DOI: 10.1002/chem.200601823

Cobalt-Mediated [2+2+2] Cycloaddition versus C–H and N–H Activation of Pyridones and Pyrazinones with Alkynes: An Experimental Study

Corinne Aubert,[a] Patrick Betschmann,[b] Michael J. Eichberg,[b] Vincent Gandon,[a] Thilo J. Heckrodt,[b] Jürg Lehmann,[b] Max Malacria,[a] Birgit Masjost,[b] Elisa Paredes,[b] K. Peter C. Vollhardt,*[b] and Glenn D. Whitener[b]

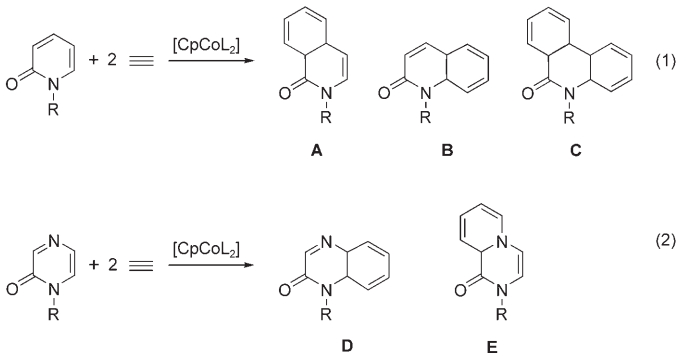
Abstract: The reactivity of a range of pyridone and pyrazinone derivatives towards alkynes in the presence of cyclopentadienylcobaltbis(ethene) has been investigated. Depending on the nature of the substrates, [2+2+2]- or [2+2] cycloaddition, C–H, or N–H activation may occur. In the case of pyridones, the first three predominated with N-protected derivatives, whereas substrates containing N–H bonds followed an N–H activation pathway. The [2+2+2] cycloaddition of an *N*-butynylisoquinolone was applied successfully to the total synthesis of anhydrolycorinone. Pyrazinone substrates showed similar patterns of reactivity.

Keywords: C–H activation · cobalt · cycloaddition · heterocycles · N–H activation

Introduction

Nitrogen-containing heterocycles are present in a multitude of biologically important molecules with extremely diverse physiological activity. They are also of great importance in medicinal chemistry because of their pharmacological potential. Hence, the development of novel methods directed at the synthesis of new azacycles is of great interest. We have been engaged in the cobalt-mediated activation of double bonds in aromatic heterocycles toward the [2+2+2] cycloaddition with alkynes.[1] Remarkably, even though resonance stabilized, these systems participate readily in such cyclizations. Thus, this methodology has been applied to furans,[2] benzofurans,[3] thiophenes,[2] indoles,[4] pyrroles,[5] imidazoles,[6] and pyrimidines,[7] giving rise to fused dihydroheteroaromatics that are largely inaccessible by conventional methods. The success of these transformations led us to consider, initially, pyridine and pyrazine as potential cyclization partners and, eventually, their more reactive pyridone and pyrazinone analogues. These nuclei play a key role in medicinal chemistry and are often incorporated in active pharmaceutical ingredients.[8] They are also present in a vast variety of biologically active natural products.[9] Therefore, cycloadditions of the generic type illustrated in Scheme 1 promised to provide not only access to novel azapolycycles, but also further insights into the scope of the methodology.

Moreover, pyridines (and pyridones) can themselves be constructed by cobalt- (and other metal-) catalyzed alkyne cooligomerizations with nitriles and isocyanates, respective-



Scheme 1. Generic cobalt-mediated [2+2+2] cycloadditions of ethyne to pyridone [Eq. (1)] and pyrazinone [Eq. (2)].

[a] Dr. C. Aubert, Dr. V. Gandon, Prof. Dr. M. Malacria
Université Pierre et Marie Curie-Paris 6
Laboratoire de Chimie Organique (UMR CNRS 7611)
Institut de Chimie Moléculaire (FR 2769), case. 229
4 place Jussieu, 75252 Paris cedex 05 (France)

[b] Dr. P. Betschmann, Dr. M. J. Eichberg, Dr. T. J. Heckrodt, Dr. J. Lehmann, Dr. B. Masjost, Dr. E. Paredes, Prof. Dr. K. P. C. Vollhardt, Dr. G. D. Whitener
Department of Chemistry, University of California at Berkeley and the Chemical Sciences Division, Lawrence Berkeley National Laboratory, Berkeley, CA 94720–1460 (USA)
Fax: (+1) 510-643-5208
E-mail: kpcv@berkeley.edu

 © 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim WILEY InterScience DISCOVER SOMETHING GREAT

ly,[10] opening an avenue to sequential cyclizations with even greater changes in complexity. Herein, we report the results of our initial forays into this chemistry, which revealed a puzzling divergence in reactivity from the expected [2+2+2] cycloaddition mode to one in which C–H or N–H bond activation with simultaneous double alkyne insertion took place, depending on the nature of the substrates.

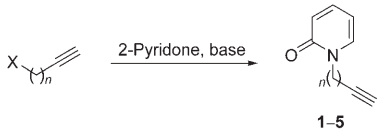
Results and Discussion

Initial attempts: Early experiments revealed that pyridine and pyrazine themselves do not enter into the cobalt-mediated [2+2+2] cycloaddition, even under conditions that have proven to be most favorable for these reactions in other cases. It was hoped, however, that some type of activation might render the heterocycles more compliant. Unfortunately, focusing on the pyridine nucleus, neither modification to pyridinium salts, nor precomplexation to osmium[11] were productive. Inspired by previous findings that the (formal) enamine double bond needs to be alkanoylated to render it a successful cocyclization partner,[4,6,12] it was decided to switch to the oxo derivatives of pyridine and pyrazine as substrates. Such a change is known to attenuate aromaticity,[13] which appears to play a role in the energetics of the alkene metal-complexation and insertion steps of the mechanism of the cobalt-mediated cyclization.[14] An experimental indication of increased reactivity toward cycloadditions is given by numerous Diels–Alder reactions of pyridones[15] and pyrazinones.[16]

Preparation of starting materials: Alkynyl-2-pyridones **1**–**7** (only the first two of which were known)[17,18] were prepared by adaptation or application of standard literature procedures for such compounds (Table 1 and Table 2). The alkylation of pyridones is complicated by the possibility of attack at either nitrogen or oxygen, as well as the further ability of the products to isomerize by inter- or intramolecular transfer of the alkyl or acyl group. Therefore, alkynyloxypyridines resulting from *O*-alkylation were common side products which could, however, be readily separated by column chromatography.

Abstract in German: *Eine Reihe von Pyridon- und Pyrazinonderivaten wurde auf ihre Reaktivität gegenüber Alkinen in der Gegenwart von Cyclopentadienylcobaltbis(ethen) untersucht. In Abhängigkeit vom Substrat traten zum einen [2+2+2] oder [2+2] Cycloadditionen auf, zum anderen auch C–H oder N–H Aktivierungsreaktionen. Die ersten drei Fälle dominierten wenn N-geschützte Pyridone verwendet wurden, wohingegen Substrate mit N–H Bindungen eine N–H Aktivierung unterliefen. Die [2+2+2] Cycloaddition eines N-Butinylisochinolons wurde erfolgreich in der Totalsynthese von Anhydrolycorinon eingesetzt. Pyrazinone zeigten ein ähnliches Reaktionsverhalten.*

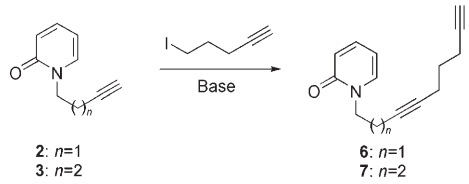
Table 1. Preparation of alkynyl-2-pyridones **1**–**5**.



1–**5**

Product	X	*n*	Yield [%]
2	TsO	2	25
3	I	3	85
4	TsO	4	46
5	TsO	5	50

Table 2. Preparation of diynyl-2-pyridones **6** and **7**.



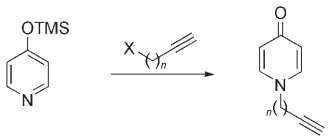
2: *n*=1
3: *n*=2

6: *n*=1
7: *n*=2

Product	*n*	Yield [%]
6	1	68
7	2	52

The problem of *O*-alkylation was pronounced with 4-pyridones. Thus, treatment with alkynyl tosylates or iodides in the presence of base in DMF or DMSO led to alkoxypyridines in low overall yields. This difficulty was circumvented by using the method of Guerry and Neier[19] and 4-trimethylsilyloxypyridine (**8**)[20] as the nucleophile (Table 3).

Table 3. Preparation of alkynyl-4-pyridones **9**–**12**.



8

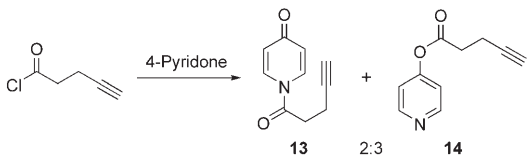
9–**12**

Product	X	*n*	Yield [%]
9	Br	1	85
10	I	2	17
11	I	3	85
12	I	4	60

N-Acylpyridones pose the additional dilemma of facile acyl migration. For example *N*-acetyl-2-pyridone cannot be isolated at room temperature and is in equilibrium with the *O*-acetyl derivative at −40 °C.[21] In contrast, its 4-pyridone isomer exists as the amide at room temperature in the solid state, although equimolar equilibration with the ester form occurs in solution.[22] Consequently, it was not surprising that reaction of 4-pyridone with 4-pentynoyl chloride led to an inseparable 2:3 mixture of the *N*- and *O*-acylated derivatives **13** and **14**, respectively (Scheme 2).[23]

The alkynylation of pyrazinones was achieved in a manner similar to that described for the pyridone systems

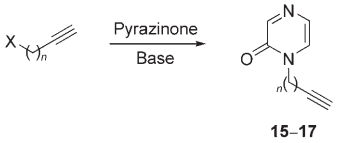
 © 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



Scheme 2. Pentynoylation of 4-pyridone.

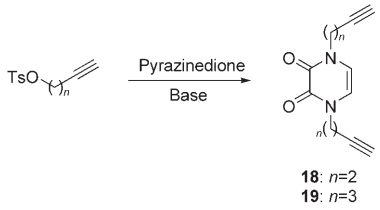
(Table 4). Precursors for all-intramolecular cyclizations were obtained by double alkynylation of pyrazinediones (Table 5).

Table 4. Preparation of *N*-alkynylpyrazinones **15**–**17**.



Product	X	*n*	Yield [%]
15	TsO	2	41
16	TsO	3	52
17	I	4	60

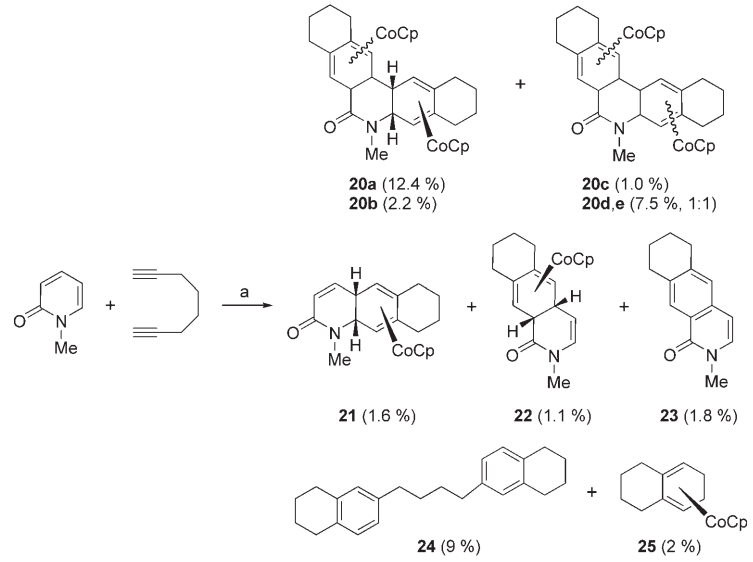
Table 5. Preparation of dialkynylpyrazinediones **18** and **19**.



Product	*n*	Yield [%]
18	2	39
19	3	60

Cycloadditions of 1,7-octadiyne to *N*-methylpyridones: First experiments investigated the potential of 1,7-octadiyne to cycloadd to the two *N*-methylpyridones in the presence of $[CpCo(C_2H_4)_2]$. The juxtaposition of these reagents was chosen in order to establish the basic feasibility of the proposed chemistry on the N-protected heterocyclic core, to probe for the possible occurrence of double additions as in **C** (Scheme 1), and to compare the stereochemistry of the products with that obtained in analogous cycloadditions, particularly that found in the most closely related pyrimidine adducts.[7] Thus, treatment of excess *N*-methyl-2-pyridone (6 equiv) and 1,7-octadiyne with $[CpCo(C_2H_4)_2]$ resulted in a number of products arising from both single and double [2+2+2] cycloaddition to the pyridone double bonds (Scheme 3). These included five isomeric double adducts, three of which (**20a**–**c**) were separable, two of which formed an inseparable mixture (**20d**,**e**, 1:1), in a total yield of 23%. In addition, single adducts to the enamine (**21**, 1.6%) and enone (namely **22**, 1.1%, and its aromatized congener **23**, 1.8%) units were isolated. Finally, trimer **24** and diene complex **25** were generated in 11% overall yield, based on the (limiting) diyne starting material. The former arises from catalytic cyclotrimerization of octadiyne and is a common side product in reactions employing this substrate,[24] while the latter is the result of a cocyclization of the diyne with a cobalt ethene ligand (Scheme 3). In line with the exploratory nature of these investigations (and those following in this paper), systematic efforts to optimize yields were not undertaken, but past experience has shown that improvements, often substantial, are possible by variation of reaction conditions.[3–7]

All five isomers of **20** displayed similar mass spectral characteristics, including the expected molecular ion at *m*/*z* 569, sequential loss of two CpCo moieties, and the presence of a fragment peak at *m*/*z* 256, corresponding to CpCo-tetrahydronaphthalene. Structural assignments of the isomers of **20** were hampered by the complexity of their NMR spectra and the failure to produce X-ray quality crystals. Double activation of the pyridone core could generate eight distinct diastereomers of **20**, reasonably assuming *cis* fusion of the C3–C4 and C5–C6 carbons of the lactam ring. For the major product, **20a**, the ^{1}H NMR spectrum showed two signals for the Cp peaks at $\delta = 4.50$ and $\delta = 4.43$ ppm (s, 5H), and one for the *N*-methyl peak at $\delta = 3.01$ ppm (s, 3H). In addition, three resolved doublets and a broadened singlet were ob-

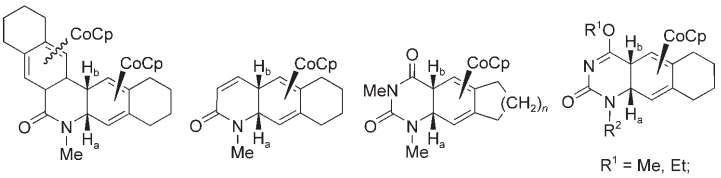


Scheme 3. Reaction of 1,7-octadiyne with *N*-methyl-2-pyridone (6 equiv). Reagents and conditions: a) $[CpCo(C_2H_4)_2]$, THF, reflux, 2.5 h.

 © 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

served at $\delta = 3.78$ ($J = 2.7$ Hz, 1H), 2.86 ($J = 4.2$ Hz, 1H), 2.54 ($J = 3.1$ Hz, 1H), and 2.50 ppm (br s, 1H), and these were assigned to the four complexed alkene protons shifted upfield by the anisotropy of the cobalt. The only resolved ring fusion proton signal was a doublet of doublets at $\delta =$ 3.54 ppm ($J = 8.89$, 4.2 Hz, 1H), assigned to the methane-hydrogen atom H_a, α to the nitrogen atom. This characteristically large chemical shift (relative to those in related *anti* complexes;[7] see also, e.g., **33** and **34**) corresponds well to those for closely related pyrimidinedione derivatives, in which the CpCo moiety is *syn* to the ring fusion hydrogens (for selected examples, see Table 6), suggesting the same arrangement for at least this half of the molecule. The ^{13}C-DEPT NMR displayed the number and type of signals expected for this structure. A total of eight signals for the methylene carbons appeared in two clusters at $\delta = 23.9$–24.3 ppm and $\delta = 29.3$–29.7 ppm, the. Similarly, two groups of peaks were observed for the eight methine carbon atoms of the complexed cyclohexadiene rings at $\delta = 42.1$–48.4 ppm and $\delta = 53.0$–57.1 ppm. Another series of peaks, identified as the its four quaternary carbons, were seen at $\delta = 92.0$–95.1 ppm. Signals at $\delta = 169.5$, 81.5, 81.3, and 32.8 were assigned to the carbonyl, two Cp rings, and the methyl carbon atoms, respectively.

Table 6. Chemical shifts [ppm] and vicinal coupling constants [Hz] for the *syn* hydrogen H_a in pyridones **20a** and **21**, and pyrimidinediones **26** and **27**.



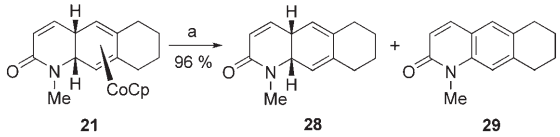
	20a	**21**	**26**[a]	**27**[a]
δ_{Ha}	3.54	3.44	3.03–3.14	3.25–3.34
J_{HaHb}	8.89	10.0	10.7–11.0	10.8–12.6

[a] Ref. [7a].

Thus, while the spectral data support the formulation of **20a** as a double adduct, only the stereochemistry of the 3,4-pyridone ring fusion, or the right half of the molecule, can be assigned with reasonable certainty, and the orientation of the cyclohexadiene with its attached CpCo moiety of the left half remains unknown. Unfortunately, attempted oxidative demetalation led to decomposition.

Compound **20b** appears to be a "left half" isomer of **20a**. It displayed all of the four olefinic hydrogen resonances in the ^{1}H NMR spectrum distinctly, at $\delta = 3.53$ (d, $J = 4.4$ Hz, 1H), 2.84 (d, $J = 3.4$ Hz, 1H), 2.78 (d, $J = 3.6$ Hz, 1H), and 2.76 ppm (d, $J = 3.3$ Hz, 1H). As with **20a**, a signal assigned to the ring junction hydrogen at C6 of the lactam moiety appeared at $\delta = 3.17$ ppm (dd, $J = 9.0$, 3.6 Hz, 1H), again suggesting a *syn* relationship to the metal at this (and the adjacent) position. The two Cp peaks at $\delta = 4.44$ and 4.39 ppm (s, 5 H each), as well as the methyl resonance at $\delta =$ 2.72 ppm (s, 3H) could also be identified. The ^{13}C NMR spectrum appeared similar to that of **20a**. Stereochemical assignments of isomers **20c**–**20e** were not possible.

The monoadducts **21** and **22** displayed similar mass spectral patterns, including a molecular ion at m/z 339, a base peak at m/z 337 due to loss of the two ring fusion hydrogens,[25] and peaks at m/z 271 and 215 corresponding to the stepwise loss of Cp and Co. For **21**, the ^{1}H NMR spectrum displayed two downfield, slightly broad doublets at $\delta = 5.69$ ($J = 9.6$ Hz, 1H) and $\delta = 5.58$ ppm ($J = 9.6$ Hz, 1H), assigned to the uncomplexed vinyl hydrogen atoms. In keeping with the chemical shift reasoning described above (Table 6), a signal at $\delta = 3.44$ ppm ($J_{HaHb} = 10.0$ Hz) was assigned to the ring junction proton H_a, α to the amide nitrogen. The adjacent methine hydrogen was observed at $\delta = 2.31$ ppm (br d, $J = 10.7$ Hz, 1H). These results indicate a *syn* relationship between the ring junction hydrogens and the CpCo moiety. The ^{13}C data were in accord with the structure. As expected, in this, as well as all subsequent CpCo diene compounds reported here, the terminal diene carbons appear at dramatically higher field than their internal neighbors. Demetalation of **21** with Cu^{II} afforded the free ligand **28**, contaminated with a small amount of the aromatized product **29** (4:1; Scheme 4). Most diagnostically, the ^{1}H NMR resonances of the hydrogen atoms in the vicinity of the metal in the starting complex are found at the expected higher δ values. Crucial for the confirmation of the regiochemistry of cycloaddition were the chemical shifts of quinolone **29**, which corresponded to those of the parent *N*-methylquinolone.[26]

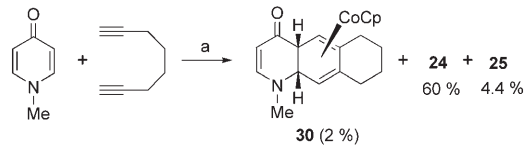


Scheme 4. Demetalation of the cyclization product **21**. Reagents and conditions: a) $CuCl_2 \cdot 2H_2O$, Et_3N, MeCN, 0 °C, 30 min.

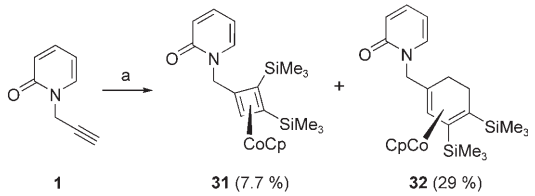
The structural assignment of the other monocyclization product **22** was made in a similar manner, the *syn* stereochemistry indicated by the methine signal next to the carbonyl, $\delta = 2.99$ (dd, $J = 12.1$, 4.2 Hz, 1H). This complex probably gives rise to the aromatic **23**, the structure of which was confirmed by comparison of its ^{1}H NMR spectrum with that of *N*-methylisoquinolone.[27]

To reduce the number of possible products and to probe the scope of this cycloaddition, the more symmetrical *N*-methyl-4-pyridone was subjected to the reaction conditions described in Scheme 3. Disappointingly, only a 2% yield of the monocyclized product **30** was isolated, diyne autooligomerization to **24** dominating the reaction path (Scheme 5). For **30**, the ring fusion methine hydrogen resonance α to the nitrogen atom appeared at $\delta = 3.19$ ppm ($J = 11.0$ Hz), and

 © 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



Scheme 5. Reaction of 1,7-octadiyne with *N*-methyl-4-pyridone (2 equiv). Reagents and conditions: a) $[CpCo(C_2H_4)_2]$, THF, reflux, 2.5 h.



Scheme 6. Cocyclotrimerization of **1** with BTMSA. Reagents and conditions: a) BTMSA, $[CpCo(C_2H_4)_2]$, THF, room temperature, 2 h.

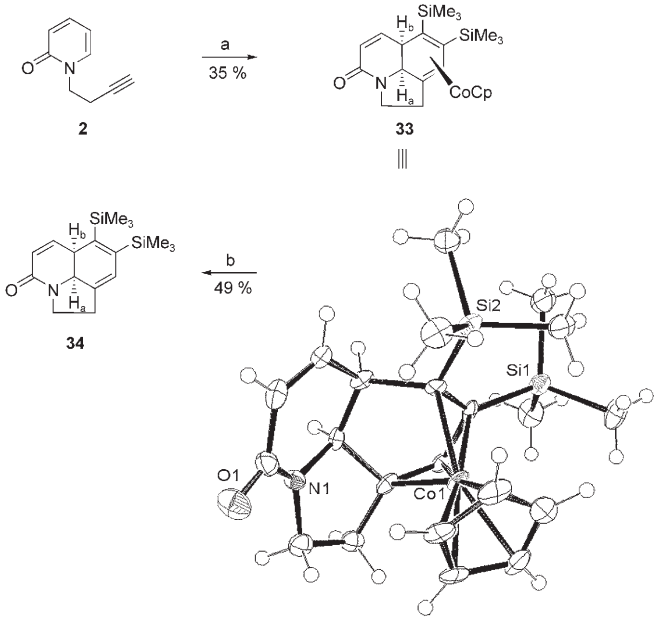
the neighboring methine proton peak at $\delta = 2.93$ ppm ($J = 11.0$ Hz) consistent with a CpCo moiety located *syn* to these hydrogens.

Thus, while the preceding chemistry demonstrates the possibility of using either or both C–C double bonds of pyridones as cocyclization partners with alkynes in the presence of CpCo, the process is plagued by competitive alkyne aromatization. The diene complexes isolated appear to show a preference for the *syn* stereochemistry noted in analogous pyrimidinone cyclizations, but mixtures ensue.[7] Indeed, DFT calculations described in the accompanying paper attest to the similarity in the energetic requirements on route to both *syn* and *anti* products.[28] Rather than tinkering with reaction conditions to improve the outcome of these transformations, the topology of the reaction partners was modified such as to maximize the likelihood of heterocycle incorporation in the products.

Cobalt-mediated [2+2+2] cycloadditions of alkyne-tethered pyridones: Tethering one or both of the alkyne cycloaddition partners to the heteroaromatic core to lower the entropic costs of the [2+2+2] cyclization has been a frequent strategy to improve reaction yields.[1] In the case of CpCo, this variant has generated a number of novel polycycles,[2–7] some of which have been utilized in total syntheses.[12,29] In this vein, the *N*-alkynylated pyridones **1**–**7** and **9**–**13** were subjected to cocyclization with a large excess of bis(trimethylsilyl)acetylene (BTMSA). The nature of the resulting products—CpCo-complexed cyclobutadienes, cyclohexadienes, and 3-butadienylpyridones—showed a remarkable dependence on the length or nature of the tether. This section will summarize examples of the first two modes, while a subsequent part will describe the third type, which involves C–H activation.

Simultaneous additions of separate solutions of *N*-2-propynylpyridone **1** and the cobalt reagent in THF to BTMSA produced, perhaps not surprisingly, only cyclobutadiene complex **31** and the ethene adduct **32**, the latter in unusually high yield (Scheme 6).[30]

However, extending the tether length by one carbon, as in *N*-3-butynyl system **2**, provided, under the same conditions, the [2+2+2] product **33** in 35% yield almost exclusively, only trace amounts of the cyclobutadiene isomer (see Experimental Section) and none of the ethene adduct being detectable (Scheme 7). The identity of **33**, including its *anti* stereochemistry, was clearly indicated by the NMR spectra, which were characteristically distinct from those for related *syn* complexes, in particular **21** (Table 6), and in line with

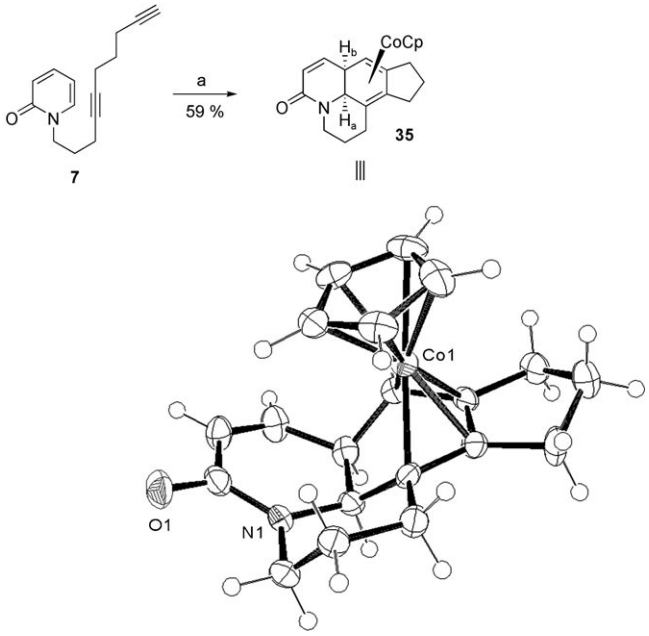


Scheme 7. Cocyclotrimerization of **2** with BTMSA and oxidative demetalation of product **33**. Reagents and conditions: a) BTMSA, $[CpCo(C_2H_4)_2]$, THF, room temperature, 2 h; b) $Fe(NO_3)_3 \cdot 9H_2O$, MeCN, THF, H_2O, 0 °C, 12 min.

the data for similar *anti* fused diene complexes.[7] Specifically, H_a and H_b give rise to relatively shielded signals at $\delta = 2.36$ ppm (d, $J = 8.0$ Hz) and $\delta = 1.48$ ppm (dd, $J = 8.0$, 4.6 Hz). Further structural confirmation was derived by oxidative demetalation (Scheme 7) to **34**. In this free ligand, the NMR resonance for H_a appears at $\delta = 4.75$ ppm and H_b at $\delta = 2.40$ ppm, while the dienyl hydrogen singlet has experienced a shift from $\delta = 4.82$ to 5.86 ppm on decomplexation. Solidification of these assignments rested on an X-ray crystal structure analysis (Scheme 7). The molecule forms a pronounced bowl, the metal located on its concave face. The energetic preference for the observed stereochemistry in this tethered system is also indicated by DFT calculations.[28] As will be described in a later section, lengthening the tether in **2** twice by increments of a methylene spacer (**3** and **4**, respectively) led to products of C–H activation, to the complete detriment of a [2+2+2] pathway. Finally, to complete this series, the *N*-heptynyl derivative **5** was tested in the process, to give, now as the sole new compound, the cyclobutadiene complex (see Experimental Section).

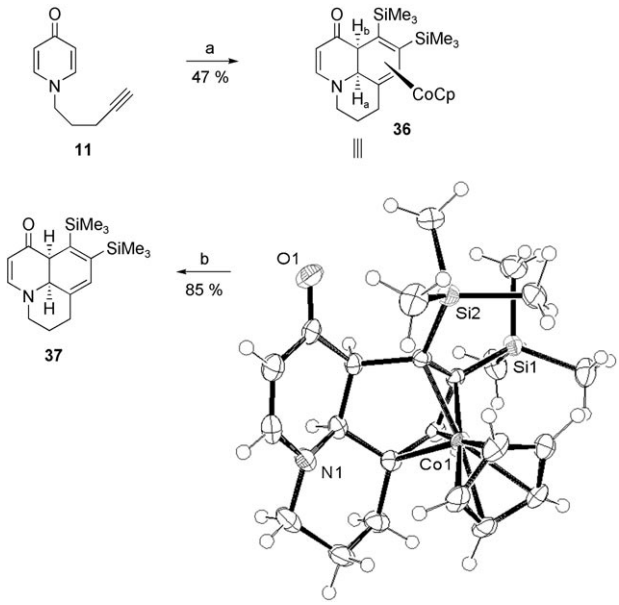
 © 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Encouraged by the result depicted in Scheme 7, all-intramolecular variants of this cycloaddition were explored with substrates **6** and **7**. The former can be viewed as an extended version of **2**, and, on the basis of Scheme 7, was thought to be an excellent substrate for [2+2+2] cycloisomerization. The homolog **7**, on the other hand, when considered as a derivative of **3**, was anticipated to enter the C–H activation manifold (vide infra). Contrary to these expectations, adding **6** under high-dilution conditions to $[CpCo(C_2H_4)_2]$ produced only an inseparable mixture of regioisomers resulting from intermolecular cycloadditions, as indicated by mass spectral analysis. On the other hand, **7** underwent smooth cyclization (and not C–H activation) to tetracycle **35** in quite acceptable yield (Scheme 8). The ^{1}H NMR spectrum of **35** reveals the complexed diene proton at $\delta = 2.40$ (br s) ppm and the tertiary nuclei at $\delta_{Ha} = 2.37$ (d, $J = 8.0$ Hz) and $\delta_{Hb} = 1.48$ ppm (m). An X-ray structural determination confirmed the structural assignment. The complete stereoselectivity of this transformation contrasts with related intramolecular cycloadditions in the indole[4b] and pyrrole series.[5] This array of atoms has not been reported in the literature, either as such or as a substructure.



Scheme 8. Cyclization of **7**. Reagents and conditions: a) $[CpCo(C_2H_4)_2]$ (1.1 equiv), THF, room temperature, 16 h. Yield based on recovered starting material (27 %).

Extending the above series to its 4-pyridone isomeric counterpart was deemed again instructive, because symmetry might lead to improved yields, the disappointing results in the cycloadditions with external diynes (vide supra) notwithstanding. Moreover, it was hoped that the changes in the outcome of the cyclization of 2-pyridone substrates might be affected in an intelligible manner by this switch. In the event, cocyclization of the *N*-alkynyl-4-pyridones **9**–**12** produced in all cases substantial amounts of bis(trimethylsilyl)cyclobutadiene cobalt complexes (50, 25, 15, and 34 %, respectively), *no* products of C–H activation, some spurious side products in the case of **9** and **10** (see Experimental Section), and, puzzlingly contrasting with the 2-pyridone series, only with *N*-4-pentynylpyridone **11** the desired fused diene **36** (47 %; Scheme 9). The structural proof of **36** rests on the same accumulated evidence as that for **33** and **35**: NMR data [e.g., $\delta_{Ha} = 2.35$ ($J = 8.8$ Hz) and $\delta_{Hb} = 1.47$ ppm ($J = 8.8$ Hz)], oxidative free ligand **37** generation, aromatization of **37** to the corresponding 4-quinolone with DDQ (see Experimental Section), and an X-ray crystallographic analysis.



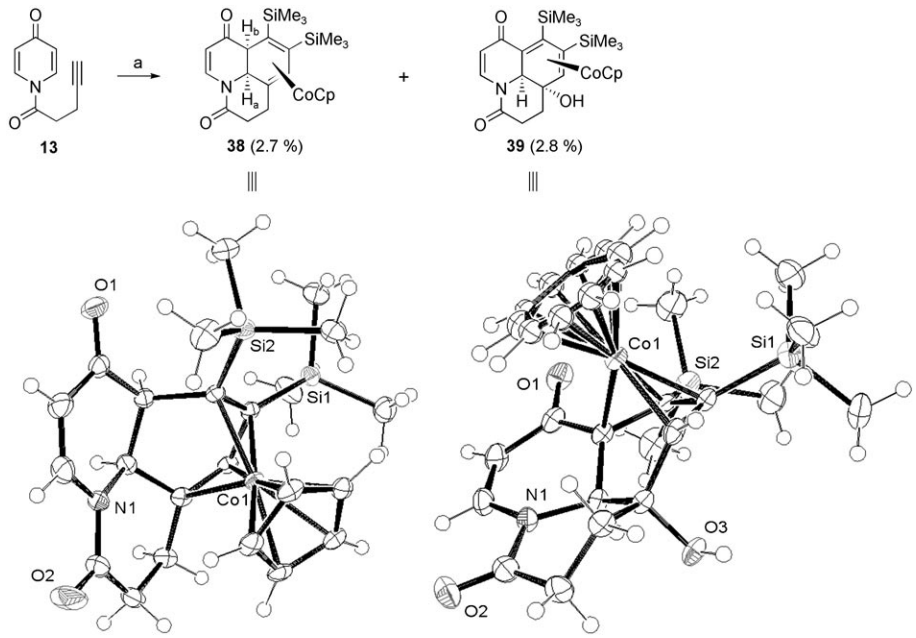
Scheme 9. Cocycloaddition of **11** to BTMSA and oxidative demetalation of product **36**. Reagents and conditions: a) BTMSA, $[CpCo(C_2H_4)_2]$, dioxane, THF, room temperature, 4.5 h; b) $Fe(NO_3)_3 \cdot 9H_2O$, MeCN, THF, H_2O, 0 °C, 10 min.

As mentioned above, *N*-acylated azaaromatics perform frequently in a superior manner in this methodology compared to their *N*-alkylated counterparts.[4,6,12] Therefore, undaunted by the lability of *N*-acylpyridones and their propensity to equilibrate with their ester isomers,[21–23] **13** (admixed with **14**) was exposed to BTMSA and $[CpCo(C_2H_4)_2]$ (Scheme 10).

The reaction furnished two products **38** and **39** of [2+2+2] cocycloaddition in a poor 5.5 % total yield and in the absence of any other tractable material. The "normal" product **38** was readily identified by spectral analysis, in particular ^{1}H NMR spectroscopy, with the characteristic absorptions for H_a [$\delta = 3.78$ ppm ($J = 6.9$ Hz), unusually deshielded relative to H_a of **37** due to the presence of the amide carbonyl], and H_b [$\delta = 1.21$ ppm ($J = 6.9$ Hz)] and, ultimately, by an X-ray structure.

The identity of the other cyclization product **39** was more difficult to establish. While the incorporation of BTMSA and CpCo was evident from resonances at $\delta = 0.32$ (s, 9H),

 © 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



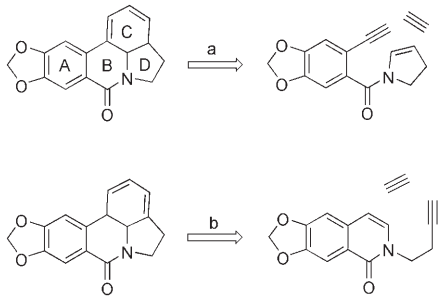
Scheme 10. Cocyclotrimerization of **13** with BTMSA. Reagents and conditions: a) BTMSA, $[CpCo(C_2H_4)_2]$, 1,4-dioxane, THF, room temperature, 1.5 h.

0.38 (s, 9H), and 4.65 ppm (s, 5H) in the ^{1}H NMR spectrum, the presence of an additional oxygen atom was suggested by a molecular ion at *m/z* 485. Rather than the two doublets for the ring fusion arrangement in **38**, three singlets were observed at $\delta = 3.11$ (s, 1H), 3.50 (s, 1H), and 1.60 ppm (br s, 1H). That the last of these corresponded to a hydroxy proton was supported by a broad absorption in the IR spectrum at 3373 cm^{-1}. The precise location of this function was determined by an X-ray structural analysis, which revealed **39** to be a hydroxylated diene isomer of **38** (Scheme 10). The structure is remarkable in as much as it constitutes a novel 4-quinolone hydrate, kinetically protected from aromatization (by dehydration) by the attached metal unit. A mechanism for this oxidation through enolization and one-electron transfer to adventitious Co^{III} is suggested by recent literature.[31]

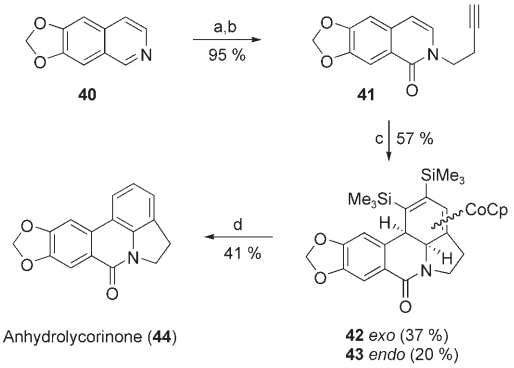
In summary of the results described in this section, it is clear that the pyridone nucleus bearing tethered C–C triple bonds is a relatively effective cocyclization partner with alkynes, but the reaction displays a subtle divergence in its outcome, which seemingly is strongly dependent on the length of the tether linking the nitrogen atom with the proximal triple bond. In accord with previous findings in the pyrimidine series,[7] tethering one or both of the alkyne units causes an inversion of the stereochemistry of the resulting cobalt complex to *anti*.

Application to the total synthesis of anhydrolycorinone: The successful execution of Scheme 7 inspired its extension to a new approach to the synthesis of the galanthan (pyrrolophenanthridine) alkaloid skeleton,[32] as exemplified by anhydrolycorinone **44**.[33] This family of natural products has been a frequent target on which to test the utility of new methodology, much of it developed toward arene couplings that construct the embedded biphenyl unit. A retro-[2+2+2]synthetic analysis of the C ring as a cyclohexadiene suggests two feasible disconnections, a and b (Scheme 11). Approach a, employing an enamide double bond as a cocyclization partner in the cobalt-mediated step has been executed by us previously.[12] Approach b constitutes a benzo-fused version of Scheme 7 and was realized according to Scheme 12.

Starting with methylenedioxyisoquinoline (papraline) **40**,[34] *N*-alkynylation with 3-butynyl-1-tosylate[35] gave the corresponding isoquinolinium salt, which was oxidized with potassium hexacyanoferrate(III) in a two-



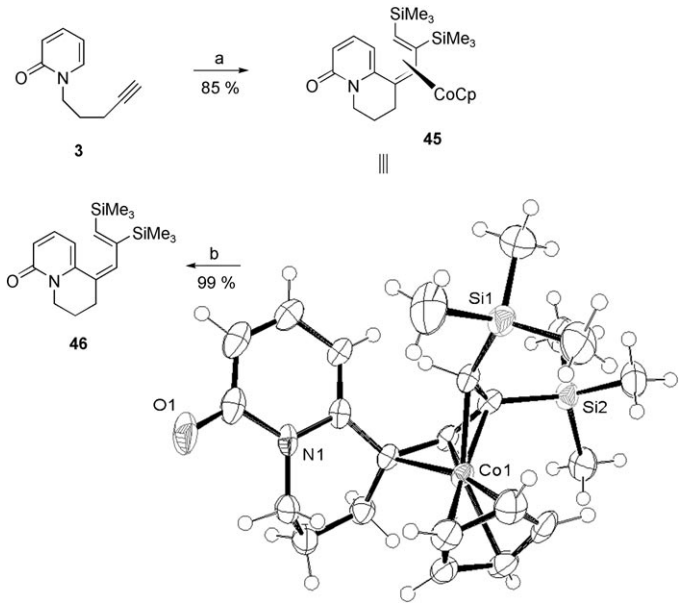
Scheme 11. Retro[2+2+2]cycloaddition disconnections of ring C of the galanthan core.



Scheme 12. Total synthesis of anhydrolycorinone. Reagents and conditions: a) 3-Butynyl tosylate, MeCN, 160 °C (microwave), 3 h; b) $K_3[Fe(CN)_6]$, H_2O, 0 °C, 1 h, then KOH, 0 °C, 0.5 h; c) $[CpCo(C_2H_4)_2]$, BTMSA, room temperature, 1 h; d) Bu_4NF, THF, room temperature, 2 h, then $Fe(NO_3)_3 \cdot 9H_2O$, THF, H_2O, room temperature, 2 min.

 © 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

step sequence[36] to the desired precursor **41** for the key step. The cobalt-mediated [2+2+2] cycloaddition delivered the pentacycles **42** and **43** in an approximate 2:1 ratio in admirable combined 57% yield (67% based on recovered starting material). It appears that the added benzofusion (in comparison to **33**) exerts a steric effect on the stereochemistry of insertion such that *endo* product formation becomes competitive.[28] The NMR spectra of these two isomers show the trends delineated above for the *exo* versus *endo* disposition of the metal (see Experimental Section). An indication of the steric encumbrance exerted by the benzene ring is hindered rotation of the trimethylsilyl groups in the bay region of the dihydrophenanthridinone skeleton on the NMR time scale at room temperature. In **43**, this effect is visible by the broadening of one of the silyl singlets; in **42** it is more pronounced, leading to the appearance of three singlets for the individual methyls. We have detected such behavior in other products of the cocyclization of BTMSA.[4b,29g,37] Removal of the two silyl groups with fluoride, followed by oxidative demetalation with $Fe(NO_3)_3 \cdot 9H_2O$,[12] furnished anhydrolycorinone (**44**) directly, without the obtention of the intermediate cyclohexadiene ligand. This material was identical with **44** prepared previously by route a in Scheme 11.[12]



Scheme 13. C–H activation in the cobalt-mediated reaction of **3** with BTMSA. Reagents and conditions: a) BTMSA, $[CpCo(C_2H_4)_2]$, THF, room temperature, 1 h; b) $Fe(NO_3)_3 \cdot 9H_2O$, MeCN, H_2O (9:1), 0 °C.

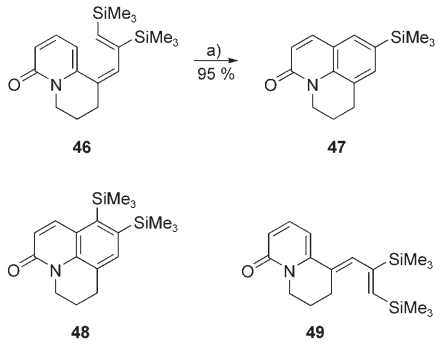
Dienylpyridones by C–H activation reactions: As alluded to in previous sections, [2+2]- and [2+2+2] cocycloadditions are not the only pathways by which pyridones transform. Alternative options for these substrates are C–H, and, as we shall describe in the next section, N–H activation, with simultaneous double alkyne stitching to provide dienylated heterocycles, isomeric to the [2+2+2] products. Such insertions have been noted previously in cobalt-mediated cyclizations of heterocycles, usually, but not always, as minor byproducts.[2,4a,7a,38,39] Experimental[40] and theoretical evidence[14] support attack of the cobaltacyclopentadiene intermediate (formed by alkyne oxidative coupling) on the C–H bond of the heterocycle. One notes that such ethynylogous hydroheteroarylations of alkynes are rare, but of obvious synthetic desirability.[41] In the present case, this process surfaces rather startlingly with 3-pentynylpyridone **3**, which, under the conditions that furnished only [2+2+2] products from the lower homologue **2** (Scheme 7) and the all-intra analogue **7** (Scheme 8), provided the fused dienylpyridone complex **45** essentially quantitatively (^{1}H NMR analysis of crude product; 85% isolated yield; Scheme 13).

That **45** was different from the expected fused quinolone complex was immediately evident in its NMR spectra. In particular, the tertiary hydrogen signals typical of the cyclohexadiene ring fusion, $H_{a,b}$, were missing and, instead, the typical pattern for a 6-substituted pyridone was evident [δ = 4.65 (dd, J = 6.0, 1.5 Hz, 1H, H5), 6.47 (dd, J = 9.1, 6.0 Hz, 1H, H4), 6.62 ppm (dd, J = 9.1, 1.5 Hz, 1H, H3)], H5 being shielded by about 0.7 ppm from its normal position by the anisotropy of the adjacent CpCodiene moiety (vide infra). Moreover, in addition to the anticipated singlet for the internal complexed diene hydrogen (δ = 4.56 ppm, br), there was a second singlet at δ = −0.64 ppm (br), pinpointing the presence of an internal, terminal diene hydrogen atom. The ^{13}C NMR spectrum, in conjunction with 2D spectra, corroborated these assignments, cemented ultimately by an X-ray crystal structure analysis (Scheme 13). The molecule is unusually deformed, such as to twist the essentially coplanar complexed diene unit away from the pyridone ring (dihedral angle around the alkylidene double bond = −55°). This distortion places H5 exactly above the terminal diene carbon centroid, the vector H5-centroid-Co deviating from linearity by only 1°. The switch from [2+2+2] chemistry (Scheme 7) to C–H activation on simple lengthening of the tether is qualitatively in accord with DFT estimates, which reveal a narrowing of energetic requirements for the two respective pathways on going from **2** to **3**, although the pronounced switchover in mechanism is not reproduced computationally.[28]

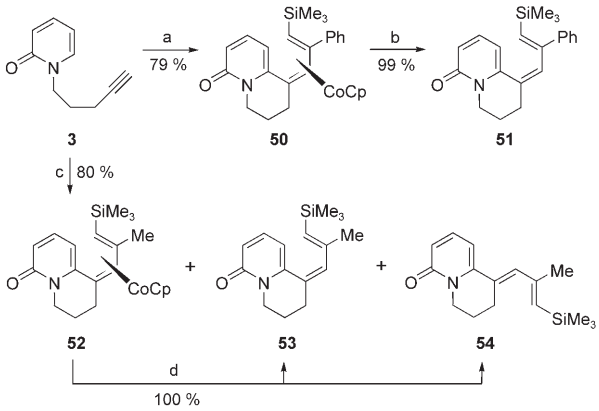
Quantitative decomplexation of **45** was achieved with $Fe(NO_3)_3$ (Scheme 13), and the changes in the NMR spectra in going from **45** to the unknown system **46** were exactly as expected. Significant with respect to the structural assignments of related dienes (vide infra), the terminal diene signal appears as a doublet (J = 2.0 Hz) at δ = 6.33 ppm, whereas its internal counterpart produces a doublet of triplets [δ = 6.06 ppm (J = 1.8, 1.7 Hz)] due to additional allylic coupling. With reasonable quantities of **46** in hand, its potential to undergo thermal electrocyclic ring closure was tested. Butadienylbenzene and 2-(butadienyl)pyridine have been shown to follow such a pathway during gas-phase pyrolyses to furnish 1,2-dihydronaphthalene and 5,6-dihydroquinoline, respectively.[42] Indeed, when **46** was heated to 110 °C for 12 h, aromatization with concomitant protodesilylation was the result, yielding **47** quantitatively (NMR). Monitoring this re-

 © 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

action revealed the intermediacy of two compounds, **48** and **49**, both of which could be purified by HPLC and independently thermolyzed to **47**, quantitatively (Scheme 14). It is



Scheme 14. Electrocyclic ring closure of the free ligand **46**. a) Toluene, 110 °C, 12 h.

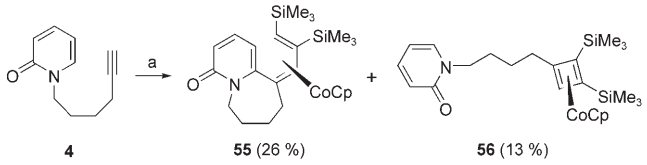


Scheme 15. Regioselective C–H activation–insertion of **3** with unsymmetrical alkynes. Reagents and conditions: a) Phenyl(trimethylsilyl)acetylene (100 equiv), $[CpCo(C_2H_4)_2]$, THF, room temperature, 1 h; b) $Fe(NO_3)_3 \cdot 9H_2O$, $MeCN/H_2O$ (9:1), 0 °C; c) 1-trimethylsilylpropyne (135 equiv), $[CpCo(C_2H_4)_2]$, THF, room temperature, 1 h; d) $Fe(NO_3)_3 \cdot 9H_2O$, $MeCN/H_2O$ (9:1), 0 °C.

likely that **48** is the precursor to **47**, as the peri-silyl group should be very prone to hydrolytic removal.[43] The structure of **49**, clearly an isomer of **48** on the basis of spectral data, was assigned in analogy to similar isomerizations in the furan and thiophene series[2] and the observation of substantial deshielding of the signals for the methylene hydrogens proximal to the butadienylidene substituent when going from **46** to **49**. Moreover, the internal diene hydrogen experiences a downfield shift of about 0.4 ppm on moving *syn* to the pyridone function. This isomer must be in equilibrium with its precursor to be converted to **48** and eventually **47**. We suspect that this isomerization is catalyzed by adventitious acid.

The high yielding conversion depicted in Scheme 13 stimulated a brief exploration of its scope with other symmetrical and unsymmetrical monoalkynes. Thus, the reaction of a large excess phenyl(trimethylsilyl)acetylene with pyridone **3** gave **50** regioselectively in 79% yield (Scheme 15). The ^1H and ^{13}C NMR spectral features of **50** were remarkably similar to those of **45**, except for the signal for the carbon atom bearing the phenyl substituent and that of the hydrogen next to it. The position of the phenyl group was ascertained by 2D spectroscopy (HMQC). The observed regioselectivity is in accord with the strong preference of silyl groups to occupy the positions α to the metal center in the intermediate cobaltacyclopentadienes.[1g,h] Removal of the cobalt with $Fe(NO_3)_3$ furnished the free ligand **51** quantitatively (Scheme 15). A similar result was observed with 1-trimethylsilylpropyne as the cocyclization partner, which gave only regioisomer **52** (33%), admixed with the free ligand **53** and its isomer **54** (10:1, 47%) (Scheme 15). This mixture could be converted quantitatively to **53** and **54** (4:1) with Fe^{III}. In these compounds, the regiochemical identity was readily verified by the absence of coupling between the methyl substituent on the butadienylidene fragment and the terminal hydrogen. The *syn* disposition of this fragment with respect to the pyridone nucleus is again manifest in the unusually shielded H5 signal of the latter [$\delta = 4.53$ ppm (d, $J = 6.6$ Hz)]. The identity of **54** was surmised on the basis of the changes in the NMR data when compared to those of its isomer **53**, similar to those noted for **49** relative to **46**.

While the examples above attest to the potentially remarkable efficiency of a C–H activation pathway in the cobalt-mediated reaction of tethered 2-pyridones with certain alkynes, limitations were encountered with other substrates. Thus, the reaction of **3** with ethyne, even at −70 °C, in the presence of $[CpCo(C_2H_4)_2]$ supplied only *N*-(3-phenylpropyl)-2-pyridone in 65% yield, derived by alkyne cotrimerization of the triple bond of **3** with ethyne (see Experimental Section).[44] Similarly, dimethyl butynedioate gave *N*-[3-(2,3,4,5-tetramethyoxycarbonylphenyl)propyl]-2-pyridone (56%, see Experimental Section). On the other hand, homologation of the tether as in **4** gave diene complex **55** in 26% yield, in addition to cyclobutadiene complex **56** (13%; Scheme 16).



Scheme 16. Cobalt-mediated reaction of **4** with BTMSA. Reagents and conditions: a) BTMSA, $[CpCo(C_2H_4)_2]$, THF, room temperature, 1 h.

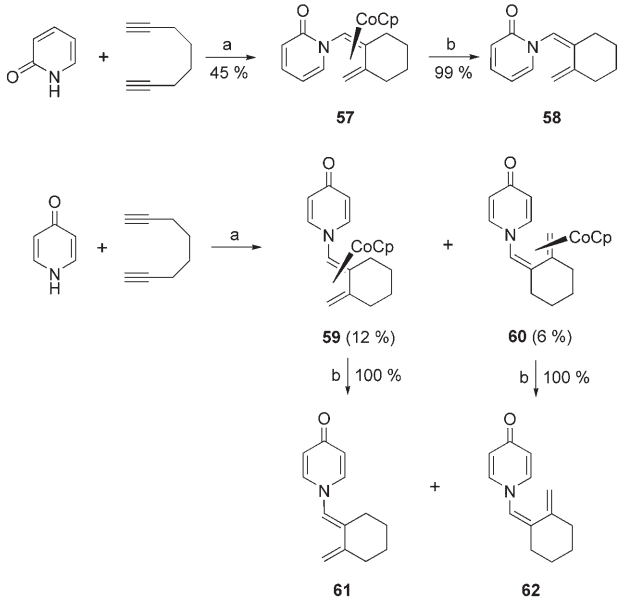
In summary of this section, C–H activation with simultaneous double alkyne stitching replaces [2+2+2] cycloadditions in the reactions of N-protected pyridones in a subtle and unpredictable way. While products derived from both options simultaneously were not found for any particular reaction discussed so far, such direct competition is evident in other systems.[4a,7a] Thus, it is clear that the two reaction manifolds are close energetically, as corroborated by compu-

 © 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

tational estimates.[28] In view of the above, the question arose whether N–H activation was another alternative, answered in the next section.

N–H activation reactions: The catalytic hydroamination of alkynes to enamines is a subject of considerable current interest.[45] Hydroamination occurring with simultaneous alkyne coupling to furnish dienylamines is rare.[46] Wakatsuki and Yamazaki have reported that thioacetanilide and thiourea derivatives add to Cpcobaltacyclopentadienes in this fashion, whereas pyrrole underwent C–H activation.[40b] On consideration of these results, it appeared reasonable to expect that the parent 2- and 4-pyridones would react by N–H insertion, an expectation reinforced by a DFT appraisal of the comparative energetics involved.[28]

Indeed, when excess 2-pyridone (53 equiv, to maximize cocycloaddition) was treated with 1,7-octadiyne and [CpCo(C_2H_4)$_2$], cobalt complex **57** was recovered with exclusive *Z*-configuration in 45% yield, remarkably high in view of the intermolecular nature of this heterocycle activation (Scheme 17). The structure of **57** was indicated by the absence of an infrared band for an N–H bond and the presence of a complete set of four pyridone protons, notably a doublet characteristic of pyridone H-6 next to nitrogen [$\delta =$ 7.27 ppm ($J = 5.5$ Hz)]. In addition, there were three broadened singlets assigned to CpCo-bound dienyl hydrogens at $\delta = -0.15$, 1.71, and 3.08 ppm, the first two chemical shifts typical of terminal *Z* and *E* positions, the third consistent with an *E*-hydrogen atom appropriately shifted by the neighboring enamido group.[47] Oxidative demetalation delivered free ligand **58**, a novel array, in quantitative yield.

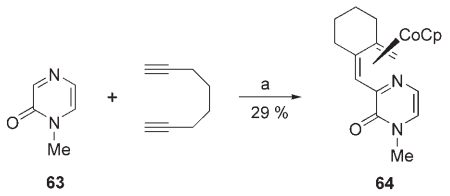


Scheme 17. N–H activation of 2- and 4-pyridone. Reagents and conditions: a) [CpCo(C_2H_4)$_2$], MeOH, THF, room temperature, 1 h; b) Fe(NO_3)$_3$·9H_2O, MeCN, H_2O, 0 °C, 15 min.

Execution of the same protocol with 4-pyridone also led to N-H activation, albeit less efficiently and stereoselectively, furnishing the two isomers **59** and **60** (2:1), separated by HPLC, in 18% combined yield (Scheme 17). The difference in nature of the stereochemistry of these two complexes is clearly evident in the chemical shifts of the diene hydrogen atoms next to the pyridone substituent: $\delta = 0.92$ (**59**) and 4.11 ppm (**60**). Both complexes delivered their free ligands **61** and **62**, respectively, on oxidation.

The above results are gratifying, albeit limited to the two examples investigated, in as much as they indicate that, indeed, in addition to the two modes of cycloaddition and to C–H activation, N–H activation is feasible and, considering the other possible modes of reactivity, most facile for pyridones in the presence of CpCo. Future experimentation is warranted in order to explore the synthetic utility of this reaction, as it generates valuable synthetic building blocks. Having explored at some length the reactivity of pyridones by variation of substituents, another attempt at delineating the scope of this chemistry was made by replacing C4 in the heterocycle by nitrogen, as in pyrazinone. The results are instructive in comparison to those collected in the pyridinone (vide supra) and pyrimidinone series.[7]

Cobalt-mediated activation of pyrazinones: Like pyridine, pyrazine itself is left untouched by CpCo. Therefore, in analogy to Scheme 3 and in anticipation of a [2+2+2] cycloaddition, *N*-methylpyrazinone **63** and 1,7-octadiyne were treated with [CpCo(C_2H_4)$_2$]. Surprisingly, complex **64** was formed regioselectively (22% yield; 29% based on converted **63**) via C-H activation (Scheme 18). The NMR spectra of this compound showed the disappearance of the low field peak associated with H-3 in pyrazinones, but the preservation of the characteristic doublets for the other hydrogen atoms of the heterocycle. The presence of the cobalt-complexed diene unit and its stereochemistry was evident in the ^{13}C and ^{1}H NMR spectra, the latter through three diagnostic singlets at $\delta = 4.65$ and 2.51 ppm, for the two *E* hydrogen atoms, the former relatively deshielded by the adjacent heterocyclic substituent, and 0.37 ppm, for the *Z* hydrogen atom at the terminus.

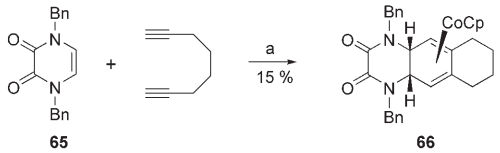


Scheme 18. Reaction of pyrazinone **63** with 1,7-octadiyne (1.9 equiv). Reagents and conditions: a) [CpCo(C_2H_4)$_2$], C_6H_6, Δ, 4 h. Yield based on recovered **63** (24%).

While C–H activations of similar functions are unprecedented to our knowledge, it appears that the imine C–H bond in **63** is particularly reactive, obviating the expected

 © 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

cycloaddition pathway. Tentative confirmation of this notion was sought by removing this site, as in *N*,*N*′-dibenzylpyrazinedione **65**,[48] for which the relative propensity to enter the [2+2+2] versus C–H activation manifold could be properly evaluated. In the event, the former wins out, as reaction with 1,7-octadiyne formed linear tricycle **66** in 15% isolated yield (Scheme 19). In this reaction, substantial quantities of

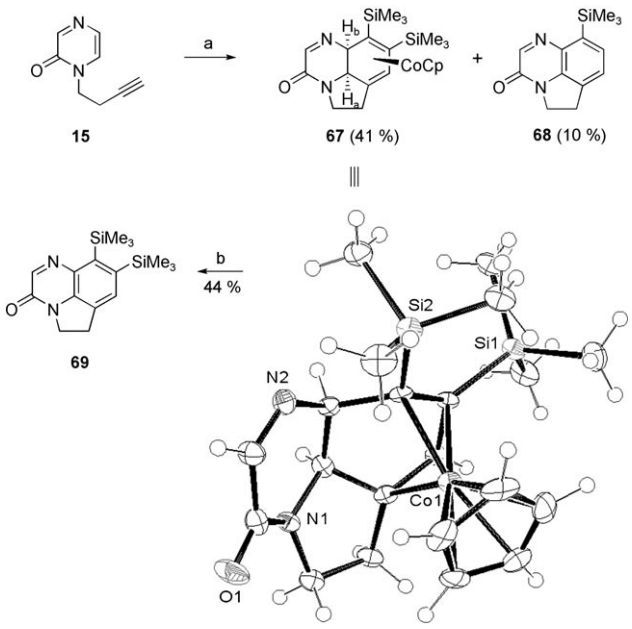


Scheme 19. Reaction of pyrazinedione **65** with 1,7-octadiyne (3.6 equiv). Reagents and conditions: a) $[CpCo(C_2H_4)_2]$ (1.1 equiv), toluene, room temperature, 18 h. Yield based on recovered **65**: 54%.

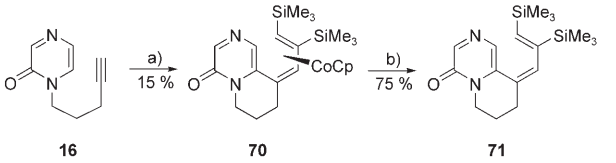
unreacted **65** were recovered (72%), indicating that competitive diyne cyclotrimerization is detrimental. Based on converted heterocycle, the yield is an admirable 54%. The symmetry in **66** is reflected in the simple ^{1}H NMR spectrum and its *syn* stereochemistry surmised by the position of the peaks for the tertiary hydrogens [$\delta = 3.71$ ppm (br s)] (Table 6), in accord with related cyclizations in the pyridone (Scheme 3–5) and pyrimidinone series.[7]

To prevent the C–H activation pathway of Scheme 18 and improve the competitiveness of heterocycle incorporation at the expense of external alkyne cyclotrimerization, recourse was again taken to the attachment of one or both of the triple bonds by a tether. Gratifyingly, in analogy to Scheme 7, the 3-butynyl substituted system **15** was transformed to **67** (41%), in addition to a small amount of aromatized and partly desilylated **68** (10%). The NMR spectra clearly indicated that [2+2+2] cycloaddition had occurred, its stereopreference revealed by $\delta_{Ha} = 1.94$ (d, $J = 8.4$ Hz) and $\delta_{Hb} = 3.20$ (dd, $J = 8.4$, 2.8 Hz), the latter showing a small coupling to the imine hydrogen at $\delta = 7.88$ (d, $J =$ 2.8 Hz). An X-ray diffraction analysis confirmed these assignments and presented a molecule with a three-dimensional disposition almost identical to that of the pyridone analog **33** (Scheme 7). Curiously, attempted decomplexation of **67** with Fe^{III} led to a complex mixture of unidentified products. More successful was Cu^{II}, although it caused aromatization to **69** (44%) together with some, presumably subsequent, monodesilylation to **68** (5%; Scheme 20). The pyrroloquinoxalinone system represented by **69** is very rare.[49]

In consonance with the pyridone (Scheme 13 and 15) and pyrimidinone analogues,[7] extending the tether length by one methylene group caused C–H activation to resurface, albeit in much poorer yield (**70** in Scheme 21). Decomplexation of **70** under standard conditions furnished **71** (Scheme 21). The NMR data of these compounds were as expected in comparison to those of **45** and **46**, respectively. An attempt to extend the series to the hexynylpyrazinone **17**, by analogy to Scheme 16, was unsuccessful.



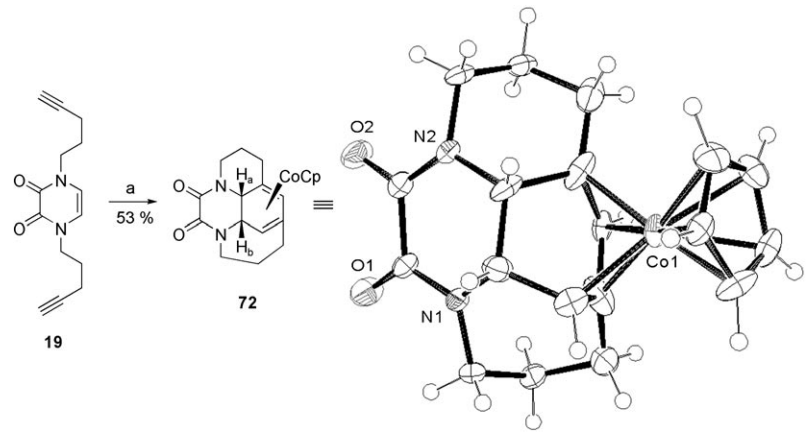
Scheme 20. Cobalt-mediated [2+2+2] cycloaddition of BTMSA to alkyne tethered pyrazinone **15**. Reagents and conditions: a) BTMSA, $[CpCo(C_2H_4)_2]$ (1.2 equiv), THF, room temperature, 3 h; b) $CuCl_2 \cdot H_2O$, NEt_3, THF, 0°C to room temperature, 7 h.



Scheme 21. Cobalt-mediated C–H activation of alkyne tethered pyrazinone **16**. Reagents and conditions: a) BTMSA, $[CpCo(C_2H_4)_2]$, THF, room temperature, 2.5 h; b) $Fe(NO_3)_3 \cdot 9H_2O$, MeCN, H_2O, 0°C, 1.5 min.

Finally, in the spirit of Scheme 8, an all-intramolecular isomerization of *N*,*N*′-dipentynylpyrazinedione **19** was executed (Scheme 22), fully expecting a symmetrical structure with the carbon tether emanating from the terminal diene carbons in the anticipated cyclohexadiene cobalt complex, such as found in the cycloisomerization of the all carbon analogue tetradeca-7-ene-1,13-diyne.[50] Surprisingly, an unsymmetrical molecule ensued, the puzzling spectral data of which were demystified only by an X-ray structural analysis (Scheme 22). It showed that one of the terminal triple bonds had been incorporated in a way that was regioisomeric to normal, the resulting bowl shaped ligand bearing the metal on its convex face. Remarkably, the bond lengths and (dihedral) angles around the metalated diene unit in this (formally) anti-Bredt[51] molecule are unexceptional. The relatively large chemical shifts of H_a [$\delta = 3.93$ (d, $J = 7.9$ Hz)] and H_b [$\delta = 3.76$ (dd, $J = 7.8$, 5.5 Hz)] corroborate the stereochemical assignments of **66** (*syn*) and **67** (*anti*). DFT computations of the system revealed that the pathway from **19** to **72** is not only perfectly feasible thermodynamically, but also that it proceeds by a new mechanism.[28] Attempts to affect

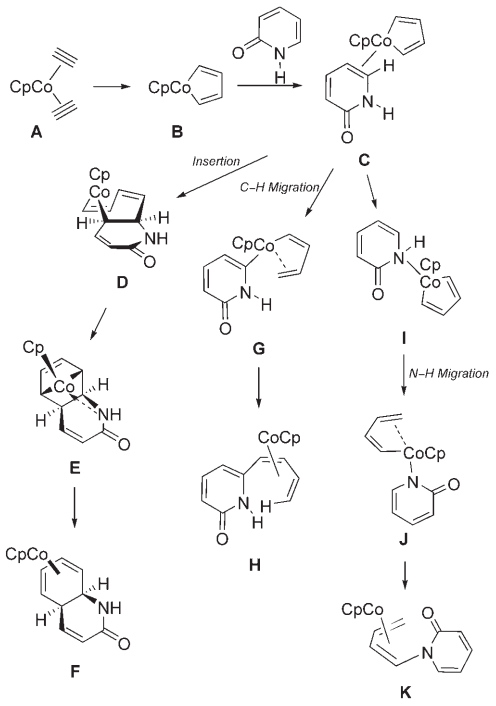
 © 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



Scheme 22. All-intramolecular [2+2+2] cycloaddition of **19**. Reagents and conditions: a) $[CpCo(C_2H_4)_2]$, toluene, room temperature, 3.5 h.

this process by shortening the tether, as in **18**, failed to give identifiable products.

General mechanistic considerations: While a more detailed mechanistic discussion is relegated to an accompanying publication dealing with DFT computations of the specific pathways of reactivity encountered in this work,[28] this and a recently published calculational appraisal[14] leads to the generic picture outlined in Scheme 23 for the reaction of 2-pyridone with ethyne. The key intermediate is the cobaltacyclopentadiene **B** derived by oxidative coupling of two ethynes in **A**. This intermediate may valence tautomerize to the corresponding cyclobutadiene complex, be trapped by addition-



Scheme 23. Generic mechanisms of the cobalt-mediated reaction of ethyne with 2-pyridone.

al ethyne to generate benzene, or by ethene to produce [CpCo(η^4-cyclohexadiene)], all types of which are observed as undesired products. The desired intermediate is η^2-pyridone complex **C** (in equilibrium with its various isomers). This species (when N-protected) may undergo insertion to cobaltacycloheptadiene **D**, giving rise to [2+2+2] adducts **F** via **E**. Alternatively, it may enter a proton transfer manifold (C–H activation) to furnish **G**, which subsequently provides dienylpyridone **H**. Finally, for N-unprotected systems, the metallotropomer **I** of **C** can undergo proton migration (N–H activation) to **J** and, eventually, *N*-dienylpyridone **K**.

Conclusion

In summary, we have extended the cobalt-mediated heterocycle activation methodology to the nuclei of pyridone and pyrazinone. The diversity of the resulting products attests to the fact that the metal has several energetically close-lying trajectories at its disposal, a finding that is corroborated by DFT calculations in an accompanying study. Synthetically, some potentially quite useful molecular alterations were uncovered, namely, in addition to [2+2+2] cycloadditions, dienylations at carbon and nitrogen proceeding by alkyne stitching. While it is, at present, difficult to predict the overall efficiency and relative preponderance of the former two pathways, it appears that the latter mode prevails for N-unprotected systems. Further experimentation should shed further light on these issues.

Experimental Section

General methods: Unless otherwise stated, all starting materials were obtained from commercial suppliers and used without further purification. DME, THF, and Et_2O were freshly distilled from sodium benzophenone; toluene and xylene were distilled from potassium and sodium, respectively, and DMSO was stored over 4 Å molecular sieves. Unless otherwise specified, all reactions that involved air- or moisture-sensitive materials were carried out under an atmosphere of dry nitrogen or argon with glassware that was oven-dried overnight at 130 °C. In these experiments, reagents were usually added via Hamilton gas tight syringes mounted on a syringe pump. Column chromatography was performed on flash silica gel (Merck Reagents silica gel 60, 230–400 mesh ASTM). Thin-layer chromatography (TLC) was carried out on a 250 μm coating with fluorescent indicator. Melting points were observed in open Pyrex capillary tubes with a Thomas-Hoover Unimelt apparatus and are uncorrected. Infrared spectra were obtained either on neat compounds (NaCl plates), in solution (solvent, NaCl cells), or with KBr pellets. ^{1}H NMR assignments, when given, were made on the basis of correlation spectroscopy. Low-

 © 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

and high-resolution mass spectra were provided by the Mass Spectral Service at the University of California at Berkeley. Elemental analyses were executed by the Microanalytical Laboratory, UCB. Microwave-assisted reactions were run in a Smith Synthesizer single-mode microwave cavity, producing continuous radiation at 2450 MHz.

***N*-(3-Butynyl)-2-pyridone (2)**: This compound was prepared by an alternative route to that published.[18] A solution of 2-pyridone (freshly recrystallized, washed with EtOAc, 98%, 2.49 g, 25.7 mmol), NaOH (1.05 g, 25.7 mmol), and 3-butynyl tosylate (96%, 5 g, 21.4 mmol)[52] in MeOH (15 mL) was heated to reflux for 21 h, during which additional MeOH (15 mL) was added to minimize foaming. The mixture was poured into water and extracted with CH_2Cl_2. The organic phase was washed with sat. Na_2CO_3, dried over $MgSO_4$, and the solvent removed in vacuo. Chromatography (hexanes/EtOAc 1:1–1:2) gave first 2-(3-butynyloxy)pyridine (121 mg, 4%). Colorless oil; IR (film): $\tilde{\nu}$3299, 2960, 2122, 1597, 1572, 1477, 1434, 1250, 1143, 1046, 1017, 780, 644 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=8.18 (dd, J=4.8, 1.2 Hz, 1H), 7.57 (dd, J=6.4, 5.2 Hz, 1H), 6.88 (dd, J=6.4, 5.2 Hz, 1H), 6.77 (d, J=8.4 Hz, 1H), 4.44 (t, J=6.8 Hz, 2H), 2.69 (td, J=6.8, 2.8 Hz, 2H), 2.03 ppm (t, J=2.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ=163.2, 146.7, 138.5, 116.8, 111.1, 80.8, 69.5, 63.5, 19.2 ppm; MS (70 eV, EI): *m/z* (%): 147 (52) [M^+], 118 (8), 108 (19), 95 (100), 78 (53), 67 (40); HRMS: Calcd for C_9H_9NO: 147.0684; found: 147.0683. Subsequent fractions contained **2** (796 mg, 25%). Colorless powder; m.p. 81–83 °C; IR (film): $\tilde{\nu}$=3451, 3295, 3232, 2961, 2117, 1660, 1582, 1539, 1438, 1353, 1168, 1147, 767 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.30–7.19 (m, 2H), 6.45 (d, J=9.2 Hz, 1H), 6.17 (t, J=6.6 Hz, 1H), 3.96 (t, J=6.4 Hz, 2H), 2.58 (m, 2H), 1.96 ppm (t, J=2.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=162.3, 139.9, 138.4, 120.7, 105.6, 80.5, 71.1, 48.8, 18.5 ppm; MS (70 eV, EI): *m/z* (%): 147 (100) [M^+], 118 (6), 108 (7), 95 (99), 80 (30), 67 (28); elemental analysis calcd (%) for C_9H_9NO: C 73.45, H 6.16, N 9.52; found: C 73.16, H 6.25, N 9.53.

***N*-(4-Pentynyl)-2-pyridone (3)**: 5-Iodo-1-pentyne (11.3 g, 52.0 mmol)[53] was added to a solution of 2-pyridone (4.94 g, 52.0 mmol) and potassium carbonate (7.16 g, 52.0 mmol) in DMSO (150 mL). The mixture was heated to 100 °C for 48 h, filtered, and solvent removed by distillation at 0.001 torr. The residue was extracted with chloroform (200 mL) and the resulting solution washed with 1.00 N HCl (2×50 mL), saturated NaCl (2×50 mL), and dried over sodium sulfate. Chromatography ($CHCl_3$/MeOH 9:1) gave **3** (7.10 g, 85%). Light yellow liquid; IR (KBr) $\tilde{\nu}$=3296, 3228, 3075, 2940, 2116, 1659, 1588, 1539, 1465, 1434, 1348, 1242, 1164, 1144, 846, 767 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=7.30 (m, 2H), 6.46 (d, J=9.7 Hz, 1H), 6.15 (td, J=6.7, 1.0 Hz, 1H), 4.04 (t, J=6.8 Hz, 2H), 2.22 (td, J=6.8, 2.6 Hz, 2H), 2.02 (t, J=2.6 Hz, 1H), 1.97 ppm (quin, J=6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=161.9, 139.4, 137.9, 121.0, 105.8, 82.7, 69.7, 48.6, 27.1, 15.4 ppm; MS (70 eV, EI): *m/z* (%): 161 (50) [M^+], 144 (8), 109 (100), 95 (19), 81 (36), 67 (32), 53 (15); HRMS: Calcd for $C_{10}H_{11}NO$: 161.0841; found: 161.0842. Further elution furnished 2-(4-pentynyloxy)pyridine (100 mg, 1%). ^1H NMR (300 MHz, $CDCl_3$): δ=2.28–2.20 (m, 3H), 2.38 (td, J=7.2, 2.6 Hz, 2H), 4.40 (t, J=6.2 Hz, 2H), 6.75 (dd, J=8.4, 2.0 Hz, 1H), 6.88 (ddd, J=8.4, 5.2, 2.0 Hz, 1H), 7.59 (td, J=8.4, 2.0 Hz, 1H), 8.15 ppm (dd, J=5.2, 2.0 Hz, 1H).

***N*-(5-Hexynyl)-2-pyridone (4)**: A solution of 2-pyridone (freshly recrystallized, washed with EtOAc, 98%, 485 mg, 5 mmol), NaOH (245 mg, 6 mmol), and 5-hexynyl tosylate (1.51 g, 6 mmol)[54] in MeOH (5 mL) was heated to refluxed for two days, during which additional MeOH (5 mL) was added after 18 h. The mixture was poured into water, extracted with CH_2Cl_2, the organic phase washed with saturated Na_2CO_3, dried over $MgSO_4$, and the solvent removed in vacuo. Chromatography (hexanes/EtOAc 1:1–1:2) eluted first 2-(5-hexynyloxy)pyridine (142 mg, 16%). Colorless oil; IR (film) $\tilde{\nu}$=3300, 2948, 2117, 1596, 1570, 1478, 1469, 1434, 1252, 1049, 989, 781, 637 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=8.15 (dt, J=4.3, 1.0 Hz, 1H), 7.56 (dd, J=2.0, 1.2 Hz, 1H), 6.85 (ddd, J=7.1, 5.1, 0.8 Hz, 1H), 6.77 (dt, J=8.4, 0.8 Hz, 1H), 4.31 (t, J=6.4 Hz, 2H), 2.28 (m, 2H), 1.97 (t, J=2.8 Hz, 1H), 1.91 (m, 2H), 1.72 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=163.9, 146.8, 138.6, 116.6, 111.1, 84.2, 68.6, 65.3, 28.2, 25.1, 18.2 ppm; MS (70 eV, EI): *m/z* (%): 175 (22) [M]$^+$, 147 (16), 146 (26), 96 (51), 95 (100), 79 (36), 78 (36), 67 (74); HRMS: Calcd for $C_{11}H_{13}NO$: 175.0997. Found: 175.0995. Further fractions provided **4** (406 mg, 46%). Colorless oil; IR (film): $\tilde{\nu}$=3445, 3296, 3230, 2944, 2115, 1660, 1583, 1539, 1465, 1435, 1145, 768 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.33–7.25 (m, 2H), 6.56 (d, J=9.2 Hz, 1H), 6.16 (td, J=6.7, 1.1 Hz, 1H), 3.95 (t, J=7.4 Hz, 2H), 2.25 (td, J=6.9, 2.7 Hz, 2H), 1.96 (t, J=2.6 Hz, 1H), 1.88 (m, 2H), 1.58 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=162.6, 139.4, 137.5, 121.1, 106.1, 83.7, 68.9, 49.2, 28.4, 25.4, 18.1 ppm; MS (70 eV, EI): *m/z* (%): 175 (89) [M^+], 136 (100), 133 (49), 109 (65), 95 (69), 80 (79), 67 (49); HRMS: Calcd for $C_{11}H_{13}NO$: 175.0997; found: 175.0994.

***N*-(6-Heptynyl)-2-pyridone (5)**: A solution of 2-pyridone (freshly recrystallized, washed with EtOAc, 98%, 1.227 g, 12.9 mmol), NaOH (0.52 g, 12.9 mmol), and 6-heptynyl tosylate (4.12 g, 15.5 mmol)[55] in MeOH (15 mL) was heated to reflux for 22 h. It was then poured into water, extracted with CH_2Cl_2, the organic phase washed with sat. Na_2CO_3, dried over Na_2SO_4, and the solvent removed in vacuo. Chromatography (hexanes/EtOAc 1:1–1:2) delivered **5** (1.226 g, 50%). Slightly reddish oil; IR (film): $\tilde{\nu}$=3449, 3297, 3230, 2940, 2862, 2115, 1659, 1584, 1539, 1465, 1434, 1159, 1144, 768 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.32–7.23 (m, 2H), 6.56 (dd, J=9.0, 0.6 Hz, 1H), 6.16 (td, J=6.6, 1.3 Hz, 1H), 3.92 (t, J=7.4 Hz, 2H), 2.25 (td, J=6.9, 2.7 Hz, 2H), 1.93 (t, J=2.6 Hz, 1H), 1.79–1.71 (m, 2H), 1.59–1.50 (m, 2H), 1.50–1.40 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=162.6, 139.3, 137.5, 121.2, 105.9, 84.2, 68.5, 49.8, 28.8, 28.0, 25.7, 18.3 ppm; MS (70 eV, EI): *m/z* (%): 189 (84) [M^+], 188 (100), 150 (69), 109 (61), 96 (48); HRMS: Calcd for $^{12}C_{11}{}^{13}CH_{15}NO$: 190.1187; found: 190.1187.

***N*-(3,8-Nonadiynyl)-2-pyridone (6)**: To a solution of *N*-3-butynyl-2-pyridone (**2**) (1.21 g, 8.22 mmol) in dry THF (50 mL) was added BuLi (2.5 M, 4.6 mL, 11.5 mmol) via syringe at −78 °C and the mixture stirred for 1 h at −78 °C. Neat 5-iodo-1-pentyne (6.38 g, 32.9 mmol)[53] was added, the solution allowed to warm to room temperature overnight, the mixture poured into H_2O (80 mL), and the aqueous layer extracted with Et_2O (4×50 mL). After drying over $MgSO_4$, the volatiles were removed under reduced pressure, and the crude product purified by column chromatography ($CHCl_3$) to yield **6** (1.21 g, 68%). Pale amber oil; IR (thin film): $\tilde{\nu}$=3274, 2858, 1660, 1582, 1531, 1424, 1180, 1131, 834 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ=7.31–7.21 (m, 2H), 6.41 (d, J=8.6, 1H), 6.05 (d, J=8.6, 1H), 3.95–3.86 (m, 2H), 2.59–2.48 (m, 2H), 2.19–2.08 (m, 4H), 1.85 (t, J=2.7 Hz, 1H), 1.61–1.47 ppm (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=165.2, 136.3, 134.4, 124.7, 103.2, 83.2, 79.5, 72.4, 68.6, 46.3, 23.4, 18.5, 17.9, 17.1 ppm; MS (70 eV, EI): *m/z* (%): 213 (18) [M^+], 212 (79), 196 (56), 184 (61), 134 (31), 117 (100); HRMS: Calcd for $C_{14}H_{15}NO$: 213.1118; found: 213.1153; elemental analysis calcd (%) for $C_{14}H_{15}NO$: C 78.84, H 7.09, N 6.57; found: C 78.57, H 7.22, N 6.63.

***N*-(4,9-Decadiynyl)-2-pyridone (7)**: To a solution of *N*-4-pentynyl-2-pyridone (**3**) (3.00 g, 18.6 mmol) in dry THF (120 mL) was added BuLi (2.5 M, 10.4 mL, 26 mmol) via syringe at −78 °C. The solution was stirred for 1 h at −78 °C, neat 5-iodo-1-pentyne (16 g, 82.5 mmol) added and the reaction mixture allowed to warm to room temperature overnight. The mixture was poured into water (150 mL), extracted with ethyl ether (4×60 mL), the organic layer dried over $MgSO_4$, and solvents removed under reduced pressure. Column chromatography (hexanes/EtOAc 2:1) gave **7** (2.20 g, 52%). Brown oil; IR (thin film): $\tilde{\nu}$=3293, 2936, 2866, 1659, 1586, 1539, 1434, 1335, 1169, 1164, 1145, 846, 767 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.12 (m, 2H), 6.30 (d, J=10.0 Hz, 1H), 5.97 (t, J=7.0 Hz, 1H), 3.81 (t, J=7.0 Hz, 2H), 2.21 (m, 4H), 1.97 (td, J=6.4, 2.7 Hz, 2H), 1.82 (t, J=2.7 Hz, 1H), 1.71 (q, J=6.6 Hz, 2H), 1.48 ppm (q, J=7.0 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$): δ=162.6, 139.4, 137.9, 121.0, 105.8, 83.5, 80.4, 79.2, 60.3, 48.9, 27.9 (2C), 17.7, 17.4, 15.8 ppm; MS (70 eV, EI): *m/z* (%): 227 (2) [M^+], 226 (7) [M^+-H], 132 (52), 109 (100); HRMS: Calcd for $C_{15}H_{17}NO$: 227.1310; found: 227.1303.

***N*-(2-Propynyl)-4-pyridone (9)**: To a mixture of 3-bromopropyne (80% w/w in toluene, 300 μL, 2.69 mmol) in MeCN (9 mL) at reflux was added 4-trimethylsilyloxypyridine (**8**) (336 mg, 2.01 mmol)[20] in MeCN (3 mL) via syringe pump over a period of 45 min. After a total of 3 h, the reaction mixture was cooled to room temperature and treated with MeOH (3.7 mL) and solid K_2CO_3 (750 mg). Following a further 30 min, the suspension was filtered and concentrated in vacuo. The residue was purified by chromatography (CH_2Cl_2/MeOH 8:1) to give compound **9** (229 mg,

 © 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

85%). Blue-green oil; IR (film): $\tilde{\nu}$ = 3405, 3080, 2955, 2123, 1640, 1546, 1183, 853, 574 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.72 (d, J = 7.5 Hz, 2H), 6.49 (d, J = 7.6 Hz, 2H), 4.80 (d, J = 2.5 Hz, 2H), 2.65 ppm (t, J = 2.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.3, 140.3, 118.2 (br), 77.4, 75.2, 45.9 ppm; MS (70 eV, EI): m/z (%): 133 (100) [M^+], 105 (31), 104 (63), 78 (14), 52 (16); HRMS: Calcd for C_8H_7NO: 133.0528; found: 133.0526.

***N*-(3-Butynyl)-4-pyridone (10)**: A solution of impure 4-iodo-1-butyne (550 mg, 3.05 mmol) in MeCN (15 mL) was combined with **8** (540 mg, 3.23 mmol) in MeCN (6 mL). Treatment of the reaction mixture with MeOH (6 mL) and K_2CO_3 (1.2 g, 8.7 mmol) was followed by filtration and concentration in vacuo to leave a white solid residue. Chromatography (CH_2Cl_2/MeOH 10:1–8:1) gave **10** (76 mg, 17%). Colorless solid; m.p. 97–100 °C; IR (film): $\tilde{\nu}$ = 3383, 3291, 2962, 2925, 2116, 1641, 1557, 1404, 1187, 854 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.34 (d, J = 5.9 Hz, 2H), 6.34 (d, J = 5.9 Hz, 2H), 3.90 (t, J = 6.4 Hz, 2H), 2.63 (td, J = 6.4, 2.6 Hz, 2H), 2.10 ppm (t, J = 2.6 Hz, 1H); ^{13}C-DEPT NMR (125 MHz, $CDCl_3$): δ = 178.7 (C), 140.1 (CH), 118.1 (CH), 78.8 (C), 72.4 (CH), 54.7 (CH_2), 20.9 (CH_2); MS (70 eV, EI): m/z (%): 147 (44) [M^+], 118 (4), 109 (7), 108 (100), 95 (3), 82 (19), 53 (6); HRMS: Calcd for C_9H_9NO: 147.0684; found: 147.0682.

***N*-(4-Pentynyl)-4-pyridone (11)**: Following the procedure described above, a solution of 5-iodo-1-pentyne (1.2 g, 6.2 mmol) in MeCN (10 mL) was combined with **8** (795 mg, 4.75 mmol) in MeCN (4 mL). After 3.5 h, the reaction mixture was treated with MeOH (4 mL) and K_2CO_3 (800 mg). Filtration and concentration in vacuo left a white solid residue. Chromatography (CH_2Cl_2/MeOH 10:1) furnished **11** (655 mg, 85%). Yellow oil; IR (film): $\tilde{\nu}$ = 3291, 1640, 1548, 1194, 854 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.33 (d, J = 7.2 Hz, 2H), 6.38 (d, J = 7.1 Hz, 2H), 3.95 (t, J = 6.8 Hz, 2H), 2.23 (td, J = 6.4, 2.6 Hz, 2H), 2.08 (t, J = 2.6 Hz, 1H), 1.95 ppm (quin, J = 6.6 Hz, 2H); ^{13}C-DEPT NMR (125 MHz, $CDCl_3$): δ = 178.6 (C), 139.8 (CH), 118.4 (CH), 81.3 (C), 70.5 (CH), 54.6 (CH_2), 28.7 (CH_2), 14.8 ppm (CH_2); MS (70 eV, EI): m/z (%): 161 (100) [M^+], 133 (19), 132 (49), 120 (16), 108 (96), 107 (30), 82 (25), 81 (41), 67 (13); HRMS: Calcd for $C_{10}H_{11}N_1O_1$: 161.0841; found: 161.0838.

***N*-(5-Hexynyl)-4-pyridone (12)**: Following the procedure described above, a solution of 6-iodo-1-hexyne (501 g, 2.40 mmol)[56] in MeCN (8 mL) was combined with compound **8** (357 mg, 2.13 mmol) in MeCN (3 mL). After 3 h, the reaction mixture was treated with MeOH (2.5 mL) and K_2CO_3 (550 mg) and then filtered and concentrated in vacuo. Chromatography (CH_2Cl_2/MeOH 10:1) gave compound **12** (222 mg, 60%). White solid; m.p. 121–124 °C; IR (KBr): $\tilde{\nu}$ = 3192, 2942, 2862, 1675, 1639, 1553, 1520, 1510, 1190, 853, 722, 534 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.26 (d, J = 7.6 Hz, 2H), 6.29 (d, J = 7.5 Hz, 2H), 3.76 (t, J = 7.3 Hz, 2H), 2.19 (td, J = 6.8, 2.6 Hz, 2H), 1.94 (t, J = 2.6 Hz, 1H), 1.85 (quin, J = 7.5 Hz, 2H), 1.48 ppm (quin, J = 7.3 Hz, 2H); ^{13}C-DEPT NMR (125 MHz, $CDCl_3$): δ = 178.7 (C), 139.5 (CH), 118.7 (CH), 82.8 (C), 69.4 (CH), 56.3 (CH_2), 29.6 (CH_2), 24.6 (CH_2), 17.8 ppm (CH_2); MS (70 eV, EI): m/z (%): 175 (64) [M^+], 146 (31), 121 (28), 120 (23), 108 (100), 82 (23), 67 (10), 53 (13); HRMS: Calcd for $C_{11}H_{13}NO$: 175.0997; found: 175.0998.

***N*-(4-Pentynoyl)-4-pyridone (13) and pyridin-4-yl pent-4-ynoate (14)**: To a solution of 4-pyridone (1.04 g, 10.9 mmol) in CH_2Cl_2 (20 mL) at room temperature was added a solution of 4-pentynoyl chloride (625 mg, 5.46 mmol) in CH_2Cl_2 (5 mL) over 3 min. After 30 min, the reaction mixture was transferred via canula to a Schlenk flask fitted with a glass frit. The mixture was filtered through the frit into another Schlenk flask and concentrated in vacuo to give a solid consisting of **13** and **14** (545 mg, 58%) in an approximate ratio of 3:2 (^1H NMR). White solid; ^1H NMR (300 MHz, CD_2Cl_2) signals attributable to **13**: δ = 8.10 (dd, J = 8.2 Hz, 2H), 6.28 (d, J = 8.3 Hz, 2H), 3.10 (t, J = 6.9 Hz, 2H), 2.68 (td, J = 7.3, 2.6 Hz, 2H), 2.08 ppm (t, J = 2.6 Hz, 1H). Chromatography of the mixture (MeOH) afforded only **14** contaminated with methyl 4-pentynoate. Colorless oil; IR (film): $\tilde{\nu}$ = 3298, 3061, 2943, 2118, 1763, 1593, 1470, 1434, 1196, 1128, 734, 647 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.60 (d, J = 5.6 Hz, 2H), 7.10 (d, J = 6.1 Hz, 2H), 2.80 (t, J = 7.2 Hz, 2H), 2.59 (td, J = 7.3, 2.6 Hz, 2H), 2.02 ppm (t, J = 2.6 Hz, 1H); ^{13}C NMR-DEPT (125 MHz, $CDCl_3$): δ = 168.9 (C), 157.2 (C), 151.4 (CH), 116.8 (CH), 81.6 (C), 69.6 (CH), 33.5 (CH_2), 14.3 ppm (CH_2). No attempts were made to obtain these compounds completely pure.

1-(3-Butynyl)-2-pyrazinone (15): A mixture of 2-pyrazinone (507 mg, 5.28 mmol), 3-butynyl tosylate (1.24 g, 5.6 mmol),[52] and K_2CO_3 (1.50 g, 11.7 mmol) in CH_3CN (130 mL) was stirred under reflux for 6 h. The mixture was then allowed to cool to room temperature, concentrated on a rotary evaporator, and extracted with CH_2Cl_2 and H_2O. The combined organic phases were dried over $MgSO_4$, filtered, and concentrated. Chromatography (CH_2Cl_2/MeOH 20:1) gave the known *O*-alkynylation side product (224 mg, 29%) 2-(3-butynyloxy)pyrazine[57] and then **15** (322 mg, 41%). IR (KBr): $\tilde{\nu}$ = 3225, 3075, 3050, 3020, 2960, 2920, 1650, 1585, 1500, 1455, 1445, 1430, 1365, 1355, 1310, 1185, 1125, 1060, 1000, 920, 810, 745, 710, 615, 595, 550, 525 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ = 8.15 (s, 1H), 7.32 (d, J = 4.4 Hz, 1H), 7.20 (dd, J = 4.4, 1.2 Hz, 1H), 4.01 (t, J = 6.3 Hz, 2H), 2.70 (td, J = 6.3, 2.7 Hz, 2H), 2.04 ppm (t, J = 2.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 156.0, 149.5, 129.5, 123.5, 79.7, 71.8, 48.5, 18.1 ppm; MS (70 eV, EI): m/z (%): 148 (92) [M^+], 119 (19), 96 (100), 81 (50), 68 (30), 54 (18); HRMS: Calcd for $C_8H_8N_2O$: 148.0637; found: 148.0637.

1-(4-Pentynyl)-2-pyrazinone (16): A mixture of 2-pyrazinone (154 mg, 1.60 mmol), 4-pentynyl tosylate (425 mg, 1.91 mmol),[58] and $CsCO_3$ (1.06 g, 5.50 mmol) in CH_3CN (40 mL) was stirred under reflux for 1 h. The mixture was allowed to cool to room temperature, concentrated on a rotary evaporator, and extracted with CH_2Cl_2 and H_2O. The combined organic phases were dried over $MgSO_4$, filtered, and concentrated. Column chromatography (hexanes/CH_2Cl_2/EtOAc 3:1:1-CH_2Cl_2/MeOH 9:1) gave **16** (135 mg, 52%). Colorless oil; IR (KBr): $\tilde{\nu}$ = 3220, 3080, 3060, 3015, 2960, 1655, 1585, 1490, 1460, 1435, 1340, 1270, 1215, 1165, 1125, 1075, 1050, 915, 815, 760, 734, 690, 620, 575 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ = 8.13 (d, J = 0.9 Hz, 1H), 7.31 (d, J = 4.4 Hz, 1H), 7.16 (dd, J = 4.4, 1.1 Hz, 1H), 4.02 (t, J = 6.9 Hz, 2H), 2.25 (td, J = 6.6, 2.6 Hz, 2H), 2.05 (t, J = 2.6 Hz, 1H), 1.97 ppm (quin, J = 6.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 156.0, 149.4, 129.1, 123.6, 82.1, 70.3, 48.3, 26.4, 15.4 ppm; MS (70 eV, EI): m/z (%): 162 (49) [M^+], 145 (9), 133 (8), 120 (33), 110 (100), 106 (8), 97 (28), 82 (47), 79 (10), 68 (28), 66 (17), 54 (13), 52 (6); HRMS: Calcd for $C_9H_{10}N_2O$: 162.0793; found: 162.0793. A subsequent fraction gave 2-(4-pentynyloxy)pyrazine (110 mg, 42%). Colorless oil; IR (KBr): $\tilde{\nu}$ = 3625, 3060, 2965, 2945, 2905, 1585, 1535, 1470, 1420, 1375, 1310, 1295, 1200, 1155, 1075, 1060, 1035, 1010, 935, 845, 755, 690, 650, 615 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ = 8.22 (s, 1H), 8.10 (ABm, 2H), 4.42 (t, J = 6.9 Hz, 2H), 2.40 (td, J = 7.1, 2.6 Hz, 2H), 2.02 ppm (quin, J = 6.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 160.2, 140.6, 136.6, 136.0, 83.2, 69.1, 64.7, 27.8, 15.3 ppm; MS (70 eV, EI): m/z (%):162 (22) [M^+], 147 (9), 134 (79), 123 (9), 106 (5), 96 (100), 79 (27), 68 (66), 66 (24), 52 (18); HRMS: Calcd for $C_9H_{10}N_2O$: 162.0793; found: 162.0792.

1-(5-Hexynyl)-2-pyrazinone (17): A mixture of 2-pyrazinone (216 mg, 2.23 mmol), 6-iodo-1-hexyne (521 mg, 2.50 mmol)[56] and K_2CO_3 (623 mg, 4.51 mmol) in CH_3CN (50 mL) was stirred under reflux for 19 h. The mixture was allowed to cool to room temperature, concentrated on a rotary evaporator, and extracted with CH_2Cl_2 and H_2O. The combined organic phases were dried over $MgSO_4$, filtered, and concentrated. Chromatography (CH_2Cl_2/MeOH 20:1) furnished **17** (237 mg, 60%). Colorless oil; IR (KBr): $\tilde{\nu}$ = 3225, 3085, 2960, 2905, 1655, 1630, 1580, 1560, 1490, 1460, 1430, 1375, 1340, 1310, 1285, 1240, 1210, 1155, 1120, 1090, 1015, 920, 820, 740, 720, 625, 585, 555, 525 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ = 8.14 (d, J = 1.2 Hz, 1H), 7.32 (d, J = 4.4 Hz, 1H), 7.09 (dd, J = 4.4, 1.2 Hz, 1H), 3.92 (t, J = 7.3 Hz, 2H), 2.27 (td, J = 6.9, 2.6 Hz, 2H), 1.97 (t, J = 2.6 Hz, 1H), 1.95–1.85 (m, 2H), 1.63–1.53 ppm (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 156.2, 149.7, 128.6, 124.0, 84.4, 69.3, 48.9, 27.8, 25.2, 18.0 ppm; MS (70 eV, EI): m/z (%): 176 (30) [M^+], 175 (30), 159 (19), 147 (15), 137 (38), 134 (100), 120 (11), 110 (38), 96 (60), 79 (75), 68 (60), 53 (27); HRMS: Calcd for $C_{10}H_{12}N_2O$: 176.0948; found: 176.0950. A subsequent fraction gave 2-(5-hexynyloxy)pyrazine (103 mg, 26%). Colorless oil; IR (KBr): $\tilde{\nu}$ = 3300, 3060, 2950, 2870, 2115, 1580, 1535, 1470, 1415, 1380, 1310, 1290, 1195, 1180, 1155, 1060, 1050, 1000, 950, 920, 840, 750, 735, 640, 610, 540 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ = 8.22 (d, J = 1 Hz, 1H), 8.08 (ABm, 2H), 4.33 (t, J = 6.4 Hz, 2H), 2.28 (td, J = 7.1, 2.6 Hz, 2H), 1.96 (t, J = 2.6 Hz, 1H), 1.96–1.87 (m, 2H), 1.75–1.65 ppm

 © 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

(m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 160.4, 140.6, 136.5, 136.1, 84.0, 68.9, 65.8, 27.9, 25.1, 18.2 ppm; MS (70 eV, EI): *m/z* (%): 176 (4) [M^+], 175 (12), 147 (58), 135 (6), 120 (7), 107 (6), 96 (90), 79 (100), 68 (68), 53 (32); HRMS: Calcd for $C_{10}H_{12}N_2O$: 176.0948; found: 176.0950.

***N,N′*-Di(3-butynyl)-2,3-pyrazinedione (18)**: To a solution of 1,4-dihydro-2,3-pyrazinedione (300 mg, 2.68 mmol) in DMSO (50 mL) was added a 60% NaH dispersion (235 mg, 5.87 mmol) under H_2 evolution. After 10 min, 3-butynyl tosylate (1.26 g, 5.632 mmol)[52] was added and the mixture stirred at room temperature for 3.5 days. The DMSO was removed under high vacuum, the brown residue transferred into a separatory funnel, extracted with CH_2Cl_2/H_2O, and the combined organic layers dried over $MgSO_4$, filtered and concentrated. Column chromatography (CH_2Cl_2/MeOH 20:1) delivered compound **18** (227 mg, 39%). White solid; IR (KBr): $\tilde{\nu}$ = 3245, 3110, 2960, 2115, 1685, 1655, 1640, 1590, 1460, 1420, 1385, 1320, 1275, 1225, 1175, 1000, 815, 720, 685, 625, 575, 525 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.28 (s, 2H), 3.91 (t, *J* = 6.5 Hz, 4H), 2.65 (td, *J* = 6.5, 2.6 Hz, 4H), 2.02 (t, *J* = 2.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 155.7, 113.4, 80.4, 71.2, 48.0, 18.1; MS (70 eV, EI): *m/z* (%): 216 (100) [M^+], 177 (11), 164 (94), 149 (31), 112 (47), 97 (26), 83 (18), 69 (20); HRMS: Calcd for $C_{12}H_{12}N_2O_2$: 217.0932; found: 217.0933.

***N,N′*-Di(4-pentynyl)-2,3-pyrazinedione (19)**: To a solution of 1,4-dihydro-2,3-pyrazinedione (349 mg, 3.11 mmol) in DMSO (50 mL) was added a 60% NaH dispersion (270 mg, 6.75 mmol) generating H_2. After 10 min, 4-pentynyl tosylate (1.49 g, 6.24 mmol)[58] was added and the mixture stirred at room temperature for 18 h. Purification as for **18** provided **19** (458 mg, 60%). White solid; IR (KBr): $\tilde{\nu}$ = 3245, 2945, 1685, 1675, 1650, 1590, 1460, 1425, 1335, 1315, 1275, 1220, 1005, 860, 805, 765, 725, 680, 575, 540, 510 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.39 (s, 2H), 3.90 (t, *J* = 6.9 Hz, 4H), 2.26 (td, *J* = 6.9, 2.6 Hz, 4H), 2.02 (t, *J* = 2.6 Hz, 2H), 1.94 ppm (quin, *J* = 6.9 Hz, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 155.8, 113.1, 82.5, 69.9, 47.8, 26.5, 15.7 ppm; MS (70 eV, EI): *m/z* (%): 244 (84) [M^+], 227 (9), 215 (5), 192 (100), 175 (10), 163 (18), 150 (20), 136 (22), 126 (54), 120 (35), 108 (22), 97 (21), 81 (18), 65 (35), 55 (22); HRMS: Calcd for $C_{14}H_{16}N_2O_2$: 244.1212; found: 244.1217.

Cobalt-mediated cycloaddition of *N*-methyl-2-pyridone to 1,7-octadiyne: To a refluxing solution of *N*-methyl-2-pyridone (985 mg, 9.03 mmol) in dry THF (40 mL) was added 1,7-octadiyne (180 μL, 144 mg, 1.36 mmol) in THF (8 mL) and [$CpCo(C_2H_4)_2$] (268 mg, 1.49 mmol) in THF (8 mL) via separate syringes over a period of 110 min. After a total of 2.5 h, the mixture was concentrated in vacuo and the residue subjected to chromatography (hexanes/EtOAc 3:1) to yield five sets of fractions A, B, C, D, and E, in order of increasing polarity. Fractions A were rechromatographed (hexanes/EtOAc 100:1–20:1) to afford trimer **24** (13 mg, 9%)[24] preceded by diene complex **25** (7.1 mg, 2%). Red-brown oil; UV/Vis (CH_3OH): λ_{max} (logε) = 260 (4.00), 348 (2.90), 389 (2.78) nm; IR (thin film): $\tilde{\nu}$ = 2936, 2841, 1450, 1437, 1354, 1165, 1114, 1016, 806 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6): δ = 4.59 (s, 5H), 2.98 (d, *J* = 2.4 Hz, 2H), 2.42 (dt, *J* = 16.2, 6.2 Hz, 2H), 2.17 (dt, *J* = 16.0, 6.3 Hz, 2H), 2.03 (m, 2H), 1.71 (m, 2H), 1.62 (AA′m, 2H), 0.97 ppm (BB′m, 2H); ^{13}C NMR (75 MHz, C_6D_6): δ = 93.8, 80.6, 50.4, 29.5, 26.2, 24.0 ppm; MS (EI, 70 eV): *m/z* (%): 258 (100) [M^+], 256 (70), 252 (58), 188 (73), 187 (80), 124 (12); HRMS: Calcd for $C_{15}H_{19}Co$: 258.0819; found: 258.0818; elemental analysis calcd (%) for $C_{15}H_{19}Co$: C 69.76, H 7.42; found C 69.66, H 7.48.

Fractions B were concentrated and rechromatographed (hexanes/EtOAc 2:1) to give, in order, **22** (5.3 mg, 1.1%), the aromatic **23** (5.1 mg, 1.8%), and impure complex **20c** (3.7 mg, 1.0%).

Compound 22: Orange oil; IR (film): $\tilde{\nu}$ = 2929, 2360, 1652, 1262, 1094, 1024, 801 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6): δ = 5.06 (dd, *J* = 8.0, 1.7 Hz, 1H), 4.56 (dd, *J* = 8.0, 3.3 Hz, 1H), 4.41 (s, 5H), 3.62 (d, *J* = 4.2 Hz, 1H), 2.99 (dd, *J* = 12.1, 4.2 Hz, 1H), 2.83 (d, *J* = 4.2 Hz, 1H), 2.59 (s, 3H), 2.32 (m, 3H), 1.99 (m, 2H), 1.77 (m, 2H), 1.53 ppm (m, 2H); ^{13}C NMR (125 MHz, C_6D_6): δ = 170.5, 125.0, 107.9, 93.4, 93.1, 81.4 (Cp), 54.1, 53.4, 45.2, 38.8, 34.1, 30.2, 29.5, 24.0, 23.9 ppm; MS (70 eV, EI): *m/z* (%): 339 (33) [M^+], 338 (21), 337 (100), 271 (54), 269 (29), 267 (13), 215 (13), 214 (14), 187 (8), 172 (9); HRMS: Calcd for $C_{19}H_{22}CoNO$: 339.1033; found: 339.1034.

Compound 23: Yellow oil; IR (film): $\tilde{\nu}$ = 2928, 2857, 1647, 1630, 1604, 794 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.12 (s, 1H), 7.19 (s, 1H), 6.95 (d, *J* = 7.3 Hz, 1H), 6.37 (d, *J* = 7.3 Hz, 1H), 3.57 (s, 3H), 2.92 (m, 2H), 2.88 (m, 2H), 1.83 ppm (m, 4H); ^{13}C NMR-DEPT (125 MHz, $CDCl_3$): δ = 142.4 (C), 137.0 (C), 134.8 (C), 131.4 (CH), 127.4 (CH), 125.5 (CH), 105.7 (CH), 36.9 (CH_3), 29.8 (CH_2), 29.4 (CH_2), 23.1 (CH_2), 22.9 ppm (CH_2), signals for the carbonyl and one quaternary carbon not detected; MS (70 eV, EI): *m/z* (%): 213 (100) [M^+], 212 (72), 198 (12), 185 (26), 128 (12), 115 (17); HRMS: Calcd for $C_{14}H_{15}NO$: 213.1154; found: 213.1155.

Compound 20c: Orange oil; IR (film): $\tilde{\nu}$ = 2928, 2855, 1615, 1435, 1265, 805, 335 cm^{-1}; partial ^{1}H NMR (300 MHz, C_6D_6): δ = 4.52 (s, 5H), 4.46 (s, 5H), 3.99 (d, *J* = 3.0 Hz, 1H), 3.15 (s, 3H), 2.92 (d, *J* = 3.7 Hz, 1H), 2.75 (m, 1H), 2.50–1.40 (m, 19H), 0.80 (d, *J* = 7.7 Hz, 1H), 0.68 ppm (d, *J* = 6.6 Hz, 1H); MS (70 eV, EI): *m/z* (%): 569 (100) [M^+], 503 (8), 445 (33), 443 (23), 441 (32), 380 (41), 378 (67), 376 (30), 337 (11), 317 (10), 256 (25), 191 (23), 189 (52), 187 (33), 171 (12), 124 (39). HRMS: Calcd for $C_{32}H_{37}Co_2NO$: 569.1539; found: 569.1541.

Fractions C were concentrated and rechromatographed (hexanes/EtOAc 2:1) to give **20a** (48.3 mg, 12.4%). Orange waxy solid; m.p. 76–78 °C; IR (KBr): $\tilde{\nu}$ = 3091, 2927, 2852, 1623, 1432, 802 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6): δ = 4.50 (s, 5H), 4.43 (s, 5H), 3.78 (d, *J* = 2.7 Hz, 1H), 3.54 (dd, *J* = 8.89, 4.2 Hz, 1H), 3.01 (s, 3H), 2.86 (d, *J* = 4.2 Hz, 1H), 2.54 (d, *J* = 3.1 Hz, 1H), 2.50 (br s, 1H), 2.43 (dt, *J* = 16.1, 6.4 Hz, 1H), 2.38 (dt, *J* = 8.8, 3.4 Hz, 1H), 2.26 (m, 2H), 2.13 (m, 3H), 1.97 (m, 3H), 1.87 (m, 4H), 1.73 (m, 1H), 1.67 (m, 1H), 1.57 (m, 2H), 0.60 ppm (br s, 1H); ^{13}C NMR-DEPT (125 MHz, C_6D_6): δ = 169.5 (C), 95.1 (C), 93.3 (C), 93.0 (C), 92.0 (C), 81.5 (CH, Cp), 81.3 (CH, Cp), 57.1 (CH), 55.1 (CH), 54.1 (CH), 53.0 (CH), 48.4 (CH), 45.2 (CH), 43.6 (CH), 42.1 (CH), 32.8 (CH_3), 29.7 (CH_2), 29.63 (CH_2), 29.59 (CH_2), 29.3 (CH_2), 24.3 (CH_2), 24.2 (CH_2), 24.0 (CH_2), 23.9 ppm (CH_2); MS (70 eV, EI): *m/z* (%): 569 (52) [M^+], 503 (8), 445 (10), 444 (10), 380 (10), 257 (17), 256 (100), 252 (10), 187 (10), 124 (7); HRMS: Calcd for $C_{32}H_{37}Co_2NO$: 569.1539; found: 569.1536.

Fractions D were concentrated and rechromatographed (hexanes/EtOAc 1:1) to give a 1:1 mixture of **20d** and **20e** (29 mg, 7.5%) and pure **20b** (8.6 mg, 2.2%).

Mixture 20d/e (1:1): Orange oil; ^{1}H NMR (500 MHz, C_6D_6): δ = 4.44 (s, 5H, Cp), 4.39 (s, 5H, Cp), 4.32 (s, 5H, Cp), 4.27 (s, 5H, Cp), 3.57 (br s, 2H), 3.52 (d, *J* = 4.4 Hz, 1H), 3.44 (br s, 1H), 3.34 (br s, 1H), 3.16 (dd, *J* = 9.0, 3.6 Hz, 1H), 2.97 (m, 1H), 2.83 (d, *J* = 3.6 Hz, 1H), 2.78 (d, *J* = 3.6 Hz, 1H), 2.76 (d, *J* = 3.6 Hz, 1H), 2.71 (s, 3H, *N*-Me), 2.57 (s, 3H, *N*-Me), 2.50–0.70 ppm (m, 38H); ^{13}C NMR (125 MHz, C_6D_6): δ = 170.9, 170.5, 93.8, 93.1, 91.8, 91.5, 83.5 (Cp), 83.0 (Cp), 80.5 (2Cp), 73.8, 69.7, 67.4, 63.8, 61.6, 58.4, 56.7, 53.8, 52.4, 50.5, 50.4, 49.7, 48.0, 46.4, 45.0, 44.8, 43.1, 41.2, 37.1, 31.6, 30.0, 29.8, 29.5, 29.4, 29.2, 29.0, 28.9, 28.8, 28.7, 28.4, 27.5, 27.3, 23.60, 23.58, 23.5, 23.3, 23.2, 22.8 ppm; MS (70 eV, EI): *m/z* (%): 569 (59) [M^+], 501 (5), 445 (17), 378 (21), 376 (26), 339 (17), 257 (19), 256 (100), 252 (8), 189 (10), 187 (16), 124 (13).

Compound 20b: Orange oil; IR (film): $\tilde{\nu}$ = 2924, 2854, 1622, 1456, 1378, 802 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6): δ = 4.44 (s, 5H), 4.39 (s, 5H), 3.53 (d, *J* = 4.4 Hz, 1H), 3.17 (dd, *J* = 9.0, 3.6 Hz, 1H), 2.84 (d, *J* = 3.4 Hz, 1H), 2.78 (d, *J* = 3.6 Hz, 1H), 2.76 (d, *J* = 3.3 Hz, 1H), 2.72 (s, 3H), 2.45 (dd, *J* = 6.0, 1.1 Hz, 1H), 2.40 (dt, *J* = 16.2, 6.4 Hz, 1H), 2.28 (m, 3H), 2.22 (m, 1H), 2.10 (m, 2H), 1.98 (m, 2H), 1.89 (m, 3H), 1.81 (m, 4H), 1.60 ppm (m, 2H); ^{13}C NMR (125 MHz, C_6D_6): δ = 171.0, 94.3, 93.5, 92.2, 91.8, 80.91 (Cp), 80.89 (Cp), 58.7, 52.8, 51.0, 50.7, 48.3, 46.9, 45.5, 41.4, 32.0, 29.8, 29.33, 29.28, 29.2, 24.0, 23.9, 23.6, 23.5 ppm; MS (70 eV, EI): *m/z* (%): 569 (36) [M^+], 501 (7), 445 (29), 443 (19), 441 (19), 378 (26), 376 (23), 375 (23), 257 (17), 256 (100), 187 (8), 124 (6); HRMS: Calcd for $C_{32}H_{37}Co_2NO$: 569.1539; found: 569.1540.

Fractions E were concentrated and rechromatographed (hexanes/EtOAc 1:4) to give compound **21** (7.5 mg, 1.6%). Orange oil; IR (film): $\tilde{\nu}$ = 2928, 1663, 1608, 1108, 810 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6): δ = 5.69 (d, *J* = 9.6 Hz, 1H), 5.58 (d, *J* = 9.6 Hz, 1H), 4.35 (s, 5H), 3.44 (dd, *J* = 10.0, 2.7 Hz, 1H), 2.93 (s, 3H), 2.49 (d, *J* = 4.4 Hz, 1H), 2.31 (d, *J* = 10.7 Hz, 1H), 2.12 (dt, *J* = 16.2, 6.3 Hz, 1H), 2.01 (dt, *J* = 16.3, 6.0 Hz, 1H), 1.94 (dt, *J* = 16.1, 6.0 Hz, 1H), 1.76 (m, 4H), 1.52 (m, 1H), 1.42 ppm (m, 1H); ^{13}C NMR-DEPT (125 MHz, C_6D_6): δ = 161.2 (C), 140.4 (CH), 119.5 (CH), 94.1 (C), 93.0 (C), 81.3 (CH, Cp), 60.5 (CH), 50.5 (CH), 48.3

 © 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

(CH), 36.3 (CH), 32.4 (CH_3), 29.9 (CH_2), 29.2 (CH_2), 23.9 (CH_2), 23.7 ppm (CH_2); MS (70 eV, EI): *m/z* (%): 339 (52) [M^+], 338 (21), 337 (100), 271 (22), 241 (10), 215 (13), 214 (14), 213 (12); HRMS: Calcd for $C_{19}H_{22}CoNO$: 339.1033; found: 339.1032.

Quinolone derivatives 28 and 29 by oxidative demetalation of 21: To a solution of **21** (8.7 mg, 0.026 mmol) and Et_3N (20 μL, 0.14 mmol) in MeCN (2 mL) at 0 °C was added solid $CuCl_2{\cdot}2H_2O$ (23 mg, 0.14 mmol). After 30 min, the mixture was diluted with CH_2Cl_2, washed with water and brine, and dried over Na_2SO_4. Concentration left a residue which was purified by chromatography (CH_2Cl_2/MeOH 20:1) to give a mixture of **28** and **29** (5.4 mg, 96%) in a ratio of 4:1. Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) signals attributable to **29**: $\delta = 7.56$ (d, $J = 9.4$ Hz, 1H), 7.23 (s, 1H), 7.04 (s, 1H), 6.60 (d, $J = 9.2$ Hz, 1H), 3.68 (s, 3H); GC-MS for **29**: *m/z* (%): 213 (100) [M^+], 212 (45), 209 (30), 198 (10), 185 (79), 167 (12), 156 (21), 139 (20), 128 (16), 115 (20), 63 (20). Another run performed as above [**21** (5.1 mg, 0.015 mmol), Et_3N (20 μL, 0.14 mmol), $CuCl_2{\cdot}2H_2O$ (24 mg, 0.14 mmol), MeCN (2 mL)] provided uncontaminated **28** (1 mg, 31%). Yellow oil; IR (film): $\tilde{\nu} = 2931$, 2858, 1662, 1609, 1435, 1398, 1247, 1108, 822 cm^{-1}; ^{1}H (300 MHz, $CDCl_3$): $\delta = 6.06$ (dd, $J =$ 9.7, 2.8 Hz, 1H), 5.88 (dd, $J = 9.7$, 2.6 Hz, 1H), 5.41 (d, $J = 6.1$ Hz, 1H), 5.27 (m, 1H), 4.16 (m, 1H), 3.20 (m, 1H), 2.98 (s, 3H), 2.25 (m, 4H), 1.66 ppm (m, 4H); MS (70 eV, EI): *m/z* (%): 215 (69) [M^+], 214 (100), 213 (22), 186 (72), 173 (28), 172 (48), 158 (20), 144 (18), 129 (22), 128 (22), 115 (29), 91 (16), 77 (12).

Complex 30 from cocyclization of *N*-methyl-4-pyridone with 1,7-octadiyne: To a solution of *N*-methyl-4-pyridone (207 mg, 1.90 mmol) in degassed, refluxing THF (25 mL) was added 1,7-octadiyne (120 μL, 96 mg, 0.91 mmol) in THF (4.5 mL) and [CpCo(C_2H_4)$_2$] (164 mg, 0.91 mmol) in THF (4.5 mL) via separate syringes over 75 min. After a further 70 min, the reaction mixture was concentrated in vacuo and the residue purified by chromatography (hexanes/EtOAc 1:0–1:1) to afford **24** (11.5 mg, 4.4%), **25** (63.5 mg, 60%), and an impure, polar fraction. This latter material was rechromatographed (CH_2Cl_2/MeOH 20:1) to give complex **30** (7.3 mg, 2%). Orange oil; IR (film): $\tilde{\nu} = 2927$, 1575, 1319, 1241, 806 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6): $\delta = 5.69$ (d, $J = 7.5$ Hz, 1H), 4.81 (d, $J =$ 7.5 Hz, 1H), 4.37 (s, 5H), 3.63 (d, $J = 4.1$ Hz, 1H), 3.19 (dd, $J = 11.4$, 3.6 Hz, 1H), 2.93 (dd, $J = 10.7$, 4.4 Hz, 1H), 2.79 (d, $J = 3.6$ Hz, 1H), 2.39 (dt, $J = 16.5$, 7.4 Hz, 1H), 2.17 (s, 3H), 1.94 (m, 2H), 1.72 (m, 2H), 1.53 (m, 2H), 1.33 ppm (m, 1H); ^{13}C NMR (125 MHz, C_6D_6): $\delta = 150.8$, 94.3, 92.4, 91.8, 81.0 (Cp), 59.2, 52.7, 47.8, 40.5, 29.1, 28.8, 23.3, 23.2 ppm, signals for the carbonyl and one alkenyl carbon not observed; MS (70 eV, EI): *m/z* (%): 339 (18) [M^+], 257 (17), 256 (100), 252 (11), 213 (35), 212 (19), 187 (14), 159 (6), 124 (8).

Complexes 31 and 32 from the reaction of 1, BTMSA, and [CpCo(C_2H_4)$_2$]: A solution of *N*-2-propynyl-2-pyridone (**1**) (133 mg, 1 mmol) in dry, degassed THF (2 mL) and a solution of [CpCo(C_2H_4)$_2$] (180 mg, 1 mmol) in dry, degassed THF (2 mL) were added simultaneously over 1 h to degassed BTMSA (15 mL). Subsequently, the mixture was stirred for 1 h, THF and excess BTMSA removed in vacuo, and the residue purified by chromatography (hexane/EtOAc 1:1) to give compounds **31** (32.9 mg, 7.7%) and **32** (134 mg, 29%).

Complex 31: Yellow solid; m.p. 93–95 °C; IR (film): $\tilde{\nu} = 2954$, 1662, 1588, 1538, 1438, 1246, 839 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6): $\delta = 6.90$ (d, $J =$ 6.2 Hz, 1H), 6.62 (dd, $J = 7.5$, 6.8 Hz, 1H), 6.52 (d, $J = 9.2$ Hz, 1H), 5.49 (dd, $J = 6.5$, 6.4 Hz, 1H), 4.71 (s, 5H), 4.32 (d, $J = 15.1$ Hz, 1H), 4.21 (d, $J = 15.1$ Hz, 1H), 4.18 (s, 1H), 0.17 (s, 9H), 0.07 ppm (s, 9H); ^{13}C NMR (125 MHz, C_6D_6): $\delta = 161.7$, 138.5, 136.3, 121.1, 104.3, 84.2, 79.5, 70.0, 69.1, 66.6, 47.1, 0.60, 0.17 ppm; MS (70 eV, EI): *m/z* (%): 427 (56) [M^+], 333 (100), 163 (57), 152 (33), 147 (22); elemental analysis calcd (%) for $C_{21}H_{30}CoNOSi_2$: C 58.99, H 7.07, N 3.27; found: C 58.75, H 7.32, N 3.54.

Complex 32: Dark red solid; m.p. 117–118 °C; IR (film): $\tilde{\nu} = 2955$, 1736, 1659, 1588, 1538, 1438, 1246, 839 cm^{-1}; ^{1}H NMR (400 MHz, C_6D_6): $\delta =$ 6.69 (d, $J = 5.8$ Hz, 1H), 6.64 (d, $J = 6.9$ Hz, 1H), 6.56 (d, $J = 8.9$ Hz, 1H), 5.48 (dd, $J = 6.8$, 6.2 Hz, 1H), 5.41 (s, 1H), 4.57 (s, 5H), 3.94 (d, $J =$ 13.3 Hz, 1H), 3.77 (d, $J = 13.3$ Hz, 1H), 1.43–1.35 (m, 2H), 0.87 (m, 2H), 0.38 (s, 9H), 0.17 ppm (s, 9H); ^{13}C NMR (100 MHz, C_6D_6): $\delta = 162.2$, 138.4, 137.3, 121.7, 103.9, 87.7, 85.9, 80.8, 74.2, 67.2, 57.9, 30.3, 25.8, 2.46, 2.39 ppm; MS (70 eV, EI): *m/z* (%): 455 (41) [M^+], 389 (100), 361 (78), 316 (51), 295 (25), 288 (36); elemental analysis calcd (%) for $C_{23}H_{34}CoNOSi_2$: C 60.63, H 7.52, N 3.07; found: C 60.35, H 7.64, N 3.18.

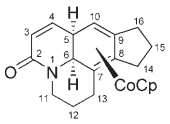
Complex 33 from the cocyclization of 2 with BTMSA: *N*-3-Butynyl-2-pyridone (**2**) (147 mg, 1 mmol), [CpCo(C_2H_4)$_2$] (180 mg, 1 mmol), and BTMSA (20 mL) were reacted as in the preceding preparation of **31** and **32** to give complex **33** (153 mg, 35%). Red solid; m.p. 124–125 °C; IR (film): $\tilde{\nu} = 2952$, 2896, 1666, 1606, 1248, 836, 811 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6): $\delta = 6.10$ (dd, $J = 10.1$, 4.6 Hz, 1H), 6.06 (d, $J = 9.0$ Hz, 1H), 4.82 (s, 1H), 4.52 (s, 5H), 4.19 (dt, $J = 12.1$, 8.9 Hz, 1H), 3.28 (quin, $J = 5.9$ Hz, 1H), 2.36 (d, $J = 8.9$ 0 Hz, 1H), 1.48 (dd, $J = 8.0$, 4.6 Hz, 1H), 1.32–1.27 (m, 2H), 0.29 (s, 9H), 0.15 ppm (s, 9H); ^{13}C NMR (125 MHz, C_6D_6): $\delta = 161.0$, 139.3, 124.3, 83.9, 81.6, 78.8, 77.2, 62.1, 60.0, 43.3, 41.0, 32.2, 4.21, 3.31 ppm; MS (70 eV, EI): *m/z* (%): 441 (38) [M^+], 243 (55), 228 (100); elemental analysis calcd (%) for $C_{22}H_{32}CoNOSi_2$: C 59.85, H 7.31, N 3.17; found: C 59.58, H 7.37, N 3.13. Shortening the mixing times of the reagents to 30 min diminished the yield of **33** (18%) and led to the detection of the faster eluting 1-[2-(*N*-2-oxopyridinyl)ethyl]-2,3-bis(trimethylsilyl)cyclobudadiene CpCo complex (2.4%). Colorless solid; m.p. 110–111 °C; IR (film): $\tilde{\nu} = 2953$, 1660, 1585, 1538, 1243, 836 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6): $\delta = 6.66$ (dd, $J = 8.7$, 7.1 Hz, 1H), 6.53 (d, $J =$ 9.2 Hz, 1H), 6.47 (d, $J = 4.9$ Hz, 1H), 5.45 (dd, $J = 6.3$, 5.6 Hz, 1H), 4.77 (s, 5H), 3.97 (s, 1H), 3.62 (m, 2H), 2.28 (m, 1H), 2.12 (m, 1H), 0.16 (s, 9H), 0.13 ppm (s, 9H); ^{13}C NMR (125 MHz, C_6D_6): $\delta = 161.8$, 138.8, 137.8, 121.4, 104.2, 87.9, 79.4, 73.3, 68.8, 49.8, 30.0, 0.83, 0.27 ppm, one cyclobutadienylcarbon signal not detected; MS (70 eV, EI): *m/z* (%): 441 (13) [M^+], 346 (100), 294 (32), 248 (23); HRMS: Calcd for $C_{22}H_{32}CoNOSi_2$: 441.1355; found: 441.1357.

Oxidative demetalation of 33 to 34: A solution of $Fe(NO_3)_3{\cdot}9H_2O$ (100 mg, 0.25 mmol) in MeCN (1 mL) and H_2O (1 mL) was added to a solution of complex **33** (22 mg, 0.05 mmol) in MeCN (1 mL) and THF (1 mL) at 0 °C. After stirring for 12 min, the mixture was poured into ice water and extracted with CH_2Cl_2. The combined organic layers were washed with H_2O, dried over Na_2SO_4, and the solvent was removed in vacuo. Chromatography (hexanes/EtOAc 1:2) delivered the free ligand **34** (7.8 mg, 49%). White solid; m.p. 153–154 °C; IR (film): $\tilde{\nu} = 2957$, 1656, 1608, 1420, 1249, 837 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6): $\delta = 5.97$ (dd, $J =$ 10.1, 3.3 Hz, 1H), 5.86 (d, $J = 2.1$ Hz, 1H), 5.69 (dd, $J = 10.1$, 2.2 Hz, 1H), 4.76 (m, 1H), 3.62 (dd, $J = 12.6$, 2.2 Hz, 1H), 3.54 (d, $J = 12.6$ Hz, 1H), 2.41 (m, 1H), 2.11 (m, 1H), 1.92 (dd, $J = 17.5$, 8.0 Hz, 1H), 0.18 (s, 9H), 0.15 ppm (s, 9H); ^{13}C NMR (100 MHz, C_6D_6): $\delta = 166.1$, 146.9, 141.8, 139.7, 136.8, 123.4, 118.9, 58.3, 45.1, 36.1, 29.1, 2.2, 1.5 ppm; MS (70 eV, EI): *m/z* (%): 317 (50) [M^+], 316 (100), 302 (11), 274 (11), 244 (17), 228 (16), 73 (49); elemental analysis calcd (%) for $C_{17}H_{27}NOSi_2$: C 64.29, H 8.57, N 4.41; found: C 64.06, H 8.81, N 4.10.

Cocyclization of 5 with BTMSA: Heptynylpyridone **5** (189 mg, 1 mmol), [CpCo(C_2H_4)$_2$] (180 mg, 1 mmol), and BTMSA (20 mL) were treated as in the preparation of **31** and **32** to generate 1-[5-(*N*-2-oxopyridinyl)pentyl]-2,3-bis(trimethylsilyl)cyclobudadiene CpCo complex (132 mg, 27%). Light yellow oil; IR (film): $\tilde{\nu} = 2918$, 1662, 1591, 1539, 1245, 837 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6): $\delta = 6.66$ (t, $J = 6.9$ Hz, 1H), 6.53 (d, $J =$ 9.2 Hz, 1H), 6.35 (d, $J = 6.1$ Hz, 1H), 5.45 (t, $J = 6.4$ Hz, 1H), 4.78 (s, 5H), 4.17 (s, 1H), 3.53 (m, 2H), 1.79 (t, $J = 7.6$, 2H), 1.49 (m, 2H), 1.36–1.24 (m, 2H), 1.12 (m, 2H), 0.22 (s, 9H), 0.16 ppm (s, 9H); ^{13}C NMR (125 MHz, C_6D_6): $\delta = 162.0$, 138.5, 137.5, 121.4, 104.2, 92.7, 79.3, 68.8, 66.7, 64.2, 49.2, 30.3, 29.5, 29.3, 26.7, 0.90, 0.34 ppm; MS (70 eV, EI): *m/z* (%): 483 (100) [M^+], 410 (9), 385 (6), 320 (11), 313 (15), 294 (12), 152 (12), 73 (22); elemental analysis calcd (%) for $C_{25}H_{38}CoNOSi_2$: C 62.08, H 7.92, N 2.90; found: C 61.90, H 7.85, N 2.58.

Cyclization of 7 to 35: Decadiyne **7** (330 mg, 1.45 mmol) was dissolved in dry, degassed THF (10 mL) and added during 4 h to a solution of [CpCo(C_2H_4)$_2$] (287 mg, 1.59 mmol) in THF (50 mL). The mixture was stirred overnight at room temperature. The solvent was removed in vacuo and the residue was purified by chromatography (hexane/EtOAc 2:1) to give unreacted starting material (89 mg, 27%) and complex **35** (219 mg, 43%, 59% based on consumed starting material). Red crystals; m.p. 126–127 °C; IR (film): $\tilde{\nu} = 2800$, 2934, 1655, 1593, 1539, 1435, 1280, 1143, 868, 806 cm^{-1};

 © 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



^{1}H NMR (500 MHz, C_6D_6, assignments according to the numbering in the structure shown): $\delta = 6.07$ (d, $J = 10.0$ Hz, 1H, H3), 5.62 (dd, $J = 10.0$, 4.0 Hz, 1H, H4), 5.19 (d, $J = 10.8$ Hz,1H, H11), 4.25 (s, 5H, Cp), 2.40 (br s, 1H, H10), 2.37 (d, $J = 8.0$ Hz, 1H, H6), 2.28(m, 1H, H16), 2.22–2.06 (m, 4H, H11, H13, H14, H16), 2.05–1.85 (m, 2H, H13, H14), 1.64 (m, 1H, H12), 1.50–1.46 (m, 2H, H5, H15), 1.38 (m, 1H, H12), 1.27 ppm (m, 1H, H15); ^{13}C NMR (500 MHz, C_6D_6): $\delta = 161.5$ (C2), 140.2 (C4), 122.2 (C3), 98.5 (C9 or C8), 97.0 (C8 or C9), 80.7 (5C, Cp), 64.8 (C7), 61.1 (C6), 50.1 (C10), 42.9 (C11), 36.3 (C5), 33.1 (C15), 32.5(C16), 29.8 (C14), 24.8 (C12), 24.5 ppm (C13); MS (70 eV, EI): m/z (%): 351 (98) [M^+], 349 (100), 281 (44), 254 (51), 227 (20), 225 (32), 198 (35); elemental analysis calcd (%) for $C_{20}H_{22}CoNO$: C 68.37, H 6.31, N 3.99; found: C 68.94, H 6.38, N 3.95.

Reaction of 9, BTMSA, and [CpCo(C_2H_4)$_2$]: To stirred, degassed BTMSA (15 mL) at room temperature was added **9** (149 mg, 1.12 mmol) in 1,4-dioxane (6 mL) and EtOH (3 mL), and [CpCo(C_2H_4)$_2$] (220 mg, 1.22 mmol) in THF (8.5 mL) via separate syringes over a period of 2.5 h. After a total of 4 h, the solvent was removed and the residue subjected to chromatography (CH_2Cl_2/MeOH 20:1) to afford 1-(*N*-4-oxopyridyl)-methyl-2,3-bis(trimethylsilyl)cyclobutadiene CpCo (232 mg) and a mixed fraction, purified by HPLC (C18, 100% MeOH), containing more of this complex (7 mg, for a total of 239 mg, 50%) and 1*Z*,3*E*-5-(*N*-4-oxopyridyl)-1,2-bis(trimethylsilyl)-1,3-pentadiene (8 mg, 2.4%).

Cyclobutadiene complex. Yellow crystals; m.p. 148–150 °C; IR (KBr): $\tilde{\nu} =$ 2955, 2898, 2192, 1638, 1560, 1248, 1156, 840, 814, 727 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.22$ (d, $J = 7.3$ Hz, 2H), 6.26 (d, $J = 7.4$ Hz, 2H), 4.82 (s, 5H), 4.25 (s, 1H), 4.21 (d, $J = 14.8$ Hz, 1H), 4.16 (d, $J = 14.8$ Hz, 1H), 0.013 (s, 9H), 0.0024 ppm (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta =$ 178.8 (br), 138.8, 118.3 (br), 80.9, 79.1 (Cp), 69.2, 68.8, 67.8, 55.7, 0.31, −0.23 ppm; MS (70 eV, EI): m/z (%): 427 (20) [M^+], 354 (11). 334 (17), 333 (54), 163 (28), 124 (32), 108 (22), 73 (100); elemental analysis calcd (%) for $C_{21}H_{30}CoNOSi_2$: C 58.99, H 7.07, N 3.28; found: C 58.60, H 7.20, N 3.25.

Pentadienylpyridone: Colorless oil; IR (film): $\tilde{\nu} = 3365$, 2954, 2898, 1641, 1557, 1249, 1180, 837 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6): $\delta = 6.59$ (s, 1H), 6.34 (d, $J = 7.4$ Hz, 2H), 6.27 (d, $J = 7.8$ Hz, 2H), 6.00 (d, $J = 15.2$ Hz, 1H), 5.14 (dt, $J = 15.3$, 6.3 Hz, 1H), 3.16 (dd, $J = 6.2$, 1.2 Hz, 2H), 0.19 (s, 9H), 0.14 ppm (s, 9H); MS (70 eV, EI): m/z (%): 305 (24) [M^+], 290 (5), 225 (9), 168 (47), 123 (48), 73 (100).

Reaction of 10, BTMSA, and [CpCo(C_2H_4)$_2$]: In a manner similar to the conversion of **9** described above, compound **10** (87.5 mg, 0.591 mmol) in 1,4-dioxane (5 mL) and [CpCo(C_2H_4)$_2$] (112 mg, 0.623 mmol) in THF (5 mL) were added to BTMSA (7 mL) over 1.5 h. After a total of 3 h, the mixture was chromatographed (CH_2Cl_2/MeOH 10:1) to afford 1-[2-(*N*-4-oxopyridyl)ethyl]-2,3-bis(trimethylsilyl)cyclobutadiene CpCo (50.3 mg) and mixed fractions, purified by HPLC (C18, CH_3CN/MeOH 1:4), containing more of this complex (15 mg, for a total of 65.3 mg, 25%) and 1-[2-(*N*-4-oxopyridyl)ethyl]-3,4-bis(trimethylsilyl)cyclohexadiene CpCo (15 mg, 3.3%).

Cyclobutadiene complex: Yellow crystals (from Et_2O); m.p. 138–141 °C; IR (film): $\tilde{\nu} = 3229$, 2955, 2897, 1640, 1549, 1401, 1244, 1193, 836, 811, 734 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.15$ (d, $J = 6.4$ Hz, 2H), 6.24 (d, $J = 6.6$ Hz, 2H), 4.84 (s, 5H), 3.98 (s, 1H), 3.79 (ddd, $J = 12.8$, 5.7, 5.7 Hz, 1H), 3.66 (ddd, $J = 14.4$, 7.7, 7.7 Hz, 1H), 2.34 (m, 2H), 0.13 (s, 9H), 0.41 ppm (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 139.6$, 118.6 (br), 85.2, 79.1 (Cp), 69.0, 67.1, 66.3, 56.9, 32.5, 0.75, −0.11 ppm, signal for carbonyl not observed; MS (70 eV, EI): m/z (%): 441 (100) [M^+], 343 (41), 333 (58), 294 (23), 271 (43), 167 (9), 163 (24), 149 (25), 124 (11), 73 (20); HRMS: Calcd for $C_{22}H_{32}CoNOSi_2$: 441.1354; found: 441.1356.

Cyclohexadiene complex: Red oil; IR (film): $\tilde{\nu} = 2954$, 2901, 2838, 1641, 1564, 1246, 1191, 841 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6): $\delta = 6.38$ (d, $J =$ 5.7 Hz, 2H), 6.33 (d, $J = 6.9$ Hz, 2H), 4.52 (s, 5H), 4.24 (s, 1H), 2.85 (m, 2H), 1.61 (dt, $J = 13.7$, 5.8 Hz, 1H), 1.43 (m, 1H), 1.33 (m, 1H), 1.25 (dt, $J = 13.7$, 8.4 Hz, 1H), 0.90 (dd, $J = 14.9$, 7.5 Hz, 1H), 0.35 (s, 9H), 0.21 (s, 9H), −0.009 ppm (dt, $J = 13.2$, 7.6 Hz, 1H); ^{13}C NMR (125 MHz, C_6D_6): $\delta = 139.4$, 119.1 (br), 85.6, 85.3, 81.0 (Cp), 66.9, 58.7, 53.5, 43.0, 31.7, 25.4, 2.44, 1.24 ppm, signal for carbonyl not observed; MS (70 eV, EI): m/z (%): 469 (52) [M^+], 467 (19), 385 (32), 344 (17), 330 (16), 133 (19), 124 (12), 108 (37), 84 (100), 73 (77); HRMS: Calcd for $C_{24}H_{36}CoNOSi_2$: 469.1668; found: 469.1671.

Complex 36: In a manner similar to the conversion of **9** described above, compound **11** (140 mg, 0.864 mmol) in 1,4-dioxane (7 mL) and [CpCo(C_2H_4)$_2$] (160 mg, 0.889 mmol) in THF (7 mL) were added to BTMSA (10 mL) over 2 h. After a total of 2.5 h, the mixture chromatographed (CH_2Cl_2/MeOH 20:1) to provide **36** (192 mg, 47%) and 1-[3-(*N*-4-oxopyridyl)propyl]-2,3-bis(trimethylsilyl)cyclobutadiene CpCo (70 mg, 15%).

Complex 36: Red crystals (from CH_2Cl_2/hexanes); m.p. 168–169 °C; IR (KBr): $\tilde{\nu} = 2961$, 1595, 1244, 1230, 1173, 837, 730 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6): $\delta = 6.06$ (d, $J = 7.6$ Hz, 1H), 4.94 (d, $J = 7.7$ Hz, 1H), 4.68 (s, 5H), 4.48 (s, 1H), 2.58 (dd, $J = 12.6$, 5.0 Hz, 1H), 2.35 (d, $J =$ 8.8 Hz, 1H), 2.24 (td, $J = 10.4$, 2.0 Hz, 1H), 1.56 (m, 1H), 1.47 (d, $J =$ 8.8 Hz, 1H), 1.08 (m, 3H), 0.57 (s, 9H), 0.41 ppm (s, 9H); ^{13}C NMR-DEPT (125 MHz, C_6D_6): $\delta = 191.6$ (C), 150.7 (CH), 97.7 (CH), 87.6 (C), 82.9 (CH), 81.9 (CH, Cp), 70.5 (C), 66.2 (CH), 63.5 (C), 53.4 (CH_2), 50.0 (CH), 34.8 (CH_2), 24.9 (CH_2), 5.66 (CH_3), 3.59 ppm (CH_3); MS (70 eV, EI): m/z (%): 455 (97) [M^+], 440 (9), 390 (8), 362 (10), 331 (31), 330 (100), 316 (46), 314 (35), 242 (33), 124 (7), 73 (17); HRMS: Calcd for $C_{23}H_{34}CoNOSi_2$: 455.1511; found: 455.1515.

Cyclobutadiene complex: Yellow crystals (from Et_2O); m.p. 155–157 °C; IR (KBr): $\tilde{\nu} = 3060$, 2952, 1638, 1562, 1244, 1188, 851, 835, 808 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) $\delta = 7.23$ (d, $J = 6.9$ Hz, 2H), 6.38 (d, $J =$ 6.9 Hz, 2H), 4.81 (s, 5H), 4.14 (s, 1H), 3.75 (m, 2H), 1.95 (m, 2H), 1.84 (m, 2H), 0.082 (s, 9H), 0.061 ppm (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) $\delta = 139.4$, 118.9, 89.4, 79.0 (Cp), 68.0, 67.0, 65.0, 56.5, 30.8, 26.9, 0.66, 0.039 ppm, carbonyl signal not observed; MS (70 eV, EI): m/z (%): 455 (55) [M^+], 430 (25), 358 (39), 357 (28), 322 (100), 314 (29), 285 (27), 175 (36), 149 (29), 108 (72), 69 (41), 57 (52); elemental analysis calcd (%) for $C_{23}H_{34}CoNOSi_2$: C 60.63, H 7.52, N 3.07; found: C 60.32, H 7.51, N 3.10.

Reaction of 12, BTMSA, and [CpCo(C_2H_4)$_2$]: In a manner similar to the conversion of **9** described above, **12** (177 mg, 1.00 mmol) in 1,4-dioxane (8 mL) and EtOH (1 mL) and [CpCo(C_2H_4)$_2$] (198 mg, 1.10 mmol) in THF (9 mL) were added to BTMSA (20 mL) over 2.25 h. After a total of 3.25 h, the mixture was (CH_2Cl_2/MeOH 15:1) to deliver 1-[4-(*N*-4-oxopyridyl)butyl]-2,3-bis(trimethylsilyl)cyclobutadiene CpCo (158 mg, 34%). Yellow-black crystals (from Et_2O); m.p. 151–153 °C; IR (KBr): $\tilde{\nu} = 3078$, 3036, 2947, 2897, 1637, 1570, 1244, 1194, 856, 807 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.34$ (d, $J = 6.9$ Hz, 2H), 6.51 (d, $J = 6.9$ Hz, 2H), 4.80 (s, 5H), 4.12 (s, 1H), 3.80 (m, 2H), 1.92 (m, 2H), 1.78 (m, 2H), 1.38 (m, 2H), 0.89 (s, 9H), 0.048 ppm (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$: $\delta = 178.8$, 139.5, 118.8, 90.9, 78.9 (Cp), 73.0, 68.2, 64.7, 50.8, 30.7, 29.6, 26.1, 0.65, 0.046 ppm; MS (70 eV, EI): m/z (%): 469 (100) [M^+], 454 (7), 371 (51), 299 (51), 294 (16), 272 (12), 124 (30), 108 (14), 73 (83); elemental analysis calcd (%) for $C_{24}H_{36}CoNOSi_2$: C 61.38, H 7.73, N 2.98; found: C 60.90, H 7.59, N 2.98.

Oxidative demetalation of 36 to 37: To a solution of complex **36** (55 mg, 0.12 mmol) in MeCN (1 mL) and THF (1 mL) at 0 °C was added dropwise a cooled solution of $Fe(NO_3)_3 \cdot 9H_2O$ (240 mg, 0.590 mmol) in H_2O (0.5 mL). After 10 min, the mixture was poured onto H_2O (5 mL) and extracted with CH_2Cl_2 (3×5 mL). The organic layers were dried over $MgSO_4$ and concentrated in vacuo, and the residue was chromatographed (CH_2Cl_2/MeOH 20:1) to furnish compound **37** (34 mg, 85%). Yellow solid; m.p. 122–123 °C; IR (KBr): $\tilde{\nu} = 3439$, 2951, 2898, 1624, 1578, 1247, 1197, 858, 833, 758 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 6.82$ (d, $J =$ 7.7 Hz, 1H), 5.99 (d, $J = 1.6$ Hz, 1H), 5.01 (d, $J = 7.8$ Hz, 1H), 4.30 (dd, $J = 10.1$, 1.9 Hz, 1H), 3.55 (d, $J = 10.1$ Hz, 1H), 3.44 (dt, $J = 12.0$, 5.3 Hz, 1H), 3.35 (ddd, $J = 13.6$, 8.7, 5.0 Hz, 1H), 2.32 (m, 2H), 1.75 (m, 2H), 0.22 (s, 9H), 0.20 ppm (s, 9H); ^{13}C NMR-DEPT (125 MHz, $CDCl_3$): $\delta =$ 192.7 (C), 152.9 (CH), 146.2 (C), 144.8 (C), 130.6 (C), 127.1 (CH), 100.9 (CH), 59.7 (CH), 53.6 (CH_2), 45.8 (CH), 28.2 (CH_2), 23.9 (CH_2), 1.63 (CH_3), 1.28 ppm (CH_3); MS (70 eV, EI): m/z (%): 331 (18) [M^+], 316 (43), 242 (23), 83 (100), 73 (33), 55 (9); elemental analysis calcd (%) for $C_{18}H_{29}NOSi_2$: C 65.20, H 8.81, N 4.22; found: C 65.10, H 8.82, N 4.30.

Aromatization of 37: To a solution of **37** (12.8 mg, 0.039 mmol) in toluene (1 mL) at 70 °C was added solid 2,3-dichloro-5,6-dicyano-1,4-benzoqui-

 © 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

none (DDQ, 12.5 mg, 0.055 mmol). After 10 min, the mixture was concentrated in vacuo and the residue chromatographed (CH_2Cl_2/MeOH 30:1) to give the aromatized product (1.8 mg, 14%). Orange oil; IR (film): $\tilde{\nu}$ = 2950, 1623, 1590, 1533, 1470, 1240, 1165, 844 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.56 (s, 1H), 7.40 (d, J = 7.4 Hz, 1H), 6.23 (d, J = 7.4 Hz, 1H), 4.07 (t, J = 5.7 Hz, 2H), 3.01 (t, J = 6.2 Hz, 2H), 2.19 (quin, J = 6.0 Hz, 2H), 0.38 (s, 9H), 0.37 ppm (s, 9H); ^{13}C NMR-DEPT (125 MHz, $CDCl_3$): δ = 179.5 (C), 151.1 (C), 144.6 (C), 141.2 (CH), 137.6 (C), 137.1 (CH), 132.2 (C), 124.1 (C), 109.6 (CH), 52.2 (CH_2), 27.0 (CH_2), 21.3 (CH_2), 5.00 (CH_3), 2.43 ppm (CH_3); MS (FAB): m/z (%): 330 (41) [MH^+], 314 (100); HRMS (FAB): Calcd for $C_{18}H_{28}NOSi_2$: 330.1710; found: 330.1719.

Complexes 38 and 39: To stirring, degassed BTMSA (12 mL) at room temperature was added a mixture of **13** and **14** (150 mg, 0.85 mmol) in 1,4-dioxane (7 mL) and [$CpCo(C_2H_4)_2$] (160 mg, 0.89 mmol) in THF (7 mL) via separate syringes over 80 min. After a total of 1.5 h, the mixture was concentrated in vacuo and the residue chromatographed on alumina (activity III; hexanes/EtOAc 100:1–1:100, then CH_2Cl_2-CH_2Cl_2/MeOH 10:1) to give **38** (10.6 mg, 2.7%) and **39** (11.7 mg, 2.8%).

Complex 38: Red needles (from THF/pentane); m.p. 157–160 °C; IR (KBr): $\tilde{\nu}$ = 3443, 2948, 1677, 1649, 1612, 1348, 1243, 1225, 855, 832, 810, 735 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.15 (d, J = 8.4 Hz, 1H), 5.27 (d, J = 8.4 Hz, 1H), 4.90 (s, 1H), 4.76 (s, 5H), 3.78 (d, J = 6.9 Hz, 1H), 2.93 (ddd, J = 18.1, 9.9, 5.6 Hz, 1H), 2.80 (ddd, J = 18.1, 10.9, 4.7 Hz, 1H), 2.08 (ddd, J = 5.6, 10.9, 15.7 Hz, 1H), 1.81 (ddd, J = 14.9, 10.0, 4.7 Hz, 1H), 1.21 (d, J = 6.9 Hz, 1H), 0.40 (s, 9H), 0.16 ppm (s, 9H); ^{13}C NMR-DEPT (125 MHz, $CDCl_3$): δ = 195.1 (C), 171.0 (C), 138.1 (CH), 107.8 (CH), 88.5 (C), 82.9 (CH), 81.5 (CH, Cp), 67.2 (C), 62.2 (CH), 60.1 (C), 48.6 (CH), 30.9 (CH_2), 30.5 (CH_2), 4.02 (CH_3), 2.90 ppm (CH_3); MS (70 eV, EI): m/z (%): 469 (100) [M^+], 454 (10), 404 (23), 376 (29), 330 (94), 256 (49), 124 (9), 84 (42), 73 (34); HRMS: Calcd for $C_{23}H_{32}CoNO_2Si_2$: 469.1304; found: 469.1302.

Complex 39: Red plates (from Et_2O); m.p. 195 °C (decomp); IR (KBr): $\tilde{\nu}$ = 3373, 2957, 1698, 1622, 1245, 846, 810 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.07 (d, J = 8.4 Hz, 1H), 5.48 (d, J = 8.4 Hz, 1H), 4.65 (s, 5H), 3.50 (s, 1H), 3.11 (s, 1H), 2.56 (m, 2H), 2.44 (ddd, J = 13.3, 10.1, 6.5 Hz, 1H), 1.98 (dt, J = 13.4, 3.8 Hz, 1H), 1.60 (br s, 1H), 0.38 (s, 9H), 0.32 ppm (s, 9H); ^{13}C NMR-DEPT (125 MHz, $CDCl_3$): δ = 193.9 (C), 172.1 (C), 137.3 (CH), 110.0 (CH), 95.0 (C), 87.6 (C), 82.8 (CH, Cp), 82.6 (CH), 77.8 (C), 68.85 (CH), 68.78 (C), 34.0 (CH_2), 29.1 (CH_2), 4.31 (CH_3), 1.59 ppm (CH_3); MS (70 eV, EI): m/z (%): 485 (3) [M^+], 470 (49), 412 (9), 346 (17), 328 (60), 300 (16), 286 (24), 270 (22), 256 (14), 228 (14), 214 (10), 198 (14), 124 (100), 73 (99); elemental analysis calcd (%) for $C_{23}H_{32}CoNO_3Si_2$: C 56.89, H 6.64, N 2.88; found: C 56.56, H 6.62, N 2.99.

Isoquinolone 41: A solution of **40** (173 mg, 1 mmol) and 3-butynyl tosylate (500 mg, 2.2 mmol) in MeCN (2 mL) in a sealed tube was heated to 160 °C for 3 h by microwave irradiation. The mixture was diluted with Et_2O and extracted three times with water (15 mL total). A solution of $K_3[Fe(CN)_6]$ (3.29 g, 10 mmol) in H_2O (10 mL) was added over 1 h at 0 °C to the aqueous phase containing the crude isoquinolinium salt, followed by a solution of KOH (841 mg, 15 mmol) in H_2O (2 mL) over 30 min at 0 °C. After the addition of toluene (20 mL), the mixture was stirred for 30 min at 40 °C and extracted three times with CH_2Cl_2. The combined organic phases were dried with $MgSO_4$ and the solvent removed in vacuo, yielding isoquinolone **41** (230 mg, 95%). White solid; m.p. 177–178 °C; IR (film): $\tilde{\nu}$ = 3226, 2774, 2391, 1974, 1654, 1611, 1466, 1253, 839, 788 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.77 (s, 1H), 7.09 (d, J = 7.3 Hz, 1H), 6.86 (s, 1H), 6.38 (d, J = 7.3, 1H), 6.08 (s, 2H), 4.12 (t, J = 6.6 Hz, 2H), 2.72 (td, J = 6.6, 2.7 Hz, 2H), 2.02 ppm (t, J = 2.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.1, 151.8, 147.8, 134.4, 131.1, 121.6, 105.6, 105.6, 103.6, 101.7, 80.9, 70.6, 48.4, 18.7 ppm; MS (70 eV, EI): m/z (%): 241 (73) [M^+], 202 (20), 189 (100), 172 (60); elemental analysis calcd (%) for $C_{14}H_{11}NO_3$: C 69.70, H 4.60, N 5.81; found: C 69.43, H 4.67, N 5.67.

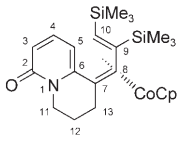
Complexes 42 and 43: A solution of isoquinolone **41** (121 mg, 0.5 mmol) in dry, degassed THF (4 mL) and a solution of [$CpCo(C_2H_4)_2$] (90 mg, 0.5 mmol) in dry, degassed THF (4 mL) were added simultaneously over 1 h to a mixture of degassed BTMSA (6 mL). The mixture was stirred for another 1 h, THF and excess BTMSA removed in vacuo, and the residue purified by chromatography (hexane/EtOAc 1:2) to return some **41** (16.4 mg, 14%), the *exo* complex **42** (98.4 mg, 37%, 43% based on converted starting material), and the *endo* complex **43** (54.6 mg, 20%, 24% based on converted starting material).

Complex 42: Red solid; m.p. 110–112 °C; IR (film): $\tilde{\nu}$ = 2954, 2895, 2849, 1645, 1609, 1473, 1248, 1038, 836 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.60 (s, 1H), 6.65 (s, 1H), 6.03 (AB, 2H), 5.21 (s, 1H), 4.72 (s, 5H), 4.32 (m, 1H), 3.49 (m, 1H), 2.85 (d, J = 7.3 Hz, 1H), 2.08 (d, J = 7.5 Hz, 1H), 2.04 (m, 1H), 1.90 (m, 1H), 0.41 (s, 9H), 0.29 (s, 3H), 0.08 (s, 3H), −0.57 ppm (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.3, 149.4, 147.1, 132.5, 127.7, 125.7, 111.1, 108.4, 101.4, 85.1, 82.1 (Cp), 78.4, 64.8, 61.7, 43.7, 43.2, 33.7, 6.21, 5.73, 3.16, 2.22 ppm; MS (70 eV, EI): m/z (%): 535 (100) [M^+], 533 (40), 460 (16), 73 (16); HRMS: Calcd for $C_{27}H_{34}CoNO_3Si_2$: 535.1409; found: 535.1407.

Complex 43: Brown solid; m.p. 145–146 °C; IR (film): $\tilde{\nu}$ = 3449, 2955, 2896, 1649, 1474, 1261, 1037, 834 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.13 (s, 1H), 7.22 (s, 1H), 5.41 (s, 1H), 5.30 (s, 2H), 4.38 (s, 5H), 4.00 (m, 1H), 3.87 (d, J = 10.9 Hz, 1H), 3.85 (m, 1H), 1.81 (d, J = 10.9 Hz, 1H), 1.31 (m, 2H), 0.44 (br s, 9H), 0.41 ppm (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.9, 149.4, 145.8, 139.4, 128.3, 109.6, 104.3, 101.3, 93.6, 81.7 (Cp), 77.4, 66.9, 62.9, 62.5, 55.5, 44.6, 32.1, 5.43 (br), 2.65 ppm; MS (70 eV, EI): m/z (%): 535 (34) [M^+], 462 (100), 410 (10), 395 (16), 73 (11); elemental analysis calcd (%) for $C_{27}H_{34}NO_3Si_2Co$: C 60.48, H 6.35, N 2.61; found: C 60.38, H 6.41, N 2.65.

Anhydrolycorinone 44: A mixture of **42** and **43** (2:1, 29.5 mg, 0.55 mmol) in THF (1 mL) was treated with Bu_4NF (28.8 mg, 1.10 mmol) for 2 h, before the addition of $Fe(NO_3)_3{\cdot}9H_2O$ (66.7 mg, 0.165 mmol) in THF (2 mL) and H_2O (1 mL). After 2 min, the mixture was subjected to aqueous work up, dried ($MgSO_4$), and chromatographed (ether/hexane 4:1) to give **44** (5.9 mg, 41%).[12]

Cocyclization of 3 with BTMSA to give 45: Pentynylpyridone **3** (161 mg, 1.00 mmol) and [$CpCo(C_2H_4)_2$] (180 mg, 1.00 mmol), both dissolved in degassed THF (2 mL each), were added through separate syringes to degassed BTMSA (20 mL) under argon over 1 h at room temperature. Subsequently, solvents were removed in vacuo and the resulting residue chromatographed (EtOAc/hexanes 8:2) under N_2 to give complex **45** (387 mg, 85%). Dark violet crystals (from pentane/EtOAc); m.p. 198–199 °C; IR (KBr): $\tilde{\nu}$ = 2955, 2897, 1651, 1570, 1538, 1456, 1300, 1245, 1138, 1064, 961, 834 cm^{-1}; ^1H NMR (300 MHz, C_6D_6, assignments according to the numbering in the structure shown): δ = 6.62 (dd, J = 9.1, 1.5 Hz, 1H, H3), 6.47 (dd, J = 9.1, 6.0 Hz, 1H, H4), 5.60 (dd, J = 13.5, 6.2 Hz, 1H, H11), 4.65 (dd, 6.0, 1.5 Hz, 1H, H5), 4.56 (br s, 1H, H8), 4.49 (s, 5H, Cp), 3.80 (td, J = 12.7, 5.5 Hz, 1H, H11), 1.55–1.28 (m, 2H, H12), 1.19 (m, 2H, H13), 0.25 (s, 9H, TMS), 0.06 (s, 9H, TMS), −0.64 ppm (br s, 1H, H10); ^{13}C NMR (100 MHz, C_6D_6): δ = 162.7 (C2), 149.8 (C6), 136.4 (C4), 115.9 (C3), 101.2 (C5), 90.2 (C9), 80.8 (C8), 80.7 (Cp), 56.9 (C7), 48.1 (C10), 37.7 (C11), 33.7 (C13), 20.6 (C12), 1.98 (TMS), 1.13 ppm (TMS); MS (70 eV, EI): m/z (%): 455 (40) [M^+], 382 (10), 330 (52), 316 (18), 258 (100), 242 (39), 228 (7), 184 (7), 170 (9), 73 (100), 59 (9); HRMS: Calcd for $C_{23}H_{34}CoNOSi_2$: 455.1511; found: 455.1506; elemental analysis calcd (%) for $C_{23}H_{34}CoNOSi_2$: C 60.63, H 7.52, N 3.07; found: C 60.83, H 7.48, N 3.26.



Oxidative demetalation of 45 to 46: Complex **45** (199 mg, 0.438 mmol) in MeCN (10 mL) and THF (10 mL) at 0 °C was treated with $Fe(NO_3)_3{\cdot}9H_2O$ (1.00 g, 2.5 mmol) in MeCN (10 mL) and H_2O (4 mL) for 15 min. The mixture was poured into ice water (50 mL), extracted with CH_2Cl_2 (3×50 mL), the combined organic layers washed with H_2O (50 mL), dried over sodium sulfate, and the solvent removed under reduced pressure. Column chromatography (EtOAc/hexanes) furnished **46** (145 mg, 100%). Colorless crystals; m.p. 59–60 °C; IR (KBr): $\tilde{\nu}$ = 2960, 1652, 1574, 1526, 1447, 1260, 1152, 1024, 914, 800, 693 cm^{-1}; ^1H NMR (300 MHz, C_6D_6): δ = 6.62 (dd, J = 9.1, 6.9 Hz, 1H, H4), 6.49 (dd, J = 9.1, 1.4 Hz, 1H, H3), 6.33 (d, J = 2.0 Hz, 1H, H10), 6.15 (dd, J = 6.9, 1.4 Hz, 1H, H5), 6.06 (q, J = 1.9 Hz, 1H, H8), 3.84 (t, J = 6.8 Hz, 2H, H11), 1.85

© 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

(td, $J=7.0$, 1.6 Hz, 2H, H13), 1.29 (quin, $J=6.9$ Hz, 2H, H12), 0.09 (s, 9H, TMS), 0.001 ppm (s, 9H, TMS); ^{13}C NMR (100 MHz, C_6D_6): $\delta=$ 162.2 (C2), 160.2 (C6), 148.3 (C10), 145.9 (C9), 138.9 (C8), 137.1 (C4), 127.9 (C7), 118.7 (C3), 107.4 (C5), 41.4 (C11), 29.6 (C13), 22.9 (C12), 1.22 (TMS), 0.84 ppm (TMS); MS (70 eV, EI): m/z (%): 331 (48) [M^+], 330 (64), 316 (20), 258 (100), 242 (65), 73 (74); HRMS: Calcd for $C_{18}H_{29}NOSi_2$: 331.1788; found: 331.1789; elemental analysis calcd (%) for $C_{18}H_{29}NOSi_2$: C 65.20, H 8.81, N 4.22; found: C 65.02, H 9.02, N 3.96.

Thermolysis of 46 to 47, 48, and 49: Dienylpyridone **46** (100 mg, 0.30 mmol) in toluene (30 mL) was heated at 110 °C for 1.5 h. The toluene was removed and the mixture subjected to HPLC (EtOAc/hexanes 7:3) to separate **47** (65%), **48** (25%), and **49** (10%). Species **48** degraded to **47** within 12 h, while **49** converted to **47** quantitatively on heating. More simply, heating **46** (100 mg) in toluene at 110 °C for 12 h gave **47** (73.0 mg, 95%).

Quinolone 47: Colorless solid; IR (KBr): $\tilde{\nu}=$2954, 2896, 1660, 1651, 1645, 1574, 1479, 1423, 1313, 1251, 1143, 914, 838, 754 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=$7.68 (d, $J=9.5$ Hz, 1H, H4), 7.52 (d, $J=1.0$ Hz, 1H, H10), 7.41 (d, $J=1.0$ Hz, 1H, H8), 6.68 (d, $J=9.4$ Hz, 1H, H3), 4.19 (t, $J=6.0$ Hz, 2H, H11), 2.99 (t, $J=6.1$ Hz, 2H, H13), 2.09 (quin, $J=$ 6.1 Hz, 2H, H12), 0.29 ppm (s, 9H, TMS); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=$161.0 (C2), 139.0 (C4), 137.2 (C6), 134.5 (C8), 133.3 (C9), 131.9 (C10), 124.1 (C7), 121.2 (C3), 120.0 (C5), 42.2 (C11), 27.6 (C13), 20.7 (C12), −1.10 ppm (TMS); MS (70 eV, EI): m/z (%): 257 (60) [M^+], 242 (100), 113 (5); HRMS: Calcd for $C_{15}H_{19}NOSi$: 257.1236; found: 257.1238.

Quinolone 48: Colorless solid; IR (KBr): $\tilde{\nu}=$2954, 2896, 1660, 1651, 1645, 1574, 1479, 1423, 1313, 1251, 1143, 914, 838, 754 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=$8.08 (d, $J=9.9$ Hz, 1H, H4), 7.53 (s, 1H, H8), 6.64 (d, $J=9.9$ Hz, 1H, H3), 4.21 (t, $J=6.0$ Hz, 2H, H11), 2.96 (t, $J=$ 6.0 Hz, 2H, H13), 2.09 (quin, $J=6.0$ Hz, 2H, H12), 0.47 (s, 9H, TMS), 0.39 ppm (s, 9H, TMS); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=$161.0 (C2), 139.7 (C4), 138.9 (C6), 136.5 (C8), 134.4 (C9), 128.1 (C10), 125.0 (C7), 121.3 (C5), 119.2 (C3), 42.5 (C11), 27.6 (C13), 20.7 (C12), 4.08 (TMS), 2.80 ppm (TMS); MS (70 eV, EI): m/z (%): 329 (13) [M^+], 314 (10), 257 (55), 242 (100), 113 (5); HRMS: Calcd for $C_{18}H_{27}NOSi_2$: 329.1631; found: 329.1632.

Diene 49: Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=$7.19 (dd, $J=$ 9.0, 7.0 Hz, 1H), 6.50 (dd, $J=9.0$, 2.0 Hz, 1H), 6.46 (q, $J=1.8$ Hz, 1H), 6.34 (dd, $J=7.0$ Hz, 2.0 Hz, 1H), 6.33 (d, $J=2.1$ Hz, 1H), 4.05 (t, $J=$ 6.2 Hz, 2H), 2.48 (td, $J=6.9$, 1.5 Hz, 2H), 2.01 (quin, $J=6.3$ Hz, 2H), 0.12 (s, 9H), 0.09 ppm (s, 9H); MS (70 eV, EI): m/z (%): 331 (58) [M^+], 330 (40), 316 (20), 258 (100), 244 (65), 73 (69); HRMS: Calcd for $C_{18}H_{29}NOSi_2$: 331.1788; found: 331.1793.

Cocyclization of 3 with 1-trimethylsilyl-2-phenylacetylene to give 50: *N*-(4-Pentynyl)-2-pyridone (**3**) (161 mg, 1.00 mmol) and [$CpCo(C_2H_4)_2$] (180 mg, 1.00 mmol) in degassed THF (5 mL each) were added through separate syringes to degassed 1-trimethylsilyl-2-phenylacetylene (20 mL) over 1 h at room temperature. The volatiles were removed by distillation at 0.001 torr and the residue chromatographed (EtOAc/hexanes 9:1) under N_2 to give **50** (362 mg, 79%). Dark-brown crystals (from pentane/EtOAc); m.p. 209–210 °C; IR (KBr): $\tilde{\nu}=$3448, 2950, 1655, 1561, 1535, 1384, 835 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6): $\delta=$7.62 (br s, 2H, PhH), 7.26 (m, 3H, PhH), 6.62 (dd, $J=9.1$, 1.5 Hz, 1H, H3), 6.45 (dd, $J=9.1$, 6.0 Hz, 1H, H4), 5.59 (m, 1H, H11), 4.73 (d, $J=6.0$ Hz, 1H, H5), 4.64 (br s, 1H, H8), 4.45 (s, 5H, Cp), 3.72 (m, 1H, H11), 1.73–1.53 (m, 2H, H12), 1.32–1.10 (m, 2H, H13), −0.10 (s, 9H, TMS), −0.32 ppm (br s, 1H, H10); ^{13}C NMR (100 MHz, C_6D_6): $\delta=$162.9 (C2), 149.2 (C6), 136.8 (C4), 130.4 (Ph), 128.1 (Ph), 127.8 (Ph), 115.8 (C3), 106.6 (Ph_{quat}), 101.0 (C5), 81.8 (Cp), 79.7 (C8), 69.8 (C9), 52.1 (C7), 48.4 (C10), 37.7 (C11), 33.3 (C13), 20.8 (C12), 1.28 ppm (TMS); MS (70 eV, EI): m/z (%): 459 (35) [M^+], 386 (25), 335 (55), 320 (24), 73 (100); HRMS: Calcd for $C_{26}H_{30}CoNOSi$: 459.1429; found: 459.1430; elemental analysis calcd (%) for $C_{26}H_{30}CoNOSi$: C 67.95, H 6.59, N 3.05; found: C 68.06, H 6.32, N 3.35.

Oxidative demetalation of 50 to 51: Complex **50** (100 mg, 0.220 mmol) was treated according to the procedure that led to **46** to provide **51** (74.0 mg, 99%). Colorless oil; IR (KBr): $\tilde{\nu}=$2964, 1652, 1575, 1539, 1417, 1261, 1020, 799 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6): $\delta=$7.29 (m, 2H, *o*-PhH), 7.13 (m, 3H, PhH), 6.79 (q, $J=1.8$ Hz, 1H, H8), 6.76 (dd, $J=9.0$, 7.0 Hz, 1H, H4), 6.59 (dd, $J=9.0$, 1.2 Hz, 1H, H3), 6.22 (d, $J=1.5$ Hz, 1H, H10), 6.10 (dd, $J=7.1$, 1.2 Hz, 1H, H5), 3.70 (t, $J=6.0$ Hz, 2H, H11), 1.77 (td, $J=6.6$, 1.8 Hz, 2H, H13), 1.03 (quin, $J=6.2$ Hz, 2H, H12), 0.29 ppm (s, 9H, TMS); ^{13}C NMR (300 MHz, C_6D_6): $\delta=$161.1 (C2), 152.2 (Ph_{quat}), 146.8 (C6), 142.1 (C9), 137.8 (C4), 134.5 (C7), 131.8 (C10), 129.5 (C8), 127.9 (*p*-Ph), 128.9 (*o*-Ph), 126.6 (*m*-Ph), 118.9 (C3), 101.6 (C5), 42.1 (C11), 25.1 (C13), 21.7 (C12), 1.35 ppm (TMS); MS (70 eV, EI): m/z (%): 335 (100) [M^+], 320 (20), 262 (58), 73 (36); HRMS: Calcd for $C_{21}H_{25}NOSi$: 335.1705; found: 335.1697.

Cocyclization of 3 with 1-trimethylsilylpropyne to give 52–54: Pentynyl pyridone **3** (161 mg, 1.00 mmol) and [$CpCo(C_2H_4)_2$] (180 mg, 1.00 mmol), both dissolved in degassed THF (5 mL each), were added through separate syringes to degassed 1-(trimethylsilyl) propyne (20 mL, 135 mmol) under argon over 1 h at room temperature. Subsequently, solvents were removed in vacuo and the resulting residue chromatographed (EtOAc/hexanes 9:1) under N_2 to give a mixture of **52** (33% by ^{1}H NMR), admixed with the free ligand **53** and its isomer **54** (10:1, 47% by ^{1}H NMR), as a brown oil. The identity of **52** was ascertained by the diagnostic signals in the ^{1}H NMR spectrum (C_6D_6, 300 MHz): selected $\delta=$4.53 (d, $J=$ 6.6 Hz, 1H, H5), 4.48 (br s, 1H, H8), 4.36 (s, 5H, Cp), 1.89 (s, 3H, CH_3), 0.03 (s, 9H, TMS), −0.59 ppm (br s, 1H, 10H), and a mass spectrum of the mixture: MS (70 eV, EI): m/z (%): 397 (95) [M^+]. The identity of **53** and **54** in the mixture was confirmed by oxidative demetalation of the crude cyclization mixture and chromatography (EtOAc/hexanes 9:1) to elute **53** (175 mg, 64%), then **54** (44 mg, 16%).

Diene 53: Colorless oil; IR (KBr): $\tilde{\nu}=$2956, 1660, 1652, 1575, 1539, 1408, 1248, 1141, 1071, 1038, 839, 801 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6): $\delta=$6.68 (dd, 1H, $J=9.12$, 6.8 Hz, 1H, H4), 6.56 (dd, $J=9.1$, 1.3 Hz, 1H, H3), 5.94 (dd, $J=6.8$, 1.3 Hz, 1H, H5), 5.89 (br s, 1H, H8), 5.54 (s, 1H, H10), 3.84 (t, $J=6.0$ Hz, 2H, H11), 1.82 (td, $J=6.6$, 1.5 Hz, 2H, H13), 1.17 (s, 3H, CH_3), 1.28 (quin, $J=6.3$ Hz, 2H, H12), 0.12 ppm (s, 9H, TMS); ^{13}C NMR (100 MHz, C_6D_6): $\delta=$161.9 (C2), 149.8 (C9), 145.9 (C6), 137.3 (C4), 136.5 (C8), 132.4 (C10), 129.9 (C7), 119.1 (C3), 105.9 (C5), 40.4 (C11), 29.4 (C13), 22.5 (C12), 21.2 (CH_3), 1.34 ppm (TMS); MS (70 eV, EI): m/z (%): 273 (100) [M^+], 256 (90), 199 (100), 184 (60), 73 (43); HRMS: Calcd for $C_{16}H_{23}NOSi$: 273.1549; found: 273.1546.

Diene 54: Colorless oil; IR (KBr): $\tilde{\nu}=$2956, 1660, 1652, 1575, 1539, 1408, 1248, 1141, 1071, 1038, 839, 801 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6): $\delta=$6.76 (dd, $J=8.8$, 7.1 Hz, 1H, H4), 6.62 (d, $J=8.8$ Hz, 1H, H3), 6.24 (br s, 1H, H8), 5.91 (d, $J=6.9$ Hz, 1H, H5), 5.49 (br s, 1H, H10), 3.77 (t, $J=6.0$ Hz, 2H, H11), 2.10 (td, $J=6.9$, 1.5 Hz, 2H, H13), 1.13 (quin, $J=6.1$ Hz, 2H, H12), 0.30 ppm (s, 9H, TMS); ^{13}C NMR (100 MHz, C_6D_6): $\delta=$161.0 (C2), 149.5 (C9), 137.9 (C4), 134.9 (C8), 133.0 (C10), 128.2 (C7), 118.3 (C3), 101.9 (C5), 46.1 (C11), 24.8 (C13), 22.4 (CH_3, C12), 1.35 ppm (TMS); the signal for C6 could not be detected; MS (70 eV, EI): m/z (%): 273 (100) [M^+], 258 (90), 199 (100), 184 (60), 73 (43).

***N*-(3-Phenylpropyl)-2-pyridone**: Pentynylpyridone **3** (161 mg, 1.00 mmol) in THF (50 mL) was degassed with argon, cooled to −70 °C, and purged with ethyne for 1 h. A solution of [$CpCo(C_2H_4)_2$] (180 mg, 1.00 mmol) in THF (15 mL) was then added via a syringe pump over 1 h and the mixture allowed to warm to room temperature slowly, while maintaining a continuous flow of ethyne. Solvents were removed in vacuum and the crude product chromatographed (EtOAc/hexanes 9:1) to give the product (138 mg, 65%). Yellow resin; IR (KBr): $\tilde{\nu}=$3392, 3027, 2957, 2930, 2861, 1658, 1580, 1540, 1497, 1455, 1275, 1074, 768, 700 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6): $\delta=$7.08 (m, 3H), 6.94 (d, $J=7.5$ Hz, 2H), 6.69 (br t, $J=6.9$ Hz, 1H), 6.55 (br d, $J=9.1$ Hz, 1H), 6.29 (br d, $J=6.8$ Hz, 1H), 5.44 (br t, $J=6.8$ Hz, 1H), 3.51 (t, $J=7.4$ Hz, 2H), 2.34 (t, $J=7.2$ Hz, 2H), 1.76 ppm (quin, $J=7.5$ Hz, 2H); ^{13}C NMR (100 MHz, C_6D_6): $\delta=$ 167.5, 141.3, 138.9, 137.7, 130.8, 128.6, 126.2, 121.2, 104.9, 49.3, 32.9, 30.8 ppm; MS (70 eV, EI): m/z (%): 213 (39) [M^+], 109 (100), 91 (60); HRMS: Calcd for $C_{13}H_{15}NO$: 213.1154; found: 213.1153.

***N*-[3-(2,3,4,5-Tetramethyoxycarbonylphenyl)propyl]-2-pyridone**: [$CpCo(C_2H_4)_2$] (180 mg, 1 mmol) and dimethyl butynedioate (1.42 g, 10.0 mmol) in degassed THF (10 mL each) were added through separate syringes over 75 min to pentynylpyridone **3** (161 mg, 1.00 mmol) dissolved in degassed THF (15 mL). After evaporation of solvents, the residue was chromatographed (EtOAc/MeOH 8:2) under N_2 to give the tetraester

 © 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

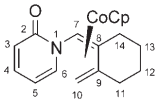
(250 mg, 56%). Red resin; IR (KBr): $\tilde{\nu}$=2954, 1733, 1659, 1582, 1541, 1441, 1374, 1248, 1212, 1161, 1114, 1047, 1000, 888, 811, 770 cm^{-1}; ^1H NMR (300 MHz, C_6D_6): δ=7.59 (s, 1H), 6.64 (ddd, J=9.1, 6.6, 2.1 Hz, 1H), 6.49 (br d, J=9.1 Hz, 1H), 6.27 (dd, J=6.8, 2.1 Hz, 1H), 5.45 (td, J=6.8, 2.0 Hz, 1H), 3.66 (s, 3H), 3.53 (s, 3H), 3.42 (s, 3H), 3.40 (s, 3H), 2.36 (t, J=8.4 Hz, 2H), 1.62 (quin, J=7.5 Hz, 2H), 0.91 ppm (t, J=7.1 Hz, 2H); ^{13}C NMR (100 MHz, C_6D_6): δ=167.4, 167.3, 166.4, 165.3, 162.4, 141.9, 139.1, 137.9, 136.6, 133.5, 133.5, 131.4, 131.2, 120.9, 105.1, 52.8, 52.7, 52.6, 52.5, 49.0, 30.6, 30.4 ppm; MS (70 eV, EI): m/z (%): 445 (20) [M^+], 415 (20), 122 (38), 108 (100), 94 (42); HRMS: Calcd for $C_{22}H_{23}NO_9$: 445.1373; found: 445.1371.

Cocyclization of 4 with BTMSA to give 55 and 56: A solution of hexynylpyridone **4** (175 mg, 1 mmol) in dry, degassed THF (2 mL) and a solution of [$CpCo(C_2H_4)_2$] (180 mg, 1 mmol) in dry, degassed THF (2 mL) were added simultaneously over 1 h to degassed BTMSA (10 mL). The mixture was stirred for another h, the volatiles removed in vacuo, and the residue purified by chromatography (hexane/EtOAc 1:1–7:3–3:1) to deliver **55** (123 mg, 26%) and **56** (60.3 mg, 13%).

Complex 55: Dark red solid; m.p. 130–131 °C (decomp); IR (film): $\tilde{\nu}$= 2950, 1652, 1536, 1246, 833 cm^{-1}; ^1H NMR (300 MHz, C_6D_6): δ=7.10 (d, J=7.0 Hz, 1H), 6.89 (dd, J=9.0, 7.0 Hz, 1H), 6.50 (d, J=7.9 Hz, 1H), 5.24 (m, 1H), 4.84 (s, 1H), 4.58 (s, 5H), 3.33 (m, 1H), 1.37–1.10 (m, 6H), 0.30 (s, 9H), 0.02 (s, 9H), −0.41 ppm (s, 1H); ^{13}C NMR (125 MHz, C_6D_6): δ=161.8, 155.5, 138.2, 116.9, 110.4, 92.4, 85.0, 81.5, 65.1, 48.0, 43.6, 41.7, 27.6, 26.5, 1.73, 1.11 ppm; MS (70 eV, EI): m/z (%): 469 (100) [M^+], 396 (7), 358 (13), 73 (17); HRMS: Calcd for $C_{24}H_{36}CoNOSi_2$: 469.1667; found: 469.1673; elemental analysis calcd (%) for $C_{24}H_{36}CoNOSi_2$: C 61.38, H 7.73, N 2.98; found: C 61.13, H 8.06, N 2.82.

Complex 56: Light yellow oil; IR (film): $\tilde{\nu}$=2952, 1661, 1591, 1538, 1245, 837 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ=7.31 (ddd, J=9.0, 6.7, 2.1 Hz, 1H), 7.25 (d, J=6.7 Hz, 1H), 6.57 (d, J=9.0 Hz, 1H), 6.16 (t, J=6.6 Hz, 1H), 4.80 (s, 5H), 4.15 (s, 1H), 3.92 (t, J=7.3 Hz, 2H), 1.91 (m, 2H), 1.75 (quin, J=7.2 Hz, 2H), 1.42 (m, 2H), 0.10 (s, 9H), 0.05 ppm (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ=162.6, 139.2, 137.4, 121.1, 105.8, 91.9, 78.9, 68.2, 66.8, 64.3, 49.6, 29.7, 29.2, 26.4, 0.60, 0.04 ppm; MS (70 eV, EI): m/z (%): 469 (100) [M^+], 396 (13), 306 (19), 299 (18), 294 (24), 152 (19), 73 (23); elemental analysis calcd (%) for $C_{24}H_{36}CoNOSi_2$: C 61.38, H 7.73, N 2.98; found: C 61.56, H 7.96, N 2.95.

Reaction of 2-pyridone with 1,7-octadiyne to give 57: [$CpCo(C_2H_4)_2$] (180 mg, 1.00 mmol) and 1,7-octadiyne (106 mg, 1.00 mmol), both in degassed THF (2 mL each), were added through separate syringes over 1 h to a solution of 2-pyridone (5.04 g, 53.0 mmol) in dry and degassed MeOH (30 mL) at room temperature. Removal of solvents and chromatography (EtOAc/hexanes 8:2) resulted in complex **57** (146 mg, 45%). Orange resin; IR (KBr): $\tilde{\nu}$=3083, 2932, 2858, 1652, 1581, 1532, 1447, 1354, 1275, 1138, 899, 848, 817, 766 cm^{-1}; ^1H NMR (300 MHz, C_6D_6, assignments according to the numbering in the structure shown): δ=7.27 (br d, J=5.5 Hz, 1H, H6), 6.74 (br t, J=9.0 Hz, 1H, H4), 6.59 (d, J=9.0 Hz, 1H, H3), 5.61 (br t, J=6.1 Hz, 1H, H5), 4.23 (s, 5H, Cp), 3.08 (br s, 1H, H7), 2.21 (m, 2H), 1.83–1.55 (m, 4H), 1.71 (br s, 1H, H10), 1.20 (m, 2H), −0.15 ppm (br s, 1H, H10); ^{13}C NMR (100 MHz, C_6D_6): δ=162.9 (C2), 137.7 (C6), 137.4 (C4), 120.7 (C3), 102.8 (C5), 90.4 (C8 or C9), 86.8 (C8 or C9), 81.7 (Cp), 60.0 (C7), 31.3 (C10), 30.7, 25.7, 23.7, 22.9 ppm (C11–14); MS (70 eV, EI): m/z (%): 325 (100) [M^+], 257 (45), 201 (44), 153 (34); HRMS: Calcd for $C_{18}H_{20}CoNO$: 325.0877; found: 325.0873.



Oxidative demetalation of 57 to 58: Complex **57** (100 mg, 0.31 mmol) was treated according to the procedure that led to **46** to provide **58** (63.0 mg, 100%). Colorless oil; IR (KBr): $\tilde{\nu}$=3079, 2934, 2858, 1668, 1586, 1532, 1447, 1275, 1145, 896, 841, 771 cm^{-1}; ^1H NMR (300 MHz, C_6D_6): δ=6.86 (s, 1H, H7), 6.64 (ddd, J=9.0, 6.4, 1.5 Hz, 1H, H4), 6.52 (dd, J=8.8, 1.4 Hz, 1H, H3), 6.45 (dd, J=6.5, 1.5 Hz, 1H, H6), 5.41 (td, J=6.5, 1.4 Hz, 1H, H5), 4.91 (br s, 1H, H10), 4.64 (br s, 1H, H10), 2.07 (t, J=6.3 Hz, 2H, H11), 1.91 (t, J=6.1 Hz, 2H, H14), 1.33 (AA′m, 2H, H12), 1.19 ppm (BB′m, 2H, H13); ^{13}C NMR (100 MHz, C_6D_6): δ=161.9 (C2), 147.2 (C8), 138.8 (C4), 138.2 (C9), 137.9 (C6), 122.3 (C7), 121.9 (C3), 110.4 (C10), 103.8 (C5), 41.7 (C11), 34.9 (C14), 26.6 (C12), 25.7 ppm (C13); MS (70 eV, EI): m/z (%): 201 (100) [M^+], 184 (24), 172 (42); HRMS: Calcd for $C_{13}H_{15}NO$: 201.1154; found: 201.1153; elemental analysis calcd (%) for $C_{13}H_{15}NO$: C 77.58, H 7.51, N 6.96; found: C 77.45, H 7.25, N 6.98.

Reaction of 4-pyridone with 1,7-octadiyne to give 59 and 60: [$CpCo(C_2H_4)_2$] (180 mg, 1.00 mmol) and 1,7-octadiyne (106 mg, 1.00 mmol), both dissolved in THF (2 mL each), were added through separate syringes over 1 h to a solution of 4-pyridone (5.04 g, 53.0 mmol) in dry and degassed MeOH (30 mL) at room temperature. Evaporation of the solvents and chromatography (EtOAc/hexanes 8:2) provided a mixture, which was separated by HPLC (silica gel, EtOAc/MeOH 9:1) to access **59** (40.0 mg, 12%) and **60** (20.0 mg, 6%).

Compound 59: Orange resin; ^1H NMR (300 MHz, C_6D_6): δ=6.65 (m, 2H), 6.41 (m, 2H), 4.25 (s, 5H, Cp), 1.68 (br s, 1H), 1.99–1.59 (m, 4H), 1.29–1.14 (m, 4H), 0.92 (br s, 1H), −0.72 ppm (br s, 1H); ^{13}C NMR (100 MHz, C_6D_6): δ=140.3, 101.5, 90.2, 86.0, 82.0 (Cp), 63.8, 35.2, 31.2, 29.6, 25.4, 23.2 ppm, signal for carbonyl carbon not detected; MS (70 eV, EI): m/z (%): 325 (80) [M^+], 219 (15), 200 (75), 172 (100), 144 (20); HRMS: Calcd for $C_{18}H_{20}CoNO$: 325.0877; found: 325.0874.

Compound 60: Orange resin; ^1H NMR (300 MHz, C_6D_6): δ=6.37 (m, 2H), 6.29 (m, 2H), 4.24 (s, 5H, Cp), 4.12 (br s, 1H), 2.19 (dt, J=13.6, 4.1 Hz, 1H), 1.96 (m, 1H), 1.81 (s, 1H), 1.80–1.60 (m, 6H), −0.37 ppm (br s, 1H); ^{13}C NMR (100 MHz, C_6D_6): δ=144.8, 101.4, 86.1, 81.9 (Cp), 81.8, 63.6, 35.2, 30.9, 29.7, 23.2, 23.0 ppm, signal for carbonyl carbon not detected.

Oxidative demetalation of 59 to 61: Complex **59** (40 mg, 0.123 mmol) was treated according to the procedure that led to **46**, resulting in **61** (24.0 mg, 100%). Colorless oil; ^1H NMR (300 MHz, C_6D_6) δ=6.36 (d, J=7.8 Hz, 2H), 6.19 (d, J=7.8 Hz, 2H), 5.70 (br s, 1H), 4.66 (br s, 1H), 4.56 (br s, 1H), 1.97 (t, J=6.0 Hz, 2H), 1.62 (t, J=6.0 Hz, 2H), 1.28 ppm (m, 4H).

Oxidative demetalation of 50 to 62: Complex **60** (20.0 mg, 0.06 mmol) was treated according to the procedure that led to **46**, resulting in **62** (12 mg, 100%).Colorless oil; ^1H NMR (300 MHz, C_6D_6): δ=6.37 (br s, 4H), 5.28 (br s, 1H), 4.56 (br s, 1H), 4.30 (br s, 1H), 1.77 (m, 2H), 1.69 (m, 2H), 1.32 ppm (m, 4H); MS (70 eV, EI): m/z (%): 201 (62) [M^+], 200 (100), 172 (96).

Reaction of 1-methyl-2-pyrazinone (63) with 1,7-octadiyne to give 64: A solution of 1-methyl-2-pyrazinone (**63**) (90.1 mg, 0.82 mmol) in C_6H_6 (5 mL) and of [$CpCo(C_2H_4)_2$] (153 mg, 0.849 mmol) in C_6H_6 (3 mL) were syringe-pumped separately into a boiling solution of 1,7-octadiyne (164 mg, 1.54 mmol) in C_6H_6 (3 mL) over a period of 4 h. After solvent removal, column chromatography (EtOAc/MeOH 1:0–10:1) of the black residue gave complex **64** (61.3 mg, 22%) and starting **63** (21.5 mg, 24%). Orange oil; IR (KBr): $\tilde{\nu}$=3080, 2930, 2865, 2830, 1645, 1590, 1485, 1435, 1405, 1355, 1325, 1275, 1255, 1205, 1165, 1140, 1110, 1040, 1010, 925, 900, 860, 835, 810, 730, 705, 650, 620, 600, 575 cm^{-1}; ^1H NMR (C_6D_6, 300 MHz): δ=6.61 (d, J=4.3 Hz, 1H), 5.78 (d, J=4.3 Hz, 1H), 4.75 (s, 5H), 4.65 (s, 1H), 2.71 (s, 3H), 2.51 (s, 1H), 2.50–2.32 (m, 3H), 2.24 (m, 1H), 1.99–1.71 (m, 2H), 1.58–1.48 (m, 2H), 0.37 ppm (s, 1H); ^{13}C NMR (C_6D_6, 100 MHz): δ=160.3, 157.0, 123.5, 122.4, 99.4, 94.4, 81.7, 42.5, 39.3, 36.4, 32.6, 32.2, 24.2, 24.1 ppm; MS (70 eV, EI): m/z (%): 340 (74) [M^+], 272 (29), 259 (9), 242 (18), 215 (100); HRMS: Calcd for $C_{18}H_{21}CoN_2O$: 340.0990; found: 340.0988.

***N,N′*-Dibenzyl-2,3-pyrazinedione (65)**:[44] A solution of 1,4-dihydro-2,3-pyrazinedione (104.1 mg, 0.93 mmol) in DMSO (15 mL) was treated with a 60% NaH dispersion (83 mg, 2.08 mmol). After 10 min, benzylbromide (360 mg, 0.21 mmol) was added and the mixture stirred at room temperature for 2 h. DMSO was removed under high vacuum, the brown residue extracted with CH_2Cl_2/H_2O, and the extract dried over $MgSO_4$, and chromatographed (CH_2Cl_2/MeOH 20:1) to give **65** (236 mg, 87%). White solid; IR (KBr): 3100, 3065, 3030, 2945, 1685, 1640, 1585, 1495, 1445, 1420, 1395, 1360, 1355, 1320, 1225, 1200, 1150, 1080, 1020, 945, 835, 755, 730, 695, 635, 620, 605, 555 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ=7.46–7.28 (m, 10H), 6.08 (s, 2H), 4.96 ppm (s, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=155.9, 135.0, 128.9, 128.5, 128.4, 112.1, 51.3 ppm; MS

© 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

(70 eV, EI): *m/z* (%): 292 (50) [M^+], 281 (9), 207 (32), 201 (21), 91 (100), 65 (26); HRMS: Calcd for $C_{18}H_{16}N_2O_2$ 292.1212; found: 292.1212.

Reaction of 65 with 1,7-octadiyne to give 66: 1,7-Octadiyne (65.0 mg, 0.61 mmol) and [$CpCo(C_2H_4)_2$] (71.0 mg, 0.39 mmol) in toluene (3 mL each) were syringe-pumped separately to 1,4-dibenzyl-1,4-dihydropyrazine-2,3-dione (**65**) (107 mg, 0.37 mmol) in toluene (10 mL) over a period of 3 h. TLC analysis (CH_2Cl_2/MeOH 20:1) showed mainly starting material, therefore, the red solution was stirred for another 2 h under reflux. Subsequently, more 1,7-octadiyne (75.0 mg, 0.71 mmol) dissolved in toluene (5 mL) was added to the boiling solution by syringe pump over a period of approximately 15 h. The solvent was removed and the black mixture purified by column chromatography (CH_2Cl_2/MeOH 20:1) to yield **66** (29 mg, 15%) and recovered starting material **65** (77 mg, 72%). Red oil; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 7.38$–7.24 (m, 10H), 5.21 (d, $J =$ 14.8 Hz, 2H), 4.59 (s, 5H), 4.24 (d, $J = 14.8$ Hz, 2H), 3.71 (br s, 2H), 3.03 (br s, 2H), 2.36–2.20 (m, 2H), 2.2.-1.92 (m, 4H), 1.80 ppm (m, 2H); MS (70 eV, EI): *m/z* (%): 522 (36) [M^+], 456 (18), 236 (30), 91 (100); HRMS: Calcd for $C_{31}H_{31}CoN_2O_2$: 522.1718; found: 522.1714.

Cocyclization of 15 with BTMSA to give 67 and 68: Butynylpyrazinone **15** (98.3 mg, 0.66 mmol) and [$CpCo(C_2H_4)_2$] (145 mg, 0.805 mmol) in THF (3 mL each) were added separately by syringe pump to BTMSA (10 mL) at room temperature over a period of 3 h. The solvents were removed, and column chromatography (EtOAc/hexane 1:1) of the black residue provided **67** (119 mg, 41%) and compound **68** (15.8 mg, 10%).

Complex 67: Red solid; IR (KBr): $\tilde{\nu} = 3110$, 2955, 2900, 2845, 1670, 1630, 1475, 1445, 1330, 1280, 1245, 1215, 1205, 1170, 1110, 1085, 1035, 1015, 970, 925, 860, 820, 810, 760, 680, 660, 635, 615 cm^{-1}; ^{1}H NMR (C_6D_6, 300 MHz): $\delta = 7.88$ (d, $J = 2.8$ Hz, 1H), 4.86 (s, 1H), 4.49 (s, 5H), 4.13 (dt, $J = 12.3$, 8.7 Hz, 1H), 3.20 (dd, $J = 8.4$, 2.8 Hz, 1H), 3.00 (dt, $J = 12.3$, 6.0 Hz, 1H), 1.94 (d, $J = 8.4$ Hz, 1H), 1.17 (t, $J = 8.3$ Hz, 2H), 0.35 (s, 9H), 0.34 ppm (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 154.5$, 153.3, 84.8, 81.8, 78.8, 77.0, 66.7, 64.1, 58.1, 43.7, 31.4, 4.7, 3.7 ppm; MS (70 eV, EI): *m/z* (%): 442 (100) [M^+], 427 (7), 317 (24), 229 (6), 124 (14), 73 (31); elemental analysis calcd (%) for $C_{21}H_{31}CoN_2OSi_2$: C 56.99, H 7.06, N 6.33; found: C 57.03, H 7.22, N 6.30.

Compound 68: White solid; IR (KBr): $\tilde{\nu} = 3045$, 2950, 2895, 1670, 1615, 1575, 1480, 1430, 1400, 1330, 1310, 1255, 1245, 1110, 1095, 1045, 990, 925, 880, 835, 755, 690, 625, 595, 580, 550 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 8.26$ (s, 1H), 7.37 (ABq, 2H), 4.46 (t, $J = 2.6$ Hz, 2H), 3.42 (t, $J =$ 2.6 Hz, 2H), 0.39 ppm (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 151.0$ (2C), 138.3, 135.9, 134.7, 132.4, 130.7, 125.3, 47.3, 27.2, −0.20 ppm; MS (70 eV, EI): *m/z* (%): 244 (20) [M^+], 229 (100), 201 (7). HRMS: Calcd for $C_{13}H_{16}N_2OSi$: 244.1032; found: 244.1031.

Oxidative demetalation of 67 to 69: A solution of $CuCl_2 \cdot 2H_2O$ (60.5 mg, 0.35 mmol) in THF (2 mL) and H_2O (0.5 mL) was added to an ice-cooled solution of complex **67** (32.1 mg, 0.073 mmol) and NEt_3 (20 μL, 0.143 mmol) in THF (2 mL). After 5 min of stirring at 0°C, TLC analysis (EtOAc) showed only starting material, therefore, the ice bath was removed and the solution was stirred at room temperature. After 7 h, the starting material had disappeared, and the deep red solution was diluted with H_2O/CH_2Cl_2 and extracted with CH_2Cl_2. Column chromatography (hexane/EtOAc 1:1) gave **69** (10 mg, 44%) and some **68** (1 mg, 5%). Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 8.23$ (s, 1H), 7.68 (t, $J =$ 1.1 Hz, 1H), 4.42 (br t, $J = 7.8$ Hz, 2H), 3.41 (dt, $J = 7.8$, 1.1 Hz, 2H), 0.48 (s, 9H), 0.41 ppm (s, 9H); MS (70 eV, EI): *m/z* (%): 316 (28) [M^+], 301 (100), 285 (27), 243 (18), 229 (7), 143 (14), 73 (16).

Reaction of 16 with BTMSA and [$CpCo(C_2H_4)_2$] to give 70: Pentynylpyrazinone **16** (101 mg, 0.62 mmol) and [$CpCo(C_2H_4)_2$] (115 mg, 0.638 mmol) in THF (3 mL each) were added separately by syringe pump to BTMSA (10 mL) at room temperature over a period of 2.5 h. After removal of the volatiles, column chromatography (EtOAc/hexane 3:1) provided **70** (43.0 mg, 15%). Thick, red-green oil; IR (KBr): $\tilde{\nu} = 3095$, 3010, 2960, 2900, 1655, 1560, 1475, 1460, 1425, 1400, 1325, 1300, 1260, 1245, 1180, 1160, 1140, 1105, 1015, 965, 855, 830, 750, 685, 655, 623, 595, 552 cm^{-1}; ^{1}H NMR (C_6D_6, 300 MHz): $\delta = 8.40$ (br s, 1H), 6.17 (br s, 1H), 5.26 (dd, $J = 12.7$, 5.5 Hz, 1H), 4.57 (s, 1H), 4.45 (s, 5H), 3.65 (td, $J =$ 12.5, 5.5 Hz, 1H), 1.37–1.06 (m, 4H), 0.20 (s, 9H), 0.03 (s, 9H), −0.60 ppm (br s, 1H); ^{13}C NMR (C_6D_6, 100 MHz): $\delta = 157.7$, 143.3, 142.7, 119.6, 91.5, 81.0, 84.0, 53.0, 49.1, 37.7, 33.6, 20.5, 2.31, 1.45 ppm; MS (70 eV, EI): *m/z* (%): 456 (100) [M^+], 383 (35), 332 (24), 317 (36), 73 (88); HRMS: Calcd for $C_{22}H_{33}CoN_2OSi_2$: 456.1463; found: 456.1459.

Oxidative demetalation of 70 to 71: To a solution of complex **70** (46.1 mg, 0.101 mmol) in THF (2 mL) and CH_3CN (2 mL) at 0°C was added $Fe(NO_3)_3$?$9H_2O$ (210 mg, 0.520 mmol) dissolved in CH_3CN (2 mL) and H_2O (0.5 mL). The dark green solution turned orange. After 1.5 min, the mixture was poured into ice water and extracted three times with CH_2Cl_2. The combined organic layers were dried ($MgSO_4$), filtered and concentrated in vacuo. Column chromatography (hexanes/EtOAc 1:1) furnished **71** (25.0 mg, 75%). White solid; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 7.97$ (s, 1H), 7.53 (s, 1H), 6.55 (q, $J = 1.6$ Hz, 1H), 6.38 (d, $J = 2.1$ Hz, 1H), 3.97 (t, $J = 6.4$ Hz, 2H), 2.49 (td, $J = 6.6$, 1.5 Hz, 2H), 2.05 (quin, $J =$ 6.6 Hz, 2H), 0.14 (s, 9H), 0.11 ppm (s, 9H); HRMS: Calcd for $C_{17}H_{28}N_2OSi_2$: 332.1740; found: 332.1743.

Cyclization of 19 to 72: To dipentynylpyrazinedione **19** (106.1 mg, 0.43 mmol) in toluene (25 mL) was added [$CpCo(C_2H_4)_2$] (86.2 mg, 0.479 mmol) in toluene (6 mL). The mixture was stirred at room temper-

Table 7. Crystal data and structure refinement for complexes **33**, **35**, **36**, **38**, **39**, **45**, **67**, and **72**.

	33	**35**	**36**	**38**	**39**	**45**	**67**	**72**
formula	$C_{22}H_{32}CoNOSi_2$	$C_{20}H_{22}CoNO$	$C_{23}H_{34}CoNOSi_2$	$C_{23}H_{32}CoNO_2Si_2$	$C_{23}H_{32}CoNO_3Si_2$	$C_{23}H_{34}CoNOSi_2$	$C_{21}H_{31}CoN_2OSi_2$	$C_{19}H_{21}CoN_2O_2$
F_w	441.59	351.32	455.62	469.13	485.61	455.62	442.59	368.31
temperature [K]	293(2)	153(2)	157(2)	146(2)	155(2)	440(2)	135(2)	132(2)
wavelength [Å]	0.71073	0.71073	0.71073	0.71073	0.71073	0.71073	0.71073	0.71073
crystal system	triclinic	triclinic	monoclinic	monoclinic	monoclinic	monoclinic	triclinic	triclinic
space group	$P\bar{1}$	$P\bar{1}$	$P2_1/c$	$C2/c$	$C2/c$	$P2_1/n$	$P\bar{1}$	$P\bar{1}$
a [Å]	7.7555(6)	7.802(4)	19.9466(13)	23.2021(18)	29.458(3)	18.3427(4)	7.5467(8)	9.3495(3)
b [Å]	9.5294(7)	9.424(5)	14.1688(9)	17.7971(14)	10.1754(9)	7.41830(10)	9.0865(10)	9.7539(3)
c [Å]	16.6462(12)	12.258(6)	18.0408(12)	13.6060(10)	16.5627(15)	19.8862(3)	16.8965(18)	19.7948(5)
α [°]	89.549(2)	73.603(6)	90	90	90	90	82.937(2)	99.923(2)
β [°]	78.700(2)	87.129(6)	116.1060(10)	118.9050(10)	105.9150(10)	117.0160(10)	77.934(2)	101.4510(10)
γ [°]	68.163(2)	65.985(5)	90	90	90	90	73.230(2)	94.22
V [Å^3]	1116.97(14)	787.6(7)	4578.5(5)	4918.4(7)	4774.4(7)	2410.67(7)	1082.4(2)	1731.88(9)
Z	2	2	8	8	8	4	2	4
ρ_{calcd} [g cm^{-3}]	1.340	1.481	1.322	1.362	1.351	1.255	1.358	1.522
μ [mm^{-1}]	0.890	1.093	0.868	0.820	0.843	0.824	0.917	1.012
R_1 [$I > 2\sigma(I)$]	0.0679	0.0364	0.0276	0.0286	0.0317	0.0642	0.0504	0.0527
wR_2 (all data)	0.1715	0.0806	0.0764	0.0722	0.0696	0.1480	0.1213	0.1493

 © 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

ature for 3.5 h, the solvent removed, and the black residue purified by column chromatography (CH_2Cl_2/MeOH 15:1) to give **72** (84.0 mg, 53%). Red oil; IR (KBr): $\tilde{\nu}$ = 3085, 2900, 2910, 2850, 2230, 1655, 1600, 1465, 1435, 1410, 1390, 1350, 1330, 1305, 1290, 1255, 1175, 1150, 1120, 1045, 1010, 930, 905, 860, 825, 810, 735, 725, 645, 620, 565 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ = 4.68 (s, 5H), 4.46 (m, 1H), 4.19 (m, 1H), 4.10 (br s, 1H), 3.93 (d, J = 7.9 Hz, 1H), 3.76 (dd, J = 7.8, 5.5 Hz, 1H), 2.83 (t, J = 12.6 Hz, 1H), 2.75–2.70 (m, 2H), 2.43 (td, J = 13.5, 4.8 Hz, 1H), 2.33 (dd, J = 5.4, 1.0 Hz, 1H), 2.01–1.89 (m, 2H), 1.82 (m, 1H), 1.67–1.44 ppm (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 154.5, 153.3, 92.1, 81.5, 74.0, 69.3, 61.6, 48.4, 45.5, 43.3, 36.5, 33.6, 31.5, 30.0, 29.2 ppm; MS (70 eV, EI): *m/z* (%): 368 (100) [M^+], 340 (7), 302 (7), 244 (11), 124 (17); HRMS: Calcd for $C_{19}H_{21}CoN_2O_2$: 368.0935; found: 368.0939.

Crystal structure determinations: X-ray intensity data were recorded on a Bruker SMART 1000 CCD area detector[59] with monochromated $Mo_{K\alpha}$ radiation (λ = 0.71073 Å). Data collection strategies were assigned based on the apparent Laue symmetry obtained from a preliminary examination of the unit cell (full sphere for a triclinic setting and an arbitrary hemisphere for higher symmetries). Data were integrated with the SAINT software package[60] and corrected for Lorentz polarization effects and an empirical absorption correction applied within SADABS.[61] The space group for each compound was assigned based on systematic absences observed within the data.[62] Structures were solved by direct methods[63] and expanded using Fourier methods and refined routinely.[64] Except where disorder is indicated, all non-hydrogen atoms were refined with anisotropic thermal motion parameters. Hydrogen atoms were included in geometrically calculated positions with thermal parameters tied to the atom to which they are bonded. The water hydrogens in **33** and **72** were included in their observed positions but were restrained to have O–H distances of 0.86 Å. A summary of the crystal and structure refinement data can be found in Table 7.

CCDC-630383–CCDC-630390 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data request/cif.

Acknowledgements

This work was supported by CNRS, MRES, and the NSF (CHE 0451241). We thank the Swiss National Science Foundation and the Roche Research Foundation (J. L., P.B.), the Humboldt Foundation (T.H.), the Studienstiftung des deutschen Volkes (B.M.), the NSF predoctoral program (M. J.E.), and OAS-LASPAU (E.P.).

[1] For general reviews of transition-metal-mediated [2+2+2] cycloadditions, see: a) P. R. Chopade, J. Louie, *Adv. Synth. Catal.* **2006**, *348*, 2307; b) V. Gandon, C. Aubert, M. Malacria, *Chem. Commun.* **2006**, 2209; c) S. Kotha, E. Brahmachar, K. Lahiri, *Eur. J. Org. Chem.* **2005**, 4741; d) Y. Yamamoto, *Curr. Org. Chem.* **2005**, *9*, 503; e) S. Saito, Y. Yamamoto, *Chem. Rev.* **2000**, *100*, 2901; f) M. Lautens, W. Klute, W. Tam, *Chem. Rev.* **1996**, *96*, 49; g) I. Ojima, M. Tzamarioudaki, Z. Li, R. J. Donovan, *Chem. Rev.* **1996**, *96*, 635; h) D. B. Grotjahn in *Comprehensive Organometallic Chemistry II, Vol. 12* (Eds.: E. W. Abel, F. G. A. Stone, G. Wilkinson, L. Hegedus), Pergamon Press, Oxford, **1995**, pp. 741. For an early review of CpCo-mediated [2+2+2] cycloadditions, see: i) K. P. C. Vollhardt, *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 539.

[2] R. Boese, D. F. Harvey, M. J. Malaska, K. P. C. Vollhardt, *J. Am. Chem. Soc.* **1994**, *116*, 11153.

[3] D. Peréz, B. A. Siesel, M. J. Malaska, E. David, K. P. C. Vollhardt, *Synlett* **2000**, 306.

[4] a) R. Boese, A. P. Van Sickle, K. P. C. Vollhardt, *Synthesis* **1994**, 1374; b) D. B. Grotjahn, K. P. C. Vollhardt, *J. Am. Chem. Soc.* **1986**, *108*, 2091.

[5] G. S. Sheppard, K. P. C. Vollhardt, *J. Org. Chem.* **1986**, *51*, 5496.

[6] R. Boese, H.-J. Knölker, K. P. C. Vollhardt, *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 1035.

[7] a) H. Pellissier, J. Rodriguez, K. P. C. Vollhardt, *Chem. Eur. J.* **1999**, *5*, 3549; b) R. Boese, J. Rodriguez, K. P. C. Vollhardt, *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 993.

[8] a) N. Sato in *Science of Synthesis, Vol. 16* (Ed.: Y. Yamamoto), Thieme, Stuttgart, **2004**, p. 751; b) N. Sato in *Comprehensive Heterocyclic Chemistry II, Vol. 6* (Eds.: A. R. Katritzky, C. W. Rees, E. F. V. Scriven), Elsevier, Oxford, **1996**, p. 233; c) G. B. Barlin, *The Pyrazines*, Interscience, New York, **1982**.

[9] For selected recent illustrative examples, see: a) V. G. Pawar, W. M. De Borggraeve, *Synthesis* **2006**, 2799; b) L. A. Mitscher, *Chem. Rev.* **2005**, *105*, 559; c) X. Ma, D. R. Gang, *Nat. Prod. Rep.* **2004**, *21*, 752; d) P. J. Tobin, L. P. Rivory, *Drug Des. Rev.–Online* **2004**, *1*, 341; e) M. Adamczyk, S. R. Akireddy, D. D. Johnson, P. G. Mattingly, Y. Pan, R. E. Reddy, *Tetrahedron* **2003**, *59*, 8129; f) D. E. N. Jacquot, H. Hoffmann, K. Polborn, T. Lindel, *Tetrahedron Lett.* **2002**, *43*, 3699; g) K. Hirano, T. Kubota, M. Tsuda, K. Watanabe, J. Fromont, J. Kobayashi, *Tetrahedron* **2000**, *56*, 8107.

[10] a) For a review, see: J. A. Varela, C. Saá, *Chem. Rev.* **2003**, *103*, 3787; for some recent pertinent investigations, see: b) K. Tanaka, Y. Hagiwara, M. Hirano, *Angew. Chem. Int. Ed.* **2006**, *45*, 2734; c) R. T. Yu, T. Rovis, *J. Am. Chem. Soc.* **2006**, *128*, 2782, and references therein.

[11] a) W. D. Harman, *Top. Organomet. Chem.* **2004**, *7*, 95; b) R. Cordone, H. Taube, *J. Am. Chem. Soc.* **1987**, *109*, 8101; c) P. A. Lay, R. H. Magnuson, J. Sen, H. Taube, *J. Am. Chem. Soc.* **1982**, *104*, 7658.

[12] D. B. Grotjahn, K. P. C. Vollhardt, *Synthesis* **1993**, 579.

[13] a) A. R. Katritzky, K. Jug, D. C. Oniciu, *Chem. Rev.* **2001**, *101*, 1421; b) A. R. Katritzky, A. F. Pozharskii, *Handbook of Heterocyclic Chemistry*, 2nd Ed.; Pergamon Press, Amsterdam, **2000**, p. 47; c) C. W. Bird, *Tetrahedron* **1992**, *48*, 7857; d) A. J. Boulton, A. McKillop in *Comprehensive Heterocyclic Chemistry, Vol. 2* (Eds.: A. McKillop, A. J. Boulton, A. McKillop, A. R. Katritzky, C. W. Rees), Pergamon Press, Oxford, **1984**, p. 151, 156; e) J. Elguero, C. Marzin, A. R. Katritzky, P. Linda, *The Tautomerism of Heterocycles*, Academic Press, New York, **1976**, p. 84.

[14] V. Gandon, N. Agenet, K. P. C. Vollhardt, M. Malacria, C. Aubert, *J. Am. Chem. Soc.* **2006**, *128*, 8509, and references therein.

[15] For reviews, see: a) K. Afarinkia, V. Vinader, T. Nelson, G. H. Posner, *Tetrahedron* **1992**, *48*, 9111; b) A. R. Katritzky, N. Dennis, *Chem. Rev.* **1989**, *89*, 827; for examples of pyridone reacting as a diene, see: c) K. Matsumoto, M. Ciobanu, M. Yoshida, T. Uchida, *Heterocycles* **1997**, *45*, 15; d) G. H. Posner, V. Vinader, K. Afarinkia, *J. Org. Chem.* **1992**, *57*, 4088; e) H. Nakano, T. Sate, K. Okamura, H. Tomisawa, H. Hongo, *Chem. Pharm. Bull.* **1991**, *39*, 2471; f) M. Kuzuya, A. Noguchi, E. Mano, T. Okuda, *Bull. Chem. Soc. Jpn.* **1985**, *58*, 1149; g) R. Gompper, A. Schmidt, *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 463; h) H. Tomisawa, H. Hongo, R. Fujita, H. Kato, *Heterocycles* **1977**, *6*, 1765; as dienophile, see: i) R. Fujita, M. Hoshino, H. Tomisawa, H. Matsuzaki, H. Hongo, *Chem. Pharm. Bull.* **2001**, *49*, 497; j) R. Fujita, K. Watanabe, W. Ikeura, Y. Ohtake, H. Hongo, *Heterocycles* **2000**, *53*, 2607; k) R. Fujita, M. Hoshino, H. Tomisawa, H. Hongo, *Chem. Pharm. Bull.* **2000**, *48*, 1814; l) H. Kato, R. Fujita, H. Hongo, H. Tomisawa, *Heterocycles* **1979**, *12*, 1.

[16] For selected recent examples, see: a) N. Kaval, D. Ermolat′ev, P. Appukkuttan, W. Dehaen, C. O. Kappe, E. van der Eycken, *J. Comb. Chem.* **2005**, *7*, 490, and references therein; b) B. M. P. Verbist, W. M. De Borggraeve, S. Toppet, F. Compernolle, G. J. Hoornaert, *Eur. J. Org. Chem.* **2005**, 2941; c) N. Kaval, W. Dehaen, C. O. Kappe, E. van der Eycken, *Org. Biomol. Chem.*, **2004**, *2*, 154; d) F. J. R. Rombouts, D. A. J. Vanraes, J. Wynendaele, P. K. Loosen, I. Luyten, S. Toppet, F. Compernolle, G. J. Hoornaert, *Tetrahedron* **2001**, *57*, 3209.

[17] A. Casaschi, R. Grigg, J. M. Sansano, *Tetrahedron* **2001**, *57*, 607.

[18] A.-S. Bessis, C. Bolea, B. Bonnet, M. Epping-Jordan, N. Poirier, S.-M. Poli, J.-P. Rocher, Y. Thollon, Patent PCT Int. Appl. WO 2005123703, **2005**.

 © 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

[19] P. Guerry, R. Neier, *Synthesis* **1984**, 485.
[20] H. Kaye, S.-H. Chang, *Tetrahedron* **1970**, *26*, 1369.
[21] A. McKillop, M. J. Zelesko, *Tetrahedron Lett.* **1968**, *9*, 4945.
[22] I. Fleming, D. Philippides, *J. Chem. Soc. C* **1970**, *17*, 2426.
[23] M. R. Del Giudice, G. Settimj, M. Delfini, *Tetrahedron* **1984**, *40*, 4067.
[24] A. J. Hubert, J. Dale, *J. Chem. Soc.* **1965**, 3160; K. P. C. Vollhardt, R. G. Bergman, *J. Am. Chem. Soc.* **1974**, *96*, 4996.
[25] a) K. Yasufuku, H. Yamazaki, *Org. Mass Spectrom.* **1970**, *3*, 23; b) W. G. Dauben, M. E. Lorber, *Org. Mass Spectrom.* **1970**, *3*, 211.
[26] A. P. Venkov, S. M. Statkova-Abeghe, *Tetrahedron* **1996**, *52*, 1451.
[27] S. L. Spassov, I. A. Atanassova, M. Haimova, *Org. Magn. Reson.* **1984**, *22*, 194.
[28] C. Aubert, V. Gandon, A. Geny, T. J. Heckrodt, M. Malacria, E. Paredes, K. P. C. Vollhardt, *Chem. Eur. J.* **2007**, *13*, 10.1002/chem.200601822.
[29] Strychnine: a) M. J. Eichberg, R. L. Dorta, D. B. Grotjahn, K. Lamottke, M. Schmidt, K. P. C. Vollhardt, *J. Am. Chem. Soc.* **2001**, *123*, 9324; b) M. J. Eichberg, R. L. Dorta, K. Lamottke, K. P. C. Vollhardt, *Org. Lett.* **2000**, *2*, 2479; LSD: c) C. Saá, D. D. Crotts, G. Hsu, K. P. C. Vollhardt, *Synlett* **1994**, 487; stemodin: d) J. Germanas, C. Aubert, K. P. C. Vollhardt, *J. Am. Chem. Soc.* **1991**, *113*, 4006; illudol: e) E. P. Johnson, K. P. C. Vollhardt, *J. Am. Chem. Soc.* **1991**, *113*, 381; steroids: f) S. H. Lecker, N. H. Nguyen, K. P. C. Vollhardt, *J. Am. Chem. Soc.* **1986**, *108*, 856; g) H. Butenschön, M. Winkler, K. P. C. Vollhardt, *J. Chem. Soc. Chem. Commun.* **1986**, 388; h) K. P. C. Vollhardt, *Pure Appl. Chem.* **1985**, *57*, 1819; camptothecin: i) R. A. Earl, K. P. C. Vollhardt, *J. Org. Chem.* **1984**, *49*, 4786; j) R. A. Earl, K. P. C. Vollhardt, *J. Am. Chem. Soc.* **1983**, *105*, 6991.
[30] For the recent disclosure of high-yielding CpCo-mediated cocyclizations of ethene with diboryldiynes, see: V. Gandon, D. Leboeuf, S. Amslinger, K. P. C. Vollhardt, M. Malacria, C. Aubert, *Angew. Chem. Int. Ed.* **2005**, *44*, 7114.
[31] Q. Zhang, J. O. Rich, I. C. Cotterill, D. P. Pantaleone, P. C. Michels, *J. Am. Chem. Soc.* **2005**, *127*, 7286.
[32] For recent reviews, see: a) U. Rinner, T. Hudlicky, *Synlett* **2005**, 365; b) Z. Jin, *Nat. Prod. Rep.* **2005**, *22*, 111; c) O. Hoshino in *The Alkaloids, Vol. 51* (Ed.: G. A. Cordell), Academic Press, San Diego, **1998**, p. 323.
[33] For some very recent work, see: T. Harayama, A. Hori, H. Abe, Y. Takeuchi, *Heterocycles* **2006**, *67*, 385; M. D. Ganton, M. A. Kerr, *Org. Lett.* **2005**, *7*, 4777; J. C. Torres, A. C. Pinto, S. J. Garden, *Tetrahedron* **2004**, *60*, 9889; T. Harayama, A. Hori, H. Abe, Y. Takeuchi, *Tetrahedron* **2004**, *60*, 1611, and references therein.
[34] D. L. Boger, C. E. Brotherton, M. D. Kelley, *Tetrahedron* **1981**, *37*, 3977.
[35] G. Eglinton, M. C. Whiting, *J. Chem. Soc.* **1950**, 3650.
[36] D. Gnecco, C. Marazano, R. G. Enríquez, J. L. Terán, M. del Rayo Sánchez S. , A. Galindo, *Tetrahedron: Asymmetry* **1998**, *9*, 2027.
[37] J.-C. Clinet, E. Duñach, K. P. C. Vollhardt, *J. Am. Chem. Soc.* **1983**, *105*, 6710.
[38] V. Gandon, K. P. C. Vollhardt, unpublished results.
[39] Related solvent dienylations by alkynes in the presence of complexes of Ir (and possibly Rh) in boiling arenes have been reported, see: a) M. C. Comstock, J. R. Shapley, *Organometallics* **1997**, *16*, 4816; b) S. A. Gardner, P. S. Andrews, M. D. Rausch, *Inorg. Chem.* **1973**, *12*, 2396. For the analogous dienylation of a Cp ring in the reaction of $[CpRh(C_2H_4)_2]$ with 2-butyne, see: c) J. Müller, T. Akhnoukh, P. Escarpa Gaede, A. Guo, P. Moran, K. Qiao, *J. Organomet. Chem.* **1997**, *541*, 207. For a recent advance, see: d) K. Tanaka, Y. Otake, A. Wada, K. Noguchi, M. Hirano, *Org. Lett.* **2007**, *9*, 2203.
[40] a) H. Yamazaki, Y. Wakatsuki, *J. Organomet. Chem.* **1978**, *149*, 377; b) Y. Wakatsuki, H. Yamazaki, *J. Organomet. Chem.* **1978**, *149*, 385. c) For a recent Ru-catalyzed version of this process with alkenes, see: J. A. Varela, S. G. Rubín, C. González-Rodríguez, L. Castedo, C. Saá, *J. Am. Chem. Soc.* **2006**, *128*, 9262.
[41] For relevant reviews dealing with synthetic aspects of hydroarylations of alkynes, see: a) C. Nevado, A. M. Echavarren, *Synthesis* **2005**, 167; b) F. Kakiuchi, N. Chatani, *Top. Organomet. Chem.* **2004**, *11*, 45; c) F. Kakiuchi, N. Chatani, *Adv. Synth. Catal.* **2003**, *345*, 1077; d) M. Miura, M. Nomura, *Top. Curr. Chem.* **2002**, *219*, 211; e) V. Ritleng, C. Sirlin, M. Pfeffer, *Chem. Rev.* **2002**, *102*, 1731; f) C. Jia, T. Kitamura, Y. Fujiwara, *Acc. Chem. Res.* **2001**, *34*, 633; g) Y. Guari, S. Sabo-Etienne, B. Chaudret, *Eur. J. Inorg. Chem.* **1999**, 1047.
[42] a) P. B. Valkovich, J. L. Conger, F. A. Castiello, T. D. Brofie, W. P. Weber, *J. Am. Chem. Soc.* **1975**, *97*, 901; b) B. I. Rosen, W. P. Weber, *J. Org. Chem.* **1977**, *42*, 47.
[43] R. L. Hillard III, K. P. C. Vollhardt, *J. Am. Chem. Soc.* **1977**, *99*, 4058.
[44] This compound is mentioned in a review without experimental details: J. Sivaguru, A. Natarajan, L. S. Kaanumalle, J. Shailaja, S. Uppili, A. Joy, V. Ramamurthy, *Acc. Chem. Res.* **2003**, *36*, 509.
[45] For recent reviews, see: a) M. Beller, J. Seayad, A. Tillack, H. Jiao, *Angew. Chem. Int. Ed.* **2004**, *43*, 3368; b) F. Alonso, I. P. Beletskaya, M. Yus, *Chem. Rev.* **2004**, *104*, 3079; c) I. Nakamura, Y. Yamamoto, *Chem. Rev.* **2004**, *104*, 2127; d) F. Pohlki, S. Doye, *Chem. Soc. Rev.* **2003**, *32*, 104; e) T. E. Müller, M. Beller, *Chem. Rev.* **1998**, *98*, 675. For a recent summary of the importance of enamides, see: f) J. M. Lee, D.-S. Ahn, D. Y. Jung, J. Lee, Y. Do, S. K. Kim, S. Chang, *J. Am. Chem. Soc.* **2006**, *128*, 4058.
[46] For a recent assessment of the importance of this class of compounds, see: G. Reginato, F. Gaggini, A. Mordini, M. Valacchi, *Tetrahedron* **2005**, *61*, 12954.
[47] For the chemical shifts of (di)enamides, see, e.g.: a) A. Bayer, M. E. Maier, *Tetrahedron* **2004**, *60*, 6665; b) A. Fürstner, C. Brehm, V. Cancho-Grande, *Org. Lett.* **2001**, *3*, 3955.
[48] This compound is known: G. W. H. Cheeseman, R. A. Godwin, *J. Chem. Soc. C* **1971**, *18*, 2973, but was prepared directly from pyrazinedione (see Experimental Section).
[49] A combined search with Scifinder and Beilstein Crossfire retrieved only three references: a) Nissan Chemical Industries, Ltd., Japan, Jpn. Kokai Tokkyo Koho, JP 60084287, **1985**; b) K. Makino, G. Sakata, K. Morimoto, Y. Ochiai, *Heterocycles* **1985**, *23*, 1729; c) H. Suschitzky, B. J. Wakefield, R. A. Whittaker, *J. Chem. Soc. Perkin Trans. 1* **1975**, 401.
[50] T. R. Gadek, K. P. C. Vollhardt, *Angew. Chem. Int. Ed. Engl.* **1981**, *20*, 802.
[51] For reviews of bridgehead alkenes, see: a) W. E. Billups, M. M. Haley, G. Lee, *Chem. Rev.* **1989**, *89*, 1147; b) P. M. Warner, *Chem. Rev.* **1989**, *89*, 1067; c) R. Keese, *Angew. Chem. Int. Ed. Engl.* **1975**, *14*, 528.
[52] a) B.-L. Deng, T. L. Hartman, R. W. Buckheit, Jr., C. Pannecouque, E. De Clercq, P. E. Fanwick, M. Cushman, *J. Med. Chem.* **2005**, *48*, 6140; b) T. Harada, K. Iwazaki, T. Otani, A. Oku, *J. Org. Chem.* **1998**, *63*, 9007.
[53] E. R. Koft, A. B. Smith III, *J. Org. Chem.* **1984**, *49*, 832.
[54] Y. Yang, T. M. Swager, *Macromolecules* **2006**, *39*, 2013.
[55] F. F. Knapp, P. C. Srivastava, A. P. Callahan, E. B. Cunningham, G. W. Kabalka, K. A. R. Sastry, *J. Med. Chem.* **1984**, *27*, 57.
[56] P. M. Jackson, C. J. Moody, P. Shah, *J. Chem. Soc. Perkin Trans. 1* **1990**, 2909.
[57] D. A. De Bie, A. Ostrowica, G. Geurtsen, H. C. Van Plas, *Tetrahedron* **1988**, *44*, 2977.
[58] G. L. Edwards, C. A. Muldoon, D. J. Sinclair, *Tetrahedron* **1996**, *52*, 7779.
[59] [Bruker SMART Vol. 5.052, Bruker AXS Inc, Madison, WI, **1998**.
[60] Bruker SAINT Vol. 5.12, Bruker AXS Inc, Madison, WI, **1998**.
[61] SADABS Vol. 2.01, G. M. Sheldrick, University of Göttingen, **1996**.
[62] XPREP Vol. 5, Bruker AXS Inc, Madison, WI, **1998**.
[63] SIR-92, A. Altomare, M. Cascarano, C. Giacovazzo, A. Guagliardi, *J. Appl. Crystallogr.* **1993**, *26*, 343.
[64] SHELXL-97, G. M. Sheldrick, University of Göttingen, **1997**.

Received: December 19, 2006
Revised: March 28, 2007
Published online: June 20, 2007

 © 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim