Tetrahydrofuran-Mediated Stereoselective Radical C−C Bond Formation in Dicobalthexacarbonyl−Propargyl Complexes

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An extensive study on the mechanism of novel tetrahydrofuran (THF)-mediated coupling of $Co_2(CO)_6$-complexed propargyl alcohols and cations was carried out. On the basis of the stoichiometry of the process, the measurement of the kinetic isotope effect (KIE) in the competitive and noncompetitive settings (THF-d_0 and THF-d_8), ligand substitution experiments with ^{13}CO, kinetic studies with model compounds—$Co_2(CO)_6$-complexed 1-phenyl-2-propyne (**6**), tetrahydrothiophene, cobalt−alkyne anchored tetrahydropyran (THP, **21**)—and ab initio calculations, the mechanism of the reaction was proposed. It includes a reversible coordination of two THF molecules with an α-cationic center in a π-bonded propargyl moiety, followed by a single-electron transfer from the THF-sandwiched cobalt complex toward an electron-deficient propargyl cation. Although used in a 2-fold excess, THF acts *as a catalyst*, altering, both electronically and structurally, the requisite $Co_2(CO)_6$-complexed cations and breaking away from the organometallic scaffold, upon radical generation, in a chemically unchanged form. By triggering disproportionation between cobalt-complexed propargyl cations, THF acts in an unusual capacity of a *radical mediator,* previously being known in organic chemistry as a Lewis donor and donor of H atoms and hydride ions. The novel process that provides a facile entry to *d*,*l*-3,4-diphenyl-1,5-hexadiyne can be expanded toward stereo-, chemo-, and regioselective synthesis of polysubstituted *d*,*l*-3,4-diaryl-1,5-alkadiynes otherwise hardly accessible.

Introduction

The stereocontrol in radical reactions remains one of the major research thrusts in modern synthetic chemistry.[1] Both conceptually and experimentally, the most developed domain is substrate control in intramolecular cyclizations utilizing nucleophilic radical moieties. Intermolecular radical reactions, on the contrary, are less advanced, exhibiting various levels of selectivity under both substrate and chiral auxiliary control. Among the most promising strategies is the coordination of organic radicals with transition metals, which moderates the behavior of transient species that are otherwise unruly. The very topology of metal complexes allows for altering of the electronic, steric, and conformational parameters of π-bonded ligands by varying the nature of the transition metal, its oxidation state, and attendant with it, the mode of interaction with an organic moiety. Although the chemistry of organometallic radicals, in particular those with an unpaired electron localized on the α-carbon atom in a π-bonded ligand, has received relatively little attention,[2] the synthetic potential uncovered so far is truly remarkable: it provides novel methods for inter- and intramolecular radical C−C bond formation, which readily occurs, in a selective manner, in a diverse polyfunctional environment.[2,3] A systematic study of the chemistry of transition metal-templated propargyl

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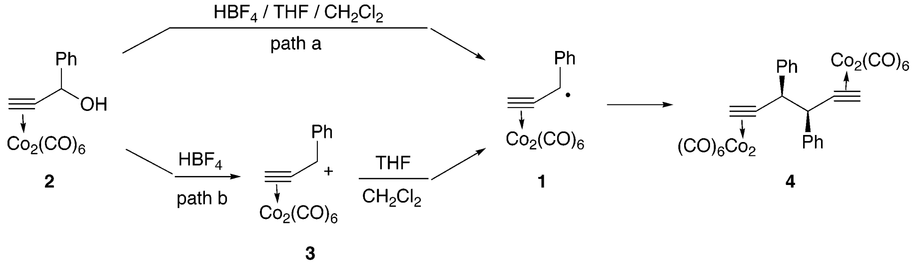
(1) (a) Curran, D. P. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: London, 1992; Vol. 5. (b) Malacria, M. *Chem. Rev.* **1996**, *96*, 289. (c) Giese, B.; Kopping, B.; Gobel, T.; Dickhaut, J.; Thoma, G.; Kulicke, K. J.; Trach, F. In *Organic Reactions*; Paquette L., Ed.; John Wiley: New York, 1996; Vol. 48, p 301. (d) Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Radical Reactions*; VCH: Weinhein, 1997. (e) Sibi, M. P.; Porter, N. A. *Acc. Chem. Res.* **1999**, *32*, 163.

(2) (a) *Organometallic Radical Processes*; Trogler, W. C., Ed.; Elsevier: Amsterdam, 1990; Chapters 3, 4, 9, 10. (b) Collman, J. R.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987. (c) Astruc, D. *Acc. Chem. Res.* **1991**, *24*, 36. (d) Astruc, D. *Electron Transfer and Radical Processes in Transition-Metal Chemistry*; VCH: New York, 1995; Chapters 3, 5, 6. (e) Torraca, K. E.; McElwee-White, L. *Coord. Chem. Rev.* **2000**, *206−207*, 469. (f) Melikyan, G. G. In *Frontiers in Organometallic Chemistry*; Nova Science Publishers: New York, 2006; p 155.

(3) (Pentadienyl radical)$Fe(CO)_3$: (a) Mahler, J. E.; Gibson, D. H.; Pettit, R. *J. Am. Chem. Soc.* **1963**, *85*, 3959. (b) Sapienza, R. S.; Riley, P. E.; Davis, R. E.; Pettit, R. *J. Organomet. Chem.* **1976**, *121*, C35. (c) Pearson, A. J.; Chen, Y.-S.; Daroux, M. L.; Tanaka, A. A.; Zettler, M. *J. Chem. Soc., Chem. Commun.* **1987**, 155. (Propargyl radical)$Cp_2Mo_2(CO)_4$: (d) Le Berre-Cosquer, N.; Kergoat, R.; L'Haridon, P. *Organometallics* **1992**, *11*, 721. (Benzyl radical)$Cr(CO)_3$: (e) Top, S.; Jaouen, G. *J. Organomet. Chem.* **1987**, *336*, 143. (f) Merlic, C. A.; Walsh, J. C.; Tantillo, D. J.; Houk, K. N. *J. Am. Chem. Soc.* **1999**, *121*, 3596. Ferrocenyl radical: (g) Cais, M.; Eisenstadt, A. *J. Chem. Soc.* **1965**, *30*, 1148. (h) Cais, M.; Askhenazi, P.; Dani, S.; Gottlieb, J. *J. Organomet. Chem.* **1977**, *540*, 127. CpCo(η^5-C_7H_9) radical: (i) Geiger, W. E.; Genneth, Th.; Lane, G. A. *Organometallics* **1986**, *5*, 1352. (Propargyl radical)$Co_2(CO)_6$: (j) Padmanabhan, S.; Nicholas, K. M. *J. Organomet. Chem.* **1981**, *212*, 115. (k) Salazar, K. L.; Khan, M. A.; Nicholas, K. M. *J. Am. Chem. Soc.* **1997**, *119*, 9053. (l) Salazar, K. L.; Khan, M. A.; Nicholas, K. M. *Tetrahedron* **2000**, *56*, 2211.

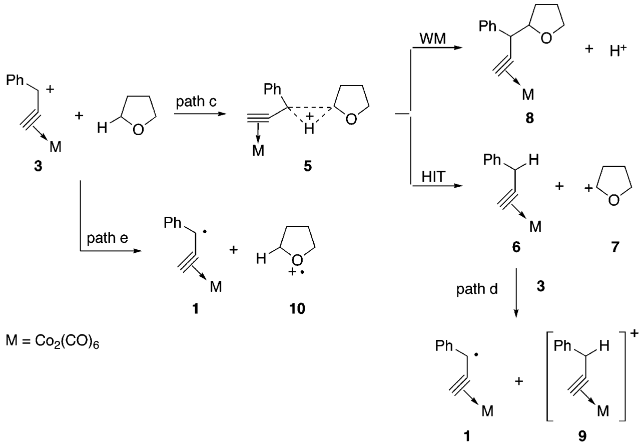
10.1021/om060579v CCC: $33.50

Scheme 1



radicals and cations[4] led us to the discovery of the novel THF-mediated generation, and coupling, of the $Co_2(CO)_6$-coordinated propargyl radicals.[4c,d] *One*- and *two-step protocols* utilize metal-templated propargyl alcohols, as substrates, and include either in situ generation or isolation of respective cationic species. Thus, secondary radical **1**, derived from propargyl alcohol **2**, via cation **3**, was shown to dimerize to *d*,*l*-**4** with an excellent diastereoselectivity (de 90%,[4c,d] Scheme 1). The *path a*—one-step protocol—is considered to be more efficient than *path b,* since it bypasses a laborious isolation of the requisite cation **3**. The synthetic versatility of the reaction was proven by the stereoselective construction of eight- and nine-membered 1,5-cycloalkadiynes[4d] and *d*,*l*-hexestrol, an inhibitor of microtubule assembly.[4f] It is noteworthy that the level of stereocontrol achieved in these reactions (up to 94% *d*,*l*-) remains unprecedented for organometallic radical dimerizations.[2,3] The intimate details of the THF-mediated process—*a mode of radical generation, the genesis of a single electron converting the cations to the respective radicals, the fate of the THF molecule*—remain unclear. It is worthy to mention that an alleged mediation of the radical reaction is not quite consistent with THF's synthetic profile. As a mild Lewis donor, it is widely used in organic chemistry as a solvent with an enhanced solvating power. As a reagent, it is known to donate H atoms[5a−c] and hydride ions,[5d] but not to mediate, or directly participate, in a single-electron transfer (SET) processes. Also "ionic" in nature is the alkylative cleavage of cyclic ethers by Lewis acids, abundantly illustrated in the literature.[5e−i] The current study was undertaken to shed light on the mechanism of the THF-mediated radical process, first, by identifying chemically conceivable alternatives and, second, by designing a series of control experiments that would allow us to unequivocally confirm, or exclude, certain mechanistic pathways.

Scheme 2



Results and Discussion

Mechanistic Alternatives. The most conceivable mechanistic pathways by which a two-component composition—cation **3** and THF—could yield a dimeric product **4** are shown in Scheme 2. An interaction could occur by a p−σ coordination mechanism involving an empty p-orbital in cation **3**, a Lewis acid, and an α-C−H bond in THF, an entity of a higher electron density (path c). The coordination is analogous to that first postulated for boron−hydrogen bond hydrolysis;[6] it was also invoked to interpret the mechanism of the transition metal-induced C−H[7a−c] and H−H[7d] bond activation, as well as the structural features of boranes[8] and stable organic cations.[9] The structure of intermediate **5** is also based on calculation data that revealed a two-electron, three-membered (3c-2e) transition state for a hydride-ion transfer reaction between propargyl cation and THF.[10] The conversion of TS-**5** to the stable organic products could occur by two mechanistically distinct pathways. A *two-electron shift* in (3c-2e) assembly **5**, to form a new C−H bond, would formally represent a hydride-ion transfer (HIT)[11] toward the cationic center, giving rise to hydrocarbon **6** and the THF-derived cation **7**. An alternative *two-electron shift* would form a new C−C bond in complex **8**, reminescent of the Wagner−

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(4) (a) Melikyan, G. G.; Vostrowsky, O.; Bauer, W.; Bestmann, H. J. *J. Organomet. Chem.* **1992**, *423*, C24. (b) Melikyan, G. G.; Bright, S.; Monroe, T.; Hardcastle, K. M.; Ciurash, J. *Angew. Chem., Int. Ed.* **1998**, *37*, 161. (c) Melikyan, G. G.; Deravakian, A. *J. Organomet. Chem.* **1997**, *544*, 143. (d) Melikyan, G. G.; Deravakian, A.; Myer, S.; Yadegar, S.; Hardcastle, K. I.; Ciurash, J.; Toure, P. *J. Organomet. Chem.* **1999**, *578*, 68. (e) Toure, P.; Melikyan, G. G.; Villena, F. *Org. Lett.* **2002**, *4*, 3989. (f) 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. (g) Melikyan, G. G.; Villena, F.; Sepanian, S.; Pulido, M.; Sarkissian, H.; Florut, A. *Org. Lett.* **2003**, *5*, 3395.

(5) (a) Olah, G. A.; Krishnamurthy, V. V. *J. Am. Chem. Soc.* **1982**, *104*, 3987. (b) Ruiz, J.; Lacoste, M.; Astruc, D. *J. Am. Chem. Soc.* **1990**, *112*, 5471, and references therein. (c) Baati, R.; Valleix, A.; Mioskowski, C.; Barma, D. K.; Falck, J. R. *Org. Lett.* **2000**, *2*, 485. (d) Nenitzescu, C. D. In *Carbonium Ions*; Olah, G. A., Schleyer, P. v. R., Eds.; Wiley: New York, 1968; Vol. 2, p 484. (e) Mudryk, B.; Cohen, T. *J. Am. Chem. Soc.* **1991**, *113*, 1867. (f) Yu, Y.; Zhang, Y.; Ling, R. *Synth. Commun.* **1993**, *23*, 1973. (g) Boisson, C.; Berthet, J. C.; Lance, M.; Nierlich, M.; Ephritikhine, M. *Chem. Commun.* **1996**, 2129. (h) Avens, L. R.; Barnhart, D. M.; Burns, C. J.; McKee, S. D. *Inorg. Chem.* **1996**, *35*, 537. (i) Dalko, P. I.; Langlois, Y. *J. Org. Chem.* **1998**, *63*, 8107.

(6) Hawthorne, M. F.; Lewis, E. S. *J. Am. Chem. Soc.* **1958**, *80*, 4296.

(7) (a) Hall, C.; Perutz, R. N. *Chem. Rev.* **1996**, *96*, 3125. (b) Crabtree, R. H. *Chem. Rev.* **1995**, *95*, 987. (c) Arndtsen, B. A.; Bergman, R. G.; Mobley, T. A.; Peterson, T. H. *Acc. Chem. Res.* **1995**, *28*, 154. (d) Kubas, G. J. *Acc. Chem. Res.* **1988**, *21*, 120.

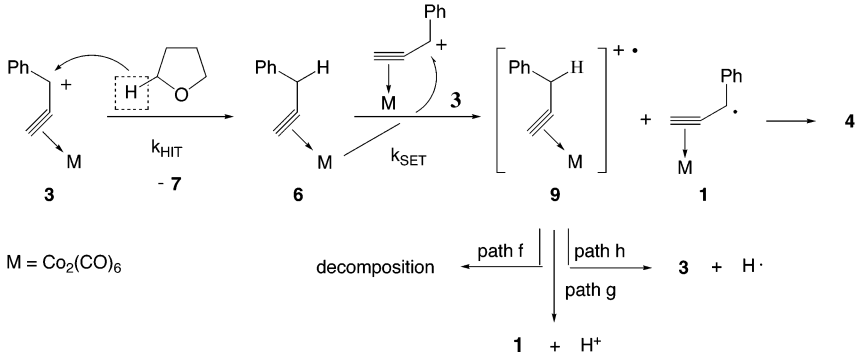
(8) (a) Brown, H. C.; Klender, G. J. *Inorg. Chem.* **1962**, *1*, 204. (b) Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*, 5th ed.; Wiley: New York, 1988; Chapter 6.

(9) (a) Laube, T. *Acc. Chem. Res.* **1995**, *28*, 399. (b) Sorensen, T. S. In *Stable Carbocation Chemistry*; Prakash, G. K. S., Schleyer, P. v. R., Eds.; Wiley: New York, 1997; Chapter 3.

(10) Toure, P.; Myer, S.; Melikyan, G. G. *J. Phys. Chem. A* **2001**, *105*, 4579.

(11) (a) Nenitzescu, C. D. In *Carbonium Ions*; Olah, G. A., Schleyer, P. v. R., Eds.; Wiley: New York, 1968; Vol. 4, Chapter 13. (b) Meerwein, H.; Hederich, V.; Morschel, H.; Wunderlich, K. *Ann. Chem.* **1960**, *635*, 1.

Scheme 3



Meerwein (WM) rearrangement.[12] The formation of HIT-**6** does not preclude the generation of the radical species **1**: due to its neutral character, hydrocarbon **6** would have a higher electron density on the cluster compared to cation **3**, which, in turn, could trigger a *cluster-to-cluster reduction* process (path d).[2,13] Thus, an "ionic-radical" sequence represented by path c/path d could generate propargyl radical **1**, along with an oxidized complex **9**. An alternative, "most obvious" mechanistic pathway is a *direct SET* from an O atom in THF toward the cationic center in a metal complex, affording radical **1** along with cation-radical **10** (path e). Thus, our initial efforts were focused on these mechanistic alternatives in an attempt to prove, or exclude, either one of them.

Does HIT Represent a Viable Mechanistic Pathway? In the preliminary set of experiments, it was established that an optimal ratio of carbocation **3** to THF is 1:2, bringing the reaction to completion in 35 min and 3 h, for two- and one-step procedures, respectively. A larger excess of THF, up to 10-fold, was found not to affect the rate of reaction. If HIT product **6** were in fact a key intermediate, then, dependent upon the fate of the oxidized species **9**, the stoichiometry would change from a **3**:THF ratio of 2:1—in the case of a gross decomposition (Scheme 3, path f) or release of hydrogen ion and radical species **1** (path g)—to 1:1, when cation **3** gets regenerated, along with a hydrogen atom (path h). These data provided an early indication that the HIT process is most probably not involved in the mechanistic path leading to *d*,*l*-**4** (Scheme 3). The tentative formation of HIT product **6** and its subsequent interaction with cation **3** involve the alternative scenarios—"*fast-slow*" and "*slow-fast*"—differing in the relative rates of generation (k_{HIT}) and consumption (k_{SET}) of HIT product **6** (Scheme 3). The former implies a rapid accumulation of hydrocarbon **6** in the reaction mixture and a slow consumption of it ($k_{HIT} \gg k_{SET}$), while the latter would maintain a low, and constant, concentration of the intermediate **6** throughout the reaction ($k_{HIT} \ll k_{SET}$). Careful monitoring of the process (^{1}H NMR; TLC) revealed that the concentration profile of HIT product **6** corresponds to a "*slow-fast*" mechanism: its amount in the reaction mixture remains constant, around 1%, starting from an early stage in the reaction. These data allowed us to conclude that the formation of HIT product **6** might only occur at a *slow, rate-determining step*, which can further be probed by measuring the primary *kinetic isotope effect (KIE)*.[14] It is noteworthy that examination of the decomplexed crude mixtures by means of ^{1}H NMR and GC-MS provided no indication for the formation of Wagner—Meerwein product **8** (Scheme 2). This finding is in accord with previous calculation data suggesting that a transfer of two electrons within the (3c-2e) transition state **5** (Scheme 2) would be thermodynamically disfavored.[10]

Kinetic Isotope Effect. The unique nature of this reaction does not allow us to use a "classical" approach—determination of isotopic distribution in end products[14]—since the HIT product **6** itself is formed only in trace amounts. Instead, an alleged C—H bond stretching in TS-**5** and HIT, as a rate-determining step, are followed by a cluster-to-cluster reduction, producing *nonisotopic* dimer **4**. This leaves us with two options, either to apply a *noncompetitive technique and determine the fractional amounts of conversion, F*, or to use a *competitive technique with isotopic reagents and determine their ratio at an early stage of conversion*.[14] On the basis of literature data for hydride-ion transfer, KIE values would lie in a range k_H/k_D 1.5—2.0, suggesting a nonlinear, three-membered transition state.[6,14] In the series of preliminary kinetic studies, it was established that the cation quenching with methanol needs to be standardized to avoid irreproducible kinetic data. The reason was that an interaction of electrophilic cationic species with methanol is a highly exothermic process, and a local overheating, if allowed, can result in a higher degree of conversion that does not adequately reflect the genuine product distribution in the reaction mixture.[15]

In a *competitive setting*, cation **3** was treated with equimolar quantities of THF-d_0 and THF-d_8, and their fractional amounts were then determined by capillary GC-MS (Scheme 4). The reaction was stopped after 1min by quenching with MeOH;[15] according to GC data, a ratio of the isotopic mediators—THF-d_0 and THF-d_8—remains the same as before the reaction, 1:1. These data were in accord with measurement of the KIE in a *noncompetitive setting*: cation **3** (1 equiv) was separately treated with a 2-fold excess of THF-d_0 (1 equiv) and THF-d_8 (1 equiv), and the reaction mixture, upon quenching with methanol,[15] was analyzed by ^{1}H NMR. In both cases, after 1 min, the ratio of dimer **4**:Me-ether **11** was equal to 18:82 (Scheme 5). The fact that the KIE was equal to 1 for both protocols provided us with

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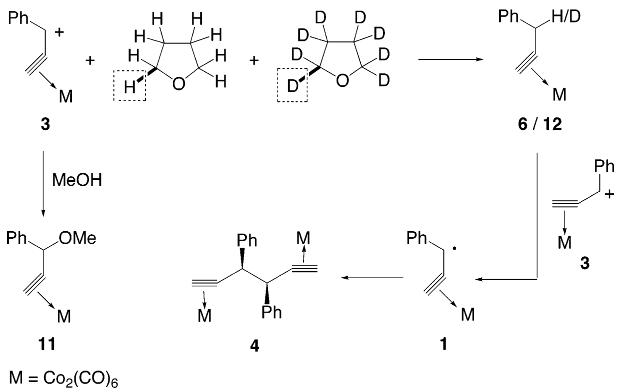
[12] Kaupp, G. *Top. Curr. Chem.* **1988**, *146*, 57.

[13] (a) Astruc, D. *Acc. Chem. Res.* **1997**, *30*, 383. (b) Barlow, S.; O'Hare, D. *Chem. Rev.* **1997**, *97*, 637.

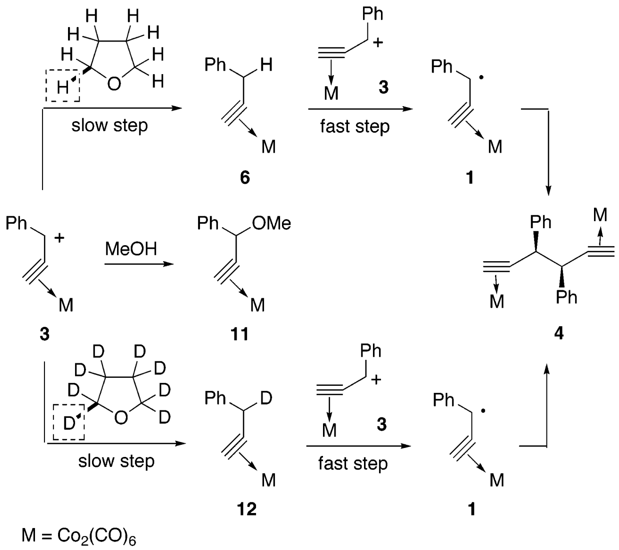
[14] (a) Kwart, H. *Acc. Chem. Res.* **1982**, *15*, 401. (b) Melander, L.; Saunders, W. H. *Reaction Rates of Isotopic Molecules*; Wiley: New York, 1980. (c) Cheng, T. Y.; Bullock, R. M. *J. Am. Chem. Soc.* **1999**, *121*, 3150.

[15] A series of control experiments were carried out to determine the conditions for sampling the reaction mixture and also quenching it with methanol. The experimental protocols tested were as follows: (1) an aliquot (0.1 mL) dispersed into MeOH (2 mL) at 20 °C; (2) an aliquot (0.1 mL) dispersed into MeOH (2 mL) at −20 °C; (3) an "*in-flask*" quenching, at −20 °C, using precooled (−20 °C) MeOH (2 mL; slow addition onto the walls of the flask); (4) an "*in-flask*" quenching using precooled (−78 °C) MeOH (2 mL; slow addition onto the walls of the flask cooled to −78 °C). An interaction of unreacted cation **3** with methanol yielded the respective Me-ether, [HC≡C—CH(OMe)-Ph]Co$_2$(CO)$_6$ (**11**), and the ratio of dimer **4**:Me-ether **11** was determined by ^{1}H NMR. On the basis of these data, two experimental procedures were adopted for *sampling* and "*in-flask*" quenching: first, dispersing an aliquot (0.1 mL) into MeOH (2 mL) at 20 °C and, second, an addition of precooled methanol (−20 °C) to the reaction mixture at −20 °C.

Scheme 4



Scheme 5



another line of evidence that the α-C−H bond in THF is not involved in a rate-determining step, and formation of the HIT products **6**/**12** does not precede the generation of propargyl radical **1**.

Tandem Action of THF and HIT Product 6. Since the measurement of the KIE showed that formation of HIT product **6** did not occur at a rate-determining step, then the control experiment was carried out to probe *the effect of HIT product* **6**, as an additive, upon the rate of the reaction. The rationale behind this was that if, in fact, a hydride-ion transfer takes place at a slow step, then introducing the tentative intermediate into the reaction mixture should substantially accelerate the process. Methodologically, cation **3** was treated with THF (2 equiv) and HIT product **6** (1 equiv) simultaneously, and the reaction progress was monitored by NMR, upon quenching the aliquots with MeOH.[15] When compared with the parent process mediated by THF alone (Figure 1, A), a tandem action aided by HIT **6** did not result in any acceleration (Figure 1, B). To the contrary, and quite unexpectedly, a noticeable retardation of the reaction was observed: even in 90 min, the conversion reaches only 80% (Figure 1, B), while the parent reaction came to completion in 35 min (Figure 1, A). The retardation in question might be accounted for in terms of dilution of the reaction mixture with 1 equiv of HIT **6**, thus affecting the intermolecular dimerization reaction rate. Most importantly, these data allowed us to conclude that HIT is not a main mechanistic pathway responsible for the formation of radical dimers, and the validity of an alternative pathway—path e—should be carefully examined (Scheme 2).

Testing Path e. Path e (Scheme 2) involves a direct electron transfer from THF, acting *as a source of* an electron, toward an α-cationic center in cation **3**. The literature precedent does not support this hypothesis: an interaction of topologicaly diverse Co-complexed propargyl cations with a variety of O-, S-, P-, N-, and H-nucleophiles was reported to yield the respective solvolysis products, while the formation of radical dimers was not observed, even with thiolate ions.[16,17] The very protocol for cation isolation[16] suggests that path e can hardly be a major source of transient radicals **1**: upon treatment with HBF_4, cation **3** is washed with large quantities of diethyl ether (0.25 mmol of **3**; 60 mL of Et_2O), but the respective radical reaction does not take place. The ionization potentials of THF and diethyl ether are relatively close to each other (9.38 vs 9.52 eV),[18] and this makes an observed disparity in their behavior difficult to interpret. To fully exclude path e from consideration, a surrogate of THF with a lower ionization potential (8.62 eV)[18]—tetrahydrothiophene—was used as a radical mediator (Scheme 6). The concentration curves derived from ^{1}H NMR data showed that the reaction, contrary to our expectations, was even slower than a THF-assisted process: a complete conversion was achieved in 90 min versus 35 min for the parent reaction (Figure 2).

Effect of Steric Bulkiness upon Reaction Rate. Since the most probable mechanistic pathways (c/d/e, Scheme 2) were not supported by the experimental evidence, we looked for alternative avenues that could explain an observed *"radicalization"* of cation **3** in the presence of THF. One of the key parameters to examine was the coordination between an α-cationic center, a Lewis acid, and an O atom in THF, a Lewis base, affording the oxonium salt **13** (Scheme 7). The rationale behind this is that since an α-carbon atom in a propargyl moiety is located in a sterically congested area of the molecule, due to the presence of the Co_2-core and phenyl group, then the reaction might be sensitive toward a bulkiness of the Lewis base. One could also envision that a sterically hindered Lewis base, not capable of accessing a cationic center, will not be efficient in mediating the radical process. To test this hypothesis, 2,5-dimethyltetrahydrofuran and 2,2,5,5-tetramethyltetrahydrofuran were used as potential radical mediators, and the reaction mixtures were quenched with MeOH[15] after 35 min, the reaction time for the parent process mediated by THF. According to ^{1}H NMR spectra, the ratios of dimer **4**:Me-ether **11** were equal to 62:38 and 11:89, respectively, indicating that the *bulkiness of*

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(16) (a) Melikyan, G. G.; Nicholas, K. M. In *Modern Acetylene Chemistry*; Stang, P. J., Diederich, F., Ed.; VCH Publishers: Weinheim, 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.

(17) (a) Saha, M.; Nicholas, K. M. *J. Am. Chem. Soc.* **1984**, *49*, 417. (b) Gruselle, M.; Philomin, V.; Chaminant, F.; Jaouen, G.; Nicholas, K. M. *J. Organomet. Chem.* **1990**, *399*, 317. (c) Amouri, H.; Gruselle, M.; Jaouen, G.; Daran, J. C.; Vaissermann, J. *Inorg. Chem.* **1990**, *29*, 3238. (d) Bennett, S. C.; Gelling, A.; Went, M. J. *J. Organomet. Chem.* **1992**, *439*, 189. (e) Roth, K. D.; Muller, U. *Tetrahedron Lett.* **1993**, 2919. (f) Gelling, A.; Mohmand, F.; Jeffery, J. C.; Went, M. J. *J. Chem. Soc., Dalton Trans.* **1993**, 1857. (g) Gruselle, M.; Kondratenko, M. A.; Amouri, H.; Vaissermann, J. *Organometallics* **1995**, *14*, 5242. (h) Kuhn, O.; Rau, D.; Mayr, H. *J. Am. Chem. Soc.* **1998**, *120*, 900. (i) Amouri, H.; Begue, J. P.; Chennoufi, A.; Bonnet-Delpon, D.; Gruselle, M.; Malezieux, B. *Org. Lett.* **2000**, *2*, 807. (j) Gruselle, M.; Malezieux, B.; Andres, R.; Amouri, H.; Vaissermann, J.; Melikyan, G. G. *Eur. J. Inorg. Chem.* **2000**, 359. (k) Amouri, H.; Thouvenot, R.; Gruselle, M.; Malezieux, B.; Vaissermann, J. *Organometallics* **2001**, *20*, 1904. For reduction of ferrocenylcarbonium ion with ethyldiisopropylamine see: Cais, M.; Askhenazi, P.; Dani, S.; Gottlieb, J. *J. Organomet. Chem.* **1976**, *122*, 403.

(18) NIST database: http://webbook.nist.gov/chemistry.

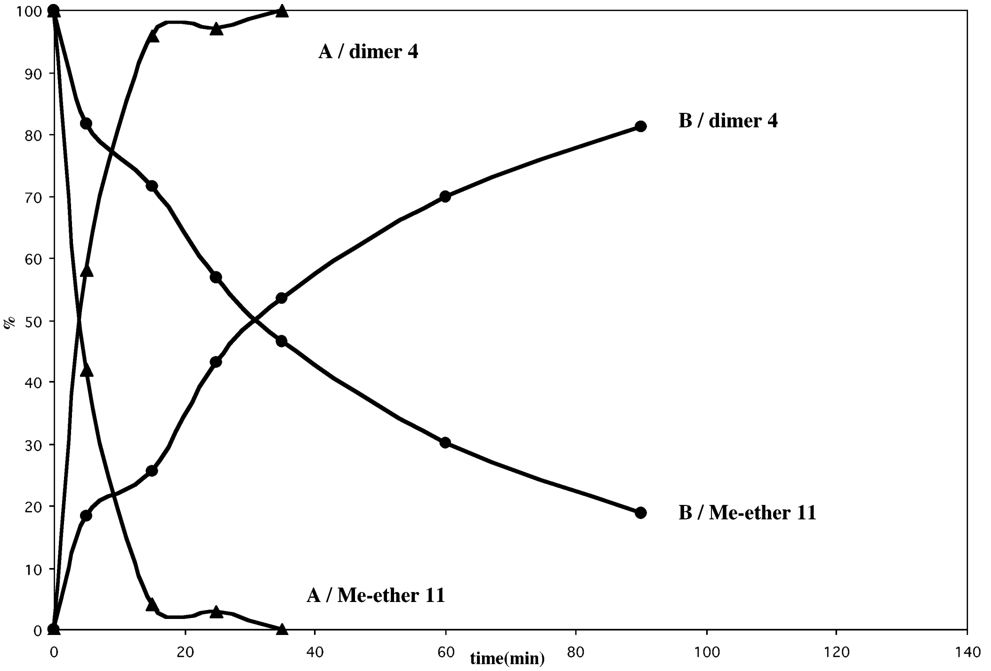
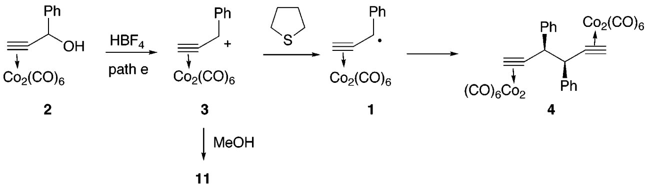


Figure 1. Concentration curves for coupling reaction mediated by THF (A) and THF/HIT **6** (B).

Scheme 6



the radical mediator—increasing from 100 Å^3, via 158 Å^3, to 202 Å^3—*is inversely proportional to the reaction rate* (Scheme 7). From a mechanistic viewpoint, this finding proved that *donor*−*acceptor coordination is the initial mode of interaction between propargyl cation **3** and oxygen-containing radical mediators*.

Complexation of Propargyl Cation and THF: Calculation Data. Our studies on the stoichiometry of the process revealed that the molar ratio of **3**:THF, 1:2, is optimal for the rapid completion of the reaction. Since the very fact of coordination was experimentally confirmed, it was of utmost importance to evaluate its feasibility from a thermodynamic perspective. Thus, an interaction of propargyl cation **14** (Figure 3) with THF was probed with the geometries being optimized by the Hartree−Fock method (6-31G* basis sets).[19] The coordination of a first molecule of THF was found to be highly exothermic (−54.7 kcal/mol), yielding the oxonium ion **15**. Less predictably, the addition of the second molecule of THF to form adduct **16** also exhibited an exothermicity of −11.5 kcal/mol (Figure 3). Conceptually, this interaction has a precedence in the formation of stable complexes between a proton and two THF molecules.[20] By using pulsed electron beam mass spectroscopy, the bond energies were measured for dimer cations of heterocyclic compounds, THF and tetrahydrophiophene.[20a] Curiously enough, the former yielded a much more stable cluster complex than its sulfur-containing counterpart (−29.9 vs −16.9 kcal/mol). These data shed light on an observed retardation of the reaction when THF is replaced by tetrahydrothiophene (Figure 2, Scheme 6): the alleged 1:2 complex of cation **3** with the latter might be energetically inferior to that of THF. More recent data on the solvated proton with carborane anion, [H(THF)$_2$][CHB$_{11}$H$_5$Br$_6$], provided a crystallographic description of these unique species having short oxygen−oxygen separations and relatively strong, linear H-bonding.[20c] The calculation data involving an *uncomplexed* propargyl cation **14** indicated that the formation of the analogous THF-sandwiched 1:2 complex might also take place in the case of the *cobalt-complexed* propargyl cation **3**. Molecular modeling further confirmed the feasibility of this parallel: with the α-Ph group present, two THF molecules were easily accommodated by the cationic center without causing any significant structural deviation. The totality of calculation and literature data and molecular modeling made an empirically found ratio of cation **3**:THF of 1:2 quite sensible: the consecutive coordination of two THF molecules with an electrophilic center in cation **3** constitutes an initial stage of the process, triggering a series of transformations responsible for generation of key radical **1**.

Model Studies with [4-Ethynyltetrahydropyran]dicobalthexacarbonyl (21). One of the most critical questions with regard to the mechanism of the radical coupling reaction is the *fate of the mediator, a THF molecule*. Systematic efforts were made to trap the ring-opening products—4-hydroxy- and 4-methoxybutanals and 3-butenal—that might have been derived from the oxidized forms of THF, such as α-cationic species **7** or oxonium ion **10** (Scheme 2; GC-MS, trapping with 2,4-dinitrophenylhydrazine). After these attempts proved unsuccessful, we decided to anchor a "light" molecule of THF by tethering it to a larger, and colored, molecular assembly, a Co$_2$(CO)$_6$-alkyne unit. An organometallic moiety would then allow

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[19] Titan program from Wavefunction, Inc. All geometries were optimized by the Hartree−Fock method using 3-21G* and 6-31G* basis sets.

[20] (a) Hiraoka, K.; Takimoto, H.; Yamade, S. *J. Am. Chem. Soc.* **1987**, *109*, 7346. (b) Stoyanov, E. S. *Phys. Chem. Chem. Phys.* **2000**, *2*, 1137. (c) Stasko, D.; Hoffman, S. P.; Kim, K.; Fackler, L. P.; Larsen, A. S.; Drovetskaya, T.; Tham, F. S.; Reed, C. A.; Rickard, C. E. F.; Boyd, P. D. W.; Stoyanov, E. S. *J. Am. Chem. Soc.* **2002**, *124*, 13869, and references therein. For synthetic and computational studies on pentacoordinate carbon compounds see, respectively: Yamashita, M.; Yamamoto, Y.; Akiba, K.; Hashizume, D.; Iwasaki, F.; Takagi, N.; Nagase, S. *J. Am. Chem. Soc.* **2005**, *127*, 4354. Raghavachari, K.; Chandrasekhar, J.; Burnier, R. C. *J. Am. Chem. Soc.* **1984**, *106*, 3124.

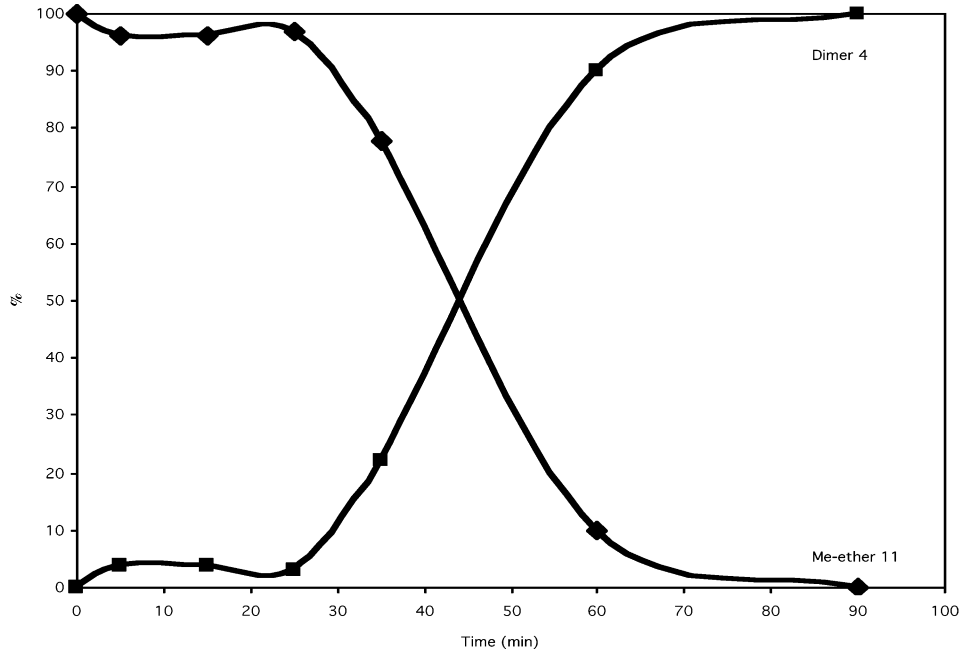
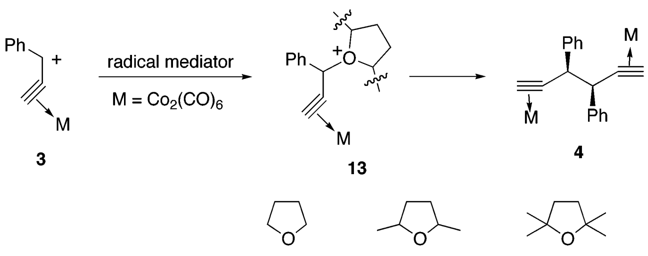


Figure 2. Concentration curves for coupling reaction mediated by tetrahydrothiophene.

Scheme 7



Dimer **4** : Me-ether **11**	100 : 0	62 : 38	11 : 89
Molecular volume, Å^3	100	158	202

us to easily detect, isolate, and characterize any derivatives formed by the structural alteration of the heterocyclic unit. 4*H*-Tetrahydropyran-4-one (**17**) was condensed with sodium acetylide, and the crude alcohol, without any additional purification, was allowed to complex with dicobaltoctacarbonyl (Scheme 8). The treatment of the resulting cobalt complex **18** with tetrafluoroboric acid was aimed at generation of propargyl cation **19**, which could further be reduced to the respective hydrocarbon. Instead, even at low temperatures, up to −78 °C, the cationic species could not be isolated from an ethereal solution, undergoing a rapid β-deprotonation to enyne complex **20**. Attempts to reduce an internal double bond in **20** in the presence of heterogeneous catalysts were unsuccessful (Pd/C, PtO_2), apparently for steric reasons. An alternative approach to the THP derivative **21** was the direct treatment of alcohol **18** with BH_3/CF_3COOH,[21] affording the target molecule in a high yield (Scheme 8). The very design of the anchored THP **21** limits, due to its symmetrical nature, the number of chemically conceivable products derived from the ring opening; at the same time, the peripheral location of an anchor will not alter, either electronically or sterically, the heterocyclic region of the molecule.

The treatment of propargyl cation **3** with THP derivative **21** was carried out under standard conditions (CH_2Cl_2, 20 °C), and the reaction was monitored by TLC and ^{1}H NMR. Coordination was expected to take place yielding the oxonium ion **22** (might also contain two molecules of THP initiator **21**), followed by the generation of *d*,*l*-**4** and other products derived from the radical mediator. A careful examination of the reaction mixture showed that *no new cobalt complexes, either stable or transient in nature, were formed in the course of the reaction*: THP derivative **21** was instead recovered, by PTLC, in a 86% yield. These data indicate that THP initiator **21**, and, by analogy, a THF molecule in the parent reaction, does not undergo any chemical transformation. Its role, most probably, consists of the coordination with a cationic center, alteration of the propargyl complex both electronically and sterically, and breaking away from the organometallic scaffold upon initiation of the radical process. In fact, *heterocyclic molecules, THF or THP, act as catalysts of radical coupling reaction, although the very nature*

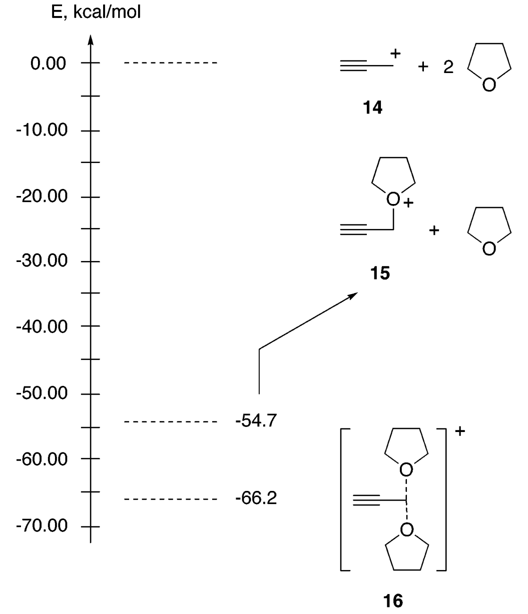


Figure 3. Thermodynamics of the coordination of propargyl cation **14** with THF.

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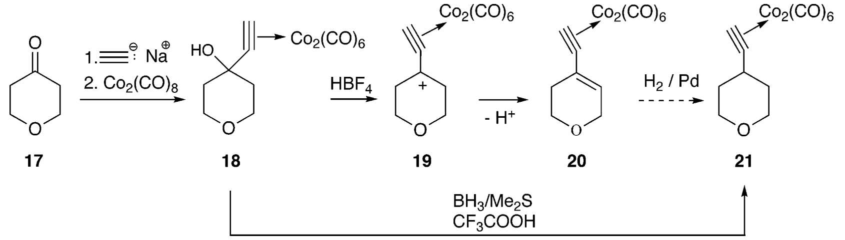
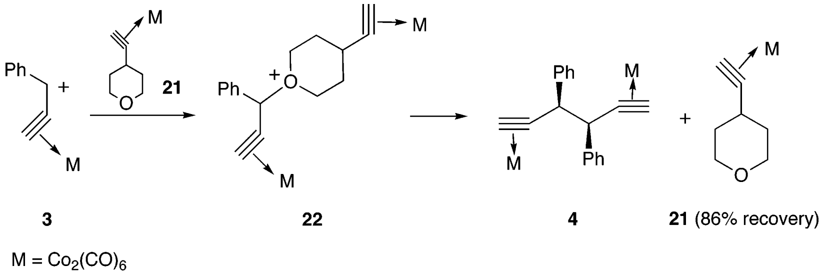
(21) McComsey, D. F.; Reitz, A. B.; Maryanoff, C. A.; Maryanoff, B. E. *Synth. Commun.* **1986**, *16*, 1535.

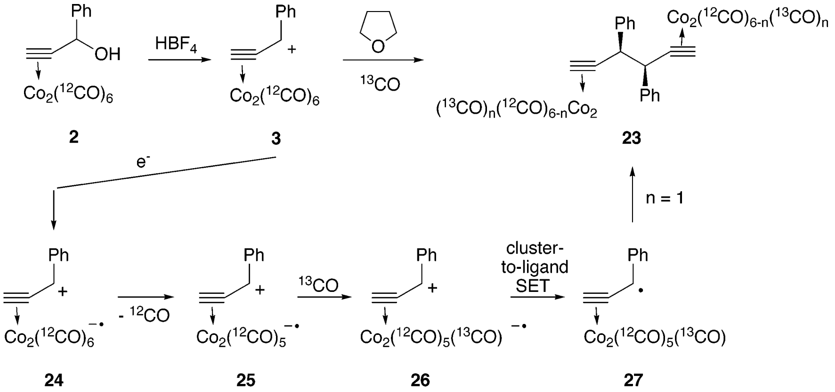
Scheme 8



Scheme 9



Scheme 10



of the process requires not catalytic but stoichiometric quantities of these reagents.

^{13}CO Incorporation in Ligand Substitution Experiments. The mechanism of the radical process mediated by THF includes the formation of cobalt-complexed propargyl radical **1**, which, in turn, originates from its ionic counterpart, propargyl cation **3**. It is conceivable that, along the reaction coordinate, upon electronic and structural alterations of the requisite propargyl cations, a single-electron transfer occurs between metal clusters of various levels of electrophilicity. In cluster redox chemistry, the mono- and polymetallic metal cores are known to undergo one-electron transfer reactions, to act as electron reservoirs, and also to be reduced, and oxidized, either by chemical or electrochemical means.[2,5b,16,22,23] If the hypothesis is correct, then the formation of the reduced metal clusters could be detected by a ligand substitution reaction: 19e$^-$ species—generated by reduction of the polynuclear metal carbonyls with Na/Ph$_2$CO, or electrochemically—are reported to undergo an accelerated, by a factor of $>10^6$, ligand displacement at ambient temperatures.[23] Propargyl alcohol **2** was converted to cation **3**, which was then treated with a 2-fold excess of THF in ^{13}CO atmosphere (Scheme 10). Dimer **23** was isolated by PTLC and analyzed by ^{13}C NMR and MS-FAB. The former revealed a sharp increase in the peak intensity of cobalt-coordinated ^{13}CO signals (199/200 ppm), indicating an incorporation of "heavy" carbon monoxide into the product (SI). A comparison of MS-FAB data for dimer **23** and isotopically nonlabeled species **4** revealed an incorporation of at least four molecules of ^{13}CO (**23** m/z M$^+$ − 3CO 718, 719, 720, 721, 722; **4** m/z M$^+$ − 3CO 718) into the metal cluster (SI). The actual level of incorporation might be even higher, since CO ligands most susceptible to substitution might also be those initially released in the fragmentation of molecular ion. Thus, we concluded that redox processes do occur *prior to the generation of key radical **1***. Most probably, cation **3** undergoes a one-electron reduction to anion-radical **24** with a subsequent ligand replacement by a dissociative mechanism. The tentative 37e$^-$ species **24** could lose a ^{12}CO molecule, forming the dicobaltpentacarbonyl complex **25**, which, in turn, is attacked by an incoming ligand, ^{13}CO, to form the isotopically mixed complex **26**. A subsequent one-electron transfer—from the cluster on the π-bonded ligand—will give rise to propargyl radical **27** and dimer **23**, upon dimerization. Complex **26** might also enter another two-step

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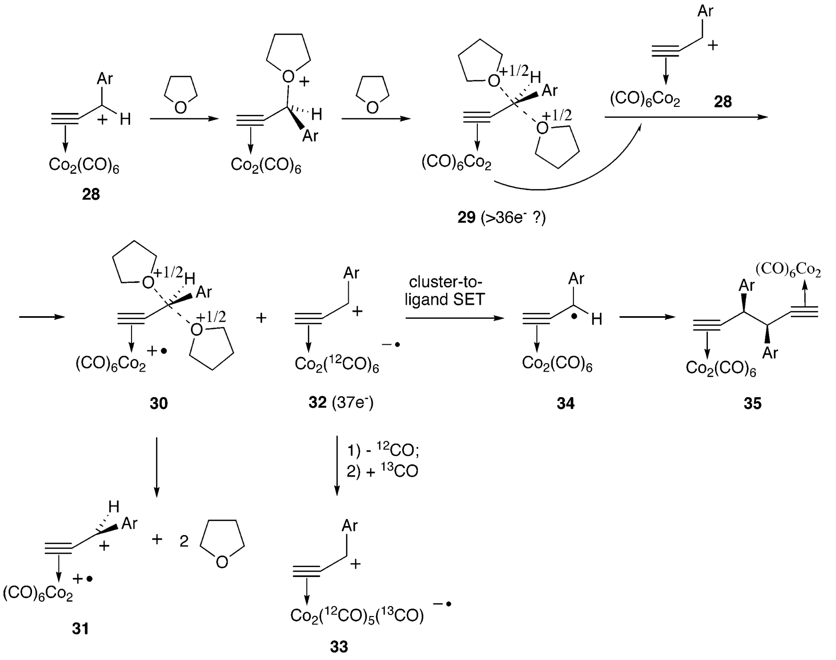
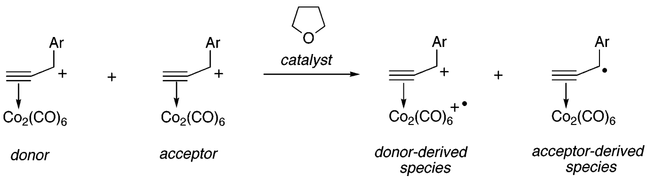
(22) (a) Davies, S. G.; McCarthy, T. D. In *Comprehensive Organometallic Chemistry II;* Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon Press: New York, 1995; Vol. 12, p 1039. (b) Semmelhack, M. F. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon Press: New York, 1995; Vol. 12, p 979. (c) *Electron Transfer in Inorganic, Organic and Biological Systems*; Bolton, J. R., Mataga, N., McLendon, G., Eds.; *Advances in Chemistry Series 328*; American Chemical Society: Washington, DC, 1991. (d) Colbran, S. B.; Robinson, B. H.; Simpson, J. *Organometallics* **1983**, *2*, 943, and references therein.

(23) (a) Arewgoda, C. M.; Robinson, B. H.; Simpson, J. *J. Am. Chem. Soc.* **1983**, *105*, 1893, and references therein. (b) Kochi, J. K. In *Organometallic Radical Processes*; Trogler, W. C., Ed.; Elsevier: Amsterdam, 1990; p 201.

Scheme 11



Scheme 12



cycle of ligand replacement, yielding radical species, and dimers, of a higher degree of isotopic enrichment ($n = 1-4$).

Proposed Mechanism for THF-Mediated Coupling of Cobalt-Complexed Propargyl Systems. On the basis of the totality of experimental data available to date, the following mechanism for THF-mediated reaction is proposed (Scheme 11). The initial stage of the process includes the coordination of two molecules of THF with an electrophilic center in cation **28**. Several lines of supporting evidence include (a) kinetic data on THF and its 2,5-dimethyl- and 2,2,5,5-tetramethyl derivatives with reaction rates declining with an increase in steric hindrance (Scheme 7); (b) stoichiometry studies with an empirically found optimal ratio of cation:THF equal to 1:2; (c) calculation data on propargyl cation−THF complexes (Figure 3); and (d) literature precedence on the formation of the stable and structurally characterizable proton−heterocycle clusters.[20] Complex **29**, a tentative key intermediate, would represent a significant departure from the original species **28**, in both steric and electronic terms. The cationic center in the cobalt-complexed propargyl cation is known to be shifted toward one of the cobalt atoms in a metal core (X-ray crystallography[4b]), a structural reflection of the stabilizing overlap of the empty p-orbital of the cationic center and a filled d-orbital of the metal atom. Introducing THF molecules, Lewis donors, into the molecule would disrupt the p−d interaction between a metal core and a π-bonded ligand, reverse the flow of electrons, and also cause a major charge redistribution in the cobalt−propargyl moiety. The electron density on the cluster in complex **29** should be higher ($>36e^-$) than that in cation **28**, thus enabling the former to act as a reducing agent and transfer an electron toward a second molecule of cation **28**. The complex **29** is analogous to *radical anions* that can be generated from metal carbonyls by reduction with Na/Ph_2CO, or electrochemically, and exhibit a significant stability—in air, up to several hours—and increased reactivity in ligand displacement reactions.[23] Conceptually, it is reminiscent of the $(18+\delta)$ complexes[24] with an electron density higher than that of traditional 18-electron complexes and known to act as strong reducing agents.[24c] The oxidized complex **30** might undergo decomposition, releasing bis-cationic species **31** and THF molecules, the process mimicked by a high recovery of cobalt-anchored THP derivative **21** (Scheme 9). Among the alternative modes of the intermolecular SET—*cluster-to-cluster* and *cluster-to-ligand* —the former is most consistent with the experimental data. The formation of anion-radical **32** accounts for an extensive ligand replacement (**33**, $n = 1$) observed in the presence of “heavy” carbon monoxide (Scheme 10). This observation is fully consistent with ample literature evidence that reduced transition metal complexes are susceptible to ligand displacement by a dissociative mechanism.[2,23] The conversion of anion-radicals **32** to key radicals **34** might occur through an intramolecular cluster-to-ligand reduction reminiscent of the spontaneous, albeit slow, dimerization of the related species yielding dimer **35**.[4g] *Thus we conclude that THF acts as a catalyst that accelerates the process by forming the electronically enriched, and structurally altered, transient species **29** and then breaking away, upon reaction completion, from the organometallic scaffold, in a chemically unchanged form.*

Conclusion

The proposed mechanism, by its very nature, is unorthodox for transition metal π-complexes: the THF molecule accelerates cluster-to-cluster electron transfer by structurally and electronically modifying a π-bonded ligand and converting cobalt-complexed propargyl cations into a source of electrons. Although used in a 2-fold excess, THF acts *as a catalyst*, altering the requisite $Co_2(CO)_6$-complexed cations and breaking away from the organometallic scaffold in a chemically unchanged form.

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(24) (a) Tyler, D. R. *Acc. Chem. Res.* **1991**, *24*, 325. (b) Meyer, R.; Schut, D. M.; Keana, K. J.; Tyler, D. R. *Inorg. Chim. Acta* **1995**, *240*, 405. (c) Zavarine, I. S.; Kubiak, C. P. *Coord. Chem. Rev.* **1998**, *171*, 419.

Phenomenologically, the new reaction represents a disproportionation between cobalt-complexed propargyl cations with THF—known in organic chemistry as a Lewis donor and donor of H atoms and hydride ions—acting in an unusual capacity of a *radical mediator* (Scheme 12). The novel process that provides a facile access to *d*,*l*-3,4-diphenyl-1,5-hexadiyne can be expanded toward stereo-, chemo-, and regioselective synthesis of *d*,*l*-3,4-diaryl-1,5-alkadiynes otherwise hardly accessible. While we rationalized most of the observed phenomenon, further studies are needed to isolate and structurally characterize a key intermediate, **29**, and to gain full insight into factors controlling the stereoselectivity of the reaction.

Experimental Section

General Information. 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 including ^{13}CO were purchased from Aldrich and used as received. $Co_2(CO)_8$ was received from Strem. NMR solvents and THF-d_8 were supplied by Cambridge Isotope Laboratories. ^1H and ^{13}C NMR spectra were recorded on Bruker DRX-400 (^1H, 400 MHz) and Bruker ACF-200 (^1H, 200 MHz). 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 Desert Analytics (Tucson, AZ). Melting temperatures (uncorrected) were measured on a Mel-Temp II (Laboratory Devices) apparatus. Silica gel S733-1 (200−425 mesh; Fisher) was used for flash column chromatography. Analytical and preparative TLC analyses were conducted on silica gel 60 F_{254} (EM Science; aluminum sheets) and silica gel 60 PF_{254} (EM Science; w/gypsum), respectively. Mass spectra were run at the Regional Center on Mass Spectroscopy, UC Riverside, Riverside, CA (FAB, ZAB-SE; CI-NH_3, 7070EHF; Micromass). GC-MS analysis was conducted on a Hewlett-Packard G1800 GCD (SE-52, 30 m × 0.25 mm).

***d*,*l*- and *meso*-μ-η^2-(3,4-Diphenyl-1,5-hexadiyne)bisdicobalthexacarbonyl (4). Development of Quenching Protocol for Cation 3.** Under nitrogen atmosphere, alcohol **2** (105 mg, 0.25 mmol) was transferred to a flame-dried flask and dissolved in diethyl ether (20 mL). The solution was cooled to −20 °C, and $HBF_4{\cdot}Et_2O$ (162 mg, 1 mmol) was added dropwise. After stirring for 1 h, the ethereal layer was removed, and the cation **3** was washed with diethyl ether (3 × 15 mL) at −20 °C. Residual ether was stripped under reduced pressure (−5 °C) to afford the cation **2** as a dark red solid. Methylene chloride (2.5 mL) was added, and the reaction mixture was warmed to 20 °C. After 35 min, the alternative quenching procedures were applied. *Protocol #1 (sampling):* an aliquot (0.1 mL) was dispersed in MeOH (2 mL, 20 °C). The sample was diluted with H_2O (2 mL) and then extracted with ether (2 mL). The solvent was evaporated under vacuum, and the crude mixture was analyzed by ^1H NMR to determine the ratio of dimer **4** and Me-ether **11**. *Protocol #2 (sampling):* an aliquot (0.1 mL) was dispersed in MeOH (2 mL, −20 °C) and worked up analogously. *Protocol #3 (in-flask quenching):* the reaction mixture was cooled to −20 °C and quenched with precooled MeOH (2 mL, −20 °C). After stirring for 15 min, the reaction mixture was warmed to 20 °C, diluted with H_2O (5 mL), and extracted with ether (6 mL). The solvent was evaporated under vacuum, and the crude mixture was analyzed by ^1H NMR to determine the ratio of dimer **4** and Me-ether **11**. *Protocol #4 (in-flask quenching):* the reaction mixture was cooled to −78 °C, quenched with precooled MeOH (2 mL, −78 °C), and worked up analogously. On the basis of ^1H NMR data, protocols #1 (sampling) and #3 (in-flask quenching) were chosen and used throughout the mechanistic study. The ratios of dimer **4**:Me-ether **11** were equal to 11:89 and 10:90, respectively. The conversion observed in these experiments reflects the extent of spontaneous generation of requisite radicals within 35 min.[4g] Multiple runs showed variation of quantitative data by only 2%.

d,*l*-**4**: TLC (PE): R_f 0.26. Mp: 132−133 °C (partial dec; sealed capillary; coevaporation with benzene, 3 × 1 mL). ^1H NMR ($CDCl_3$): δ 4.33 (s, 2H, CH), 6.33 (s, 2H, HC≡), 7.10−7.30 (m, 10H, $2C_6H_5$). MS-FAB: m/z 774 ($M^+ - CO$), 718 ($M^+ - 2CO$), 690 ($M^+ - 3CO$), 662 ($M^+ - 4CO$), 634 ($M^+ - 5CO$), 606 ($M^+ - 6CO$), 578 ($M^+ - 7CO$), 550 ($M^+ - 8CO$), 522 ($M^+ - 9CO$), 494 ($M^+ - 10CO$), 466 ($M^+ - 12CO$). *meso*-**4**: TLC (PE): R_f 0.42. T_{dec}: 140−155 °C (sealed capillary; coevaporation with benzene, 3 × 1 mL). ^1H NMR ($CDCl_3$): δ 4.38 (s, 2H, CH), 4.96 (s, 2H, HC≡), 7.10−7.30 (m, 10H, $2C_6H_5$). MS-FAB: same as that of *d*,*l*-isomer **4**. Anal. Calcd for $C_{30}H_{14}O_{12}Co_4$ (*d*,*l*-**4** + *meso*-**4**): C, 44.89; H, 1.75. Found: C, 45.08; H, 2.00. Me-ether **11**: TLC (PE): $R_f = 0.11$. ^1H NMR ($CDCl_3$): δ 3.46 (s, 3H, OMe), 5.29 (d, 1H, CH, $J = 0.83$), 6.03 (d, 1H, HC≡, $J = 0.92$), 7.28−7.42 (m, 5H, C_6H_5). MS-FAB: m/z 432 (M^+, 3%), 348 ($M^+ - 3CO$, 100%).

Two-Step Dimerization Protocol. Under nitrogen atmosphere, alcohol **2** (105 mg, 0.25 mmol) was transferred to a flame-dried flask and dissolved in diethyl ether (20 mL). The solution was cooled to −20 °C, and $HBF_4{\cdot}Et_2O$ (162 mg, 1 mmol) was added dropwise. After stirring for 1 h, the ethereal layer was removed and the cation **3** was washed with diethyl ether (3 × 15 mL) at −20 °C. Residual ether was stripped under reduced pressure (−5 °C) to afford the cation **3** as a dark red solid. Methylene chloride (2.5 mL) and THF (36 mg, 0.5 mmol) were added, and the reaction mixture was warmed to 20 °C. Aliquots of the solution (0.1 mL) were withdrawn via syringe and quenched in 2 mL of methanol at the intervals 5, 15, 25 and 35 min. ^1H NMR analysis showed that reaction was over in 35 min (*d*,*l*-**4**, 4.33 and 6.43 ppm; *meso*-**4**, 4.96 ppm; Me-ether **11**, 5.29 ppm).

One-Step Dimerization Protocol. At 20 °C, under nitrogen atmosphere, alcohol **2** (105 mg, 0.25 mmol) was dissolved in methylene chloride (2.5 mL) and treated with THF (36 mg, 0.5 mmol) and $HBF_4{\cdot}Et_2O$ (81 mg, 0.5 mmol). Aliquots of the solution (0.1 mL) were withdrawn via syringe and quenched in 2 mL of methanol at the intervals 5, 15, 25, 35, 60, 90, 120, 150, and 180 min. ^1H NMR analysis showed that reaction was over in 3 h.

Tetrahydrothiophene as a Radical Mediator. Under nitrogen atmosphere, alcohol **2** (105 mg, 0.25 mmol) was transferred to a flame-dried flask and dissolved in diethyl ether (20 mL). The solution was cooled to −20 °C, and $HBF_4{\cdot}Et_2O$ (162 mg, 1 mmol) was added dropwise. After stirring for 1 h, the ethereal layer was removed and the cation **3** was washed with diethyl ether (3 × 15 mL) at −20 °C. Residual ether was stripped under reduced pressure (−5 °C) to afford the cation **3** as a dark red solid. Methylene chloride (2.5 mL) and tetrahydrothiophene (44 mg, 0.5 mmol) were added, and the reaction mixture was warmed to 20 °C. Aliquots of the solution (0.1 mL) were withdrawn via syringe and quenched in 2 mL of methanol at the intervals 5, 15, 25, 35, 60, and 90 min. The concentration curves reflecting the ratio of dimer **4** and Me-ether **11** were plotted (Figure 2) on the basis of ^1H NMR data.

2,5-Dimethyltetrahydrofuran as a Radical Mediator. Under nitrogen atmosphere, alcohol **2** (105 mg, 0.25 mmol) was placed in a flame-dried flask and dissolved in diethyl ether (20 mL). The solution was cooled (−20 °C) and treated with $HBF_4{\cdot}Me_2O$ (134 mg, 1.0 mmol). After stirring for 1 h, the ethereal layer was removed, and precipitate was washed with diethyl ether (3 × 15 mL) at −20 °C. Residual ether was stripped off under reduced pressure (−5 °C) to afford the cation **3** as a dark red solid. Methylene chloride (2.5 mL) was added at −20 °C followed by 2,5-dimethyltetrahydrofuran (50 mg, 0.5 mmol), and the reaction mixture was warmed to 20 °C. Upon stirring for 35 min, the reaction mixture was cooled to −20 °C, quenched with precooled MeOH (2 mL, −20 °C), and stirred for an additional 15 min at −20 °C. The reaction mixture was then brought to ambient temperature and diluted with H_2O (5 mL) and ether (10 mL). The organic layer was separated, an aqueous layer was extracted with ether (2 × 5 mL), and the combined organic extracts were dried (Na_2SO_4). Solvents were evaporated under reduced pressure, and the residue was fractionated by preparative TLC (silica gel, PE:E, 20:1) to yield a mixture of dimer **4** (*d*,*l* + *meso*):Me-ether **11**:hydrocarbon **6** (77 mg) in the ratio of 38:23:39, by ^{1}H NMR. The ratio of *d*,*l*-**4**:*meso*-**4** was equal to 94:6, de 88%. The ratio dimer **4**:Me-ether **11** was determined to be 62:38 (*d*,*l*-**4**, 4.33 and 6.43 ppm; *meso*-**4**, 4.96 ppm; Me-ether **11**, 5.29 ppm; hydrocarbon **6** 6.09 ppm).

2,2,5,5-Tetramethyltetrahydrofuran as a Radical Mediator. Under analogous conditions, with 2,2,5,5-tetramethyltetrahydrofuran (64 mg, 0.5 mmol) acting as a radical mediator, the dimer **4**:Me-ether **11** ratio was equal to 11:89. This ratio indicates that the steric hindrance in 2,2,5,5-tetramethyltetrahydrofuran precludes its coordination with the cationic center in cation **3** and the conversion observed should be completely attributed to the spontaneous process.[4g]

Determination of the Kinetic Isotope Effect: Noncompetitive Technique. (a) THF-d_0. Under nitrogen atmosphere, alcohol **2** (105 mg, 0.25 mmol) was placed in a flame-dried flask and dissolved in dry diethyl ether (20 mL). The solution was cooled (−20 °C) and treated with $HBF_4\cdot Et_2O$ (162 mg, 1 mmol). After stirring for 1 h, the ethereal layer was removed, and the cation **3** was washed with dry ether (3 × 20 mL) at −20 °C. Residual ether was removed under reduced pressure at −5 °C to afford the cation **3** as a dark red solid. Methylene chloride (2.5 mL) was added at −5 °C, and the temperature was raised to 20 °C. THF-d_0 was then added (36 mg, 0.5 mmol) in one portion. At exactly 1 min after the addition of THF, methanol (505 μL) was added and the solution was stirred for 10 min. The reaction mixture was then poured into a separatory funnel containing distilled Et_2O (7 mL) and deionized water (25 mL). The aqueous layer was drained off, and the organic layer was washed (3 × 25 mL) with deionized water. The organic layer was evaporated under reduced pressure and prepared for NMR analysis by dissolving the crude product in $CDCl_3$ and filtering it through a short bed of Celite (500 mg). NMR analysis showed the ratio of dimer **4**:Me-ether **11** to be 18:82.

(b) THF-d_8. The above procedure was repeated in all respects except that THF-d_8 (39 mg, 0.5 mmol) was used. NMR analysis of the crude mixture showed the ratio of dimer **4**:Me-ether **11** to be 18:82.

Determination of the Kinetic Isotope Effect: Competitive Technique. Under nitrogen atmosphere, alcohol **2** (105 mg, 0.25 mmol) was transferred to a flame-dried flask and dissolved in diethyl ether (20 mL). The solution was cooled to −20 °C, and $HBF_4\cdot Et_2O$ (162 mg, 1 mmol) was added dropwise. After stirring for 1 h, the ethereal layer was removed and the cation **3** was washed with diethyl ether (3 × 15 mL) at −20 °C. Residual ether was stripped under reduced pressure (−5 °C) to afford the cation **2** as a dark red solid. Methylene chloride (2.5 mL) was added at −5 °C, and the solution was warmed to 20 °C. THF-d_0 (18 mg, 20 μL, 0.25 mmol) and THF-d_8 (20 mg, 20 μL, 0.25 mmol) were simultaneously added, and the reaction mixture was quenched with MeOH (1 mL) after 1 min. The ratio of THF-d_0:THF-d_8 was equal to 1:1 according to GC-MS analysis [31 °C, 0.5 mL/min, T_{inj} 100 °C, t_R (THF-d_8) 3.37 min; t_R (THF-d_8) 3.43 min].

Synthesis of (4-Ethynyltetrahydropyran)dicobalthexacarbonyl (21). (4-Ethynyl-4-hydroxytetrahydropyran)dicobalthexacarbonyl (18). Under an atmosphere of nitrogen, a solution of tetrahydro-4*H*-pyran-4-one (**17**, 1.00 g, 10 mmol) in dry THF (8 mL) was added dropwise (8 min) to a suspension of sodium acetylide (0.72 g, 15 mmol) in dry THF (32 mL) at −20 °C. The reaction mixture was stirred overnight at 20 °C, diluted with saturated aqueous ammonium chloride (40 mL) at 0 °C, and extracted with ether (3 × 25 mL), and the combined ethereal extracts were dried over Na_2SO_4. Upon filtration under an atmosphere of nitrogen, a solution of crude alcohol was added dropwise (60 min) to a solution of $Co_2(CO)_8$ (1.26 g, 10 mmol) in degassed ether (50 mL) at 20 °C. Upon stirring overnight (TLC control), the reaction mixture was concentrated and chromatographed on Florisil (200 g, PE:E, 2:1) to yield **18** (3.16 g, 76.7%) as brick-red crystals. Mp: 62−63 °C (sealed capillary; coevaporation with benzene, 3 × 1 mL). TLC (PE:E, 1:1): R_f 0.28. ^{1}H NMR ($CDCl_3$): δ 1.70−2.03 (4H, m, $2CH_2$), 3.82 (4H, m, $2CH_2O$), 6.07 (1H, s, HC≡). Anal. Calcd for $C_{13}H_{10}O_8Co_2$: C, 37.86; H, 2.43. Found: C, 37.67; H, 2.36.

(4-Ethynyl-5,6-dihydro-2*H*-pyran)dicobalthexacarbonyl (20). Under an atmosphere of nitrogen, a solution of tetrahydro-4*H*-pyran-4-one (**17**, 1.00 g, 10 mmol) in THF (7 mL) was added dropwise (15 min) to a suspension of sodium acetylide (0.72 g, 15 mmol) in THF (33 mL) at −20 °C. The reaction mixture was stirred overnight at 20 °C, refluxed for 1 h, diluted with saturated aqueous ammonium chloride (40 mL) at 0 °C, and extracted with ether (3 × 20 mL), and the combined ethereal extracts were dried over Na_2SO_4. The solution, under an atmosphere of nitrogen, was added dropwise (60 min) to a solution of $Co_2(CO)_8$ (3.76 g, 11 mmol) in degassed ether (100 mL) at 20 °C. Upon stirring overnight (TLC control), the reaction mixture was centrifuged and the crude cobalt complex **18** was treated with $HBF_4\cdot Me_2O$ (6.70 g, 50 mmol) at −20 °C, under an atmosphere of nitrogen. Upon stirring overnight at ambient temperature, the reaction mixture was cannulated, washed with water (15 × 25 mL), and dried ($MgSO_4$). The solvents were stripped off under reduced pressure, and the residue was chromatographed on a silica gel column (100 g, PE:E, 10:1) to afford **20** (1.24 g, 31.5%) as brick-red crystals. Mp: 46−47 °C (sealed capillary; coevaporation with benzene, 3 × 1 mL). TLC (PE:E, 1:1): R_f 0.61. ^{1}H NMR ($CDCl_3$): δ 2.40 (2H, m, CH_2), 3.89 (2H, t, CH_2, $J = 5.4$), 4.22 (2H, q, CH_2, $J = 2.7$), 6.15 (1H, m, HC=), 6.21 (1H, s, HC≡). Anal. Calcd for $C_{13}H_8O_7Co_2$: C, 39.59; H, 2.03. Found: C, 39.39; H, 2.16.

(4-Ethynyltetrahydropyran)dicobalthexacarbonyl (21). At 0 °C, under N_2 atmosphere, a solution of complex **18** (309 mg, 0.75 mmol) in dry CH_2Cl_2 (7.5 mL) was treated with $BH_3\cdot Me_2S$ in toluene (120 mg, 1.575 mmol). The reaction mixture was stirred for 3 min, then CF_3COOH (750μL) was added and stirring was continued for an additional 30 min (TLC control). The organic layer was washed with cold H_2O (3 × 8 mL), separated, and dried over Na_2SO_4. Upon removal of solvent, the crude mixture was fractionated by preparative TLC (3 plates, PE:E, 2:1) to afford **21** (220 mg, 74.1%) as a dark red oil. TLC (PE:E, 1:1): R_f 0.59. ^{1}H NMR ($CDCl_3$): δ 1.54−1.75 (2H, m, CH_2), 1.84−1.92 (2H, m, CH_2), 2.89 (1H, ttd, 1H, $J = 11.4$, $J = 4.0$, $J = 1.0$), 3.51 (2H, td, CH_2, $J = 12.0$, $J = 2.2$), 4.05 (2H, dd split, CH_2, $J = 11.4$, $J = 4.3$), 6.06 (1H, d, HC≡). Anal. Calcd for $C_{13}H_{10}O_7Co_2$: C, 39.40; H, 2.53. Found: C, 37.39; H, 2.37.

***d*,*l*- and *meso*-μ-η^2-(3,4-Diphenyl-1,5-hexadiyne)bisdicobalthexacarbonyl (4). (4-Ethynyltetrahydropyran)dicobalthexacarbonyl (21) as a Radical Mediator.** Under an atmosphere of nitrogen, alcohol **2** (105 mg, 0.25 mmol) was placed in a flame-dried flask and dissolved in diethyl ether (20 mL). The solution was cooled (−20 °C) and treated with $HBF_4\cdot Me_2O$ (134 mg, 1.00 mmol). After stirring for 1 h at −20 °C, an ethereal layer was removed, and the cation **3** was washed with diethyl ether (3 × 15 mL) at −20 °C. The residual amount of ether was stripped under reduced pressure (−5 °C), the cation **3** was dissolved in dry methylene chloride (2.5 mL), and a solution of complex **21** (99 mg, 0.25 mmol) in dry CH_2Cl_2 (2.5 mL) was added at −20 °C. The reaction mixture was warmed and stirred at 20 °C overnight (19 h), the solvent was removed under reduced pressure, and the crude mixture was fractionated on a preparative TLC plate. Obtained were *d*,*l*-**4** and *meso*-**4** (45 mg, 90.0%; de 86%) and complex **21** (85 mg, 85.9% recovery).

Isotopically Enriched *d*,*l*- and *meso*-μ-η^2-(3,4-Diphenyl-1,5-hexadiyne)bisdicobalthexacarbonyl (23). ^{13}CO Incorporation Experiments. Under an atmosphere of nitrogen, alcohol **2** (105 mg, 0.25 mmol) was placed in a flame-dried flask and dissolved in diethyl ether (20 mL). The solution was cooled (−20 °C) and treated with $HBF_4 \cdot Me_2O$ (134 mg, 1.00 mmol). After stirring for 1 h at −20 °C, an ethereal layer was removed, and cation **3** was washed with diethyl ether (3 × 15 mL) at −20 °C. Residual ether was stripped under reduced pressure (−5 °C), a ^{13}CO atmosphere was introduced to the reaction mixture, and the cation **3** was dissolved in CH_2Cl_2 (2.5 mL). Upon addition of THF (36 mg, 0.50 mmol), the reaction temperature was raised to 20 °C (35 min). Dimer **23** was isolated by preparative TLC (PE:E, 15:1) and analyzed by ^{13}C NMR (Figures A, B; Supporting Information) and MS-FAB (Figure C; Supporting Information) spectroscopy.

d,*l*-**23**: ^{13}C NMR ($CDCl_3$): δ 54.4, 77.0, 101.7, 127.0, 128.1, 128.7, 143.2, 198.7, 200.0 (high intensity). *d*,*l*-**4**: ^{13}C NMR ($CDCl_3$): δ 54.4, 77.1, 101.7, 127.0, 128.1, 128.7, 143.2, 198.7, 200.0 (low intensity). The gross incorporation of ^{13}CO ligand into the cobalt cluster was evident from an unusually extensive carbonyl signal (198.7, 200.0 ppm) in the ^{13}C NMR spectrum (Figure B; Supporting Information).

The MS-FAB spectrum of dimer **23** contained $M^+ - 3CO$ signals of higher molecular weights, from 718 to 725 (Figure C; Supporting Information). Analysis of line intensities revealed an introduction of, at least, four ^{13}CO ligands into the metal cluster (*m*/*z* 719, 720, 721, 722; *m*/*z* $M^+ - CO$ 718). The actual level of incorporation might be even higher since CO ligands most susceptible to substitution might be those initially released in the fragmentation of the molecular ion under MS conditions.

Without THF, the isotope exchange can hardly be detected since it depends on the rate of the spontaneous reaction,[4g] a process shown to be much slower than the THF-catalyzed reaction (total conversion: 9 h vs 35 min; only 11% conversion in 35 min).

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Supporting Information Available: ^{13}C NMR spectra of unlabeled and ^{13}CO-labeled *d*,*l*-3,4-diphenyl-1,5-hexadiyne (**4**, Figure A; **23**, Figure B); MS-FAB spectra of ^{13}CO-labeled and unlabeled *d*,*l*-3,4-diphenyl-1,5-hexadiyne (**23** (a), **4** (b), Figure C). Calculated total electronic energies (in hartrees) for propargyl cation **14** derived 1:1 oxonium complex **15** [HF/3-21G*; HF/6-31G*] and 1:2 oxonium complex **16** [HF/3-21G*; HF/6-31G*] (Table 1, Figure D). This material is available free of charge via the Internet at http://pubs.acs.org.

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