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Stoichiometric and Catalytic (η^5-Cyclopentadienyl)cobalt-Mediated Cycloisomerizations of Ene-Yne-Ene Type Allyl Propargyl Ethers

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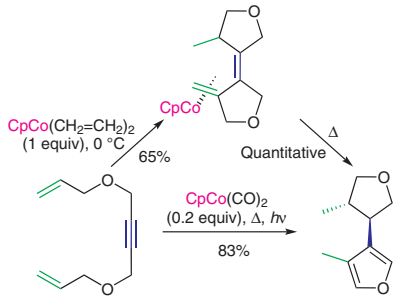

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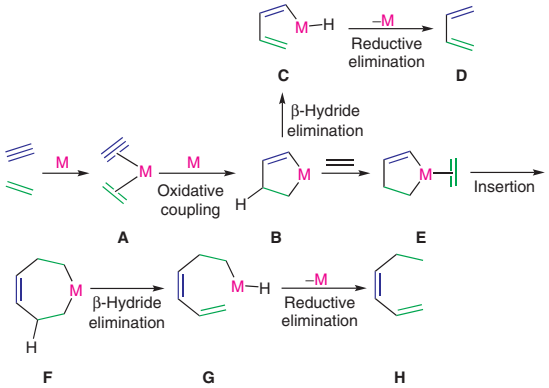
Abstract The complexes $CpCoL_2$ (Cp = C_5H_5; L = CO or CH_2=CH_2) mediate the cycloisomerizations of α,δ,ω-enynenes containing allylic ether linkages to 3-(oxacyclopentyl or cycloalkyl)furans via the intermediacy of isolable CpCo-η^4-dienes. A suggested mechanism comprises initial complexation of the triple bond and one of the double bonds, then oxidative coupling to a cobalt-2-cyclopentene, terminal double bond insertion to assemble a cobalta-4-cycloheptene, β-hydride elimination, and reductive elimination to furnish a CpCo-η^4-diene. When possible, the cascade continues through cobalt-mediated hydride shifts and dissociation of the aromatic furan ring. The outcome of a deuterium labeling experiment supports this hypothesis. The reaction exhibits variable stereoselectivity with a preference for the *trans*-product (or, when arrested, its *syn*-Me CpCo-η^4-diene precursor), but is completely regioselective in cases in which the two alkyne substituents are differentiated electronically by the presence or absence of an embedded oxygen. Regioselectivity is also attained by steric discrimination or blocking one of the two possible β-hydride elimination pathways. When furan formation is obviated by such regiocontrol, the sequence terminates in a stable CpCo-η^4-diene complex. The conversion of the cyclohexane-fused substrate methylidene-2-[5-(2-propenyloxy)-3-pentynyl]cyclohexane into mainly 1-[(1*R**,3a*S**,7a*S**)-7a-methyloctahydroinden-1-yl]-1-ethanone demonstrates the potential utility of the method in complex synthesis.

Key words enynes, β-hydride elimination, cobalt, cycloisomerization, furans

Transition-metal-catalyzed hydroalkenylative coupling reactions of alkenes with alkynes, particularly their intramolecular variants ('enyne cycloisomerizations') constitute powerful additions to the arsenal of the synthetic chemist.[1] Depending on substrates, the choice of the metal, and conditions, various products may arise, including conjugated and skipped dienes or their reduced analogues, as well as cyclobutane and cyclopropane derivatives. Among the mechanisms proposed for these conversions, particularly prevalent (and relevant within the context of this report) is the oxidative coupling pathway that engenders conjugated dienes, as depicted in its simplest form in Scheme 1. Here, the metal first enables the reorganization of the two types of ligands in **A** to generate **B**, which, in the majority of cases, undergoes rapid β-hydride elimination to **C**, followed by reductive elimination to liberate butadiene **D**. Much rarer is the interception of **B** by another alkene component, as in **E**, followed by insertion to metalla-4-cycloheptene **F**, its β-hydride elimination to **G**, and final reductive elimination from **G** to give hexadiene **H**. The paucity of this pathway can be traced to the intervention of competing trajectories, dominant among which are the alternative to intermolecular **B** → **E**, namely intramolecular **B** → **C**,[1] or reductive elimination from **F** to create the [2+2+2] cycloaddition products.[2] In order to minimize the former and enhance the likelihood of the incorporation of the second alkene unit, a number of studies have employed all-intramolecular options with mixed results (Scheme 2).



Scheme 1 Generic oxidative coupling mechanism of the hydroalkenylation of alkynes to give 1,3-butadienes and 1,3-hexadienes

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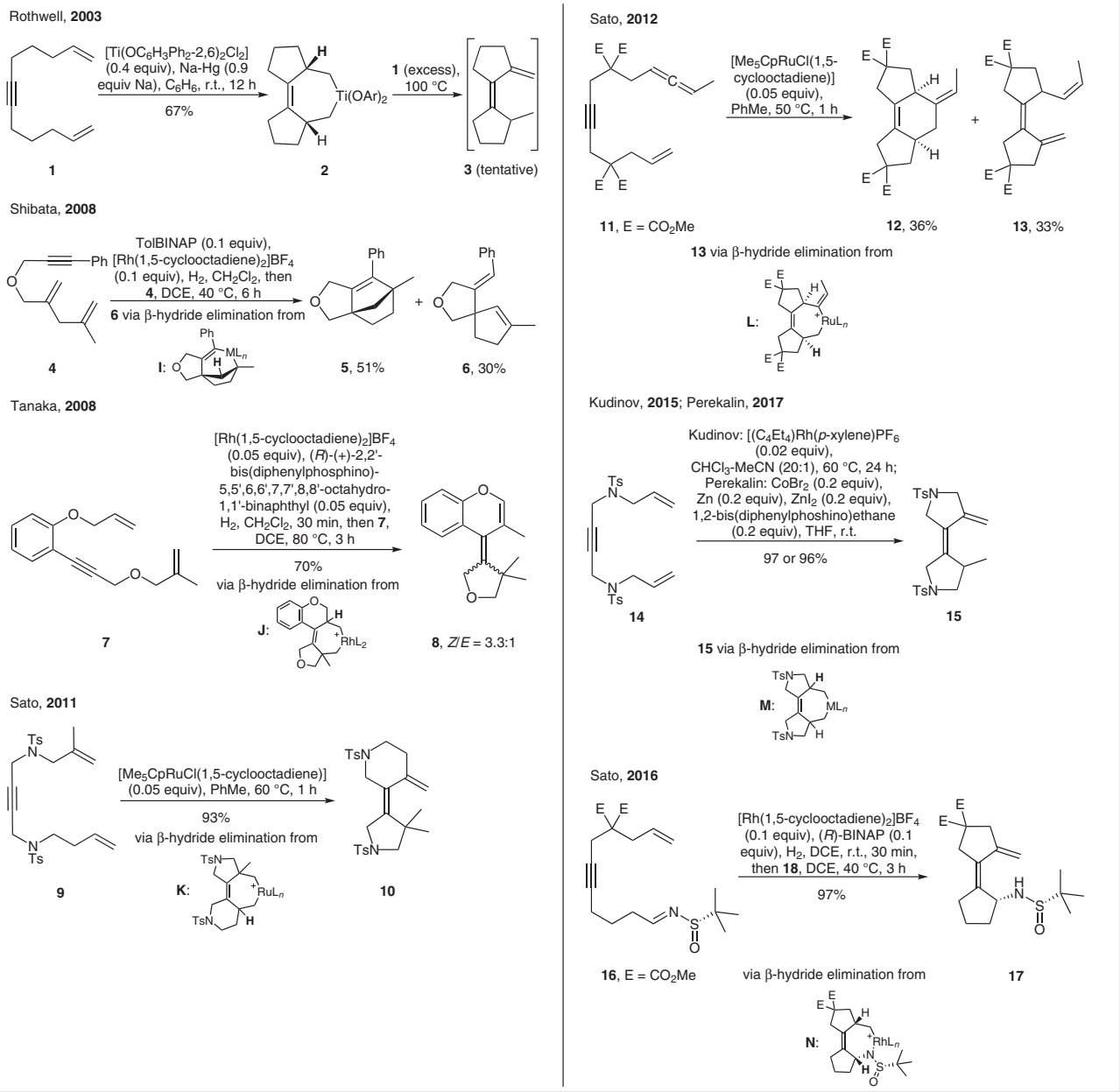
Thus, titanacycloheptane **2**, made from **1**, converted **1** catalytically into a mixture of hydrocarbons, in which **3** was believed to be the major component, although no spectral data were given.[3] A series of investigations aimed primarily at effecting [2+2+2] cycloadditions of enynenes and dienynes to assemble the corresponding cyclohexenes describe the occasional generation of cycloisomerization products according to Scheme 1 (in addition to other structures formed by competing mechanisms),[1e] their relative preponderance depending on substrates and reaction conditions. For example, a cationic Rh catalyst rearranged **4** to **5** and **6** via presumed intermediate **I**, the route to **6** obviated by changing the tether between the double bonds or the triple bond substituent.[4] The postulate of **I** is unusual, in as much as it features insertion of the second double bond into the usually less favored alkylmetal side of the initial metallacyclopentene. In a report of thirteen examples of the [2+2+2] cycloaddition of enynenes bearing oxa- and azatethers mediated by cationic Rh, **7** was unique in its transformation into the diene stereoisomers (*E*)- and (*Z*)-**8**, presumably emerging via β-hydride elimination from **J**.[5] Similarly, [Me_5CpRuCl(1,5-cyclooctadiene)] accomplished



Scheme 2 Pertinent intramolecular cycloisomerizations of enynenes and dienynes, including imine analogue **16**, to furnish various 1,2- or 1,4-dienes according to the general mechanism in Scheme 1

mostly [2+2+2] cyclizations of enynenes, with minor exceptions, one of which is depicted in Scheme 2, namely the almost quantitative evolution of **10** from **9** via metallacycle **K**.[1m,6] The same catalyst effects analogous reorganizations for thirteen enynallenes, and only in the case of **11** was the cycloisomerization endpoint **13** isolated, in addition to equal quantities of the cycloaddition framework **12**.[7] Perhaps not unexpectedly, in light of the observations made with **9**, **14** converted exclusively into **15** in the presence of a cationic cyclobutadiene Rh complex.[8] Remarkable, however, is the dependence of the product selectivity from **14** (and the corresponding ether analogues) using Co (in the form of a mixture of $CoBr_2$, Zn, and ZnI_2) on the nature of added phosphine ligands. Hence, as shown, 1,2-bis(diphenylphoshino)ethane led only to **15**, whereas Ph_3P created exclusively the [2+2+2] cycloadducts.[9] The latter were completely avoided in the cationic Rh-enabled cycloisomerization of seven imines of the type **16**, giving only products of the type **17**.[10]

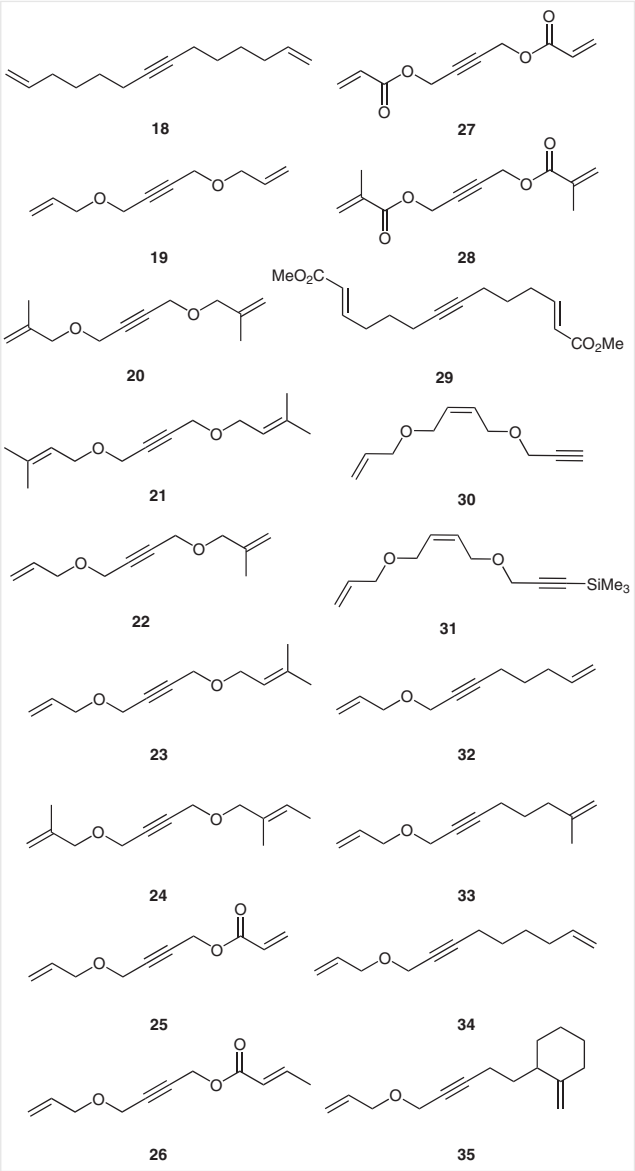


Figure 1 Starting materials used in this study

As the preceding summary illustrates, there is poor control over the outcome of the intramolecular transition-metal-catalyzed stitching of two double bonds with a C≡C bond. In this paper, we expand the range of current knowledge by adding $CpCoL_2$ (Cp = C_5H_5; L = CO or CH_2=CH_2) to the number of catalysts that can be employed, leading to complementary insights.[11]

The requisite starting materials, shown in Figure 1, were either known (**19**,[12] **20**,[12] **22**,[13] **27**,[12] **28**,[14] and **30**[15]) or made by established strategies [see experimental section and Supporting Information (SI)].

Our experiments commenced with enynene **18**, the bishomologue of **1**. Exposure to $CpCo(CO)_2$ (0.3 equiv) in boiling *m*-xylene under irradiation for six hours led to the complete disappearance of starting material and formation of a complex mixture of products (see experimental section). Varying the reaction conditions [$CpCo(CO)_2$ (1 equiv), boiling decalin; $CpCo(CH_2$=$CH_2)_2$, with and without irradiation from –50 to 80 °C; $CpCo(CH_2$=$CH_2)_2$, PPh_3 (1 equiv) with and without irradiation from 0 to 50 °C; $CpCo(PPh_3)_2$,[16] 60 °C] and following the progress of the disappearance of **18** by GC, MS, TLC, and NMR suggested the occurrence of double bond isomerization,[1a,b,11,17] dimerization, trimerization, and alkyne cleavage to a biscarbyne[18] (see experimental section). While the presence of the desired bishomologue of **3** in the mixture could not be ruled out, this possibility was not investigated further. Rather, and exploiting the long-known accelerating effect of allylic and propargylic heteroatoms in transition-metal-catalyzed cyclizations (which also appear to be of benefit in the relevant examples of Scheme 2),[19] we turned to **19** as the next substrate.

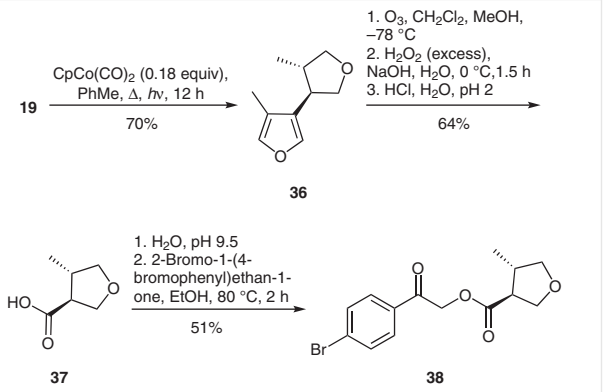
Gratifyingly, exposure of **19** to catalytic $CpCo(CO)_2$ in boiling and irradiated PhMe effected clean isomerization to furan **36** in the form of only one isolated stereoisomer (Scheme 3). However, the presence of another isomer in the crude reaction mixture was suggested by low intensity (2.5%) ^{1}H NMR signals at δ = 1.90 (s) and 0.75 (d, *J* = 6.7 Hz).

A control experiment verified the necessity of the catalyst in this process, as **19** is untouched under these conditions without it. The gross structural features of **36** were corroborated by its NMR data. Thus, the ^{1}H NMR spectrum revealed two singlets in the aromatic region [δ = 7.18 (1 H), 7.14 (1 H)], as well as two methyl resonances, one a singlet at δ = 1.96, the other a doublet at δ = 1.05 (*J* = 6.6 Hz). Absorptions attributable to the four protons on the oxygen-bearing carbons appeared as ABM spin systems between δ = 4.5 and 3.5, and the remaining tetrahydrofuran peaks showed up in the alkyl region. The ^{13}C NMR spectrum exhibited the expected ten peaks, occurring in three groups,

assignable to the furan (δ = 140.0, 138.6, 124.7, 119.8), tetrahydrofuran (δ = 75.1, 73.7, 43.0, 40.3), and methyl carbons (δ = 16.0, 8.48), respectively.

Unfortunately, the proton couplings were undiagnostic for the assignment of the stereochemistry in **36**,[20] and an NOE experiment proved inconclusive for this purpose. Consequently, and also because of the profound reorganization occurring during the genesis of **36**, X-ray structural support for the formulated structure was sought. Since the substance was an oil, a sequence was devised that transformed it into a crystalline derivative without compromising the configuration around the stereocenters (Scheme 3). A mild protocol of choice presented itself in the initial ozonolysis-oxidation of the furan ring to the carboxylic acid, namely **37** (or its *cis*-isomer),[21] which, if not crystalline, could then be further altered to such a derivative. Confidence in the stereoretentive nature of this oxidation was derived from the finding that the two stereoisomers of 2-methylcyclopentanecarboxylic acid do not epimerize in strong acid (3 N HCl).[22] Moreover, the half-life for epimerization of the corresponding methyl esters with strong base at 35 °C (NaOMe, MeOH) was estimated to be 8–29 hours, with a ratio of *trans*/*cis* = 9.4 at equilibrium.[23] In the event, ozonolysis and oxidative workup of **36** with careful control of the pH proceeded uneventfully (Scheme 3). Acid **37** emerged as an oil that could not be crystallized and was therefore reacted with 2-bromo-1-(4-bromophenyl)ethan-1-one, again under pH control,[24] to afford **38**. Crystallization from hot hexane supplied material suitable for X-ray analysis (Figure 2).[25] The stereochemistry is unequivocally *trans* in **38** and thus, by inference, in **36**.

A mechanism for the catalytic reorganization of **19** to **36**, patterned after the general outline of Scheme 1, is depicted in Scheme 4. It features initial complexation of the triple bond and one of the double bonds, as in **O**, then oxidative coupling to the cobalt-2-cyclopentene **P**, terminal



Scheme 3 Cycloisomerization of **19** to **36** and derivatization to crystalline **38**

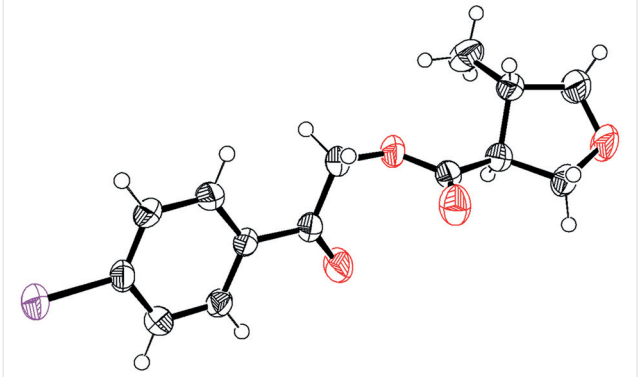
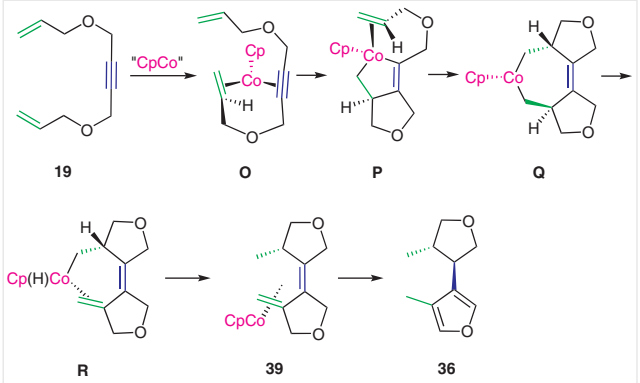


Figure 2 Structure of **38** in the crystal

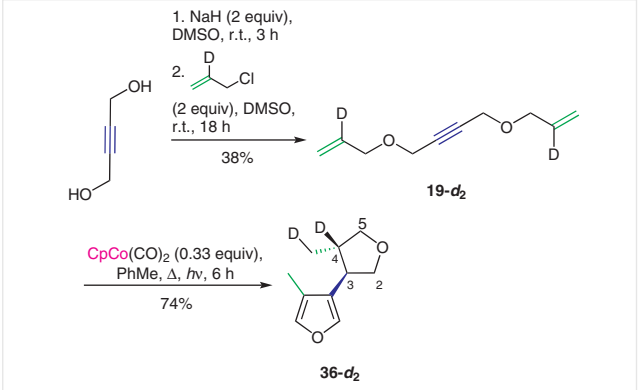
double bond insertion to assemble **Q**, β-hydride elimination to **R**, and reductive elimination to diene complex **39**. Finally, cobalt-mediated *syn*-hydride shifts[1a,b,11,17] and departure of the metal from the aromatized ring[26] finishes the sequence. As the color in Scheme 4 indicates, the process involves an extensive redistribution of hybridization states. While the stereochemistry of **O** (with the complexed alkenyl hydrogen positioned *syn* to the Cp) and of **P** (with the complexed alkenyl hydrogen positioned *anti* to the Cp and the tertiary hydrogen) are written such as to lead to that observed in **36**, there are complementary alternatives that accomplish the same. Thus, most steps are likely reversible,[1,27] the mechanism is expected to involve rapidly inverting triplet 16-electron CpCo intermediates ('dual state mechanism'),[27h,l] and the complexed diene unit in **39** may be subject to double inversion by an envelope flip,[28] adding a plethora of additional mechanistic options. Therefore, in the absence of a computational treatment, Scheme 4 is meant to be only suggestive. Finally, while the pronounced stereoselectivity towards **36** invites mechanistic speculation about its origins, the validity of such an effort is negated by the much less selective outcomes of additional examples (vide infra).



Scheme 4 Mechanism of the cycloisomerization of **19** to **36**

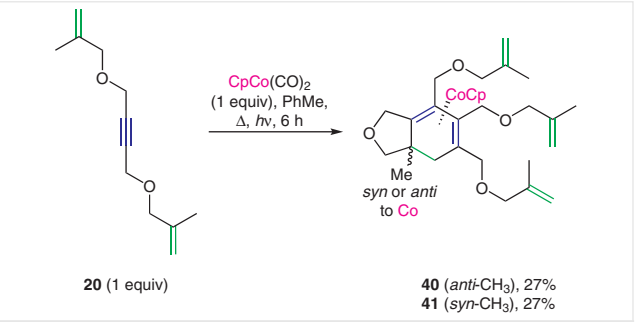
Notwithstanding the preceding disclaimers, two additional experiments supported aspects of Scheme 4. The first addressed the topological veracity of the β-hydride transfer process. For this purpose, **19-*d*$_2$** (97% label incorporation by ^{1}H NMR spectroscopy) was prepared from 3-chloro-1-propene-2-*d*[29] and 2-butyne-1,4-diol and subjected to the isomerization conditions (Scheme 5). The ^{1}H NMR spectrum of **19-*d*$_2$**, when compared to that of **19**[12] exhibited the expected (near) disappearance of the absorption at δ = 5.87 due to the internal alkenyl hydrogens and the corresponding simplification of the splitting patterns of their neighbors (for a comparison of the spectra, see SI). In consonance with Scheme 4, the resulting **36-*d*$_2$** (94% label incorporation by ^{1}H NMR spectroscopy) showed the presence of the label only in the 4-methyl and 4-position of the tetrahydrofuranyl substituent (for numbering, see Scheme 5), as indicated by the metamorphosis of the original methyl doublet into a broad singlet, the (near) disappearance of the multiplet at δ = 2.28 arising from H4, and the simplification of its three neighboring signals by removal of one coupling each.

The second experiment was aimed at arresting the progress of the isomerization at the stage of the diene complex **39** by exposing **19** to the reactive CpCo source CpCo(CH$_2$=CH$_2$)$_2$ at 0 °C, inspired by a related strategy in the [2+2+2] cycloaddition of α,δ,ω-enediynes.[17a] Gratifyingly, this treatment produced **39** in 70% yield. Its structure was strongly supported by the NMR spectra, in which the attached metal serves to cause characteristic structurally and stereochemically diagnostic shieldings.[17,30] Specifically, apart from the ^{1}H NMR signals for the eight methylene hydrogens next to oxygen between δ = 4.7 and 3.3, the two terminal complexed diene protons appeared at δ = 1.86 (outer or *E*-position) and 0.28 (inner or *Z*-position). The location of the methyl group as *syn* to CpCo was divulged by its relatively deshielded peak at δ = 1.10, while the neighboring tertiary *anti*-H exhibited a correspondingly relatively shielded multiplet at δ = 0.55. The ^{13}C NMR spectrum identified the complexed diene carbons at δ = 100.0 and 95.8 (internal), and at 59.8 and 23.2 (terminal), in addition to exhibiting lines for the remaining carbons with the expected chemical shifts. In further support of the proposed mechanism in Scheme 4, **39** converted cleanly into **36** at 80–100 °C in PhMe (^{1}H NMR).



Scheme 5 Fate of the deuterium label in the cycloisomerization of **19-*d*$_2$** to **36-*d*$_2$**

To investigate the scope of this cycloisomerization, several variations of the enynene substrates were scrutinized, including adding alkyl substituents to the double bonds, incorporating electron-withdrawing units, changing the relative positioning of the triple bond, and replacing one of the oxygens by carbon. First on the list was dimethylated **20**, in which the substituents obviate β-hydride elimination, therefore perhaps allowing the detection of competing pathways of reactivity. Indeed, under standard cyclization conditions and employing **20** and CpCo(CO)$_2$ in equimolar quantities, the air-sensitive diene complexes **40** and **41** were formed in a 1:1 ratio and 54% yield (Scheme 6). With CpCo(CH$_2$=CH$_2$)$_2$ at 0 °C and starting materials in the stoichiometric ratio of 2:1, the products emerged in 80% yield and a 1:3 ratio.



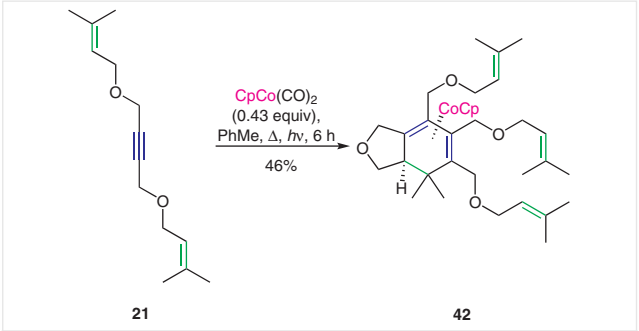
Scheme 6 [2+2+2] Cocycloaddition of **20** to furnish **40** and **41**

Their structural assignments rested on mass spectral and NMR data. Most diagnostic with respect to stereochemistry were the positions of the angular methyl hydrogen signals in the ^{1}H NMR spectra, characteristically shielded for **40** (δ = 0.79) relative to those of **41** (δ = 1.43). In addition, accidentally isochronous peaks were observed for the respective three terminal 2-propenyl hydrogens (δ = 4.87–4.97) and distinct AB quartets for one of the methylene fragments of the tetrahydrofuran ring (δ = 3.48 and 3.47, respectively), the others overlapping to give rise to multiplets. The corresponding pairs of doublets for the CH$_2$ moiety of the complexed cyclohexadiene ring occurred at δ = 1.89 and 1.21, and at 1.03 and 0.06, respectively. The ^{13}C NMR spectrum of only **41** was recorded and it exhibited all of the expected lines, several of which were assignable. For example, there were two sets of three singlets due to the terminal alkene carbons around 142 and 111 ppm, respectively; the complexed internal diene carbons resonated at δ = 90.7 and 85.5, close to the Cp signal at δ = 81.0; ten lines from δ = 75.8–66.0 included all carbons attached to oxygen and the

complexed terminal diene carbons; the peak at δ = 51.0 arose from the tertiary ring carbon, those at δ = 32.4 and 29.2 from the cyclohexadiene CH_2 and the methyl group, and a broad singlet at δ = 19.5 was assigned to the three accidentally isochronous alkenyl methyls.

A plausible mechanistic rationale for the emergence of **40** and **41** from **20** is via the interception of the dimethyl analogue of **P** in Scheme 4 (possibly in equilibrium with the dimethyl analogue of **Q**, both frustrated with respect to β-hydride elimination) by another molecule of **20**, thus entering the [2+2+2] cocycloaddition pathway to the product. Alternatively, and perhaps more likely, the increased steric encumbrance of the double bond (relative to **19**) may slow its participation in metallacycle of type **P** formation to favor initial oxidative coupling of the triple bonds of two molecules of **20** to the corresponding cobaltacyclopentadiene, followed by incorporation of the alkene moiety to give **40** and **41**.[31]

Next to be examined was **21**, in which the β-hydride elimination pathway was enabled and the terminal methyl groups served to test the tolerance of the cyclization to steric hindrance. From a practical standpoint, the latter would also simplify the NMR spectral analysis of eventual products. In the event, the fate of **21**, when confronted with $CpCo(CO)_2$, equaled that of **20**, except that only diastereomer **42** was generated (Scheme 7).

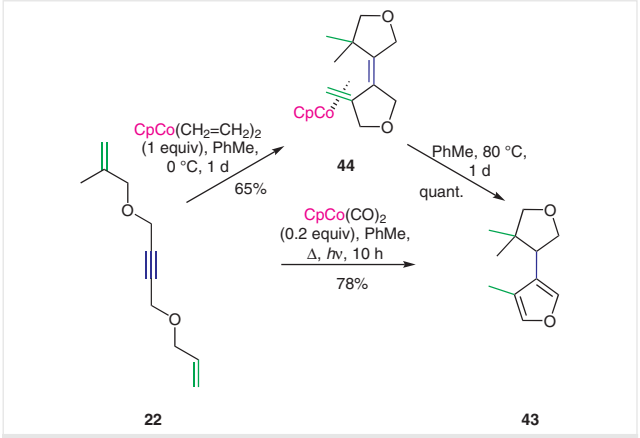


Scheme 7 [2+2+2] Cocycloaddition of **21** to furnish **42**

As hoped, the ^{1}H NMR spectrum of **42** was largely resolved to render first order patterns, facilitating the assignment of the stereochemistry of the tertiary hydrogen of the complexed cyclohexadiene ring as located *syn* to the metal [δ = 3.52 (dd, *J* = 7.1, 7.1 Hz)]. Its neighboring nuclei are clearly differentiated with respect to their relative position: δ = 1.10 (CH_3-*syn*), 0.57 (CH_3-*anti*); 2.68 (C*H*-*syn*), 2.24 (C*H*H-*anti*); remote tetrahydrofuran-CH_2: 3.82 (C*H*-*syn*), 3.25 (C*H*H-*anti*). The ^{13}C NMR spectrum gave rise to the complexed cyclohexadiene absorptions at δ = 90.1 and 87.4 (internal) and 66.5 and 65.4 (terminal; pinpointed by DEPT), the two remaining six-membered-ring carbons resonating at δ = 61.1 (tertiary) and 28.8 (quaternary), the two methyl carbons at δ = 31.6 (*syn* to CpCo) and 27.2 (*anti*), respectively.

Mechanistically, while it is tempting to assume that the steric bulk around the neopentylic hydrogen renders the endocyclic β-hydride elimination process from the tetramethyl species analogous to **P** and **Q** (Scheme 4) relatively noncompetitive,[1,27c,32] it is difficult to rationalize the absence of its exocyclic counterpart involving the hydrogens of one of the methyl groups, leading to the skipped diene topology (an option deliberately omitted from Scheme 1, because it was not recorded in the chemistry described in this paper). Moreover, such an endocyclic β-hydride elimination is observed for **23** (vide infra). We therefore prefer, as above for **40** and **41**, initial oxidative alkyne coupling as the pathway to **42**.

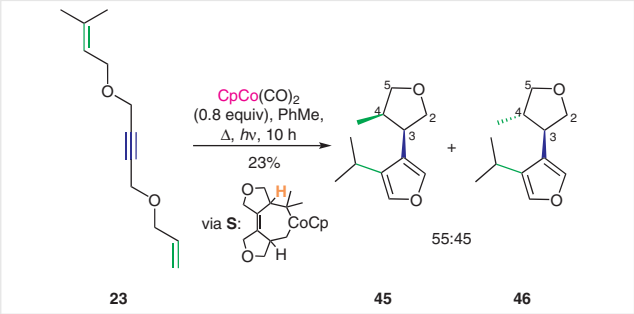
In view of the results with **20** and **21**, it was of interest to test **22** and **23**, in which the level of impedance to cycloisomerization had been attenuated such as to leave one of the termini of **19** intact. Indeed, as shown in Schemes 8 and 9, these substrates mimicked the behavior of **19**.



Scheme 8 Cycloisomerization of **22** to **43** directly and via **44**

The structures of compounds **43** and **44** were readily ascertained by the similarity of their NMR spectra to those of **36** and **39**, respectively, including the changes expected by the presence of the extra methyl group (see experimental section and SI). The furans isolated from the cyclization of **23** were inseparable. Nevertheless and fortunately, the ^{1}H NMR spectrum was completely resolved, allowing the recognition of the two isomers **45** and **46**, present in the ratio 55:45, and assigned as the *cis*- and *trans*-isomers, respectively. The regiochemistry of the alkyl groups was indicated by the relatively deshielded positions and multiplicity of the isopropyl methine resonances at δ = 2.67 (sept) and 2.69 (sept), respectively, clearly pinpointing their attachment to the furan ring. Conversely, the unique C4-methyl groups (for numbering see Scheme 9) gave rise to doublet absorptions at δ = 0.74 and 1.07, respectively, confirming their connectivity to the tetrahydrofuran substructure.

The designation of the stereochemistry of **46** as *trans* rested on the similarity of the ^{1}H NMR data for its tetrahy-



Scheme 9 Cycloisomerization of **23** to **45** and **46**

Table 1 Selection of Comparative ^{1}H NMR data (ppm) for **45**, **46**, and **36**[a]

Complex	H2 (δ)	H3 (δ)	H4 (δ)	H5 (δ)	C4-CH_3 (δ)
45	4.07, 3.50	3.26	2.52	4.05, 3.78	0.74
46	4.18, 3.56	2.77	2.26	4.10, 3.44	1.07
36	4.14, 3.60	2.72	2.28	4.08, 3.43	1.05

[a] For numbering, see Scheme 9.

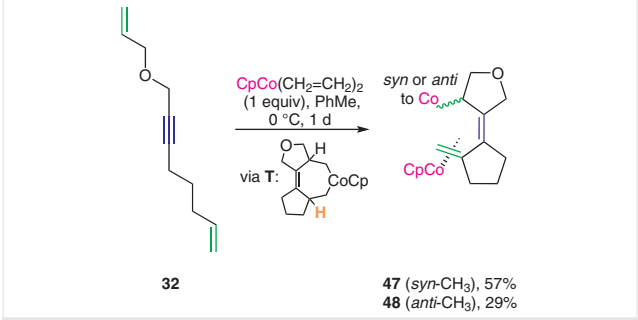
drofuran ring with those of **36** and their divergence from those of **45** (Table 1).

The outcome of the cycloisomerization depicted in Scheme 9 provides some mechanistic insight. First, the near equimolar formation of *cis*- and *trans*-isomers shows that the reaction is not generally stereoselective, as implied earlier by the (possibly) exclusive formation of the *trans* compound **36** from **19**. Therefore, cobalt-4-cycloheptene intermediates of the type **Q** (Scheme 4) may be accessible in both stereoisomeric forms (see also the conversion of **1** into the *cis* complex **2** in Scheme 2). Such lack of stereoselectivity will repeat itself in other examples (vide infra). Second, the regioselective formation of **45** and **46** signals that β-hydride elimination from the dimethyl analogue of **Q**, namely **S** (Scheme 9), favors the more substituted trajectory, the result of stereoelectronic effects.[1,27c,32]

One notes that, as in the case of **21**, β-hydride elimination to the terminal methyl substituent in **23** was not observed. Therefore, an attempt was made to enforce such a pathway by exploring the reactivity of **24** (Figure 1), in which the endocyclic pathway is blocked, but its *exo* counterpart remains enabled. Unfortunately, its reaction with $CpCo(CO)_2$ under the standard conditions led to a complex mixture that was not further characterized.

At this stage, it was thought instructive to activate (potentially) the double bonds in **18** and **19** with electron-withdrawing groups, as in the esters **25**–**29**. Lamentably, this exercise turned into a fiasco, as the starting materials, on attempted cycloisomerization, polymerized. This methodology could also not be extended to include enynenes such as **30** and **31**, in which the triple bond locus was terminal. While complete consumption of the starting materials was noted, no desired products were formed. A possible explanation for this failure is that the insertion of the terminal double bond into the saturated alkylcobalt side of the initial cobaltacyclopentene intermediate is prohibitively slow.[16]

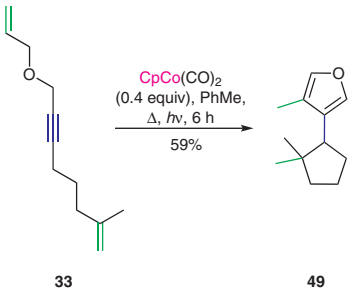
An important aspect of this chemistry to be probed was the necessity of the diallyl ether array for its success, prompting the interrogation of monoallyl ethers **32**–**35**. Puzzlingly, when **32** was treated with $CpCo(CO)_2$ in boiling toluene, the consequence was a complex mixture, containing several complexes, as highlighted by their orange-red color on TLC analysis. In an effort to access any free ligands, the crude product was treated with $CuCl_2{\cdot}2H_2O$,[30] prompting decomposition. The issue was resolved by carrying out a low temperature experiment with $CpCo(CH_2{=}CH_2)_2$, which provided the two complexes **47** and **48** in high yield, in a ratio of 2:1 (Scheme 10). While inseparable, their ^{1}H NMR spectrum exhibited resolved features for each isomer, assignable by comparison with the corresponding data for **39** and **44** (see experimental section and SI). Similarly, the ^{13}C NMR spectrum showed the expected doubling of relevant absorptions. Attempted oxidative demetalation led to polymerization, likely a reflection of the sensitivity of the free ligand.[33] Interestingly, although not unexpectedly,[1,27c,32] β-hydride elimination from the desymmetrized version of **Q**, namely **T** (Scheme 10), occurs away from the oxygen to construct only the bis(alkylidenecyclopentane) regioisomers shown in Scheme 10, evidently incapable of entering the hydrogen shift manifold that leads to the emergence of aromatic furans.



Scheme 10 Cycloisomerization of **32** to **47** and **48**

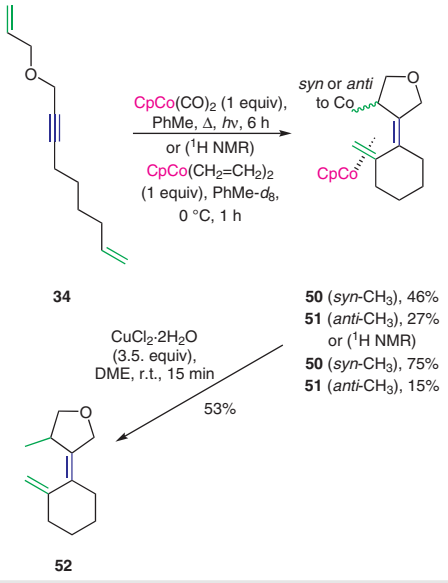
The preceding conjecture was tested with the derivative **33**, in which the pathway traversed by **32** is blocked. Indeed, standard cyclization of this substrate led to furan **49** in good yield (Scheme 11), revealing spectral data that compared well with those of its relatives **36**, **43**, **45**, and **46**.

On the other hand, simple chain extension of **32**, as in **34**, reproduced the trajectory depicted in Scheme 10, except that the resulting diene complexes were stable to the higher temperature conditions of their generation from $CpCo(CO)_2$ in boiling PhMe.



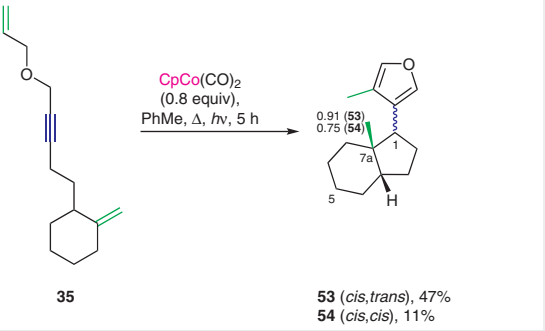
Scheme 11 Cycloisomerization of **33** to **49**

Here, the main consequence of switching to $CpCo(CH_2{=}CH_2)_2$ at 0 °C was an increased ratio of *syn* to *anti* complexes **50** and **51** (Scheme 12). The structural assignments of these compounds followed those made for their analogues **39**, **44**, **47**, and **48**. Further chemical corroboration of their identities as diastereomers was obtained by oxidative demetalation, which provided a single diene **52** (Scheme 12).



Scheme 12 Cycloisomerization of **34** to **50** and **51**, followed by demetalation to **52**

A final substrate to be inspected was the annulated enynene **35**, in which substitution at the alkyl end was expected to ensure furan formation, and the presence of a stereocenter raised the issue of potential diastereoselectivity. Cycloisomerization of **35** in the presence of $CpCo(CO)_2$ under the usual conditions led to a mixture of only two of the four possible furylhydrindanes **53** and **54**, which could not be separated preparatively by standard column chromatography (Scheme 13). Segregation occurred on GC, however, allowing for the recording of the individual mass spectra



Scheme 13 Cycloisomerization of **35** to **53** and **54** and the ^{1}H NMR chemical shifts of the methyl groups in the products

and determination of their ratio of 4:1, the latter confirmed by ^{1}H NMR spectroscopy.

The NMR spectra of **53** and **54** were sufficiently resolved to allow assignments of all signals but for the six methylene groups (see experimental section and SI), a finding that, unfortunately, did not reveal stereochemical identity. Two considerations led us to adopt a bias toward the formulation of the hydrindane fusion as being *cis*. The first was mechanistic and based on molecular models, which showed that the approach **U** of the methylidenecyclohexane double bond to the metal that leads to the *cis* configuration is sterically considerably more favorable than the alternative **V** (Figure 3).

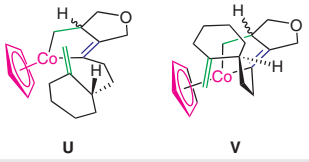
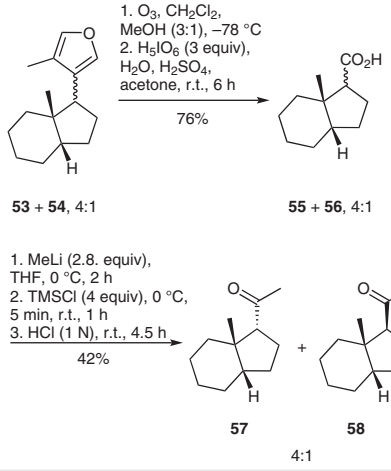


Figure 3 The two approaches of the methylidenecyclohexane double bond to cobalt: **U** leads to the eventual *cis*-hydrindane fusion, **V** to the *trans*-alternative

The second rested on the relatively greater similarities of the NMR chemical shifts of the atoms at the fusion of **53** and **54** – ^{1}H NMR: δ (CH_3) = 0.91 and 0.75, δ_{Htert} = 1.94 and 2.11; ^{13}C NMR: δ (CH_3) = 23.4 and 24.0, δ_{fusion} = 42.3/47.5 and 43.6/45.2 – when compared to the dissimilarities at the point of attachment of the furyl substituent ^{1}H NMR: δ = 2.51 and 2.93; ^{13}C NMR: δ = 45.5 and 39.2.

Turning to the choice of the disposition of the furyl group in the major isomer **53** as *trans* to the adjacent methyl, it was indicated by the larger chemical shift of the angular methyl group compared to that in **54** (Scheme 13). This assignment finds precedence in the reported larger chemical shifts (Δδ = 0.2–0.3) for related *trans*- versus *cis*-isomers of a series of *cis*-fused 7a-methyl-5-oxooctahydroindene-1-carboxylic acid derivatives (Scheme 13 and vide infra).[34]

The tenuousness of these arguments prompted an effort to convert the mixture of **53** and **54** into known compounds (Scheme 14). In this vein, ozonolysis, using a modified literature procedure,[35] furnished a 4:1 mixture of the carboxylic acids **55** and **56**,[36] exhibiting the expected IR and NMR spectral fingerprints, in particular the projected changes when going from starting materials to products. Moreover, and strengthening the preceding argument for the relative stereochemistry at C1, the major isomer exhibited δ (CH_3) = 1.19, its minor kin δ (CH_3) = 0.93. The corresponding 5-oxoacids show δ (CH_3) = 1.45 and 1.14, respectively.[34] Treatment of **55** and **56** with MeLi, TMSCl, and aqueous HCl[37] in sequence supplied a 4:1 mixture of the known[38] diastereomeric methyl ketones **57** and **58**, whose stereochemistry was corroborated by comparison of the ^{1}H NMR chemical shifts of the angular CH_3 groups [δ (CH_3) = 1.25 and 0.87] with those in the literature [δ (CH_3) = 1.27 and 0.88].[38] Note that the ratio of diastereomers remained constant throughout the sequence from furans to methyl ketones, making epimerization highly unlikely, thus lending credibility to the assigned structures for **53** and **54**.



Scheme 14 Sequential conversion of **53** and **54** via **55** and **56** into **57** and **58**

To conclude, we have shown that the complexes $CpCoL_2$ (Cp = C_5H_5; L = CO or CH_2=CH_2) facilitate the cycloisomerizations of α,δ,ω-enynenes containing allylic ether linkages, thus complementing related chemistry in the literature. Uniquely, the reaction cascades can be arrested at the stage of the intermediate CpCo-η^4-diene complexes derived from β-hydride elimination of the postulated cobalta-4-cycloheptenes (Schemes 8, 10, and 12). Similarly, when possible, these complexes can proceed by hydride shifts to furan products, thus rendering the process catalytic (Schemes 3, 8, 9, 11, and 13). The transformation is not stereoselective, but exhibits a preference for the *trans*-furan product (Schemes 3, 9, and 13) or, when arrested, the *syn*-Me CpCo-η^4-diene complex (Schemes 10 and 12). It is, however, completely regioselective in cases in which the starting alkyne is unsymmetrical: When one side of the enynene is blocked with respect to β-hydride elimination, the other side is chosen (Scheme 8); when one side features terminal substitution, the intermediate cobaltacycloheptene favors a hydride shift from the more substituted site (Scheme 9); when only one side contains an electron-withdrawing oxygen, β-hydride elimination is directed away from it (Scheme 12), unless this option is blocked (Scheme 11). When both double bonds are blocked or excessively encumbered by substitution, the cycloisomerization option is outcompeted by [2+2+2] cycloaddition to produce CpCo-η^4-cyclohexadiene products derived from the coupling of two substrate molecules (Schemes 6 and 7). The synthetic potential of the method is highlighted by the conversion of methylidene-2-[5-(2-propenyloxy)-3-pentynyl]cyclohexane into 1-[(1*R**,3a*S**,7a*S**)-7a-methyloctahydroinden-1-yl]-1-ethanone as the major isomer.

Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification. Solvents and/or reactants were degassed by purging with dry N_2 or argon for 3 min. All reactions with water-sensitive materials were carried out under dry N_2. Melting points were obtained with a Büchi melting point apparatus and are uncorrected. THF, DME, and Et_2O were distilled directly from Na/benzophenone ketyl prior to use. CH_2Cl_2, DMSO, pyridine, and Et_3N were distilled from CaH_2 and stored over 3Å molecular sieves. PhMe was extracted sequentially with concd H_2SO_4 at 0 °C (4 × 100 mL per L of solvent), H_2O (2 × 100 mL), and sat aq $NaHCO_3$, then predried via azeotropic distillation, and stored over 3Å molecular sieves. MeOH was distilled from Mg under N_2. *t*-BuOH was recrystallized until its melting point exceeded 24.5 °C. TLC was performed on commercial silica gel (Analtech, GHLF 250 micron, 10 × 2.5 cm glass, containing $CaSO_4$ and fluorescent indicator) plates, and visualizations were accomplished with anisaldehyde-H_2SO_4, phosphomolybdic acid-Ce^{4+}-H_2SO_4 spray, or UV illumination. GC was performed on either a Shimadzu Mini-2 instrument, interfaced with a Model TPM 2R temperature programmer and Hewlett-Packard Model 3390A Integrator, or a Hewlett-Packard Model 5880A integrating chromatograph, both equipped with 12 m OV-101 fused silica capillary columns. ^{1}H NMR spectra were recorded on any of these superconducting FT instruments: Varian EM-390, UCB-250, BVX-300, Bruker AM-400, or AM-500 MHz, respectively. They are reported on the δ scale in ppm, with chemical shifts referenced to the residual signal of the solvent, and are tabulated in the order: multiplicity (standard abbreviations), coupling constant(s), number of protons, and, if possible, assignment. Assignments (see SI) were made using the COSY pulse sequence or by decoupling experiments. ^{1}H-Decoupled ^{13}C NMR spectra were obtained on either the BVX-300 or Bruker AM-400 spectrometers. Chemical shifts are referenced to the residual signal of the solvent. Unless trivial, assignments were made routinely with the assistance of the DEPT 135° pulse sequence and/or by comparison with the spectra of similar compounds. ^{31}P NMR (relative to the chemical shift of 85% H_3PO_4) data are the result of proton decoupling. IR spectra were measured on PerkinElmer Model 681 or 137 instruments, referenced to polystyrene (1601 cm^{-1}); liquids were analyzed neat on NaCl plates and solids in KBr pellets. Low-resolution mass spectra are given as *m*/*z* values and were obtained at 70 eV with Atlas MS-12, Hewlett-Packard 5970A, or Finnigan 4000 mass spectrometers. Peak intensity

is expressed as percent total ion current normalized with respect to the base peak. High-resolution mass spectra were determined with a Consolidated 12-110B mass spectrometer. Elemental analyses were performed by the Microanalytical Laboratory operated by the College of Chemistry, University of California at Berkeley.

1,13-Tetradecadien-7-yne (18)

To anhydrous liquid NH_3 (freshly distilled from Na; 150 mL) were added Na (1.20 g, 52 mmol) and a few crystals of anhyd $Fe(NO_3)_3$. The mixture was stirred for 1 h at –33 °C, cooled to –78 °C, and then treated with a solution of 1-octen-7-yne[39] (2.80 g, 25.9 mmol) in Et_2O (150 mL) for 30 min. To this solution was added slowly 6-bromo-1-hexene (5.00 g, 30.6 mmol) in Et_2O (150 mL) and the resulting reaction mixture stirred at r.t. until the solvent had evaporated. The residual material was taken up in Et_2O, washed with H_2O (3 × 50 mL), the solvent evaporated, and the remaining oil distilled through a Kugelrohr to give **18** as a colorless liquid; yield: 3.00 g (61%); bp 80–85 °C/5 Torr.

IR (film): 3100, 2950, 2850, 1820, 1640, 1460, 1440, 1330, 1000, 910 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.78 (ddt, *J* = 16.5, 9.0, 7.5 Hz, 2 H), 4.99 (dd, *J* = 16.5, 1.5 Hz, 2 H), 4.85 (dd, *J* = 9.0, 1.5 Hz, 2 H), 2.35 (m, 4 H), 2.03 (m, 4 H), 1.48 (m, 8 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.7, 114.5, 80.1, 33.4, 28.7, 28.2, 18.7.

^{13}C NMR (75 MHz, PhMe-d_8): δ = 138.9, 114.7, 80.4, 33.8, 29.1, 28.6, 19.1.

MS (EI, 70 eV): *m*/*z* (%) = 190 ([M^+], 2), 147 (10), 133 (18), 119 (19), 107 (54), 93 (74), 79 (100), 67 (67).

Anal. Calcd for $C_{14}H_{22}$: C, 88.42; H, 11.57. Found: C, 88.21; H, 11.49.

General Etherification Procedure for the Synthesis of 21, 23, and 24[40]

To a vigorously stirred solution of the unsaturated alcohol in DMSO contained in a 125 mL conical flask was added KOH in one portion. The brown slurry was stirred for 45 min at r.t. and the neat halide dripped in at 0–5 °C over 15–30 min. The mixture was stirred for 30 min at 0 °C, then 1–3 h at 40–45 °C. The brown slurry was poured into ice-H_2O (200 mL) and extracted with hexane (3 × 85 mL). The combined organic phases were washed with H_2O (100 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to yield the crude product.

1,4-Bis[(3-methyl-2-butenyl)oxy]but-2-yne (21)

The general etherification procedure was employed using 2-butyne-1,4-diol (491 mg, 5.70 mmol), KOH (1.45 g, 25.8 mmol), DMSO (10 mL), and 1-bromo-3-methyl-2-butene (1.000 g, 6.710 mmol). Extractions were performed with pentane (3 × 10 mL). Column chromatography on silica gel, eluting with Et_2O/hexane (1:4), rendered **21** as an air-sensitive oil; yield: 398 mg (31%).

IR (film): 2970, 2920, 2850, 1670, 1445, 1375, 1350, 1110, 1070, 930 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.31 (tsept, *J* = 7.0, 1.4 Hz, 2 H), 4.15 (s, 4 H), 4.02 (d, *J* = 7.0 Hz, 4 H), 1.73 (br s, 6 H), 1.68 (br s, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.2, 120.2, 82.4, 66.0, 57.1, 25.8, 18.0.

1-(3-Methyl-2-butenyloxy)-4-(2-propenyloxy)-2-butyne (23)

The general etherification procedure was implemented using 4-(2-propenyloxy)-2-butyn-1-ol[41] (500 mg, 3.96 mmol), KOH (890 mg, 15.9 mmol), DMSO (10 mL), and 4-bromo-2-methyl-2-butene (671 mg, 4.50 mmol). Extractions were performed with pentane (3 × 10 mL). Column chromatography on silica gel, eluting with Et_2O/hexane (3:50), furnished **23** as a colorless, moderately air-sensitive oil; yield: 530 mg (69%).

IR (film): 2970, 2920, 2850, 1445, 1375, 1350, 1120, 1070, 1020, 990, 925 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.88 (ddt, *J* = 17.3, 11.3, 5.7 Hz, 1 H), 5.31 (m, 1 H), 5.28 (br d, *J* = 17.3 Hz, 1 H), 5.19 (br d, *J* = 10.8 Hz, 1 H), 4.18 (t, *J* = 2.6 Hz, 2 H), 4.15 (t, *J* = 2.7 Hz, 2 H), 4.05 (m, 2 H), 4.02 (m, 2 H), 1.73 (s, 3 H), 1.68 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.2, 133.9, 120.2, 117.8, 82.6, 82.0, 70.5, 66.0, 57.4, 57.1, 25.8, 18.0.

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.83; H, 9.37.

1-[(*E*)-2-Methyl-2-butenyloxy]-4-(2-methyl-2-propenyloxy)-2-butyne (24)

The general etherification procedure was executed using 4-(2-methyl-2-propenyloxy)-2-butyn-1-ol[42] (2.300 g, 16.41 mmol), KOH (4.33 g, 77 mmol), DMSO (50 mL), and 1-bromo-2-methyl-2-butene[43] (2.446 g, 16.41 mmol). Column chromatography on silica gel, eluting with Et_2O/hexane (1:20), afforded **24** as a colorless oil; yield: 2.231 g (65%).

IR (film): 3080, 2970, 2940, 2910, 2840, 1650, 1445, 1370, 1345, 1200, 1140, 1115, 1070, 895, 835 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 5.49 (m, 1 H), 4.95 (br s, 1 H), 4.89 (br s, 1 H), 4.14 (t, *J* = 1.7 Hz, 2 H), 4.09 (t, *J* = 1.7 Hz, 2 H), 3.93 (s, 2 H), 3.89 (s, 2 H), 1.71 (br s, 3 H), 1.61 (s, 3 H), 1.58 (br d, *J* = 8.3 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.4, 132.1, 123.6, 112.8, 82.5, 82.0, 75.8, 73.5, 57.2, 56.7, 19.5, 13.6, 13.2.

1-[4-(2-Propenyloxy)-2-butynyl] Propenoate (25)

To a stirred solution of 4-(2-propenyloxy)-2-butyn-1-ol[41] (1.000 g, 7.927 mmol) and Et_3N (2.2 mL, 1.6 g, 16 mmol) in CH_2Cl_2 (20 mL) at 0 °C was added neat propenoyl chloride (1.086 g, 12.00 mmol) via syringe over 5 min with the formation of a brown precipitate. The mixture was stirred for 12 h at r.t., treated with sat. aq NaOAc (10 mL), the layers separated, and the aqueous phase extracted with CH_2Cl_2 (20 mL). The combined organic layers were dried ($MgSO_4$), filtered, concentrated in vacuo, and subjected to column chromatography on silica gel, eluting with Et_2O/hexane (1:9), to sequester **25** as a faintly yellow, unstable oil; yield: 670 mg (47%).

IR (film): 3070, 2980, 2940, 2850, 1735, 1635, 1435, 1410, 1355, 1265, 1180, 1140, 1080, 1050, 980, 930, 810 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 6.43 (dd, *J* = 17.3, 1.4 Hz, 1 H), 6.11 (dd, *J* = 17.3, 10.4 Hz, 1 H), 5.86 (ddt, *J* = 17.2, 10.4, 5.8 Hz, 1 H), 5.85 (dd, *J* = 10.4, 1.4 Hz, 1 H), 5.27 (ddt, *J* = 17.2, 1.6, 1.5 Hz, 1 H), 5.22 (ddt, *J* = 10.4, 1.6, 1.5 Hz, 1 H), 4.78 (t, *J* = 1.8 Hz, 2 H), 4.17 (t, *J* = 1.8 Hz, 2 H), 4.02 (ddd, *J* = 5.8, 1.3, 1.3 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.2, 133.7, 131.7, 127.6, 117.9, 82.8, 80.2, 70.7, 57.3, 52.3.

1-[4-(2-Propenyloxy)-2-butynyl] (*E*)-2-Butenoate (26)

To a solution of 4-(2-propenyloxy)-2-butyn-1-ol[41] (700 mg, 5.55 mmol) and anhyd pyridine (8 mL) in CH_2Cl_2 (30 mL) at r.t. was introduced *trans*-2-butenoyl chloride (0.70 mL, 76 mg, 73 mmol) via syringe in one portion. The mixture was stirred for 12 h, H_2O (20 mL) added, the layers separated, and the aqueous phase extracted with hexane (15 mL). The combined organic fractions were extracted successively with H_2O (15 mL) and sat. aq $CuSO_4$ (15 mL), filtered, dried

($MgSO_4$), and concentrated in vacuo to give a yellow syrup that was subjected to Kugelrohr distillation to supply **26** as a faintly yellow, unstable oil; yield: 873 mg (81%); bp 120–129 °C/15 Torr.

IR (film): 3060, 2920, 2830, 1715, 1640, 1435, 1355, 1295, 1235, 1150, 1125, 1070, 1010, 980, 955, 920 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.95 (dq, *J* = 15.6, 6.9 Hz, 1 H), 5.80 (m, 2 H), 5.21 (dt, *J* = 17.2, 1.7 Hz, 1 H), 5.12 (dt, *J* = 10.4, 1.3 Hz, 1 H), 4.69 (t, *J* = 1.8 Hz, 2 H), 4.10 (t, *J* = 1.8 Hz, 2 H), 3.96 (ddd, *J* = 5.8, 1.3, 1.3 Hz, 2 H), 1.81 (dd, *J* = 6.9, 1.7 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.3, 145.7, 133.6, 121.6, 117.6, 82.4, 80.3, 70.4, 57.1, 51.7, 17.9.

Dimethyl *trans*,*trans*-Tetradeca-2,12-dien-7-ynedioate (29)

5-Decynedial

To a suspension of powdered PCC (1.80 g, 8.35 mmol) and NaOAc (150 mg, 1.82 mmol) in CH_2Cl_2 was added 5-decyn-1,10-diol[30d] (400 mg, 2.35 mmol) at r.t. After stirring for 1.5 h, the solvent was evaporated and the dark residue chromatographed on silica gel, eluting with Et_2O, to lead to 5-decynedial as a colorless oil; yield: 250 mg (64%).

IR (film): 2950, 2740, 1730, 1395, 1340, 1135, 1080, 940 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 9.77 (t, *J* = 1.2 Hz, 2 H), 2.53 (dt, *J* = 7.2, 1.2 Hz, 4 H), 2.19 (t, *J* = 5 Hz, 4 H), 1.78 (m, 4 H).

MS (EI, 70 eV): *m*/*z* (%) = 166 ([M^+], 0.5), 123 (23), 110 (30), 95 (44), 78 (91), 55 (100).

29

5-Decynedial (400 mg, 2.41 mmol) and methoxycarbonylmethylenetriphenylphosphorane (2.23 g, 6.67 mmol) were stirred in benzene (15 mL) at r.t. for 3 h and at 80 °C for 8 h. The solvent was evaporated and the residue chromatographed on neutral alumina (activity), eluting with Et_2O/pentane (3:2), to deliver **29** as a colorless oil; yield: 194 mg (29%).

IR (film): 2942, 1726, 1658, 1432, 1325, 1272, 1200, 1150, 1095, 1043, 979, 913, 856 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 6.93 (dt, *J* = 15.6, 7.0 Hz, 2 H), 5.81 (dt, *J* = 15.6, 1.5 Hz, 2 H), 3.70 (s, 6 H), 2.28 (m, 4 H), 2.15 (t, *J* = 7.0 Hz, 4 H), 1.61 (m, 4 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 167.8, 149.4, 122.3, 80.8, 52.2, 32.0, 28.1, 19.0.

MS (EI, 70 eV): *m*/*z* (%) = 278 ([M^+], 2), 277 (5), 263 (15), 187 (37), 159 (70), 91 (84), 81 (100).

HRMS (EI, 70 eV): *m*/*z* [M^+ – 1] calcd for $C_{16}H_{21}O_4$: 277.1439; found: 277.1434.

cis-1-(2-Propenyloxy)-4-(3-trimethylsilyl-2-propynyloxy)-2-butene (31)

To a stirred solution of **30**[15] (1.000 g, 6.016 mmol) in Et_2O (100 mL) at 0 °C was added BuLi (3.4 mL, 1.8 M in hexane, 6.12 mmol) over 5 min via syringe, giving a yellow suspension. After 1 h, TMSCl (1.0 mL, 860 mg, 7.9 mmol) was introduced via syringe over 5 min. The mixture was stirred at 23 °C for 3 h, treated with sat. aq $NaHCO_3$ (100 mL), and the layers separated. The organic phase was dried ($MgSO_4$), filtered, and concentrated in vacuo to leave a yellow oil. Chromatography on silica gel, eluting with Et_2O/hexane (1:9), afforded **31** as a faint yellow oil; yield: 849 mg (59%).

^1H NMR (250 MHz, $CDCl_3$): δ = 5.88 (ddt, *J* = 17.2, 10.3, 5.7 Hz, 1 H), 5.71 (ABX_4m, 2 H), 5.24 (ddt, *J* = 17.2, 1.6, 1.6 Hz, 1 H), 5.15 (ddt, *J* = 10.3, 1.4, 1.3 Hz, 1 H), 4.10 (s, 2 H), 4.10 (br d, *J* = 5.3 Hz, 2 H), 4.05 (br d, *J* = 5.4 Hz, 2 H), 3.95 (dt, *J* = 5.6, 1.4 Hz, 2 H), 0.15 (s, 9 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 134.5, 130.3, 128.4, 117.2, 101.3, 91.4, 71.2, 65.6, 64.9, 57.8, –0.19.

Synthesis of 32–35 from 3-(2-Propynyloxy)-1-propene; General Procedure

A 100 mL round-bottomed flask fitted with a septum was charged with NaH (1.05 equiv), rendered oil-free by washing with anhyd Et_2O (3 × 10 mL), and DMSO (30 mL). The resulting slurry was heated to 65–75 °C in an oil bath with stirring until the NaH had dissolved, giving a green-grey solution. After cooling to r.t., 3-(2-propynyloxy)-1-propene was added via syringe over 5 min, the mixture stirred for 1 h, and the bromoalkene introduced via syringe over 10 min with sufficient cooling to maintain a reaction temperature below 30 °C. After 6–12 h, the mixture was diluted with H_2O (60 mL) and extracted with hexane (3 × 20 mL). The combined organic phases were washed with H_2O (50 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to supply the crude product.

8-(2-Propenyloxy)-1-octen-6-yne (32)

The preceding general procedure was employed using NaH (669 mg, 27.86 mmol), 3-(2-propynyloxy)-1-propene (2.500 g. 26.01 mmol), and 5-bromo-1-pentene (4.024 g. 27.00 mmol). Kugelrohr distillation presented **32** as a colorless oil; yield: 2.795 g (65%); bp 94–104 °C/18 Torr.

IR (film): 3080, 2980, 2940, 2860, 1645, 1445, 1355, 1135, 1090, 990, 910 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.88 (ddt, *J* = 17.2, 11.4, 5.7 Hz, 1 H), 5.76 (ddt, *J* = 16.9, 13.4, 6.7 Hz, 1 H), 5.27 (dd, *J* = 17.2, 1.5 Hz, 1 H), 5.18 (dd, *J* = 10.4, 1.5 Hz, 1 H), 5.01 (dd, *J* = 18.5, 1.4 Hz, 1 H), 4.96 (dd, *J* = 10.1, 1.0 Hz, 1 H), 4.11 (t, *J* = 2.0 Hz, 2 H), 4.02 (dd, *J* = 4.7, 1.0 Hz, 2 H), 2.22 (tt, *J* = 7.0, 1.9 Hz, 2 H), 2.12 (dt, *J* = 7.4, 7.3 Hz, 2 H), 1.59 (tt, *J* = 7.3, 7.3 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.7, 134.1, 117.6, 115.1, 86.6, 76.1, 70.4, 57.7, 32.8, 27.7, 18.2.

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.30; H, 9.94.

2-Methyl-8-(2-propenyloxy)-1-octen-6-yne (33)

The preceding general procedure was employed using NaH (264 mg, 11.0 mmol), 3-(2-propynyloxy)-1-propene (1.153 g, 12.00 mmol), and 5-bromo-2-methyl-1-pentene (1.600 g, 9.812 mmol). The crude product was chromatographed on silica gel, eluting with Et_2O/hexane (1:20), to give **33** as a colorless oil; yield: 627 mg (36%).

IR (film): 3070, 2930, 2850, 1650, 1450, 1370, 1350, 1135, 1085, 1020, 995, 925, 890 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.89 (ddt, *J* = 16.2, 10.4, 5.8 Hz, 1 H), 5.27 (dd, *J* = 17.3, 1.5 Hz, 1 H), 5.18 (d, *J* = 10.4 Hz, 1 H), 4.71 (br s, 1 H), 4.67 (br s, 1 H), 4.12 (t, *J* = 2.0 Hz, 2 H), 4.03 (br dt, *J* = 5.8, 1.1 Hz, 2 H), 2.20 (tt, *J* = 7.2, 1.9 Hz, 2 H), 2.09 (br t, *J* = 7.4 Hz, 2 H), 1.70 (s, 3 H), 1.64 (tt, *J* = 7.5, 7.0 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.9, 134.1, 117.6, 110.4, 86.7, 76.0, 70.4, 57.7, 36.8, 26.5, 22.3, 18.3.

Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.69; H, 10.26.

9-(2-Propenyloxy)-1-nonen-7-yne (34)

The preceding general procedure was employed using NaH (324 mg, 13.5 mmol), 3-(2-propynyloxy)-1-propene (1.300 g, 13.52 mmol), and 6-bromo-1-hexene (2.201 g, 13.50 mmol). The crude product was chromatographed on silica gel, eluting with Et_2O/pentane (3:50), to afford **34** as a colorless oil; yield: 1.519 g (63%).

IR (film): 3080, 2980, 2940, 2860, 1645, 1445, 1355, 1135, 1085, 995, 915 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.89 (ddt, *J* = 17.2, 10.4, 5.8 Hz, 1 H), 5.78 (ddt, *J* = 17.0, 10.3, 6.6 Hz, 1 H), 5.28 (ddt, *J* = 17.2, 1.6, 1.6 Hz, 1 H), 5.18 (dtd, *J* = 10.4, 1.4, 1.2 Hz, 1 H), 4.98 (ddt, *J* = 17.2, 1.7, 1.6 Hz, 1 H), 4.92 (dtd, *J* = 10.2, 2.1, 1.2 Hz, 1 H), 4.11 (t, *J* = 2.1 Hz, 2 H), 4.03 (ddd, *J* = 5.7, 1.3, 1.3 Hz, 2 H), 2.21 (tt, *J* = 6.8, 2.1 Hz, 2 H), 2.05 (dt, *J* = 7.0, 7.0 Hz, 2 H), 1.50 (AA′BB′m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.5, 134.2, 117.6, 114.5, 86.8, 75.9, 70.4, 57.7, 33.2, 28.02, 28.01, 18.6.

Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.84; H, 10.04.

Methylidene-2-[5-(2-propenyloxy)-3-pentynyl]cyclohexane (35)

2-(2-Methylidenecyclohexyl)ethyl Methanesulfonate

To a stirred solution of 2-(2-methylidenecyclohexyl)ethanol[44] (2.137 g, 15.24 mmol) and MsCl (1.3 mL, 1.9 g, 17 mmol) in CH_2Cl_2 (50 mL) at 0 °C was added Et_3N (2.2 mL, 1.6 g, 16 mmol) dropwise via syringe over 2 min, causing the formation of a colorless precipitate. The mixture was stirred for 12 h at r.t., diluted with hexane (80 mL) and H_2O (40 mL), and the separated aqueous phase extracted with hexane (30 mL). The combined organic layers were washed with H_2O (50 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to yield 2-(2-methylidenecyclohexyl)ethyl methanesulfonate[44] as a colorless oil, to be applied directly to the next reaction; yield: 3.192 g (96%).

IR (film): 2920, 2850, 1640, 1445, 1355, 1170, 970, 955, 890, 835, 820, 790 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.70 (br s, 1 H), 4.57 (br s, 1 H), 4.22 (m, 2 H), 2.94 (s, 3 H), 2.20 (m, 2 H), 2.05 (m, 2 H), 1.77–1.42 (m, 6 H), 1.31 (m, 1 H).

1-(2-Bromoethyl)-2-methylidenecyclohexane

To a stirred solution of 2-(2-methylidenecyclohexyl)ethyl methanesulfonate (3.187 g, 14.60 mmol) in acetone (50 mL) at r.t. was added anhyd LiBr (2.606 g, 30.01 mmol) in one portion. After 24 h, the solvent was removed in vacuo at 0 °C, pentane (60 mL) and H_2O (30 mL) were added to the residue, and the separated aqueous layer extracted with pentane (20 mL). The combined organic phases were washed with H_2O, dried ($MgSO_4$), filtered, and concentrated in vacuo at 0 °C. Chromatography on silica gel, eluting with pentane, gave 1-(2-bromoethyl)-2-methylidenecyclohexane[44] as a colorless oil; yield: 2.609 g (88%).

IR (film): 3170, 2930, 2860, 1645, 1445, 1260, 1240, 1210, 895 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.68 (br s, 1 H), 4.58 (br s, 1 H), 3.40 (m, 2 H), 2.28 (m, 1 H), 2.16 (m, 2 H), 2.01 (m, 1 H), 1.79 (m, 2 H), 1.53 (m, 4 H), 1.28 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.9, 106.6, 41.5, 35.1, 34.2, 33.3, 32.3, 28.5, 23.9.

Anal. Calcd for $C_9H_{15}Br$: C, 53.22; H, 7.44. Found: C, 53.44; H, 7.49.

35

The preceding general synthetic procedure was employed using NaH (216 mg, 9.00 mmol), 3-(2-propynyloxy)-1-propene (961 mg, 10.0 mmol), and 1-(2-bromoethyl)-2-methylidenecyclohexane (1.692 g, 8.330 mmol). The crude product was chromatographed on silica gel, eluting with Et_2O/hexane (1:50), to supply **35** as a colorless oil; yield: 952 mg (52%).

IR (film): 3080, 2930, 2850, 1640, 1445, 1350, 1135, 1080, 925, 890 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.89 (ddt, *J* = 17.2, 10.4, 5.8 Hz, 1 H), 5.28 (ddt, *J* = 17.3, 1.6, 1.6 Hz, 1 H), 5.18 (ddt, *J* = 10.3, 1.3, 1.2 Hz, 1 H), 4.65 (br s, 1 H), 4.55 (br s, 1 H), 4.12 (t, *J* = 2.1 Hz, 2 H), 4.03 (dt, *J* = 5.8, 1.3 Hz, 2 H), 2.19 (m, 4 H), 2.02 (m, 1 H), 1.84 (m, 1 H), 1.73 (m, 1 H), 1.62 (m, 1 H), 1.51 (m, 4 H), 1.26 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.8, 134.2, 117.6, 106.1, 87.1, 75.8, 70.4, 57.8, 42.1, 34.4, 33.4, 31.0, 28.7, 24.0, 16.8.

Anal. Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.43; H, 10.10.

Attempted CpCo-Mediated Cycloisomerization of 18

Reactions were performed with 1–2 mmol of **18** or, on a smaller scale, in NMR tubes with thoroughly degassed reagents and solvents. Their progression was followed by GC, MS, TLC, and ^1H/^{13}C NMR spectroscopy, until all of **18** had disappeared or conversion stopped. When a workup was executed, the reaction mixture was filtered through a short column of neutral alumina, eluting with pentane/Et2O (95:5).

In a typical experiment, **18** (115 mg, 0.60 mmol) and $CpCo(CO)_2$ (25 µL, 33.8 mg, 0.19 mmol) in decalin (1:1 mixture of *cis*- and *trans*-isomers; 10 mL) was heated to reflux for 4 h. The deep red solution slowly turned brown with concurrent formation of a fine black precipitate. After workup, the product oil (90 mg, 78% mass recovery) showed a ^1H NMR spectrum ($CDCl_3$) in which the terminal alkene signal at δ = 5.78 had disappeared and absorptions at δ = 5.3 (m), 2.1 (m), 1.6 (m), 1.3 (m), and 0.9 (m) in the ratio of 1:2:1:2:1 were evident.

IR (film): 2950, 1450, 1380, 1330, 960 cm^{-1}.

MS (EI, 70 eV): *m*/*z* (%) = 190 ([M^+], 1), 175 (13), 161 (50), 147 (50), 133 (44), 122 (65), 107 (71), 93 (83), 79 (84), 67 (83), 55 (83), 41 (100).

In another experiment, **18** (255 mg, 1.34 mmol) and $CpCo(CO)_2$ (50 µL, 67.6 mg, 0.38 mmol) in boiling *m*-xylene (10 mL) was irradiated with a projector lamp for 2 h, the light turned off, and reflux continued for another 4 h. Chromatography on alumina, eluting with Et_2O/pentane (1:1), separated first an oil (159 mg, 62% mass recovery) of similar composition to that above (^1H NMR), followed by a purple fraction of biscarbyne complex {$[CpCo]_3[\mu_3$-*trans*-CH=CH$(CH_2)_3CH_3]_2$} (14 mg, 20%).

^1H NMR (90 MHz, $CDCl_3$): δ = 8.84 (dt, *J* = 15, 1.5 Hz, 2 H), 6.70 (dt, *J* = 15, 7.2 Hz, 2 H), 4.30 (s, 15 H), 2.37 (m, 4 H), 1.60 (m, 8 H), 1.05 (t, *J* = 8 Hz, 6 H).

MS (EI, 70 eV): *m*/*z* (%) = 686 ([M^+], 11), 578 (12), 562 (43), 438 (1), 314 (2), 213 (13), 199 (37), 189 (76), 97 (40), 71 (51), 69 (61), 57 (100).

Allylic Ether Cyclizations with $CpCo(CO)_2$; General Procedure

A solution of $CpCo(CO)_2$ (0.2 or 1 equiv) and the enynene in anhyd, degassed, alkene-free PhMe (5–10 mL) was introduced via syringe pump over several h to boiling, stirred, anhyd, degassed, alkene-free PhMe (25–35 mL), contained in a 100 mL round-bottomed flask that had been pretreated with hexamethyldisilazane. The vessel was irradiated with a filtered (Corning GS0-52-1, 340 nm cutoff) slide projec-

tor lamp (Sylvania ELH 120 V, 300 W) controlled by a voltage regulator set at 50 V during the entire addition to ensure continuous decarbonylation of $CpCo(CO)_2$. Boiling was sustained for several hours, until all of the starting material had disappeared, the mixture cooled to r.t., and the volatiles were removed by vacuum transfer. The orange-brown residue was chromatographed on silica gel, eluting with Et_2O/hexane.

Allylic Ether Cyclizations with $CpCo(CH_2{=}CH_2)_2$; General Procedure

To $CpCo(CH_2{=}CH_2)_2$ (100 mg, 0.56 mmol) in PhMe (2 mL) at 0 °C was added the enynene (1 equiv) dropwise by syringe over a few min and the mixture allowed to stir at r.t. for several h. The color changed from deep-brown to dark red. To complete conversion, the mixture was heated 50 °C for several min. The solvent was removed in vacuo and the residue purified by chromatography on basic Al_2O_3, eluting with Et_2O/hexane. The so-obtained dark red or dark orange neat oils were stable to air for several h, but decomposed relatively rapidly in solution.

trans-3-Methyl-4-(4-methyloxacyclopent-3-yl)furan (36)

$CpCo(CO)_2$ (510 µL, 689 mg, 3.82 mmol) and **19** (3.600 g, 21.66 mmol) were subjected to the general cyclization conditions over 12 h to result in **36** as a colorless oil; yield: 2.524 g (70%).

IR (film): 2960, 2930, 2870, 1465, 1390, 1365, 1150, 1055, 870, 790 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 7.18 (s, 1 H), 7.14 (s, 1 H), 4.14 (dd, *J* = 8.0, 7.7 Hz, 1 H), 4.08 (dd, *J* = 7.9, 7.5 Hz, 1 H), 3.60 (dd, *J* = 8.4, 8.4 Hz, 1 H), 3.43 (dd, *J* = 8.2, 8.2 Hz, 1 H), 2.72 (ddd, *J* = 8.3, 8.3, 8.3 Hz, 1 H), 2.28 (m, 1 H), 1.96 (s, 3 H), 1.05 (d, *J* = 6.6 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.0, 138.6, 124.7, 119.8, 75.1, 73.7, 43.0, 40.3, 16.0, 8.48.

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.93; H, 8.55.

trans-4-Methyl-3-oxacyclopentanecarboxylic Acid (37)

Through a solution of **36** (400 mg, 2.41 mmol) in CH_2Cl_2/MeOH (1:3, 35 mL) was passed ozone at –78 °C until a green color persisted. The mixture was purged with N_2 and treated with aq H_2O_2 (8 mL, 30% by wt) and aq 3 N NaOH (4 mL). After stirring at 0 °C for 1.5 h, the volatiles were removed in vacuo, and the residue was extracted with Et_2O (30 mL). The pH of the aqueous layer was adjusted to 2 with aq HCl and the solution saturated with NaCl, followed by extraction with Et_2O (3 × 20 mL). The combined organic phases were dried ($MgSO_4$), filtered, concentrated in vacuo, and the resulting pink oil subjected to Kugelrohr distillation to afford **37** as a colorless oil; yield: 201 mg (64%); bp 125–131 °C/13 Torr.

IR (film): 3300–2800 (br), 2970, 2870, 1720, 1460, 1415, 1380, 1180, 1055, 915 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 9.10 (br s, 1 H), 4.05 (m, 3 H), 3.36 (dd, *J* = 7.9, 7.9 Hz, 1 H), 2.67 (ddd, *J* = 7.3, 7.3, 7.3 Hz, 1 H), 2.57 (dddq, *J* = 7.0, 7.0, 6.9, 6.9 Hz, 1 H), 1.13 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 179.2, 75.2, 70.1, 51.5, 38.5, 17.1.

MS (EI, 70 eV): *m*/*z* (%) = 130 ([M$^+$], 2), 112 (5), 100 (29), 88 (27), 85 (36), 82 (28), 73 (100).

HRMS (EI, 70 eV): *m*/*z* [M$^+$] calcd for $C_6H_{10}O_3$: 130.0630; found: 130.0625.

2-(4-Bromophenyl)-2-oxoethyl *trans*-4-Methyl-3-oxacyclopentanecarboxylate (38)

A solution of **37** (250 mg, 1.92 mmol) in H_2O (3 mL) stirred at r.t. was treated with a few crystals of phenolphthalein and a sufficient number of drops of aq 3 N NaOH to turn the solution pink. Enough HCl (0.3 N) was then added to discharge the pink color, followed by 2-bromo-1-(4-bromophenyl)-1-ethanone (500 mg, 1.80 mmol) in EtOH (17 mL). A precipitate formed, which dissolved on heating to reflux for 2 h. The EtOH was removed in vacuo, the residue covered with H_2O (20 mL), and the mixture extracted with CH_2Cl_2 (2 × 30 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a yellow oil. Crystallization from hexane provided **38** as a colorless solid; yield: 300 mg (51%); mp 74–75 °C.

IR (KBr): 2930, 2880, 1735, 1705, 1590, 1425, 1385, 1190, 1080, 985, 930, 830, 815 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 7.74 (d, *J* = 8.6 Hz, 2 H), 7.61 (d, *J* = 8.6 Hz, 2 H), 5.30 (ABq, 2 H), 4.06 (m, 3 H), 3.38 (dd, *J* = 8.1, 7.6 Hz, 1 H), 2.82 (ddd, *J* = 7.4, 7.4, 7.4 Hz, 1 H), 2.68 (dddq, *J* = 7.0, 7.0, 6.9, 6.9 Hz, 1 H), 1.18 (d, *J* = 6.7 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 190.9, 172.9, 132.7, 132.2, 129.2, 129.1, 75.2, 70.3, 65.9, 51.5, 38.8, 17.2.

MS (EI, 70 eV): *m*/*z* (%) = 328 ([M$^+$], 0.1), 326 ([M$^+$], 0.1), 200 (60), 198 (61), 185 (83), 183 (84), 157 (41), 155 (43), 129 (70), 113 (56), 84 (40), 83 (75), 76 (47), 75 (35), 69 (49), 57 (70), 55 (100).

Anal. Calcd for $C_{14}H_{15}BrO_4$: C, 51.40; H, 4.62. Found: C, 51.33; H, 4.60.

1,4-Bis(2-deuterio-2-propenyloxy)-2-butyne (19-d_2)

To a slurry of NaH (744 mg, 31.00 mmol) in DMSO (25 mL) at r.t. was added 2-butyne-1,4-diol (1.310 g, 15.22 mmol) in DMSO (10 mL) over 15 min via syringe. The brown mixture was stirred until H_2 evolution had ceased (3 h) and then 3-chloro-1-propene-2-*d*[29] (2.360 g, 30.44 mmol) in DMSO (5 mL) introduced via syringe, while keeping the temperature below 30 °C. After stirring for 18 h, the mixture was treated with sat. aq $NaHCO_3$ (60 mL) and hexane (75 mL). The layers were separated and the aqueous phase extracted with hexane (2 × 25 mL). The combined organic layers were washed with brine (50 mL), dried (Na_2SO_4), filtered, and concentrated in vacuo to furnish a yellow oil. Kugelrohr distillation provided **19-d_2** as a colorless oil; yield: 961 mg (38%); bp 107–110 °C/12 Torr (Lit. **19**[12] bp 104–106/10 Torr).

^1H NMR (250 MHz, $CDCl_3$): δ = 5.87 (m, 0.06 H), 5.28 (narrow m, 2 H), 5.18 (narrow m, 2 H), 4.17 (s, 4 H), 4.03 (br s, 4 H).

trans-3-Methyl-4-(4-deuterio-4-deuteriomethyloxacyclopent-3-yl)furan (36-d_2)

The deuterated enynene **19-d_2** (168 mg, 1.00 mmol) was subjected to the general enynene cyclization procedure in the presence of $CpCo(CO)_2$ (42 µL, 57 mg, 0.32 mmol) over 6 h. The orange-brown residue was chromatographed on silica gel, eluting with Et_2O/hexane (1:9), to give **36-d_2** as a colorless oil; yield: 125 mg (74%).

IR (film): 2930, 2860, 2180, 1675, 1440, 1280, 1140, 1050, 920, 785 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 7.18 (s, 1 H), 7.14 (s, 1 H), 4.14 (dd, *J* = 8.0, 7.7 Hz, 1 H), 4.08 (d, *J* = 7.9 Hz, 1 H), 3.60 (dd, *J* = 8.4, 8.4 Hz, 1 H), 3.43 (d, *J* = 8.2 Hz, 1 H), 2.72 (dd, *J* = 8.3, 8.3 Hz, 1 H), 2.28 (m, 0.07 H), 1.96 (s, 3 H), 1.05 (br s, 2.06 H).

Diene Complex 39

$CpCo(CH_2{=}CH_2)_2$ (100 mg, 0.56 mmol) and enynene **19** (93 mg, 0.56 mmol) were transformed according to the general cyclization protocol and subjected to chromatography on alumina, eluting with hexane/Et_2O (10:1), to sequester **39** as a dark red oil; yield: 114 mg (70%).

IR (film): 2970, 2930, 2850, 1675, 1473, 1459, 1377, 1342, 1265, 1113, 1080, 1063, 1042, 1027, 943, 910, 741 cm^{-1}.

^1H NMR (300 MHz, PhMe-d_8): δ = 4.59 (br s, 2 H), 4.53 (d, *J* = 9 Hz, 1 H), 4.33 (s, 5 H), 4.32 (d, *J* = 9 Hz, 1 H), 3.64 (d, *J* = 9 Hz, 1 H), 3.40 (m, 3 H), 1.86 (d, *J* = 2 Hz, 1 H), 1.10 (d, *J* = 7 Hz, 3 H), 0.55 (m, 1 H), 0.28 (d, *J* = 2 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$, DEPT): δ = 100.0 (C_{quat}), 95.8 (C_{quat}), 81.9 (CH), 74.9 (CH_2), 73.9 (CH_2), 73.7 (CH_2), 73.4 (CH_2), 59.8 (C_{quat}), 34.7 (CH), 23.2 (CH_2), 21.0 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 290 ([M^+], 16), 286 (2), 262 (8), 260 (8), 217 (7), 166 (7), 124 (100).

Cyclohexadiene Complexes 40 and 41

Enynene **20** (194 mg, 1.00 mmol) and $CpCo(CO)_2$ (127 μL, 171 mg, 0.95 mmol) were subjected to the general enynene cyclization conditions over 6 h. Chromatography on silica gel, eluting with Et_2O/hexane (3:7), afforded first **40** as an air-sensitive orange syrup; yield: 70 mg (27%, based on **20**).

^1H NMR (250 MHz, $CDCl_3$): δ = 4.97 (br s, 3 H), 4.90 (br s, 3 H), 4.62 (s, 5 H), 4.54 (m, 1 H), 4.16 (m, 1 H), 3.96 (m, 12 H), 3.48 (ABm, 2 H), 1.89 (d, *J* = 15 Hz, 1 H), 1.74 (br s, 9 H), 1.21 (d, *J* = 15 Hz, 1 H), 0.79 (s, 3 H).

MS (FAB, 70 eV): *m*/*z* (%) = 512 ([M^+], 83), 511 (100).

A second band contained **41**, also as an air-sensitive orange syrup; yield: 70 mg (27%, based on **20**).

^1H NMR (250 MHz, $CDCl_3$): δ = 4.96 (br s, 3 H), 4.87 (br s, 3 H), 4.63 (s, 5 H), 4.56 (m, 1 H), 4.30 (m, 1 H), 3.95 (m, 11 H), 3.47 (ABm, 2 H), 2.70 (d, *J* = 7.5 Hz, 1 H), 1.74 (br s, 9 H), 1.43 (s, 3 H), 1.03 (d, *J* = 15 Hz, 1 H), 0.06 (d, *J* = 15 Hz, 1 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 142.6, 142.51, 142.47, 111.94, 111.89, 111.55, 90.7, 85.5, 81.0, 75.8, 75.7, 74.89, 74.85, 74.52, 74.08, 68.6, 67.8, 66.7, 66.0, 51.0, 32.4, 29.2, 19.5 (br, 3 C).

HRMS (FAB, 70 eV): *m*/*z* [M^+] calcd for $C_{29}H_{41}CoO_4$: 512.2337; found: 512.2341.

Cyclohexadiene Complex 42

Enynene **21** (198 mg, 0.891 mmol) and $CpCo(CO)_2$ (51 μL, 69 mg, 0.38 mmol) were subjected to the general cyclization method over 6 h. Chromatography on silica gel, eluting with Et_2O/hexane (3:7), afforded **42** as an orange syrup; yield: 100 mg (46%).

^1H NMR (300 MHz, $CDCl_3$): δ = 5.37 (tsept, *J* = 7.0, 1.4 Hz, 1 H), 5.32 (tsept, *J* = 7.0, 1.4 Hz, 2 H), 4.51 (s, 5 H), 4.48 (d, *J* = 11.0 Hz, 1 H), 4.45 (d, *J* = 11.3 Hz, 1 H), 4.24 (d, *J* = 11.0 Hz, 1 H), 4.17 (m, 1 H), 4.10 (d, *J* = 11.4 Hz, 1 H), 4.09 (d, *J* = 9.7 Hz, 1 H), 4.04 (m, 3 H), 3.88 (m, 3 H), 3.82 (d, *J* = 10.0 Hz, 1 H), 3.52 (dd, *J* = 7.1, 7.1 Hz, 1 H), 3.25 (d, *J* = 10.1 Hz 1 H), 2.68 (dd, *J* = 11.5, 7.1 Hz, 1 H), 2.24 (dd, *J* = 11.5, 7.1 Hz, 1 H), 1.73 (s, 3 H), 1.72 (s, 6 H), 1.67 (s, 3 H), 1.65 (s, 3 H), 1.64 (s, 3 H), 1.10 (s, 3 H), 0.57 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$, DEPT): δ = 136.2 (C_{quat}), 135.8 (C_{quat}), 135.6 (C_{quat}), 121.9 (CH), 121.8 (CH), 121.6 (CH), 90.1 (C_{quat}), 87.4 (C_{quat}), 81.0 (CH), 74.1 (CH_2), 72.1 (CH_2), 70.2 (CH_2), 67.3 (CH_2), 67.2 (CH_2), 67.1 (CH_2), 66.6 (CH_2), 66.5 (C_{quat}), 66.1 (CH_2), 65.4 (C_{quat}), 61.1 (CH), 31.6 (CH_3), 28.8 (C_{quat}), 27.2 (CH_3), 25.76 (2 CH_3), 25.74 (CH_3), 18.09 (CH_3), 18.07 (2 CH_3).

Anal. Calcd for $C_{33}H_{49}CoO_4$: C, 69.70; H, 8.68. Found: C, 69.32; H, 8.63.

4-Methyl-3-(4,4-dimethyloxacyclopent-3-yl)furan (43)

Enynene **22** (2.381 g, 13.21 mmol) and $CpCo(CO)_2$ (381 μL, 514 mg, 2.86 mmol) were subjected to the general cyclization protocol over 10 h. Chromatography on silica gel, eluting with Et_2O/hexane (1:4), presented **43** as a colorless oil; yield: 1.856 g (78%).

IR (film): 2960, 2925, 2870, 1465, 1385, 1365, 1150, 1055, 920, 870, 790 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 7.17 (br s, 2 H), 4.18 (dd, *J* = 8.2, 8.0 Hz, 1 H), 3.82 (dd, *J* = 8.6, 8.5 Hz, 1 H), 3.63 (ABq, 2 H), 2.92 (dd, *J* = 8.3, 8.2 Hz, 1 H), 1.96 (s, 3 H), 1.09 (s, 3 H), 0.83 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.6, 139.4, 122.5, 120.3, 80.7, 73.1, 45.00, 41.9, 25.8, 21.6, 8.63.

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.43; H, 9.02.

Diene Complex 44

$CpCo(CH_2{=}CH_2)_2$ (100 mg, 0.56 mmol) and enynene **22** (101 mg, 0.56 mmol) were transformed according to the general cyclization routine over 1 d and subjected to chromatography on alumina, eluting with hexane/Et_2O (1:1), to secure **44** as a dark red oil; yield: 111 mg (65%).

IR (film): 3100, 2970, 2930, 2840, 1670, 1470, 1415, 1390, 1370, 1360, 1340, 1265, 1110, 1080, 1060, 1020, 950, 920, 890, 810, 760, 710 cm^{-1}.

^1H NMR (300 MHz, PhMe-d_8): δ = 4.63 (d, *J* = 8 Hz, 1 H), 4.61 (br s, 2 H), 4.37 (d, *J* = 8 Hz, 1 H), 4.35 (s, 5 H), 3.48 (ABq, 2 H), 3.45 (d, *J* = 8 Hz, 1 H), 3.21 (d, *J* = 8 Hz, 1 H), 1.78 (d, *J* = 4 Hz, 1 H), 1.22 (s, 3 H), 0.69 (d, *J* = 4 Hz, 1 H), 0.24 (s, 3 H).

^{13}C NMR (75 MHz, C_6D_6, DEPT): δ = 100.3 (C_{quat}), 94.8 (C_{quat}), 83.7 (CH_2), 82.2 (CH), 79.7 (CH_2), 75.3 (CH_2), 74.4 (CH_2), 65.0 (C_{quat}), 41.2 (C_{quat}), 29.8 (CH_3), 27.1 (CH_3), 22.0 (CH_2).

MS (EI, 70 eV): *m*/*z* (%) = 304 ([M^+], 39), 180 (36), 124 (100), 109 (89), 108 (78), 95 (56), 79 (56), 66 (55).

***cis*-3-(1-Methylethyl)-4-(4-methyltetrahydrofuran-3-yl)furan (45) and *trans*-3-(1-Methylethyl)-4-(4-methyltetrahydrofuran-3-yl)furan (46)**

Enynene **23** (230 mg, 1.18 mmol) and $CpCo(CO)_2$ (127 μL, 172 mg, 0.95 mmol) were subjected to the general cyclization technique over 10 h. The orange-brown crude product was chromatographed, eluting with Et_2O/hexane (1:9), to give an inseparable mixture of **45** and **46** in the ratio 55:45; yield: 54 mg (23%).

45

^1H NMR (300 MHz, $CDCl_3$): δ = 7.16 (br s, 1 H), 7.13 (br s, 1 H), 4.07 (dd, *J* = 8.0, 7.4 Hz, 1 H), 4.05 (dd, *J* = 8.0, 7.4 Hz, 1 H), 3.78 (dd, *J* = 7.9, 7.7 Hz, 1 H), 3.50 (dd, *J* = 8.3, 5.6 Hz, 1 H), 3.26 (ddd, *J* = 7.1, 7.1, 7.1 Hz, 1 H), 2.67 (sept, *J* = 6.6 Hz, 1 H), 2.52 (dddq, *J* = 7.0, 7.0, 6.9, 5.7 Hz, 1 H), 1.21 (d, *J* = 6.9 Hz, 3 H), 1.17 (d, *J* = 7.4 Hz, 3 H), 0.74 (d, *J* = 6.9 Hz, 3 H).

46

^1H NMR (300 MHz, $CDCl_3$): δ = 7.20 (br s, 1 H), 7.14 (br s, 1 H), 4.18 (dd, *J* = 7.9, 7.8 Hz, 1 H), 4.10 (dd, *J* = 8.1, 7.7 Hz, 1 H), 3.56 (dd, *J* = 8.3, 8.3 Hz, 1 H), 3.44 (dd, *J* = 8.2, 8.2 Hz, 1 H), 2.77 (ddd, *J* = 8.3, 8.1, 8.1 Hz, 1 H), 2.69 (sept, *J* = 6.6 Hz, 1 H), 2.26 (dddq, *J* = 7.8, 7.4, 7.3, 7.3 Hz, 1 H), 1.19 (d, *J* = 7.0 Hz, 3 H), 1.17 (d, *J* = 7.4 Hz, 3 H), 1.07 (d, *J* = 7.1 Hz, 3 H).

Diene Complexes 47 and 48

$CpCo(CH_2{=}CH_2)_2$ (100 mg, 0.56 mmol) and enynene **32** (92 mg, 0.56 mmol) were transformed according to the general cyclization scheme over 1 d and subjected to chromatography on alumina, eluting with hexane/Et_2O (1:1), to yield an inseparable mixture of **47** and **48** in a 2:1 ratio as a dark red oil; yield: 145 mg (86%).

IR (film): 2970, 2930, 2860, 1740, 1470, 1270, 1110, 1090, 1080, 1020, 920, 810, 750 cm^{-1}.

^1H NMR (300 MHz, PhMe-d_8; tentative assignments): δ (**47**) = 4.65 (m, 2 H), 4.36 (s, 5 H), 3.65 (ABq, 2 H), 2.4–1.2 (m, 6 H), 1.92 (br s, 1 H), 1.18 (d, *J* = 7 Hz, 3 H), 0.65 (m, 1 H), 0.47 (br s, 1 H); δ (**48**) = 4.43 (m, 2 H), 4.41 (s, 5 H), 3.48 (m, 2 H), 2.4–1.2 (m, 6 H), 1.78 (br s, 1 H), 1.10 (d, *J* = 7 Hz, 3 H), 0.92 (m, 1 H), 0.36 (br s, 1 H).

^{13}C NMR (75 MHz, C_6D_6, DEPT): δ = 103.6 (C_{quat}), 99.3 (C_{quat}), 99.1 (C_{quat}), 97.6 (C_{quat}), 82.1 (CH), 81.3 (CH), 75.6 (CH_2), 73.9 (CH_2, 2 C), 73.7 (CH_2), 60.5 (br, C_{quat}, 2 C), 35.5 (CH_2), 34.8 (CH_2), 34.2 (CH), 32.8 (CH_2), 31.7 (CH), 26.7 (br, CH_2, 2 C), 23.9 (CH_2), 23.5 (CH_2), 23.3 (CH_3), 21.9 (CH_2), 21.0 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 288 ([M⁺], 74), 271 (33), 269 (30), 203 (100), 124 (65), 91 (57), 79 (43), 59 (50).

Anal. Calcd for $C_{16}H_{21}CoO$: C, 66.66; H, 7.34. Found: C, 66.75; H, 7.68.

3-(2,2-Dimethylcyclopentyl)-4-methylfuran (49)

Enynene **33** (250 mg, 1.40 mmol) and $CpCo(CO)_2$ (76 μL, 103 mg, 0.57 mmol) were subjected to the general cyclization protocol over 6 h. Chromatography on silica gel, eluting with hexane, produced **49** as a colorless oil; yield: 153 mg (59%).

IR (film): 2955, 2925, 2870, 1465, 1380, 1365, 1155, 1055, 850, 785 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 7.13 (s, 2 H), 2.52 (dd, *J* = 10.4, 7.8 Hz, 1 H), 2.00 (m, 1 H), 1.94 (s, 3 H), 1.70 (m, 3 H), 1.56 (m, 2 H), 0.97 (s, 3 H), 0.72 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$, DEPT): δ = 139.7 (CH), 138.9 (CH), 125.9 (C_{quat}), 120.6 (C_{quat}), 45.2 (CH), 41.8 (CH_2), 41.3 (C_{quat}), 31.8 (CH_2), 28.6 (CH_3), 23.0 (CH_3), 21.3 (CH_2), 8.85 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 178 ([M⁺], 91), 163 (26), 135 (34), 122 (24), 109 (33), 108 (29), 96 (100), 71 (35).

HRMS (EI, 70 eV): *m*/*z* [M⁺] calcd for $C_{12}H_{18}O$: 178.1358; found: 178.1358.

Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.96; H, 10.09.

Diene Complexes 50 and 51

Enynene **34** (600 mg, 3.37 mmol) and $CpCo(CO)_2$ (431 μL, 582 mg, 3.23 mmol) were subjected to the general cyclization routine over 8.5 h. Chromatography on silica gel, eluting with Et_2O/hexane (1:20), gave first **51**, followed by **50** as orange oils.

50

Yield: 446 mg (46%).

^1H NMR (300 MHz, C_6D_6): δ = 4.38 (s, 5 H), 3.81 (s, 2 H), 3.58 (apparent d, *J* = 3.3 Hz, 2 H), 2.38 (m, 4 H), 1.85 (m, 2 H), 1.83 (d, *J* = 1.9 Hz, 1 H), 1.70 (m, 1 H), 1.49 (m, 1 H), 1.17 (d, *J* = 7.0 Hz, 3 H), 0.81 (qd, *J* = 6.9, 3.4 Hz, 1 H), 0.45 (br s, 1 H).

^{13}C NMR (75 MHz, C_6D_6, DEPT): δ = 97.3 (C_{quat}), 91.0 (C_{quat}), 81.8 (CH), 73.3 (CH_2), 71.9 (CH_2), 61.9 (C_{quat}), 34.9 (CH), 32.8 (CH_2), 31.0 (CH_2), 28.4 (CH_2), 24.4 (CH_2), 23.6 (CH_2), 20.0 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 302 ([M⁺], 92), 300 (39), 243 (30), 230 (53), 124 (100), 73 (88), 59 (64).

51

Yield: 268 mg (27%).

^1H NMR (300 MHz, C_6D_6): δ = 4.50 (s, 5 H), 4.48 (d, *J* = 9.7 Hz, 1 H), 4.42 (dd, *J* = 7.7, 7.5 Hz, 1 H), 3.61 (ABq, 2 H), 2.50 (m, 1 H), 2.08–1.51 (m, 8 H), 1.76 (br s, 1 H), 0.42 (d, *J*= 6.9 Hz, 3 H), 0.11 (br s, 1 H).

^{13}C NMR (75 MHz, C_6D_6, DEPT): δ = 95.9 (C_{quat}), 89.1 (C_{quat}), 82.1 (CH), 77.7 (CH_2), 77.1 (CH_2), 64.2 (C_{quat}), 40.5 (CH), 32.6 (CH_2), 31.4 (CH_2), 29.7 (CH_2), 24.2 (CH_2), 23.5 (CH_2), 22.0 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 302 ([M⁺], 73), 300 (63), 243 (30), 230 (37), 124 (100), 59 (82).

(*E*)-3-Methyl-4-(2-methylenecyclohexylidene)oxacyclopentane (52)

Note: Because of the air-sensitivity of **52**, all operations were carried out under argon in degassed solvents. To a mixture of **50** and **51** (1.7:1, 516 mg, 1.71 mmol) in DME (15 mL) at r.t. was added $CuCl_2{\cdot}2H_2O$ (1.023 g, 6.00 mmol) in one portion. The resulting green solution was stirred for 15 min, followed by the addition of hexane (30 mL) and H_2O (100 mL). The mixture was shaken in a separatory funnel, the sequestered organic layer washed with H_2O (50 mL), dried ($MgSO_4$), filtered, concentrated in vacuo, and chromatographed on silica gel, eluting with Et_2O/hexane (1:9), to afford **52** as an air-sensitive colorless oil; yield: 161 mg (53%).

IR (film): 3075, 2930, 2850, 1633, 1444, 1370, 1098, 1085, 1077, 1043, 972, 925, 895, 822, 700 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 4.82 (br s, 1 H), 4.78 (br s, 1 H), 4.39 (d, *J* = 13.0 Hz, 1 H), 4.24 (d, *J* = 13.0 Hz, 1 H), 3.83 (dd, *J* = 8.3, 5.9 Hz, 1 H), 3.56 (dd, *J* = 8.3, 2.9 Hz, 1 H), 3.03 (m, 1 H), 2.26 (m, 1 H), 2.03 (m, 3 H), 1.68 (m, 2 H), 1.52 (m, 2 H), 1.05 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$, DEPT): δ = 149.2 (C_{quat}), 136.2 (C_{quat}), 131.3 (C_{quat}), 109.0 (CH_2), 76.0 (CH_2), 69.6 (CH_2), 37.4 (CH_2), 36.1 (CH), 33.3 (CH_2), 27.9 (CH_2), 26.9 (CH_2), 18.7 (CH_3).

Anal. Calcd for $C_{12}H_{18}O_2$: C, 80.85; H, 10.18. Found: C, 80.85; H, 10.16.

3-Methyl-4-[(1*R,3a*S**,7a*S**)-7a-methyloctahydro-1-indenyl]furan and (53) 3-Methyl-4-[(1*S**,3a*S**,7a*S**)-7*a*-methyloctahydro-1-indenyl]furan (54)**

Enynene **35** (380 mg, 1.74 mmol) and $CpCo(CO)_2$ (178 μL, 240 mg, 1.34 mmol) were subjected to the general cyclization conditions over 5 h. Chromatography on silica gel, eluting with hexane, afforded an inseparable (except by GC) mixture of **53** and **54** as a colorless oil, in the ratio 4:1, as determined by capillary GC and ^1H NMR spectroscopy; yield: 221 mg (58%).

IR (film): 2950, 2930, 2870, 1462, 1445, 1372, 1153, 1055, 855, 783 cm^{-1}.

53

^1H NMR (300 MHz, C_6D_6; assigned from the mixture of **53** and **54**): δ = 7.14 (d, *J* = 1.5 Hz, 1 H), 7.08 (m, 1 H), 2.51 (dd, *J* = 10.6, 8.9 Hz, 1 H), 1.94 (m, 1 H), 1.84 (d, *J* = 1.0 Hz, 3 H), 1.72–1.00 (m, 12 H), 0.91 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$, DEPT; assigned from the mixture of **53** and **54**): δ = 139.86 (CH), 138.79 (CH), 124.63 (C_{quat}), 120.66 (C_{quat}), 47.5 (CH), 45.5 (CH), 42.3 (C_{quat}), 29.4 (CH_2), 28.05 (CH_2), 25.1 (CH_2), 24.8 (CH_2), 23.4 (CH_3), 21.8 (CH_2), 20.7 (CH_2), 8.84 (CH_3).

GCMS: *m*/*z* (%) = 218 ([M$^+$], 18), 203 (5), 122 (14), 109 (31), 108 (100), 96 (38), 95 (11), 79 (16), 77 (10), 41 (14).

54

^{1}H NMR (300 MHz, C_6D_6; assigned from the mixture of **53** and **54**): δ = 7.11 (d, *J* = 1.4 Hz, 1 H), 7.06 (m, 1 H), 2.93 (dd, *J* = 8.8, 8.6 Hz, 1 H), 2.11 (m, 1 H), 1.83 (d, *J* = 2.0 Hz, 3 H), 1.72–1.00 (m, 12 H), 0.75 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$, DEPT; assigned from the mixture of **53** and **54**): δ = 139.94 (CH), 138.75 (CH), 124.76 (C_{quat}), 120.78 (C_{quat}), 45.2 (CH), 43.6 (C_{quat}), 39.2 (CH), 34.3 (CH_2), 29.9 (CH_2), 28.9 (CH_2), 28.09 (CH_2), 24.3 (CH_2), 24.0 (CH_3), 22.4 (CH_2), 8.88 (CH_3).

GCMS: *m*/*z* (%) = 218 ([M$^+$], 16), 122 (12), 108 (100), 96 (28), 79 (16), 77 (10), 41 (15).

Anal. Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.27; H, 10.13.

(1*R,3a*S**,7a*S**)-7a-Methyloctahydroindene-1-carboxylic Acid (55) and (1*S**,3a*S**,7a*S**)-7a-Methyloctahydroindene-1-carboxylic Acid (56)**

Ozone was passed through a mixture of **53** and **54** (4:1, 320 mg, 1.47 mmol) in CH_2Cl_2 (15 mL) at –78 °C until a green color persisted. Excess ozone was purged with O_2, the solution warmed to r.t., and the solvent removed in vacuo to give a yellow oil. The residue was stirred with added H_5IO_6 (1.071 g, 4.698 mmol), acetone (3 mL), and aq H_2SO_4 (6 M, 2 mL) for 6 h, the solution partitioned between H_2O (50 mL) and Et_2O (20 mL) with shaking, and the separated aqueous phase washed with Et_2O (3 × 15 mL). The combined organic layers were extracted with sat. aq $NaHCO_3$ (2 × 25 mL) and the resulting basic solution acidified to pH 2 with aq 6 N HCl. This mixture was washed with Et_2O (4 × 10 mL), and the combined Et_2O solutions were dried ($MgSO_4$), filtered, and concentrated in vacuo to afford a 4:1 mixture of **55** and **56** as a waxy pink solid, used as such in their conversion into **57** and **58**; yield: 203 mg (76%).

IR (KBr): 3000 (br), 2973, 2930, 2860, 1705, 1465, 1455, 1420, 1380, 1290, 1255, 1235, 1123, 1083, 1047, 890, 875 cm^{-1}.

55

^{1}H NMR (300 MHz, $CDCl_3$; assigned from the mixture of **55** and **56**): δ = 2.52 (dd, *J* = 9.0, 8.8 Hz, 1 H), 2.09 (m, 1 H), 1.97–1.08 (m, 13 H), 1.19 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$, DEPT; assigned from the mixture of **55** and **56**): δ = 180.63 (C_{quat}), 56.4 (CH), 45.9 (C_{quat}), 43.7 (CH), 27.81 (CH_2), 25.7 (CH_2), 24.04 (CH_2), 23.59 (CH_3), 23.55 (CH_2), 21.77 (CH_2), 20.10 (CH_2).

56

^{1}H NMR (300 MHz, $CDCl_3$; assigned from the mixture of **55** and **56**): δ = 2.81 (dd, *J* = 8.8, 7.8 Hz, 1 H), 2.09 (m, 1 H), 1.97–1.08 (m, 13 H), 0.93 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$, DEPT; assigned from the mixture of **55** and **56**): δ = 181.95 (C_{quat}), 49.06 (CH), 46.1 (CH), 45.0 (C_{quat}), 34.1 (CH_2), 28.33 (CH_2), 28.07 (CH_2), 24.11 (CH_2), 23.69 (CH_3), 21.88 (CH_2); one signal could not be located.

1-[(1*R,3a*S**,7a*S**)-7a-Methyloctahydroinden-1-yl]-1-ethanone (57) and 1-[(1*S**,3a*S**,7a*S**)-7a-Methyloctahydroinden-1-yl]-1-ethanone (58)**

To a stirred mixture of **55** and **56** (4:1, 148 mg, 0.812 mol) in THF (10 mL) at 0 °C was added MeLi (2.14 mL, 1.4 M in hexane, 3.00 mmol) via syringe over 30 sec. After 2 h, TMSCl (444 μL, 380 mg, 3.50 mmol) was introduced rapidly via syringe and the mixture allowed to warm to r.t. Treatment with aq 1 N HCl (15 mL) was followed by vigorous stirring of the resulting biphasic mixture for 4.5 h. The layers were separated, and the aqueous phase was extracted with Et_2O (3 × 20 mL). The combined organic portions were dried ($MgSO_4$), filtered, and concentrated in vacuo to afford a pink oil. This material was chromatographed on silica gel, eluting with Et_2O/hexane (1:9), to give a 4:1 mixture of **57** and **58** as a pink oil; yield: 62 mg (42%).

IR (film): 2960, 2930, 2860, 1705, 1470, 1450, 1355, 1210, 1165 cm^{-1}.

57

^{1}H NMR (300 MHz, $CDCl_3$/TMS; assigned from the mixture of **57** and **58**): δ = 2.69 (dd, *J* = 9.1, 9.0 Hz, 1 H), 2.13 (s, 3 H), 2.09 (m, 1 H), 1.73–0.88 (m, 13 H), 1.25 (s, 3 H) (Lit.[37] δ = 1.27).

58

^{1}H NMR (300 MHz, $CDCl_3$/TMS; assigned from the mixture of **57** and **58**): δ = 2.98 (dd, *J* = 9.0, 7.2 Hz, 1 H), 2.12 (s, 3 H), 2.09 (m, 1 H), 1.73–0.88 (m, 13 H), 0.87 (s, 3 H) (Lit.[37] δ = 0.88).

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Supporting Information

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References

(1) For pertinent reviews, see: (a) Liu, X.; Li, B.; Liu, Q. *Synthesis* **2019**, *51*, 1293. (b) Ai, W.; Zhong, R.; Liu, X.; Liu, Q. *Chem. Rev.* **2019**, *119*, 2876. (c) Hirano, M. *ACS Catal.* **2019**, *9*, 1408. (d) Pellissier, H. *Coord. Chem. Rev.* **2018**, *360*, 122. (e) Hu, Y.; Bai, M.; Yang, Y.; Zhou, Q. *Org. Chem. Front.* **2017**, *4*, 2256. (f) Chen, W.-W.; Xu, M.-H. *Org. Biomol. Chem.* **2017**, *15*, 1029. (g) Roese, P.; Hilt, G. *Synthesis* **2016**, *48*, 463. (h) Stathakis, C. I.; Gkizis, P. L.; Zografos, A. L. *Nat. Prod. Rep.* **2016**, *33*, 1093. (i) Gandeepan, P.; Cheng, C.-H. *Acc. Chem. Res.* **2015**, *48*, 1194. (j) Micalizio, G. C.; Hale, S. B. *Acc. Chem. Res.* **2015**, *48*, 663. (k) Aissa, C. *Synlett* **2014**, *25*, 2379. (l) Müller, T. J. J. In *Molecular Catalysts: Structure and Functional Design*; Gade, L. H.; Hofmann, P., Ed.; Wiley-VCH: Weinheim, **2014**, 255. (m) Saito, N.; Tanaka, D.; Mori, M.; Sato, Y. *Chem. Rec.* **2011**, *11*, 186. (n) Watson, I. D. G.; Toste, F. D. *Chem. Sci.* **2012**, *3*, 2899. (o) Watson, I. D. G.; Toste, F. D. In *Science of Synthesis, Stereoselective Synthesis, Vol. 3*; Evans, P. A., Ed.; Thieme: Stuttgart, **2011**, 243. (p) Gandon, V.; Thorimbert,

S.; Malacria, M. In *Science of Synthesis, 1,3-Dienes, Vol. 46*; Rawal, V. H.; Kozmin, S. A., Ed.; Thieme: Stuttgart, **2009**, 173. (q) Kulkarni, A. A.; Daugulis, O. *Synthesis* **2009**, 4087. (r) Jeganmohan, M.; Cheng, C.-H. *Chem. Eur. J.* **2008**, *14*, 10876. (s) Michelet, V.; Toullec, P. Y.; Genêt, J.-P. *Angew. Chem. Int. Ed.* **2008**, *47*, 4268. (t) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326. (u) Echavarren, A. M.; Nevado, C.; Nieto-Oberhuber, C.; Muñoz, M. P.; López, S. In *NATO Science Series, II: Mathematics, Physics and Chemistry, New Methodologies and Techniques for a Sustainable Organic Chemistry, Vol. 246*; Mordini, A.; Faigl, F., Ed.; Springer: Dordrecht, **2008**, 246 99. (v) Bruneau, C. In *Metathesis Chemistry: From Nanostructure Design to Synthesis of Advanced Materials*; İmamoğlu, Y.; Dragutan, V., Ed.; Springer: Dordrecht, **2007**, 375. (w) Bruneau, C. *Angew. Chem. Int. Ed.* **2005**, *44*, 2328. (x) Yamamoto, Y.; Itoh, K. In *Ruthenium in Organic Synthesis*; Murahashi, S. I., Ed.; Wiley-VCH: Weinheim, **2004**, 95. (y) Aubert, C.; Buisine, O.; Malacria, M. *Chem. Rev.* **2002**, *102*, 813.

(2) For a recent topical review, see: Domínguez, G.; Pérez-Castells, J. *Chem. Eur. J.* **2016**, *22*, 6720.

(3) Himes, R. A.; Fanwick, P. E.; Rothwell, I. P. *Chem. Commun.* **2003**, 18.

(4) Shibata, T.; Tahara, Y.; Tamura, K.; Endo, K. *J. Am. Chem. Soc.* **2008**, *130*, 3451.

(5) Sagae, H.; Noguchi, K.; Hirano, M.; Tanaka, K. *Chem. Commun.* **2008**, 3804.

(6) Interestingly, the same catalyst causes the analogous intermolecular reaction of enynes with ethene to generate only β-hydride elimination products.

(7) (a) Saito, N.; Ichimaru, T.; Sato, Y. *Chem. Asian J.* **2012**, *7*, 1521. (b) Interestingly, the analogous intermolecular reaction of enallenes with alkenes in the presence of a Ni catalyst results in only β-hydride elimination products: Noucti, N. N.; Alexanian, E. J. *Angew. Chem. Int. Ed.* **2013**, *52*, 8424.

(8) Perekalin, D. S.; Shvydkiy, N. V.; Nelyubina, Y. V.; Kudinov, A. R. *Chem. Eur. J.* **2015**, *21*, 16344.

(9) Suleymanov, A. A.; Vasilyev, D. V.; Novikov, V. V.; Nelyubina, Y. V.; Perekalin, D. S. *Beilstein J. Org. Chem.* **2017**, *13*, 639.

(10) Oonishi, Y.; Hato, Y.; Sato, Y. *Adv. Synth. Catal.* **2016**, *358*, 2273.

(11) For the precedent-setting cycloisomerization of 1,n-enynes in the presence of stoichiometric $CpCo(CO)_2$ to give CpCo(1,3-diene) complexes, see: Buisine, O.; Aubert, C.; Malacria, M. *Chem. Eur. J.* **2001**, *7*, 3517; and references cited therein.

(12) See SI in: Clavier, H.; Correa, A.; Escudero-Adán, E. C.; Benet-Buchholz, J.; Cavallo, L.; Nolan, S. P. *Chem. Eur. J.* **2009**, *15*, 10244.

(13) Sashuk, V.; Grela, K. *J. Mol. Catal. A: Chem.* **2006**, *257*, 59.

(14) Wiggins, L. F.; Wood, D. J. C. *J. Chem. Soc.* **1949**, 2371.

(15) Marco-Contelles, J. *Synth. Commun.* **1997**, *27*, 3163.

(16) (a) Yamazaki, H.; Hagihara, N. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 2260. (b) See also: Wakatsuki, Y.; Aoki, K.; Yamazaki, H. *J. Am. Chem. Soc.* **1979**, *101*, 1123.

(17) (a) Cammack, J. K.; Jalisatgi, S.; Matzger, A. J.; Negrón, A.; Vollhardt, K. P. C. *J. Org. Chem.* **1996**, *61*, 4798. (b) King, J. A.; Vollhardt, K. P. C. *J. Organomet. Chem.* **1993**, *460*, 91.

(18) Fritch, J. R.; Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 559.

(19) See, for example: (a) Tamao, K.; Kobayashi, K.; Ito, Y. *J. Am. Chem. Soc.* **1988**, *110*, 1286. (b) Grigg, R.; Scott, R.; Stevenson, P. *Tetrahedron Lett.* **1982**, *23*, 2691.

(20) $J_{H3,4cis} \cong J_{H3,4trans}$ in substituted tetrahydrofurans: (a) Wu, A.; Cremer, D. *Int. J. Mol. Sci.* **2003**, *4*, 158. (b) Dana, G.; Touboul, E.; Convert, O.; Pascal, Y. L. *Tetrahedron* **1988**, *44*, 429. (c) Lambert, J. B.; Papay, J. J.; Khan, S. A.; Kappauf, K. A.; Magyar, E. S. *J. Am. Chem. Soc.* **1974**, *96*, 611 .

(21) Inspired by: Bednarski, M.; Danishefsky, S. *J. Am. Chem. Soc.* **1986**, *108*, 7060.

(22) Meyers, A. I.; Mihelich, E. D.; Kamata, K. *J. Chem. Soc., Chem. Commun.* **1974**, 768.

(23) Hine, J.; Hahn, S. *J. Org. Chem.* **1982**, *47*, 1738.

(24) Wolinsky, L. E.; Faulkner, D. J.; Finer, J.; Clardy, J. *J. Org. Chem.* **1976**, *41*, 697.

(25) CCDC 1948834 (**38**) contains the supplementary crystallographic data for this paper. They can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/getstructures.

(26) (a) Transition-metal-catalyzed cycloisomerizations of allyl propargyl ethers typically stop at the 3,4-dimethylidenetetrahydrofuran stage, see refs 9 and 10, and a review, ref. 1p. (b) For an exception that features furan formation, see: Kawai, H.; Oi, S.; Inoue, Y. *Heterocycles* **2006**, *67*, 101.

(27) (a) Hartwig, J. F. *Organotransition Metal Chemistry: From Bonding to Catalysis*; University Science Books: Sausalito, **2009**. For selected DFT treatments of (possibly) relevant analogous steps, see: (b) Yang, T.; Ehara, M. *J. Org. Chem.* **2017**, *82*, 2150. (c) Kiyota, S.; In, S.; Komine, N.; Hirano, M. *Chem. Lett.* **2017**, *46*, 1040. (d) Mekareeya, A.; Walker, P. R.; Couce-Rios, A.; Campbell, C. D.; Steven, A.; Paton, R. S.; Anderson, E. A. *J. Am. Chem. Soc.* **2017**, *139*, 10104. (e) Hirano, M.; Ueda, T.; Komine, N.; Komiya, S.; Nakamura, S.; Deguchi, H.; Kawauchi, S. *J. Organomet. Chem.* **2015**, *797*, 174. (f) Liu, T.; Han, L.; Han, S.; Bi, S. *Organometallics* **2015**, *34*, 280. (g) Dachs, A.; Pla-Quintana, A.; Parella, T.; Solà, M.; Roglans, A. *Chem. Eur. J.* **2011**, *17*, 14493. (h) Lebœuf, D.; Iannazzo, L.; Geny, A.; Malacria, M.; Vollhardt, K. P. C.; Aubert, C.; Gandon, V. *Chem. Eur. J.* **2010**, *16*, 8904. (i) Montero-Campillo, M. M.; Rodríguez-Otero, J.; Cabaleiro-Lago, E. *J. Phys. Chem. A* **2008**, *112*, 2423. (j) Aubert, C.; Gandon, V.; Geny, A.; Heckrodt, T. J.; Malacria, M.; Paredes, E.; Vollhardt, K. P. C. *Chem. Eur. J.* **2007**, *13*, 7466. (k) Geny, A.; Lebœuf, D.; Rouquié, G.; Vollhardt, K. P. C.; Malacria, M.; Gandon, V.; Aubert, C. *Chem. Eur. J.* **2007**, *13*, 5408. (l) Gandon, V.; Agenet, N.; Vollhardt, K. P. C.; Malacria, M.; Aubert, C. *J. Am. Chem. Soc.* **2006**, *128*, 8509.

(28) Baldridge, K. K.; O'Connor, J. M.; Chen, M.-C.; Siegel, J. S. *J. Phys. Chem. A* **1999**, *103*, 10126.

(29) (a) Li, L.; Zhu, X.-Q.; Zhang, Y.-Q.; Bu, H.-Z.; Yuan, P.; Chen, J.; Su, J.; Deng, X.; Ye, L.-W. *Chem. Sci.* **2019**, *10*, 3123. (b) Kwart, H.; Miles, W. H.; Horgan, A. G.; Kwart, L. D. *J. Am. Chem. Soc.* **1981**, *103*, 1757.

(30) For some pertinent examples, see: (a) Aubert, C.; Gandon, V.; Han, S.; Johnson, B. M.; Malacria, M.; Schömenauer, S.; Vollhardt, K. P. C.; Whitener, G. D. *Synthesis* **2010**, 2179. (b) Amslinger, S.; Aubert, C.; Gandon, V.; Malacria, M.; Paredes, E.; Vollhardt, K. P. C. *Synlett* **2008**, 2056; and references cited therein. (c) Duñach, E.; Halterman, R. L.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1985**, *107*, 1664. (d) Malacria, M.; Vollhardt, K. P. C. *J. Org. Chem.* **1984**, *49*, 5010. (e) Sternberg, E. D.; Vollhardt, K. P. C. *J. Org. Chem.* **1984**, *49*, 1574. (f) Sternberg, E. D.; Vollhardt, K. P. C. *J. Org. Chem.* **1984**, *49*, 1564. (g) Gadek, T. R.; Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 802.

(31) For a related scenario see: Yamamoto, Y.; Kuwabara, S.; Ando, Y.; Nagata, H.; Nishiyama, H.; Itoh, K. *J. Org. Chem.* **2004**, *69*, 6697.

(32) For selected pertinent discussions of steric and electronic effects on β-hydride eliminations, see: (a) Chen, Z.-M.; Liu, J.; Guo, J.-Y.; Loch, M.; DeLuca, R. J.; Sigman, M. S. *Chem. Sci.* **2019**, *10*, 7246; and references cited therein. (b) Giri, R.; Shekhar, K. C. *J. Org. Chem.* **2018**, *83*, 3013. (c) Hong, X.; Liu, P.; Houk, K. N. C. *J. Am. Chem. Soc.* **2013**, *135*, 1456. (d) Jana, R.; Pathak, T. P.; Sigman, M. S. *Chem. Rev.* **2011**, *111*, 1417. (e) Lu, X. *Top. Catal.* **2005**, *35*, 73. (f) Trost, B. M.; Romero, D. L.; Rise, F. *J. Am. Chem. Soc.* **1994**, *116*, 4268. (g) Trost, B. M.; Tanoury, G. J.; Lautens, M.; Chan, C.; MacPherson, D. T. *J. Am. Chem. Soc.* **1994**, *116*, 4255. (h) Trost, B. M.; Lautens, M.; Chan, C.; Jebaratnam, D. J.; Mueller, T. *J. Am. Chem. Soc.* **1991**, *113*, 636. (i) Trost, B. M.; Lee, D. C.; Rise, F. *Tetrahedron Lett.* **1989**, *30*, 651. (j) Doherty, N. M.; Bercaw, J. E. *J. Am. Chem. Soc.* **1985**, *107*, 2670.

(33) (a) Ventre, S.; Simon, C.; Rekhroukh, F.; Malacria, M.; Amatore, M.; Aubert, C.; Petit, M. *Chem. Eur. J.* **2013**, *19*, 5830. (b) Grigg, R.; Scott, R.; Stevenson, P. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1365.

(34) Inubushi, Y.; Kikuchi, T.; Ibuka, T.; Tanaka, K.; Saji, I.; Tokane, K. *Chem. Pharm. Bull.* **1974**, *22*, 349.

(35) Bednarski, M.; Danishefsky, S. *J. Am. Chem. Soc.* **1986**, *108*, 7060.

(36) These acids are described in the literature, but without NMR spectral data: (a) Los, M. US Patent 3331856, **1967**. (b) Raymahasay, S.; Sengupta, S. K.; Bhattacharyya, B. K. *J. Indian Chem. Soc.* **1959**, *36*, 765.

(37) Rubottom, G. M.; Kim, C.-W. *J. Org. Chem.* **1983**, *48*, 1550.

(38) (a) Lansbury, P. T.; Demmin, T. R.; DuBois, G. E.; Haddon, V. R. *J. Am. Chem. Soc.* **1975**, *97*, 394. (b) Lansbury, P. T.; Briggs, P. C.; Demmin, T. R.; DuBois, G. E. *J. Am. Chem. Soc.* **1971**, *93*, 1311. (c) Zeeh, B.; Jones, G.; Djerassi, C. *Chem. Ber.* **1968**, *101*, 1018.

(39) Black, H. K.; Weedon, B. C. L. *J. Chem. Soc.* **1953**, 1785.

(40) Modified from: Barbot, F.; Dauphin, B.; Miginiac, P. *Synthesis* **1985**, 768.

(41) Padwa, A.; Meske, M.; Murphree, S. S.; Watterson, S. H.; Ni, Z. *J. Am. Chem. Soc.* **1995**, *117*, 7071.

(42) Kitamura, T.; Sato, Y.; Mori, M. *Adv. Synth. Catal.* **2002**, *344*, 678.

(43) Grdina, M. B.; Orfanopoulos, M.; Stephenson, L. M. *J. Org. Chem.* **1979**, *44*, 2936.

(44) (a) Ikeda, T.; Yue, S.; Hutchinson, C. R. *J. Org. Chem.* **1985**, *50*, 5193. (b) In addition to the preparation of 2-(2-methylidenecyclohexyl)ethanol, this paper describes its conversion into the bromide (characterized only by ^{1}H NMR) via the corresponding unisolated methanesulfonate.