

## Helicenes

International Edition: DOI: 10.1002/anie.201915870  
German Edition: DOI: 10.1002/ange.201915870

## Enantioselective Synthesis of 1,12-Disubstituted [4]Helicenes

Thierry Hartung, Rafael Machleid, Martin Simon, Christopher Golz, and Manuel Alcarazo\*

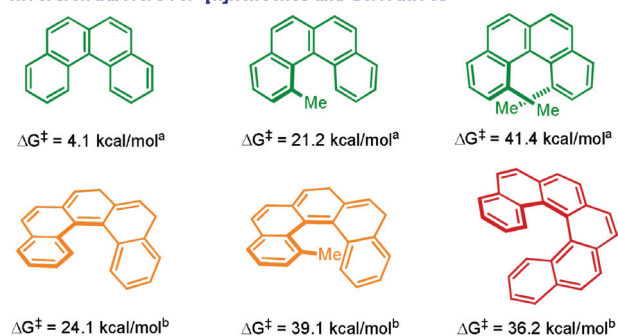
**Abstract:** A highly enantioselective synthesis of 1,12-disubstituted [4]carbohelicenes is reported. The key step for the developed synthetic route is a Au-catalyzed intramolecular alkyne hydroarylation, which is achieved with good to excellent regio- and enantioselectivity by employing TADDOL-derived ( $\alpha,\alpha,\alpha,\alpha$ -tetraaryl-1,3-dioxolane-4,5-dimethanol)  $\alpha$ -cationic phosphonites as ancillary ligands. Moreover, an appropriate design of the substrate makes the assembly of [4]helicenes of different substitution patterns possible, thus demonstrating the synthetic utility of the method. The absolute stereochemistry of the newly prepared structures was determined by X-ray crystallography and characterization of their photophysical properties is also reported.

Carbohelicenes are screw-shaped molecules formally derived from the *ortho*-condensation of benzene rings.<sup>[1]</sup> Even though no stereogenic centers are present in their structures, the twisted geometry imposed by their connectivity makes them chiral. The energetic barrier for the interconversion between the two enantiomeric forms is strongly dependent on the number of *ortho*-fused benzene units. The first member of the carbohelicene family with a helicoidal structure is [4]helicene, which is configurationally unstable under ambient conditions.<sup>[2]</sup> [5]helicene can be resolved, but the low activation energy of racemization ( $\Delta G^\ddagger = 24.1$  kcal mol<sup>-1</sup>) does not hamper the slow interconversion of the enantiomers. Hence, the racemization of these structures is typically complete after a couple of days at room temperature.<sup>[3]</sup> The first configurationally stable member of the helicene family is [6]helicene. Racemization of [6]helicene only occurs after intensive heating ( $\Delta G^\ddagger = 36.2$  kcal mol<sup>-1</sup>;  $t_{1/2}(\text{rac}) = 48$  min at 205 °C), making this scaffold the first carbohelicene intrinsically useful for the design of thermally stable chiral architectures.<sup>[4]</sup>

Nevertheless, the absolute configuration of low-order [4] and [5]helicenes can be fixed either by installation of appropriate substituents at one or both termini of their fjord region, or by embedment of the helicene moiety into

a more extended  $\pi$ -conjugated scaffold.<sup>[5]</sup> As an illustrative example, on the incorporation of a methyl substituent in the 1-position of [5]helicene, the enantiomerization barrier increases up to  $\Delta G^\ddagger = 39.1$  kcal mol<sup>-1</sup>, making 1-(methyl)-[5]helicene even more reluctant to racemize than [6]helicene.<sup>[6]</sup> The situation is analogous for [4]helicenes, but these structures require positions 1- and 12- to be simultaneously substituted to freeze the racemization process (Figure 1).<sup>[7]</sup>

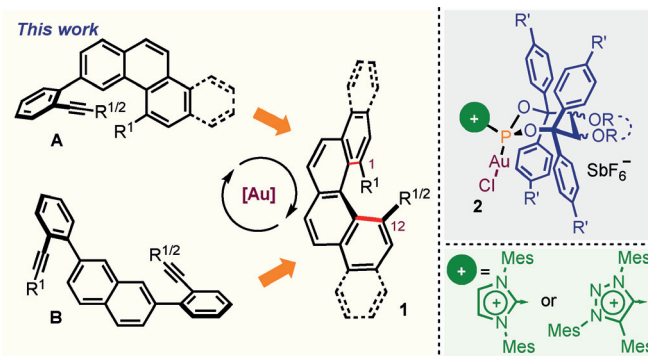
## Inversion barriers for [n]helicenes and derivatives



**Figure 1.** Inversion barriers for [4]-, [5]-, and [6]helicenes and their Me-substituted derivatives; [a] Calculated values at the B3LYP/6-31G(d) level of theory; [b] Experimental values.

Despite the impressive development already achieved in the synthesis of helicenes,<sup>[1]</sup> and the number of applications that configurationally stable low-order helicenes have found in diverse areas such as asymmetric catalysis,<sup>[8]</sup> chiral recognition,<sup>[9]</sup> or the design of molecular machines,<sup>[10]</sup> highly enantioselective syntheses of [5]carbohelicene derivatives are scarce.<sup>[11,12]</sup> To the best of our knowledge, no enantioselective route is available for the preparation of 1,12-disubstituted[4]helicenes.<sup>[13]</sup>

Being aware of the potential offered by Au-catalyzed hydroarylation reactions for the assembly of conveniently designed alkynes into polyarenes,<sup>[14]</sup> we conceived the enantiomeric synthesis of 1,12-disubstituted [4]helicenes from substrates of general formulae **A** or **B** (Figure 2).



**Figure 2.** Synthetic approaches to the enantioselective synthesis of 1,12-disubstituted [4]helicenes.

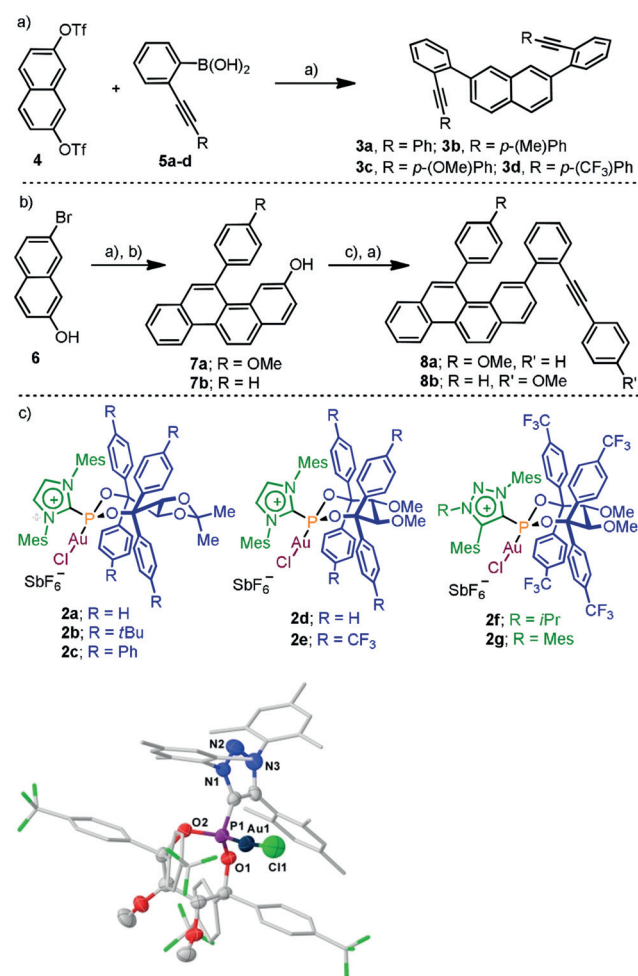
[\*] T. Hartung, R. Machleid, M. Simon, Dr. C. Golz, Prof. Dr. M. Alcarazo  
Institut für Organische und Biomolekulare Chemie  
Georg-August-Universität Göttingen  
Tammannstr 2, 37077 Göttingen (Germany)  
E-mail: malcara@gwdg.de

Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under:  
<https://doi.org/10.1002/anie.201915870>.

© 2020 The Authors. Published by Wiley-VCH Verlag GmbH & Co. KGaA. This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

TADDOL-derived  $\alpha$ -cationic phosphonites recently developed in our laboratory were chosen as ancillary ligands for the preparation of the necessary Au precatalysts **2** because of their high modularity, which allows easy tuning of the chiral pocket around the Au atom; and their cationic character, ultimately responsible for the enhanced activity of the actual catalytic species if compared with other Au catalysts of similar structure but derived from neutral ligands.<sup>[15]</sup>

We began our investigation by synthesizing dialkyne **3a**, which was obtained by Suzuki coupling between known bistriflate **4** and boronic acid **5a** (Scheme 1a).<sup>[17]</sup> Subsequently, a complete array of Au precatalysts **2a–g** were screened for the successive double hydroarylation required to transform the model substrate into [4]helicene **1a**. Our initial explorative conditions were set up as follows: catalyst loading of 10 mol %, fluorobenzene as solvent, and a working temper-



**Scheme 1.** Synthesis of [4]helicene precursors and structures of the catalysts tested. Reagents and conditions: a) Pd<sub>2</sub>(dba)<sub>3</sub> (5 mol %), SPhos (10 mol %), Cs<sub>2</sub>CO<sub>3</sub> (4 equiv), THF/H<sub>2</sub>O (10:1), 80 °C, 24 h, **3a**, 62%; **3b**, 67%; **3c**, 65%; **3d**, 89%; b) **19** (9 mol %), AgSbF<sub>6</sub> (9 mol %), DCM, **7a**, 87%; **7b**, 42%, both from **6** (two steps); c) Tf<sub>2</sub>O (1.5 equiv), pyridine (4.0 equiv), and then **5a** or **5c**, Pd<sub>2</sub>(dba)<sub>3</sub> (5 mol %), SPhos (10 mol %), Cs<sub>2</sub>CO<sub>3</sub> (2 equiv), THF/H<sub>2</sub>O (10:1), 80 °C, 24 h, **8a**, 60%; **8b**, 25% (two steps). X-ray structure of **2g**, H atoms, co-crystallized solvents and SbF<sub>6</sub> anions are removed for clarity. Arene moieties are drawn as reduced sticks, ellipsoids drawn at 50% probability level.<sup>[16]</sup>

ature of –20 °C. All reactions were allowed to proceed for 96 hours or until total consumption of the starting material.

The performance of catalysts **2a–c**, all containing an acetamide backbone, was modest in terms of regio- and enantioselectivity (Table 1, Entries 1–3). Interestingly, replacement of the acetamide motif by methoxy groups,

**Table 1:** Screening of chiral Au-phosphonite complexes in the hydroarylation of mono- and diynes towards [4]helicenes.<sup>[a]</sup>

Entry	Au catalyst	Substrate	Yield [%]	1:9	1 ( <i>ee</i> [%])
1	<b>2a</b>	<b>3a</b>	50	75:25	<b>1a</b> (–36)
2	<b>2b</b>	<b>3a</b>	13	50:50	<b>1a</b> (–30)
3	<b>2c</b>	<b>3a</b>	91	94:6	<b>1a</b> (–8)
4	<b>2d</b>	<b>3a</b>	52	68:32	<b>1a</b> (28)
5	<b>2e</b>	<b>3a</b>	94	98:2	<b>1a</b> (97)
6	<b>2f</b>	<b>3a</b>	97	99:1	<b>1a</b> (98)
7 <sup>[b]</sup>	<b>2g</b>	<b>3a</b>	98	98:2	<b>1a</b> (99)
8 <sup>[b,c]</sup>	<b>2g</b>	<b>3a</b>	95	96:4	<b>1a</b> (98)
9 <sup>[b]</sup>	<b>2g</b>	<b>3b</b>	94	97:3	<b>1b</b> (97)
10 <sup>[b,d]</sup>	<b>2g</b>	<b>3c</b>	84	93:7	<b>1c</b> (89)
11 <sup>[b,c]</sup>	<b>2g</b>	<b>3d</b>	4	> 99:1	<b>1d</b> (95)
12 <sup>[b,d]</sup>	<b>2g</b>	<b>8a</b>	57	98:2	<b>1e</b> (88)
13 <sup>[b,d]</sup>	<b>2g</b>	<b>8b</b>	65	94:6	<b>1e</b> (97)

[a] Reaction conditions: **3a–d** (0.02 mmol), catalysts **2a–g**, 10 mol %, AgSbF<sub>6</sub> 10 mol %, FC<sub>6</sub>H<sub>5</sub> (0.05 M), –20 °C, 96 h. Yields are of the isolated **1:9** mixtures; regioisomer ratios were determined by <sup>1</sup>H NMR spectroscopy and *ee* values by chiral HPLC. [b] CH<sub>2</sub>Cl<sub>2</sub> was used as solvent (0.05 M). [c] Reaction carried out at 0 °C. [d] Catalyst loading of 5 mol %.

such as in Au complexes **2d,e**, improved the performance of the catalysts.<sup>[18]</sup> Specifically, catalyst **2e**, which contains four *p*-(CF<sub>3</sub>)Ph substituents, was able to promote the desired double cyclization towards [4]helicene **1a** with excellent enantio- (97% *ee*) and regioselectivity (**1a:9a**; 98:2) (Table 1, Entry 5). The catalytic system suffers, however, from low reactivity, and reaction times of up to four days were necessary.

In an attempt to solve this issue, the imidazolium moiety in ligand **2e** was exchanged by more-electron-withdrawing 1,2,3-triazolium units, and the already optimal chiral environment around the Au atom was maintained. Both resulting catalysts, **2f** and **2g**, were able to match, or even slightly overtake, the already outstanding regio- and enantioselectivities of **2e** (Table 1, Entries 6 and 7), and by employing **2g** the reaction times were shortened to only two days. No product derived from the 5-*exo*-dig cyclization of the substrate was observed in any of these experiments. A final solvent screening indicated that **2g** does not require the employment of fluorobenzene to maintain excellent levels of enantioinduction; highly competitive results were also obtained working in dichloromethane (Table 1, Entry 8).<sup>[15a]</sup> Finally, crystals of precatalyst **2g** were obtained, and its molecular connectivity was confirmed by X-ray diffraction (see Scheme 1c and the Supporting Information).

By using the conditions already optimized, the respective cyclization reactions of diynes **3b,c** into **1b,c** took place with high levels of regio- and enantioselectivity (Table 1, Entries 9 and 10). Interestingly, the more reactive nature of **3c**, decorated with terminal *p*-anisyl substituents allowed a reduction of the catalyst loading to only 5 mol % without significant erosion of the yield. On the other hand, the cyclization of diyne **3d**, bearing strong electron-withdrawing CF<sub>3</sub> substituents proved to be difficult and only traces of the desired [4]helicene **1d** was obtained under the standard reaction conditions, although with outstanding *ee* (4 % yield of isolated product, 95 % *ee*). The mono-cyclized intermediate is the main species present in the mixture (Table 1, Entry 11).

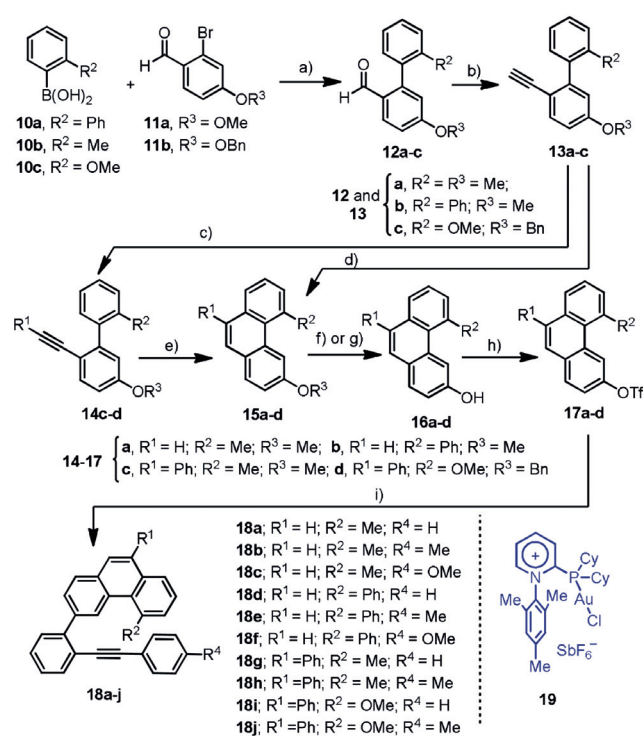
The hydroarylation of substrates **8a** and **8b** towards non C<sub>2</sub>-symmetrically substituted **1e** proceeded in both cases with acceptable yields. The same major enantiomer was obtained from both reactions, albeit the enantioselectivity of the cyclization is slightly eroded when using **8a** as the substrate (Table 1, Entries 12 and 13). Considering that only one hydroarylation event is required to obtain **1e** from these substrates, it is not surprising that only 5 mol % of precatalyst **2g** is required for the reactions to conclude in 48 h. The X-ray structure of substrate **8a** and precursor **7a** are depicted in the Supporting Information.

Encouraged by these results, and seeking to further explore the viability of our cycloisomerization protocol towards other [4]helicene structures, additional alkyne precursors were evaluated. Thus, phenanthrene derivatives **18a–j** were prepared following a multistep route, which is described in detail in Scheme 2.

Key for the success of this synthetic plan was the effective preparation of phenanthrene intermediates **15a–d** by intramolecular hydroarylation of the corresponding alkynes. Although for substrates **13a,b**, containing a terminal alkyne, the cycloisomerization proceeded successfully in the presence of catalytic amounts of PtCl<sub>2</sub>,<sup>[19]</sup> neither PtCl<sub>2</sub> or Ph<sub>3</sub>PAuCl/AgSbF<sub>6</sub> were able to satisfactorily promote the hydroarylation step for internal alkynes **14c,d**. Only the employment of Au precatalyst **19**, containing a strong  $\pi$ -acceptor *N*-arylpyridinium phosphine as an ancillary ligand, induced the formation of **15c,d** in synthetically practical yields.<sup>[20]</sup>

For substrates **18a–c** (R<sup>2</sup> = Me), the performance of **2g** (5 mol %) is mediocre in terms of regio- and enantioselectivity (Table 2, Entries 1–3), and significant amounts of undesired benzo[*m*]tetraphenes **21a–c** were obtained as side products. Interestingly, complete control over the enantioselectivity (97–99% *ee*) is achieved by formal exchange of the methyl groups at position R<sup>2</sup> by phenyl groups (substrates **18d–f**); however, the regioselectivity of the cyclization for these substrates is still far from ideal (Table 2, Entries 4–6). Note that **8a,b** only differs from **18d–f** in a remote benzanulation, but this seems to be crucial to effectively direct the hydroarylation to the inner position of the phenanthrene (Table 1, Entries 11–12).

Similarly, alkynes **18g,h** only differs from **18a,b** in a phenyl substituent from the outer rim of the phenanthrene; however, for these structures the cyclization is again selectively directed to the desired position affording **20g,h** with high regioselectivity (Table 2, Entries 7–8). The best results of



**Scheme 2.** Synthesis of non-symmetric [4]helicene precursors.

Reagents and conditions: a) Pd(AcO)<sub>2</sub> (3 mol %), SPhos, (3 mol %), K<sub>3</sub>PO<sub>4</sub> (2.0 equiv), toluene/dioxane (10:1), **12a**, 92%, **12b**, 91%, **12c**, 87%; b) Ohira-Bestmann reagent (3.0 equiv), K<sub>2</sub>CO<sub>3</sub> (3.0 equiv), MeOH, **13a**, 95%, **13b**, 99%, **13c**, 87%; c) PhI (1.0 equiv), Cul (3 mol %), PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (2 mol %), Et<sub>3</sub>N (5 mL), **14c**, 89%, **14d**, 71%; d) PtCl<sub>2</sub> (10 mol %), toluene, 85 °C, **15a**, 60%; **15b**, 89%; e) **19** (10 mol %), AgSbF<sub>6</sub> (10 mol %), DCM, **15c**, 73%; **15d**, not isolated; f) BBr<sub>3</sub>, DCM, **16a**, 99%; **16b**, 85%; **16c**, 73%; g) BCl<sub>3</sub> (2 equiv), C<sub>6</sub>HMe<sub>5</sub> (3 equiv), **16d**, 67% (two steps); h) Tf<sub>2</sub>O (1.2 equiv), Et<sub>3</sub>N, **17a**, 79%; **17b**, 75%; **17c**, 98%; **17d**, 95%; i) **5a–c**, Pd<sub>2</sub>(dba)<sub>3</sub> (5 mol %), SPhos (10 mol %), Cs<sub>2</sub>CO<sub>3</sub> (2 equiv), THF/H<sub>2</sub>O (10:1), 80 °C, 24 h, **18a**, 89%; **18b**, 92%; **18c**, 68%; **18d**, 51%; **18e**, 43%; **18f**, 38%; **18g**, 67%; **18h**, 75%; **18i**, 62%; **18j**, 81%.

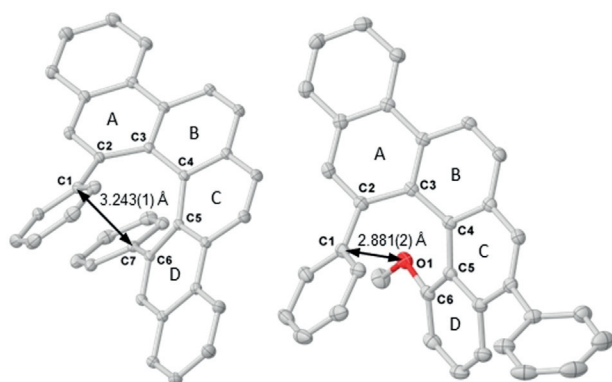
the series were obtained for substrates **18i,j** (R<sup>1</sup> = Ph, R<sup>2</sup> = OMe), which were transformed into **20i,j** with excellent regio- and enantioselectivities. Further scrutiny is ongoing to fully understand the effect of remote substitutions on the hydroarylation site, but it seems to be consistent that catalyst **2g** promotes higher enantioselectivities for  $\pi$ -extended structures.<sup>[15]</sup>

The connectivity of parent [4]helicene **1a** was unambiguously confirmed by X-ray crystallography employing a racemic single crystal (Figure 3). In this compound the vertical distance between the overlapping C1 and C7 carbon atoms is 3.243(1) Å, which is basically identical to the value in [6]helicene (3.215 Å). On the other hand, the torsion angles along the inner rim in **1a** (from C1 to C7,  $\varphi = 20.3, 27.6, 27.6, 20.3^\circ$ ) vary significantly if compared with those in [6]helicene ( $\varphi = 11.2, 30.1, 31.0, 15.2^\circ$ ), in particular for rings A and D. This difference is likely to be caused by the higher tolerance to geometrical distortion of the one-point-connected phenyl groups.<sup>[21]</sup> To examine the chiral stability of the [4]helicenes prepared, enantioenriched **1a** (98% *ee*) was heated at 180 °C in 1,2-dichlorobenzene for 24 h and later monitored by chiral

**Table 2:** Scope of the Au-catalyzed hydroarylation of **18a–j** towards [4]helicenes.<sup>[a]</sup>

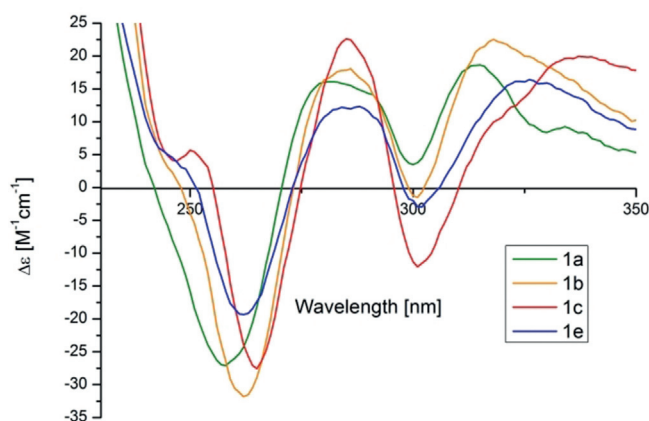
Entry	Substrate	Yield [%]	20:21	20 ( <i>ee</i> [%])
1	<b>18a</b>	93	63:37	<b>20a</b> (60)
2	<b>18b</b>	43	42:58	<b>20b</b> (75)
3	<b>18c</b>	85	44:56	<b>20c</b> (70)
4	<b>18d</b>	93	69:31	<b>20d</b> (97)
5	<b>18e</b>	93	54:46	<b>20e</b> (99)
6	<b>18f</b>	75	38:62	<b>20f</b> (98)
7	<b>18g</b>	87	90:10	<b>20g</b> (67)
8	<b>18h</b>	93	98:2	<b>20h</b> (79)
9	<b>18i</b>	93	99:1	<b>20i</b> (92)
10	<b>18j</b>	94	95:5	<b>20j</b> (90)

[a] Reaction conditions: **18a–j** (0.02 mmol), catalyst **2g**, 5 mol%, AgSbF<sub>6</sub> 10 mol%, CH<sub>2</sub>Cl<sub>2</sub> (0.05 M), –20 °C, 96 h. Yields are of the isolated **20:21** mixtures; regioisomer ratios were determined by <sup>1</sup>H NMR spectroscopy and *ee* values by chiral HPLC.

**Figure 3.** X-ray structure of *rac*-**1a** (left) and **20j** (right). H atoms are removed for clarity and ellipsoids drawn at 50% probability level.<sup>[16]</sup>

HPLC. No erosion of the *ee* value was observed, highlighting the configurational stability of 1,12-disubstituted [4]helicenes.

The absolute configuration of the newly prepared helicenes was determined to be *P* from the X-ray analyses of single crystals of **20i** and **20j** (See Figure 3 and the Supporting Information).<sup>[22]</sup> For **20i**, both the Flack and Hooft parameters (0.01(4) and 0.04(3), respectively) unambiguously support this assignment. For **20j** an identical conclusion can be reached (0.01(12) and 0.09(5) for the Flack and Hooft parameters, respectively). The higher estimated standard deviation for the latter case is attributed to lower data redundancy for this measurement. Importantly, both independent results point to the same absolute configuration. Additionally, the circular dichroism spectra for [4]helicenes **1a–e** are shown in Figure 4. Comparison of these EDC spectra with that reported by Yamaguchi and co-workers for a 1,12-dimethyl substituted [4]helicene further confirms the assignment of the helicity made by crystallographic techniques.<sup>[23]</sup>

**Figure 4.** Circular dichroism spectra of **1a–e** in dichloromethane.

The absorption and fluorescence spectra of the [4]helicenes synthesized can be found in the Supporting Information. Interestingly, compounds **1a–e** display blue fluorescence, with the emission maximum being located at 438–440 nm. The emission bands for **20a–j**, architectures characterized by only one benzannulation of the parent [4]helicene, are slightly blue-shifted and appear at 426–433 nm.

In summary, we report herein the first highly enantioselective synthesis of 1,12-disubstituted [4]carbohelicenes, achieved through the Au-catalyzed intramolecular hydroarylation of appropriate alkynes and employing a TADDOL-derived  $\alpha$ -cationic phosphinite as an ancillary ligand. Single-crystal X-ray analysis unambiguously determined the connectivity of the new structures obtained and established their absolute configuration. Ongoing work in our laboratory is focused on the further optimization of the catalytic system developed towards the enantioselective synthesis of higher-order carbohelicenes and other polyhelic scaffolds.

## Acknowledgements

Financial support from the Deutsche Forschungsgemeinschaft (AL 1348/8-1, INST 186/1237-1 and INST 186/1324-1) is gratefully acknowledged.

## Conflict of interest

The authors declare no conflict of interest.

**Keywords:** [4]helicenes · asymmetric catalysis · Au catalysis · enantioselective synthesis · ligand design

**How to cite:** *Angew. Chem. Int. Ed.* **2020**, *59*, 5660–5664  
*Angew. Chem.* **2020**, *132*, 5709–5713

- [1] a) Y. Shen, C.-F. Chen, *Chem. Rev.* **2012**, *112*, 1463–1535; b) M. Gingras, *Chem. Soc. Rev.* **2013**, *42*, 968–1006; c) M. Gingras, G. Félix, R. Peresutti, *Chem. Soc. Rev.* **2013**, *42*, 1007–1050; d) M. Gingras, *Chem. Soc. Rev.* **2013**, *42*, 1051–1095; e) C.-F. Chen, Y. Shen, *Helicene Chemistry, From Synthesis to Applications*, Springer, Berlin, **2017**.

- [2] a) J. Elm, J. Lykkebo, T. J. Sørensen, B. W. Laursen, K. V. Mikkelsen, *J. Phys. Chem. A* **2011**, *115*, 12025–12033; b) K. Kato, Y. Segawa, K. Itami, *Synlett* **2019**, *30*, 370–377.
- [3] C. Goedicke, H. Stegemeyer, *Tetrahedron Lett.* **1970**, 937–940.
- [4] R. H. Martin, M. J. Marchant, *Tetrahedron Lett.* **1972**, 3707–3708.
- [5] H. Marom, S. Pogodin, I. Agranat, *Polycyclic Aromat. Compd.* **2007**, *27*, 295–310.
- [6] P. Ravat, R. Hinkelmann, D. Steinebrunner, A. Prescimone, I. Bodoky, M. Juriček, *Org. Lett.* **2017**, *19*, 3707–3710.
- [7] a) M. S. Newman, R. M. Wise, *J. Am. Chem. Soc.* **1956**, *78*, 450–454; b) C. M. Kemp, S. F. Mason, *Chem. Commun.* **1965**, 559–560.
- [8] D. Nakano, M. Yamaguchi, *Tetrahedron Lett.* **2003**, *44*, 4969–4971.
- [9] K. Kano, H. Kamo, S. Negi, T. Kitae, R. Takaoka, M. Yamaguchi, H. Okubo, M. Hiram, *J. Chem. Soc. Perkin Trans. 2* **1999**, 15–21.
- [10] T. R. Kelly, X. Cai, F. Damkaci, S. B. Panicker, B. Tu, S. M. Bushell, I. Cornella, M. J. Piggott, S. Richard, M. Caverio, Y. Zhao, S. Jasmin, *J. Am. Chem. Soc.* **2007**, *129*, 376–386.
- [11] a) J. Caeiro, D. Peña, A. Cobas, D. Pérez, E. Guitián, *Adv. Synth. Catal.* **2006**, *348*, 2466–2474; b) I. G. Stará, I. Starý, M. Tichý, J. Závada, V. Hanuš, *J. Am. Chem. Soc.* **1994**, *116*, 5084–5088.
- [12] For diastereoselective syntheses, see: a) M. C. Carreño, S. García-Cerrada, A. Urbano, *J. Am. Chem. Soc.* **2001**, *123*, 7929–7930; b) Y. Ogawa, T. Ueno, M. Karikomi, K. Seki, K. Haga, T. Uyehara, *Tetrahedron Lett.* **2002**, *43*, 7827–7782; c) Y. Ogawa, M. Toyama, M. Karikomi, K. Seki, K. Haga, T. Uyehara, *Tetrahedron Lett.* **2003**, *44*, 2167–2170; d) M. C. Carreño, S. García-Cerrada, A. Urbano, *Chem. Eur. J.* **2003**, *9*, 4118–4131; e) M. Šámal, S. Chercheja, J. Rybáček, J. V. Chocholoušová, J. Vacek, L. Bednářová, D. Šaman, I. G. Stará, I. Starý, *J. Am. Chem. Soc.* **2015**, *137*, 8469–8474; f) A. Urbano, A. M. del Hoyo, A. Martínez-Carrión, M. C. Carreño, *Org. Lett.* **2019**, *21*, 4623–4627.
- [13] For diastereoselective syntheses, see: a) M. C. Carreño, S. García-Cerrada, M. J. Sanz-Cuesta, A. Urbano, *Chem. Commun.* **2001**, 1452–1453; b) M. C. Carreño, A. Enríquez, S. García-Cerrada, M. J. Sanz-Cuesta, A. Urbano, F. Maseras, A. Nonell-Canals, *Chem. Eur. J.* **2008**, *14*, 603–620; c) A. Latorre, A. Urbano, M. C. Carreño, *Chem. Commun.* **2011**, *47*, 8103–8105.
- [14] a) M. Alcarazo, *Chem. Eur. J.* **2014**, *20*, 7868–7877; b) M. Alcarazo, *Acc. Chem. Res.* **2016**, *49*, 1797–1805; c) L. D. M. Nicholls, M. Alcarazo, *Chem. Lett.* **2019**, *48*, 1–13.
- [15] a) E. González-Fernández, L. D. M. Nicholls, L. D. Schaaf, C. Farès, C. W. Lehmann, M. Alcarazo, *J. Am. Chem. Soc.* **2017**, *139*, 1428–1431; b) L. D. M. Nicholls, M. Marx, T. Hartung, E. González-Fernández, C. Golz, M. Alcarazo, *ACS Catal.* **2018**, *8*, 6079–6085; c) J. Zhang, M. Simon, C. Golz, M. Alcarazo, *Angew. Chem. Int. Ed.* **2020**, <https://doi.org/10.1002/anie.201915456>; *Angew. Chem.* **2020**, <https://doi.org/10.1002/ange.201915456>.
- [16] CCDC 1958105, 1958106, 1958107, 1958108, 1958109, 1958110, 1958111, and 1958146 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.
- [17] a) A. C. Shaikh, D. S. Ranade, P. R. Rajamohanan, P. P. Kulkarni, N. T. Patil, *Angew. Chem. Int. Ed.* **2017**, *56*, 757–761; *Angew. Chem.* **2017**, *129*, 775–779; b) A. S. Hacker, M. Pavano, J. E. Wood, C. E. Immoos, H. Hashimoto, S. P. Genis, D. K. Frantz, *J. Org. Chem.* **2018**, *83*, 510–515.
- [18] The same effect has been observed in TADDOL-derived phosphoramidites, see: H. Teller, M. Corbet, L. Mantilli, G. Gopakumar, R. Goddard, W. Thiel, A. Fürstner, *J. Am. Chem. Soc.* **2012**, *134*, 15331–15342.
- [19] a) A. Fürstner, V. Mamane, *J. Org. Chem.* **2002**, *67*, 6264–6267; b) V. Mamane, P. Hannen, A. Fürstner, *Chem. Eur. J.* **2004**, *10*, 4556–4575.
- [20] H. Tinnermann, L. D. M. Nicholls, T. Johannsen, C. Wille, C. Golz, R. Goddard, M. Alcarazo, *ACS Catal.* **2018**, *8*, 10457–10463.
- [21] Y. Yoshida, Y. Nakamura, H. Kishida, H. Hayama, Y. Nakano, H. Yamoshi, G. Saito, *CrystEngComm* **2017**, *19*, 3626–3632.
- [22] H. D. Flack, G. Bernardinelli, *Chirality* **2008**, *20*, 681–690.
- [23] H. Okubo, M. Yamaguchi, C. Kabuto, *J. Org. Chem.* **1998**, *63*, 9500–9509.

Manuscript received: December 11, 2019

Accepted manuscript online: January 21, 2020

Version of record online: February 20, 2020