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Chiral cobalt^I and nickel^0 complexes in the synthesis of nonracemic helicenes through the enantioselective [2 + 2 + 2] cyclotrimerisation of alkynes

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ABSTRACT

The enantioselective intramolecular [2 + 2 + 2] cycloisomerisation of triynes under catalysis by chiral transition-metal complexes (Co^I, Ni^0) in order to receive nonracemic helicene derivatives was explored. The use of the chiral neomenthylindene Co^I complex led to a moderate 25% ee of tetrahydro[6]helicene, which was the first example of such a reaction catalysed by the chiral Co^I complex. The alternative Ni^0 catalysis employing privileged axially chiral monophosphines such as (−)-(*aS*)-NAPHEP led to tetrahydro[6]helicene with 64% ee, which is among the highest enantiomeric excesses so far observed for this Ni^0-catalysed reaction.

1. Introduction

The chemistry and physics of carbohelicenes, heterohelicenes and their helicene-like congeners (generally helicenes) have recently experienced renewed interest as evidenced by the increasing number of papers related to this topic [1]. This trend putting under the spotlight the highly promising helicene entities is fuelled by remarkable achievements in the field of transition-metal enantioselective catalysis [2], enantioselective organocatalysis [3], molecular recognition [4], chiral materials [5], self-assembly [6], surface science [7] and other branches of chemistry [8]. Evidently, there are increasing demands for the development of effective accesses to nonracemic helicenes and their derivatives. Besides the resolution of racemic helicenes by liquid chromatography on chiral stationary phases (limited by the prices of the preparative columns) [9], by crystallisation with chiral resolving agents [8a,9d,10], enzymatic resolution [11] or the separation of diastereomeric pairs formed from properly functionalised racemic helicenes (all limited to specific cases) [12], asymmetric synthesis remains a challenging task to develop a general approach to optically pure helicenes [13]. Along with the recent advances in the diastereoselective synthesis of nonracemic helicenes [14], enantioselective catalysis has been envisaged to play an important role [15].

As far as the recently emerged approaches to helicenes are concerned, transition-metal-mediated [2 + 2 + 2] cyclotrimerisation of alkynes to form the helical backbone is receiving more attention now, which can be seen from the contributions by Stará et al. [16], Vollhardt et al. [17], Tanaka et al. [15b,c,e], Teplý et al. [8], Carbery et al. [3b] and Shibata et al. [15a]. Since an organometallic intermediate is involved in the helicity-forming step, this methodology calls for utilising chiral ligands coordinated to catalytically active transition metals to control the stereochemical output of the cyclisation. Indeed, enantioselective intramolecular triyne [2 + 2 + 2] cyclotrimerisation under Ni^0 catalysis in the helicene synthesis has been attempted by Stará et al. to reach moderate enantiomeric excess of tetrahydro[6]helicene (48% ee) [18b], which has further been improved to 64% ee [18a]. Similarly, Tanaka et al. applied the enantioselective Rh^I catalysis to the [2 + 2 + 2] cyclotrimerisation of triynes obtaining oxa[7]helicene-like molecules with up to 85% ee [15e] or to double cyclotrimerisation of tetraynes and diynes forming oxa[7]- or oxa[9]helicene derivatives with up to 38% or 60% ee, respectively [15c]. Most recently, Shibata et al. have developed an approach to highly enantioenriched silahelicenes with up to 93% ee, which was based

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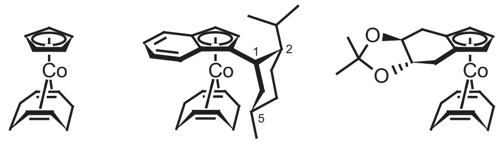
on a two-step process comprising the enantioselective Ir-catalysed intermolecular [2 + 2 + 2] cycloaddition of tetraynes with diynes followed by stereoconservative Ni-mediated intramolecular [2 + 2 + 2] cycloaddition [15a], and Tanaka et al. achieved a highly enantioselective synthesis of helically chiral 1,1′-bistriphenylenes via rhodium-catalysed double [2 + 2 + 2] cycloaddition of biaryl-linked tetraynes with 1,4-diynes (up to 93% ee) [15b].

Herein, we report on the formation of nonracemic helicene scaffolds by intramolecular enantioselective [2 + 2 + 2] cycloisomerisation of triynes when employing chiral Co^I complexes (bearing chiral cyclopentadienyl/indenyl ligands) or Ni^0 complexes (bearing chiral phosphines). This contribution covers the second part of a broader study on enantioselective cycloisomerisation (the first part has recently been published) [18a].

2. Results and discussion

Cobalt^I-catalysed or -mediated intramolecular [2 + 2 + 2] cycloisomerisation of triynes has been proved to be an efficient way to synthesise helicenes and their congeners [1b]. Although various Co^I complexes such as the commercially available $CpCo(CO)_2$, easy-to-prepare and stable CpCo(fumarate)(CO) [19], or highly reactive albeit less stable $CpCo(H_2C{=}CH_2)_2$ [20] or $CpCo(H_2C{=}CHSiMe_3)_2$ [21] can be used as pre-catalysts, a virtual CpCo fragment is generally proposed to play a catalytic major role as an active catalyst [22]. Obviously, the Cp ligand is expected to reside on cobalt during all of the elemental steps of the catalytic cycle of alkyne cycloisomerisation. Provided that the Cp ligand bears a chiral moiety [23], a certain level of the stereocontrol might occur in the helicity-forming step during cycloisomerisation of an achiral triyne to a helicene scaffold. However, to the best of our knowledge, chiral Co^I complexes have never been used in the asymmetric synthesis of helicenes by enantioselective cycloisomerisation of alkynes. Therefore, we paid attention to the chiral Co^I complexes **2** [24] and **3** [25], whose reactivity was compared with that of the achiral parent complex **1** [26] (Fig. 1).

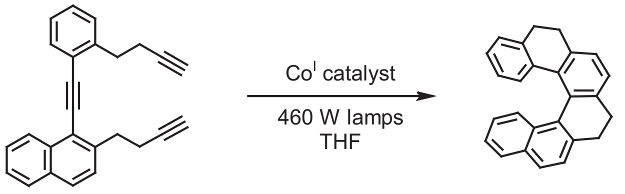
To begin with, we performed a cycloisomerisation of triyne **4** [18b,26] to tetrahydro[6]helicene **5** [18b,28] in the presence of the achiral Co^I complex **1**, which proceeded smoothly (Table 1, entry 1). This fact prompted us to utilise the chiral analogues **2** and **3**. The choice of triyne **4** was derived from the fact that it was found configurationally stable under the reaction conditions that we planned to use [18]. When we applied the neomenthylindene Co^I catalyst **2**, which combined elements of central and planar chirality, the cyclisation at 10 °C provided product **5** in a quantitative yield and we monitored a moderate enantiomeric excess (18% ee; Table 1, entry 2). This result confirmed that the chiral Co^I complex could control the helicity of the product but the reaction conditions required an optimisation to achieve higher ee. Hence, we lowered the temperature to −10 °C to observe a slightly better enantioselectivity of the reaction (25% ee; Table 1, entry 3). By further decreasing the temperature to −30 °C, we unfortunately faced a diminished reactivity of triyne **4**, which was accompanied by lowering the enantiomeric excess of **5** (17% ee; Table 1, entry 4). The use of the chiral tartrate-derived Co^I catalyst **3** led to the formation of **5** in a quantitative yield, but practically no enantiomeric excess of the product was monitored (Table 1, entry 5).



1 (-)-(1*S*,2*S*,5*R*,*pS*)-**2** (+)-(*S*,*S*)-**3**

Fig. 1. The Co^I complexes **1**–**3** employed in [2 + 2 + 2] cycloisomerisation of triynes to helicene scaffolds.

Table 1
Cycloisomerisation of triyne **4** to tetrahydro[6]helicene **5** catalysed by Co^I complexes **1**–**3**.[a]



4 **5**

Entry	Catalyst (mol%)	Time (h)	Temperature (°C)	ee (%)[b]	Yield (%)[c]
1	**1** (10)	20	25	–	>99
2	**2** (10)	24	10	18 (+)	>99
3	**2** (10)	18	−10	25 (+)	>99
4	**2** (10)	21	−30	17 (+)	81
5	**3** (10)	19	25	0	>99

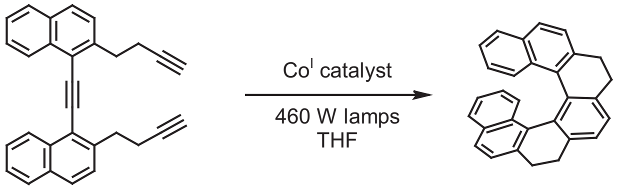
[a] The reaction mixture irradiated by two 460 W lamps ($\lambda \approx 420$ nm).
[b] Determined by HPLC on a Chiracel OJ-H column, the +/− sign indicates the sense of the optical rotation of **5**.
[c] Determined by GC.

Next, we focused on the symmetrical triyne **6** [9h] and its Co^I-catalysed cyclisation to tetrahydro[7]helicene **7** [9h] (Table 2). We checked the reactivity of triyne **6** in the presence of the achiral parent Co^I complex **1** to observe its smooth conversion to product **7** (Table 2, entry 1). When we applied the chiral neomenthylindene Co^I catalyst **2**, we could see quantitative yields of **7** regardless of the temperature used, but the enantiomeric excess of **7** was moderate at 25 or 10 °C (20% ee) and low at 0 °C (9% ee; Table 2, entries 2–4).

Obviously, we demonstrated for the first time that chiral Co^I complexes could indeed control the stereochemical outcome of the enantioselective [2 + 2 + 2] cycloisomerisation of triynes to provide nonracemic helicene derivatives. However, the enantiomeric excesses so far achieved underlined the need for a diligent optimisation of the structure of the chiral Co^I catalysts.

Alternatively, a nickel^0 catalysis employing chiral ligands could be applied to the enantioselective [2 + 2 + 2] cycloisomerisation of triynes to receive nonracemic helicene derivatives. However, we found that most phosphines, phosphites, phosphinites and aminophosphines possessing elements of central, axial or planar

Table 2
Cycloisomerisation of triyne **6** to tetrahydro[7]helicene **7** catalysed by Co^I complexes **1** and **2**.[a]



6 **7**

Entry	Catalyst (mol%)	Time (h)	Temperature (°C)	ee (%)[b]	Yield (%)[c]
1	**1** (10)	20	25	–	>99
2	**2** (10)	20	25	20 (+)	>99
3	**2** (10)	20	10	20 (+)	>99
4	**2** (10)	20	0	9 (+)	>99

[a] The reaction mixture irradiated by two 460 W lamps ($\lambda \approx 420$ nm).
[b] Determined by HPLC on a Chiracel OD-H column, the +/− sign indicates the sense of the optical rotation of **7**.
[c] Determined by GC.