ORGANOMETALLICS

Article

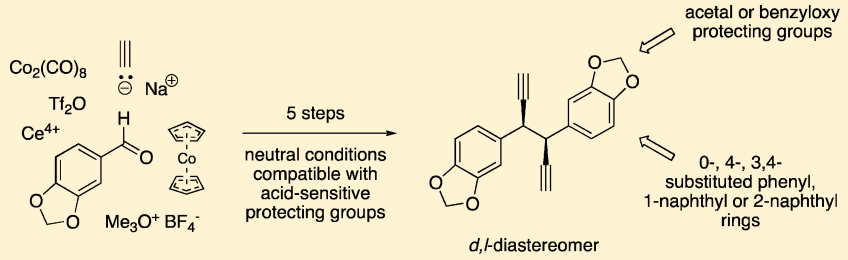
pubs.acs.org/Organometallics

Cobaltocene-Induced Low-Temperature Radical Coupling Reactions in a Cobalt−Alkyne Series

Gagik G. Melikyan,* Bianca Rivas, Stepan Harutyunyan, Louis Carlson, and Ruth Sepanian

Department of Chemistry and Biochemistry, California State University Northridge, Northridge, California 91330-8262, United States

Supporting Information



ABSTRACT: A novel method for the low-temperature generation of $Co_2(CO)_6$-complexed propargyl radicals is developed. It consists of an in situ preparation of the respective cationic species (−50 to −10 °C) and their rapid reduction with cobaltocene, Cp_2Co, at −50 °C. The optimized experimental protocol is applied to both inter- and intramolecular reactions, affording topologically diverse *α*-aryl and *α*-napthyl, *d,l*- and *meso*-1,5-hexadiynes and 1,5-cyclodecadiynes. The *d,l* configuration is the most preferable steric arrangement in intermolecular radical C−C bond-forming reactions (*d,l* 69−92%), while a reversal of stereoselectivity is observed in intramolecular cyclizations (*meso* 79%). Under oxidizing conditions (Ce^{4+}), decomplexation affords *d,l*-3,4-diaryl- and *d,l*-3,4-(1-/2-naphthyl)-1,5-hexadiynes in good to excellent yields (47−98%). An enhanced *functional tolerance* is showcased by introducing peripheral acid-sensitive functionalities, such as benzyloxy and methylenedioxy groups, and carrying out a five-step conversion scheme—from commercial aromatic aldehydes to radical dimers—under *nonacidic conditions*.

INTRODUCTION

Recently we reported[1] on high-temperature generation of $Co_2(CO)_6$-stabilized propargyl cations under neutral conditions, involving the treatment of the respective methyl propargyl ethers with triflic or trifluoroacetic anhydrides. In contrast to the conventional cation generation that utilizes a variety of Brønsted−Lowry and Lewis acids,[2,3] the novel method could potentially tolerate the acid-sensitive moieties and functional groups susceptible to protonation. It could also become a key carbon−carbon bond-forming step in total syntheses of complex molecular assemblies when an incompatibility of the reagents, or reaction conditions, with peripheral functionalities may cause unwanted chemical alterations. The main drawback still remained a relatively high reaction temperature (83−147 °C), which caused a partial decomplexation of radical dimers that, in turn, required a recomplexation of the crude products.[1] Among the disadvantages were also an inherently low atom economy, given the spontaneous nature of the radical generation reaction (2 equiv of propargyl substrate → 1 equiv of propargyl radicals),[1,4c,e] and the formation of the respective hydrocarbons as side products.[1] Herein we report on the novel low-temperature generation of cobalt-stabilized propargyl cations (−50 to −10 °C) under neutral conditions and inter- and intramolecular radical coupling reactions induced by cobaltocene, an external reducing agent (−50 °C). Carrying out the radical coupling reaction at low temperatures allowed us to achieve a number of synthetic objectives: in particular, the elimination of the laborious cation isolation step and minimization of a partial decomplexation of the triple bonds, while maintaining the neutrality of the medium. An enhanced functional tolerance was showcased by engaging the substrates with acid-sensitive functionalities—benzyloxy and methylenedioxy—located on the periphery of the aromatic nuclei.

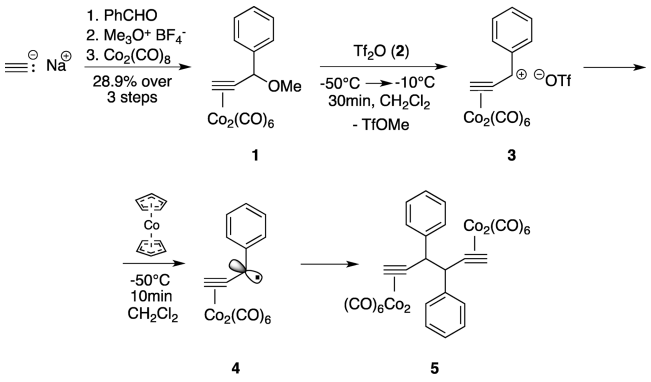
RESULTS AND DISCUSSION

Methyl propargyl ether **1** was synthesized under nonacidic conditions (Scheme 1) by the condensation of sodium acetylide with benzaldehyde,[5] followed by in situ methylation of sodium alkoxide with trimethyloxonium tetrafluoroborate and complexation of the triple bond with dicobalt octacarbonyl.[6] Developing a three-step sequence that affords the requisite methyl ethers under nonacidic conditions is of utmost importance. It allows for the whole synthetic scheme—from commercially available products to radical dimers—to be carried out *without using either Lewis or Brønsted−Lowry acids*. Methyl propargyl ethers were previously synthesized—under acidic conditions—from the respective $Co_2(CO)_6$ propargyl alcohols by using either HBF_4/MeOH (*with isolation of*

Received: July 19, 2011
Published: February 15, 2012

dx.doi.org/10.1021/om2006497 | *Organometallics* 2012, 31, 1653−1663

Scheme 1. Low-Temperature Generation of Propargyl Cations *under Neutral Conditions* and a Low-Temperature Reduction with Cobaltocene



intermediate cations),[1] or BF_3/MeOH (*without isolation of intermediate cations*).[7] The only "nonacidic" protocol, previously developed by us,[1] was less efficient, utilizing a large excess of an alternative alkylating agent (20 equiv of MeI vs 1.1 equiv of $Me_3O^+BF_4^-$) and suffering from an extended reaction time (19 h vs 1.5 h) and a lower overall yield (17.5% vs 28.9%).

An interaction of methyl propargyl ether **1** with triflic anhydride (**2**) occurred at low temperatures, albeit at a slow pace. An optimized experimental protocol included a gradual elevation of the reaction temperature from −50 to −10 °C, within 30 min, thus fully converting methyl ether **1** to ionic propargyl triflate **3** (Scheme 1). Cobaltocene, a 19e reducing agent,[8] was shown by us[4h] to operate in the T domain different from that of zinc. The latter is capable of reducing cobalt-complexed propargyl cations only at 20 °C,[4b,e] while cobaltocene, given its reducing power and a good solubility in CH_2Cl_2, even at −78 °C, rapidly reduces bis-propargyl cations to *meso*-1,5-cyclodecadiynes with an excellent stereoselectivity (up to 97%).[4h] The reduction of propargyl triflate **3** occurred at −50 °C (10 min), forming the requisite radicals **4**, which then underwent intermolecular dimerization to 1,5-hexadiyne **5** (61.9%; *d,l*-**5**:*meso*-**5** = 69:31). The facile reduction of propargyl triflate **3** with cobaltocene attests to its presumed ionic nature, since analogous conditions were employed with propargyl tetrafluoroborates, the intrinsically ionic compounds.[4e,h]

The generation of the propargyl cations under neutral conditions and their reduction with cobaltocene at low temperatures (−50 °C) allowed us to achieve five synthetic objectives, while maintaining the neutrality of the medium. First, we avoided the high temperatures (83−147 °C) that are typical for the spontaneous generation of radicals carried out *in the absence of the external reducing agent*.[1] Second, we proved that cobalt-complexed propargyl triflates are *propargyl cation mimics* due to the high polarizability of the carbon−triflate bond located α to the metal core. Third, we enhanced the atom economy with respect to the spontaneous radical reactions, for which 2 equiv of cobalt-complexed propargyl cations is required for generation of 1 equiv of the requisite propargyl radicals.[4c,e] Fourth, we minimized the partial decomplexation of the triple bonds, a known deficiency in high-temperature processes that, in turn, requires a recomplexation of the respective mono complexes.[1,4e,g] Fifth, we achieved a long sought after compatibility between the cation generation conditions and a reducing agent that would potentially eliminate the laborious cation isolation step. The existing methods utilize Brønsted−Lowry acids, such as HBF_4, and zinc, as a standard reductant, *the combination of reagents that requires an isolation of the requisite cations prior to the reduction step*.[2−4]

The standardized protocol for generating cobalt-complexed propargyl cations at low temperatures, under neutral conditions, was applied to para-substituted alkoxy derivatives **6** (4-OMe) and **7** (4-OBn) (Table 1). The conversion to the respective propargyl triflates was carried out with Tf_2O (**2**), followed by reduction with cobaltocene at −50 °C (10 min). Radical dimers **8** and **9** were formed in good yields (73.3% and 68.6%), both being represented by a mixture of diastereomers (**8**, *d,l*:*meso* = 72:28; **9**, *d,l*:*meso* = 69:31). The successful application of the standardized conditions to substrate **7**, bearing a protecting benzyl group,[9] represents experimental proof that the neutrality of the medium is maintained throughout the cation generation−reduction steps. The benzyl group is known to be removable under mild conditions by a variety of Brønsted−Lowry and Lewis acids (CF_3COOH, BF_3, $AlCl_3$),[9] and it can hardly "survive" under standard cation generation conditions, employing HBF_4 as an acid.[2,3a,4b,e]

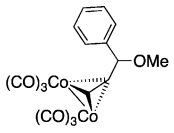
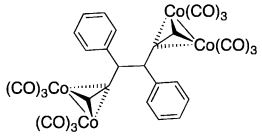
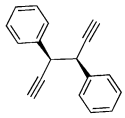
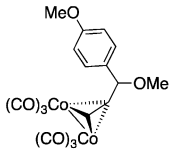
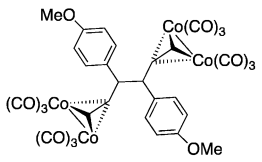
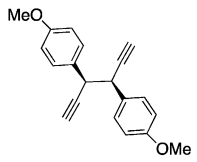
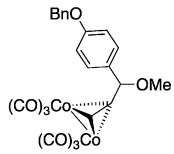
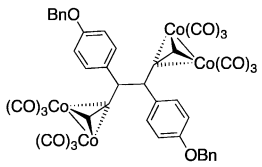
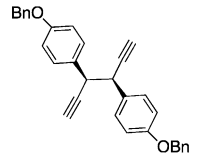
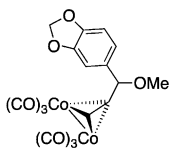
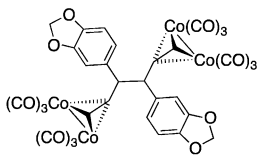
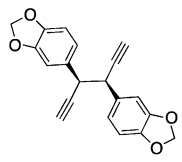
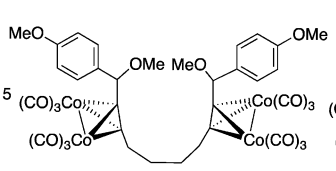
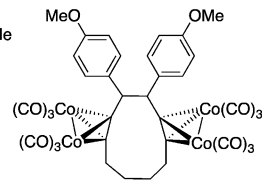
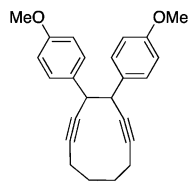
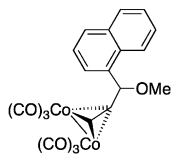
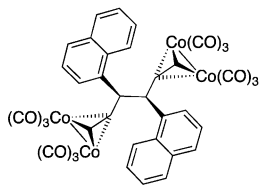
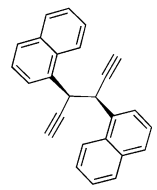
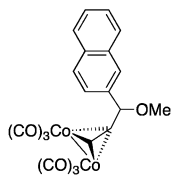
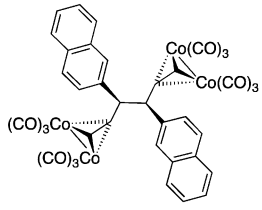
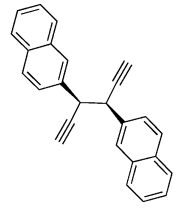
A methylenedioxy moiety —OCH_2O[9]— represents an alternative acid-sensitive functionality that can hardly maintain its structural integrity under conventional acid-induced cation generation protocols.[2,3,4b,e] To test the scope and applicability of the low-temperature cation generation method under neutral conditions, methyl ether **10** was synthesized in three steps from commercially available benzaldehyde and treated with Tf_2O (**2**) at −50 °C (Scheme 2). The latter acts as an electrophile, releasing a triflate anion and forming the highly substituted oxonium ion **11**. The C−O bond heterolysis occurs at −10 °C, forming propargyl triflate **12**, a key cationic intermediate, and methyl triflate, which provides for a continuous neutrality of the reaction medium. A rapid reduction with cobaltocene, at −50 °C (10 min), generates the requisite propargyl radicals **13**, which dimerize, supposedly in a diffusion-controlled step, to 1,5-hexadiyne **14** (*d,l*-**14**:*meso*-**14** = 85:15; *d,l*-**14** 46.8%). The major diastereomer, *d,l*-**14**, can be relieved from metal bondage under oxidative conditions,[2a,g] thus concluding a five-step conversion of commercial aromatic aldehyde to a radical coupling product bearing acid-sensitive functional groups on the periphery of the aromatic nuclei (Scheme 2).

To further expand the scope of the reaction, an *intramolecular variant* was explored in order to develop access to 1,5-cyclodecadiynes[10] with acid-sensitive moieties located on the periphery of the aromatic rings. Given the structural proximity to the cytotoxic enediynes,[11] radical cyclization products can provide a novel carbon framework in the development of the new generation of nontoxic prodrugs[12] for cancer treatment. Dimethyl ether **15** was synthesized from the respective bis alcohol[4f] by treatment with methanol in the presence of $BF_3{\cdot}Me_2O$.[7] The interaction with a 2-fold excess of Tf_2O (**2**), within an optimized −50 to −10 °C temperature range, followed by reduction with a 4-fold excess of cobaltocene afforded 1,5-cyclodecadiyne **16** (56.7%), with the *meso* diastereomer being predominantly formed (*d,l*-**16**:*meso*-**16** = 21:79). For comparison, zinc-induced cyclizations[4f] yielded 1,5-cyclodecadiynes with lower yields (28.7−43.3%) and featured a reversed stereoselectivity: i.e., predominant formation of the respective *d,l* diastereomers (*d,l* 54−80%).

An optimized protocol for α-phenyl propargyl cation generation and its in situ reduction was further expanded to include topologically diverse α-naphthyl substrates (Table 1;

dx.doi.org/10.1021/om2006497 | *Organometallics* 2012, 31, 1653−1663

Table 1. Low-Temperature, Cobaltocene-Induced Inter- and Intramolecular Radical Coupling Reactions

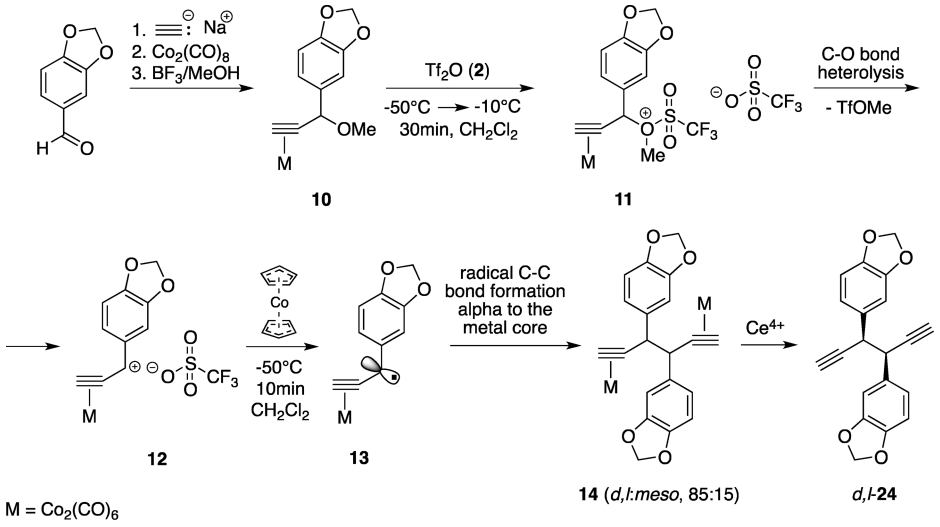
Entry	Substrate	Bis-cluster	Ratio, *d,l* : *meso* (yield, %)	Organic product[c]
1	 **1**	 **5**	69 : 31[a] (61.9)	 **21** (100% *d,l*)
2	 **6**	 **8**	72 : 28[a] (73.3)	 **22** (100% *d,l*)
3	 **7**	 **9**	69 : 31[a] (68.6)	 **23** (100% *d,l*)
4	 **10**	 **14**	85 : 15[a] (46.8)	 **24** (100% *d,l*)
5	 **15**	 **16**	21 : 79[b] (56.7)	 **25** (73 : 27, *d,l* : *meso*)[d]
6	 **17**	 **19**	81 : 19[a] (22.2)	 **26** (100% *d,l*)
7			87 : 13[e] (48.8)	
8	 **18**	 **20**	92 : 8[a] (31.9)	 **27** (100% *d,l*)
9			74 : 26[e] (57.5)	

[a]Chromatographically separable. [b]Chromatographically inseparable. [c]Only major *d,l* diastereomers were decomplexed with ceric ammonium nitrate unless indicated otherwise. [d]1,5-Cyclodecadiyne with a diastereomeric ratio of 67:33 (Zn reduction)[4f] was used as a substrate in the decomplexation reaction. [e]Reduction of the isolated propargyl cations with Zn.

entries 6 and 8). Thus, 1- and 2-naphthyl group containing ethers **17** and **18** were converted to the respective dimeric products **19** and **20**, each represented by a mixture of stereoisomers (**19**, *d,l*:*meso* = 81:19; **20**, *d,l*:*meso* = 92:8). An increased bulkiness of the α substituent (PCModel, v9.1: $\Delta V = V(C_6H_6) - V(C_{10}H_8) = 56$ Å^3) did not interfere with the formation of a C−C bond; to the contrary, the diastereoselectivities observed are systematically higher than that with a

dx.doi.org/10.1021/om2006497 | *Organometallics* 2012, 31, 1653−1663

Scheme 2. "Survival" of an Acetal Protection Group



much smaller α-phenyl group (**5**, *d,l*:*meso* = 69:31). A higher level of diastereoselection observed with the 2-naphthyl substrate **18** indicates that the orientation of converging propargyl radicals is dependent upon the substitution pattern (1-naphthyl vs 2-naphthyl) and, attendant with it, the disparity in the steric hindrance. An impact of the reducing agent was probed by using an alternative dimerization procedure[4b,e,j,k] that includes an isolation of the respective propargyl cations and their subsequent reduction with zinc. Curiously, for 1-naphthyl-substituted methyl ether **17**, *d,l* diastereoselectivity was improved (**19**: Zn, *d,l*:*meso* = 87:13; Cp_2Co, *d,l*:*meso* = 81:19; Table 1, entries 6 and 7), while for 2-naphthyl derivative **18**, a significant decline in diastereoselection was detected (**20**: Zn, *d,l*:*meso* = 74:26; Cp_2Co, *d,l*:*meso* = 92:8; Table 1, entries 8 and 9). An impact of the reducing agent upon the stereoselectivity was previously observed by us[4e] in cross-coupling radical reactions, with Cp_2Co systematically favoring a *meso* configuration. To what extent the observed disparity can be attributed to the solubility of the reducing agents in methylene chloride (hetero- vs homogeneous) still remains to be seen. However, the experimental data on hand allow us to conclude that $Co_2(CO)_6$-complexed propargyl radicals are not kinetically independent, and the conformational and rotational flexibilities depend upon the structure and composition of the intermediate radical ion species.

The diastereoselectivity of radical coupling reactions was determined by using the diagnostic value of acetylenic protons in NMR spectra:[4a,b,e,k] in *meso* diastereomers, respective signals are shifted upfield, up to 1.25 ppm, due to the spatial proximity to the centroid of the aromatic ring (*HC*≡, *d,l*, 5.83−6.33 ppm; *meso*, 4.69−5.06 ppm). The same disposition of the acetylenic protons was observed in benzyloxy and methylenedioxy derivatives **9** and **14**, with the respective signals in *meso* diastereomers being shifted upfield, on average, by 1.18 ppm (*HC*≡, *d,l*, 6.28−6.29 ppm; *meso*, 5.01−5.20 ppm). The replacement of α-phenyl groups with much larger 1- and 2-naphthyl moieties substantially affected the chemical shifts of acetylenic and methyne hydrogens, to the extent that a correlation with previously reported data[4] did not allow for an unambiguous stereochemical assignment. In the case of α-phenyl derivatives such as **5**, the chemical shifts of methyne hydrogens do not have any diagnostic value because of the close proximity of the respective signals in *d,l* and *meso* diastereomers (4.33 and 4.38 ppm; $\Delta\delta$ = 0.05 ppm). With a 1-naphthyl group introduced α to the metal core (**19**), methyne hydrogens drastically shift downfield, by 1.33 ppm, for one of the diastereomers, creating a significant gap ($\Delta\delta$ = 0.87 ppm) between the respective proton resonances in opposite stereoisomers. Both acetylenic and methyne hydrogen signals were found outside the established ranges of chemical shifts, with the topology of the naphthyl group (1 vs 2) being another contributing, and complicating, factor. To unambiguously establish the relative configurations of naphthyl dimers, the structure of the major stereoisomer, as *d,l*-**20**, was determined by X-ray crystallography (Figure 1).[13] The diagnostic methyne hydrogens—H_{15} and H_{16}—are positioned anti to each other ($\theta_{H15-C15-C16-H16}$ = 170.8°), by arranging the bulky cobalt alkyne moieties in an ideally gauche fashion ($\theta_{C14-C15-C16-C17}$ = 62.1°). The acetylenic hydrogens are forced into close proximity to each other (H_{13}−H_{18} = 2.31 Å), with the nonbonding distance slightly exceeding the sum of VdW radii (2.20 Å[14]). This is the reason why introducing any γ substituents at the acetylenic termini (t-Bu,[4k] Ph,[4e] Et[4j]) resulted in substantial conformational changes, positioning the cobalt alkyne units anti to each other. Metal cores—Co_2C_2—represent the tetrahedra with a skew geometry where the angles between Co−Co and C−C triple bonds significantly deviate from the perpendicular arrangement (70.4, 69.2°).[2] Other noteworthy structural features of *d,l*-**20** include (a) an essentially undistorted linearity of alkyne moieties (H_{13}−C_{13}−C_{14}−C_{15} = 0.1°, C_{16}−C_{17}−C_{18}−H_{18} = 2.9°), (b) a bent geometry[2] for coordinated alkyne units (H_{13}−C_{13}−C_{14} = 135.1°, C_{13}−C_{14}−C_{15} = 145.4°, H_{13}−C_{13}−C_{14} = 136.2°, C_{16}−C_{17}−C_{18} = 142.2°), reflecting a substantial rehybridization of acetylenic carbons and strong back-bonding from the cobalt carbonyl moiety, and (c) a lengthened coordinated C−C triple bond (C_{13}−C_{14} = 1.32 Å vs ∼1.21 Å for free ligand) attendant with complexation to the transition metal.[2]

An oxidative decomplexation with cerium(IV) ammonium nitrate[2a,g] was carried out for major *d,l* diastereomers (*d,l*-**5**, *d,l*-**8**, *d,l*-**9**, *d,l*-**14**, *d,l*-**19**, *d,l*-**20**), or an inseparable stereoisomeric mixture derived from the intramolecular cyclization reaction (*d,l*-**16** + *meso*-**16**). Metal-free organic products **21**−**27** were obtained in good to excellent yields (up to 98%), mostly in an

dx.doi.org/10.1021/om2006497 | *Organometallics* 2012, 31, 1653−1663

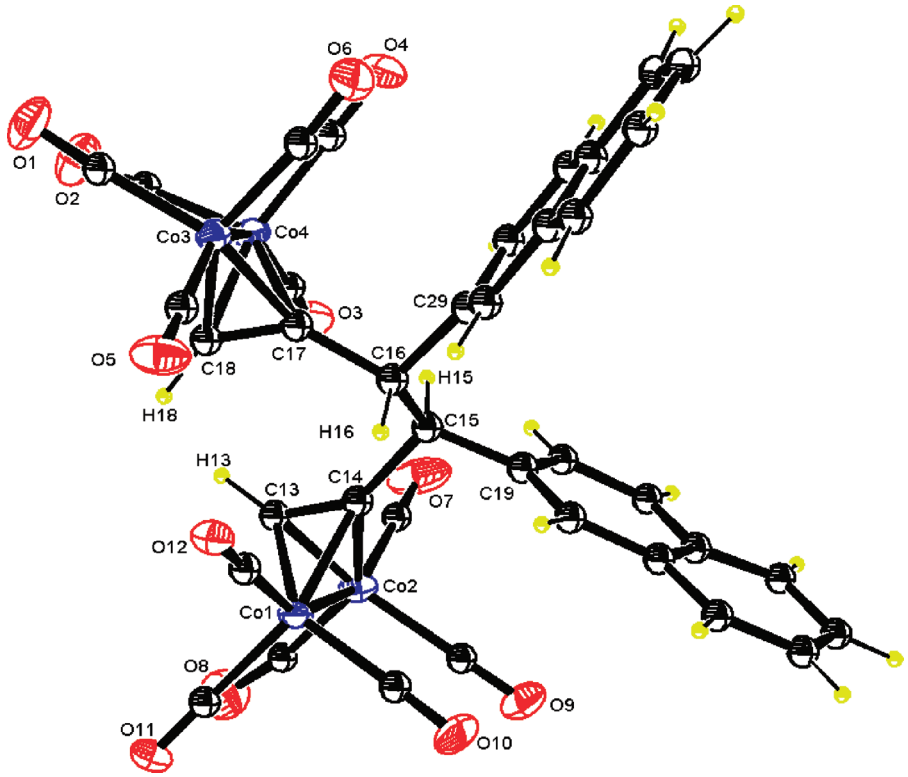


Figure 1. ORTEP diagram of *d,l*-[μ,η^2-3,4-bis(2′-naphthyl)-1,5-hexadiyne]bis(dicobalt hexacarbonyl) (**20**). Selected bond distances (Å), interatomic distances (Å), and bond and torsion angles (deg): H18−H13 = 2.31, C13−C14 = 1.32, C14−C15 = 1.53, C15−C16 = 1.50, Co1−Co2 = 2.47, H13−C13−C14 = 135.1, C13−C14−C15 = 145.4, H18−C18−C17 = 136.2, C16−C17−C18 = 142.2, C13−C14−Co1−Co2 = 70.4, C17−C18−Co3−Co4 = 69.2, H16−C16−C15−H15 = 170.8, H13−C13−C14−C15 = 0.1, C16−C17−C18−H18 = 2.9, C29−C16−C15−C14 = 47.3, C14−C15−C16−C17 = 62.1, C19−C15−C16−C29 = 47.3.

isomerically pure *d,l* form (Table 1). The relative configuration for naphthyl derivative *d,l*-**27** was established by X-ray crystallography (Figure 2).[13] Conformationally, the X-ray structure of *d,l*-**27** represents a striking departure from that of its metal-clustered counterpart *d,l*-**20**. The latter positioned bulky cobalt alkyne units and 2-naphthyl groups gauche to each other, with internal hydrogen atoms exhibiting only a slight deviation from an expected value ($\theta_{H15-C15-C16-H16}$ = 170.8°). The removal of metal cores and, attendant with it, a substantial steric relief caused the naphthyl rings to spring out to a nearly ideal anti disposition ($\theta_{C10-C11-C12-C13}$ = 173.8°). The triple bonds retained their steric relationship ($\theta_{C23-C11-C12-C25}$ = 67.1°), while the hydrogen atoms, reflecting a decomplexation-derived conformational change, appear gauche to each other (*d,l*-**27**, $\theta_{H11-C11-C12-H12}$ = 60.1°; *d,l*-**20**, $\theta_{H15-C15-C16-H16}$ = 170.8°).

The novel method for radical C−C bond formation, α to the metal core, represents a viable approach to the synthesis of acyclic and cyclic alkadiynes with 1,5-disposition of the triple bonds. The latter can readily be converted, via conventional methods, to a variety of classes of organic compounds, such as 1,5-alkadienes, 1,4-/1,6-diketones, cyclopentenes, cyclopentenones, cycloalkane-1,2-diols, enediynes, and fused and bridged carbocycles. It should be emphasized that *d,l* 3,4-disubstituted 1,5-alkadiynes are not easily accessible by alternative means.[15] In a purely "organic" setting, propargyl−propargyl coupling exhibits a poor regioselectivity due to unwanted acetylene−allene rearrangement and, attendant with it, the formation of inseparable mixtures of isomeric dimers (*head-to-head, head-to-tail, tail-to-tail*).[15a] Another drawback is that organic molecules do not provide the anchoring points in proximity to the stereogenic centers, so that the stereochemistry of the head-to-head coupling products—1,5-alkadiynes—could be controlled by auxiliary functional groups, either sterically or electronically. Even in transition-metal-catalyzed processes (Ti, Ru, Pd),[15b−d] isomeric allenes are formed in significant quantities (45−50%),[15b] along with poor diastereo- and regioselectivities and low conversions (~70%).[15c,d] The very nature of propargyl radicals—prone to rearrangement and featuring a low chemoselectivity—triggered an interest toward developing their synthetic equivalents.[16] The complexation of the triple bonds with a $Co_2(CO)_6$ protecting group allowed us to preclude an unwanted acetylene−allene rearrangement, thus providing for an exclusive formation of head-to-head radical dimers, in a highly regioselective manner. In addition to this, well-known ionic transformations of propargyl derivatives, such as Rupe and Meyer−Schuster rearrangements,[17] were not observed in cobalt-protected propargyl systems, even in the presence of strong acids. Another advantage of having a bulky protecting group is its potential ability to favorably affect the stereochemical outcome of radical C−C formation by altering the orientations of converging propargyl radicals and limiting their conformational freedoms. It should also be mentioned that synthesizing propargyl cations under nonacidic conditions has long been a synthetic challenge. In organometallic chemistry, a standard protocol involves treatment of transition metal π-complexed organic derivatives, typically alcohols, with strong acids, such as H_2SO_4, HBF_4, CF_3COOH, HBr, TfOH, TsOH, and FSO_3H. Under these conditions, the existing methods could be of limited use when applied to larger polyfunctional

dx.doi.org/10.1021/om2006497 | *Organometallics* 2012, 31, 1653−1663

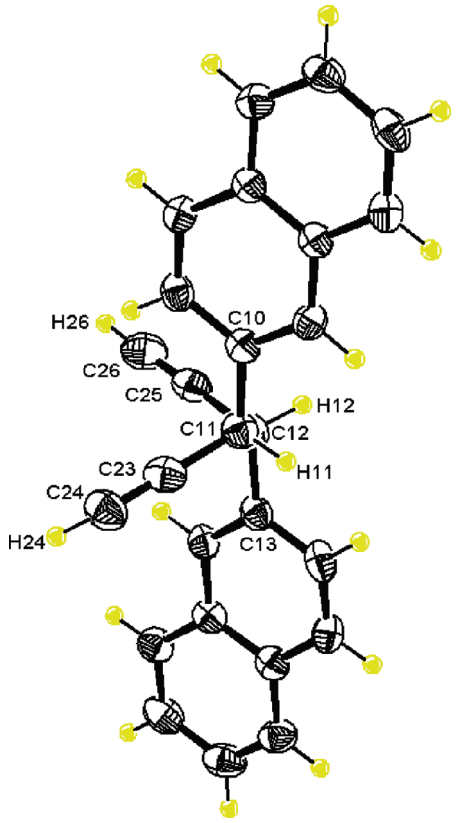


Figure 2. ORTEP diagram of *d,l*-3,4-bis(2′-naphthyl)-1,5-hexadiyne (**27**). Selected bond lengths (Å) and torsion angles (deg): C11−C12 = 1.57, H11−C11−C12−H12 = 60.1, C23−C11−C12−C25 = 67.1, C10−C11−C12−C13 = 173.8.

molecules containing acid-sensitive functionalities. The novel method substantially enhances the *function compatibility* of transition-metal-mediated radical reactions, allowing for functionalization of propargyl positions, as key steps, in the multistep synthesis of biologically relevant molecules.

The stereoselectivity observed in low-temperature cobaltocene-induced radical coupling reactions indicates that in intermolecular reactions the *d,l* configuration is favored for topologically diverse 1,5-hexadiynes **5**, **8**, **9**, **14**, **19**, and **20** (Table 1). The level of *d,l* stereocontrol is dependent upon the nature and bulkiness of the α substituent, ranging from 69% to 92%. Figure 3 represents the preferential orientations for converging propargyl radicals containing α-phenyl (**A**), α-1-naphthyl (**B**), and α-2-naphthyl (**C**) substituents. All three pre-*d,l* spatial arrangements place aromatic rings gauche to each other, with the number of gauche interactions being equal to 2. A higher *d,l* diastereoselectivity observed in the presence of α-naphthyl groups (*d,l*-**19**, 81%; *d,l*-**20**, 92%), relative to that in α-phenyl containing substrate (*d,l*-**5**, 69%), can be attributed to the larger size of the naphthyl group. In other words, by introducing a bulkier substituent α to the metal core, we were able to achieve a better discrimination between the alternative spatial arrangements, leading to *d,l* and *meso* diastereomers. In the *intramolecular cyclization* reaction, an opposite trend was observed, with the *meso* diastereomer being the dominant stereoisomer (Table 1: **16**, *d,l*:*meso* = 21:79). The alternative orientations for converging propargyl radicals, designated **D** (pre-*meso*) and **E** (pre-*d,l*) (Figure 3), feature three and two gauche interactions, respectively. With the current level of understanding of cyclization kinetics, it is difficult to unambiguously explain why the pre-*meso* orientation **D** is energetically favored, despite the larger number of potentially destabilizing gauche interactions. Given the reducing power of cobaltocene, providing for a rapid reduction at temperatures as low as −50 °C, and its relatively high bulkiness (199.56 Å^3) comparable with that of requisite substrates (e.g., **1** 358.72 Å^3), it is conceivable that the cyclizing diradicals are not kinetically independent species comparable to those in intermolecular reactions. To the contrary, a one-electron transfer toward cationoid species can generate diradicals that could remain associated with oxidized Cp_2Co^+ species. The latter in turn could act as counterions and affect, both sterically and conformationally, the converging propargyl radical ions in such a way that the pre-*meso* orientation **D** becomes energetically more favorable.

CONCLUSION

A novel method for the generation of propargyl triflates at low temperatures—by interaction of $Co_2(CO)_6$-complexed methyl propargyl ethers with triflic anhydride—was developed. Their ionic nature, at temperatures as low as −50 °C, was demonstrated by a successful reduction with cobaltocene. The requisite substrates, metal-complexed methyl propargyl ethers, can be synthesized under nonacidic conditions, allowing for the whole scheme—from commercial aromatic aldehydes and alkynes to 1,5-alkadiynes and 1,5-cyclodecadiynes—to be carried out in an acid-free environment. The compatibility of

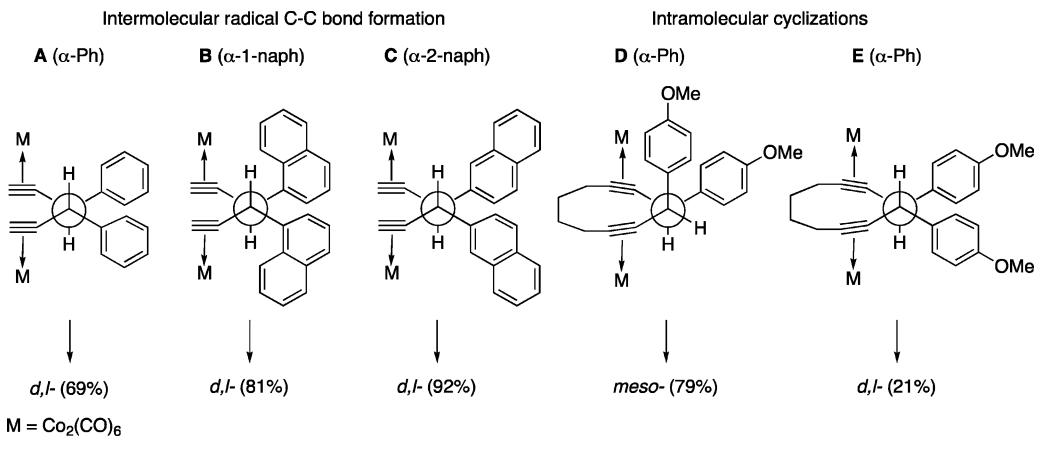


Figure 3. Preferential orientations of converging propargyl radicals.

dx.doi.org/10.1021/om2006497 | *Organometallics* 2012, 31, 1653−1663

the reaction conditions, throughout a five-step synthetic sequence, with acid-sensitive structural units was successfully demonstrated by engaging substrates with benzyloxy and methylenedioxy protecting groups. The latter are textbook examples of functionalities that are poorly compatible with strong acids, such as HBF_4. It is worth mentioning that the temperature domain for reduction of propargyl triflates, previously falling in the range of 20−147 °C,[1,4c,g] was expanded toward much lower temperatures, down to −50 °C. A newly acquired ability to generate cationoid species and form a carbon−carbon bond at low temperatures, while maintaining the neutrality of the medium, substantially enhances the synthetic potential of transition-metal-mediated radical chemistry. In particular, this method can now be used, as a key step, in targeted synthesis of larger organic assemblies wherein the compatibility of reaction conditions and reagents with peripheral functionalities becomes pivotal.

EXPERIMENTAL SECTION

All manipulations of air-sensitive materials were carried out in flame-dried Schlenk-type glassware on a dual-manifold Schlenk line interfaced to a vacuum line. Argon and nitrogen (Airgas, ultrahigh purity) were dried by passing through a Drierite tube (Hammond). All solvents were distilled before use under dry nitrogen over appropriate drying agents (ether, THF, from sodium benzophenone ketyl; CH_2Cl_2, from CaH_2; benzene, from sodium). All reagents were purchased from Sigma-Aldrich and Acros and used as received. $Co_2(CO)_8$ and $Ce(NH_4)_2(NO_3)_4$ were purchased from Strem. NMR solvents were supplied by Cambridge Isotope Laboratories. ^1H and ^{13}C NMR spectra were recorded on a Bruker DRX-400 (^1H, 400 MHz) spectrometer. Chemical shifts were referenced to internal solvent resonances and are reported relative to tetramethylsilane. Spin−spin coupling constants (J) are given in hertz. Elemental analyses were performed by Columbia Analytical Services (Kelso, WA). Melting temperatures (uncorrected) were measured on a Mel-Temp II (Laboratory Devices) apparatus and Optimelt Automated Meltemp. Silica Gel S735-1 (60−100 mesh; Fisher) was used for flash column chromatography. Analytical and preparative TLC analyses (PTLC) were conducted on silica gel 60 F_{254} (EM Science; aluminum sheets) and silica gel 60 PF_{254} (EM Science; w/gypsum, 20 × 20 cm), respectively. Eluents are ether (E), petroleum ether (PE), pentane (P), and benzene (B). Mass spectra were run at the Regional Center on Mass Spectroscopy, UC Riverside, Riverside, CA (FAB, ZAB-SE; CI-NH_3, 7070EHF; Micromass; TOF Agilent 6210 LCTOF instrument with a Multimode source).

Synthesis of Methyl Propargyl Ethers under Nonacidic Conditions (Protocol A): (μ,η^2-1-Methoxy-1-phenyl-2-propyne)dicobalt Hexacarbonyl (1). Under an atmosphere of nitrogen, at −50 °C, a solution of benzaldehyde (212 mg, 2 mmol) in dry THF (8 mL) was added dropwise (15 min) to a suspension of sodium acetylide (106 mg, 2.2 mmol; 587 mg, 18% suspension in xylene) in dry THF (12 mL), and the reaction mixture was stirred for 4 h at 20 °C. Trimethyloxonium tetrafluoroborate (326 mg, 2.2 mmol) was added at −20 °C, in one portion, and the reaction mixture was stirred for 1.5 h at −20 °C (TLC control). The mixture was quenched with water (25 mL) at −20 °C, the aqueous layer was extracted with ether (3 × 20 mL), and the combined ethereal fractions were dried (Na_2SO_4). Upon concentration under reduced pressure (1/3 v/v), under an atmosphere of nitrogen, the crude methyl ether (292 mg, 2 mmol; assuming 100% yield) was added dropwise (25 min) to a solution of dicobalt octacarbonyl (1.64 g, 4.8 mmol) in dry ether (40 mL). The reaction mixture was stirred for 4 h at 20 °C, concentrated under reduced pressure, and fractionated on a silica gel column (132 g, PE) to give **1** (250 mg, 28.9% over three steps). Spectral and physicochemical data are analogous with those reported earlier.[4a]

Low-Temperature Generation and Cp_2Co Reduction of $Co_2(CO)_6$-Complexed Cations (Protocol B): *d,l*- and *meso*-(μ,η^2-3,4-Diphenyl-1,5-hexadiyne)bis(dicobalt hexacarbonyl) (5). Under an atmosphere of nitrogen, Tf_2O (**2**; 73 mg, 0.26 mmol) was added dropwise (11 min) to a solution of methyl ether **1** (108 mg, 0.25 mmol) in dry methylene chloride (4 mL) at −50 °C. The reaction mixture was brought to −10 °C in 30 min (NMR control), and then a solution of Cp_2Co (49 mg, 0.26 mmol) in dry methylene chloride (1 mL) was added dropwise at −50 °C. The reaction mixture was stirred for 10 min, diluted with saturated brine (10 mL), warmed to 0 °C in 40 min, and then extracted with ether (10 mL), washed with water (2 × 15 mL), and dried (Na_2SO_4). By NMR, the crude mixture contained *d,l*-**5**, *meso*-**5**, and $(HC{\equiv}CCH_2Ph)Co_2(CO)_6$ in the ratio of 64, 30, and 6 (*d,l*-**5**:*meso*-**5** = 69:31). Organic solvents were evaporated under reduced pressure, and the residue was fractionated by preparative TLC (PE:CH_2Cl_2 = 10:1) to afford *d,l*-**5** and *meso*-**5** (62.1 mg, 61.9%; *d,l*-**5**:*meso*-**5** = 68:32). Both diastereomers were fully characterized in the previous account.[4d]

***d,l*- and *meso*-[μ,η^2-3,4-Bis(4′-methoxyphenyl)-1,5-hexadiyne]bis(dicobalt hexacarbonyl) (8).** According to protocol B, methyl ether **6**[1] (116 mg, 0.25 mmol), Tf_2O (**2**, 73 mg, 0.26 mmol), and Cp_2Co (49 mg, 0.26 mmol) afforded the crude mixture, containing, by NMR, *d,l*-**8**, *meso*-**8**, and $[HC{\equiv}CCH_2C_6H_4(4\text{-}OMe)]$-$Co_2(CO)_6$ in the ratio of 69:28:3 (*d,l*-**8**:*meso*-**8** = 72:28). Organic solvents were evaporated under reduced pressure, and the residue was fractionated by preparative TLC (PE:E = 20:1) to yield *d,l*-**8** and *meso*-**8** (79 mg, 73.3%; *d,l*-**8**:*meso*-**8** = 74:26). Both diastereomers were fully characterized in the previous account.[4b]

[μ,η^2-3-(4′-Benzyloxyphenyl)-3-methoxy-1-propyne]-dicobalt Hexacarbonyl (7). *[μ,η^2-1-(4′-Benzyloxyphenyl)-2-propyn-1-ol]dicobalt Hexacarbonyl.* Under an atmosphere of nitrogen, a solution of 4-benzyloxybenzaldehyde (2.12 g, 10.0 mmol) in dry THF (10 mL) was added dropwise (10 min) to a suspension of sodium acetylide (4.0 g, 18% w/w in xylene; 0.72 g, 15 mmol) in dry THF (30 mL) at −50 °C. Upon addition, the reaction mixture was stirred for 5 min, warmed to 20 °C, and then stirred for 6 h (TLC monitoring). Degassed saturated aqueous ammonium chloride (40 mL) was added at 0 °C, the crude mixture was diluted with water (50 mL), and then ether (150 mL), and the ethereal layer was separated. The aqueous layer was extracted with ether (5 × 50 mL), and the combined ethereal fractions were dried (Na_2SO_4). Under reduced pressure, crude alcohol (2.38 g, 10 mmol; assuming 100% yield) was stripped of organic solvents, redissolved in ether (100 mL), and added dropwise (20 min) to a solution of dicobalt octacarbonyl (3.76 g, 11 mmol) in dry ether (100 mL) under a flow of nitrogen. The reaction mixture was stirred at 20 °C for 2 h (TLC control), concentrated under reduced pressure, and fractionated on the silica gel column (75 g, PE:E = 5:1) to afford $[HC{\equiv}CCH(OH)C_6H_4(4'\text{-}OBn)]Co_2(CO)_6$ (1.49 g, 28.4% yield) as red crystals. An analytical sample was obtained with preparative TLC (PE:B = 1:1). Mp: 70−72 °C (sealed capillary; dried by coevaporation with benzene, 3 × 1 mL). TLC (PE:E = 3:1): R_f 0.35. ^1H NMR (400 MHz, $CDCl_3$): δ 2.25 (1H, d, OH, J = 3.6), 5.07 (2H, s, OCH_2Ph), 5.86 (1H, d, CH), 6.06 (1H, s, HC≡), 6.96 (2H, d, aromatic H, J = 8.8), 7.30−7.44 (7H, m, aromatic H). MS-HR-TOF: calcd for $C_{22}H_{13}O_7Co_2$ $(M - OH)^+$ 506.9320, found 506.9323.

Methylation Step (Protocol C): HBF_4/MeOH. Under an atmosphere of nitrogen, $HBF_4{\cdot}Me_2O$ (804 mg, 6.0 mmol) was added dropwise in four equal portions to a solution of $[HC{\equiv}CCH(OH)C_6H_4$-$(4'\text{-}OBn)]Co_2(CO)_6$ (786 mg, 1.5 mmol) in dry ether (35 mL) at −20 °C. Introduction of each portion took 3 min, and the reaction mixture was stirred for 5 min after each addition. The cation was allowed to settle, and the ethereal layer was removed. At −20 °C, dry ether (20 mL) was added along the inner wall of the flask, stirring was resumed for 5 min, the cation was allowed to settle, and the ethereal layer was removed. The washing was repeated once with an additional portion of dry ether (20 mL). The residual amount of ether was removed under reduced pressure, and the cation was suspended in dry ether (20 mL) at −20 °C. Dry methanol (1 mL) was then added dropwise (3 min) to the reaction mixture, which was stirred for 5 min at −20 °C and then for 1.5 h at 20 °C (TLC control). The reaction mixture was diluted with water (15 mL) and ether (5 mL). The ethereal layer was washed with water (2 × 15 mL), dried over molecular sieves (4 Å), and evaporated to dryness to yield **7** (689 mg, 85.4% yield) as a red

dx.doi.org/10.1021/om2006497 | Organometallics 2012, 31, 1653−1663

solid. Mp: 66−68 °C (sealed capillary; dried by coevaporation with benzene, 3 × 1 mL). TLC (PE:E = 5:1): R_f 0.48. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.44 (3H, s, OMe), 5.08 (2H, s, OCH_2Ph), 5.25 (1H, s, CH), 6.03 (1H, s, HC≡), 6.98 (2H, spl d, aromatic H, J = 8.8), 7.28−7.46 (7H, m, aromatic H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 57.4, 70.3, 72.3, 83.4, 99.0, 115.1, 127.6, 127.7, 128.1, 128.7, 134.9, 137.2, 158.9, 199.5. MS-HR-TOF: calcd for $C_{24}H_{19}O_9Co_2$ (M + OMe)$^-$ 568.9699, found 568.9682.

***d,l*- and *meso*-[μ,η^2-3,4-Bis(4′-benzyloxyphenyl)-1,5-hexadiyne]bis(dicobalt hexacarbonyl) (9).** According to protocol B, methyl ether **7** (135 mg, 0.25 mmol), Tf_2O (**2**; 73 mg, 0.26 mmol), and Cp_2Co (49 mg, 0.26 mmol) afforded the crude mixture, containing, by NMR, *d,l*-**9** and *meso*-**9** in a ratio of 69:31. Organic solvents were evaporated under reduced pressure, and the residue was fractionated by column chromatography (Florisil, 40 g; PE:E = 20:1) followed by preparative TLC (2 plates; PE:CH_2Cl_2:E = 10:1:0.5) to afford *d,l*-**9** and *meso*-**9** (87.0 mg, 68.6%; *d,l*-**9**:*meso*-**9** = 69:31). Individual diastereomers were isolated on a Florisil column (P:B = 2:1) under anaerobic conditions, with *d,l*-**9** being repurified by preparative TLC (P:B = 5:1).

d,l-**9**: red crystals. T_{dec} = 118.4−123.8 °C (sealed capillary; dried by coevaporation with benzene, 3 × 1 mL). TLC (P:B = 2:1): R_f 0.38. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.30 (2H, s, HC), 4.97 (4H, s, OCH_2Ph), 6.28 (2H, s, HC≡), 6.78 (4H, d, 3′-H, 5′-H, J = 8.8), 7.00 (2H, d, 2′-H, 6′-H, J = 8.4), 7.28−7.39 (10H, m, aromatic H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 54.2, 70.2, 77.0, 102.5, 114.8, 127.6, 128.0, 128.6, 129.9, 136.2, 137.2, 157.9, 199.1, 200.2. HR-MS ESI/APCI: calcd for $C_{44}H_{26}O_{14}KCo_4$ MK^+ 1052.8288, found 1052.8260.

meso-**9**: red solid. T_{dec} 133.2−137.8 °C (sealed capillary; dried by coevaporation with benzene, 3 × 1 mL). TLC (P:B = 2:1): R_f 0.63. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.31 (2H, s, HC), 5.01 (2H, s, HC≡), 5.15 (4H, s, OCH_2Ph), 6.97−7.51 (18H, m, aromatic H). HR-MS ESI/APCI: calcd for $C_{44}H_{26}O_{14}KCo_4$ 1052.8288, found 1052.8274.

Synthesis of Methyl Propargyl Ethers under Acidic Conditions (Protocol D): [μ,η^2-3-Methoxy-3-(3′,4′-methylenedioxyphenyl)-1-propyne]dicobalt Hexacarbonyl (10). Under an atmosphere of nitrogen, at 0 °C, methanol (0.5 mL) and BF_3·Me_2O (166 mg, 1.46 mmol) were added to a solution of [HC≡CCH(OH)C_6H_3(3′,4′-OCH_2O)]$Co_2(CO)_6$ (270 mg, 0.584 mmol) in dry methylene chloride (3 mL). The reaction mixture was stirred for 1 h at 0 °C, poured into saturated aqueous $NaHCO_3$ (10 mL), and extracted with methylene chloride (3 × 10 mL). The combined organic fractions were dried ($MgSO_4$), concentrated under reduced pressure, and chromatographed on a silica gel column (60 g; PE:E = 10:1) to afford **10** (228 mg, 82.0%) as red crystals. Mp: 44−46 °C (sealed capillary; dried by coevaporation with benzene, 3 × 1 mL). TLC (PE:E = 10:1): R_f 0.42. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.43 (3H, s, OMe), 5.19 (1H, m, CH), 5.95 (2H, AB spectrum, CH_2, $J_{H(A)-H(B)}$ = 1.4), 6.02 (1H, d, HC≡, J = 1.2), 6.79 (1H, dd, 5′-H, J = 8.0, J = 0.4), 6.85 (1H, ddd, 6′-H, J = 2.0, 0.4), 6.90 (1H, dt, 2′-H, J = 2.0, 0.4). MS TOF FD$^+$: m/z calcd for $C_{17}H_{10}O_9Co_2$ [M$^+$] 475.8983, found 475.8983. Anal. Found: C, 42.63; H, 2.16. Calcd for $C_{17}H_{10}O_9Co_2$: C, 42.88; H, 2.12.

***d,l*- and *meso*-[μ,η^2-3,4-Bis(3′,4′-methylenedioxyphenyl)-1,5-hexadiyne]bis(dicobalt hexacarbonyl) (14).** According to protocol B, methyl ether **10** (119 mg, 0.25 mmol), Tf_2O (**2**; 73 mg, 0.26 mmol), and Cp_2Co (49 mg, 0.26 mmol) afforded the crude mixture, containing, by NMR, *d,l*-**14** and *meso*-**14** in a ratio of 85:15. The reaction mixture was treated with dicobalt octacarbonyl (13 mg, 0.0375 mmol; 20 °C, 2 h), and organic solvents were evaporated under reduced pressure. The residue was fractionated by preparative TLC (PE:CH_2Cl_2:E = 18:1:0.5); repurification by preparative TLC afforded *d,l*-**14** (PE:E = 10:1; 2 runs; 52.1 mg, 46.8%).

d,l-**14**: red crystals. T_{dec} = 117−120 °C (sealed capillary; dried by coevaporation with benzene, 3 × 1 mL). TLC (PE:E = 10:1): R_f 0.25. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.18 (2H, s, CH), 5.87 (4H, AB spectrum, OCH_2O, J = 1.2), 6.29 (2H, s, HC≡), 6.53−6.67 (6H, m, aromatic H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 54.3 (CH), 77.3 (HC≡C), 101.1 (OCH_2O), 102.1 (HC≡C), 108.2, 109.1, 122.4, 137.5, 146.6, 147.6 (aromatic C), 199.0, 200.1 (C═O). HR-MS ESI/APCI: calcd for $C_{33}H_{17}O_{17}Co_4$ [M + MeO]$^-$ 920.7799, found 920.7780.

[μ,η^2-1,10-Dimethoxy-1,10-bis(4′-methoxyphenyl)-2,8-decadiyne]bis(dicobalt hexacarbonyl) (15). According to protocol D, [(4′-$OMeC_6H_4$CH(OH)C≡C$(CH_2)_4$C≡CCH(OH))C_6H_4(4′-OMe)][$Co_2(CO)_6$]$_2$[4f] (570 mg, 0.6 mmol), methanol (0.5 mL), and BF_3·Me_2O (342 mg, 3 mmol) afforded, after chromatographic isolation on a silica gel column (150 g; PE:E = 10:1), bis methyl ether **15** (326 mg, 55.6%) as dark red crystals. Mp: 72−87 °C (sealed capillary; dried by coevaporation with benzene, 3 × 1 mL). TLC (PE:E = 7:1): R_f 0.45. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.72 (4H, m, $2CH_2$), 2.73 (4H, m, $2CH_2$), 3.41 (6H, s, OMe), 3.81 (6H, s, OMe), 5.26 (2H, s, CH), 6.92 (4H, d, aromatic H, J = 8.4), 7.30 (4H, d, aromatic H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.68, 33.42 (C4, C5, C6, C7), 55.30, 57.12 (OMe), 83.48 (C1, C10), 98.11, 100.00 (C2, C3, C8, C9), 113.92, 127.41, 134.02, 159.55 (aromatic C), 199.70 (C═O). MS TOF: m/z calcd for $C_{38}H_{30}O_{16}ClCo_4$ [M + Cl]$^-$ 1012.8556, found 1012.8584. Anal. Found: C, 46.65; H, 3.22. Calcd for $C_{38}H_{30}O_{16}Co_4$: C, 46.65; H, 3.09.

***d,l*- and *meso*-[μ,η^2-3,4-Bis(4′-methoxyphenyl)-1,5-cyclodecadiyne]bis(dicobalt hexacarbonyl) (16).** According to protocol B, bis methyl ether **15** (98 mg, 0.1 mmol), Tf_2O (**2**; 62 mg, 0.22 mmol), and Cp_2Co (76 mg, 0.4 mmol) afforded the crude mixture, containing, by NMR, *d,l*-**16** and *meso*-**16** in a ratio of 21:79. Organic solvents were evaporated under reduced pressure, and the residue was fractionated by preparative TLC (2 plates; PE:E = 10:1) to afford *d,l*-**16** and *meso*-**16** (52 mg, 56.7%; *d,l*-**16**:*meso*-**16** = 18:82). Both diastereomers were fully characterized in the previous account.[4f]

[μ,η^2-3-Methoxy-3-(1′-naphthyl)-1-propyne]dicobalt Hexacarbonyl (17) (Protocol E). Under an atmosphere of nitrogen, 1-naphthaldehyde (1.03 g, 6.63 mmol) in dry THF (5 mL) was added dropwise (5 min) to a suspension of sodium acetylide (350 mg, 7.29 mmol; 1.94 g, 18% suspension in xylene) in dry THF (20 mL) at −50 °C. The reaction mixture was stirred for 4 h at 20 °C and then was quenched with water (25 mL). An aqueous layer was extracted with ether (3 × 20 mL), and the combined ethereal fractions were dried (Na_2SO_4). Under an atmosphere of nitrogen, a solution of crude HC≡CCH(OH)(1-naphthyl) (1.21 g, 6.63 mmol; assuming 100% yield) in dry ether (20 mL) was added dropwise (25 min) to a solution of dicobalt octacarbonyl (2.38 g, 6.96 mmol) in dry ether (20 mL). The reaction mixture was stirred for 3 h at 20 °C, concentrated under reduced pressure, and fractionated on a silica gel column (230 g; PE:E = 15:1) to afford [HC≡CCH(OH)(1-naphthyl)]$Co_2(CO)_6$ (746 mg, 24.1%) as a red oil. Under an atmosphere of nitrogen, at 0 °C, methanol (2 mL) and BF_3·Me_2O (912 mg, 8.0 mmol) were added to a solution of alcohol (746 mg, 1.59 mmol) in dry methylene chloride (10 mL). The reaction mixture was stirred for 2 h at 0 °C, poured into saturated aqueous $NaHCO_3$ (20 mL), and extracted with ether (3 × 20 mL). The combined organic fractions were dried ($MgSO_4$) and then evaporated to dryness to afford **17** (704 mg, 91.9%) as a dark red oil. TLC (PE:E = 10:1): R_f 0.59. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.55 (3H, s, OMe), 5.89 (1H, s, CH), 6.01 (1H, s, HC≡), 7.47−7.55 (2H, m, aromatic H), 7.56−7.61 (1H, m, aromatic H), 7.69 (1H, d, aromatic H, J = 7.2), 7.81 (1H, d, aromatic H, J = 8.4), 7.89 (1H, dd, aromatic H, J = 8.2, J = 0.6), 8.16 (1H, d, aromatic H, J = 8.4). ^{13}C NMR (100 MHz, $CDCl_3$): δ 57.4 (OMe), 71.9 (CH), 80.9, 97.8 (HC≡C), 123.1, 123.4, 125.4, 125.6, 125.9, 128.4, 128.9, 130.3, 134.0, 137.4 (aromatic C), 199.0, 199.5 (C═O). MS TOF EI: m/z calcd for $C_{21}H_{15}O_8Co_2$ [M + MeO]$^-$ 512.9436, found 512.9428. MS TOF FD$^+$: m/z M$^+$ 482. Anal. Found: C, 49.59; H, 2.89. Calcd for $C_{20}H_{12}O_7Co_2$: C, 49.82; H, 2.51.

***d,l*- and *meso*-[μ,η^2-3,4-Bis(1′-naphthyl)-1,5-hexadiyne]bis(dicobalt hexacarbonyl) (19).** *(a). Zn-Mediated, Two-Step Dimerization Reaction (Protocol F).* Under an atmosphere of nitrogen, at −20 °C, a solution of HBF_4·Me_2O (201 mg, 1.5 mmol) was added dropwise to a solution of methyl ether **17** (121 mg, 0.25 mmol) in dry pentane (10 mL). The reaction mixture was stirred for 5 min at −20 °C and then for an additional 1.5 h at 0 °C. The cation was washed with dry pentane (3 × 20 mL) at −30 °C, the residual

dx.doi.org/10.1021/om2006497 | Organometallics 2012, 31, 1653−1663

amount of pentane was removed under reduced pressure, and the precipitate was dissolved in dry methylene chloride (10 mL) at −20 °C. The reaction mixture was treated with zinc (650 mg, 10 mmol), stirred for 5 min at −20 °C, and then the temperature was raised to 20 °C, and zinc was mechanically scraped from the walls of the flask. The reaction mixture was stirred for 20 min at 20 °C (TLC control), and zinc was filtered off on a short bed of Florisil (1 in.). The crude mixture (NMR: *d,l*-**19**:*meso*-**19** = 87:13) was fractionated on a silica gel column (40 g; PE) to afford a mixture of *d,l*-**19** and *meso*-**19** (55 mg, 48.8%). The individual diastereomers were isolated by preparative TLC (PE:CH_2Cl_2 = 5:1; two runs) to afford *d,l*-**19** (42 mg, 37.3%) and *meso*-**19** (6 mg, 5.3%).

d,l-**19**: dark red solid. T_{dec} = 137−145 °C (sealed capillary; dried by coevaporation with benzene, 3 × 1 mL). TLC (PE:CH_2Cl_2 = 3:1): R_f 0.44. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.66 (2H, s, 2CH), 6.51 (2H, s, HC≡), 7.07 (2H, dd, aromatic H, J = 7.6, J = 8.4), 7.39−7.48 (4H, m, aromatic H), 7.51−7.58 (4H, m, aromatic H), 7.69 (2H, d, aromatic H, J = 8.4), 8.11 (2H, d, aromatic H, J = 8.4). ^{13}C NMR (100 MHz, $CDCl_3$): δ 46.9 (CH), 77.5, 101.4 (C≡C), 121.8, 124.6, 124.9, 125.2, 126.2, 127.3, 129.0, 131.0, 133.5, 139.6 (aromatic C), 198.3, 200.1 (C═O). MS TOF EI: m/z calcd for $C_{39}H_{21}O_{13}Co_4$ [M + MeO]$^-$ 932.8316, found 932.8325. MS TOF FD$^+$: m/z M$^+$ 902. Anal. Found: C, 50.57; H, 2.51. Calcd for $C_{38}H_{18}O_{12}Co_4$: C, 50.58; H, 2.01.

meso-**19**: dark red solid. T_{dec} = 124−133 °C (sealed capillary; dried by coevaporation with benzene, 3 × 1 mL). TLC (PE:CH_2Cl_2 = 5:1): R_f 0.53. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.79 (2H, s, 2CH), 5.78 (2H, s, HC≡), 7.60 (4H, m, aromatic H), 7.70 (2H, t, aromatic H, J_{av} = 7.8), 7.83 (2H, d, aromatic H, J = 7.2), 7.98 (4H, dd, aromatic H, J = 8.0, J = 10.0), 8.23 (2H, d, aromatic H, J = 8.0). MS TOF EI: m/z calcd for $C_{39}H_{21}O_{13}Co_4$ [M + MeO]$^-$ 932.8316, found 932.8273. MS TOF FD$^+$: m/z M$^+$ 902. Anal. Found: C, 50.67; H, 3.14. Calcd for $C_{38}H_{18}O_{12}Co_4$: C, 50.58; H, 2.01.

(b). Cp_2Co-Mediated Dimerization Reaction (Protocol B). According to protocol B, methyl ether **17** (121 mg, 0.25 mmol), Tf_2O (**2**; 92 mg, 0.325 mmol; stirred for 2 h at −10 °C), and Cp_2Co (71 mg, 0.375 mmol; stirred for 2 h at −30 °C) afforded the crude mixture, containing, by NMR, *d,l*-**19** and *meso*-**19** in the ratio of 81:19. Fractionation by column chromatography (SiO_2, 54 g; PE:E = 100:1), yielded *d,l*-**19** (25 mg, 22.2%) and [HC≡CCH_2(1-naphthyl)]-$Co_2(CO)_6$ (7 mg, 6.2%; repurification by preparative TLC, pentane).

[HC≡CCH_2(1-Naphthyl)]$Co_2(CO)_6$: dark red oil. TLC (PE:E = 15:1): R_f 0.57. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.58 (2H, s, CH_2), 5.97 (1H, s, HC≡), 7.39 −7.47 (2H, m, aromatic H), 7.52 (1H, td, aromatic H, J = 8.0, J = 1.2), 7.58 (1H, td, aromatic H, J = 6.8, J = 1.2), 7.79 (1H, t, aromatic H, J = 5.2), 7.88 (1H, d, aromatic H, J = 7.6), 8.10 (1H, d, aromatic H, J = 8.4). MS TOF FD$^+$: M$^+$ 452.

[μ,η^2-3-Methoxy-3-(2′-naphthyl)-1-propyne]dicobalt Hexacarbonyl (18). According to protocol E, 2-naphthaldehyde (1.87 g, 12 mmol; THF, 10 mL), sodium acetylide (634 mg, 13.2 mmol; 3.52 g, 18% suspension in xylene; THF, 40 mL), and dicobalt octacarbonyl (4.31 g, 12.6 mmol; ether, 40 mL) afforded, upon chromatographic isolation (silica gel, 250 g; PE:E = 10:1), [HC≡CCH(OH)-(2-naphthyl)]$Co_2(CO)_6$ (1.13 g, 20.2%) as a red oil. Methylation with methanol (1 mL) and BF_3·Me_2O (1.38 g, 12.1 mmol), at 0 °C, yielded **18** (937 mg, 80.4%; 16.2% over three steps) as a dark red solid. Mp: 73−76 °C (sealed capillary; dried by coevaporation with benzene, 3 × 1 mL). TLC (PE:E = 5:1): R_f 0.63. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.50 (3H, s, OMe), 5.45 (1H, s, CH), 6.05 (1H, d, HC≡, J = 0.8), 7.45−7.55 (3H, m, aromatic H), 7.81−7.89 (4H, m, aromatic H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 57.3 (OCH_3), 71.9 (CH), 83.7, 97.8 (C≡C), 124.0, 125.2, 125.9, 126.2, 127.6, 127.8, 128.2, 128.4, 133.1, 139.4 (aromatic C), 199.2 (C═O). MS TOF EI: m/z calcd for $C_{19}H_9O_7Co_2$ [M − Me]$^-$ 466.9018, found 466.9036. MS TOF FD$^+$: m/z M$^+$ 482. Anal. Found: C, 49.87; H, 2.53. Calcd for $C_{20}H_{12}O_7Co_2$: C, 49.82; H, 2.51.

***d,l*- and *meso*-[μ,η^2-3,4-Bis(2′-naphthyl)-1,5-hexadiyne]bis-(dicobalt hexacarbonyl) (20).** *(a). Zn-Mediated, Two-Step Dimerization Reaction.* According to protocol F, HBF_4·Me_2O (201 mg, 1.5 mmol), methyl ether **18** (121 mg, 0.25 mmol), and zinc (325 mg, 5 mmol) afforded crude **20** (NMR: *d,l*-**20**:*meso*-**20** = 74:26), which was fractionated on a silica gel column (20 g; PE:E = 15:1) to yield a mixture of *d,l*-**20** and *meso*-**20** (65 mg, 57.5%; *d,l*-**20**:*meso*-**20** = 75:25). The individual diastereomers were isolated by preparative TLC (PE:E = 10:1) to afford *d,l*-**20** (50 mg, 44.1%) and *meso*-**20** (10 mg, 8.5%).

d,l-**20**: dark red solid. T_{dec} = 127−135 °C (sealed capillary; dried by coevaporation with benzene, 3 × 1 mL). TLC (PE:E = 5:1): R_f 0.64. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.68 (2H, s, 2CH), 6.38 (2H, s, HC≡), 7.30−7.40 (6H, m, aromatic H), 7.54−7.73 (8H, m, aromatic H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 54.4 (CH), 77.0, 101.6 (C≡C), 125.4, 125.8, 127.4, 127.5, 127.9, 132.3, 132.9, 140.6 (aromatic C), 198.6, 199.8 (C═O). MS TOF EI: m/z calcd for $C_{39}H_{21}O_{13}Co_4$ [M + MeO]$^-$ 932.8316, found 932.8278. MS TOF FD$^+$: m/z M$^+$ 902. Anal. Found: C, 51.12; H, 2.27. Calcd for $C_{38}H_{18}O_{12}Co_4$: C, 50.58; H, 2.01. Single crystals suitable for X-ray structure analysis (Figure 1) were obtained by ethanol vapor diffusion into a solution of *d,l*-**20** in pentane and methylene chloride (5:1, v/v) at 0 °C (1 day).

meso-**20**: dark red solid. T_{dec} = 165−170 °C (sealed capillary; dried by coevaporation with benzene, 3 × 1 mL). TLC (PE:E = 5:1): R_f 0.68. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.69−4.87 (2H, m, 2CH), 4.89−5.08 (2H, m, HC≡), 7.53−8.10 (16H, m, arom H). MS TOF EI: m/z calcd for $C_{39}H_{21}O_{13}Co_4$ [M + MeO]$^-$ 932.8316, found 932.8271.

(b). Cp_2Co-Mediated Dimerization Reaction (Protocol B). According to protocol B, methyl ether **18** (121 mg, 0.25 mmol), Tf_2O (**2**; 92 mg, 0.325 mmol; stirred for 2 h at −10 °C), and Cp_2Co (142 mg, 0.75 mmol; stirred for 2 h at −30 °C) afforded, upon partial recomplexation with $Co_2(CO)_8$ (13 mg, 0.0375 mmol; ether, 13 mL) and fractionation by preparative TLC (PE:CH_2Cl_2 = 10:1; two plates, two runs), *d,l*-**20** (33 mg, 29.2%) and *meso*-**20** (3 mg, 2.7%; repurification by preparative TLC, PE:CH_2Cl_2 = 20:1). The mass ratio of *d,l*-**20** and *meso*-**20** was equal to 92:8.

***d,l*-3,4-Bis(4′-benzyloxyphenyl)-1,5-hexadiyne (23) (Protocol G).** Under an atmosphere of nitrogen, a solution of degassed $Ce(NH_4)_2(NO_3)_6$ (121 mg, 0.22 mmol) in acetone (5 mL) was added to a solution of *d,l*-**9** (20 mg, 0.02 mmol) in acetone (5 mL) at −78 °C. The reaction mixture was warmed to −30 °C, stirred for 1 h (TLC control), cooled to −78 °C, and quenched with degassed saturated NaCl solution (5 mL). The reaction mixture was then diluted with water (10 mL), warmed to 20 °C, and extracted with ether (5 × 20 mL). The combined ethereal layers were concentrated to about one-fifth of their original volume and dried over molecular sieves (4 Å). The molecular sieves were filtered off, the ethereal layer was evaporated to dryness, and the residual tan powder was washed with pentane (5 × 5 mL). The residual pentane was removed under reduced pressure, and product was coevaporated with benzene (5 mL) to give *d,l*-**23** (8.7 mg, 98.4%) as an off-white powder. Mp: 153−154 °C (with partial decomposition; sealed capillary; dried by coevaporation with benzene, 3 × 1 mL). TLC (B): R_f 0.54. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.37 (2H, s, HC≡), 3.94 (2H, s, CH), 5.05 (4H, s, OCH_2Ph), 6.88 (4H, d, aromatic 3′-H and 5′-H, J = 8.4), 7.19 (4H, d, aromatic H, J = 8.8), 7.31−7.47 (10H, m, aromatic H). HR-MS ESI/APCI: calcd for $C_{32}H_{30}O_5$ MNH_4^+ 460.2277, found 460.2263.

***d,l*-3,4-Diphenyl-1,5-hexadiyne (21), *d,l*-3,4-Bis(4′-methoxyphenyl)-1,5-hexadiyne (22), and *d,l*- and *meso*-3,4-Bis(4′-methoxyphenyl)-1,5-cyclodecadiyne (25).** Decomplexation of *d,l*-**5**, *d,l*-**8**, and *d,l*- and *meso*-**16** was carried out according to protocol G and described in the previous accounts.[1,4f]

***d,l*-3,4-Bis(3′,4′-methylenedioxyphenyl)-1,5-hexadiyne (24).** According to protocol G, the treatment of *d,l*-**14** (36 mg, 0.04 mmol) with degassed $Ce(NH_4)_2(NO_3)_6$ (241 mg, 0.44 mmol; −78 °C, 2 h; 0 °C 30 min), followed by purification on a preparative TLC plate (PE:E = 3:1) afforded *d,l*-**24** (11 mg, 89.0%) as an off-white solid. Mp: 140−141 °C (sealed capillary; dried by coevaporation with benzene, 3 × 1 mL). TLC (PE:E = 3:1): R_f 0.22. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.39 (2H, s, HC≡), 3.89 (2H, s, CH), 5.96 (4H, AB spectrum, OCH_2O, J = 1.4), 6.72 (4H, s, aromatic H), 6.88 (2H, s, aromatic H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 45.4 (CH), 73.6, 83.1 (C≡CH), 101.2 (OCH_2O), 108.1, 109.0, 122.0, 132.1, 147.1, 147.6 (aromatic

dx.doi.org/10.1021/om2006497 | *Organometallics* 2012, 31, 1653−1663

C). MS TOF EI$^+$: m/z calcd for $C_{20}H_{14}O_4$ M^+ 318.0887, found 318.0897.

***d,l*-3,4-Bis(1′-naphthyl)-1,5-hexadiyne (26).** According to protocol G, the treatment of *d,l*-**19** (26 mg, 0.029 mmol) with degassed $Ce(NH_4)_2(NO_3)_6$ (127 mg, 0.232 mmol; −78 °C, 30 min; −50 °C, 30 min; −30 °C, 30 min), followed by repeated purification on a preparative TLC plate (PE:CH_2Cl_2 = 5:1; PE:CH_2Cl_2 = 10:1) afforded *d,l*-**26** (4.5 mg, 47.0%) as a light yellow solid. Mp: 133−135 °C (sealed capillary; dried by coevaporation with benzene, 3 × 1 mL). TLC (PE:CH_2Cl_2 = 2:1): R_f 0.47. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.47 (2H, d, HC≡, J = 0.8), 4.95 (2H, s, 2CH), 7.47−7.59 (6H, m, aromatic H), 7.83 (2H, d, aromatic H, J = 8.4), 7.88−7.96 (2H, m, aromatic H), 8.03−8.19 (4H, m, aromatic H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 39.5 (CH), 73.6, 83.2 (C≡C), 122.3, 125.3, 125.4, 126.1, 126.9, 128.2, 129.1, 130.3, 133.8, 134.5 (aromatic C). MS TOF EI: m/z calcd for $C_{26}H_{18}$ M^+ 330.1409, found 330.1417.

***d,l*-3,4-Bis(2′-naphthyl)-1,5-hexadiyne (27).** According to protocol G, the treatment of *d,l*-**20** (40 mg, 0.044 mmol) with degassed $Ce(NH_4)_2(NO_3)_6$ (193 mg, 0.352 mmol; −78 °C, 30 min; −50 °C, 1 h), followed by purification on a preparative TLC plate (activation at 130 °C, 1 h; PE:CH_2Cl_2 = 10:1; THF extraction) afforded *d,l*-**27** (9.7 mg, 68.9%) as a light yellow solid. Mp: 143−145 °C (sealed capillary; dried by coevaporation with benzene, 3 × 1 mL). TLC (PE:E = 2:1): R_f 0.64. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.453 (1H, d, HC≡, J = 0.8), 2.457 (1H, d, HC≡, J = 0.8), 4.33 (2H, s, 2CH), 7.44−7.52 (6H, m, aromatic H), 7.74−7.89 (8H, m, aromatic H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 45.4 (CH), 73.7, 82.5 (C≡C), 125.8, 126.0, 126.2, 127.4, 127.5, 127.7, 127.9, 132.6, 133.0, 135.4 (aromatic C). MS TOF EI: m/z calcd for $C_{26}H_{18}$ M^+ 330.1409, found 330.1399. Single crystals suitable for X-ray structure analysis (Figure 2) were obtained by ethanol vapor diffusion into a solution of *d,l*-**27** in methylene chloride at 0 °C (2 days).

X-ray Crystallography of *d,l*-20 and *d,l*-27. Suitable crystals of *d,l*-**20** and *d,l*-**27** were coated with Paratone N oil, suspended in small fiber loops, and placed in a cooled nitrogen gas stream at 173 K on a Bruker D8 APEX II CCD sealed-tube diffractometer with graphite-monochromated Cu Kα (1.541 78 Å) radiation. Data were measured for each crystal using a series of combinations of ψ and ω scans with 10 s frame exposures and 0.5° frame widths. Data collection, indexing, and initial cell refinements were all carried out using APEX 2[13a] software. Frame integration and final cell refinements were done using SAINT[13b] software. The structures were solved using direct methods and difference Fourier techniques (SHELXTL V6.12).[13c] Hydrogen atoms were placed in their expected chemical positions using the HFIX command and were included in the final cycles of least squares with isotropic U_{ij} values related to the atoms ridden upon, except for H24 and H26 in *d,l*-**27**, which were found in a difference Fourier map and refined. All non-hydrogen atoms were refined anisotropically for *d,l*-**27**, but only the Co and O atoms were refined anisotropically for *d,l*-**20**. Scattering factors and anomalous dispersion corrections are taken from ref 13d. Structure solution, refinement, graphics, and generation of publication materials were performed by using SHELXTL V6.12 software.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

CIF files and tables giving crystallographic details, bond distances and angles, atomic coordinates and equivalent isotropic displacement parameters, and torsion angles for *d,l*-**20** and *d,l*-**27** and figures giving ^{1}H and ^{13}C NMR spectra of *d,l*-**9**, *meso*-**9**, *d,l*-**14**, *meso*-**20**, *d,l*-**23**, *d,l*-**24**, *d,l*-**26**, and *d,l*-**27**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: gagik.melikyan@csun.edu.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This material is based upon work supported by the National Science Foundation under Grant No. CHE-1112129. We are also greatly indebted to the Office of Graduate Studies, Research and International Programs, and University Corporation, California State University Northridge, for their generous support.

■ REFERENCES

(1) Melikyan, G. G.; Sepanian, R.; Spencer, R.; Rowe, A.; Toure, P. *Organometallics* **2009**, *28*, 5541.

(2) (a) Melikyan, G. G.; Nicholas, K. M. In *Modern Acetylene Chemistry*; Stang, P. J., Diederich, F., Ed.; VCH: Weinheim, Germany, 1995; Chapter 4. (b) McGlinchey, M. J.; Girard, L.; Ruffolo, R. *Coord. Chem. Rev.* **1995**, *143*, 331. (c) Amouri, H. E.; Gruselle, M. *Chem. Rev.* **1996**, *96*, 1077. (d) Went, M. *Adv. Organomet. Chem.* **1997**, *41*, 69. (e) Green, J. R. *Curr. Org. Chem.* **2001**, *5*, 809. (f) Muller, T. J. J. *Eur. J. Org. Chem.* **2001**, 2021. (g) Teobald, B. J. *Tetrahedron* **2002**, *58*, 4133. (h) Omae, I. *Appl. Organomet. Chem.* **2007**, *21*, 318.

(3) Representative examples are as follows. HBF_4: (a) Varghese, V.; Saha, M.; Nicholas, K. M. *Org. Synth.* **1989**, *67*, 141. BF_3: (b) Saha, M.; Nicholas, K. M. *J. Org. Chem.* **1984**, *49*, 417. CF_3COOH: (c) Nicholas, K. M.; Siegel, J. *J. Am. Chem. Soc.* **1985**, *107*, 4999. H_2SO_4: (d) Top, S.; Jaouen, G. *J. Org. Chem.* **1981**, *46*, 78. HBr: (e) Descoins, C.; Samain, D. *Tetr.ahedron Lett.* **1976**, 745. $TiCl_4$: (f) Magnus, P.; Pitterna, T. *J. Chem. Soc., Chem. Commun.* **1991**, 541. Bu_2BOTf: (g) Schreiber, S. L.; Klimas, M. T.; Sammakia, T. *J. Am. Chem. Soc.* **1987**, *109*, 5749. $MeAl(OR)_2$: (h) Nakamura, T.; Matsui, T.; Tanino, K.; Kuwajima, I. *J. Org. Chem.* **1997**, *62*, 3032. Me_2AlCN: (i) Stuart, J. G.; Nicholas, K. M. *Synthesis* **1989**, 454. TfOH: (j) Tanaka, S.; Isobe, M. *Tetrahedron* **1994**, *50*, 5633. TsOH: (k) Hosokawa, S.; Isobe, M. *J. Org. Chem.* **1999**, *64*, 37. $AgBF_4$: (l) Vizniowski, G. S.; Green, J. R.; Breen, T. L.; Dalacu, A. V. *J. Org. Chem.* **1995**, *60*, 7496. FSO_3H: (m) Reutov, O. A.; Barinov, I. V.; Chertkov, V. A.; Sokolov, V. I. *J. Organomet. Chem.* **1985**, *297*, C25.

(4) (a) Melikyan, G. G.; Deravakian, A.; Myer, S.; Yadegar, S.; Hardcastle, K. I.; Ciurash, J.; Toure, P. *J. Organomet. Chem.* **1999**, *578*, 68. (b) Melikyan, G. G.; Sepanian, S.; Riahi, B.; Villena, F.; Jerome, J.; Ahrens, B.; McClain, R.; Matchett, J.; Scanlon, S.; Abrenica, E.; Paulsen, K.; Hardcastle, K. I. *J. Organomet. Chem.* **2003**, *683*, 324. (c) Melikyan, G. G.; Villena, F.; Sepanian, S.; Pulido, M.; Sarkissian, H.; Florut, A. *Org. Lett.* **2003**, *5*, 3395. (d) Melikyan, G. G.; Villena, F.; Florut, A.; Sepanian, S.; Sarkissian, H.; Rowe, A.; Toure, P.; Mehta, D.; Christian, N.; Myer, S.; Miller, D.; Scanlon, S.; Porazik, M. *Organometallics* **2006**, *25*, 4680. (e) Melikyan, G. G.; Floruti, A.; Devletyan, L.; Toure, P.; Dean, N.; Carlson, L. *Organometallics* **2007**, *26*, 3173. (f) Melikyan, G. G.; Wild, C.; Toure, P. *Organometallics* **2008**, *27*, 1569. (g) Melikyan, G. G.; Mikailian, B.; Sepanian, R.; Toure, P. *J. Organomet. Chem.* **2009**, *694*, 785. (h) Melikyan, G. G.; Spencer, R.; Abedi, E. *J. Org. Chem.* **2009**, *74*, 8541. (i) Melikyan, G. G.; Voorhees, E.; Wild, C.; Spencer, R.; Molnar, J. *Tetrahedron Lett.* **2010**, *51*, 2287. (j) Melikyan, G. G.; Spencer, R. *Tetrahedron* **2010**, *66*, 5321. (k) Melikyan, G. G.; Spencer, R.; Rowe, A. *Organometallics* **2010**, *29*, 3556.

(5) Brandsma, L.; Verkruijsse, H. D. *Synthesis of Acetylenes, Allenes and Cumulenes*: Elsevier: New York, 1981; p 80.

(6) Greenfield, H.; Sternberg, H. W.; Friedel, R. A.; Wotiz, J. H.; Markby, R.; Wender, I. *J. Am. Chem. Soc.* **1956**, *78*, 120.

(7) Olier, C.; Gastaldi, S.; Gil, G.; Bertrand, M. P. *Tetrahedron Lett.* **2007**, *48*, 7801.

(8) (a) Tyler, D. R. *Acc. Chem. Res.* **1991**, *24*, 325. (b) Zavarine, I. S.; Kubiak, C. P. *Coord. Chem. Rev.* **1998**, *171*, 419. For the X-ray structure of cobaltocene see: (c) Antipin, M. Yu.; Boese, R.; Augart, N.; Schmid, G. *Struct. Chem.* **1993**, *4*, 91.

(9) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; Wiley: New York, 1999; pp 266−269, 287−288.
(10) (a) Gleiter, R.; Kratz, D.; Schafer, W.; Schehlmann, V. *J. Am. Chem. Soc.* **1991**, *113*, 9258. (b) Haberhauer, G.; Roers, R.; Gleiter, R. *Tetrahedron Lett.* **1997**, *38*, 8679. (c) Semmelhack, M. F.; Gallagher, J. *Tetrahedron Lett.* **1993**, 4121. (d) Boss, C.; Keese, R. *Tetrahedron* **1997**, *53*, 3111. (e) Myers, A. G.; Dragovich, P. S. *J. Am. Chem. Soc.* **1992**, *114*, 5859. (f) Klein, M.; Zabel, M.; Bernhardt, G.; König, B. *J. Org. Chem.* **2003**, *68*, 9379. (g) Pitsch, W.; Klein, M.; Zabel, M.; König, B. *J. Org. Chem.* **2002**, *67*, 6805.
(11) (a) Grissom, J. W.; Gunawardena, G. U.; Klingberg, D.; Huang, D. *Tetrahedron* **1996**, *52*, 6453. (b) Smith, A. L.; Nicolaou, K. C. *J. Med. Chem.* **1996**, *39*, 2103. (c) Basak, A.; Mandal, S.; Bag, S. S. *Chem. Rev.* **2003**, *103*, 4077.
(12) (a) Testa, B.; Mayer, J. M. *Hydrolysis in Drug and Prodrug Metabolism*; VHCA, Zurich/Wiley-VCH: Weinheim, Germany, 2003; p 780. (b) Balant, L. P.; Doelker, E. In *Burger's Medicinal Chemistry and Drug Discovery*; Wolff, M. E., Ed.; Wiley: New York, 1995; p 949.
(13) (a) *Bruker APEX 2 SAINT Version 6.45A*; Bruker AXS Inc., Madison, WI, 2003. (b) *Bruker SAINT*; Bruker AXS Inc., Madison, WI. (c) Sheldrick, G. M. A short history of SHELX. *Acta Crystallogr.* **2008**, *A64*, 112−122. (d) Wilson, A. J. C., Ed. *International Tables for X-ray Crystallography*; Kynoch Academic: Dordrecht, The Netherlands, 1992; Vol. *C*, Tables 6.1.1.4 (pp 500−502) and 4.2.6.8 (pp 219−222).
(14) (a) Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441. (b) Mantina, M.; Chamberlin, A. C.; Valero, R.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem. A* **2009**, *113*, 5806.
(15) (a) Badanyan, Sh. O.; Voskanyan, M. G.; Chobanyan, Zh. A. *Russ. Chem. Rev.* **1981**, *50*, 1074. (b) Onodera, G.; Nishibayashi, Y.; Uemura, S. *Organometallics* **2006**, *25*, 35. (c) Yang, F.; Zhao, G.; Ding, Y.; Zhao, Z.; Zheng, Y. *Tetrahedron Lett.* **2002**, *43*, 1289. (d) Ogoshi, S.; Nishiguchi, S.; Tsutsumi, K.; Kurosawa, H. *J. Org. Chem.* **1995**, *60*, 4650.
(16) Boutillier, P.; Zard, S. Z. *Chem. Commun.* **2001**, 1304.
(17) Swaminathan, S.; Narayanan, K. V. *Chem. Rev.* **1971**, *71*, 429.