Synthesis of Sterically Hindered Biaryls by Zr-Mediated Co-cyclotrimerization of Alkynes

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Treatment of zirconacyclopentadienes with *ortho*-substituted arylpropynoates in the presence of stoichiometric amounts of CuCl or $NiBr_2(PPh_3)_2$ represents a novel approach to the synthesis of biaryls, formed in good yields. The CuCl-mediated reaction proceeded through two reaction mechanisms, also affording Dewar benzenes together with the corresponding biaryls.

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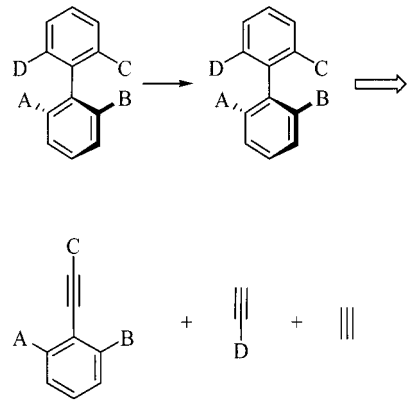
Introduction

Hindered biaryl compounds have numerous applications in organic synthesis. Biaryl backbones constitute important moieties in many natural compounds[1] and are also used as chiral scaffolds in many chiral ligands (phosphanes, pyridines, etc).[2] Biaryls are most frequently prepared by transition metal-catalyzed cross-coupling reactions between aryl metals and aryl halides or esters (e.g., triflates).[2,3] Although this approach has its merits and has been extensively studied, it may suffer drawbacks in cases of coupling of heavily substituted partners in which steric hindrance may severely retard the course of the cross-coupling reaction. In view of this, it is of general synthetic interest to develop new pathways for the preparation of highly substituted biaryls, and one possible approach is outlined in Scheme 1. Retrosynthetic analysis of the upper benzene ring of the biaryl compound clearly shows that it could be constructed from different alkynes: an *ortho*-substituted arylalkyne containing the necessary functional groups (A, B, C) and two other alkynes bearing between them the rest of the substituents (D). In this way the whole problem of the preparation of the substituted biaryl is reduced to the preparation of the *ortho*-substituted arylalkyne and its combination with the other two alkynes to complete the desired molecule. An ideal reaction for such a process is [2+2+2] cyclotrimerization of alkynes. As for the *ortho*-substituted arylalkyne, it would be beneficial if it could bear functional groups that would ensure its synthetic flexibility with regard to further organic transformations.



Scheme 1. Retrosynthetic analysis of biaryl formation by cyclotrimerization.

Although cyclotrimerization of alkynes has been a well known reaction for 30 years,[4] its application for the construction of chiral centers has started to gain attention only recently.[5] However, because of selectivity problems these approaches are usually applied to cyclotrimerization of α,ω-diynes with alkynes. As for the cyclotrimerization of three alkynes to highly substituted arenes with potential atropoisomeric properties, one convenient method is based on the treatment of zirconacyclopentadienes[6] with alkynes in the presence of stoichiometric amount of CuCl,[7] $NiBr_2(PPh_3)_2$,[8] or $NiBr_2(PMe_3)_2$.[9] This method has been successfully applied for the synthesis of polysubstituted aromatic compounds such as benzoheterocycles containing group 14 elements,[10] haloterphenyls,[11] haloterphenyls

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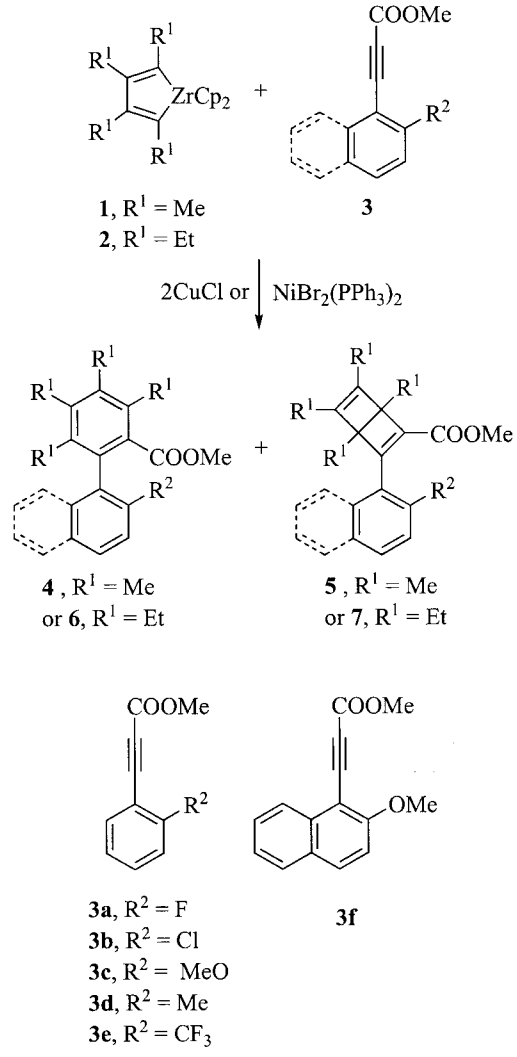
with chiral backbones,[12] perfluoroalkyl-substituted terphenyls,[13] polyacenes,[14] and ferrocenylalkynes.[15] There are several factors that favor the above method: firstly, zirconacyclopentadienes are easily prepared with a great variety of substituents and they are stable at room temperature, and secondly, arylalkynes can be easily prepared from commonly accessible starting material. Additionally, both CuCl and $NiBr_2(PPh_3)_2$ are stable and cheap compounds. Although there are plenty of examples of reactions between zirconacyclopentadienes and arylalkynes proceeding in good to excellent yields, no data are available on how *ortho*-substitution in the aromatic rings in the arylalkynes will affect the course of the reaction. It is reasonable to assume that *ortho*-substitution might cause undesirable steric hindrance that would result in a slower reaction rate. Although there had previously been a lack of information on the influence of the *ortho*-effect on the course of the reactions of *ortho*-substituted alkynes in transition metal-induced reactions, this topic has recently started to gain attention. Knowledge of this effect is important in the search for new synthetic methods for the preparation of potentially atropoisomeric biaryls, such as in the Dötz reaction between *ortho*-substituted arylalkynes and chromium carbenes.[16]

Results and Discussion

In this study we focused on reactions between alkyl-substituted zirconacyclopentadienes and various *ortho*-substituted arylpropynotes in an approach to substituted biaryls with potentially atropoisomeric properties. To compare the synthetic suitabilities of these methods we carried out the reactions in the presence of CuCl and $NiBr_2(PPh_3)_2$. The choice of arylpropynoates as the arylalkyne representatives was based on three facts: firstly, the presence of the ester group next to the triple bond is a prerequisite for the successful course of the reaction in the presence of CuCl,[7] secondly, the ester group can easily be converted into other functional groups, and, last but not least, the arylpropynoates can readily be prepared in great structural variety by simple synthetic procedures. Tetramethyl- (**1**) and tetraethylzirconacyclopentadiene (**2**) were chosen as typical representatives of zirconacycles (Scheme 2).

The results of Cu-mediated reactions of tetramethylzirconacyclopentadiene (**1**) and tetraethylzirconacyclopentadiene (**2**) are summarized in Table 1. The reactions proceeded with various levels of success in all cases; in addition to the expected biaryls, Dewar benzenes[17] were also formed as minor side-products (Scheme 2). Generally, the reaction rates were slow in all cases and reaction times of 148 h (1 week) were necessary in order to achieve reasonable yields of the products. This is in sharp contrast to the reaction with unsubstituted phenylpropynoate, which proceeded in excellent yield (85%) within a reasonable reaction time of 48 h.[7b] The reactions between tetramethylzirconacyclopentadiene (**1**) and *ortho*-halophenylpropynoates **3a** and **3b** gave the corresponding biaryls **4a** and **4b** in 60 and 36% yields. According to NMR analysis of the reaction mixtures, the Dewar benzenes **5a** and **5b** were formed in 32 and 20% yields, respectively. However, the Dewar benzenes **5a** and **5b** probably decomposed during isolation and only the biaryls **4a** and **4b** were isolated. Interestingly, in the cases



Scheme 2. Reactions between zirconacyclopentadienes and *ortho*-substituted arylpropynoates.

Table 1. Reactions between zirconacyclopentadienes **1** and **2** and arylpropynoates **3** in the presence of stoichiometric amounts of CuCl.

Zirconacycle	Propynoate	Products	Yield [%][a]
1	**3a**	**4a** + **5a**	60 + 32 (57)
2	**3a**	**6a** + **7a**	59 + 38 (52)
1	**3b**	**4b** + **5b**	36 + 20 (32)
2	**3b**	**6b** + **7b**	48 + 15 (38)
1	**3c**	**4c**	50 (47)
2	**3c**	**6c** + **7c**	32 + 12 (30 + 10)
1	**3d**	**4d**	55 (40)
2	**3d**	**6d** + **7d**	17 + 15 (30)
1	**3e**	**4e** + **5e**	22 + 10 (16 + 6)
2	**3e**	**6e** + **7e**	26 + 25 (23 + 20)
2	**3e**	**6f**	10 (7)

[a] ^1H NMR yields, isolated yields are in parentheses.

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of the *ortho*-methoxy- and methylphenylpropynoates **3c** and **3d**, only the formation of the biaryls **4c** and **4d** was observed, in 50 and 55% yields. The reaction with the *ortho*-(trifluoromethyl)phenylarylpropynoate **3e** again furnished a mixture of the biaryl **4e** and Dewar benzene **5e**.

Treatment of the tetraethylzirconacyclopentadiene **2** with the arylpropynoates **3** afforded mixtures of biaryls and Dewar benzenes in all the cases but one. The reactions with the haloarylpropynoates **3a** and **3b** thus gave mixtures of the biaryls and Dewar benzenes **6a** and **7a** (59 and 38%) and **6b** and **7b** (48 and 15%), respectively. Also, as in the previous two instances, the Dewar benzenes **7a** and **7b** probably decomposed during isolation and only the biaryls **6a** and **6b** were isolated. Analogously, the reactions with the methoxy, methyl, and trifluoromethyl *ortho*-substituted arylpropynoates **3c**, **3d**, and **3e** resulted in mixtures of the corresponding biaryls and Dewar benzenes **6c** and **7c** (32 and 12%), **6d** and **7d** (17 and 15%), and **6e** and **7e** (26 and 25%), respectively. Finally, treatment with methyl 2-methoxynaphthylpropynoate (**3f**) gave a rather disappointing low yield of the biaryl **6f** (10%). Several general trends can be inferred from the results presented in Table 1. Firstly, higher yields were obtained with **1** then with **2**; the observed difference might be caused by the greater size of the Et group than the Me group. Secondly, the yields of products decrease roughly with the size of the *ortho*-substituents,[18] increasing steric hindrance of which may have negative effects on the course of the reaction.

A single-crystal X-ray structure of the biaryl **4c** showed that the two phenyl rings are almost perpendicular to each other in the solid state (Figure 1). The orientation of the carboxyl plane is affected by extensive weak intermolecular hydrogen bonding O..H–C between the carbonyl oxygen and the methyl groups of the ester moiety or the hydrogen of the less substituted aromatic ring.

The reactions between the tetraethylzirconacyclopentadiene (**2**) and the arylpropynoates **3a**–**f** carried out in the presence of stoichiometric amounts of $NiBr_2(PPh_3)_2$ complex proceeded in most cases with good yields to give only the biaryls **6a**–**f** (Table 2). In this case no formation of the Dewar benzenes was observed, and obviously they would not be able to form because of the reaction mechanism.[8] In addition, the reaction between **2** and **3c** was carried out in the presence of $NiBr_2(PBu_3)_2$, because it had recently been shown that the use of Ni complexes with alkylphosphanes was advantageous in certain cases.[9] Nonetheless, the biaryl **6c** was formed in only 42% yield.

Table 2. Reactions between tetraethylzirconacyclopentadiene (**2**) and arylpropynoates **3** in the presence of stoichiometric amounts of $NiBr_2(PPh_3)_2$.

Zirconacycle	Propynoate	Product	Yield [%][a]
2	**3a**	**6a**	67 (45)
2	**3b**	**6b**	71 (46)
2	**3c**	**6c**	90 (52)
2	**3d**	**6d**	53 (33)
2	**3e**	**6e**	44 (23)
2	**3f**	**6f**	24 (20)

[a] ^{1}H NMR yields, isolated yields are in parentheses.

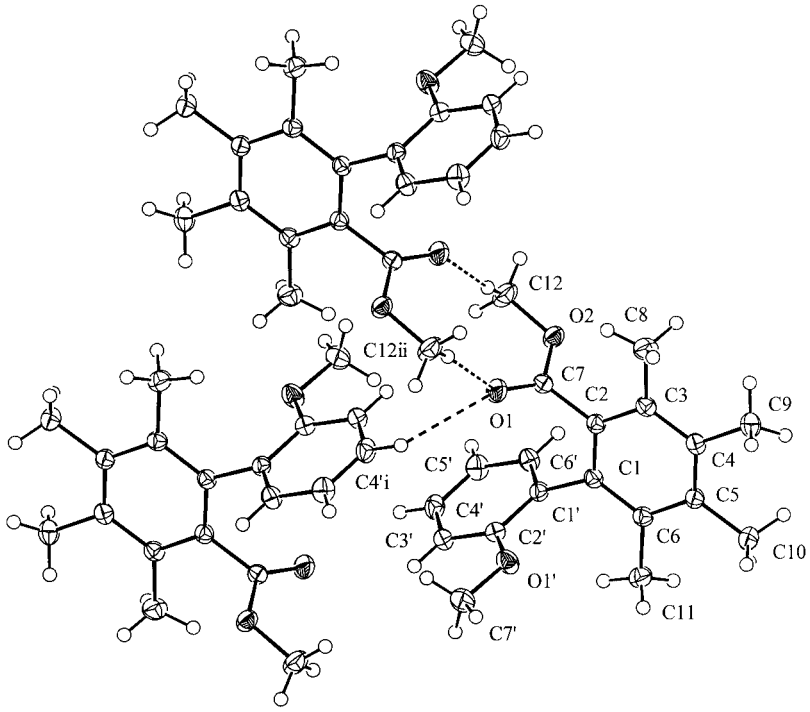

Figure 1. View of part of the network of **4c** with atom numbering. The dihedral angle of the least-squares planes of the aromatic rings is 74.29(4)°. The parameters of hydrogen bonds $C4^{i}$–$H4^{i}$···O1: $C4^{i}$···O1 3.230(2) Å, $C4^{i}$–$H4^{i}$···O1 131.5° and $C12^{ii}$-$H12C^{ii}$···O1: $C12^{ii}$···O1 3.449(2) Å, $C12^{ii}$–$H12C^{ii}$···O1 171.5°, symmetry codes (i) $-x, -y, 1-y$, (ii) $-x, 1-y, 1-y$. The displacement ellipsoids are drawn at the 50% probability level (PLATON).

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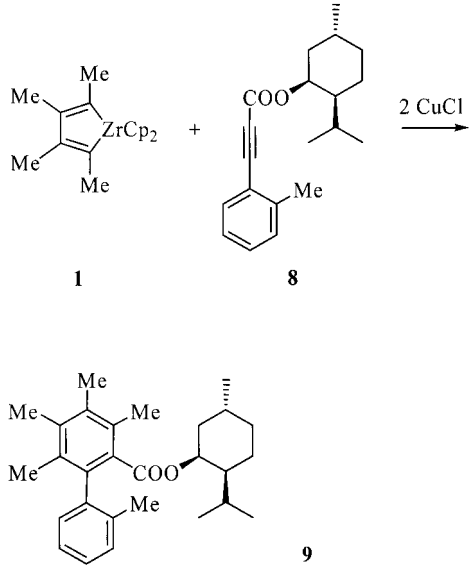
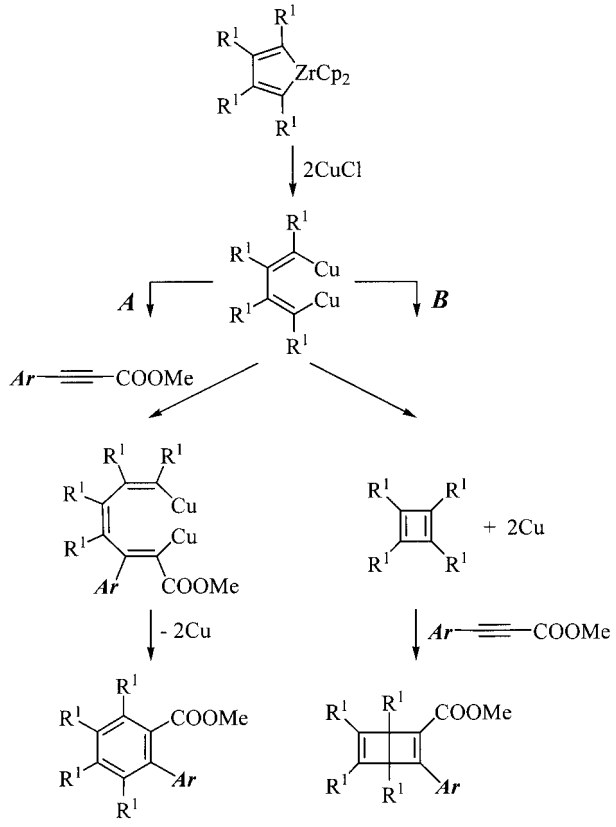
In the next step we attempted to carry out a diastereoselective reaction between tetramethylzirconacyclopentadiene (**1**) and the (–)-menthyl ester **8** in the presence of a stoichiometric amount of CuCl (Scheme 3). However, the result was rather disappointing: the corresponding product **9** was obtained in unimpressive yield (19%) and the diastereoselectivity was also low (2:1). The diastereoselectivity ratio was determined by integration of ^{1}H NMR signals of each diastereoisomer. The major diastereoisomer was obtained as a single compound by HPLC. (However, the configuration of the biaryl moiety remains unknown, because it was not possible to grow crystals suitable for X-ray analysis and the use of other methods also did not provide clearcut information.) The obtained diastereoisomer was tested for configurational stability by heating it at different temperatures for various periods of times, but we did not observe any indication of racemization (i.e., lost of axial chirality about the C–C bond connecting the two aryl rings) even on heating it at 200 °C. This indicates that the *ortho*-substitution provides considerable steric hindrance to block rotation about the C–C bond connecting the both aryl rings.



Scheme 3. Reaction between the zirconacyclopentadiene **1a** and the (–)-menthyl ester **8**.

As far as a reaction mechanism is concerned, it is worth noting that the formation of the Dewar benzenes in CuCl-mediated reactions between zirconacyclopentadienes and activated alkynes has not been observed previously. There is some evidence, and it has been generally accepted, that the mechanism of the CuCl-mediated reaction with activated alkynes proceeds through a conjugated addition of the C–Cu bond to the triple bond of the activated alkyne followed by ring closure to the aryl compound through radical decomposition of the unstable dicopper intermediate (path ***A***, Scheme 4).[7] However, it was obvious that this reaction mechanism cannot explain the formation of the Dewar benzenes and that there must be a concomitantly operating alternative reaction pathway. Generally, Dewar benzenes have usually been prepared by cycloaddition reactions between cyclobutadienes and alkynes,[19] so their formation indicates that a cyclobutadiene must be formed in one of the reaction steps. In view of this, we assume that the formation of the Dewar benzenes proceeds as follows: radical decomposition of the dicopper intermediate, formed after the transmetallation of the zirconacyclopentadiene with CuCl, results in the formation of the tetraethylcyclobutadiene, which immediately reacts with the present arylpropynoate to give the corresponding Dewar benzene (path ***B***, Scheme 4). In an attempt to confirm this assumption, the unsymmetrically substituted 4,5-diethyl-2,3-diphenylzirconacyclopentadiene was treated with the propynoate **3c** to check whether regioisomeric Dewar benzenes could be formed, but unfortunately only an intractable reaction mixture was obtained. Nevertheless, the cyclobutadiene pathway is supported by the fact that the formation of tetraethylcyclobutadiene from tetraethylzirconacyclopentadiene—as well as its cycloaddition reaction—under similar conditions has been reported previously.[20]



Scheme 4. Mechanisms of the reactions of zirconacyclopentadienes to afford biaryls and Dewar benzenes.

Further supportive information for the above reaction mechanism appeared at just about the same time as we were concluding this study. An article reported on the generation of a cyclobutadiene from a zirconacyclopentadiene,[21] and the authors showed that the organodicopper species formed by the reaction between a zirconacyclopentadiene and CuCl underwent fast reductive elimination of copper in the presence of benzoquinone to give a cyclobutadiene dimerization product. Cyclobutadiene was regarded as the reactive inter-

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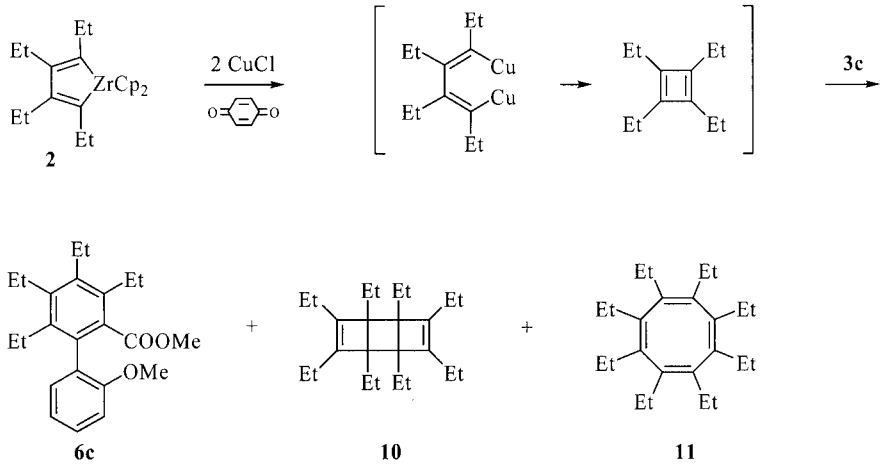

Scheme 5. Reaction between **2** and **3c** in the presence of CuCl and benzoquinone.

mediate. Although it was not stated in the report, the role of benzoquinone is quite unambiguous: it supports reductive elimination of copper from the intermediate[22] thus enhancing the formation of cyclobutadiene. We reasoned that application of these conditions to our system might give us access to reaction mixtures with higher proportions of Dewar benzenes, so the reaction between tetraethylzirconacyclopentadiene (**1**) and the propynoate **3c** in the presence of CuCl and benzoquinone was carried out at 50 °C (Scheme 5). However, the result was not encouraging: the biaryl **6c** was formed in 30% yield and the formation of the corresponding Dewar benzene **7c** was observed only in trace amounts in the initial stages of the experiment. Probably it decomposed under the reaction conditions, as we also observed its decomposition into a complex mixture of products even on standing at room temperature (20 °C). As for other products, compounds such as the tricyclooctadiene **10** and the cyclooctatetraene **11** were detected in the reaction mixture by their characteristic NMR signals.[21]

Conclusions

In conclusion, we have shown that the zirconocene-based methodology provides a simple, convenient, and one-pot procedure for coupling of two alkynes with an *ortho*-substituted arylpropynoate to provide highly substituted biaryls under mild reaction conditions. In this regard, the reaction of the intermediate zirconacyclopentadienes proceeds uneventfully in the presence of the Ni complex to give solely the corresponding biaryls. On the other hand, the reaction in the presence of CuCl apparently proceeds by two different pathways: one resulting in the formation of biaryls and the other in the formation of Dewar benzenes.

Experimental Section

General Remarks: All reactions were carried out under inert atmosphere (Ar). THF was distilled from benzophenone and sodium prior to use. $NiBr_2(PPh_3)_2$, the propynoates **3**, and the (–)-menthyl ester **8** were prepared by previously reported methods or by their modifications; for details see Supporting Information. Hex-3-yne and *n*BuLi (1.6 M solution in hexanes) were purchased from Aldrich. But-2-yne was purchased from Fluka, Buchs. All other chemicals and solvents were of commercial purity and were used without further purification.

^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Varian Unity Inova 400 spectrometer with tetramethylsilane as an internal standard. Infrared spectra were recorded on a PE-640 Perkin–Elmer spectrometer. Mass spectra were obtained on a ZAB-SEQ VG Analytical spectrometer. Elemental analyses were obtained on a Perkin–Elmer 2400 elemental analyzer. TLC was performed on Merck Silica Gel 60 F_{254} aluminium sheets and column chromatography was performed on Fluka Silica Gel 60.

General Procedure for Reactions between Zirconacylopentadienes and Arylpropynoates in the Presence of Stoichiometric Amounts of CuCl: *n*BuLi in hexanes (1.6 M, 1.25 mL, 2 mmol) was added at –78 °C to a solution of zirconocenene dichloride (292 mg, 1 mmol) in THF (5 mL) and the reaction mixture was stirred for 1 h. The alkyne (2 mmol) was then added and the reaction mixture was allowed to warm to 20 °C within 1 h. After that the arylpropynoate (1.5 mmol) and CuCl (200 mg, 2 mmol) were added, and the reaction mixture was stirred for 148 h (1 week) at 20 °C. The reaction mixture was quenched with 3 M HCl and extracted with diethyl ether (3 × 10 mL), and combined organic fractions were dried over $MgSO_4$. Removal of solvents under reduced pressure, followed by column chromatography on silica gel, afforded the corresponding products.

General Procedure for Reactions between Zirconacylopentadienes and Arylpropynoates in the Presence of Stoichiometric Amounts of $NiBr_2(PPh_3)_2$: The arylpropynoate (1.5 mmol) and $NiBr_2(PPh_3)_2$ (742 mg, 1 mmol) were added to a solution of tetraethylzirconacyclopentadiene (1 mmol) in THF (5 mL), and the reaction mixture was stirred for 24 h at 20 °C. The reaction mixture was diluted with diethyl ether (10 mL), filtered, and evaporated with silica gel. Column chromatography on silica gel afforded the corresponding products.

Methyl 2-(2-Fluorophenyl)-3,4,5,6-tetramethylbenzoate (4a). Reaction with CuCl: Column chromatography on silica gel (hexane/EtOAc, 10:1) afforded the title compound (163 mg, 57%) as colorless crystals: m.p. 76–79 °C. ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): δ = 2.01 (s, 3 H), 2.25 (s, 3 H), 2.26 (s, 3 H), 2.27 (s, 3 H), 3.42, 7.08–7.16 (m, 3 H), 7.28–7.34 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si): δ = 16.27, 16.72, 17.33, 17.61, 51.49, 115.07 (d, *J*

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= 22 Hz), 123.61 (d, J = 4 Hz), 127.73 (d, J = 18 Hz), 129.25 (d, J = 8 Hz), 129.86, 130.00, 131.42 (d, J = 3 Hz), 132.88, 135.49, 136.60, 158.68, 161.12, 170.53 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1720, 1455, 1436, 1297, 1201, 1176, 1100, 1010 cm^{-1}. HRMS calcd. for $C_{18}H_{19}FO_2$: 286.13691; found 286.13774; R_f (hexane/EtOAc, 9:1) = 0.31.

Methyl 2-(2-Chlorophenyl)-3,4,5,6-tetramethylbenzoate (4b). Reaction with CuCl: Column chromatography on silica gel (hexane/EtOAc, 10:1) afforded the title compound (97 mg, 32%) as colorless crystals: m.p. 102–104 °C. ^1H NMR (400 MHz, $CDCl_3$, Me_4Si): δ = 1.97 (s, 3 H), 2.26 (s, 3 H), 2.27 (s, 3 H), 2.28 (s, 3 H), 3.41 (s, 3 H), 7.14–7.17 (m, 1 H), 7.25–7.28 (m, 2 H), 7.42–7.45 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si): δ = 16.32, 16.71, 17.10, 17.69, 51.43, 126.24, 128.62, 128.95, 129.81, 131.22, 132.19, 132.48, 133.67, 134.37, 135.35, 136.56, 139.03, 170.42 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3009, 1721, 1436, 1296, 1201, 1176, 1060, 1054, 1010 cm^{-1}. HRMS calcd. for $C_{18}H_{19}ClO_2$: 302.10736; found 302.10779; R_f (hexane/EtOAc, 9:1) = 0.45.

Methyl 2-(2-Methoxyphenyl)-3,4,5,6-tetramethylbenzoate (4c). Reaction with CuCl: Column chromatography on silica gel (hexane/EtOAc, 4:1) afforded the title compound (140 mg, 47%) as colorless crystals: m.p. 85–86 °C. ^1H NMR (400 MHz, $CDCl_3$, Me_4Si): δ = 1.97 (s, 3 H), 2.24 (s, 3 H), 2.25 (s, 3 H), 2.26 (s, 3 H), 3.40 (s, 3 H), 3.75 (s, 3 H), 6.90–6.96 (m, 2 H), 7.05 (dd, J = 7.3, 1.8 Hz, 1 H), 7.28–7.30 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si): δ = 16.24, 16.70, 17.22, 17.66, 51.30, 55.59, 110.43, 120.06, 128.68, 129.17, 129.53, 130.85, 132.77, 132.94, 133.03, 134.61, 136.21, 157.08, 170.81 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 2947, 1727, 1660, 1581, 1495, 1462, 1434, 1293, 1245, 1197, 1027, 756 cm^{-1}. HRMS calcd. for $C_{19}H_{22}O_3$: 298.16096; found 298.15968; elemental anal. calcd. $C_{19}H_{22}O_3$: C 76.48, H 7.43, O 16.09; found C 76.41, H 7.67. R_f (hexane/EtOAc, 4:1) = 0.35.

Methyl 3,4,5,6-Tetramethyl-2-(2-methylphenyl)benzoate (4d). Reaction with CuCl: Column chromatography on silica gel (hexane/EtOAc, 10:1) afforded the title compound (113 mg, 40%) as colorless crystals: m.p. 86–89 °C. ^1H NMR (400 MHz, $CDCl_3$, Me_4Si): δ = 1.91 (s, 3 H), 2.03 (s, 3 H), 2.24 (s, 3 H), 2.27 (s, 6 H), 3.37 (s, 3 H), 7.00 (dt, J = 7.2, 1.2 Hz, 1 H), 7.14–7.18 (m, 1 H), 7.20 (d, J = 1.2 Hz, 1 H), 7.21–7.23 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si): δ = 16.18, 16.67, 16.97, 17.60, 19.78, 51.29, 125.15, 127.25, 129.30, 129.35, 129.54, 131.98, 132.45, 134.36, 135.69, 136.35, 136.93, 139.60, 170.81 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3005, 2951, 1722, 1435, 1295, 1201, 1176, 1176, 1010 cm^{-1}. HRMS calcd. for $C_{19}H_{22}O_2$: 282.16198; found 282.16229; R_f (hexane/EtOAc, 10:1) = 0.40.

Methyl 3,4,5,6-Tetramethyl-2-[2-(trifluoromethyl)phenyl]benzoate (4e) and Methyl 1,4,5,6-Tetramethyl-3-[2-(trifluoromethyl)phenyl]bicyclo[2.2.0]hexa-2,5-diene-2-carboxylate (5e). Reaction with CuCl: Column chromatography on silica gel (hexane/EtOAc, 10:1) afforded **4e** (54 mg, 16%) as a colorless solid and **5e** (20 mg, 6%) as a colorless oil, which upon further recrystallization from *n*-hexane afforded colorless crystals.

Compound 4e: M.p. 59–61 °C. ^1H NMR (400 MHz, $CDCl_3$, Me_4Si): δ = 1.88 (s, 3 H), 2.25 (s, 3 H), 2.26 (s, 3 H), 2.27 (s, 3 H), 3.38 (s, 3 H), 7.19 (d, J = 7.6 Hz, 1 H), 7.45 (t, J = 7.6 Hz, 1 H), 7.52 (t, J = 7.4 Hz, 1 H), 7.70 (d, J = 7.7 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si): δ = 16.32, 16.65, 17.79, 17.99, 51.28, 123.96 (q, $^2J_{(C–F)}$ = 273 Hz), 126.07 (q, $^4J_{(C–F)}$ = 5 Hz), 127.55, 129.28 (q, $^3J_{(C–F)}$ = 30 Hz), 129.74, 130.99, 131.99, 132.06, 132.24, 133.67, 135.24, 136.50, 138.62, 170.25 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 2950, 1723, 1436, 1316, 1296, 1174, 1153, 1129, 1060, 1035, 908 cm^{-1}. HRMS calcd. for $C_{19}H_{19}F_3O_2$: 336.13372; found 336.13303; R_f (hexane/EtOAc, 10:1) = 0.40.

Compound 5e: M.p. 51–53 °C. ^1H NMR (400 MHz, $CDCl_3$, Me_4Si): δ = 1.20 (s, 3 H), 1.36 (s, 3 H), 1.66 (d, J = 1.4 Hz, 3 H), 1.70 (d, J = 1.4 Hz, 3 H), 3.57 (s, 3 H), 7.18 (d, J = 7.6 Hz, 1 H), 7.40 (t, J = 7.5 Hz, 1 H), 7.52 (t, J = 7.6 Hz, 1 H), 7.68 (d, J = 7.9 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si): δ = 9.76, 10.54, 11.11, 11.20, 50.80, 55.25, 59.34, 123.84 (q, $^2J_{(C–F)}$ = 272 Hz), 126.28 (q, $^4J_{(C–F)}$ = 5 Hz), 127.61 (q, $^3J_{(C–F)}$ = 31 Hz), 127.63, 127.95, 131.10, 134.05, 141.50, 142.66, 144.31, 162.63, 163.71 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3016, 2957, 1710, 1647, 1436, 1317, 1216, 1212, 1170, 1133, 1115, 1037 (cm^{-1}). HRMS calcd. for $C_{19}H_{19}F_3O_2$: 336.13372; found 336.13442; R_f (hexane/EtOAc, 9:1) = 0.25.

Methyl 3,4,5,6-Tetraethyl-3-(2-fluorophenyl)benzoate (6a). Reaction with CuCl: Column chromatography on silica gel (hexane/EtOAc, 10:1) afforded the title compound (178 mg, 52%) as a yellow oil: ^1H NMR (400 MHz, $CDCl_3$, Me_4Si): δ = 0.91 (t, J = 7.5 Hz, 3 H), 1.20 (t, J = 7.5 Hz, 3 H), 1.21 (t, J = 7.5 Hz, 3 H), 1.22 (t, J = 7.5 Hz, 3 H), 2.40–2.75 (m, 8 H), 3.38 (s, 3 H), 7.08–7.14 (m, 2 H), 7.16 (td, J = 7.3, 1.8 Hz, 1 H), 7.28–7.34 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si): δ = 15.02, 15.66, 15.74, 15.95, 21.90, 22.21, 23.33, 23.98, 51.31, 115.09 (d, J = 22 Hz), 123.33 (d, J = 4 Hz), 127.33 (d, J = 18 Hz), 129.24 (d, J = 8 Hz), 130.62, 132.24 (d, J = 3 Hz), 133.59, 135.88, 138.84, 140.46, 141.64, 158.64, 161.08, 170.60 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 2970, 1722, 1493, 1451, 1438, 1279, 100, 1173, 1056, 1028 cm^{-1}. HRMS calcd. for $C_{22}H_{27}FO_2$: 342.19951; found 342.19892; R_f (hexane/EtOAc, 9:1) = 0.40.

Reaction with $NiBr_2(PPh_3)_2$: Column chromatography on silica gel (hexane/EtOAc, 9:1) afforded the title compound (154 mg, 45%) as a viscous oil.

Methyl 3-(2-Chlorophenyl)-3,4,5,6-tetraethylbenzoate (6b). Reaction with CuCl: Column chromatography on silica gel (hexane/EtOAc, 10:1) afforded the title compound (136 mg, 38%) as a yellow oil: ^1H NMR (400 MHz, $CDCl_3$, Me_4Si): δ = 0.90 (t, J = 7.6 Hz, 3 H), 1.20 (t, J = 7.4 Hz, 3 H), 1.21 (t, J = 7.4 Hz, 3 H), 1.23 (t, J = 7.5 Hz, 3 H), 2.28 (q, J = 7.6 Hz, 2 H), 2.50–2.75 (m, 6 H), 3.37 (s, 3 H), 7.23–7.26 (m, 3 H), 7.40–7.44 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si): δ = 15.01, 15.73, 15.78, 15.99, 21.91, 22.16, 23.16, 23.97, 51.20, 125.80, 128.58, 128.96, 132.05, 132.87, 134.12, 134.34, 135.90, 138.28, 138.60, 140.26, 141.68, 170.48 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 2970, 1723, 1437, 1281, 1199, 1174, 1059 cm^{-1}. HRMS calcd. for $C_{22}H_{27}ClO_2$: 358.16996; found 358.16893; R_f (hexane/EtOAc, 9:1) = 0.48.

Reaction with $NiBr_2(PPh_3)_2$: Column chromatography on silica gel (hexane/EtOAc, 9:1) afforded the title compound (165 mg, 46%) as a viscous oil.

Methyl 3,4,5,6-Tetraethyl-3-(2-methoxyphenyl)benzoate (6c) and Methyl 1,4,5,6-Tetraethyl-3-(2-methoxyphenyl)bicyclo[2.2.0]hexa-2,5-diene-2-carboxylate (7c): Reaction with CuCl. Column chromatography on silica gel (hexane/EtOAc, 9:1) afforded **6c** (106 mg, 30%) and **7c** (35 mg, 10%) as viscous oils. Reaction with $NiBr_2(PPh_3)_2$. Column chromatography on silica gel (hexane/EtOAc, 9:1) afforded 186 mg (52%) of the title compound **6c** as a viscous oil.

Compound 6c: ^1H NMR (400 MHz, $CDCl_3$, Me_4Si): δ = 0.90 (t, J = 7.5 Hz, 3 H), 1.20 (t, J = 7.5 Hz, 3 H), 1.21 (t, J = 7.5 Hz, 3 H), 1.22 (t, J = 7.5 Hz, 3 H), 2.34 (q, J = 7.5 Hz, 1 H), 2.45 (q, J = 7.5 Hz, 1 H), 2.56 (q, J = 7.5 Hz, 1 H), 2.62 (q, J = 7.5 Hz, 1 H), 2.64–2.80 (m, 4 H), 3.34 (s, 3 H), 3.74 (s, 3 H), 6.92 (t, J = 7.6 Hz, 1 H), 7.08 (dd, J = 7.6, 1.8 Hz, 1 H), 7.26 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si): δ = 14.96, 15.72, 15.81, 16.00, 21.92, 22.25, 23.25, 24.17, 51.13, 55.53, 110.48, 119.76, 128.63, 128.82,

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131.79, 133.50, 133.69, 135.56, 138.94, 139.55, 141.30, 157.07, 170.91 ppm. IR (neat): $\tilde{\nu}$ = 2950, 1704, 1595, 1487, 1466, 1434, 1270, 1248, 1192, 1173, 1069, 1026, 753 cm^{-1}. HRMS calcd. for $C_{23}H_{30}O_3$: 354.219495; found 354.220534. R_f (hexane/EtOAc, 9:1) = 0.43.

Compound 7c: ^1H NMR (400 MHz, $CDCl_3$, Me_4Si): δ = 0.88 (t, J = 7.5 Hz, 3 H), 0.98 (t, J = 7.5 Hz, 3 H), 1.00 (t, J = 7.5 Hz, 3 H), 1.02 (t, J = 7.5 Hz, 3 H), 1.84–2.03 (m, 4 H), 2.05–2.24 (m, 4 H), 3.68 (s, 3 H), 3.78 (s, 3 H), 6.80 (dd, J = 7.4, 1.0 Hz, 1 H), 6.94 (td, J = 7.5, 1.1 Hz, 1 H), 7.24–7.30 (m, 1 H), 7.58 (dd, J = 7.6, 1.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si): δ = 10.71, 10.75, 11.22, 11.42, 20.53, 21.00, 21.15, 21.17, 50.69, 54.75, 110.31, 120.10, 121.65, 124.77, 130.71, 132.17, 128.87, 136.88, 142.90, 144.19, 157.11, 162.45, 164.92 ppm. IR (neat): $\tilde{\nu}$ = 2969, 1729, 1601, 1581, 1487, 1495, 1460, 1435, 1281, 1244, 1194, 1172, 1113, 1052,1027 cm^{-1}. HRMS calcd. for $C_{23}H_{30}O_3$ 354.219495; found 354.220534. R_f (hexane/EtOAc, 4:1) = 0.35.

Methyl 3,4,5,6-Tetraethyl-3-(2-methoxyphenyl)benzoate (6d) and Methyl 1,4,5,6-Tetraethyl-3-(2-methoxyphenyl)bicyclo[2.2.0]hexa-2,5-diene-2-carboxylate (7d): Reaction with CuCl: Column chromatography on silica gel (hexane/EtOAc, 9:1) afforded a inseparable mixture of **6d** and **7d** (108 mg, 30%) in 1:0.8 ratio as a viscous oil.

Compound 6d: ^1H NMR (400 MHz, $CDCl_3$, Me_4Si): δ = 0.88 (t, J = 7.3 Hz, 3 H), 1.19 (t, J = 7.3 Hz, 3 H), 1.21 (t, J = 7.3 Hz, 3 H), 1.23 (t, J = 7.3 Hz, 3 H), 2.01 (s, 3 H), 2.17 (dq, J = 13.5, 7.4 Hz, 1 H), 2.48 (dq, J = 13.5, 7.4 Hz, 1 H), 2.60 (q, J = 7.5 Hz, 2 H), 2.66–2.80 (m, 4 H), 3.32 (s, 3 H), 7.10–7.20 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si): δ = 15.14, 15.82, 15.91, 16.08, 20.02, 21.84, 22.17, 22.96, 23.97, 51.10, 124.73, 127.21, 129.28, 130.27, 133.05, 135.63, 136.16, 136.94, 137.86, 139.18, 139.40, 141.56, 170.89 ppm.

Compound 7d: ^1H NMR (400 MHz, $CDCl_3$, Me_4Si): δ = 0.88 (t, J = 7.6 Hz, 3 H), 1.00 (t, J = 7.6 Hz, 3 H), 1.01 (t, J = 7.6 Hz, 3 H), 1.02 (t, J = 7.3 Hz, 3 H), 1.91 (q, J = 7.4 Hz, 2 H), 2.05–2.20 (m, 6 H), 2.26 (s, 3 H), 3.63 (m, 3 H), 7.10–7.20 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si): δ = 10.58, 10.95, 11.96, 12.78, 19.91, 20.49, 20.77, 20.81, 21.36, 50.71, 60.15, 64.03, 124.91, 126.56, 127.66, 130.17, 133.30, 134.73, 135.89, 139.43, 146.25, 149.92; 165.97 ppm. IR (neat): $\tilde{\nu}$ = 2971, 2937, 2878, 1708, 1634, 1488, 1455, 1437, 1379, 1301, 1284, 1274, 1200, 1174, 1057 cm^{-1}. HRMS calcd. for $C_{23}H_{30}O_2$ 338.22458; found 338.22517. R_f (hexane/EtOAc, 9:1) = 0.44.

Reaction with $NiBr_2(PPh_3)_2$: Column chromatography on silica gel (hexane/EtOAc, 9:1) afforded **6d** (112 mg, 33%) as a viscous oil: ^1H NMR (400 MHz, $CDCl_3$, Me_4Si): δ = 0.88 (t, J = 7.3 Hz, 3 H), 1.19 (t, J = 7.3 Hz, 3 H), 1.21 (t, J = 7.3 Hz, 3 H), 1.23 (t, J = 7.3 Hz, 3 H), 2.01 (s, 3 H), 2.17 (dq, J = 13.5, 7.4 Hz, 1 H), 2.48 (dq, J = 13.5, 7.4 Hz, 1 H), 2.60 (q, J = 7.5 Hz, 2 H), 2.66–2.80 (m, 4 H), 3.32 (s, 3 H), 7.08–7.22 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si): δ = 15.14, 15.82, 15.91, 16.08, 20.02, 21.84, 22.17, 22.96, 23.97, 51.10, 124.73, 127.21, 129.28, 130.27, 133.05, 135.63, 136.16, 136.94, 138.86, 139.18, 139.40, 141.56, 170.89 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3014, 2973, 2938, 2878, 1723, 1453, 1438, 1379, 1332, 1303, 1286, 1273, 1219, 1216, 1199, 1174, 1083, 1056, 1040, 1028 cm^{-1}. HRMS calcd. for $C_{23}H_{30}O_2$: 338.22458; found 338.22517. R_f (hexane/EtOAc, 9:1) = 0.44.

Methyl 3,4,5,6-Tetraethyl-3-[2-(trifluoromethyl)phenyl]benzoate (6e) and Methyl 1,4,5,6-Tetraethyl-3-[2-(trifluoromethyl)phenyl]bicyclo[2.2.0]hexa-2,5-diene-2-carboxylate (7e). Reaction with CuCl: Column chromatography on silica gel (hexane/EtOAc, 9:1) afforded **6e** (90 mg, 23%) and **7e** (78 mg, 20%) as viscous oils.

Reaction with $NiBr_2(PPh_3)_2$: Column chromatography on silica gel (hexane/EtOAc, 9:1) afforded 90 mg (23%) of the title compound **6e** as a viscous oil.

Compound 6e: ^1H NMR (400 MHz, $CDCl_3$, Me_4Si): δ = 0.86 (t, J = 7.5 Hz, 3 H), 1.18 (t, J = 7.5 Hz, 3 H), 1.19 (t, J = 7.5 Hz, 3 H), 1.22 (t, J = 7.5 Hz, 3 H), 2.15 (dq, J = 14.0, 7.5 Hz, 2 H), 2.50 (dq, J = 14.0, 7.5 Hz, 2 H), 2.62 (dq, J = 14.0, 7.5 Hz, 2 H), 2.68–2.74 (m, 2 H), 3.34 (s, 3 H), 7.29 (d, J = 7.5 Hz, 1 H), 7.41–7.52 (m, 2 H), 7.68 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si): δ = 15.15, 15.68, 15.74, 16.00, 21.84, 22.05, 23.46, 23.94, 51.06, 123.93 (q, $^2J_{(C-F)}$ = 272 Hz), 126.15 (q, $^4J_{(C-F)}$ = 5 Hz), 129.37 (q, $^3J_{(C-F)}$ = 31 Hz), 130.45, 132.04, 132.36, 132.66, 133.87, 135.75, 137.87, 138.10, 140.19, 141.55, 170.40 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3016, 2974, 2938, 1721, 1453, 1316, 1289, 1275, 1263, 1213, 1176, 1131, 1035 cm^{-1}. HRMS calcd. for $C_{23}H_{27}F_3O_2$: 392.19632; found 92.19565; R_f (hexane/EtOAc, 9:1) = 0.38.

Compound 7e: ^1H NMR (400 MHz, $CDCl_3$, Me_4Si): δ = 0.86 (t, J = 7.3 Hz, 3 H), 1.05 (t, J = 7.5 Hz, 3 H), 1.01 (t, J = 7.5 Hz, 3 H), 1.07 (t, J = 7.3 Hz, 3 H), 1.85–1.91 (m, 4 H), 2.10–2.22 (m, 2 H), 2.30 (dq, J = 7.5 Hz, 2 H), 3.55 (s, 3 H), 7.20 (dt, J = 7.6, 0.9 Hz, 1 H), 7.37–7.42 (t, J = 7.5 Hz, 1 H), 7.75 (t, J = 7.6 Hz, 1 H), 7.67 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si): δ = 10.62, 10.86, 11.79, 12.92, 20.51, 20.55, 20.65, 21.88, 50.73, 60.15, 64.77, 124.43 (q, $^2J_{(C-F)}$ = 272 Hz), 125.15 (q, $^1J_{(C-F)}$ = 362 Hz), 126.10 (q, $^4J_{(C-F)}$ = 5 Hz), 127.44, 127.58, 130.99, 135.05, 141.06, 146.62, 149.67, 163.15, 163.91 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3016, 2973, 2939, 1711, 1437, 1317, 1265, 1218, 1213, 1172 cm^{-1}. HRMS calcd. for $C_{23}H_{27}F_3O_2$: 392.19632; found 392.19291; R_f (hexane/EtOAc, 9:1) = 0.38.

Methyl 3,4,5,6-Tetraethyl-2-(2-methoxynaphthyl)benzoate (6f). Reaction with $NiBr_2(PPh_3)_2$: Column chromatography on silica gel (hexane/EtOAc, 9:1) afforded the title compound (85 mg, 20%) as a viscous oil: ^1H NMR (400 MHz, $CDCl_3$, Me_4Si): δ = 0.79 (t, J = 7.5 Hz, 3 H), 1.21 (t, J = 7.5 Hz, 3 H), 1.25 (t, J = 7.5 Hz, 3 H), 1.28 (t, J = 7.5 Hz, 3 H), 2.19 (dq, J = 13.8, 7.5 Hz, 1 H), 2.35 (dq, J = 13.8, 7.5 Hz, 1 H), 2.63 (q, J = 7.5 Hz, 2 H), 2.76 (q, J = 7.5 Hz, 2 H), 2.78 (q, J = 7.5 Hz, 2 H), 3.03 (s, 3 H), 3.85 (s, 3 H), 7.18–7.22 (m, 1 H), 7.25–7.33 (m, 3 H) 7.73–7.77 (m, 1 H), 7.84 (d, J = 9 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si): δ = 14.78, 15.83, 15.96, 16.11, 22.00, 22.31, 23.60, 24.19, 50.75, 56.35, 113.13, 122.70, 123.25, 125.74, 126.03, 127.36, 128.52, 129.20, 131.19, 134.04, 134.15, 136.00, 139.57, 139.69, 141.66, 154.39, 170.67 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 2968, 2935, 1718, 1507, 1274, 1262, 1243, 1198, 1173, 1058, 908, 809 cm^{-1}. HRMS calcd. for $C_{27}H_{32}O_3$: 404.23515; found 404.23648; R_f (hexane/EtOAc, 9:1) = 0.20.

Reaction with CuCl: Column chromatography on silica gel (hexane/EtOAc, 9:1) afforded the title compound **6f** (30 mg, 7%) as a viscous oil.

(–)-Menthyl 3,4,5,6,2′-Pentamethylbiphenyl-2-carboxylate (9): *n*BuLi in hexanes (1.6 M, 1.25 mL, 2 mmol) was added at –78 °C to a solution of zirconocenene dichloride (292 mg, 1 mmol) in THF (5 mL) and the reaction mixture was stirred for 1 h. But-2-yne (314 μL, 4 mmol) was then added and the reaction mixture was allowed to warm up to 20 °C within 1 h. The menthyl ester **8** (298 mg, 1.5 mmol) and CuCl (200 mg, 2 mmol) were added, and the reaction mixture was stirred for 148 h (1 week) at 20 °C. The reaction mixture was quenched with 3 M HCl and extracted with diethyl ether (3 × 10 mL), and the combined organic fractions were dried over $MgSO_4$. Removal of solvents under reduced pressure followed by column chromatography on silica gel (hexane/EtOAc, 10:1) afforded the title compound (77 mg, 19%) as a yellow oil: ^1H NMR (400 MHz, $CDCl_3$, TMS): δ = 0.57 (d, J = 7.0 Hz, 3 H),

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0.77 (d, J = 6.4 Hz, 3 H), 0.78 (d, J = 7.0 Hz, 3 H), 0.89–0.98 (m, 2 H), 1.14–1.20 (m, 1 H), 1.19–1.28 (m, 2 H), 1.55–1.60 (m, 3 H), 1.76–1.84 (m, 1 H), 1.80 (s, 3 H), 2.01 (m, 3 H), 2.26 (s, 3 H), 2.27 (s, 3 H), 2.28 (s, 3 H), 4.50–4.60 (m, 1 H), 7.02 (d, J = 7.3 Hz, 1 H), 7.12–7.22 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 15.82, 16.28, 16.70, 16.87, 17.48, 20.03, 20.81, 21.89, 22.93, 25.65, 31.11, 34.10, 39.31, 46.62, 74.56, 125.44, 127.31, 129.18, 129.42, 129.81, 132.04, 132.91, 134.38, 135.40, 136.05, 137.37, 139.70, 169.93 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 2957, 2927, 1709, 1456, 1294, 1195, 998, 953 cm^{-1}. HRMS calcd. for $C_{28}H_{38}O_2$: 406.28718; found 406.28701; R_f (hexane/EtOAc, 9:1) = 0.50.

Separation of diastereoisomers by preparative HPLC (hexane/EtOAc, 80:1) afforded 25 mg of a single diastereomer (it was not possible to separate the minor diastereoisomer from the starting material): $[\alpha]_D^{25}$ = –30.8 (c = 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 0.64 (d, J = 7.0 Hz, 3 H), 0.74 (d, J = 6.4 Hz, 3 H), 0.80 (d, J = 7.0 Hz, 3 H), 0.89–0.98 (m, 2 H), 1.14–1.20 (m, 1 H), 1.21–1.28 (m, 2 H), 1.52–1.60 (m, 3 H), 1.76–1.84 (m, 1 H), 1.88 (s, 3 H), 2.05 (m, 3 H), 2.25 (s, 3 H), 2.26 (s, 3 H), 2.27 (s, 3 H), 4.52 (dt, J = 10.9, 4.4 Hz, 1 H), 7.02 (d, J = 7.3 Hz, 1 H), 7.12–7.22 (m, 3 H) ppm.

Crystal Data for 3c: $C_{19}H_{22}O_3$, M = 298.37, triclinic, $P\bar{1}$ (No. 2), a = 7.9730(3) Å, b = 9.0650(3) Å, c = 12.3800(4) Å, α = 74.960(2)°, β = 72.121(2)°, γ = 73.285(2)°, V = 801.06(5) Å^3, Z = 2, D_x = 1.237 Mg·m^{-3}. A colorless crystal of dimensions 0.5 × 0.35 × 0.3 mm was mounted on a glass capillary with epoxy glue and measured on a Nonius KappaCCD diffractometer with monochromatized Mo-$K\alpha$ radiation (λ = 0.71073 Å) at 150(2) K. One absorption was neglected (μ = 0.082 mm^{-1}); a total of 12195 measured reflections in the range h = –10 to 10, k = –11 to 11, l = –16 to 16 (θ_{max} = 27.5°), from which 3660 were unique (R_{int} = 0.026), 3097 observed according to the $I > 2\sigma(I)$ criterion. The structure was solved by direct methods (SIR92)[23] and refined by full-matrix least-squares based on F^2 (SHELXL97).[24] The hydrogen atoms were fixed into idealized positions (riding model) and assigned temperature factors either H_{iso}(H) = 1.2 U_{eq}(pivot atom), or H_{iso}(H) = 1.5 U_{eq}(pivot atom) for methyl moiety. The refinement converged (Δ/σ_{max} = 0.000) to R = 0.043 for observed reflections and wR = 0.119, GOF = 1.029 for 205 parameters and all 3660 reflections. The final difference map displayed no peaks of chemical significance ($\Delta\rho_{max}$ = 0.270, $\Delta\rho_{min}$ = –0.249 e·Å^{-3}). CCDC-233093 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; Fax: +44-1223-336-033; or deposit@ccdc.cam.ac.uk).

Supporting Information (see also the footnote on the first page of this article): Synthesis, spectroscopic, and spectrometric data of propynoates **3** and **8**.

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[1] a) G. Bringmann, D. Menche, *Acc. Chem. Res.* **2001**, *34*, 615–624; b) P. Lloyd-Williams, E. Giralt, *Chem. Soc. Rev.* **2001**, *30*, 145–157; c) K. W. Bentley, *Nat. Prod. Rep.* **1993**, *10*, 449–470.

[2] For application of biaryls as ligands, see: a) P. Kočovský, Š. Vyskočil, M. Smrčina, *Chem. Rev.* **2003**, *103*, 3213–3246; b) Y. Chen, S. Yekta, A. K. Yudin, *Chem. Rev.* **2003**, *103*, 3155–3212; c) T. Hayashi, *Acc. Chem. Res.* **2000**, *33*, 354–362; d) S. Akutagawa, *App. Cat. A: General* **1995**, *128*, 171–207; e) *Chiral Auxiliaries and Ligands in Asymmetric Synthesis* (Ed.: J. Seyden-Penne); John Wiley & Sons: New York, **1995**; f) *Asymmetric Catalysis in Organic Synthesis* (Ed.: R. Noyori); Wiley Europe: Weinheim, **1994**.

[3] a) G. Bringmann, S. Tasler, R. M. Pfeifer, M. Breuning, *J. Organomet. Chem.* **2002**, *661*, 49–65; b) S. P. Stanforth, *Tetrahedron* **1998**, *54*, 263–303.

[4] a) H.-H. Frühauf, *Chem. Rev.* **1997**, *97*, 523–596; b) M. Lautens, W. Tam, *Chem. Rev.* **1996**, *96*, 49–92; c) D. B. Grotjahn, *Comprehensive Organometallic Chemistry II*; E. W. Abel, F. G. A. Stone, G. Wilkinson, Eds.; Elsevier Science Ltd: Oxford, **1995**; Vol. 12; pp. 741–770; d) N. E. Schore, *Comprehensive Organic Synthesis* (Eds.: B. M. Trost, I. Fleming), Pergamon Press Ltd: Oxford, **1991**, Vol. 5; pp. 1129–1162; e) P. J. Harrington, *Transition Metals in Total Synthesis*; John Wiley & Sons: New York, **1990**, pp. 200–240; f) N. E. Schore, *Chem. Rev.* **1988**, *88*; 1081–1119; g) K. P. C. Vollhardt, *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 539–556; h) K. C. Nicolaou, E. J. Sorensen, *Classics in Organic Synthesis (Targets, Strategies, Methods)*; VCH: Weinheim, **1996**; i) C. P. Dell, *J. Chem. Soc., Perkin Trans. 1* **1998**, 3873–3905; j) S. Saito, Y. Yamamoto, *Chem. Rev.* **2000**, *100*, 2901–2916.

[5] For reactions catalyzed by chiral complexes see: a) Y. Sato, T. Nishimata, M. Mori, *J. Org. Chem.* **1994**, *59*, 6133–6135; b) Y. Sato, T. Nishimata, M. Mori, *Heterocycles* **1997**, *44*, 443–4457; c) I. G. Stará, I. Starý, A. Kollárovič, F. Teplý, Š. Vyskočil, D. Šaman, *Tetrahedron Lett.* **1999**, *40*, 1993–1996; d) T. Shibata, T. Fujimoto, K. Yokota, K. Tatagi, *J. Am. Chem. Soc.* **2004**, *126*, 8382–8383; e) K. Tanaka, G. Nishida, A. Wada, K. Noguchi, *Angew. Chem.* **2004**, *116*, 6672–6674; *Angew. Chem. Int. Ed.* **2004**, *43*, 6510–6512. For cyclotrimerization of alkynes bearing chiral centers, see: f) B. Witulski, A. Zimmermann, *Synlett* **2002**, 1855–1859.

[6] a) E. Negishi, S. J. Holmes, J. Tour, J. A. Miller, F. E. Cederbaum, D. R. Swanson, T. Takahashi, *J. Am. Chem. Soc.* **1989**, *111*, 3336–3346; b) S. L. Buchwald, R. B. Nielsen, *J. Am. Chem. Soc.* **1989**, *111*, 2870–2874; c) T. V. RajanBabu, W. A. Nugent, D. F. Taber, P. J. Fagan, *J. Am. Chem. Soc.* **1988**, *110*, 7128–7135; d) E. Negishi, F. E. Cederbaum, T. Takahashi, *Tetrahedron Lett.* **1986**, *27*, 2829–2832.

[7] a) T. Takahashi, Z. F. Xi, M. Kotora, *J. Chem. Soc., Chem. Commun.* **1995**, 361–362; b) T. Takahashi, Z. F. Xi, A. Yamazaki, Y. H. Liu, K. Nakajima, M. Kotora, *J. Am. Chem. Soc.* **1998**, *120*, 1672–1680.

[8] T. Takahashi, F. Y. Tsai, Y. Z. Li, K. Nakajima, M. Kotora, *J. Am. Chem. Soc.* **1999**, *121*, 11093–11100.

[9] For reactions of alkynes with other zirconacycles in the presence of Ni complexes, see: a) P. R. Sharp, *J. Am. Chem. Soc.* **2000**, *122*, 9880–9881; b) J. S. Brown, P. R. Sharp, *Organometallics* **2003**, *22*, 3604–3607.

[10] Y. Z. Li, Y. Ura, F. Y. Tsai, F. Xu, T. Takahashi, *Heterocycles* **2001**, *54*, 943–949.

[11] T. Takahashi, F. Y. Tsai, Y. Z. Li, *Chem. Lett.* **1999**, 1173–1174.

[12] K. T. Wong, R. T. Chen, *Tetrahedron Lett.* **2002**, *43*, 3313–3317.

[13] S. A. Johnson, F.-Q. Liu, M. C. Suh, S. Zürcher, M. Haufe, S. S. H. Mao, T. D. Tilley, *J. Am. Chem. Soc.* **2003**, *125*, 4199–4211.

[14] T. Takahashi, M. Kitamura, B. Shen, K. Nakajima, *J. Am. Chem. Soc.* **2000**, *122*, 12876–12877.

[15] L. Dufková, H. Matsumura, D. Nečas, P. Štěpnička, F. Uhlík, M. Kotora, *Collect. Czech. Chem. Commun.* **2004**, *69*, 351–365.

[16] a) J. C. Anderson, J. W. Cran, N. P. King, *Tetrahedron Lett.* **2002**, *43*, 3849–3852; b) J. C. Anderson, J. W. Cran, N. P. King, *Tetrahedron Lett.* **2003**, *44*, 7771–7774.

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[17] Some of the Dewar benzenes **6** were independently prepared to confirm their structures by characteristic ^{1}H and ^{13}C NMR signals (for reaction conditions see: J. B. Koster, G. J. Timmermans, H. van Bekkum, *Synthesis* **1971**, 139–140). We plan to give a full account of these results in an independent article in the near future.
[18] a) *Stereochemistry of Organic Compounds* (Eds.: E. L. Eliel, S. H. Wilen), John Wiley & Sons, New York, **1994**, 1144; b) K. Mikami, Y. Itoh, M. Yamanaka, *Chem. Rev.* **2004**, *104*, 1–16.
[19] T. Bally, S. Masamune, S. *Tetrahedron* **1980**, *36*, 343–370.
[20] H. Ubayama, W.-H. Sun, Z. Xi, T. Takahashi, *Chem. Commun.* **1998**, 1931–1932.
[21] C. Chen, C. Xi, C. Lai, R. Wang, X. Hong, *Eur. J. Org. Chem.* **2004**, 647–650.
[22] L. S. Hegedus, *Transition Metals in the Synthesis of Complex Organic Molecules*, University Science Books, Mill Valley, California, **1993**.
[23] A. Altomare, M. C. Burla, M. Camalli, G. L. Cascarano, A. G. G. Moliterni, C. Giacovazzo, A. Guagliardi, G. Polidori, R. Spagna, *J. Appl. Crystallogr.* **1999**, *32*, 115–119.
[24] G. M. Sheldrick, *SHELXL-97*, Program for Crystal Structure Refinement from Diffraction Data; University of Göttingen, Göttingen, **1997**.

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