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# Asymmetric Synthesis of Axially Chiral 1-Aryl-5,6,7,8-tetrahydroquinolines by Cobalt-Catalyzed [2 + 2 + 2] Cycloaddition Reaction of 1-Aryl-1,7-octadiynes and Nitriles

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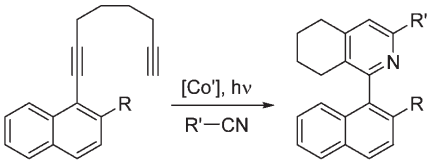


up to 94% *ee*

R = OMe, OCO*t*-Bu, OBn, COOMe, $CH_2OH$

R' = Ph, Me, *t*-Bu, 2-furyl, substituted Ph, piperidinyl

The asymmetric synthesis of a range of axially chiral 2-arylpyridines by a cobalt-catalyzed [2 + 2 + 2] cycloaddition reaction is described. The use of a planar chiral (1-neomenthylindenyl)cobalt(COD) complex under photochemical conditions is the key for reacting the 1-naphthyldiynes with a range of differently functionalized nitriles, giving the enantiomeric atropoisomers with high chemical yields and enantiomeric excesses of up to 94% ee.

## Introduction

The synthesis of axially chiral biaryls has attracted a lot of attention in the recent decades due to the emergence in a large number of natural products containing structures with a stereogenic biaryl axis, chiral auxiliaries and as ligands of catalyst systems.[1] Furthermore, their chiral element atropisomerism has received increased attention because of its occurrence in different drugs.[2] Although a number of chiral biaryls are commercially available, a set of methodologies for the direct stereoselective access to compounds possessing a chiral biaryl fragment and avoiding separation steps has been explored.[3] The experimental work reported so far showed that asymmetric catalytic cross-coupling reactions have been found to be one of the most popular and versatile methodologies for this purpose.[4] Among the different cross-coupling reactions the asymmetric Suzuki−Miyaura coupling has since the developments during the past decade proven to be most versatile and valuable for the preparation of specific chiral biaryls.[5] Another important method that has initially seen largely achiral applications in biaryl synthesis partially coupled with subsequent resolution of the racemates is the transition-metal-mediated oxidative coupling of arenes.[6] Recently, an increasing number of asymmetric metal-catalyzed oxidative couplings have been studied, especially those based

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(3) General reviews on transition-metal-mediated aryl−aryl coupling reactions: (a) Hassan, J.; Sévignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359. (b) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174.

(4) General overviews: (a) Bolm, C.; Hildebrand, J. P.; Muñiz, K.; Hermanns, N. *Angew. Chem., Int. Ed.* **2001**, *40*, 3284. (b) Wallace, T. W. *Org. Biomol. Chem.* **2006**, *4*, 3197.

(5) Recent work: (a) Uozumi, Y.; Matsuura, Y.; Arakawa, T.; Yamada, Y. M. A. *Angew. Chem., Int. Ed.* **2009**, *48*, 2708. (b) Bermejo, A.; Ros, A.; Fernández, R.; Lassaletta, J. M. *J. Am. Chem. Soc.* **2008**, *130*, 15798. (c) Sawai, K.; Tatumi, R.; Nakahodo, T.; Fujihara, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 6917. (d) Genov, M.; Almorín, A.; Espinet, P. *Tetrahedron: Asymmetry* **2007**, *18*, 625. (e) Genov, M.; Almorín, A.; Espinet, P. *Chem.—Eur. J.* **2006**, *12*, 9346. Overview on the early developments: (f) Baudoin, O. *Eur. J. Org. Chem.* **2005**, 4223.

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on copper, vanadium, and ruthenium complexes containing chiral ligands.[7]

In the recent decade the [2 + 2 + 2] cycloaddition reactions have evolved into a versatile member of the synthetic chemists' toolbox for the preparation of functionalized arenes.[8] Its potential as a key transformation in total synthesis has been demonstrated.[9] Cobalt complexes have continuously found widespread use in a number of cycloaddition reactions, and new catalyst complexes have been reported.[10] However, the use of CpCo(COD) in combination with irradiation for the activation of the catalyst turned out to be an especially mild method.[8e,11] It can be used in combination with asymmetric reactions, such as, e.g., cyanations for the racemization-free preparation of chiral compounds.[12] We first reported chiral cobalt(I) catalysts suitable for the asymmetric version of the [2 + 2 + 2] cycloaddition reaction,[13] in particular for the preparation of atropoisomeric chiral pyridines and biaryls.[14] The catalyst complex **1a/b** has been found to be most effective for this kind of transformation (Scheme 1), which otherwise needed an additional resolution step.[15] Others have developed catalyst systems based on Rh or Ir complexes.[16,17] The use of these late transition metals in the selective preparation of atropochiral biaryls has been compiled only recently.[18]

**SCHEME 1. Chiral Cobalt(I) Catalyst 1**

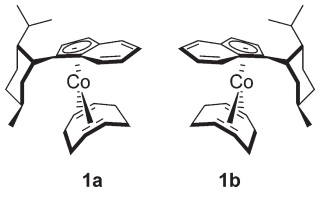
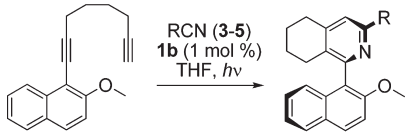



**TABLE 1. Asymmetric Synthesis of Enantiomeric Isoquinolines Using the Chiral Co Complex 1b**




| nitrile | biaryl | $T$ (°C) | yield[a] (%) | selectivity (% *ee*)[b] |
|---|---|---|---|---|
| PhCN (**3**) | **6** | −20 | 86 | 93 |
| MeCN (**4**) | **7** | 3 | 88 | 88 |
| *t*-BuCN (**5**) | **8** | 3 | 74 | 88 |

[a]Yield after chromatography. [b]Measured in reaction mixture.

We report here on our investigations using the chiral cobalt(I) complex **1** for the preparation of functionalized chiral biaryls using different diynes and nitriles to gain information on the broadness of this particular cobalt-based asymmetric methodology and structural features required to obtain good yields and high enantioselectivities.

## Results and Discussion

During our initial experiments, we investigated the use of catalyst **1a** or **1b** for the preparation of chiral isoquinoline derivatives from diynes and rather simple nitriles containing alkyl groups or a phenyl group as the only substituents.[14] The obtained results showed that the performance of the reaction of diyne **2** with benzonitrile (**3**), acetonitrile (**4**), or *tert*-butylnitrile (**5**) and catalyst **1b** under irradiation of the reaction mixture with visible light ($\lambda$ = 350−500 nm) led to successful asymmetric induction in the cycloaddition process, yielding the desired (*R*)-configured atropochiral isoquinolines **6**−**8** with very good yields and enantioselectivities (Table 1).

The screening for the optimal reaction conditions proved −20 °C as the optimal temperature for obtaining the highest enantiomeric excess for the cycloaddition product while at higher temperatures slightly lower selectivities were observed.

Our hitherto obtained data show that the chirality of the intact catalyst provided by the neomenthyl group attached to the indenyl ring is responsible for the chiral induction during the cycloaddition process. This also rules out any other predominant catalytically active species that might result from the decomposition of the chiral complex **1** leading to metallic cobalt, which has also been shown to be catalytically active.[19]

(7) Chiral Cu complexes: (a) Kozlowski, M. C.; Morgan, B. J.; Linton, E. C. *Chem. Soc. Rev.* **2009**, *38*, 3193 and references cited therein. Chiral V complexes: (b) Takizawa, S.; Katayama, T.; Sasi, H. *Chem. Commun.* **2008**, 4113 and references cited therein. Chiral Ru complexes: (c) Irie, R.; Masutani, K.; Katsuki, T. *Synlett* **2000**, 1433.

(8) Recent reviews: (a) Galan, B. R.; Rovis, T. *Angew. Chem., Int. Ed.* **2009**, *48*, 2830 and references cited therein. (b) Varela, J. A.; Saá, C. *Synlett* **2008**, 2571. (c) Scheuermann neé Taylor, C. J.; Ward, B. D. *New J. Chem.* **2008**, *32*, 1850. (d) Hess, W.; Treutwein, J.; Hilt, G. *Synthesis* **2008**, 3537. (e) Agenet, N.; Busine, O.; Slowinski, F.; Gandon, V.; Aubert, C.; Malacria, M. *Org. React.* **2007**, *68*, 1. (f) Heller, B.; Hapke, M. *Chem. Soc. Rev.* **2007**, *36*, 1085. (g) Tanaka, K. *Synlett* **2007**, 1977. (h) Chopade, P. R.; Louie, J. *Adv. Synth. Catal.* **2006**, *348*, 2307.

(9) First reported use in the synthesis of (±)-estrone: (a) Funk, R. L.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1980**, *102*, 5253 and references cited therein. Recently reported example: (b) Nicolaou, K. C.; Tang, Y.; Wang, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 597. (c) Li, P.; Menche, D. *Angew. Chem., Int. Ed.* **2009**, *48*, 5078.

(10) Examples: (a) Geny, A.; Agenet, N.; Iannazzo, L.; Malacria, M.; Aubert, C.; Gandon, V. *Angew. Chem., Int. Ed.* **2009**, *48*, 1810. (b) Hilt, G.; Hengst, C.; Hess, W. *Eur. J. Org. Chem.* **2008**, 2293.

(11) (a) Heller, B.; Sundermann, B.; Buschmann, H.; Drexler, H.-J.; You, J.; Holzgrabe, U.; Heller, E.; Oehme, G. *J. Org. Chem.* **2002**, *67*, 4414. (b) Heller, B.; Sundermann, B.; Fischer, C.; You, J.; Chen, W.; Drexler, H.-J.; Knochel, P.; Bonrath, W.; Gutnov, A. *J. Org. Chem.* **2003**, *68*, 9221. (c) Gutnov, A.; Abaev, V.; Redkin, D.; Fischer, C.; Bonrath, W.; Heller, B. *Synlett* **2005**, 1188.

(12) Heller, B.; Redkin, D.; Gutnov, A.; Fischer, C.; Bonrath, W.; Karge, R.; Hapke, M. *Synthesis* **2008**, 69.

(13) Synthesis of the chiral cobalt(I) complexes: (a) Gutnov, A.; Drexler, H.-J.; Oehme, G.; Spannenberg, A.; Heller, B. *Organometallics* **2004**, *23*, 1002. (b) Gutnov, A.; Heller, B.; Drexler, H.-J.; Spannenberg, A.; Oehme, G. *Organometallics* **2003**, *22*, 1550.

(14) (a) Gutnov, A.; Heller, B.; Fischer, C.; Drexler, H.-J.; Spannenberg, A.; Sundermann, C.; Sundermann, B. *Angew. Chem., Int. Ed.* **2004**, *43*, 3795. (b) Heller, B.; Gutnov, A.; Fischer, C.; Drexler, H.-J.; Spannenberg, A.; Redkin, D.; Sundermann, C.; Sundermann, B. *Chem.—Eur. J.* **2007**, *13*, 1117.

(15) Hrdina, R.; Stará, I. G.; Dufková, L.; Mitchel, S.; Císařová, I.; Kotora, M. *Tetrahedron* **2006**, *62*, 968.

(16) Recent examples for Rh-catalyzed reactions: (a) Oppenheimer, J.; Johnson, W. L.; Figueroa, R.; Hayashi, R.; Hsung, R. P. *Tetrahedron* **2009**, *65*, 5001. (b) Imase, H.; Suda, T.; Shibata, Y.; Noguchi, K.; Hirano, M.; Tanaka, K. *Org. Lett.* **2009**, *11*, 1805. (c) Doherty, S.; Smyth, C. H.; Harrington, R. W.; Clegg, W. *Organometallics* **2008**, *27*, 4837. (d) Nishida, G.; Ogaki, S.; Yusa, Y.; Yokozawa, T.; Noguchi, K.; Tanaka, K. *Org. Lett.* **2008**, *10*, 2849. (e) Shibata, T.; Otomo, M.; Tahara, Y.; Endo, K. *Org. Biomol. Chem.* **2008**, *6*, 4296. (f) Review: Tanaka, K. *Synlett* **2007**, 1977. (g) Nishida, G.; Noguchi, K.; Hirano, M.; Tanaka, K. *Angew. Chem., Int. Ed.* **2007**, *46*, 3951.

(17) Recent examples for Ir-catalyzed reactions: (a) Review: Shibata, T. In *Iridium Complexes in Organic Synthesis*; Oro, L. A., Claver, C., Eds.; Wiley-VCH Verlag: Weinheim, 2009; p 277 and references cited therein.

(18) Tanaka and Shibata have very recently compiled the use of transition-metal-catalyzed asymmetric [2 + 2 + 2] cycloaddition reactions in the synthesis of chiral biaryls; see: (a) Tanaka, K. *Chem. Asian J.* **2009**, *4*, 508. (b) Shibata, T.; Tsuchikama, K. *Org. Biomol. Chem.* **2008**, *6*, 1317.

(19) See: (a) Vitulli, G.; Bertozzi, S.; Lazzaroni, R.; Salvadori, P. *J. Organomet. Chem.* **1986**, *307*, C35. (b) Vitulli, G.; Bertozzi, S.; Vignali, M.; Lazzaroni, R.; Salvadori, P. *J. Organomet. Chem.* **1987**, *326*, C33.

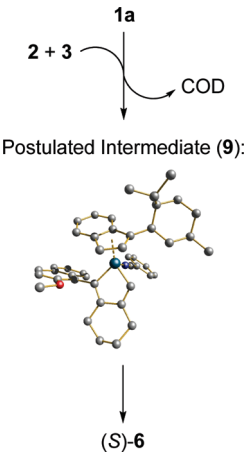


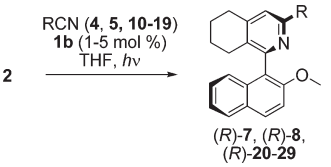

**FIGURE 1.** Proposed cobaltacyclopentadienyl intermediate (**9**) of the cycloaddition reaction.

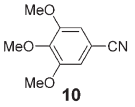
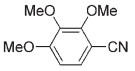
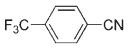
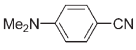
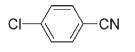
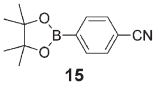
The initial idea for the formation of the chiral axis of the biaryl products points out that the chirality will be preformed in the cobaltacyclopentadienyl intermediate, which is formed during the oxidative cyclization process between the metal center and the two alkyne moieties. The subsequent coordination of the substrate nitrile molecule then only fixes the conformation, which has already been formed, no matter if it coordinates *side-on* or *end-on* to the cobalt center.[20] The energy-minimized structure (B3LYP/6-31G*) of the potential intermediate (**9**) derived from **1a** with *end-on* coordinated nitrile is displayed in Figure 1.

For the evaluation of further structural parameters in the diyne and nitrile substrates, which can play a significant role in the outcome (yield, selectivity) of the reaction, we first investigated the reaction of diyne **2** with an array of different nitriles (Table 2). In general, we used the optimized reaction conditions at −20 °C for the evaluation of the nitrile substrates to obtain comparable results.

The reaction usually requires 1−2 mol % of catalyst **1b** and 48−72 h irradiation time at −20 °C to be completed. The yields are in general moderate to very good, and the selectivities are generally above 75% ee. An exception is the use of nitrile **11**, possessing an ortho substituent, where 5 mol % of **1b** was needed for the reaction to yield reasonable amounts of biaryl **21**. The reaction became extremely sluggish when using the more hindered 2,4,6-trimethoxybenzonitrile even at 20 °C, and only traces of the corresponding product were determined at all. The examination of benzonitriles substituted at the 4-position, like **12**−**15** (entries 5−8, Table 2), gave lower yields compared to alkyl-substituted nitriles (entries 1, 2, and 12, Table 2) regardless of the electronic nature of the substituent. Furthermore, the nature of the substituent in the 4-position seems to have little effect on the selectivity, as exemplified by comparing entries 5 and 6 in Table 2. However, the yield of biaryl **23** for the reaction of **2** with 4-dimethylaminobenzonitrile (**13**) gave only around 6% yield of **23** with 81% ee selectivity at a reaction temperature of −20 °C.

**TABLE 2. Screening of Different Nitriles**



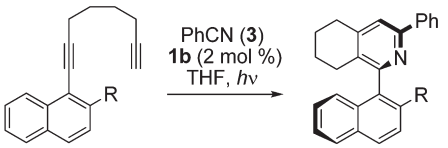

| entry | nitrile | biaryl | T/t (°C/h) | yield (%)[a] | sel. (% *ee*)[b] |
|---|---|---|---|---|---|
| 1 | MeCN (**4**) | **7**[c] | −20 / 72 | 66 | 90 |
| 2 | *t*-BuCN (**5**) | **8**[d] | −20 / 72 | 79 | 91 |
| 3 |  **10** | **20**[d] | −20 / 72 | 64 | 91 |
| 4 |  **11** | **21**[e] | −20 / 72 | 44 | 94 |
| 5 |  **12** | **22**[d] | −20 / 72 | 59 | 86 |
| 6 |  **13** | **23**[d] | −10 / 72 | 58 | 83 |
| 7 |  **14** | **24**[d] | 5 / 42 | 10 | -[f] |
| 8 |  **15** | **25**[d] | −20 / 66 | 45 | 75 |
| 9 |  **16** | **26**[c] | −20 / 48 | 81 | 91 |
| 10 |  **17** | **27** | −20 / 48 | (13)[g] | -[f] |
| 11 |  **18** | **28** | 0/15 / 48 | - | - |
| 12 |  **19** | **29**[c] | −20 / 48 | 89 | 87 |

[a]Yield after chromatography. [b]Measured in reaction mixture. [c]1 mol % of catalyst **1b**. [d]2 mol % of catalyst **1b**. [e]5 mol % of catalyst **1b**. [f]Not determined. [g]No further characterization.

Performing the reason at −10 °C provided **23** in much higher yield with no loss in selectivity. The use of 4-chlorobenzonitrile (**14**) gave only a 10% yield at a reaction temperature of 5 °C, and no further optimization was tried. The interesting boryl group-functionalized biaryl **25** resulted

(20) The modes of coordination of the nitrile to the cobalt center have been discussed on the basis of computational data: (a) Dahy, A. A.; Yamada, K.; Koga, N. *Organometallics* **2009**, *28*, 3636. The reaction pathways of the cyclotrimerization of alkynes was also the subject of detailed theoretical studies: (b) Agenet, N.; Gandon, V.; Vollhardt, K. P. C.; Malacria, M.; Aubert, C. *J. Am. Chem. Soc.* **2007**, *129*, 8860.

**TABLE 3. [2 + 2+2] Cycloaddition Reactions Using Naphthyldiynes 30−33 Differently Functionalized in the 2-Position**




**30**: R = O(CO)*t*-Bu
**31**: R = OBn
**32**: R = COOMe
**33**: R = $CH_2OH$

**34**: R = O(CO)*t*-Bu
**35**: R = OBn
**36**: R = COOMe
**37**: R = $CH_2OH$

| entry | diyne | biaryl | T/t (°C/h) | yield[a] (%) | selectivity (% *ee*)[c] |
|---|---|---|---|---|---|
| 1 | **30** | **34** | −20/72 | 11 | 52[d] |
| 2 | **31** | **35** | −20/72 | 9 | 22[d] |
| 3 | **31** | **35**[b] | +3/36 | 50 | 55 |
| 4 | **32** | **36** | −20/72 | 17 | 90 |
| 5 | **32** | **36** | +3/48 | 65 | 87 |
| 6 | **33** | **37** | −20/72 | 20 | 36 |

[a]Yield after chromatography. [b]5 mol % of catalyst **1b** was used. [c]Measured in the isolated products. [d]Determination of selectivity was difficult due to small amounts of product: the given value represents the most reliable result from the measurements.

from the successful reaction of **2** with nitrile **15** with acceptable yield and slightly lower selectivity compared to other nitriles. For the reaction of the heterocyclic nitriles **17** and **18** with diyne **2**, the reactions yielded the product either with very low (ca. 13% for **27**) or basically no yield even at 20 °C for **28**. In both cases, when either **17** or **18** was used, the reaction mixture turned red to violet over the course of the reaction, showing the typical color of cobalt complexes with heterocyclic ligands (vide infra). This is in contrast to the use of furan derivative **16**, which gave the expected cyclization product **26** with excellent enantioselectivity and very good yield. Finally, when *N*-cyanopiperidine (**19**, entry 12, Table 2) was used, both high yield and selectivity were obtained, thus making these results comparable to the values obtained for alkyl-substituted nitriles **4** and **5** (entries 1 and 2, Table 2), containing no heteroatom. Obviously, the nitrogen adjacent to the nitrile functionality lacks a negative influence on the cycloaddition reaction, contributing to the generality of the methodology.

We also investigated the effects of structural variation of the substituent in the 2-position of the diyne naphthyl ring system. Several diynes **30**−**33** bearing different functionalities, such as esters, ether, or a free hydroxyl group, were synthesized for this purpose in general using the standard Sonogashira coupling methodology.[21] Diyne **33** possessing a free hydroxyl group was conveniently prepared from diyne **32** by reduction of the ester functionality with Red-Al, yielding **33** directly with acceptable yield (69%). The cocyclotrimerization experiments of **30**−**33** with benzonitrile (**3**) were performed according to the conditions given in Table 3. Surprisingly, in the reactions performed at −20 °C, a high selectivity of 90% ee was observed only for the methyl ester substituted biaryl **36** (entry 4). In all other cases, the selectivities were rather low, especially when the results were compared with the selectivities reported in Table 2. The best selectivity after **36** was obtained in the case of biaryl **34** with the pivaloyl-protected hydroxyl group in the 2-position, although only 52% selectivity was determined (entry 1). However, the yields were very low in the cases at low temperature (9−20%, entries 1, 2, 4, and 6) and acceptable at +3 °C. Compound **34** could only be isolated containing small amounts of impurities. The presence of a free hydroxyl group as in diyne **33** obviously has no significant influence on the outcome of the cycloaddition process in either direction. We exemplarily investigated the cocyclotrimerization reaction at a higher reaction temperature (+3 °C) for diynes **31** and **32**. The results showed, in analogy to earlier observations, that at higher temperatures the yields were strongly improved, and accordingly slightly lower selectivities are usually observed, as exemplified for biaryl **36** (entry 5). Interestingly, for biaryl **35** with 55% ee, a higher selectivity was observed than at lower temperature (entry 3), which appears unusual. However, this might be due to problems of determination of the selectivity due to the low yield at the reaction temperature of −20 °C (entry 2). In comparison, the substituent in the 2-position of the naphthyl ring seems to have a higher impact, especially on the selectivity of the cycloaddition process compared to the nature of the nitrile used (Table 2). The rather small methoxy substituent therefore proves to be a highly suited functionality, as was disclosed for the carboxy methyl ester group in **36**.

The observed incompatibility of the cycloaddition reaction with heterocyclic nitriles containing sulfur or nitrogen was exemplarily addressed for 2-cyanopyridine (**18**). The expected reaction product **28** would contain the 2,2′-bipyridine moiety, which is one of the most widely used bidentate ligands for transition-metal complexes.[22] It is proposed that the formation of biaryl **28** would give rise to the formation of a stable cobalt(I) complex, leading to an inhibition of catalytic activity after formation of small amounts of **28**. To prevent this problem, the protection of the nitrogen atom in **28** was considered, which would yield a product without possessing the strong coordination abilities of the 2,2′-bipyridine fragment. A simple protection can be made by the formation of the *N*-oxide of **28**, which is an easy accessible yellow solid.[23] However, use of the *N*-oxide was found to be unsuccessful because no biaryl product from the cobalt-catalyzed cycloaddition process was observed. The fast darkening of the reaction mixture unlike the other reactions presumably indicated the occurrence of some unwanted side reactions or catalyst decomposition under our reaction conditions. Therefore, we decided to investigate the inhibition process, which is assumed in the reaction of diyne **2** with nitrile **18**. For this purpose, we synthesized the CpCo(I)−2,2′-bipyridine complex, CpCo(bpy), independently as a model compound for the catalyst inhibition product and proved its structure by X-ray crystallography (Scheme 2).[24] We also investigated if this exchange reaction can occur under photochemical conditions and found that in the reaction of CpCo(COD) with 1 equiv of bpy in THF-$d_8$ the expected complex CpCo(bpy) is indeed formed in a 3:1 ratio with unreacted starting material after 36 h of irradiation. The

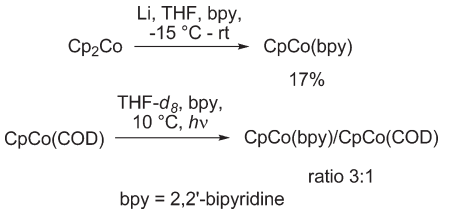
(21) The detailed synthetic procedures are given in the Experimental Section.

(22) (a) Hapke, M.; Brandt, L.; Lützen, A. *Chem. Soc. Rev.* **2008**, *37*, 2782. (b) Newkome, G. R.; Patri, A. K.; Holder, E.; Schubert, U. S. *Eur. J. Org. Chem.* **2004**, 235. (c) Kaes, C.; Katz, A.; Hosseini, M. W. *Chem. Rev.* **2000**, *100*, 3553.

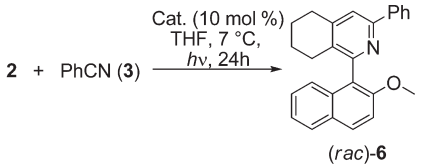
(23) Ochiai, E. *J. Org. Chem.* **1953**, *18*, 534.

(24) The complex was prepared according to the following work: (a) Jonas, K.; Deffense, E.; Habermann, D. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 716. (b) Hapke, M.; Spannenberg, A. *Acta Crystallogr.* **2009**, *E65*, m93–37.

**SCHEME 2. Synthesis of a CpCo(I)−Bipyridine Complex**




**SCHEME 3. Investigation of the Inhibition of Cycloaddition Reactions by 2,2′-Bipyridine as the Chelating Ligand**



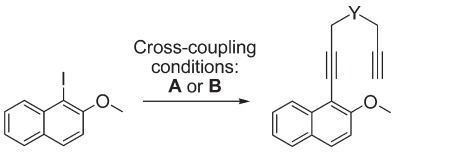

a) Cat.: CpCo(bpy)
**Cycloaddition reaction: no formation of 6**
b) Cat.: CpCo(COD), bpy (12.5 mol %)
**Cycloaddition reaction: ca. 49% GC yield of 6**
c) Cat.: CpCo(COD), bpy (60 mol %)
**Cycloaddition reaction: ca. 6% GC yield of 6**

bipyridine complex formation was proved by comparison with the $^1$H NMR spectra of a solution of isolated CpCo(bpy) in THF-$d_8$. Four protons of the coordinated 2,2′-bipyridine present remarkable proton NMR shifts (10.2 and 6.7 ppm), which are diagnostic for the coordination. The exchange process can furthermore be observed optically by the rapid change of color leading to an intense purple upon irradiation of the clear yellow solution.

Evaluation of complex CpCo(bpy) as catalyst in the cycloaddition reaction between diyne **2** and PhCN (**3**) showed that no consumption of either the diyne or the nitrile was observed (Scheme 3). However, when CpCo(COD) and 2,2′-bipyridine were added separately to the reaction mixture, the inhibition depended on the amount of bpy added. In the case of a slight excess of bpy with respect to CpCo(COD) the conversion of the diyne is still 49%, while with 6 equiv of bpy the conversion is only about 6%. These results can be therefore interpreted to mean that with only a slight excess of bpy added the cycloaddition reaction is not immediately completely inhibited and **6** can be formed to a certain extent. On the other hand, a large excess of bpy quickly led to the photochemical exchange reaction presented above, forming CpCo(bpy) as a catalytically completely inactive cobalt species.

As a final NMR experiment, we reacted CpCo(COD) with a slight excess of diyne **2** and 2-cyanopyridine (**18**) in THF-$d_8$ in a sealed tube. The $^1$H NMR analysis after irradiation for 14 h at 10 °C showed the large consumption of diyne **2** and about one-third of the CpCo(COD), indicated by the formation of free COD. The characteristically shifted signals for the formation of a CpCo−bipyridine complex were again observed in the proton NMR. The formation also became optically recognizable because we again observed the formation of a strongly colored reaction solution after a short irradiation time. After workup, the formation of biaryl **28** was corroborated by ESI mass spectroscopy. These findings can therefore be interpreted to mean that the presence of 2,2′-bipyridine as a structural fragment of the reaction product **28** from the cocyclotrimerization of **18** with **2** can indeed form a

**SCHEME 4. Synthesis of Diynes 39−43**




**38**

**39** : Y = $CH_2$ (**A**, 56%)
**40** : Y = NMe (**A**, 66%)
**41** : Y = O (**B**, 35%)
**42** : Y = $(CH_2)_3$ (**B**, 55%)
**43** : Y = $(CH_2)_4$ (**B**, 59%)

Cross-coupling conditions:
**A**) $Pd(PPh_3)_4$, $ZnCl_2$, piperidine, diyne, $I_2$, 6 h, 70 °C
**B**) $Pd(PPh_3)_4$ or $Pd_2dba_3{\cdot}CHCl_3$/dppf, CuI, THF/$Et_3N$, diyne addition via syringe pump, 45-50 °C

stable and observable cobalt complex which is able to inhibit the cycloaddition reaction under our reaction conditions. Structural parameters of the products can be a key to success, as demonstrated by Saá et al., who showed that 3-substituted 2,2′-bipyridines can be made successfully by cycloaddition reactions using $CpCo(CO)_2$ as the catalyst. This can be explained because substituents in the 3-position prevent the optimal planar arrangement of both pyridine rings necessary for the most effective complexation of the metal center.[25] However, work by Chelucci et al. provided the possibility of synthesizing substituted 2,2′-bipyridines successfully using CpCo(COD) as the catalyst with acetylene under rather harsh conditions.[26] Contrary to the behavior of the reagent based on the CpCo fragment are reagents prepared from cobalt(II) salts, bisphosphanes, and reductants like elementary zinc, as reported by Okamoto et al.[27] The generated catalysts yield a large array of 2,2′-bipyridines, including a few examples of 3-unsubstituted 2,2′-bipyridines with mostly high yields. Obviously, these catalysts are less susceptible to catalyst inhibition under the reaction conditions reported (50 °C, NMP as the solvent) compared to our approach.

To further investigate structural details and requirements for the cycloaddition reaction we evaluated the reactivity of several diyne substrates, containing different spacer units between the two alkyne functionalities. For this purpose, we needed to synthesize the various diynes **39**−**43** from 1-iodo-2-methoxynaphthalene (**38**) and the appropriate diyne using $sp^2$−sp cross-coupling methodologies (Scheme 4).[28] We utilized two slightly different coupling conditions. Procedure A used a protocol developed by Crisp et al. based on the use of $ZnCl_2$ and piperidine together with $Pd(PPh_3)_4$ as the catalyst.[29] For procedure B, traditional palladium-catalyzed Sonogashira reaction conditions were applied while adding the naphthyl iodide **38** continously over time via a syringe pump. The isolated yields for both methods are in the same range between 55 and 66%, except for the coupling of **38** with dipropargyl

(25) (a) Varela, J. A.; Castedo, L.; Saá, C. *J. Am. Chem. Soc.* **1998**, *120*, 12147. (b) Varela, J. A.; Castedo, L.; Maestro, M.; Mahía, J.; Saá, C. *Chem.—Eur. J.* **2001**, *7*, 5203.

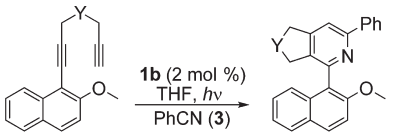
(26) (a) Chelucci, G. *Tetrahedron: Asymmetry* **1995**, *6*, 811. (b) Botteghi, C.; Chelucci, G.; Chessa, G.; Delogu, G.; Gladiali, S.; Soccolini, F. *J. Organomet. Chem.* **1986**, *304*, 217. The cycloaddition reaction was performed at 100 °C with a high acetylene pressure (12 atm).

(27) Goswami, A.; Ohtaki, K.; Kase, K.; Ito, T.; Okamoto, S. *Adv. Synth. Catal.* **2008**, *350*, 143.

(28) Negishi, E.; Anastasia, L. *Chem. Rev.* **2003**, *103*, 1979.

(29) Crisp, G. T.; Turner, P. D.; Stephens, K. A. *J. Organomet. Chem.* **1998**, *570*, 219.

**TABLE 4. Synthesis of Pyridine Derivatives with Various Ring Systems in the Backbone**




**39** : Y = $CH_2$
**40** : Y = NMe
**41** : Y = O
**42** : Y = $(CH_2)_3$
**43** : Y = $(CH_2)_4$

**44** : Y = $CH_2$
**45** : Y = NMe
**46** : Y = O
**47** : Y = $(CH_2)_3$
**48** : Y = $(CH_2)_4$

| entry | diyne | biaryl | T/t (°C/h) | yield[a] (%) | selectivity (% *ee*) |
|---|---|---|---|---|---|
| 1 | **39** | **44** | −20 | 72 | |
| 2 | **40** | **45** | −20 | 64 | |
| 3 | **41** | **46** | +5 | 59[b] | |
| 4 | **42** | **47** | +3 | [c,d] | |
| 5 | **43** | **48** | +3 | [d] | |

[a]Yield after chromatography. [b]Using 5 mol % of CpCo(COD) as catalyst. [c]6% conversion by GC. [d]Reactions using **3** and the terminally unsubstituted diynes under the same conditions for comparison did not yield any cycloaddition product either.

ether giving diyne **41**, where only 35% of the pure product was isolated.

The investigation of the [2 + 2 + 2] cycloaddition reaction of diynes **39**−**43** with benzonitrile (**3**) that could lead to either five-membered or larger rings in the backbone of the newly formed annelated pyridine was performed using catalyst **1b** or CpCo(COD) (Table 4). The results clearly show that the biaryls **44**−**46** (entries 1−3) can be formed in good chemical yields, but no enantiomeric excess was observed under these reaction conditions in either case. The use of diynes containing larger alkyl spacers between the alkyne moieties like in **42** and **43** should give rise to the formation of 7- or 8-membered rings in the backbone of the biaryls **47** and **48**, which are presumably rather stable against racemization around the biaryl axis. However, in these cases very low conversions or even no biaryl formation at all was observed. Control experiments using the terminally unsubstituted corresponding diynes did not yield any cycloaddition product either.

For a more detailed investigation on the lack of selectivity in the preparation of biaryls **44**−**46** we decided to use dynamic chiral HPLC because we were keen to find out to what extent the obvious instability of the formed biaryl axis is responsible for the racemization of the products. The investigation showed (Figure 2 shows the spectra for **44**) that at low temperatures (0 °C) both enantiomeric forms exist and that they can be separated under isothermic HPLC conditions. However, raising the temperature led to an increase of the plateau between the separated signals which belong to the achiral form, showing free, unhindered rotation around the biaryl C−C axis at temperatures higher than 30 °C. The free energy barrier to interconversion of the enantiomers of compound **44** was calculated to be $\Delta G^{\ddagger}$ = 89 kJ $mol^{-1}$ at 20 °C.[30] The barrier for the methylamino-substituted analogue **45** was found to be slightly lower, and

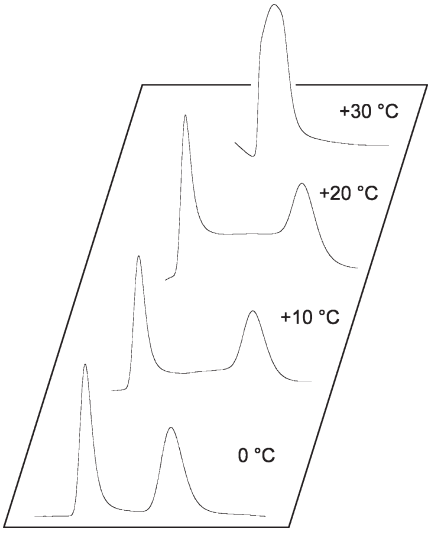



**FIGURE 2.** Dynamic HPLC of pyridine **44**.

free rotation was already observed at 20 °C. The analogous analytical chiral HPLC separation of **46** surprisingly turned out to be unsuccessful, and the enantiomers appeared to be inseparable, even when going to very low temperatures (up to −20 °C).[31] The observations are in contrast to those for the enantioselective synthesis of five-membered ring-annulated 1,4-diarylbenzenes via iridium-catalyzed [2 + 2 + 2] cycloaddition reactions from diynes and monoalkynes as recently reported by Shibata et al.[32] The products they obtained showed no racemization under conditions requiring up to 100 °C reaction temperature, therefore exhibiting a greatly enhanced stability of the configuration of the biaryl axis. It can be assumed that the presence of the sterically less demanding nitrogen (in comparison to the benzene C−H group) in the formed pyridine rings might play a vital role for the missing configurational stability of **44**−**46**.

## Conclusion

In summary, we presented an investigation of the asymmetric cobalt-catalyzed cocyclotrimerization between a range of diynes and a number of differently functionalized nitriles. The reaction can be successfully performed in general at −20 °C under optimized irradiation conditions, yielding the enantiomeric tetrahydroquinolines with mostly good yields and ee's up to 94%. We also took a closer look at the catalyst inactivation by product inhibition for heterocyclic nitriles that can form unhindered chelating ligands in the cyclization process. Finally, the synthesis of biaryls possessing a five-membered ring annulated at the pyridine moiety was investigated, and we found that the size of the ring is too small to prevent the slippage of the rings around the biaryl axis due to the presence of the ring nitrogen. Therefore, no enantioselectivity can be observed, although the obtained isolated yields were good. We are working toward the application of the cobalt-catalyzed process and the reaction of new substrates presenting interesting structural parameters.

(30) The quantitative treatment of the HPLC spectra and the calculation of the energy barrier for the interconversion from the rates following the Arrhenius equation was performed after: (a) Thede, R.; Haberland, D.; Fischer, C.; Below, E.; Langer, S. H. *J. Liq. Chromatogr. Relat. Technol.* **1998**, *21*, 2089. (b) For more recent approaches, see: Trapp, O. *Chirality* **2006**, *18*, 489 and cited references.

(31) The dynamic HPLC spectra for **45** and **46** can be found in the Supporting Information.

(32) Shibata, T.; Arai, Y.; Takami, K.; Tsuchikama, K.; Fujimoto, T.; Takebayashi, S.; Takagi, K. *Adv. Synth. Catal.* **2006**, *348*, 2475.

## Experimental Section

**General Procedures for the Synthesis of the Monoarylated Diynes. General Procedure 1.** 1-Naphthyl halides (30 mmol), $Pd(PPh_3)_4$ (1.74 g, 1.5 mmol), $ZnCl_2$ (818 mg, 6 mmol), piperidine (75 mL), diynes (60 mmol), and $I_2$ (20 mg) were stirred for 6 h at 70 °C under argon atmosphere. The reaction mixture was cooled to rt, diluted with an *n*-hexane−$Et_2O$ mixture (5:3), and stirred for an additional 1 h. Precipitated solids were filtered off and washed with the same mixture of solvents. The mother liquor was evaporated at high vacuum, and the products were separated by chromatography on silica gel using *n*-hexane−$Et_2O$ or petroleum ether/ethyl acetate in different proportions as the eluent.

**General Procedure 2.** The catalyst system (6 mol %, either $Pd(PPh_3)_4$ or $Pd_2dba_3 \cdot CHCl_3$/2 dppf) and CuI (15 mol %) were suspended in ca. 15 mL of THF in a Schlenk flask and stirred for several minutes, and then ca. 100 mL of $NEt_3$ as well as the diyne (2 equiv) were added. A solution of the naphthyl iodide in 10−15 mL THF was prepared separately. The latter solution was then charged in a 20 mL syringe and mounted to a syringe pump. The reaction mixture was then heated to 45−50 °C and the addition of the naphthyl iodide solution started (addition rate: 2.5−4 mL/h, about 10% of the solution was added immediately). After completion of the addition, the reaction mixture was stirred for another 20 h at the same temperature. After the mixture was cooled, satd $NH_4Cl$ solution was added and the mixture stirred under argon for 15 min. The crude mixture was filtered over Celite and the filtrate then extracted with ethyl acetate. The combined organic phases were washed with water and brine and dried over $Na_2SO_4$. After removal of all volatiles the residue was purified by column chromatography.

General note: During workup after the coupling reaction up to 14% of the diarylated diynes was separated as byproducts and identified by NMR and MS. However, these data are not detailed here.

**1-(1,7-Octadiynyl)-2-methoxynaphthalene (2)[14].** Compound **2** was prepared following the general procedure 1 using 1-iodo-2-methoxynaphthalene (**38**, 8.52 g, 30 mmol)[33] and 1,7-octadiyne (6.37 g, 60 mmol) to yield 5.28 g (68% yield) of pure product after chromatography with petroleum ether/ethyl acetate (6:1 v/v) on silica gel. Mp: 60−61 °C (*n*-hexane). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.27 (dd, 1H, $J$ = 8.5, 0.8 Hz), 7.80−7.75 (m, 2H), 7.53 (ddd, 1H, $J$ = 8.5, 6.8, 1.3 Hz), 7.37 (ddd, 1H, $J$ = 8.1, 6.8, 1.2 Hz), 7.23 (d, 1H, $J$ = 9.1 Hz), 4.02 (s, 3H), 2.69 (t, 2H, $J$ = 6.7 Hz), 2.32 (td, 2H, $J$ = 6.7, 2.6 Hz), 2.00 (t, 1H, $J$ = 2.6 Hz), 1.94−1.78 (m, 4H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 159.0, 135.2, 129.7, 129.0, 128.4, 127.5, 125.8, 124.5, 113.1, 107.4, 100.0, 84.7, 75.5, 68.9, 57.0, 28.4, 28.1, 20.1, 18.5. MS (EI, 70 eV) *m*/*z*: 262 (53) [$M^+$], 247 (41), 233 (38), 231 (39), 215 (30), 219 (33), 203 (34), 181 (26), 165 (100), 152 (65), 139 (23). Anal. Calcd for $C_{19}H_{18}O$ (262.35): C, 86.99; H, 6.92. Found: C, 86.90; H, 6.88.

**1-(1,7-Octadiynyl)naphthalene-2-yl Pivalate (30).** In a 250 mL Schlenk flask, 1-iodonaphthalen-2-ol (1.0 g, 6.93 mmol) and 4-dimethylaminopyridine (DMAP, 84.6 mg, 0.69 mmol) were dissolved in $CH_2Cl_2$ (25 mL) and $NEt_3$ (1.2 mL, 8.32 mmol). Pivaloyl chloride (1.0 mL, 8.31 mmol) was added slowly to the solution, which was then stirred for 4 h at rt. The reaction was quenched by addition of $NaHSO_3$ solution and extracted with $CH_2Cl_2$ several times. The combined organic phases were dried over $Na_2SO_4$, and column chromatography on silica with *n*-hexane/ethyl acetate (2:1, v/v) as eluent yielded the product 1-iodonaphthalen-2-yl pivalate (1.3 g, 53%), which was directly used for the next step. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.20 (d, 1H, $J$ = 8.5 Hz), 7.82 (d, 1H, $J$ = 8.8 Hz), 7.78 (dd, 1H, $J$ = 8.0, 1.2 Hz), 7.59 (ddd, 1H, $J$ = 8.5, 6.9, 1.4 Hz), 7.50 (ddd, 1H, $J$ = 8.0, 6.9, 1.2 Hz), 7.21 (d, 1H, $J$ = 8.8 Hz), 1.56 (s, 9H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 176.2, 150.2, 135.2, 131.9(2), 130.0, 128.3, 128.1, 126.2, 121.3, 94.3, 39.3, 27.4 ppm. MS (70 eV) *m*/*z*: 354 (15) [$M^+$], 270 (100), 114 (13), 57 (16). Diyne **30** was prepared following general procedure 2 from 1-iodonaphthalen-2-yl pivalate (1.3 g, 3.67 mmol) and 1,7-octadiyne (1.16 g, 11.0 mmol) as well as $Pd(PPh_3)_4$ (0.25 g, 0.22 mmol) as the catalyst, giving 450 mg (37%) of pure diyne **30** after chromatography on silica gel with petroleum ether/ethyl acetate (6:1 v/v). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.31 (d, 1H, $J$ = 8.3 Hz), 7.83 (d, 1H, $J$ = 8.0 Hz), 7.79 (d, 1H, $J$ = 8.9 Hz), 7.57 (ddd, 1H, $J$ = 8.3, 6.9, 1.4 Hz), 7.49 (ddd, 1H, $J$ = 8.0, 6.9, 1.3 Hz), 7.19 (d, 1H, $J$ = 8.9 Hz), 2.61 (t, 2H, $J$ = 6.8 Hz), 2.29 (td, 2H, $J$ = 6.7, 2.6 Hz), 2.00 (t, 1H, $J$ = 2.6 Hz), 1.87−1.74 (m, 4H), 1.46 (s, 9H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 176.7, 150.4, 134.3, 131.3, 128.9, 128.2, 127.1, 126.2, 126.0, 121.3, 113.7, 99.9, 84.1, 74.1, 68.8, 39.3, 27.8, 27.7, 27.4, 19.6, 18.1 ppm. MS (70 eV) *m*/*z*: 331 (15) [$M - H]^+$, 275 (100), 247 (93), 233 (29), 219 (50), 205 (16), 191 (15), 181 (30), 165 (26), 152 (41), 57 (77). HRMS (ESI) for $C_{23}H_{25}O_2$: calcd 333.1849, found 333.1849.

**1-(1,7-Octadiynyl)-2-benzyloxynaphthalene (31).** 1-Iodonaphthalen-2-ol (4.00 g, 14.8 mmol) and benzyl bromide (1.76 mL, 14.8 mmol) were dissolved in acetone (130 mL). Potassium carbonate (2.04 g, 138.2 mmol) and catalytic NaI (150 mg, 1.0 mmol) were added to the solution, and the resulting mixture was heated at reflux for 5 h. The yellow solution became orange. The mixture was cooled to rt and concentrated to a volume of about 5 mL. Water was added and the mixture extracted with ethyl acetate (3 × 15 mL). The combined organic layers were dried with $Na_2SO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (eluent: petroleum ether/ethyl acetate, 9:1 v/v) to yield 1-iodo-2-benzyloxynaphthalene as a syrup (1.65 g, 31%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.22 (dd, 1H, $J$ = 8.6, 0.9 Hz), 7.78 (d, 1H, $J$ = 8.9 Hz), 7.75 (d, 1H, $J$ = 8.4 Hz), 7.62−7.57 (m, 3H), 7.48−7.39 (m, 4H), 7.21 (d, 1H, $J$ = 8.9 Hz), 5.31 (s, 2H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 155.8, 136.7, 135.7, 131.4, 130.3, 130.1, 128.7, 128.3, 128.2, 128.0, 127.3, 124.6, 114.7, 89.1, 71.9 ppm. MS (70 eV) *m*/*z*: 360 (45) [$M^+$], 233 (29), 114 (19), 91 (100). HRMS (EI) for $C_{17}H_{13}OI$: calcd 360.0006, found 359.9996. Diyne **31** was prepared following general procedure 2 using 1-iodo-2-benzyloxynaphthalene (1.39 g, 3.86 mmol) and 1,7-octadiyne (1.23 g, 11.57 mmol) as well as $Pd(PPh_3)_4$ (0.23 g, 0.19 mmol) as the catalyst, giving 700 mg (54%) of pure diyne as a substance of syrupy consistence after chromatography with petroleum ether/ethyl acetate (19:1 v/v) as the eluent on silica gel. For use in the cycloaddition reaction the substrate was prepared as follows: **31** was dissolved in dry THF, and active molecular sieves were added for removal of residual water. After being stirred for a short period, the solution was filtered, the THF removed under reduced pressure, and the residue dried in high vacuo. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.28 (dd, 1H, $J$ = 8.6, 1.1 Hz), 7.76 (d, 1H, $J$ = 8.1 Hz), 7.72 (d, 1H, $J$ = 9.0 Hz), 7.56−7.50 (m, 3H), 7.42−7.36 (m, 3H), 7.35−7.31 (m, 1H), 7.23 (d, 1H, $J$ = 9.0 Hz), 5.32 (s, 2H), 2.68 (t, 2H, $J$ = 6.7 Hz), 2.26 (td, 2H, $J$ = 6.7, 2.7 Hz), 1.97 (t, 1H, $J$ = 2.6 Hz), 1.89−1.75 (m, 4H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 158.1, 137.4, 134.9, 129.2, 129.0, 128.6, 128.1, 127.9, 127.3, 127.2, 125.6, 124.4, 115.3, 108.6, 99.8, 84.4, 71.7, 68.7, 28.0, 27.7, 19.8, 18.1 ppm. MS (70 eV) *m*/*z*: 338 (14) [$M^+$], 257 (17), 253 (23), 247 (30), 219 (17), 165 (17), 152 (23), 91 (100). HRMS (EI) for $C_{25}H_{22}O$: calcd 338.1665, found 338.1671.

**1-(1,7-Octadiynyl)-2-carbomethoxynaphthalene (32).** The diyne was prepared using 1-bromo-2-carbomethoxynaphthalene (6.63 g, 25 mmol)[34] and 1,7-octadiyne (5.31 g, 50 mmol) following general procedure 1, yielding 4.86 g (67%) of product. Mp: 37−38 °C

(33) Preparation: Iskra, J.; Stauber, S.; Zupan, M. *Synthesis* **2004**, 1869.

(34) Weber, E.; Csöregh, I.; Stensland, B.; Czugler, M. *J. Am. Chem. Soc.* **1984**, *106*, 3297.

(pentane). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.54 (dd, 1H, $J$ = 7.9, 2.1 Hz), 7.88 (d, 1H, $J$ = 8.7 Hz), 7.84 (dd, 1H, $J$ = 7.4, 1.8 Hz), 7.77 (d, 1H, $J$ = 8.7 Hz), 7.62−7.55 (m, 2H), 3.98 (s, 3H), 2.71 (t, 2H, $J$ = 6.8 Hz), 2.31 (td, 2H, $J$ = 6.8, 2.6 Hz), 1.99 (t, 1H, $J$ = 2.6 Hz), 1.91−1.84 (m, 4H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 167.6, 134.5, 133.9, 130.5, 128.2, 128.1, 127.9, 127.6, 127.4, 125.7, 123.2, 102.1, 84.2, 77.4, 68.7, 52.3, 27.8 (2), 19.2, 18.2 ppm. MS (EI, 70 eV) $m/z$: 291 (100) [$M^+$], 275 (67), 259 (13), 231 (18). Anal. Calcd for $C_{20}H_{18}O_2$ (290.36): C, 82.73; H, 6.25. Found: C, 82.70; H, 6.24.

**1-(1,7-Octadiynyl)-2-hydroxymethylnaphthalene (33).** In a 250 mL Schlenk flask was dissolved diyne **32** (2.0 g, 6.89 mmol) in toluene and the mixture cooled to 0 °C. Red-Al (2.70 mL, 9.65 mmol, 70% solution) was added slowly, and after complete addition the mixture was stirred for 19 h at rt. Additional Red-Al (0.97 mL, 3.42 mmol, 70% solution) was added and the mixture stirred for another 4 h. The reaction was quenched by addition of $Na_2SO_4$ solution and filtered over Celite. The aqueous phase was extracted with ethyl acetate, and the combined organic phases were washed with brine. After drying over $Na_2SO_4$, column chromatography on silica using petroleum ether/ethyl acetate (6:1, v/v) as the eluent yielded the product as viscous colorless oil (1.25 g, 69%). For use in the cycloaddition reaction the substrate was prepared as follows: **33** was dissolved in dry THF, and active molecular sieves were added for removal of residual water. After being stirred for a short period, the solution was filtered, the THF removed under reduced pressure, and the residue dried under high vacuum. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.34 (d, 1H, $J$ = 8.3 Hz), 7.83 (d, 1H, $J$ = 8.1 Hz), 7.79 (d, 1H, $J$ = 8.5 Hz), 7.57 (d, 1H, $J$ = 8.5 Hz), 7.57 (ddd, 1H, $J$ = 8.3, 6.7, 1.6 Hz), 7.49 (ddd, 1H, $J$ = 8.1, 6.7, 1.3 Hz), 5.01 (s, 2H), 2.67 (t, 2H, $J$ = 6.7 Hz), 2.31 (td, 2H, $J$ = 6.7, 2.6 Hz), 2.13 (s, 1H), 2.00 (t, 1H, $J$ = 2.6 Hz), 1.90−1.76 (m, 4H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 141.0, 133.7, 132.7, 128.2 (2), 126.9, 126.3 (2), 125.4, 119.2, 100.5, 84.2, 76.6, 68.9, 64.6, 28.0, 27.8, 19.6, 18.2 ppm. MS (70 eV) $m/z$: 262 (9) [$M^+$], 233 (26), 215 (31), 202 (20), 191 (100), 178 (29), 165 (70), 152 (42). Anal. Calcd for $C_{19}H_{18}O$ (262.35): C, 86.99; H, 6.92. Found: C, 87.07; H, 7.35.

**1-(1,6-Heptadiynyl)-2-methoxynaphthalene (39).** The compound was prepared following general procedure 1 using 1-iodo-2-methoxynaphthalene (**38**, 2.84 g, 10 mmol) and 1,6-heptadiyne (1.85 g, 20 mmol), yielding 1.40 g (56%) of pure product after chromatography with petroleum ether/ethyl acetate (6:1 v/v) on silica gel. Mp: 44−45 °C (*n*-hexane). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.26 (d, 1H, $J$ = 8.5 Hz), 7.75−7.80 (m, 2H), 7.54 (ddd, 1H, $J$ = 8.5, 6.8, 1.2 Hz), 7.37 (ddd, 1H, $J$ = 8.2, 6.8, 1.2 Hz), 7.23 (d, 1H, $J$ = 9.1 Hz), 4.02 (s, 3H), 2.79 (t, 2H, $J$ = 7.0 Hz), 2.50 (dt, 2H, $J$ = 7.1, 2.7 Hz), 2.03 (t, 1H, $J$ = 2.4 Hz), 1.98 (t, 2H, $J$ = 7.0 Hz) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 158.8, 134.9, 129.5, 128.6, 128.1, 127.3, 125.4, 124.2, 112.8, 106.9, 98.9, 83.8, 75.5, 69.0, 56.7, 28.0, 19.4, 17.9 ppm. MS (70 eV) $m/z$: 248 (10) [$M^+$], 233 (30), 217 (45), 202 (53), 189 (25), 181 (21), 165 (60), 152 (76), 139 (30), 115 (19), 39 (22). Anal. Calcd for $C_{18}H_{16}O$ (248.32): C, 87.06; H, 6.49. Found: C, 87.13; H, 6.40.

**1-(3-(Prop-2-ynyl(methyl)amino)prop-1-ynyl)-2-methoxynaphthalene (40).** The compound was prepared from 1-iodo-2-methoxynaphthalene (**38**, 8.64 g, 30 mmol) and *N*-methyl-*N*,*N*-dipropargylamine (5.36 g, 50 mmol)[35] following general procedure 1, yielding 5.21 g (66%) of product after column chromatography (eluent: diethyl ether/*n*-hexane, 10:1 v/v). Mp: 76−77 °C (*n*-hexane). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.27 (dd, 1H, $J$ = 8.5, 1.2 Hz), 7.79 (d, 1H, $J$ = 9.1 Hz), 7.77 (d, 1H, $J$ = 8.2 Hz), 7.54 (ddd, 1H, $J$ = 8.5, 6.8, 1.3 Hz), 7.37 (ddd, 1H, $J$ = 8.2, 6.8, 1.2 Hz), 7.22 (d, 1H, $J$ = 9.1 Hz), 4.00 (s, 3H), 3.83 (s, 2H), 3.56 (t, 1H, $J$ = 2.4 Hz), 2.55 (s, 3H), 2.31 (d, 2H, $J$ = 2.4 Hz) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 159.2, 134.7, 130.0, 128.6, 128.1, 127.4, 125.3, 124.2, 112.8, 106.3, 94.0, 79.8, 79.3, 73.2, 56.6, 46.1, 44.8, 41.5 ppm. MS (EI, 70 eV) $m/z$: 263 (11) [$M^+$], 262 (21) [$M - H]^+$, 248 (20), 220 (100), 195 (19), 165 (39), 152 (50). Anal. Calcd for $C_{18}H_{17}NO$ (263.33): C 82.10, H 6.51, N 5.32. Found: C 82.18, H 6.60, N 5.07.

**1-(3-(Prop-2-ynyloxy)prop-1-ynyl)-2-methoxynaphthalene (41).** Diyne **41** was prepared following general procedure 2, using 1-iodo-2-methoxynaphthalene (**38**, 4 g, 14.1 mmol) and dipropargyl ether (2.65 g, 28.2 mmol) as well as $Pd(PPh_3)_4$ as the catalyst, giving 1.22 g (35%) of pure diyne after chromatography with petroleum ether/ethyl acetate (6:1 v/v) on silica gel. Mp: 62−63 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.26 (d, 1H, $J$ = 8.5 Hz), 7.82 (d, 1H, $J$ = 9.1 Hz), 7.78 (d, 1H, $J$ = 8.1 Hz), 7.55 (ddd, 1H, $J$ = 8.5, 6.8, 1.3 Hz), 7.38 (ddd, 1H, $J$ = 8.1, 6.8, 1.2 Hz), 7.23 (d, 1H, $J$ = 9.1 Hz), 4.73 (s, 3H), 4.46 (d, 1H, $J$ = 2.4 Hz), 4.01 (s, 3H), 2.52 (t,1H, $J$ = 2.4 Hz) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 159.4, 134.7, 130.5, 128.5, 128.2, 127.5, 125.2, 124.3, 112.6, 105.5, 93.7, 81.5, 79.3, 75.0, 57.9, 56.6, 56.5 ppm. MS (EI, 70 eV) $m/z$: 250 (78) [$M^+$], 221 (35), 220 (71), 219 (32), 195 (25), 191 (33), 189 (28), 181 (34), 169 (26), 165 (74), 152 (100), 151 (46), 139 (69). Anal. Calcd for $C_{17}H_{14}O_2$ (250.29): C, 81.58; H, 5.64. Found: C, 81.37; H, 5.67.

**1-(1,8-Nonadiynyl)-2-methoxynaphthalene (42).** Diyne **42** was prepared following general procedure 2, using 1-iodo-2-methoxynaphthalene (**38**, 2 g, 7.04 mmol) and 1,8-nonadiyne (1.69 g, 14.1 mmol) as well as $Pd_2dba_3 \cdot CHCl_3$ and dppf as the catalyst system (addition rate of the napthyl iodide solution: 2 mL/h for 1 h, then 0.15 mL/h), giving 1.07 g (55%) pure diyne as an oil that solidifies on standing after chromatography with petroleum ether/ethyl acetate (6:1 v/v) on silica gel. Mp: 52−54 °C (*n*-hexane). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.27 (d, 1H, $J$ = 8.5 Hz), 7.77 (d, 1H, $J$ = 8.7 Hz), 7.77 (d, 1H, $J$ = 8.5 Hz), 7.53 (ddd, 1H, $J$ = 8.5, 6.8, 1.3 Hz), 7.37 (ddd, 1H, $J$ = 8.5, 6.8, 1.2 Hz), 7.24 (d, 1H, $J$ = 8.7 Hz), 4.02 (s, 3H), 2.67 (t, 2H, $J$ = 6.8 Hz), 2.25 (td, 2H, $J$ = 6.6, 2.6 Hz), 1.96 (t, 1H, $J$ = 2.6 Hz), 1.82−1.60 (m, 6H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 158.7, 134.9, 129.3, 128.7, 128.1, 127.2, 125.5, 124.1, 112.8, 107.1, 100.1, 84.6, 75.0, 68.5, 56.8, 28.7, 28.3, 28.2, 20.2, 18.5 ppm. MS (EI, 70 eV) $m/z$: 276 [$M^+$] (57), 261 (20), 245 (23), 233 (24), 217 (20), 203 (22), 195 (43), 181 (25), 165 (100), 152 (73). Anal. Calcd for $C_{20}H_{20}O$ (276.37): C, 86.92; H, 7.29. Found: C, 86.99; H, 7.34.

**1-(1,9-Decadiynyl)-2-methoxynaphthalene (43).** Compound **43** was synthesized following general procedure 2, using 1-iodo-2-methoxynaphthalene (**38**, 2 g, 7.04 mmol) and 1,9-decadiyne (1.89 g, 14.1 mmol) as well as $Pd_2dba_3 \cdot CHCl_3$ and dppf as the catalyst system (addition rate of the napthyl iodide solution: 2 mL/h for 1 h, then 0.15 mL/h), giving 1.20 g (59%) pure diyne as an oil after chromatography with petroleum ether/ethyl acetate (6:1 v/v) on silica gel. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.26 (d, 1H, $J$ = 8.5 Hz), 7.77 (d, 1H, $J$ = 9.1 Hz), 7.77 (d, 1H, $J$ = 8.2 Hz), 7.52 (ddd, 1H, $J$ = 8.5, 6.8, 1.2 Hz), 7.36 (ddd, 1H, $J$ = 8.2, 6.8, 1.2 Hz), 7.24 (d, 1H, $J$ = 9.1 Hz), 4.02 (s, 3H), 2.65 (t, 2H, $J$ = 7.0 Hz), 2.30−2.15 (m, 2H), 1.95 (t, 1H, $J$ = 2.6 Hz), 1.81−1.71 (m, 2H), 1.64−1.47 (m, 6H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 158.7, 135.0, 129.3, 128.7, 128.1, 127.2, 125.5, 124.2, 112.9, 107.2, 100.3, 84.8, 74.9, 68.5, 56.8, 29.0, 28.6 (2), 28.5, 20.3, 18.5 ppm. MS (EI, 70 eV) $m/z$: 291 (44) [$M^+$], 195 (41), 181 (20), 165 (100), 152 (64). HRMS (EI) for $C_{21}H_{23}O$: calcd 291.1743, found 291.1741.

**General Procedure for the Enantioselective [2 + 2 + 2] Cocyclotrimerization.** An inerted and thermostated (for the corresponding temperature refer to Tables 2 and 3) reaction vessel was loaded with either diyne **2**, **30**−**33**, or **39**−**43** (2 mmol), catalyst **1b** (0.02−0.1 mmol), THF (20 mL), and nitrile (2.5−6 mmol) under argon atmosphere. The mixture was stirred thoroughly and irradiated by two 460 W lamps ($\lambda \approx$ 420 nm) for 24−72 h. The reaction was quenched by switching off the lamps and opening the reaction vessel to air. The solvent was evaporated, and the oily residue was purified on silica using *n*-hexane−$Et_2O$ or *n*-hexane−ethyl acetate in different proportions as eluent. Further purification was done by recrystallization.

(35) Iwai, I.; Yura, Y. *Chem. Pharm. Bull.* **1963**, *11*, 1049.

**(+)-(*R*)-1-(2-Methoxy-1-naphthyl)-3-phenyl-5,6,7,8-tetrahydroisoquinoline (6)[14a].** Mp: 200−201 °C (ethyl acetate). $[\alpha]^{25}_D$ = +202.5 (c = 0.1, toluene). Enantiomeric purity by HPLC analysis >98% ee. HPLC conditions: Chiralpak AD-H, *n*-hexane/ethanol 99:1, 1.0 mL/min, $T_1$ = 6.67 min, $T_2$ = 8.31 min. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.09−8.06 (m, 2H), 7.97 (d, 1H, $J$ = 9.0 Hz), 7.92−7.87 (m, 1H), 7.58 (s, 1H), 7.50−7.44 (m, 2H), 7.44−7.37 (m, 5H), 3.91 (s, 3H), 2.98 (td, 2H, $J$ = 6.1, 2.8 Hz), 2.57 (ddd, 1H, $J$ = −17.4, 7.7, 6.1 Hz), 2.27 (dd, 1H, $J$ = −17.4, 0.0 Hz), 1.92−1.84 (m, 2H), 1.84−1.77 (m, 1H), 1.75−1.66 (m, 1H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 155.8, 154.1, 153.9, 146.9, 140.1, 133.3, 132.0, 129.7, 129.3, 128.5, 128.2, 128.0, 127.1, 126.5, 124.8, 123.8, 123.6, 120.2, 113.8, 56.7, 29.7, 25.5, 23.0, 22.4 ppm. MS (70 eV) *m*/*z*: 365 (72) [$M^+$], 364 (100), 346 (40), 334 (27), 321 (18), 306 (6). Anal. Calcd for $C_{26}H_{23}NO$ (365.47)·0.5$H_2O$ (18.02): C, 83.39; H, 6.46; N, 3.74. Found: C, 83.46; H, 6.55; N, 3.13.

**(+)-(*R*)-1-(2-Methoxy-1-naphthyl)-3-methyl-5,6,7,8-tetrahydroisoquinoline (7)[14a].** Following the general procedure, biaryl **7** was obtained from **2** (525 mg, 2 mmol) and acetonitrile (**4**, 314 μL, 6 mmol) as a solid with a yield of 398 mg (66%). Mp: 160−161 °C (pentane). $[\alpha]^{25}_D$ = +138.9 (*c* = 0.1, toluene). Enantiomeric purity after recrystallization by HPLC analysis >98% ee (HPLC conditions: Chiralcel OD-H, *n*-hexane/ethanol 99.95:0.05, 1.5 mL/min, $T_1$ = 4.72 min, $T_2$ = 5.94 min). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.89 (d, 1H, $J$ = 9.0 Hz), 7.83−7.79 (m, 1H), 7.36 (d, 1H, $J$ = 9.0 Hz), 7.34−7.29 (m, 2H), 7.18−7.13 (m, 1H), 6.95 (s, 1H), 3.86 (s, 3H), 2.82 (t, 2H, $J$ = 6.3 Hz), 2.57 (s, 3H), 2.40 (dd, 1H, $J$ = −17.3, 6.4 Hz), 2.14 (dd, 1H, $J$ = −17.3, 6.1 Hz), 1.81−1.74 (m, 2H), 1.74−1.66 (m, 1H), 1.66−1.58 (m, 1H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 155.1, 154.4, 153.8, 146.6, 133.2, 130.0, 129.6, 129.3, 127.9, 126.5, 124.6, 123.6, 123.5, 122.7, 113.6, 56.6, 29.4, 25.3, 24.2, 23.0, 22.4 ppm. MS (70 eV) *m*/*z*: 303 (74) [$M^+$], 302 (100), 284 (57), 272 (38), 259 (24). Anal. Calcd for $C_{21}H_{21}NO$ (303.40): C, 83.13; H, 6.98; N, 4.62. Found: C, 83.05; H, 7.14; N, 4.50.

**(+)-(*R*)-1-(2-Methoxy-1-naphthyl)-3-*tert*-butyl-5,6,7,8-tetrahydroisoquinoline (8)[14a].** Following the general procedure, biaryl **8** was obtained from **2** (525 mg, 2 mmol) and *tert*-butylnitrile (**5**, 442 μL, 4 mmol) with a yield of 547 mg (79%) as a solid. Mp: 106−107 °C (*n*-hexane). $[\alpha]^{25}_D$ = +205.2 (*c* = 0.1, toluene). Enantiomeric purity after recrystallization by HPLC analysis >98% ee (HPLC conditions: Chiralcel OD-H, *n*-hexane/2-propanol 99.95:0.05, 1.0 mL/min, $T_1$ = 9.42 min, $T_2$ = 10.95 min). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.92 (d, 1H, $J$ = 9.0 Hz), 7.86−7.82 (m, 1H), 7.39 (d, 1H, $J$ = 9.0 Hz), 7.35−7.31 (m, 2H), 7.18−7.13 (m, 2H), 3.88 (s, 3H), 2.89 (t, 2H, $J$ = 6.3 Hz), 2.41 (dd, 1H, $J$ = −17.1, 6.6 Hz), 2.12 (dd, 1H, $J$ = −17.1, 6.1 Hz), 1.85−1.75 (m, 2H), 1.75−1.56 (m, 2H), 1.44 (s, 9H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 165.2, 154.2, 146.1, 145.7, 133.3, 129.8, 129.5, 128.0, 126.5, 126.2, 124.8, 123.7, 118.3, 114.6, 57.3, 37.0, 30.4, 29.9, 25.3, 23.0, 22.5 ppm (one quaternary carbon could not be assigned). MS (70 eV) *m*/*z*: 345 (100) [$M^+$], 330 (72), 314 (29), 303 (72). Anal. Calcd for $C_{24}H_{27}NO$ (345.48): C, 83.44; H, 7.88; N, 4.05. Found: C, 83.42; H, 7.96; N, 3.69.

**(+)-(*R*)-1-(2-Methoxy-1-naphthyl)-3-(3,4,5-trimethoxyphenyl)-5,6,7,8-tetrahydroisoquinoline (20)[36].** Diyne **2** (788 mg, 3 mmol) and 3,4,5-trimethoxybenzonitrile (**10**, 753 mg, 3.9 mmol) were reacted according to the general procedure to give compound **20** after column chromatography with 875 mg (64%) yield. Mp: 140−141 °C (benzene/*n*-hexane). $[\alpha]^{25}_D$ = +173.2 (*c* = 0.3, $CHCl_3$). Enantiomeric purity by HPLC analysis: 91% ee (HPLC conditions: Chiralpak AD, *n*-hexane/ethanol 95:5, 1.0 mL/min, $T_1$ = 13.8 min, $T_2$ = 19.8 min). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.94 (d, 1H, $J$ = 9.1 Hz), 7.86−7.81 (m, 1H), 7.47 (s, 1H), 7.38 (d, 1H, $J$ = 9.1 Hz), 7.35−7.31 (m, 2H), 7.26−7.22 (m, 1H), 7.21 (s, 2H), 3.90 (s, 6H), 3.88 (s, 3H), 3.87 (s, 3H), 2.9 (t, 2H, $J$ = 5.8 Hz), 2.48 (dd, 1H, $J$ = −16.9, 6.6 Hz), 2.23 (dd, 1H, $J$ = −16.9, 5.6 Hz), 1.88−1.79 (m, 2H), 1.77−1.63 (m, 2H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 154.2, 153.5, 153.4, 147.7, 138.8, 133.1, 132.3, 130.1, 129.2, 128.1, 126.7, 124.5, 123.6, 120.5, 113.7, 104.8 (2), 61.0, 56.7, 56.3, 29.9, 25.5, 22.8, 22.3 ppm (not all quaternary carbons could be assigned to individual peaks; given are the most clearly resolved signals). MS (70 eV) *m*/*z*: 455 (100) [$M^+$], 440 (20), 436 (25), 424 (19), 227 (12). Anal. Calcd for $C_{29}H_{29}NO_4$ (455.54): C, 76.46; H, 6.42; N, 3.07. Found: C, 76.59; H, 6.55; N, 3.05.

**(+)-(*R*)-1-(2-Methoxy-1-naphthyl)-3-(2,3,4-trimethoxyphenyl)-5,6,7,8-tetrahydroisoquinoline (21).** Following the general procedure, compound **21** was obtained from **2** (525 mg, 2 mmol) and 2,3,4-trimethoxybenzonitrile (**11**, 502 mg, 2.6 mmol) with a yield of 401 mg (44%) as a solid foam. $[\alpha]^{25}_D$ = +132.2 (*c* = 0.8, $CHCl_3$). Enantiomeric purity by HPLC analysis 94% ee. HPLC conditions: Chiracel OD-H, *n*-hexane/ethanol 99:1, 1.0 mL/min, $T_1$ = 12.94 min, $T_2$ = 14.06 min. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.93 (d, 1H, $J$ = 9.0 Hz), 7.85−7.82 (m, 1H), 7.57 (s, 1H), 7.48 (d, 1H, $J$ = 8.7 Hz), 7.38 (d, 1H, $J$ = 9.0 Hz), 7.37−7.31 (m, 2H), 6.23 (d, 1H, $J$ = 8.6 Hz), 6.73 (d, 1H, $J$ = 8.7 Hz), 3.92 (s, 3H), 3.86 (s, 3H), 3.86 (2 s, 6H), 2.96 (t, 2H, $J$ = 5.8 Hz), 2.47 (dd, 1H, $J$ = −17.2, 6.5 Hz), 2.24 (dd, 1H, $J$ = −17.2, 5.8 Hz), 1.88−1.80 (m, 2H), 1.79−1.72 (m, 1H), 1.72−1.64 (m, 1H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 155.4, 154.6, 154.3, 152.5, 151.9, 146.4, 142.4, 133.4, 131.5, 129.6, 129.2, 128.2, 128.0, 126.8, 126.0, 125.2, 124.6, 124.5, 123.7, 113.8, 107.7, 61.6, 61.1, 56.8, 56.2, 29.9, 25.5, 22.8, 22.3 ppm. MS (70 eV) *m*/*z*: 455 (48) [$M^+$], 440 (100), 424 (15), 408 (24). Anal. Calcd for $C_{29}H_{29}NO_4$ (455.54): C, 76.46; H, 6.42; N, 3.07. Found: C, 76.59; H, 6.88; N, 2.55.

**(+)-(*R*)-1-(2-Methoxy-1-naphthyl)-3-(4-trifluoromethylphenyl)-5,6,7,8-tetrahydroisoquinoline (22).** Diyne **2** (525 mg, 2 mmol) and 4-trifluoromethylbenzonitrile (**12**, 684 mg, 4 mmol) were reacted following the general procedure to yield **22** as an off-white solid (511 mg, 59%). Mp: 158−159 °C ($Et_2O$/*n*-hexane). $[\alpha]^{25}_D$ = +148.9 (*c* = 0.1, $CHCl_3$). Enantiomeric purity by HPLC analysis 86% ee (HPLC conditions: Chiralpak AD-H, *n*-hexane/ethanol 98:2, 1.0 mL/min, $T_1$ = 5.73 min, $T_2$ = 6.96 min). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.13 (d, 2H, $J$ = 8.2 Hz), 8.96 (d, 1H, $J$ = 9.1 Hz), 7.89−7.84 (m, 1H), 7.67 (d, 2H, $J$ = 8.2 Hz), 7.57 (s, 1H), 7.40 (d, 1H, $J$ = 9.1 Hz), 7.38−7.33 (m, 2H), 7.26−7.20 (m, 1H), 3.90 (s, 3H), 2.98 (t, 2H, $J$ = 6.1 Hz), 2.51 (dd, 1H, $J$ = −17.5, 6.6 Hz), 2.25 (dd, 1H, $J$ = −17.5, 6.0 Hz), 1.91−1.81 (m, 2H), 1.81−1.64 (m, 2H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 155.8, 154.2, 152.2, 148.2, 142.5, 133.6, 133.1, 130.6, 130.3 (2), 129.3, 128.2, 127.7, 126.9, 125.6 (q, $^3J_{C-F}$ = 3.7 Hz), 124.7 (q, $^1J_{C-F}$ = 272 Hz), 124.4, 123.8, 121.2, 113.7, 56.8, 29.9, 25.6, 22.8, 22.3 ppm. $^{19}$F NMR (282 MHz, $CDCl_3$): $\delta$ = 62.0 ppm. MS (70 eV) *m*/*z*: 433 (75) [$M^+$], 432 (100), 414 (51), 402 (27), 389 (23). Anal. Calcd for $C_{27}H_{22}F_3NO$ (433.46): C, 74.81; H, 5.12; N, 3.23. Found: C, 75.19; H, 5.54; N, 3.10.

**(*R*)-1-(2-Methoxy-1-naphthyl)-3-(4-dimethylaminophenyl)-5,6,7,8-tetrahydroisoquinoline (23).** When the general procedure was followed at a reaction temperature of −10 °C instead of −20 °C, biaryl **23** was obtained from diyne **2** (142 mg, 0.54 mmol) and 4-dimethylaminobenzonitrile (**13**, 158 mg, 1.08 mmol) with a yield of 127 mg (58%) as a white solid. Mp: 209−210 °C. Enantiomeric purity by HPLC analysis 83% ee (for the reaction at −10 °C). HPLC conditions: Chiralpak AD-H, *n*-heptane/ethanol 95:5, 1.0 mL/min, $T_1$ = 4.37 min, $T_2$ = 11.48 min. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.94−7.90 (m, 3H), 7.86−7.82 (m, 1H), 7.45 (s, 1H), 7.38 (d, 1H, $J$ = 9.0 Hz), 7.36−7.30 (m, 3H), 6.82 (d, 2H, $J$ = 9.0 Hz), 3.87 (s, 3H), 2.98 (s, 6H), 2.92 (t, 2H, $J$ = 6.5 Hz), 2.47 (ddd, 1H, $J$ = −17.2, 7.6, 5.8 Hz), 2.17 (dd, 1H, $J$ = −17.2, 6.0 Hz), 1.86−1.78 (m, 2H), 1.78−1.70 (m, 1H), 1.69−1.60 (m, 1H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 155.3, 154.2, 154.0, 150.7,

(36) Preliminary data: Malkov, A. V.; Westwater, M.-M.; Gutnov, A.; Ramírez-López, P.; Friscourt, F.; Kadlčíková, A.; Hodačová, J.; Rankovic, Z.; Kotora, M.; Kočovský, P. *Tetrahedron* **2008**, *64*, 11335.

146.8, 133.5, 133.4, 130.6, 129.6, 129.4, 128.2, 127.9, 126.5, 125.0, 124.1, 123.6, 119.0, 114.1, 112.4, 56.9, 40.6, 29.8, 25.5, 23.1, 22.6 ppm. MS (EI, 70 eV) *m*/*z*: 409 (28), 408 [$M^+$] (100), 407 (64), 389 (18), 377 (24), 364 (13), 188 (15). Anal. Calcd for $C_{28}H_{28}N_2O$ (408.53): C, 82.32; H, 6.91; N, 6.86. Found: C, 82.51; H, 7.04; N, 6.97.

**1-(2-Methoxy-1-naphthyl)-3-(4-chlorophenyl)-5,6,7,8-tetrahydroisoquinoline (24).** Diyne **2** (393.5 mg, 1.5 mmol) and 4-chlorobenzonitrile (**14**, 413 mg, 3 mmol) were reacted according to the general procedure to give compound **24** after column chromatography with 60 mg (10%) yield. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ = 7.94−7.89 (m, 3H), 7.85−7.81 (m, 1H), 7.47 (s, 1H), 7.38−7.30 (m, 5H), 7.23−7.18 (m, 1H), 3.87 (s, 3H), 2.96−2.90 (m, 2H), 2.46 (ddd, 1H, $J$ = −17.4, 7.9, 6.7 Hz), 2.19 (dd, 1H, $J$ = −17.4, 6.0 Hz), 1.85−1.79 (m, 2H), 1.77−1.70 (m, 1H), 1.69−1.60 (m, 1H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ = 155.4, 154.3, 152.3, 148.6, 134.9, 133.1, 130.4, 129.3, 128.9 (2), 128.3, 126.9, 124.4, 123.8, 120.9, 113.8, 56.9, 30.0, 25.5, 22.8, 22.3 ppm (not all expected signals were found due to low intensity of quarternary carbons). MS (ESI) *m*/*z*: 400 [$MH^+$] (100). HRMS (ESI): for $C_{26}H_{22}ClNO$ calcd 399.1390, found 399.1391.

**(*R*)-1-(2-Methoxy-1-naphthyl)-3-(1-phenyl-4-yl-4,4,5,5-tetramethyl-1,3-dioxa-2-borolane)-5,6,7,8-tetrahydroisoquinoline (25).** Diyne **2** (262 mg, 1 mmol) and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolyl)-benzonitrile (**15**, 300 mg, 1.3 mmol) were reacted following the general procedure to yield **25** as a nearly colorless solid (220 mg, 45%). Mp: 226−228 °C. Enantiomeric purity by HPLC analysis 75% ee. HPLC conditions: *R*,*R*-Whelk, *n*-heptane/ethanol 98:2, 0.8 mL/min, $T_1$ = 9.33 min, $T_2$ = 10.65 min. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ = 8.01 (d, 2H, $J$ = 8.2 Hz), 7.94 (d, 1H, $J$ = 9.1 Hz), 7.86 (d, 2H, $J$ = 8.2 Hz), 7.85−7.82 (m, 1H), 7.56 (s, 1H), 7.38 (d, 1H, $J$ = 9.1 Hz), 7.35−7.32 (m, 2H), 7.24−7.20 (m, 1H), 3.88 (s, 3H), 2.99−2.92 (m, 2H), 2.46 (ddd, 1H, $J$ = −17.4, 7.7, 6.7 Hz), 2.21 (dd, 1H, $J$ = −17.4, 5.9 Hz), 1.86−1.80 (m, 2H), 1.77−1.71 (m, 1H), 1.69−1.63 (m, 1H), 1.35 (s, 12H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ = 154.4, 153.2, 135.2, 133.1, 130.4, 129.3, 128.3, 126.9 (2), 124.4, 123.8, 121.3, 113.9, 83.9, 57.0, 30.0, 25.5, 25.0, 22.8, 22.3 ppm (not all expected signals were found due to low intensity of quarternary carbons). $^{11}$B NMR (160 MHz, $CDCl_3$): $\delta$ = 30.9 ppm. MS (ESI) *m*/*z*: 492 (100) [$MH^+$]. Anal. Calcd for $C_{32}H_{34}BNO_3$ (491.43): C, 78.21; H, 6.97; N, 2.85. Found: C, 78.03; H, 6.96; N, 2.50.

**(+)-(*R*)-1-(2-Methoxy-1-naphthyl)-3-(2-furyl)-5,6,7,8-tetrahydroisoquinoline (26)[36].** Following the general procedure **26** was obtained from **2** (1.05 g, 4 mmol) and 2-furonitrile (**16**, 620 $\mu$L, 7 mmol) as a solid with a yield of 1.15 g (81%). Mp: 198−199 °C (acetone). $[\alpha]^{25}_D$ = +172.5 ($c$ = 0.31, $CHCl_3$). Enantiomeric purity by HPLC analysis >98% ee. HPLC conditions: Chiracel OD-H, *n*-hexane/ethanol 99:1, 1.0 mL/min, $T_1$ = 5.76 min, $T_2$ = 7.94 min. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.94 (d, 1H, $J$ = 9.0 Hz), 7.85−7.82 (m, 1H), 7.55 (s, 1H), 7.51 (d, 1H, $J$ = 1.7 Hz), 7.38 (d, 1H, $J$ = 9.0 Hz), 7.36−7.31 (m, 2H), 7.22−7.18 (m, 1H), 6.97 (d, 1H, $J$ = 3.2 Hz), 6.49 (dd, 1H, $J$ = 3.2, 1.7 Hz), 3.89 (s, 3H), 3.19 (t, 2H, $J$ = 6.3 Hz), 2.41 (dd, 1H, $J$ = −17.5, 6.6 Hz), 2.17 (dd, 1H, $J$ = −17.5, 6.1 Hz), 1.86−1.78 (m, 2H), 1.77−1.69 (m, 1H), 1.69−1.60 (m, 1H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 155.9, 154.8, 154.0, 146.9, 146.4, 142.6, 133.3, 132.1, 129.8, 129.4, 128.5, 128.0, 126.6, 124.8, 123.6, 118.3, 113.9, 111.8, 107.8, 56.9, 29.8, 25.7, 23.0, 22.4 ppm. MS (EI, 70 eV) *m*/*z*: 355 (70) [$M^+$], 354 (100), 336 (43), 326 (25), 324 (27), 311 (20). Anal. Calcd for $C_{24}H_{21}NO_2$ (355.43): C, 81.10; H, 5.96; N, 3.94. Found: C, 81.10; H, 5.89; N, 3.61.

**(+)-(*R*)-1-(2-Methoxy-1-naphthyl)-3-(1-piperidinyl)-5,6,7,8-tetrahydroisoquinoline (29).** Diyne **2** (262 mg, 1 mmol) and piperidine-1-carbonitrile (**19**, 220 mg, 2 mmol) were reacted following the general procedure to yield **29** as an oil (332 mg, 89%). $[\alpha]^{25}_D$ = +131.2 ($c$ = 0.1, in $CHCl_3$). Enantiomeric purity by HPLC analysis 86% ee; HPLC conditions: Chiralpak AD-H, *n*-hexane/ethanol 99:1, 1.0 mL/min, $T_1$ = 6.26 min, $T_2$ = 9.58 min. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.87 (d, 1H, $J$ = 9.0 Hz), 7.79−7.83 (m, 1H), 7.36 (d, 1H, $J$ = 9.0 Hz), 7.33−7.31 (m, 3H), 6.50 (s, 1H), 3.87 (s, 3H), 3.49−3.44 (m, 4H), 2.81 (t, 2H, $J$ = 6.4 Hz), 2.52 (ddd, 1H, $J$ = −16.5, 7.8, 5.6 Hz), 2.03 (dd, 1H, $J$ = −16.5, 6.3 Hz), 1.79−1.71 (m, 2H), 1.68−1.56 (m, 8H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 158.2, 153.9, 153.3, 147.6, 133.3, 129.4, 129.2, 127.9, 126.3, 125.2, 124.8, 123.5, 122.6, 114.4, 106.3, 57.1, 47.2, 30.2, 25.6, 25.0, 24.9, 23.6, 22.9 ppm. MS (EI, 70 eV) *m*/*z*: 372 (100) [$M^+$], 343 (91), 329 (26), 316 (67), 289 (69). HRMS (EI) for $C_{25}H_{28}N_2O_1$: calcd 372.2196, found 372.2189. Anal. Calcd for the picrate salt, $C_{31}H_{31}N_5O_8$ (601.61): C, 61.89; H, 5.19; N, 11.64. Found: C, 61.44; H, 5.18; N, 11.69.

**1-(3-Phenyl-5,6,7,8-tetrahydro-1-isoquinolinyl)naphthalen-2-yl Pivalate (34).** When diyne **30** (200 mg, 0.6 mmol) and benzonitrile (**3**, 120 $\mu$l, 1.2 mmol) were reacted according to the general procedure, compound **34** was isolated after column chromatography with 30 mg (11%) yield. Enantiomeric excess by HPLC analysis 52% ee. HPLC conditions: Chiracel OD-H, *n*-heptane/ethanol 98:2, 0.3 mL/min, $T_1$ = 10.01 min, $T_2$ = 11.12 min. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.99−7.88 (m, 4H), 7.50 (s, 1H), 7.51−7.33 (m, 7H), 2.96−2.86 (m, 2H), 2.40 (ddd, 1H, $J$ = −17.4, 6.3, 6.3), 2.20 (ddd, 1H, $J$ = −17.4, 6.3, 6.3), 1.85−1.75 (m, 2H), 1.72−1.64 (m, 2H), 0.98 (s, 9H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 177.0, 154.3, 146.2, 135.9, 132.6, 132.1, 131.9, 129.3, 128.7, 128.5, 128.3, 127.2, 126.8, 125.7, 125.6 (2), 122.2, 120.5, 39.0, 29.9, 26.9, 25.7, 23.1, 22.6 ppm. MS (70 eV) *m*/*z*: 435 (29) [$M^+$], 350 (100), 322 (12). HRMS (ESI) for $C_{30}H_{30}NO_2$: calcd 436.2271, found 436.2275.

**1-(2-Benzyloxy-1-naphthyl)-3-phenyl-5,6,7,8-tetrahydroisoquinoline (35).** When diyne **31** (345 mg, 1.02 mmol) and benzonitrile (**3**, 260 $\mu$l, 2.04 mmol) were reacted according to the general procedure, compound **35** was isolated after column chromatography with 42 mg (9%) yield. Enantiomeric excess by HPLC analysis 22% ee (reaction at −20 °C) and 55% ee (reaction at 3 °C). HPLC conditions: Reprosil 100, *n*-heptane/ethanol 98:2, 0.5 mL/min, $T_1$ = 11.34 min, $T_2$ = 13.44 min. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.06−8.02 (m, 2H), 7.90 (d, 1H, $J$ = 9.1 Hz), 7.88−7.84 (m, 1H), 7.70−7.57 (m, 2H), 7.55 (s, 1H), 7.51−7.34 (m, 10H), 5.19 (s, 2H), 2.96 (t, 2H, $J$ = 6.3 Hz), 2.54 (ddd, 1H, $J$ = −17.3, 6.6, 6.6 Hz), 2.25 (ddd, 1H, $J$ = −17.3, 6.8, 6.1 Hz), 1.86−1.78 (m, 2H), 1.75−1.65 (m, 2H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 155.8, 154.0, 153.3, 147.0, 140.2, 137.7, 133.3, 132.9, 132.2, 129.7, 129.6, 129.2, 128.6, 128.4, 128.3, 128.0, 127.6, 127.1, 127.0, 126.6, 123.9, 120.2, 116.2, 71.8, 29.8, 25.7, 23.0, 22.5 ppm. MS (70 eV) *m*/*z*: 440 (74) [M − H]$^+$, 424 (44), 350 (100), 334 (45), 322 (20), 91 (37). HRMS (ESI) for $C_{32}H_{28}NO$: calcd 442.2165, found 442.2171.

**(+)-(*R*)-Methyl 1-(3-Phenyl-5,6,7,8-tetrahydro-1-isoquinolinyl)-2-naphthoate (36).** Diyne **32** (581 mg, 2 mmol) and benzonitrile (**3**, 618 $\mu$L, 6 mmol) were reacted following the general procedure to yield **36** as a white solid (509 mg, 65%). Mp: 161−162 °C (*n*-hexane). $[\alpha]^{25}_D$ = +57.4 ($c$ = 0.7, in $CHCl_3$). Enantiomeric purity by HPLC analysis 87% ee. HPLC conditions: Chiralpak AD-H, *n*-hexane/ethanol 99:1, 1.0 mL/min, $T_1$ = 9.9 min, $T_2$ = 13.9 min. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.13 (d, 1H, $J$ = 8.7 Hz), 7.99−7.91 (m, 3H), 7.97 (d, 1H, $J$ = 8.7 Hz), 7.56 (ddd, 1H, $J$ = 8.6, 6.8, 1.3 Hz), 7.55 (s, 1H), 7.45−7.32 (m, 5H), 3.70 (s, 3H), 3.02−2.93 (m, 2H), 2.34 (ddd, 1H, $J$ = −17.3, 6.9, 6.5 Hz), 2.16 (dd, 1H, $J$ = −17.3, 6.2 Hz), 1.88−1.80 (m, 2H), 1.78−1.61 (m, 2H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 167.5, 157.8, 153.9, 146.4, 141.5, 140.1, 135.4, 131.9, 131.0, 128.6, 128.3, 128.2 (2), 127.8, 127.2, 127.1, 127.0, 126.8, 126.1, 120.2, 52.2, 29.7, 26.0, 23.0, 22.5 ppm. MS (EI, 70 eV) *m*/*z*: 393 (47) [$M^+$], 360 (57), 334 (100). Anal. Calcd for $C_{27}H_{23}NO_2$: C, 82.42; H, 5.89; N, 3.56. Found: C, 82.34; H, 5.80; N, 3.52.

**1-(3-Phenyl-5,6,7,8-tetrahydro-1-isoquinolinyl)naphthalene-2-ylmethanol (37).** When diyne **33** (207 mg, 0.79 mmol) and benzonitrile (**3**, 0.02 mL, 1.58 mmol) were reacted according to the general procedure, compound **37** was isolated after

column chromatography with 59 mg (20%) yield. Enantiomeric purity by HPLC analysis 35% ee. HPLC conditions: Chiralpak AD-H, *n*-heptane/ethanol 95:5, 1.0 mL/min, $T_1$ = 9.78 min, $T_2$ = 12.21 min. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.98−7.89 (m, 4H), 7.66 (d, 1H, $J$ = 8.4 Hz), 7.60 (s, 1H), 7.47 (ddd, 1H, $J$ = 8.1, 6.4, 1.7 Hz), 7.44−7.35 (m, 5H), 4.41 (s, 2H), 3.02−2.94 (m, 2H), 2.35 (ddd, 1H, $J$ = −17.4, 8.1, 5.8 Hz), 2.13 (dd, 1H, $J$ = −17.4, 5.8 Hz), 1.89−1.59 (m, 4H) ppm (the signal for OH was undetected). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 156.9, 153.9, 148.3, 138.9, 137.1, 137.0, 133.1, 131.8, 131.6, 128.9 (3), 128.5, 127.7, 126.9, 126.7, 125.9, 125.6, 120.8, 64.4, 29.8, 26.2, 22.9, 22.4 ppm. MS (70 eV) $m/z$: 365 (53) [$M^+$], 355 (28), 346 (100), 334 (25), 281 (21), 221 (30), 147 (22), 73 (25). HRMS (ESI) for $C_{26}H_{24}NO$: calcd 366.1852, found 366.1856.

**2-(2-Methoxy-1-naphthyl)-6-phenyl-7,8-dihydro-5*H*-cyclopenta-[*c*]pyridine (44).** Following the general procedure, biaryl **44** was obtained from **39** (497 mg, 2 mmol) and benzonitrile (**3**, 412 $\mu$L, 4 mmol) as a solid with a yield of 506 mg (72%). Mp: 157−158 °C (ethyl acetate). HPLC conditions: Chiralpak AD-H, *n*-hexane/ethanol 90:10, 1.0 mL/min; $T_1$ = 5.5 min, $T_2$ = 6.54 min für 0 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.05−8.01 (m, 2H), 7.94 (d, 1H, $J$ = 9.0 Hz), 7.86−7.83 (m, 1H), 7.70 (s, 1H), 7.46−7.41 (m, 3H), 7.39 (d, 1H, $J$ = 9.0 Hz), 7.40−7.33 (m, 3H), 3.90 (s, 3H), 3.15−3.09 (m, 2H), 2.84−2.75 (m, 1H), 2.55 (ddd, 1H, $J$ = −16.4, 8.7, 5.6 Hz), 2.18−2.01 (m, 2H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 155.3, 154.4, 151.4, 140.2, 139.7, 133.1, 130.3, 129.3, 128.6 (2), 128.1, 127.5, 126.7, 124.9, 123.7, 122.4, 116.4, 113.7, 56.8, 33.4, 30.7, 24.7 ppm (one carbon signal can not be assigned). MS (EI, 70 eV) $m/z$: 351 (87) [$M^+$], 350 (100), 334 (42), 320 (21). Anal. Calcd for $C_{25}H_{21}NO$ (351.44): C, 85.44; H, 6.02; N, 3.99. Found: C, 85.44; H, 6.01; N, 3.52.

**2-(2-Methoxy-1-naphthyl)-*N*-methyl-6-phenyl-1,3-dihydro-1*H*-pyrrolo[3,4-*c*]pyridine (45).** Following the general procedure, biaryl **45** was obtained from **40** (527 mg, 2 mmol) and benzonitrile (**3**, 412 $\mu$l, 4 mmol) with a yield of 469 mg (64%) as a beige solid. Mp: 149−150 °C (MeOH). HPLC conditions: see the conditions described for **44**.[30] $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ = 8.02−7.99 (m, 2H), 7.94 (d, 1H, $J$ = 9.1 Hz), 7.85−7.82 (m, 1H), 7.66 (s, 1H), 7.51−7.48 (m, 1H), 7.44−7.40 (m, 2H), 7.39−7.34 (m, 4H), 4.26 (d, 1H, $J$ = −14.4 Hz), 4.22 (d, 1H, $J$ = −14.4 Hz), 3.99 (d, 1H, $J$ = −13.7 Hz), 3.88 (s, 3H), 3.74 (d, 1H, $J$ = −13.7 Hz), 2.63 (s, 3H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ = 156.9, 154.3, 150.5, 149.5, 139.7, 134.9, 133.1, 130.7, 129.4, 128.9, 128.8, 128.1, 127.4, 127.0, 124.9, 123.9, 122.0, 113.6, 113.5, 61.0, 59.3, 56.8, 42.4 ppm. MS (EI, 70 eV) $m/z$: 366 (74) [$M^+$], 365 (100), 351 (25), 349 (24). HRMS (ESI) for $C_{25}H_{23}N_2O$: calcd 367.1805, found 367.1805. Anal. Calcd for $2C_{25}H_{22}N_2O(366.45)\cdot 3CH_3OH(32.04)$: C, 76.78; H, 6.81; N, 6.76. Found: C, 76.63; H, 6.43; N, 6.72.

**1-(2-Methoxy-1-naphthyl)-6-phenyl-7,8-dihydrofuro[3,4-*c*]-pyridine (46).** When diyne **41** (95 mg, 0.38 mmol) and benzonitrile (**3**, 74 $\mu$L, 0.76 mmol) were reacted according to the general procedure using CpCo(COD) (4.4 mg, 0.019 mmol, 5 mol %) as the catalyst, compound **46** was isolated after column chromatography with 79 mg (59%) yield. Mp: 172−173 °C (THF/*n*-hexane). HPLC conditions: the compound turned out to be inseparable under the conditions described above.[30] $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.06−8.03 (m, 2H), 7.95 (d, 1H, $J$ = 9.0 Hz), 7.87−7.83 (m, 1H), 7.69 (s, 1H), 7.53−7.50 (m, 1H), 7.48−7.42 (m, 2H), 7.42−7.36 (m, 3H), 7.37 (d, 1H, $J$ = 9.0 Hz), 5.32−5.24 (m, 2H), 5.05 (dd, 1H, $J$ = −12.7, 2.0 Hz), 4.77 (dd, 1H, $J$ = −12.7, 1.7 Hz), 3.90 (s, 3H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 156.8, 154.3, 150.6, 149.4, 139.4, 135.4, 133.0, 130.9, 129.3, 129.0, 128.8, 128.2, 127.5, 127.1, 124.7, 123.9, 121.6, 113.4, 112.3, 73.7, 72.6, 56.6 ppm. MS (EI, 70 eV) $m/z$: 353 (50) [$M^+$], 338 (47), 324 (100), 309 (44), 294 (25). Anal. Calcd for $C_{24}H_{19}NO_2$ (353.41): C, 81.56; H, 5.42; N, 3.96. Found: C, 81.54; H, 5.64; N, 3.88.

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**Supporting Information Available:** Synthesis of cobalt complex CpCo(bpy) as well as the procedures for the reactions described in Schemes 2 and 3, copies of the proton and carbon NMR spectra for all compounds, dynamic HPLC spectra for **45** and **46**, and crystallographic data for CpCo(bpy) (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.