodivergency. Light,[11–13,20–22] redox potential,[9,23] and chemical triggers[16,24–27] are the stimuli that hold most promise for inverting the configuration of a catalyst on a timescale that is compatible with a chemical process, with the ultimate goal of controlling multiple stereogenic elements in small molecules, i.e. stereodivergency,[28] or during a polymerization.[29] However, these systems must overcome significant challenges: i) the stimulus and the substrate(s)/reactant(s),[30] or catalyst must be compatible,[31] ii) the catalyst pseudo-enantiomers must provide perfectly opposite selectivities,[20] and iii) the stereochemical switch must be rapid on the reaction timescale.[12,32] Alternative strategies have been pursued by the Leigh group[33–35] for which two pseudo-enantiomeric catalysts are present from the beginning in the reaction mixture. This yields an elegant example of stereodivergency in which a stoichiometric amount of a substrate anchored to a molecular machine is sequentially transformed by the catalyst pseudo-enantiomers (Scheme 1a2).[34] In a different design, the simultaneous operation of a pair of enantioselective switchable catalysts was prevented by mutual inhibition.[33] The implementation of a switchable asymmetric catalyst for the in-situ control of multiple stereogenic centers in a single molecular scaffold is thus an unmet challenge to date.

Recently-developed dynamic helical catalysts,[36] with intrinsically achiral metal centers anchored at the periphery of supramolecular helices,[16,37–44] have particular advantages to reach this goal. First, the direction of the asymmetric reaction is imposed by the handedness of the helices, making possible to control the direction of the catalytic process towards each enantiomer of a product by switching the catalyst handedness. Second, homochiral helical catalysts are accessible thanks to the ability of a little amount of chiral monomers or of a scalemic mixture of monomer enantiomers to impose their chiral preference to a large number of achiral metal-containing monomers, thanks to well-established “sergeants-and-soldiers” and “diluted majority rule” principles.[45,46] We previously demonstrated that helical hydrogen-bonded stacks composed of a benzene-1,3,5-tricarboxamide[47,48] (BTA) achiral phosphine ligand and a small amount of enantiopure monomers provide good enantioselectivities in the copper-catalyzed hydrosilylation of 4-nitroacetophenone[41] and in the copper-catalyzed



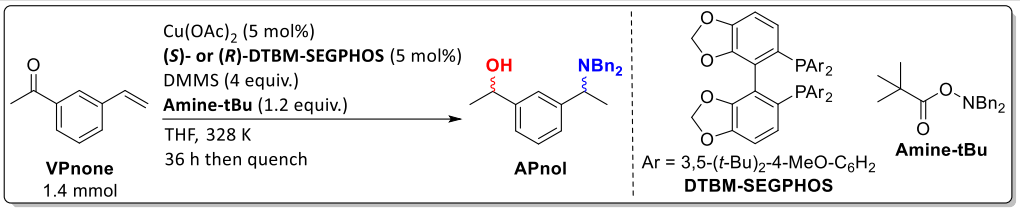
Scheme 1 a) Previous examples of reconfigurable asymmetric catalysts based on switchable asymmetric catalysts (**a1**, generation of enantiomers of **A*** from the same substrate **a**) or complementary catalysts anchored to a molecular machine (**a2**, stoichiometric control of two stereochemical centers **A*** and **B*** from the same molecular scaffold **a-b**). This work involves a stereochemically switchable helical catalyst for the catalytic control of two stereogenic centres (**a3**). The supramolecular helices in each step embed the same achiral phosphine copper complex as indicated in Scheme 1b. b) Schematic representation of the switchable supramolecular helical BTA terpolymers used in this study and the molecular structure of the corresponding BTA monomers.

hydroamination of styrene.[43] In addition, thanks to the dynamic nature of the BTA helices, their composition can be tuned by changing the nature of the major BTA enantiomer thus affording interconversion between enantiomeric helical catalysts within seconds.[16] The stereochemical switch is simply achieved by adding an enantiopure monomer that acts as a chemical stimulus to invert the selectivity of the catalyst (as represented by the addition of the red-colored monomer in Scheme 1b). Herein, we exploited these unique properties to control the configuration of two stereogenic centers of an amino alcohol thereby showcasing the first example of an asymmetric stereodivergent reaction by means of a switchable asymmetric catalyst (Scheme 1a3).

Results and Discussion

Optimization of the asymmetric hydrosilylation/hydroamination reaction. Building on our previous results with copper-functionalized BTA helices[41,43] and inspired by the possibility to engage Cu-H catalysts in sequential transformations,[49–52] we selected 3-vinylacetophenone (**VPnone**) as the substrate to implement our concept. Initial tests have been conducted with DTBM-SEGPHOS (Table 1), a covalent diphosphine ligand, since its combination with $[Cu(OAc)_2]$ proved to be highly efficient in a wide range of reactions involving Cu-H active species,[53–55] furthermore cascade hydrosilylation (HS) /hydroamination (HA) reaction of non-conjugated vinyl and ketone functions have not been reported yet. **VPnone** was first mixed with a 1:1 mixture of **(*S*)-DTBM-SEGPHOS** and **(*R*)-DTBM-SEGPHOS**, in presence of $[Cu(OAc)_2]$, with dimethoxymethylsilane (DMMS) and *N*,*N*-dibenzyl-*O*-pivaloylhydroxylamine (**Amine-tBu**) as the reducing and aminating agents, respectively. The reaction conducted in a sequential manner, *i.e.* by engaging **Amine-tBu** after completion of the hydrosilylation of the ketone function, yields the expected amino alcohol, 1-[3-(1-dibenzylaminoethyl)]-acetophenol (**APnol**), as a 1.0/1.3/1.0/1.4 mixture of the four stereoisomers according to its HPLC trace (Figure S1). The diastereomeric ratio (dr), close to 1:1, is an indication that the selectivity of the reaction is mostly controlled by the catalyst, not the substrate. Performing the reaction with **(*R*)-DTBM-SEGPHOS** under conditions resembling those reported by Buchwald and co-workers for the asymmetric HS/HA of enals,[49] yields **APnol** in 56% yield, 99% enantiomeric excess (ee) and a diastereomeric ratio of 9:1 (Table 1 and Figure S2). As expected, **(*S*)-DTBM-SEGPHOS** provides the corresponding enantiomer with similar yield and selectivity. In these reactions, 3-ethylacetophenol (**EPnol**) also forms in small amount, probably as a result of the protonation of the alkyl copper catalytic species by residual water (see Figure S1 and the SI).[56,57]

Table 1 Asymmetric hydrosilylation/hydroamination reaction of **VPnone** with DTBM-SEGPHOS as ligand. See the SI and Figure S2 for more details. The indicated yield is an isolated yield. The enantiomeric excess and diastereomeric ratio are obtained from the chiral HPLC analyses of purified **APnol**. Ee1 (positive for the (*R*)-enantiomer of the alcohol) and ee2 (positive for (*S*)-enantiomer of the amine) are extracted from the HPLC traces as indicated in Figure S2 and this convention was followed throughout this paper. Error bars: main stereoisomer ±1%, ±1% ee, ±0.2 dr, ±1% ee1, ±1% ee2 when (*R*,*R*)- or (*S*,*R*)-**APnol** is the main stereoisomer, main stereoisomer ±2%, ±1% ee, ±0.4 dr, ±3% ee1, ±1% ee2 when (*S*,*S*)- or (*R*,*S*)-**APnol** is the main stereoisomer (see the general methods in the SI).



ligand	yield in **APnol**	% of main stereoisomer of **APnol**	ee, dr	ee1 (HS), ee2 (HA)
(*R*)-DTBM-SEGPHOS	56%	90% (*R*,*S*)	99% (*R*,*S*), 9:1	84%, 94%
(*S*)-DTBM-SEGPHOS	50%	88% (*S*,*R*)	99% (*S*,*R*), 7.3:1	-80%, -94%

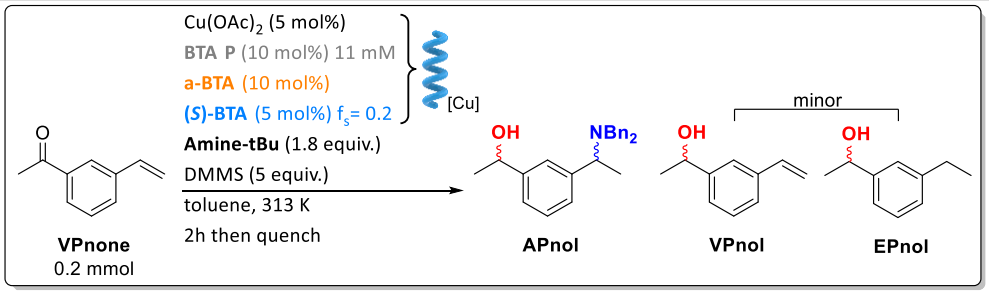
It is interesting to compare the catalytic selectivity of DTBM-SEGPHOS for the cascade transformation of **VPnone** to that previously reported for monofunctional substrates bearing either the vinyl or the ketone function. It can be concluded from the literature that **(*S*)-DTBM-SEGPHOS** yields (*S*)-acetophenol (96% ee)[58] and (*R*)-*N*,*N*-dibenzyl-1-phenylethan-1-amine (97% ee)[59] from the HS of acetophenone and the HA of styrene, respectively.[60] Therefore we expect the main isomer of the cascade reaction to be (***S***,***R***)-**APnol**. Simulated CD spectra from MM/MD optimized structure of **(*S*,*R*)-APnol** confirms that **(*S*)-DTBM-SEGPHOS** yields preferentially the stereoisomer with a (*R*) stereogenic center in α position of the amine (see the general methods in the SI). These observations not only establish the absolute and relative configurations of **APnol** but also further support that the ketone and vinyl functions of **VPnone** are transformed by the diphosphine Cu-H catalyst in an independent manner.[61]

Having established that **VPnone** is a suitable substrate to implement our concept, we next evaluated BTA helical catalysts for the same reaction. We selected BTA monomers and conditions that previously proved to be suitable for the copper-catalyzed HA of styrene (Scheme 1b):[43] **BTA P** as achiral ligand with CF_3 groups at the *meta* positions of the aryl moieties that were key for both activity and enantioselectivity, **(*S*)-BTA** as enantiopure monomer,[42] and **a-BTA** as achiral additive that was found to be beneficial for both the yield and selectivity of the reaction.[41,43,62] These monomers form helical terpolymers upon mixing in toluene, as schematically represented in Scheme 1b and previously characterized.[43] The fraction of **(*S*)-BTA** (f_s) over all BTA monomers was fixed to 20%, as it will allow to shift the handedness of the initial right-handed helices towards left-handed helices by adding a reasonable quantity of **(*R*)-BTA** monomers during the sequential transformation (*vide infra*). An excess of amine electrophile and silane was also found to enhance the yield.[43] Similar to our previous work on the HA of styrene, catalytic screening was performed without exclusion of air. In this part, silane and amine transfer reagents are engaged from the beginning of the reaction, thereby enabling both HA and HS reactions to start concomitantly.[63]

With these initial conditions in hands, **APnol** is obtained in *ca.* 66% yield, 97% ee and a dr of 3.6:1 (Table 2, entry 1). The optical purity and handedness of the BTA helical coassemblies are controlled by the combined action of **(*S*)-BTA** and **a-BTA**;[43] the achiral ligand coordinated to copper positioned in the right-handed homochiral helices provides (***R***,***S***)-**APnol** as the major stereoisomer. **APnol** is formed together with a small amount of **EPnol** (*ca.* 10%) and 3-vinylacetophenol (**VPnol**, 14%). The detection of **VPnol** but not of side products with unreacted ketone function indicates that HA is more challenging and occurs with a slower rate relatively to HS, a point confirmed by NMR monitoring of the concomitant process (Figure S3d). When **(*S*)-BTA** and **(*R*)-BTA** are engaged in equal amounts in the catalytic mixture, the resulting racemic helices furnish **APnol** as a virtually perfect equimolar mixture of its four stereoisomers, emphasizing the possibility to control the configurations of the two stereogenic centers by means of the handedness of the helical catalyst (Figure S4).[64] Concerning the influence of the nature of the amine electrophile, comparable catalytic performance is observed between 4-(((dibenzylamino)oxy)carbonyl)-*N*,*N*-dimethylaniline, an electron-rich amine transfer reagent commonly employed in Cu-H based processes,[65] and **Amine-tBu** (Table S1, entry 2). The latter was selected for further screening given its higher solubility under our reaction conditions (toluene, 313 K).

A set of tertiary phosphines was next evaluated as secondary ligands, a common strategy used to enhance the performance of Cu-H type catalysts (see Table S1 for the full screening).[58,65] Triphenylphosphine, electron-rich monophosphines and tested diphosphine ligands (dppe and dppbz) exhibit either no or detrimental effect. However, a slight but significant improvement in the yield in **APnol**, 76%, is observed upon addition of one equivalent of tris[3,5-bis(trifluoromethyl)phenyl]phosphine (P(3,5-$(CF_3)_2$-$C_6H_3)_3$) relatively to copper (Table 2, entry 2). Other stoichiometries are less advantageous. Control experiment in Table 2, entry 3 confirms the important role played by **a-BTA.** Improved yield probably stems from a more homogeneous nature of the catalytic species when **a-BTA** is present in the supramolecular terpolymers.[43] From the ee of the individual steps, it can also be seen that **a-BTA** significantly improves the ee of the HA reaction (compare ee2 in entries 2 and 3) but not of the HS step. The role of **a-BTA** in the BTA helical catalysts for the cascade reaction appears to be similar to that observed previously in the HA of styrene.[43] The amount of **a-BTA** in the

Table 2 Optimization of the asymmetric HS/HA reaction of **VPnone** with BTA helical catalysts (concomitant reactions). f_s= [**(*S*)-BTA**]/([**(*S*)-BTA**]+[**BTA P**]+[**a-BTA**]) or f_s= [**(*R*)-BTA**]/([**(*R*)-BTA**]+[**BTA P**]+[**a-BTA**]). See the SI and Figures S3 and Table S1 for more details. For entries 1-4, an internal standard is used to measure the yield in **APnol** on a crude sample whereas isolated yield is indicated for entries 5-6. The reactions on a 1 mmol scale are performed overnight. The enantiomeric excess and diastereomeric ratio are obtained from the chiral HPLC analyses of the crude (entries 1-4) or purified samples (entries 5-6). Error bars for ee and dr: see footnote of Table 1.



entry	deviation from standard conditions	NMR yield in **APnol** (±5%)	% of main stereoisomer of **APnol**	ee, dr	ee1 (HS), ee2 (HA)
1	no	66%	77% (*R*,*S*)	97% (*R*,*S*), 3.6:1	68%, 83%
2	+P(3,5-$(CF_3)_2$-$C_6H_3)_3$	76%	78% (*R*,*S*)	96% (*R*,*S*), 3.8:1	69%, 84%
3	+P(3,5-$(CF_3)_2$-$C_6H_3)_3$ without **a-BTA**[a]	61%	70% (*R*,*S*)	90% (*R*,*S*), 2.7:1	72%, 60%
4	+P(3,5-$(CF_3)_2$-$C_6H_3)_3$ with 5 mol% of **a-BTA**[a]	58%	76% (*R*,*S*)	96% (*R*,*S*), 3.4:1	68%, 80%
	optimized conditions entry 2 1 mmol scale	isolated yield in **APnol**	% of main stereoisomer of **APnol**	ee, dr	ee1 (HS), ee2 (HA)
5	with **(*S*)-BTA**	51%	77% (*R*,*S*)	96% (*R*,*S*), 3.6:1	68%, 83%
6	with **(*R*)-BTA**	48%	79% (*S*,*R*)	97% (*S*,*R*), 4.2:1	-70%, -86%

[a] f_s= 0.33 and 0.25 for entry 3 and 4, respectively.

catalytic mixtures can be decreased by two, *i.e.* [**a-BTA**]:[**BTA P**]= 0.5 instead of 1 in the standard conditions, leading to a small decrease of the yield but to the same selectivity (Table 2, entry 4), consistently with our recent findings.[62] Finally, conducting the reaction under nitrogen does not seem to significantly change the catalytic outcome of the reaction (Table S1, entry 13). Selecting the optimized conditions of Table 2, entry 2, the concomitant HS/HA reaction was performed on an approximatively 1 mmol scale yielding (***R***,***S***)-**APnol** in 51% isolated yield,[66] 96% ee and a dr of 3.6:1. Engaging **(*R*)-BTA** instead of **(*S*)-BTA** in the catalytic mixture leads to (***S***,***R***)-**APnol** with similar yield and selectivity (entries 5 and 6) as expected for homochiral BTA helical catalysts adopting opposite screw-sense preferences.

Selection of the conditions for the sequential reaction. Two prerequisites are needed in order to control the configuration of the stereogenic centers formed by sequential transformations involving a switchable asymmetric catalyst: i) different reaction rates for the two catalytic transformations, and ii) rapid and full inversion of the enantiomeric state of the catalyst. In the present copper-catalyzed transformation of **VPnone**, the HS and HA steps can be performed fully independently by adding the amine transfer reagent after completion of the HS step.[67] We thus monitored the consumption of **VPnone** under the optimized conditions reported in Table 2, entry 2 but in the absence of **Amine-tBu** (Figure S5). We found out that **VPnone** is fully consumed in *ca.* 12 minutes and that **(*R*)-VPnol** is formed in *ca.* 70% yield and 63% ee; **EPnol** (*ca.* 12%) is detected as the main byproduct (Figure 1a). Upon comparing NMR traces for the HS only reaction and the concomitant HS/HA process, it appears that the rate of the ketone reduction is drastically higher in the latter case, *i.e.* that HS of the ketone function occurs more rapidly when **Amine-tBu** is present from the beginning in the catalytic mixture (Figure S5). We also noticed that the ee in **VPnol** measured during this HS reaction (63%) is slightly lower than the ee1 determined for HS step in the concomitant HS/HA process towards **APnol** (68-71% ee, Table 2). The ee of **VPnol**, isolated from this concomitant process, is of 68%, consistently with the latter point (Figure S5). This discrepancy in the catalytic performance provided by the Cu–H helical catalyst between the HS only reaction and the concomitant HS/HA process suggests different catalytic active species for the ketone reduction depending whether the amine transfer reagent is present or not. This is not detrimental for the implementation of a sequential HS/HA reaction since side reaction at the vinyl moiety remains

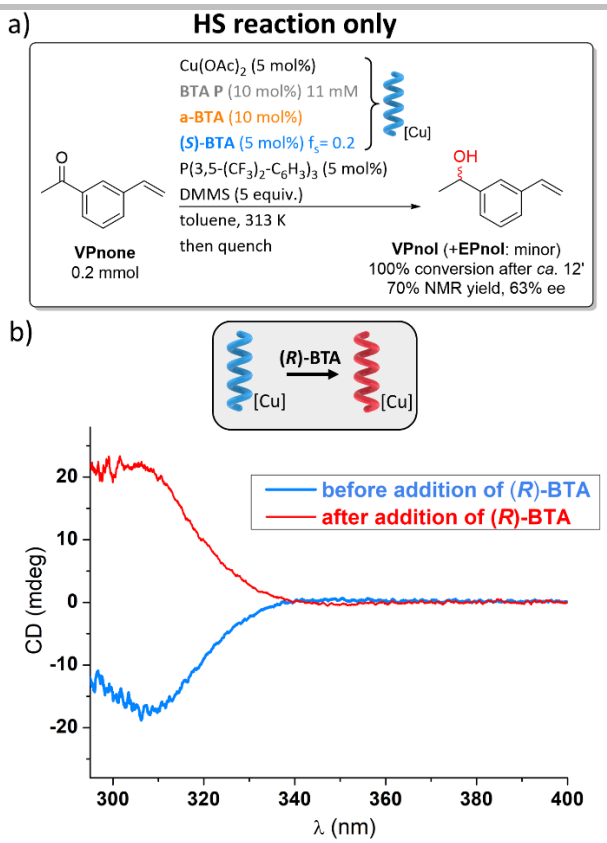


Figure 1 a) Copper-catalyzed hydrosilylation of **VPnone**. b) CD spectra of the pre-catalytic mixture before and after addition of **(*R*)-BTA** (toluene, 313 K). Composition: **BTA P** (11 mM), $Cu(OAc)_2$ (**BTA P**:[Cu]= 2), **a-BTA** (11 mM), **(*S*)-BTA** (5.5 mM, f_s= 0.2) and $P(3,5\text{-}(CF_3)_2\text{-}C_6H_3)_3$ (5.5 mM) with and without additional **(*R*)-BTA** for the red and blue spectra, respectively. After addition of **(*R*)-BTA** (36 mg in 0.2 mL of toluene, see the SI), the helical coassemblies contain 20 mM of enantiopure monomers (f_s= 0.5) with a 50% ee in favour of **(*R*)-BTA**. The small difference in CD intensity ≈15% likely comes from the use of a 0.05 mm cell needed to perform the analyses of these concentrated viscous solutions. A very small CD signal is detected at *ca.* 350 nm.

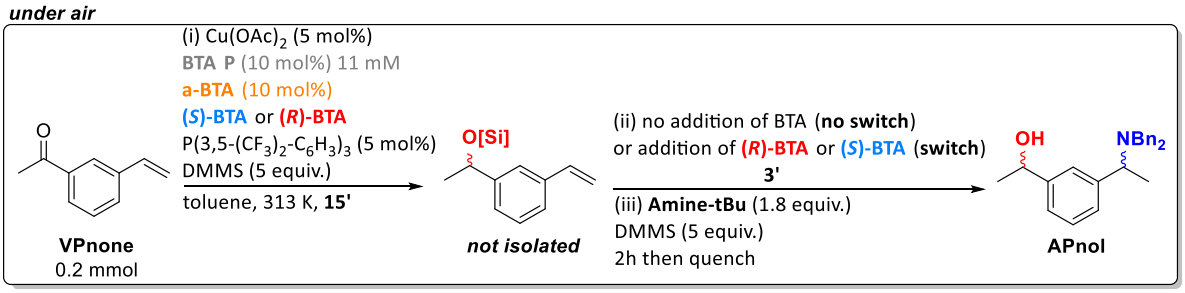
limited (≈12% of **EPnol** is formed) and the ee of the HS step is only marginally reduced.

We next probed the possibility to invert the handedness of the BTA helical catalyst under conditions similar to those used to perform the catalytic reaction. A CD spectrum of a solution containing the pre-catalytic system, *i.e.* all BTA monomers and the secondary phosphine ligand, was recorded at 313 K. **(*R*)-BTA** was then added to this solution leading to 50% ee in favour of the **(*R*)-BTA** monomers in the supramolecular terpolymer. The solution was stirred for 2 minutes and analyzed by CD. CD spectra before and after addition are almost mirror images (Figure 1b and caption).[68] These CD spectra exhibit a main CD band which belongs exclusively to **BTA P** since it is the only BTA monomer that absorbs in that region. We previously correlated this induced CD band to the selectivity observed in the copper-catalyzed HS reactions, *i.e.* the enantioselectivity (up to optimal selectivity that can be obtained by the system under study) is proportional to the intensity of this CD band.[42,44] As the present BTA coassemblies contain a sufficient number of enantiopure BTA monomers to be homochiral,[41,43] the inverted CD signals indicate that all **BTA P** monomers coordinated to copper could be positioned in opposite chiral environments as the result of a full stereochemical inversion of the handedness of the helical assemblies (from right-handed to left-handed) upon addition of **(*R*)-BTA** monomers. The exact time needed to achieve this stereochemical switch has not been determined precisely but three minutes of mixing appears reasonable to ensure full stereochemical inversion and to limit side reaction at the vinyl function.

Sequential HS/HA transformation with a stereochemically switchable BTA helical catalyst. The sequential transformation was first conducted without adding the enantiopure BTA (the chemical stimulus that triggers the stereochemical switch, *vide supra*) after completion of the HS step, *i.e.* the BTA helical catalyst has the same handedness for both HS and HA reactions. Except for the sequential addition of the reactants, the reaction was conducted similarly to the catalytic screening mentioned above, *i.e.* without exclusion of air. **APnol** also forms under these conditions but in a significantly lower yield (29±10 % NMR yield, Table 3, entry 1) compared to the aforementioned concomitant process (76±5% NMR yield, Table 2, entry 2). In addition to **APnol**, 22% and 17% of **EPnol** and **VPnol** are detected, respectively (Figure S6). The lower yield of the sequential process performed under air is thus related to the formation of by-products that likely originate from **VPnol**. However, the selectivity in **APnol** is similar to the concomitant reaction with only a small drop in the ee for the HS and HA steps which seems to be inherent to the different catalytic species present in the sequential process (see above for the discussion on the ee of the HS only reaction). Importantly, comparing the results of the entries 1 and 2 in Table 3 indicates that the optimal selectivity is reached whatever chiral induction occurs through a single enantiomer of the BTA monomer (similarly to the initial conditions before inversion of the catalyst handedness) or by means of a scalemic mixture of the BTA monomers (similarly to the conditions after inversion of the catalyst handedness).

We next envisioned to perform each step of the sequential process with the BTA helical catalyst having opposite handednesses as probed by CD spectroscopy in Figure 1b. Even though the proportion of by-products can be minimized by conducting the reaction under O_2-free and strictly anhydrous conditions (*vide infra*), the following experiments were performed under air since the time required for the HS step and the stereochemical switch have been established under these conditions (Figure 1). We were pleased to see that the (*R*,*R*) and (*S*,*S*) stereoisomers of **APnol** are now the major stereoisomers when the handedness of the catalyst is switched from right to left and left to right before the HA step, respectively (Table 3, entries 3 and 4). Enantiomeric excesses for each step have opposite signs as expected for reactions conducted with a catalyst displaying opposite intrinsic enantioselectivities. However, the values of ee2 in entries 3 and 4 indicate that the selectivity of the HA step is not optimal, thus lowering the overall selectivity of the sequential reaction. This is likely due to the fact that the stereochemical switch was not complete before the addition of

Table 3 Transformation of **VPnone** into **APnol** through sequential HS and HA steps involving the BTA helical catalyst having the same (entries 1-2) or opposite handednesses (entries 3-6) for both steps. For entries 3-6, the handedness of the BTA helical catalyst is switched after completion of the HS step as schematized by adding 15 mol% of **(*R*)-BTA** or **(*S*)-BTA** to solutions that initially contain 5 mol% of **(*S*)-BTA** or **(*R*)-BTA**. The reactions are performed without exclusion of air. See Figures S6 and S7 for the ^{1}H NMR spectra of the crude samples of entry 1 and entries 5-6, respectively. An internal standard is used to measure the yield in **APnol** on the crude samples. The enantiomeric excess and diastereomeric ratio are obtained from the chiral HPLC analyses of the crude samples. Error bars for ee and dr: see footnote of Table 1.

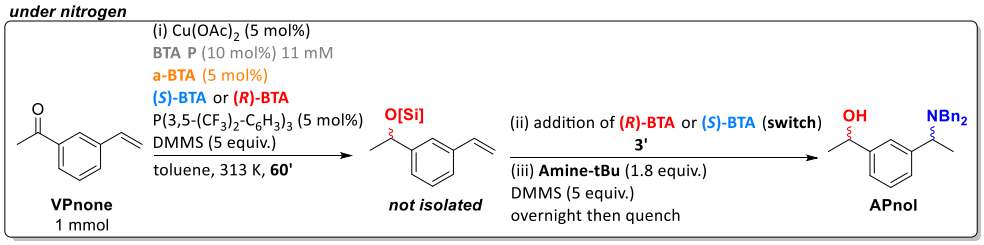


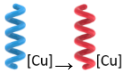
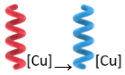
entry	conditions	schematic representation of the helical catalyst	NMR yield in **APnol** (±10%)	% of the main stereoisomer of **APnol**	ee, dr	ee1 (HS)	ee2 (HA)
1	**(*S*)-BTA**, no switch	[Cu]only	29%	72% (*R*,*S*)	89% (*R*,*S*), 3.2:1	59%	76%
2	**(*S*)-BTA**/**(*R*)-BTA** (50% ee), no switch	[Cu]only	27%	72% (*R*,*S*)	93% (*R*,*S*), 3.0:1	64%	75%
3	**(*S*)-BTA** then **(*R*)-BTA**, switch	[Cu]→[Cu]	33%	57% (*R*,*R*)	83% (*R*,*R*), 1.6:1	56%	-47%
4	**(*R*)-BTA** then **(*S*)-BTA**, switch	[Cu]→[Cu]	21%	57% (*S*,*S*)	77% (*S*,*S*), 1.8:1	-56%	42%
5	entry 3 with 5 mol% of **a-BTA** (instead of 10 mol%)	[Cu]→[Cu]	19%	71% (*R*,*R*)	95% (*R*,*R*), 2.7:1	65%	-74%
6	entry 4 with 5 mol% of **a-BTA** (instead of 10 mol%)	[Cu]→[Cu]	22%	70% (*S*,*S*)	93% (*S*,*S*), 2.7:1	-64%	71%

Amine-tBu and thus a small fraction of the silyl ether of **VPnol** (estimated to *ca.* 20%)[69] was converted by catalytic helices (or helical fragments) of the unwanted, non-switched handedness. We attribute this discrepancy between the time of stereochemical switch probed by CD spectroscopy (Figure 1) and that deduced from these catalytic experiments by a slower dynamicity of the supramolecular helices embedding the catalytic active species/resting states *versus* the pre-catalytic species. Whilst related supramolecular BTA terpolymers with copper acetate complexes anchored at their periphery have been found to be well-soluble single helices,[62] it can be surmised that the generation of hydride species, that tend to bridge several copper atoms,[70] may generate aggregated supramolecular helices through copper crosslinks that are expected to be less soluble and less dynamic under our experimental conditions.[44,62] This might also explain why the rate of the stereochemical switch in the present case (on the timescale of minutes) is slower than in our previous study dealing with HS only and for which the switch occurred on the timescale of seconds.[16] This negative effect was ultimately circumvented by lowering the amount of **a-BTA** to 5 mol% (Table 3, entries 5 and 6), which probably leads to slightly shorter and more dynamic terpolymers as a consequence of the decrease of the total BTA monomer concentration. The (*R*,*R*) and (*S*,*S*) stereoisomers of **APnol** are now obtained with a selectivity that matches the one obtained for the sequential reaction performed without stereochemical switch and is not too far from that of the concomitant process: *ca.* 70% and 78% of the main stereoisomer of **APnol** for the sequential and concomitant processes, respectively (compared data in Tables 2 and 3).

Having established that a full inversion of the catalyst handedness can be achieved under air in the conditions similar to those probed in Figure 1, we next turn to O_2-free and anhydrous conditions to improve the efficiency of the sequential reaction. Initial experiments show that the rate of the HS step is

Table 4 Sequential HS and HA reactions involving the BTA helical catalyst displaying opposite handednesses for both reactions. Reactions have been conducted on 1 mmol scale of **VPnone** under strict exclusion of air and water (see Figure S8 for ^{1}H NMR spectra of the crude samples). The handedness of the BTA helical catalyst is switched after presumed completion of the HS step as schematized by adding 15 mol% of **(*R*)-BTA** or **(*S*)-BTA** to solutions that initially contain 5 mol% of **(*S*)-BTA** or **(*R*)-BTA**. Both NMR (via an internal standard on a crude sample) and isolated yields in **APnol** are provided. The enantiomeric excess and diastereomeric ratio are obtained from the chiral HPLC analyses of the purified samples. Error bars for ee and dr: see footnote of Table 1.



conditions	schematic representation of the helical catalyst	NMR (±5%) and isolated yield in **APnol**	% of the main stereoisomer of **APnol**	ee, dr	ee1 (HS)	ee2 (HA)
(*S*)-BTA then **(*R*)-BTA**, switch		63%, 38%	50% (*R*,*R*)	79% (*R*,*R*), 1.3:1	20%	-68%
(*R*)-BTA then **(*S*)-BTA**, switch		65%, 40%	51% (*S*,*S*)	81% (*S*,*S*), 1.3:1	-21%	71%

dramatically decreased under these conditions, an observation which agrees well with the well-documented but counterintuitive ability of phosphine-based copper catalysts to exhibit enhanced activity when HS is performed under air.[71–75] The reaction time of the HS step was thus increased to one hour and the overall reaction timescale was extended (Table 4). **APnol** can now be isolated in *ca.* 40% yield, close to the isolated yield obtained in concomitant processes, confirming that by-products are significantly minimized under these conditions (Figure S8). The (*R*,*R*) and (*S*,*S*) stereoisomers of **APnol** are obtained as the main stereoisomers as expected for each step being promoted by a helical catalyst with opposite handednesses, but with a lower selectivity (*ca.* 80% ee, dr= 1.3:1) compared to the same reaction performed under air. Examining the enantiomeric excess of each step reveals that the origin of the lower selectivity comes from the HS step, which is far from being optimal, indicating that the HS of **VPnone** is not completed before the stereochemical switch. More precisely, the enantioselectivity of the HS step (ee1, Table 4) is of *ca.* 20% consistent with *ca.* 35% of **VPnone** being converted after the switch of the catalyst handedness.[69] In contrast, the selectivity of the HA step is of *ca.* 70% ee, with opposite sign compared to ee1, which is expected for HA reaction performed with the catalyst of fully inverted handedness, inferring that full stereochemical switch occurs under these conditions. Attempts to improve further the selectivity of the sequential reaction performed under nitrogen and anhydrous conditions towards the (*R*,*R*) and (*S*,*S*) stereoisomers of **APnol** were not successful since a delicate balance between catalyst activity (for HS step) and catalyst dynamicity (for the stereochemical switch) was not reached (Table S2). In overall, performing the reaction under nitrogen significantly increases the yield of the sequential reaction but drastically changes the kinetics of the HS step that makes difficult to achieve optimal selectivity under these conditions.

The four stereoisomers of **APnol** can anyway be obtained with similar selectivities either from a concomitant process in which both steps are performed with a left-handed or right-handed helical catalyst or sequential reactions (under air) in which the handedness of the BTA helical is fully switched in between the HS and HA steps (Figure 2). Dual catalysis[28] and cascade catalysis[49] are the most efficient strategies to achieve asymmetric stereodivergent with molecular catalysts but require several catalysts and/or multi-pot procedures because of the non-dynamic nature of the catalysts engaged in these reactions. The present work represents a new concept to achieve stereodivergency in which all stereoisomers can be obtained one-pot thanks to a switchable asymmetric catalyst. It is also notable that because of the efficient control of the chiral and dynamic properties of the helical coassemblies, asymmetric stereodivergency is achieved with an achiral ligand thereby representing a powerful implementation of artificial chirogenesis.[76]

Conclusion

The present work demonstrates the possibility to achieve asymmetric stereodivergency by means of a switchable asymmetric copper catalyst engaged in two transformations. The four stereoisomers of an amino alcohol are accessible one-pot, representing a totally new approach which notably avoids the purification process required when two enantiomers of a non-switchable catalyst are needed for each step of a sequential catalytic process. The approach is made possible by the incorporation of an achiral benzene-1,3,5-tricarboxamide (BTA) phosphine ligand in a supramolecular terpolymer for which the optical purity and handedness are controlled by an enantiopure BTA monomer derived from Leucine. The work benefits from the fact that the direction of the asymmetric reaction is directly

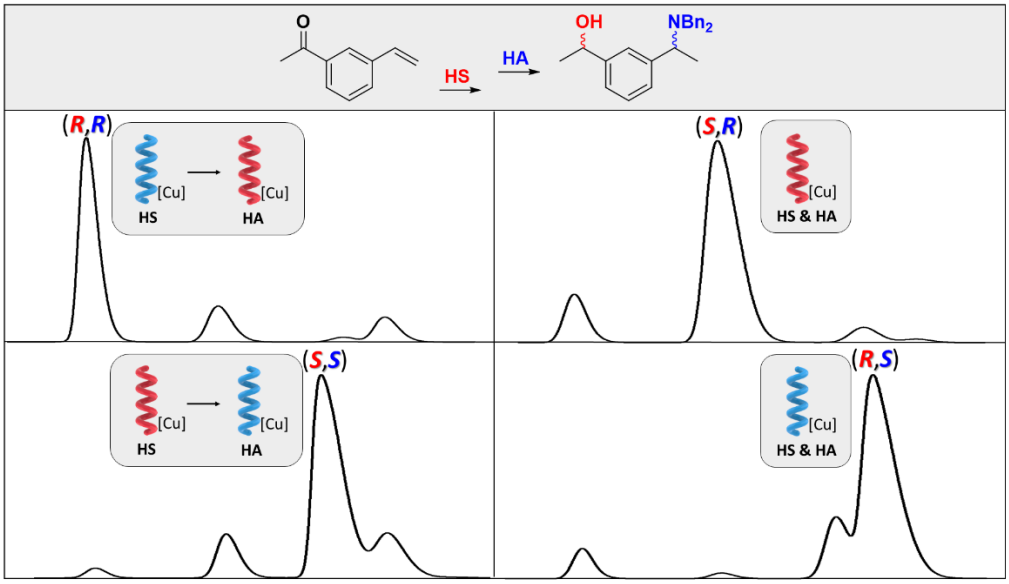


Figure 2 Asymmetric stereodivergent catalysis with a stereochemically switchable BTA helical catalyst: HPLC traces under the most selective conditions employing either the BTA helical catalyst with a single handedness for both HS and HA reactions (right, entries 5-6 of Table 2) or the BTA helical catalyst with opposite handednesses for the HS and HA reactions (left, entries 5-6 of Table 3).

related to the handedness of the helical terpolymer, which can be switched in two opposite directions by selecting the main BTA enantiomer in the terpolymers at each step of the reaction, leading to predictable configuration of two stereogenic centers. The stereochemical switch occurs through the addition of the BTA enantiomer acting as a chiral chemical trigger that inverts the stereochemical preference of the copper catalyst. The achiral BTA additive present in the supramolecular terpolymer, as well as the secondary phosphine ligand, improve the selectivity and yield of the reaction, respectively. Not only a fine tuning of the chirality of the supramolecular assemblies but also a proper control of their dynamicity is key to address stereodivergency. The present work demonstrates the feasibility of the concept to select one major (70%-79%) amongst four possible stereoisomers of an amino alcohol by applying the supramolecular helical catalyst in either concomitant (with no inversion of catalyst handedness) or sequential (with inversion of catalyst handedness) hydrosilylation and hydroamination reactions. The supramolecular helical catalyst proves to be less efficient in the sequential process, notably because of its decreased activity and selectivity for the hydrosilylation step. The concept has been demonstrated for copper hydride type catalysis but can be reasonably extended to other catalytic processes and to the control of more than two stereogenic centers in small molecules or polymers.[29] It is also conceivable that the catalytic properties and the dynamicity of this class of supramolecular helical catalysts can be improved by a proper design of the molecular structure of the monomers. Work along this direction is currently underway in our laboratory.

Supporting Information

The authors have cited additional references within the Supporting Information.[77–86]

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Keywords: supramolecular polymer • switchable catalyst • stereodivergency • chirality induction • benzene-1,3,5-tricarboxamide• dynamicity• amino alcohol• copper hydride catalysis

[1] M. Raynal, P. Ballester, A. Vidal-Ferran, P. W. N. M. van Leeuwen, *Chem. Soc. Rev.* **2014**, *43*, 1734–1787.
[2] V. Blanco, D. A. Leigh, V. Marcos, *Chem. Soc. Rev.* **2015**, *44*, 5341–5370.
[3] A. M. Lifschitz, M. S. Rosen, C. M. McGuirk, C. A. Mirkin, *J. Am. Chem. Soc.* **2015**, *137*, 7252–7261.
[4] M. Vlatković, B. S. L. Collins, B. L. Feringa, *Chem. - Eur. J.* **2016**, *22*, 17080–17111.
[5] J. Choudhury, *Tetrahedron Lett.* **2018**, *59*, 487–495.
[6] A. Goswami, S. Saha, P. K. Biswas, M. Schmittel, *Chem. Rev.* **2020**, *120*, 125–199.
[7] G. Romanazzi, L. Degennaro, P. Mastrorilli, R. Luisi, *ACS Catal.* **2017**, *7*, 4100–4114.
[8] J. Wang, B. L. Feringa, *Science* **2011**, *331*, 1429–1432.
[9] S. Mortezaei, N. R. Catarineu, J. W. Canary, *J. Am. Chem. Soc.* **2012**, *134*, 8054–8057.
[10] G. Storch, O. Trapp, *Angew. Chem. Int. Ed.* **2015**, *54*, 3580–3586.

[11] B. A. F. Le Bailly, L. Byrne, J. Clayden, *Angew. Chem. Int. Ed.* **2016**, *55*, 2132–2136.
[12] S. F. Pizzolato, P. Štacko, J. C. M. Kistemaker, T. van Leeuwen, B. L. Feringa, *Nat. Catal.* **2020**, *3*, 488–496.
[13] X. Chen, P. J. Gilissen, P. Tinnemans, N. Vanthuyne, F. P. J. T. Rutjes, B. L. Feringa, J. A. A. W. Elemans, R. J. M. Nolte, *Nat. Synth.* **2022**, *1*, 873–882.
[14] T. Yamamoto, T. Yamada, Y. Nagata, M. Suginome, *J. Am. Chem. Soc.* **2010**, *132*, 7899–7901.
[15] Y. Nagata, T. Nishikawa, M. Suginome, *J. Am. Chem. Soc.* **2015**, *137*, 4070–4073.
[16] J. M. Zimbron, X. Caumes, Y. Li, C. M. Thomas, M. Raynal, L. Bouteiller, *Angew. Chem. Int. Ed.* **2017**, *56*, 14016–14019.
[17] L. Tan, M. Sun, H. Wang, J. Wang, J. Kim, M. Lee, *Nat. Synth.* **2023**, 1–10.
[18] L. Zhang, H.-X. Wang, S. Li, M. Liu, *Chem. Soc. Rev.* **2020**, *49*, 9095–9120.
[19] D. Sahoo, R. Benny, N. K. Ks, S. De, *ChemPlusChem* **2022**, *87*, e202100322.
[20] S. F. Pizzolato, P. Štacko, J. C. M. Kistemaker, T. van Leeuwen, E. Otten, B. L. Feringa, *J. Am. Chem. Soc.* **2018**, *140*, 17278–17289.
[21] P. J. Gilissen, X. Chen, J. De Graaf, P. Tinnemans, B. L. Feringa, J. A. A. W. Elemans, R. J. M. Nolte, *Chem. – Eur. J.* **2023**, *29*, e202203539.
[22] C.-T. Chen, C.-C. Tsai, P.-K. Tsou, G.-T. Huang, C.-H. Yu, *Chem. Sci.* **2016**, *8*, 524–529.
[23] S. Mortezaei, N. R. Catarineu, X. Duan, C. Hu, J. W. Canary, *Chem. Sci.* **2015**, *6*, 5904–5912.
[24] X. Tian, C. Cassani, Y. Liu, A. Moran, A. Urakawa, P. Galzerano, E. Arceo, P. Melchiorre, *J. Am. Chem. Soc.* **2011**, *133*, 17934–17941.
[25] S. A. Moteki, J. Han, S. Arimitsu, M. Akakura, K. Nakayama, K. Maruoka, *Angew. Chem. Int. Ed.* **2012**, *51*, 1187–1190.
[26] P. Oczipka, D. Müller, W. Leitner, G. Franciò, *Chem. Sci.* **2015**, *7*, 678–683.
[27] M. Nagamoto, D. Yamauchi, T. Nishimura, *Chem. Commun.* **2016**, *52*, 5876–5879.
[28] S. Krautwald, E. M. Carreira, *J. Am. Chem. Soc.* **2017**, *139*, 5627–5639.
[29] G. W. Coates, R. M. Waymouth, *Science* **1995**, *267*, 217–219.
[30] S. Mortezaei, N. R. Catarineu, J. W. Canary, *Tetrahedron Lett.* **2016**, *57*, 459–462.
[31] D. Zhao, T. M. Neubauer, B. L. Feringa, *Nat. Commun.* **2015**, *6*, 6652.
[32] D. Sud, T. B. Norsten, N. R. Branda, *Angew. Chem. Int. Ed.* **2005**, *44*, 2019–2021.
[33] G. D. Bo, D. A. Leigh, C. T. McTernan, S. Wang, *Chem. Sci.* **2017**, *8*, 7077–7081.
[34] S. Kassem, A. T. L. Lee, D. A. Leigh, V. Marcos, L. I. Palmer, S. Pisano, *Nature* **2017**, *549*, 374–378.
[35] M. Dommaschk, J. Echavarren, D. A. Leigh, V. Marcos, T. A. Singleton, *Angew. Chem. Int. Ed.* **2019**, *58*, 14955–14958.
[36] Y. Li, L. Bouteiller, M. Raynal, *ChemCatChem* **2019**, *11*, 5212–5226.
[37] M. Raynal, F. Portier, P. W. van Leeuwen, L. Bouteiller, *J. Am. Chem. Soc.* **2013**, *135*, 17687–17690.
[38] A. Desmarchelier, X. Caumes, M. Raynal, A. Vidal-Ferran, P. W. N. M. van Leeuwen, L. Bouteiller, *J. Am. Chem. Soc.* **2016**, *138*, 4908–4916.
[39] Y. Li, X. Caumes, M. Raynal, L. Bouteiller, *Chem. Commun.* **2019**, *55*, 2162–2165.
[40] Z. Shen, Y. Sang, T. Wang, J. Jiang, Y. Meng, Y. Jiang, K. Okuro, T. Aida, M. Liu, *Nat. Commun.* **2019**, *10*, 1–8.
[41] Y. Li, A. Hammoud, L. Bouteiller, M. Raynal, *J. Am. Chem. Soc.* **2020**, *142*, 5676–5688.
[42] M. A. Martínez-Aguirre, Y. Li, N. Vanthuyne, L. Bouteiller, M. Raynal, *Angew. Chem. Int. Ed.* **2021**, *60*, 4183–4191.
[43] P. Aoun, A. Hammoud, M. A. Martínez-Aguirre, L. Bouteiller, M. Raynal, *Catal. Sci. Technol.* **2022**, *12*, 834–842.
[44] A. Hammoud, Y. Li, M. A. Martínez-Aguirre, H. Kong, L. Dubreucq, C. Troufflard, L. Bouteiller, M. Raynal, *Chem. – Eur. J.* **2023**, *29*, e202300189.
[45] E. Yashima, N. Ousaka, D. Taura, K. Shimomura, T. Ikai, K. Maeda, *Chem. Rev.* **2016**, *116*, 13752–13990.
[46] A. R. A. Palmans, E. W. Meijer, *Angew. Chem. Int. Ed.* **2007**, *46*, 8948–8968.
[47] S. Cantekin, T. F. A. de Greef, A. R. A. Palmans, *Chem. Soc. Rev.* **2012**, *41*, 6125–6138.
[48] Y. Dorca, J. Matern, G. Fernández, L. Sánchez, *Isr. J. Chem.* **2019**, *59*, 869–880.
[49] S.-L. Shi, Z. L. Wong, S. L. Buchwald, *Nature* **2016**, *532*, 353–356.
[50] Q.-F. Xu-Xu, Q.-Q. Liu, X. Zhang, S.-L. You, *Angew. Chem. Int. Ed.* **2018**, *57*, 15204–15208.
[51] S. Nishino, K. Hirano, M. Miura, *Chem. – Eur. J.* **2020**, *26*, 8725–8728.
[52] D.-W. Gao, Y. Gao, H. Shao, T.-Z. Qiao, X. Wang, B. B. Sanchez, J. S. Chen, P. Liu, K. M. Engle, *Nat. Catal.* **2020**, *3*, 23–29.
[53] C. Deutsch, N. Krause, *Chem. Rev.* **2008**, *108*, 2916–2927.
[54] M. T. Pirnot, Y.-M. Wang, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2016**, *55*, 48–57.
[55] R. Y. Liu, S. L. Buchwald, *Acc. Chem. Res.* **2020**, *53*, 1229–1243.
[56] A. Saxena, B. Choi, H. W. Lam, *J. Am. Chem. Soc.* **2012**, *134*, 8428–8431.
[57] S. Ichikawa, S. L. Buchwald, *Org. Lett.* **2019**, *21*, 8736–8739.
[58] B. H. Lipshutz, K. Noson, W. Chrisman, A. Lower, *J. Am. Chem. Soc.* **2003**, *125*, 8779–8789.
[59] S. Zhu, N. Niljianskul, S. L. Buchwald, *J. Am. Chem. Soc.* **2013**, *135*, 15746–15749.
[60] Upon considering the ee of each step for the CuH-catalyzed HS/HA reaction of **VPnone** in presence of DTBM-Segphos, it appears that the ee for the HA step is consistent with that obtained for the HA of styrene but the ee for the HS step is lower than that reported for the HS of acetophenone (see reference [58]). This might due to the fact that the former reaction is performed at 195 K instead of 313 K for **VPnone**.
[61] For all catalytic reactions performed throughout this paper, the ee in **APnol** is related to the ee of the HS and HA steps according to the formula indicated in the caption of Figure S2 and thus benefits from the statistical enhancement of the enantiomeric excess as illustrated by the ee in APnol being significantly higher than those of the independent steps (compare the value of ee versus ee1 and ee2 in Table 1).
[62] H. Kong, Y. Li, A. Hammoud, L. Dubreucq, C. Troufflard, R. Maruchenko, L. Bouteiller, M. Raynal, *ChemistryEurope* **2023**, DOI: 10.1002/ceur.202300027.
[63] Throughout this paper, HS and HA reactions are initiated at the same time in the concomitant process, but the HA reaction is slower than the HS reaction.
[64] This experiment also discards that kinetic resolution might play a role in the outcome of the asymmetric reaction. See also comment in reference [61].
[65] D. Niu, S. L. Buchwald, *J. Am. Chem. Soc.* **2015**, *137*, 9716–9721.
[66] The fact that the isolated yield in **APnol** is lower than the NMR yield is due to difficult separation of **APnol** from **EPnol** and **VPnol** (see the SI).
[67] Due to the presence of silane in both steps, HS occurs prior to HA.
[68] For CD analyses of diluted MR experiments on similar systems, showing that 10% ee in one of the enantiomer is enough to get homochiral helices, see reference [41].
[69] The calculations are made by considering that conversion occurs only before or after the switch, i.e. with catalysts displaying opposite enantioselectivities. These values are actually lower limit values if one considers that conversion occurs also during the stereochemical, e.g. with a racemic catalyst.
[70] A. J. Jordan, G. Lalic, J. P. Sadighi, *Chem. Rev.* **2016**, *116*, 8318–8372.
[71] S. Sirol, J. Courmarcel, N. Mostefai, O. Riant, *Org. Lett.* **2001**, *3*, 4111–4113.
[72] J. Courmarcel, N. Mostefaï, S. Sirol, S. Choppin, O. Riant, *Isr. J. Chem.* **2001**, *41*, 231–240.
[73] J. Wu, J.-X. Ji, A. S. C. Chan, *Proc. Natl. Acad. Sci.* **2005**, *102*, 3570–3575.
[74] N. Mostefaï, S. Sirol, J. Courmarcel, O. Riant, *Synthesis* **2007**, 1265–1271.
[75] X.-C. Zhang, Y. Wu, F. Yu, F.-F. Wu, J. Wu, A. S. C. Chan, *Chem. – Eur. J.* **2009**, *15*, 5888–5891.
[76] M. V. Escárcega-Bobadilla, A. W. Kleij, *Chem. Sci.* **2012**, *3*, 2421–2428.

Quoted in the Supporting Information:

[77] H. Sun, *Macromolecules* **1995**, *28*, 701–712.
[78] H. Sun, P. Ren, J. R. Fried, *Comput. Theor. Polym. Sci.* **1998**, *8*, 229–246.
[79] S. L. Mayo, B. D. Olafson, W. A. Goddard, *J. Phys. Chem.* **1990**, *94*, 8897–8909.
[80] S. Hoyas, V. Lemaur, Q. Duez, F. Saintmont, E. Halin, J. De Winter, P. Gerbaux, J. Cornil, *Adv. Theory Simul.* **2018**, *1*, 1800089.
[81] S. Nosé, *Mol. Phys.* **1984**, *52*, 255–268.
[82] L. Verlet, *Phys. Rev.* **1967**, *159*, 98–103.
[83] N. S. Shahana Nizar, M. Sujith, K. Swathi, C. Sissa, A. Painelli, K. George Thomas, *Chem. Soc. Rev.* **2021**, *50*, 11208–11226.
[84] J. M. Paolillo, A. D. Duke, E. S. Gogarnoiu, D. E. Wise, M. Parasram, *J. Am. Chem. Soc.* **2023**, *145*, 2794–2799.
[85] V. A. Steadman, S. B. Pettit, K. G. Poullennec, L. Lazarides, A. J. Keats, D. K. Dean, S. J. Stanway, C. A. Austin, J. A. Sanvoisin, G. M. Watt, H. G. Fliri, A. C. Liclican, D. Jin, M. H. Wong, S. A. Leavitt, Y.-J. Lee, Y. Tian, C. R. Frey, T. C. Appleby, U. Schmitz, P. Jansa, R. L. Mackman, B. E. Schultz, *J. Med. Chem.* **2017**, *60*, 1000–1017.
[86] G. A. Molander, A. R. Brown, *J. Org. Chem.* **2006**, *71*, 9681–9686.

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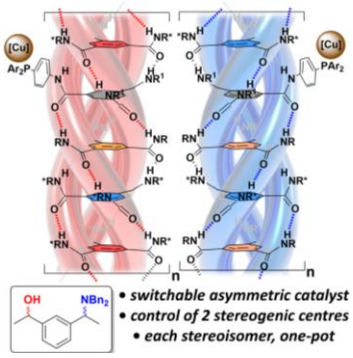

Asymmetric stereodivergency is achieved by means of a switchable supramolecular helical terpolymer consisting of an achiral benzene-1,3,5-tricarboxamide phosphine ligand (in grey) coordinated to catalytic sites, of enantiopure monomers (in blue and red) for induction and inversion of chirality, and of an achiral monomer (in orange) for increasing catalyst efficiency. All stereoisomers of an amino alcohol are obtained with similar selectivities.

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