$$\Delta H_{isom} = \frac{\Delta H_{exp}}{m_c} M_r \quad (9)$$

$\Delta H_{exp}$: experimentally determined heat of reaction (mcal)

$m_c$: amount of *cis*-azoalkane (mg)

reveal any other products other than *trans*-RNNR, RH, RR, and solvent dimers.[56] These were identified by comparing their retention times with those of authentic samples and/or by mass spectroscopy.

As *cis*-A-221 and *cis*-A-nad could be manipulated at room temperature and isomerized quantitatively to the trans isomers, all information was provided by weighing the starting material. For the other *cis*-azo compounds the procedure was more complex; the amounts of all products had to be obtained by two consecutive GC analyses.

The main product, the trans isomer, was determined by an isothermal GC analysis on capillary columns using *n*-hydrocarbons as internal standards. These had been added to the DSC pans prior to the isomerization. By making use of experimental GC factors $f$, we could determine the absolute amounts $m_1$ of the trans isomer by the usual procedure.[33] Each sample was analyzed 3–10 times.

$$m_1 = m_{St} \frac{A_{azo}}{A_{St}} f \quad (10)$$

$m_1$: yield of isomerized *trans*-azoalkanes (g)

$A$: area of the GC peak

$m_{St}$: amount of standard (g)

The minor products were determined by a temperature-programmed GC analysis using the formed trans isomer as internal standard. With the GC factors $f$ being available by an increment method[33] (the ones for the *trans*-azoalkanes could be readily reproduced within 2%) it was possible to calculate the relative yields of RH and RR based on *trans*-RNNR (set to 100%). By additionally taking into consideration the stoichiometric equations and the formula weights, the relative ratios of *cis*-azo compound going to *trans*-RNNR, RH, and RR ($m_1^{azo}$, $m_{RH}^{azo}$, $m_{RR}^{azo}$) were calculated.

$$RNNR \xrightarrow{SH} 2RH + N_2 + S\text{–}S \quad (SH: \text{solvent})$$

$$RNNR \rightarrow R\text{–}R + N_2$$

$$m_{RH}^{azo} = \frac{A_{RH}}{A_{azo}} f \frac{M_r(azo)}{2M_r(RH)} \quad (11)$$

$$m_{RR}^{azo} = \frac{A_{RR}}{A_{azo}} f \frac{M_r(azo)}{M_r(RR)} \quad (12)$$

**Acknowledgment.** We thank the Fonds der Chemischen Industrie for financial support of this work, Dr. H.-D. Beckhaus for stimulating discussions, and Sylvia Kettler for technical assistance.

# Regiospecific Synthesis of 2-Methoxy-3-methyl-1,4-benzoquinones from Maleoylcobalt Complexes and Alkynes via Lewis Acid Catalysis. A Highly Convergent Route to Isoquinoline Quinones

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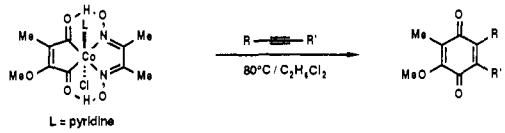
*Received October 22, 1986*

**Abstract:** Under the influence of Lewis acids such as $SnCl_4$, $BF_3{\cdot}Et_2O$, and $AgBF_4$ a maleoylcobalt complex derived from 3-methoxy-4-methylcyclobutenedione reacted with three diverse classes of alkynes (terminal, electron deficient, and propargylsilanes) at room temperature to afford moderate to good isolated yields (40–79%) of substituted benzoquinones with good to excellent regioselectivity in each case (7:1 up to >20:1). Since earlier studies had established excellent regioselectivity for the reaction of electron rich alkynyl ethers with the same maleoylcobalt complex under conditions of *thermal* activation, a wide variety of highly functionalized benzoquinones with substituents commonly encountered in bioactive natural products (2-methoxy-3-methyl-1,4-benzoquinone base) are available by this mild sequence of reactions.

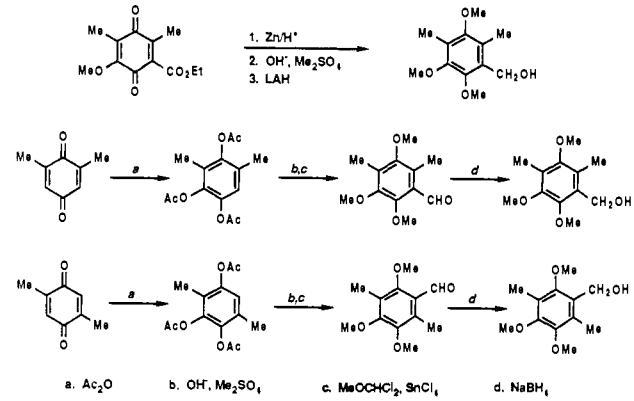
We have previously described the reaction of maleoylcobalt complex **1** with unsymmetrical acetylenes to produce benzoquinones of general structure **2** (eq 1).[2] Under our standard conditions for quinone formation from species such as **1**, reaction




1 2 (1)

at 80 °C in dichloroethane gave high yields of quinones from a wide range of alkynes. The regioselectivity of this thermal reaction varied, with terminal and electron-withdrawing alkynes showing moderate selectivity (ca. 4:1 with **2**, R = alkyl, R′ = H and **2**, R = alkyl, R′ = EWG predominating) while electron rich alkynes

Scheme I




reacted with excellent regioselectivity (13.5:1 with **2**, R = OR, R′ = alkyl predominating). Since quinones of general structure **2** are found in many important antibiotics and anticancer compounds,[3] our ability to predictably control, with good regiose-

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(2) Liebeskind, L. S.; Leeds, J. P.; Baysdon, S. L.; Iyer, S. *J. Am. Chem. Soc.* **1984**, *106*, 6451.

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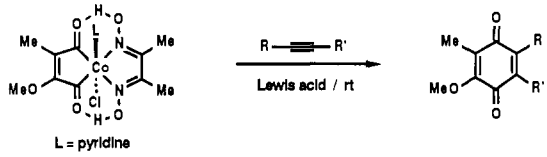
**Table I.** Lewis Acid Influence on Quinone Regiochemistry




1 2

| alkyne type | R | R′ | conditions[a] | Lewis acid | ratio[b] | yield[c] |
|---|---|---|---|---|---|---|
| terminal | *n*-Bu | H | normal | $SnCl_4$ | 10:1 | 65 |
| | *n*-Bu | H | normal | $BF_3{\cdot}Et_2O$ | 9:1 | 50 |
| | *n*-Bu | H | normal | $AgBF_4$ | 11:1 | 67 |
| | *n*-Bu | H | inv addn | $SnCl_4$ | 7:1 | 69 |
| | *n*-Bu | H | inv addn | $BF_3{\cdot}Et_2O$ | 7:1 | 35 |
| electron deficient | Me | $CO_2Et$ | normal | $SnCl_4$ | 20:1 | 62 |
| | Me | $CO_2Et$ | normal | $BF_3{\cdot}Et_2O$ | 12:1 | 62 |
| | Me | $CO_2Et$ | normal | $AgBF_4$ | 24:1 | 62 |
| | Me | $CO_2Et$ | inv addn | $SnCl_4$ | 12:1 | 62 |
| | Me | $CO_2Et$ | inv addn | $BF_3{\cdot}Et_2O$ | 10:1 | 28 |
| | Et | COMe | normal | $SnCl_4$ | 20:1 | 60 |
| propargylsilane | $CH_2SiMe_3$ | Me | normal | $SnCl_4$ | 16:1 | 40 |
| | $CH_2SiMe_2$-*t*-Bu | Me | normal | $SnCl_4$ | 20:1 | 51 |
| | $CH_2SiMe_2$-*t*-Bu | H | normal | $SnCl_4$ | 12:1 | 51 |
| control reactions | *n*-Bu | H | rt control | none | 4:1 | 10 |
| | Me | $CO_2Et$ | rt control | none | 8:1 | 10 |
| | OEt | Me | rt control | none | 14:1 | 52 |
| | (*Z*)-MeOCH=CH | H | rt control | none | 20:1 | 50 |
| | $CH_2SiMe_2$-*t*-Bu | Me | rt control | none | 18:1 | 08 |
| | $CH_2SiMe_2$-*t*-Bu | H | rt control | none | 9:1 | 16 |
| | $CH_2SiMe_2$-*t*-Bu | Me | thermal, 80 °C | none | 8:1 | 60 |
| | $CH_2SiMe_2$-*t*-Bu | H | thermal, 80 °C | none | 6:1 | 63 |

[a] Unless indicated otherwise all reactions were conducted at room temperature for 12–48 h; inverse addition refers to pretreatment of a dichloroethane solution of **1** with the Lewis acid for 1 h at room temperature prior to adding the alkyne; normal addition was addition of the Lewis acid last. [b] The major regioisomer formed is that shown in the structure used in the table; regioisomer ratios were determined by integration of appropriate resonances in the high field $^1H$ NMR spectra of the purified quinones. [c] All yields were determined by isolation of pure products.

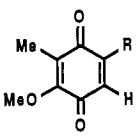
lectivity, the reaction of the three classes of alkynes mentioned above (terminal, electron rich, electron poor) according to eq 1, would provide us with a powerful synthetic entry to these target molecules. Our recent observation of the ability of $SnCl_4$ to catalyze the reaction of phthaloylcobalt complexes with alkynes to form naphthoquinones at room temperature[4] prompted us to investigate the influence of Lewis acids on the regiochemistry of the benzoquinone synthesis shown in eq 1. It was thought that improved regiochemistry for both the terminal and electron deficient alkynes could result from either the benefit of running the reaction at room temperature rather than 80 °C or from the possibility of selective coordination of the Lewis acid to one of the reactants or from both effects.

## Results

Although we tried to catalyze the quinone formation with a variety of Lewis acids, only $SnCl_4$, $BF_3{\cdot}Et_2O$, and $AgBF_4$ gave reasonable yields of quinones at room temperature. Table I lists our results of quinone formation from **1** with three classes of alkynes (terminal, electron deficient, and propargylsilanes) in the presence of Lewis acids at room temperature and demonstrates the dramatic increase in regioselectivity achievable under these conditions. Electron rich alkynes were not stable to the Lewis acidic reaction conditions, and improved regioselectivity under Lewis acid catalysis could not be probed for these substrates; however, under strictly thermal conditions (the 80 °C runs were described previously,[2] and the room temperature reactions in the absence of Lewis acid are shown in Table I) the electron rich alkynes EtOC≡CMe and (*Z*)-MeOCH=CHC≡CH reacted with very high regioselectivity. For reactions attempted with terminal alkynes that lacked functional group perturbations on the triple bond, the ratio of regioisomeric quinones **3**:**4** consistently ranged from 7:1 to 11:1 with the numbers on the lower end of the range being more typical. At room temperature, in the absence of Lewis acids, quinone formation was very slow (10% in 48 h), and the isolated quinone showed diminished regioselection (4:1 ratio) compared to the Lewis acid runs. Assignment of

(3) Saframycins: Arai, T.; Takashi, K.; Kubo, A. *J. Antibiot.* **1977**, *30*, 1015. Arai, T.; Takahashi, K.; Kubo, A.; Nakahara, S.; Sato, S.; Aiba, K.; Tamura, C. *Tetrahedron Lett.* **1979**, 2355. Arai, T.; Takahashi, K.; Nakahara, S.; Kubo, A. *Experintia* **1980**, *36*, 1025. Arai, T.; Takahashi, K.; Ishiguro, K.; Yazawa, K. *J. Antibiot.* **1980**, *33*, 951. Ishiguro, K.; Takahashi, K.; Yazawa, K.; Sakiyama, S.; Arai, T. *J. Biol. Chem.* **1981**, *256*, 2162. Ishiguro, K.; Sakayama, S.; Takahari, K.; Arai, T. *Biochem.* **1978**, *17*, 2545. Yazawa, K.; Asaoka, T.; Takahashi, K.; Mikami, Y.; Arai, T. *J. Antibiot.* **1982**, *35*, 915. Fukuyama, T.; Sachleben, R. A. *J. Am. Chem. Soc.* **1982**, *104*, 4957. Kurihara, H.; Mishima, H. *Tetrahedron Lett.* **1982**, *23*, 3639. Naphthyridinomycin: Sygusch, J.; Brisse, F.; Hanessiam, S.; Kluepfel, D. *Tetrahedron Lett.* **1974**, 4021, errata, **1975**, no. 3. Kleupfel, D.; Baker, H. A.; Piattoni, G.; Sehgal, S. N.; Sidorowicz, A.; Singh, K.; Vezina, C. *J. Antibiot.* **1975**, *28*, 497. Parker, K. A.; Cohen, I. D.; Babine, R. E. *Tetrahedron Lett.* **1984**, 3543. Danishefsky, S.; O'Neill, B. T.; Taniyama, E.; Vaughan, K. *Tetrahedron Lett.* **1984**, 4199. Danishefsky, S.; O'Neill, B. T.; Springer, J. P. *Tetrahedron Lett.* **1984**, 4203. Evans, D. A.; Biller, S. A.; *Tetrahedron Lett.* **1985**, 1907, 1911. Fukuyama, T.; Frank, R. K.; Laird, A. A. *Tetrahedron Lett.* **1985** 2955. Renieramycins: Frincke, J. M.; Faulkner, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 265, correction: 5004. Mitomycins: Hata, T.; Sano, Y.; Sugawara, R.; Matsumae, A.; Kanamori, K.; Shima, T.; Hoshi, T. *J. Antibiot.* **1956**, *9*, 141, 146. Wakaki, S.; Marumo, H.; Tomioka, K.; Simizu, G.; Kato, E.; Kamada, H.; Kudo, S.; Fujimoto, Y. *Antibiot. Chemother.* **1958**, *8*, 228. Lefemine, D. V.; Dann, M.; Barbatschi, F.; Hausmann, W. K.; Zbinovsky, V.; Monnikendam, P.; Adam, J.; Bohonos, N.; *J. Am. Chem. Soc.* **1962**, *84*, 3184. Webb, J. S.; Cosulich, D. B.; Mowat, J. H.; Patrick, J. B.; Broshcard, R. W.; Meyer, W. E.; Williams, R. P.; Wolf, C. F.; Fulmor, W.; Pidacks, C.; Lancaster, J. E. *J. Am. Chem. Soc.* **1962**, *84*, 3185, 3187. Tulinsky, A.; van den Hende, J. H. *J. Am. Chem. Soc.* **1967**, *89*, 2905. Shirahata, K.; Hirayama, N. *J. Am. Chem. Soc.* **1983**, *105*, 7199. J. Nakatsubo, F.; Kocuzza, A. J.; Kelley, D. E.; Kishi, Y. *J. Am. Chem. Soc.* **1977**, *99*, 4835. Nakatsubo, F.; Fukuyama, T.; Cocuzza, A. J.; Kishi, Y. *J. Am. Chem. Soc.* **1977**, *99*, 8115. Luly, J. R.; Rapoport, H. *J. Org. Chem.* **1982**, *47*, 2404 and references therein. Luly, J. R.; Rapoport, H. *J. Am. Chem. Soc.* **1983**, *105*, 2859. Mimosamycin: Mishima, H.; Fukumi, H.; Kurihara, H. *Heterocycles* **1977**, *6*, 1652; Fukumi, H.; Kurihara, H.; Mishima, H. *Chem. Pharm. Bull.* **1978**, *26*, 2175. Mimocin: Kubo, A.; Nakahara, S.; Iwata, R.; Takahashi, K.; Arai, T. *Tetrahedron Lett.* **1980**, *21*, 3207. Renierone: McIntyre, D. E.; Faulkner, D. J.; Van Engen, D.; Clardy, J. *Tetrahedron Lett.* **1979**, 4166. Danishefsky, S.; Berman, E.; Cvetovich, R.; Minamikawa, J. *Tetrahedron Lett.* **1980**, 4819.

(4) Liebeskind, L. S.; Baysdon, S. L.; Goedken, V. L.; Chidambaram, R. *Organometallics* **1986**, *5*, 1086.



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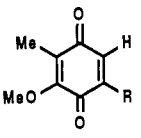

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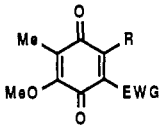
structures to the major and minor regioisomers from the terminal alkynes was performed by comparing differences in the high field $^1$H NMR spectra for both isomeric compounds with the same data for the known quinones **3** and **4**, R = Me as previously described.[2] For these two compounds, the vinyl hydrogen of **3** absorbed upfield of the corresponding resonance in **4**. In every case studied to date, the major regioisomer formed when terminal alkynes were reacted with **1** showed the olefinic absorbance upfield of the corresponding resonance for the minor isomer. This consistency in the high field NMR data was taken as proof that all major isomers formed when terminal alkynes were reacted with **1** had general structure **3**.

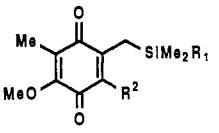
Alkynes with a directly attached electron-withdrawing group showed a dramatic improvement in regioselectivity when run at room temperature in the presence of Lewis acids. Effectively, only regioisomer **5** was formed (≥20:1 ratio) when $SnCl_4$ or $AgBF_4$



5

was used, in contrast to the 4:1 ratios previously observed under thermal activation.[2] A control reaction in the absence of Lewis acid provided significantly diminished yield and regioselection. An interesting effect of the order of addition of reactants on the regioselectivity of the quinone formation was noted for alkynes bearing an electron-withdrawing group. When the Lewis acid was added last to the reaction mixture, the selectivity was higher than when cobalt complex **1** was treated with the Lewis acid prior to addition of the alkyne. A more modest effect of order of addition was similarly observed for the terminal alkynes. Proof of the structure of the quinones derived from alkynes with electron-withdrawing groups was obtained by correlation of the quinones produced from reaction of ethyl tetrolate and **1** with materials produced by an unambiguous synthetic route (Scheme I).

Perhaps the most telling results, from the perspective of developing a consistent rationalization for the regioselectivity, were those for the propargylsilanes. Although the isolated yields of the derived quinones were lowered by their sensitivity to both heat and Lewis acid, significant regioselection (12:1–20:1) in favor of isomer **6** was observed for this class of alkyne. Again, a control



6

reaction at room temperature in the absence of Lewis acid demonstrated the catalytic influence of the Lewis acid on the rate of quinone formation, although the ability of the Lewis acid to improve the regioselection for the propargylsilanes was not great. The original observation of high regioselectivity using alkynyl ethers under thermal activation conditions and the current results with electron deficient alkynes under Lewis acid catalysis suggested that an electronic effect might be responsible for directing the regiochemical outcome of the reaction. The significant selectivity obtained from propargylsilanes further supported this suspicion.

We proved the structure of the major regioisomer of the propargylsilane reactions, **6**, by correlating a reduced derivative of **6**, $R^1 = R^2 =$ Me, obtained from the cobalt complex reaction with the same material synthesized by an unambiguous route (Scheme II).

**Scheme II**

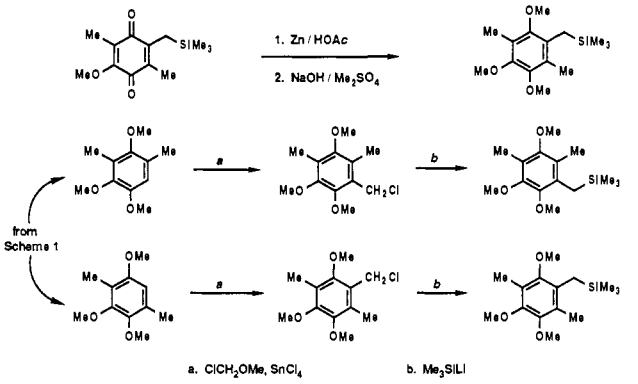
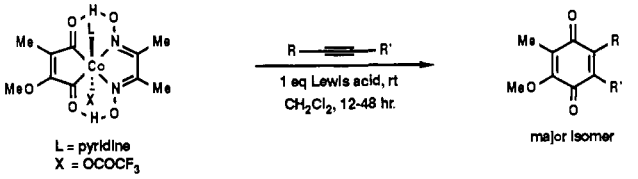



**Table II.** Reactions of the Trifluoroacetate-Substituted Cobalt Complex **7**

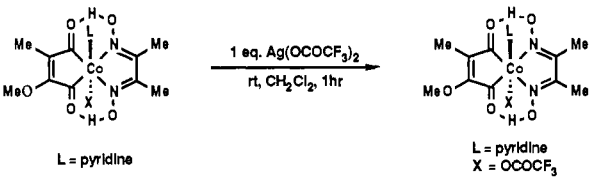



L = pyridine
X = OCOCF$_3$

7

| R | R′ | Lewis acid | ratio | yield |
|---|---|---|---|---|
| *n*-Bu | H | $SnCl_4$ | 10:1 | 71 |
| *n*-Bu | H | $Zn(SO_3CF_3)_2$ | 12:1 | 74 |
| Me | $CO_2Et$ | $SnCl_4$ | 18:1 | 76 |
| Me | $CO_2Et$ | $Zn(SO_3CF_3)_2$ | 21:1 | 79 |
| *t*-$BuMe_2SiCH_2$ | Me | $SnCl_4$ | 20:1 | 55 |
| *t*-$BuMe_2SiCH_2$ | H | $SnCl_4$ | 10:1 | 57 |

In an effort to improve the modest yields associated with formation of some of the quinones, we turned our attention to modifying the nature of the maleoylcobalt complex. In related work on the reactivity of phthaloylcobalt complexes derived from the dimethylglyoxime ligand system[4] we had noticed that quinone formation could be significantly inhibited by the addition of an equivalent of chloride or pyridine to the reaction mixture. This suggested that extraneous ligands in the reaction mixture could successfully compete with the alkyne for the coordinatively unsaturated cationic cobalt species generated when complex **1** ionized its chloride ligand. Since the Lewis acid catalyzed benzoquinone synthesis was performed in the presence of $SnCl_4$ to facilitate chloride ligand ionization, we were concerned with the possibility of chloride buildup during the reaction by degradation of the Lewis acid.[5] To probe this aspect of the chemistry we prepared a maleoylcobalt complex with a trifluoroacetate ligand in place of the chloride (eq 2, structure **7**, 78% yield) and assayed its ability




(2)

L = pyridine

1

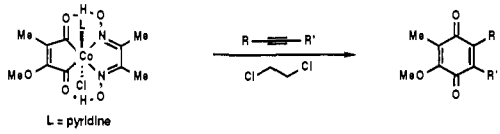
L = pyridine
X = OCOCF$_3$

7

to deliver benzoquinones regiospecifically under Lewis acid activation. These results are shown in Table II. Significantly, the trifluoroacetate based system provided improved yields in all cases investigated, and the few completely halide free attempts using

(5) For example, we have commonly observed reduction of the quinones to hydroquinones under the conditions of our chemistry. Reduction of quinones under the aprotic conditions used could generate anionic species capable of reacting with $SnCl_4$ to form tin phenoxides and free chloride. Accordingly, it often is advantageous to incorporate a dilute acid workup of the reaction mixtures followed by $FeCl_3$ oxidation (or $Ag_2O$) in order to obtain optimum yields of products.

**Table III.** Quinone Synthesis from Amino-Protected Alkynes[a]




1

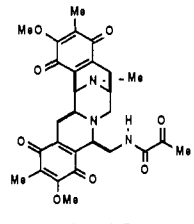
| R | R′ | conditions | ratio | yield |
|---|---|---|---|---|
| $(CH_2)_2NPhth$ | H | $SnCl_4$[c] | 7:1 | 42 |
| $(CH_2)_2NPhth$ | H | 80 °C | 3:1 | 77 |
| $(CH_2)_2NCbz(Bn)$ | H | $SnCl_4$[c] | *b* | 35 |
| $(CH_2)_2NCbz(Bn)$ | H | 80 °C | *b* | 76 |
| $(CH_2)_2NCOCF_3(Bn)$ | H | $SnCl_4$[c] | *b* | 33 |
| $(CH_2)_2NCOCF_3(Bn)$ | H | 80 °C | *b* | 72 |
| $(CH_2)_2NSO_2CF_3(Bn)$ | H | $SnCl_4$[c] | *b* | 65 |
| $(CH_2)_2NCOCO_2Et(Bn)$ | H | $SnCl_4$[c] | *b* | 30 |
| $(CH_2)_2NCOCO_2Et(Bn)$ | H | 80 °C | *b* | 76 |

[a] Isolated yields of pure product. [b] Ratios could not be obtained because of complex $^1H$ NMR spectra caused by amide rotamers. Regiochemical ratios similar to those obtained in the first two entries are presumed. [c] Room temperature.

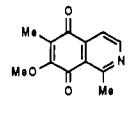
$Zn(SO_3CF_3)_2$ as the Lewis acid were superior to the $SnCl_4$ runs. These results, though small in number, suggest that quinone synthesis using the maleoylcobalt complexes can be optimized by proper choice of univalent ligand and Lewis acid.

Having established the generality and regioselectivity of the maleoylcobalt based quinone synthesis, we probed the use of this method in the synthesis of a simple isoquinoline quinone intended as a model substrate for our projected total synthesis of saframycin B and related antitumor antibiotics.[3] We first had to prove that we could perform the quinone synthesis in the presence of a nitrogen functional group on the alkyne, and after confirming our suspicion that a free amine would interfere with the quinone synthesis under Lewis acid conditions, we surveyed quinone formation from the variety of amino protected alkynes shown in Table III. It is apparent from the results that the quinone yields of the Lewis acid–room temperature runs are sensitive to the coordinating ability of the amine protecting group, with the better ligands inhibiting the formation of quinone at room temperature. This inhibition is easily overcome by running the reaction at 80 °C, but the regioselectivity must necessarily suffer at the higher temperature. Consistent with the hypothesis of ligand inhibition of quinone formation, the least coordinating nitrogen protecting group, the trifluorosulfonamide, gave the highest yield of quinone from the aminoalkynes tested in the room temperature reactions.

We chose as our model for the isoquinoline quinone derived portions of the saframycin B antitumor antibiotics, the known compound **8**.[6] In addition to providing us with information necessary for our isoquinoline quinone total synthesis project, a successful synthesis of quinone **8** would further verify our assignment of regiochemistry. Although there are numerous synthetic options for synthesizing **8** from an aminoalkyne and a maleoylcobalt complex, the route shown in Scheme III was chosen to highlight the functional group compatibility of our cobalt based quinone synthesis. By incorporating both the required amine and the electron-withdrawing acetyl group in alkyne **9** we can expect significantly improved regiochemistry over that seen for the terminal alkynes. Although the results shown above in Table III suggested that protection of the amine nitrogen as a trifluorosulfonamide would provide the highest yield of quinone under the room temperature–Lewis acid reactions conditions, for the present purposes we chose to accept lower yields and protect the nitrogen as a urethane (carbobenzyloxy:Cbz) to simplify deprotection. However, the trifluorosulfonamide is an important protecting group for future applications.

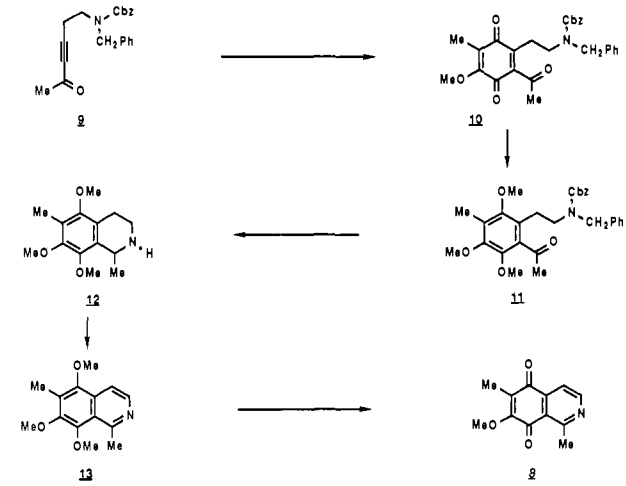


Saframycin B



8

**Scheme III**




The synthesis of isoquinoline quinone **8** commenced with commercially available 3-butyn-1-ol which was tosylated following a known procedure.[7] Reaction with benzylamine in a sealed tube at 110 °C gave *N*-benzyl-1-butynylamine in 65% yield which was converted to the ketoalkyne **9** in 50% overall yield by lithiation (*n*-BuLi at −78 °C), condensation with MeCHO, protection of the amine (CbzCl/NaOH), and finally oxidation with pyridinium dichromate. Consistent with the results listed in Table III, ketoalkyne **9** reacted with maleoylcobalt complex **1** at room temperature in the presence of $SnCl_4$ to give a modest yield of quinone **10** (35% isolated with 27% recovered alkyne) with very high regioselectivity (20:1). The analysis of regiochemistry was most easily performed by high field $^1H$ NMR on the corresponding hydroquinones. The yield of highly functionalized quinone according to Scheme III was substantially improved by conducting the reaction at 80 °C in the absence of Lewis acid (84%); however, the ratio of regioisomers fell to 3:1. For the purposes of this synthesis, we turned to reaction of ketoalkyne **9** with the trifluoroacetate substituted maleoylcobalt complex **7** at room temperature in the presence of $SnCl_4$ and obtained quinone **10** in 43% isolated yield. Reduction (Zn/HOAc) followed by methylation ($OH^-/Me_2SO_4$) gave the trimethoxyaromatic **11** in 75% yield which was reductively cyclized ($H_2$/Pd on C) to the tetrahydroisoquinoline **12** (68% yield). Conversion to the isoquinoline **13** was achieved by Pd-catalyzed dehydrogenation (Pd on C at 160 °C) in 60% yield, and then $Ag_2O$ oxidation delivered the desired isoquinoline quinone **8** in 50% isolated yield. The compound showed identical melting point and infrared and $^1H$ NMR spectra with the corresponding data in the literature[8] providing one more confirmation of our regiochemical assignment.

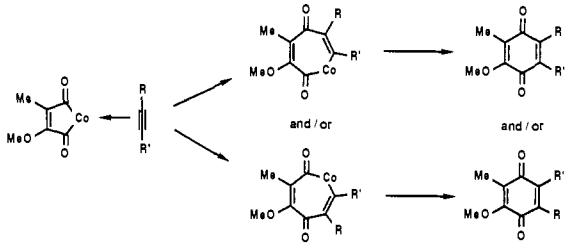
## Discussion

In order to use the results described in this manuscript in a meaningful way in synthesis, we needed to develop a rationalization of the regiochemical results observed for a variety of different alkyne structural types. In the absence of mechanistic studies, it is difficult to make firm statements about the mechanism of quinone formation from maleoylcobalt complexes and alkynes. However, for the purpose of this discussion, we point out that the quinone synthesis *might* proceed by the traditional alkyne insertion–reductive elimination pathway shown in Scheme IV.

(6) See reneiramycins under ref 3.

(7) Eglinton, G.; Whiting, M. C. *J. Chem. Soc.* **1950**, 3650.
(8) Liebeskind, L. S.; Iyer, S.; Jewell, C. F., Jr. *J. Org. Chem.* **1986**, *51*, 3065.

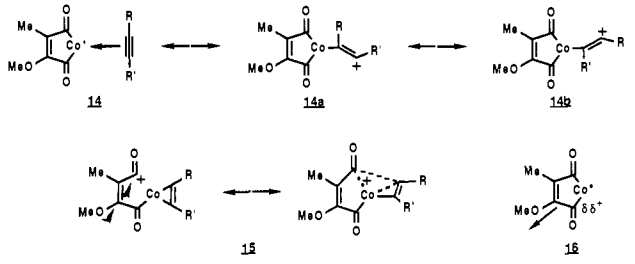
**Scheme IV**




Regioselectivity can be anticipated from the sequence shown in Scheme III only if two criteria are met. First, the alkyne must react with some preference at one or the other of the cobalt acyl bonds, and, second, the alkyne must preferentially orient its substituents relative to the cobalt–acyl carbon bond. Only when both of these conditions are met can regioselective quinone formation be expected according to Scheme IV.

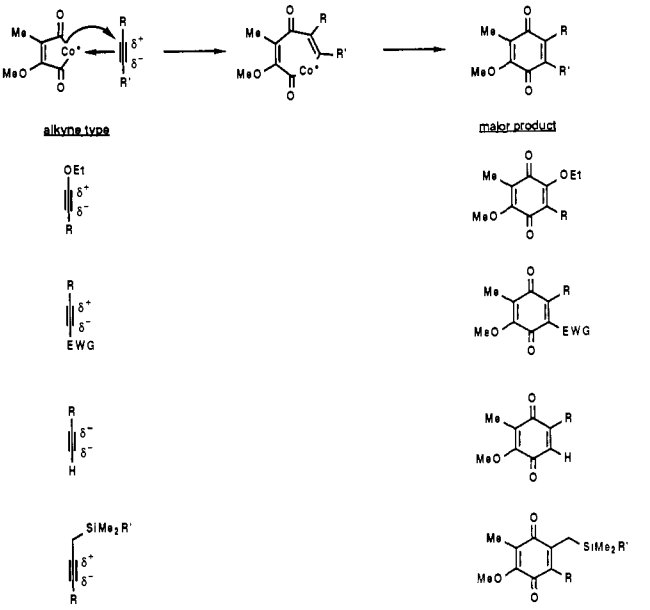
From earlier work on *phthaloyl*cobalt complexes analogous to structure **1**, we had determined that, *in the presence of Lewis acids*, chloride ligand ionization was the predominant means of achieving the coordinative unsaturation necessary to allow alkyne coordination to the cobalt prior to quinone formation.[4] The ability of the Lewis acid to facilitate ionization of the chloride ligand is definitely responsible for the increased rate of quinone formation which allows the reaction to be conducted at room temperature. However, the regiochemical outcome of the control reactions conducted in the absence of Lewis acids shown in Table I indicates that the lower reaction temperature is only partly responsible for the improved regioselectivity seen for the terminal and electron deficient alkynes. The modest improvement for the terminal alkynes (including the terminal propargylsilane) might be due to selective, kinetic coordination of the Lewis acid to one of the acyl oxygens of the maleoylcobalt complex; however, coordination of the Lewis acid to the maleoylcobalt complex under equilibrium conditions, suggested by the inverse addition results described in Table I, does not appear to contribute to improved regioselectivity. Lewis acid coordination to the electron deficient alkynes probably functions to improve selectivity as rationalized by the polarization argument advanced below.

The observation of catalysis by chloride ligand ionization restricts us to consider the mechanistic options available to cationic intermediate **14**. What effect does coordination to a cationic metal complex have on the reactivity of an alkyne? It is most reasonable to anticipate that alkynes coordinated to a cationic maleoylcobalt complex would show increased electrophilic behavior, as represented by resonance forms **14a** and **14b**. The migratory insertion




of one of the acyl groups to the coordinated alkyne can be viewed in analogy to a 1,n-shift of an organic group to an electron deficient center, with the acyl group that can best participate in stabilizing positive charge at the transition state showing the greatest migratory aptitude. Then, if that acyl group migrates preferentially to the alkyne carbon that can best support positive charge, we can meet the two criteria necessary for regioselectivity according to the insertion–reductive elimination pathway of Scheme IV. The methoxy substituent can function by resonance to delocalize partial positive charge buildup when the carbonyl group most distant from it migrates (**15**), while the methoxy substituent operates by induction to destabilize positive charge build up on the acyl carbon nearest to it (**16**). This scenario requires that the acyl carbon nearest the *methyl* group of **14** bond selectively to the most

**Chart I**




electrophilic carbon of the coordinated alkyne. All of our regiochemical results observed to date are consistent with this working model (Chart I).

The beneficial effect of Lewis acids on the regiochemistry of the reaction is to some extent due to the lower temperature at which the chemistry will operate when Lewis acids are included in the reaction mixture. However, the control reactions conducted at room temperature in the absence of Lewis acid demonstrate that Lewis acid coordination to the maleoylcobalt complex and to some of the alkynes must also contribute, in part, to the increased regioselectivity. We hesitate to overrationalize the mechanism of this latter Lewis acid effect and the previously mentioned diminished regioselectivity observed in some cases when the maleoylcobalt complex **1** is pretreated with Lewis acid, because there are multiple sites for Lewis acid coordination on the highly functionalized cobalt complex **1** as well as the problem of kinetic vs. thermodynamic coordination of the Lewis acids to the cobalt complexes. It seems clear, however, that coordination of the Lewis acid to the electron deficient alkynes should increase the polarization effects that form the basis of the rationalization of the observed regiochemistry, and it is of interest that the electron deficient alkynes show the most significant improvement of regiochemistry under Lewis acid catalysis.

A final word about the yields of these reactions is relevant. During all of our previous experiences with thermally induced quinone syntheses from cobalt complex **1** and related systems, isolated yields of quinones were routinely observed above 70% with yields of 80% or better not uncommon. Only after we tried numerous variations of the room temperature Lewis acid catalyzed system described in this manuscript could isolated yields above 70% be obtained. We have made a number of qualitative observations that suggest that *at room temperature* extraneous ligands (halide liberated from the Lewis acids, pyridine or dimethylglyoxime liberated after some of the maleoylcobalt complex begins to react, amide functional groups on the alkyne) effectively compete with the alkyne for coordination to the cationic coordinatively unsaturated maleoylcobalt species that is a presumed obligatory intermediate on the path to quinones. In fact, quinone formation at room temperature under Lewis acid catalysis seems to occur very rapidly in the initial stages of the reaction, and then significantly slows down as the reaction progresses. At the end of the reaction we can always observe unreacted alkyne and in many cases unreacted complex **1**. The inhibitory effects of internally generated ligands are easily overcome at higher temperature, since the reaction of **1** proceeds to give high yields of quinones at 80 °C; however, regioselectivity will be sacrificed at the higher reaction temperatures. As the results with the trifluoroacetate cobalt complex described above show, by the proper

combination of Lewis acid and ionizable group on the maleoylcobalt complex (replacing Cl with other univalent ligands) higher yields of quinones should be achievable without sacrificing good regioselectivity.

## Conclusions

The demonstration of effective regioselection in the synthesis of quinones from maleoylcobalt complex **1** and four diverse classes of alkynes (terminal, electron rich, electron deficient, and propargylsilanes) establishes the synthetic potential of this organotransition metal route to quinones of biological importance. Because of the generality and mildness of this transition-metal-based route to highly functionalized quinones, it should be possible to design syntheses of a wide variety of structurally diverse natural products by incorporation of appropriate functionality into the alkyne portion of the reactants. Finally, the functionalized quinone synthesis under the neutral carbon–carbon bond forming conditions described in this manuscript complements our recently discovered quinone synthesis from 3-methoxy-4-methylcyclobutenedione and unsaturated Grignard and lithium reagents.[8]

## Experimental Section

**General Methods.** Microanalyses were carried out by Galbraith Laboratories, Knoxville, TN and Atlantic Microlabs, Atlanta, GA. $^1H$ NMR spectra were recorded on a Nicolet 360-MHz spectrometer and Bruker 200- and 270-MHz spectrometers by using $CHCl_3$, benzene, acetone, or tetramethylsilane as internal standards; chemical shifts were expressed in parts per million by using the $\delta$ scale. Infrared spectra were recorded on a Perkin-Elmer Model 1420 spectrometer. High-resolution electron impact mass spectra were obtained on an A.E.I. MS-902 instrument.

All melting points were performed in open capillary tubes and are uncorrected. Analytical thin-layer chromatography was done with E. Merck silica gel 60F-254 glass-backed plates of 0.25-mm thickness which were visualized with appropriate combinations of UV light, phosphomolybdic acid stain, $KMnO_4$ (5% in water), and vanillin stain. Preparative scale separations were effected with "Flash grade" silica gel available from Aldrich Chemical Company. Dichloromethane was purified for use by distillation over $P_2O_5$ under a $N_2$ atmosphere, degassed by saturating with $N_2$, and stored over activated alumina in an amber colored bottle. Benzene, tetrahydrofuran, 1,2-dimethoxyethane, and ether were freshly distilled from sodium and benzophenone. All other solvents were reagent grade quality and used as received. Some alkynes were obtained from Farchan Chemical Company and Aldrich Chemical Company. The silylated alkynes were obtained from Petrarch or synthesized by literature procedures described below. Unless otherwise noted all other reagents were used as received.

**Syntheses of Maleoylcobalt Complexes 1 and 7.** Maleoylcobalt complexes are prepared from substituted cyclobutenediones by reaction with $ClCo(PPh_3)_3$ followed by ligand manipulation.[2] Substituted cyclobutenediones such as 3-methoxy-4-methylcyclobutenedione have been prepared by a number of different procedures.[9] However, the most convenient preparation is from squaric acid (Chickos procedure) which is now available from Aldrich Chemical Co. in *kilogram* quantities. Its price and availability seem to be related to demand, so it can be anticipated that an appropriate demand for squaric acid will increase the supply of this material at a reasonable price. There is no thorough experimental procedure for the preparation of 3-methoxy-4-methylcyclobutenedione described in the literature, so we provide one here.

Technical grade squaric acid (57 g, 0.5 mol) was dissolved in 1 L of 1:1 benzene/EtOH in a round-bottomed flask fitted with a Dean-Stark trap, and the solution was refluxed for 48 h with removal of water. The Dean-Stark trap was removed, most of the solvent was removed by distillation, and then the remaining solvent was taken off on a rotary evaporator. The residual liquid was purified by distillation by using a Kugelrohr oven (105–110 °C at 0.1 mmHg) to provide 72.2 g (85%) of diethyl squarate (Schmidt, A. H.; Reid, W. *Synthesis* **1978**, *12*, 869). Care should be taken in the handling of diethyl squarate, since it appears to be a potent vesicant and evidently can cause contact dermatitis in sensitive individuals.

Next, diethyl squarate (68 g, 0.4 mol) was added to a flame-dried, three-necked, 1-L, round-bottomed flask equipped with a mechanical stirrer. Dry ether (500 mL) was added, and the solution was cooled to −78 °C under a nitrogen atmosphere. MeMgBr (480 mmol, 171 mL of 2.8 M diethyl ether solution) was added *slowly* dropwise via an addition funnel to the cooled and vigorously stirred slurry of diethyl squarate. The addition was complete in 4 h, and stirring was continued for an additional 2 h at −78 °C at which time a minimum amount of saturated aqueous NaCl was added to quench the reaction. The ether layer was separated and combined with ether layers obtained by extracting the aqueous layer with diethyl ether, and then the organic phase was dried ($Na_2SO_4$), filtered, and concentrated to obtain a yellow oil. To the yellow oil was added a solution of concentrated HCl in acetone (5 mL in 95 mL), and the solution was stirred at room temperature for 48 h. Any insoluble solid present (squaric acid) was filtered off, and the acetone was evaporated on a rotary evaporator to leave a gum that was triturated with ether to give crude 3-hydroxy-4-methylcyclobutenedione. Recrystallization from acetone/pentane gave 20 g (44%) of pure product, mp 160 °C (Chickos, J. S. *J. Am. Chem. Soc.* **1970**, *92*, 5749).

3-Hydroxy-4-methylcyclobutenedione (11.2 g, 100 mmol) was refluxed for 48 h with 200 mL of 1:1 MeOH/benzene in a flask fitted with a Dean-Stark trap. Evaporation of the solvent followed by Kugelrohr distillation (bp 90–95 °C at 1 mmHg) gave 9.45 g (75%) of the desired product. IR and $^1H$ NMR were consistent with the values reported in the literature, mp 49–50 °C.

**Maleoylcobalt Complex 1.** A 100-mL flask equipped with a magnetic stirring bar was flame-dried under a flow of $N_2$, cooled, and charged with 2.54 g of 3-methoxy-4-methylcyclobutene-1,2-dione (20 mmol), 26.4 g of $ClCo(PPh_3)_3$ (30 mmol, 1.5 equiv; a simple preparation is described in Baysdon, S. L.; Liebeskind, L. S. *Organometallics* **1982**, *1*, 771), and 100 mL of dry $N_2$ saturated benzene. After sealing with a septum cap, the reaction mixture was placed in an oil bath maintained at 60 °C and stirred under $N_2$ for 12 h. The solvent was then removed on a rotary evaporator, the residue was dissolved in $CH_2Cl_2$ and filtered, and the filtrate was concentrated and finally diluted with absolute EtOH (100 mL). On standing a red-brown solid crystallized which was filtered and washed repeatedly with a 1:1 EtOH/water mixture until the filtrate was colorless. It was then washed again with 50 mL of absolute EtOH followed by 100 mL of hexanes. Recrystallization from $CH_2Cl_2$/ether gave 12.6 g (84%) of the chlorobis(triphenylphosphine)maleoylcobalt complex as a red-brown solid: mp 180–182 °C; IR ($CHCl_3$, $cm^{-1}$) 1665, 1610; $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$) 7.76–7.28 (m, 30 H), 3.29 (s, 3 H), 0.86 (s, 3 H). Anal. Calcd for $C_{42}H_{36}O_3P_2ClCo$: C, 67.70; H, 4.87; P, 8.31. Found: C, 67.67; H, 4.94; P, 8.16.

Next, a flame-dried, round-bottomed flask was cooled and charged with the bis(triphenylphosphine) complex (1 g, 1.34 mmol), dimethylglyoxime (0.171 g, 1.47 mmol, 1.1 equiv), and 15 mL of dry pyridine. After stirring at room temperature for 10 h under $N_2$, the reaction mixture was poured into a large excess of hexanes (200 mL). The resulting yellow solid was filtered and washed repeatedly with more hexanes. The solid residue was redissolved in $CH_2Cl_2$ and filtered to remove the excess dioxime. The resulting filtrate was then evaporated to give 0.513 g (92%) of the complex as an orange-yellow solid: mp 173 °C ($CH_2Cl_2$/ether); IR ($CHCl_3$, $cm^{-1}$) 1635, 1588, 1571; $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$) 14.07 (s, 1 H), 13.33 (s, 1 H), 8.23 (d, 2 H, $J$ = 7 Hz), 7.58 (t, 1 H, $J$ = 7 Hz), 7.10 (t, 2 H), 4.24 (s, 3 H), 2.27 (s, 6 H), 1.99 (s, 3 H). Anal. Calcd for $C_{15}H_{19}O_5N_3ClCo$: C, 43.33; H, 4.61; N, 10.11. Found: C, 43.27; H, 4.66; N, 10.27.

**Preparation of Maleoylcobalt Complex 7.** A 25-mL, flame-dried flask equipped with a magnetic stirring bar was charged with 1.0 g (2.41 mmol) of complex **1**, 0.586 g (2.65 mmol) of silver trifluoroacetate, and 15 mL of dry $CH_2Cl_2$ under $N_2$. A precipitate of AgCl was immediately formed, and the mixture was stirred under $N_2$ at room temperature for 2 h. The AgCl was removed by passing the reaction mixture through a Celite pad, and the filtrate was evaporated to afford a bright yellow solid which was recrystallized from $CH_2Cl_2$/hexanes to give 1.08 g (91%) of the trifluoroacetate complex **7**: mp 137–138 °C; IR ($CH_2Cl_2$, $cm^{-1}$) 3400–3100 (br), 2940, 1680, 1570, 1550, 1440, 1185, 1130, 1075, 920, 840; $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$) 13.821 (s, 1 H), 12.884 (s, 1 H), 8.242 (d, 2 H, $J$ = 6.22 Hz), 7.543 (t, 1 H, $J$ = 7.16 Hz), 7.066 (t, 2 H, $J$ = 6.98 Hz), 4.316 (s, 3 H), 2.259 (s, 6 H), 1.993 (s, 3 H). Anal. Calcd for $CoC_{17}H_{19}F_3N_3O_7$: C, 41.39; H, 3.88; N, 8.52. Found: C, 41.22; H, 3.87; N, 8.49.

**Alkyne Syntheses. Preparation of Propargylic Silanes.** The propargylic silanes were prepared according to the procedure of Zweifel and Rajagopalan.[10]

**Preparation of (Trimethylsilyl)-2-butyne.** 2-Butyne (1.56 mL, 1.08 g, 20 mmol) was lithiated by using 13.22 mL (1.34 g, 21 mmol, 1.7 M solution) of *t*-BuLi and 3.013 mL (2.32 g, 20 mmol) of TMEDA in 20

(9) Chickos, J. S. *J. Am. Chem. Soc.* **1970**, *92*, 5749. Bellus, D.; Fischer, H.; Greuter, H.; Martin, P. *Helv. Chim. Acta* **1978**, *61*, 1784. Brady, W. T.; Watts, R. D. **1980**, *45*, 3525. Dehmlow, E. V.; Schell, H. G. *Chem. Ber.* **1980**, *113*, 1. Bellus, D.; Martin, P.; Sauter, H.; Winkler, T. *Helv. Chim. Acta* **1980**, *63*, 1130.

(10) Zweifel, G.; Rajagopalan, S. *Synthesis* **1984**, *2*, 111.

mL of dry ether (−78 °C—room temperature) and then quenched (at −78 °C) with 3.06 mL (2.32 g, 24 mmol) of chlorotrimethylsilane. After workup and distillation 2.01 g (80%) of the product alkyne was obtained as a colorless oil with IR and $^1$H NMR consistent with values reported in the literature.[11]

**Preparation of (*tert*-Butyldimethylsilyl)-2-butyne.** 2-Butyne (1.56 mL, 1.08 g, 20 mmol) was lithiated by using 13.22 mL (1.344 g, 21 mmol, 1.7 M solution) of *t*-BuLi and 3.01 mL (2.32 g, 20 mmol) of TMEDA in 20 mL of dry ether (−78 °C—room temperature) and quenched (at −78 °C) with 3.62 g (24 mmol) of *tert*-butyldimethylsilyl chloride to give after workup and distillation (bp 110 °C/aspirator) 2.86 g (85%) of a colorless oil: IR (neat, KCl, cm$^{-1}$) 2950, 2800, 2770, 2220, 1245, 845; $^1$H NMR (360 MHz, $CDCl_3$, $\delta$) 1.75 (t, 3 H, $J$ = 2.8 Hz), 1.39 (q, 2 H, $J$ = 2.8 Hz), 0.088 (s, 9 H), 0.032 (s, 6 H).

**Preparation of 3-(*tert*-Butyldimethylsilyl)-1-propyne.** 1-(Trimethylsilyl)-1-propyne (4.43 mL, 3.36 g, 30 mmol) was lithiated by using 18.8 mL (2.04 g, 32 mmol) of 1.7 M *t*-BuLi in 30 mL of dry THF at −78 °C and quenched with 5.28 g (35 mmol) of *tert*-butyldimethylsilyl chloride dissolved in 10 mL of THF. The reaction mixture was stirred at room temperature for 12 h under $N_2$ and then quenched by adding saturated $NH_4Cl$. The reaction mixture was extracted with ether (3 × 50 mL), and the combined ether extracts were washed with 10% HCl and water, dried ($MgSO_4$), and concentrated on a rotary evaporator to obtain an oil. Distillation gave 3.44 g (50%) of an oil (bp 60–65 °C at 4–5 mmHg) which was subjected to selective desilylation according to the procedure of Zweifel et al.[10] **Selective Desilylation.** The above alkyne (2.8 g, 12 mmol) was dissolved in 20 mL of EtOH and an aqueous ethanolic solution of silver nitrate (2.6 g, 15 mmol, dissolved in 18 mL of EtOH/6 mL water) was added in four portions over a 45-min period while maintaining the temperature of the reaction mixture below 5 °C (ice bath). After having been stirred for 15 min at 0 °C the resultant white slurry was treated with a 9 M aqueous solution of KCN (8.3 mL, 75 mmol) while keeping the temperature below 5 °C during the addition. The solution was warmed to room temperature, water was added (20 mL), and the mixture was extracted with hexanes (3 × 30 mL). The combined organic extracts were washed with water and dried ($MgSO_4$), and the solvent was removed on a rotary evaporator. Distillation through a short-path column gave 1.0 g (53%) of a colorless oil (bp 65–70 °C at 30–40 mmHg): IR (neat, KCl, cm$^{-1}$) 3310, 2950, 2920, 2860, 2120, 1465, 1250, 1150, 840; $^1$H NMR (360 MHz, $CDCl_3$, $\delta$) 1.813 (t, 1 H, $J$ = 2.99 Hz), 1.490 (d, 2 H, $J$ = 2.92 Hz), 0.912 (s, 9 H), 0.080 (s, 6 H). Anal. Calcd for $C_9H_{18}Si$ ($M_r$ 154.324) C, 70.04; H, 11.76. Found: C, 70.14; H, 11.81.

**Preparation of ω-Aminoalkynes. Preparation of 4-Phthalimido-1-butyne.**[12] Phthalimide (2.94 g, 20 mmol) and 5.24 g (20 mmol) of triphenylphosphine were dissolved in 100 mL of dry THF in a 250-mL, round-bottomed flask. 3-Butyn-1-ol (1.52 mL, 1.4 g, 20 mmol) and 3.15 mL (3.48 g, 20 mmol) of diethylazodicarboxylate were added to the above solution, and the reaction mixture was stirred at room temperature under $N_2$ for 72 h. After removing the solvent on a rotary evaporator, the crude residue was passed through a column of silica gel (80–200 mesh, hexane/$CH_2Cl_2$, 1:1) to obtain 2.98 g (75%) of product as a colorless solid: mp 136–137 °C; IR ($CH_2Cl_2$, cm$^{-1}$) 3300, 3050, 2950, 2120, 1770, 1705, 1720, 1615, 1465, 1440, 1395, 1365, 1190, 1115, 1000, 870, 790, 650; $^1$H NMR (360 MHz, $CDCl_3$, $\delta$) 7.9–7.7 (m, 4 H), 3.89 (t, 2 H, $J$ = 7.04 Hz), 2.62 (dt, 2 H, $J$ = 7.1 Hz, 2.7 Hz), 1.97 (t, 1 H, $J$ = 2.7 Hz).

**Preparation of *N*-Benzyl-4-amino-1-butyne.** 4-Butynyl tosylate (6.24 g, 28 mmol) was added to a Kontes hard glass reaction vessel with 10 mL of dry DMF, 2.82 g (28 mmol) of triethylamine, and 2.99 g (28 mmol) of benzylamine. The reaction vessel was sealed and placed in an oil bath maintained at 110 °C. After having been stirred at that temperature for 10 h, the reaction vessel was cooled, and the reaction mixture was poured into 200 mL water and extracted with pentane (4 × 50 mL). The combined pentane extracts were washed with water, dried, and concentrated to obtain a pale yellow oil which was purified by flash chromatography over silica gel (230–400 mesh, hexane/ether, 2:3) to give 2.88 g (65%) of product as a colorless oil: IR (neat, KCl, cm$^{-1}$) 3300, 3040, 2920, 2840, 2120, 1600, 1500, 1450, 1120, 740, 700, 640; $^1$H NMR (90 MHz, $CDCl_3$, $\delta$) 7.33 (s, 5 H), 3.83 (s, 3 H), 2.8 (t, 2 H, $J$ = 6 Hz), 2.34 (dt, 2 H, $J$ = 6 Hz, 3 Hz), 1.9 (t, 1 H, $J$ = 3 Hz), 1.55 (br s, 1 H).

**Preparation of *N*-Benzyl-*N*-(carbobenzyloxy)-4-amino-1-butyne.** *N*-Benzyl-4-amino-1-butyne (0.96 g, 6.04 mmol) was taken in a 100-mL, round-bottomed flask. $CHCl_3$ (35 mL), 15 mL of benzene, and 30 mL of 1% aqueous NaOH were added. The vigorously stirred solution was cooled in an ice bath, and 864 μL (1.03 g, 6.04 mmol) of benzylchloroformate was added via syringe. The solution was allowed to warm to room temperature and then was stirred at ambient temperature for 5 h after which time the reaction mixture was poured into 100 mL of water, and the organic layer was separated. The aqueous layer was extracted with benzene (3 × 50 mL), and then the combined organic layers were washed thoroughly with water, 10% HCl, and water, dried ($MgSO_4$), and concentrated to obtain a gum. Purification by flash chromatography over silica gel (230–400) mesh, hexane/ether, 9:1) gave 1.56 g (88%) of the desired product: IR (neat, KCl, cm$^{-1}$) 3300, 3020, 2940, 2120, 1695, 1600, 1490, 1470, 1450, 1410, 1365, 1230, 1210, 1110, 1020, 960, 770, 730, 700; $^1$H NMR (360 MHz, $CDCl_3$, $\delta$) 7.3 (m, 10 H), 5.2 (2 s, 2 H), 4.594 (s, 2 H) 3.39 (m, 2 H), 2.4 (m, 2 H), 1.95 (s, 1 H). Anal. Calcd for $C_{19}H_{19}NO_2$: C, 77.79; H, 6.53; N, 4.77. Found: C, 77.72; H, 6.56; N, 4.72.

**Preparation of *N*-Benzyl-*N*-(4-butynyl)trifluoroacetamide.** *N*-Benzyl-4-amino-1-butyne (0.5 g, 3.15 mmol) was taken in a flame-dried, 25-mL flask equipped with a magnetic stirring bar, and 2 mL of dry pyridine was added to it. The solution was cooled in an ice bath to −10 °C and 666 μL (4.7 mmol, 1.5 equiv) of trifluoroacetic anhydride was added via a syringe. The reaction mixture was stirred at room temperature for 5 h and quenched by pouring into water. After extracting with ether (3 × 30 mL), the combined ether extracts were washed with water, diluted $H_2SO_4$, and water, dried ($MgSO_4$), and concentrated to obtain a gum. Purification by flash chromatography over silica gel (230–400 mesh, hexane/ether, 4:1) afforded 0.668 g (83%) of a clear oil: IR (neat, KCl, cm$^{-1}$) 3300, 3020, 2940, 2120, 1690, 1440, 1370, 1200, 1170, 1150, 1075, 1040, 1970, 755, 740, 700, 650; $^1$H NMR (360 MHz, $CDCl_3$, $\delta$) 7.3–7.2 (m, 5 H), 4.76 (2 s, 2 H), 3.537, 3.467 (2 t, 2 H, $J$ = 6.93 Hz), 2.48 (m, 2 H), 2.069, 2.017 (2 t, 1 H, $J$ = 2.7 Hz). Mass spectral $M_r$ calcd for $C_{13}H_{12}F_3NO$ 255.0871, found 255.0860.

**Preparation of *N*-Benzyl-*N*-(4-butynyl)trifluoromethanesulfonamide.** *N*-Benzyl-4-amino-1-butyne (0.5 g, 3.14 mmol) was taken in a 25-mL, flame-dried, round-bottomed flask, sealed with a rubber septum, and maintained under a slight flow of $N_2$. Dry $CH_2Cl_2$ (5 mL) was added to it followed by 437 μL (3.14 mmol) of triethylamine, and the solution was cooled to −78 °C. Triflic anhydride (528 μL, 3.14 mmol) was added dropwise via a syringe. The reaction mixture was stirred at −78 °C under $N_2$ for 1 h and then quenched by pouring onto ice. After extraction with ether (3 × 50 mL), the combined ether extracts were washed with water, 10% HCl, water, saturated $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated to obtain a gum. Purification was accomplished by flash chromatography over silica gel (230–400 mesh, hexane/ether, 9:1) to obtain 0.86 g (94%) of the product as a colorless oil: IR (neat, KCl, cm$^{-1}$) 3300, 3060, 3040, 2940, 2120, 1790, 1600, 1450, 1390, 1360, 1220, 1190, 1140, 1090, 1070, 985, 940, 910, 890, 800, 735, 700, 650; $^1$H NMR (360 MHz, $CDCl_3$, $\delta$) 7.388 (m, 5 H), 4.582 (br, 2 H), 3.463 (t, 2 H, $J$ = 7.43 Hz), 2.34 (br, 2 H), 2.02 (t, 1 H, $J$ = 2.63 Hz). Mass spectral $M_r$ calcd for $C_{12}H_{12}F_3NSO_2$ 291.0541, found 291.0545.

**Preparation of Ethyl *N*-Benzyl-*N*-(4-butynyl)oxamate.** *N*-Benzyl-4-amino-1-butyne (0.5 g, 3.14 mmol) was taken in a flame-dried, round-bottomed flask and 15 mL of dry ether and 0.324 g (3.2 mmol) of triethylamine were added, and the solution was cooled to 0 °C in an ice bath. Ethyloxalylchloride (361 μL, 3.24 mmol) was added, and the reaction mixture was allowed to stir at room temperature for 2 h. It was quenched by pouring into water, then was extracted with ether (3 × 30 mL), and the combined ether extracts were washed with water, diluted HCl, water, dried ($MgSO_4$), and concentrated on a rotary evaporator. Flash chromatography over silica gel (230–400 mesh, hexane/ether, 4:1) gave 0.767 g (94%) of product as a colorless oil: IR (neat, KCl, cm$^{-1}$) 3300, 2980, 2120, 1740, 1660, 1450, 1370, 1270, 1240, 1190, 1050, 870, 740, 710, 650; $^1$H NMR (360 MHz, $CDCl_3$, $\delta$) 7.3 (m, 5 H), 4.697, 4.591 (2 s, 2 H), 4.376, 4.319 (2 q, 2 H, $J$ = 7.1 Hz), 3.460, 3.400 (2 t, 2 H, $J$ = 7.05 Hz), 2.46 (m, 2 H), 2.033, 2.012 (2 t, 1 H, $J$ = 2.7 Hz), 1.391, 1.311 (2 t, 3 H, $J$ = 7.16 Hz). Anal. Calcd for $C_{15}H_{17}NO_3$ ($M_r$ 259.296) C, 69.48; H, 6.61; N, 5.40. Found: C, 69.51; H, 6.65; N, 5.39.

**General Procedures Used in Table I. $SnCl_4$ Procedure.** A 25-mL, round-bottomed flask was flame dried under $N_2$, cooled, charged with 0.104 g (0.25 mmol) of dimethylglyoxime complex **1**, and sealed with a septum. The alkyne (1.5 equiv) and 10 mL of dry, $N_2$ saturated dichloroethane were then added via a syringe. The solution was stirred under $N_2$, and $SnCl_4$ (1 M solution in $CH_2Cl_2$, 0.25 mL, 0.25 mmol) was then added via a syringe. The solution was stirred at room temperature under $N_2$ for 12–48 h. The reaction mixture was then poured into a flask containing 25 mL of 10% HCl, stirred for 1 h, and extracted with ether (3 × 25 mL), and the combined ether extracts were washed with (2 × 50 mL) 10% HCl and water, dried ($MgSO_4$), and concentrated on a rotary evaporator to give a yellow gum which was usually a mixture of quinone and hydroquinone. The mixture was stirred in a 10% solution of $FeCl_3$ in methanol (10 mL) for 1 h, poured into 50 mL water, and extracted with ether (3 × 25 mL), and the combined ether extracts

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washed with water, dried, and concentrated. The quinone was purified by flash chromatography over silica gel (230–400 mesh, hexanes/ether mixture).

**Reaction of 1-Hexyne with 1.** Cobalt complex **1** (0.104 g, 0.25 mmol), 58 μL (0.041 g, 0.5 mmol) of 1-hexyne, and 250 μL of 1 M $SnCl_4$ (0.25 mmol) after 12 h gave 0.034 g (65%) of the quinone regioisomers (10:1 ratio by $^1H$ NMR): IR ($CH_2Cl_2$, $cm^{-1}$) 2960, 2935, 2860, 1650, 1610, 1450, 1380, 1320, 1210, 1140, 990, 885; $^1H$ NMR (360 MHz, $CDCl_3$, δ) 6.378 (t, 1 H, $J$ = 1.42 Hz), isomer at 6.468 (t, $J$ = 1.42 Hz), 4.011 (s, 3 H), isomer at 3.983 (s), 2.411 (dt, 2 H, $J$ = 7.33 Hz, 1.40 Hz), 1.950 (s, 3 H), isomer at 1.938 (s), 1.50–1.35 (m, 4 H), 0.928 (t, 3 H, $J$ = 7.33 Hz). These spectral data were identical with those previously obtained for rigorously identified material.[2]

**Reaction of Ethyl Tetrolate with 1.** Cobalt complex **1** (0.104 g, 0.25 mmol), 44 μL of ethyl tetrolate (0.042 g, 0.375 mmol, 1.5 equiv), and 250 μL of 1 M $SnCl_4$ (0.25 mmol) after 12 h gave 0.037 g (62%) of the quinone regioisomers (20:1 ratio by $^1H$ NMR): IR ($CH_2Cl_2$, $cm^{-1}$) 2980, 1730, 1650, 1610, 1280, 1210, 1150, 1050, 1020, 960, 900; $^1H$ NMR (360 MHz, $CDCl_3$, δ) 4.392 (q, 2 H, $J$ = 7.22 Hz), 4.038 (s, 3 H), isomer at 4.00 (s), 2.048 (s, 3 H), isomer at 2.033 (s), 1.962 (s, 3 H), isomer at 1.953 (s), 1.376 (t, 3 H, $J$ = 7.22 Hz). These spectral data were identical with those previously obtained for rigorously identified material.[2]

**Reaction of 3-Hexyn-2-one with 1.** Cobalt complex **1** (0.104 g, 0.25 mmol), 35 μL of 3-hexyn-2-one (0.036 g, 0.375 mmol, 1.5 equiv), and 250 μL of 1 M $SnCl_4$ (0.25 mmol) after 12 h gave 0.034 g (62%) of the quinone regioisomers (20:1 ratio by $^1H$ NMR): IR ($CH_2Cl_2$, $cm^{-1}$) 2980, 2940, 1710, 1650, 1610, 1450, 1380, 1360, 1260, 1180, 1140, 980, 910, 830, 690, 650; $^1H$ NMR (360 MHz, $CDCl_3$, δ) 4.017 (s, 3 H), 2.432 (s, 3 H), isomer at 2.419 (s), 2.368 (q, 2 H, $J$ = 7.22 Hz), 1.969 (s, 3 H), isomer at 1.939 (s), 1.093 (t, 3 H, $J$ = 7.22 Hz); MS (70 eV), $m/e$ (rel intensity) 222 (M, 20), 207 (100), 179 (29), 165 (20), 161 (35), 123 (33), 83 (61), 81 (22), 79 (26), 77 (22), 67 (22), 55 (24), 53 (59), 51 (27); mass spectral $M_r$ calcd for $C_{12}H_{14}O$ 222.0891, found 222.0883.

**Reaction of (Trimethylsilyl)-2-butyne with 1.** Cobalt complex **1** (0.104 g, 0.25 mmol) was stirred with alkyne (0.063 g, 0.5 mmol) and 250 μL of 1 M $SnCl_4$ (0.25 mmol) in 10 mL of $(CH_2Cl)_2$. After 36 h 0.025 g (40%) of the quinone regioisomers was obtained (16:1 ratio by $^1H$ NMR): IR ($CH_2Cl_2$, $cm^{-1}$) 2950, 1640, 1600, 1370, 1245, 840, 680; $^1H$ NMR (360 MHz, $CDCl_3$, δ), 3.976 (s, 3 H), isomer at 3.918 (s), 2.05 (s, 2 H), 1.941 (s, 3 H), 1.92 (s, 2 H), 0.02 (s, 9 H). Further proof of the structure of this compound is given below (Confirmation of Regiochemistry).

**Reaction of (*tert*-Butyldimethylsilyl)-2-butyne with 1.** Cobalt complex **1** (0.104 g, 0.25 mmol) was stirred with 0.063 g (0.375 mmol) of the alkyne and 250 μL (0.25 mmol) of 1 M $SnCl_4$ in dichloroethane for 36 h to give, after workup, 0.038 g (51%) of the quinone regioisomers (>20:1 ratio by $^1H$ NMR): IR ($CH_2Cl_2$, $cm^{-1}$), 2980, 2940, 2860, 1645, 1610, 1390, 1115, 915, 830; $^1H$ NMR (360 MHz, $CDCl_3$), 3.975 (s, 3 H) isomer at 3.915 (s), 2.045 (s, 2 H), 1.944 (s, 3 H), 1.919 (s, 2 H), 0.945 (s, 9 H), −0.105 (s, 6 H). Anal. Calcd for $C_{16}H_{26}SiO_3$: C, 65.26; H, 8.90. Found: C, 65.97; H, 9.13.

**Reaction of 3-(*tert*-Butyldimethylsilyl)-1-propyne with 1.** Cobalt complex **1** (0.104 g, 0.25 mmol) was stirred with 0.078 g (0.5 mmol, 2 equiv) of the alkyne and 250 μL of 1 M $SnCl_4$ (0.2k mmol) in 10 mL of dichloroethane for 12 h. The usual workup gave 0.036 g (51%) of the quinone regioisomers (12:1 ratio by $^1H$ NMR): IR ($CH_2Cl_2$, $cm^{-1}$) 2950, 2925, 2855, 1645, 1600, 1465, 1375, 1320, 1210, 1135, 960, 910, 890, 825, 680; $^1H$ NMR (360 MHz, $CDCl_3$, δ) 6.245 (t, 1 H, $J$ = 1.06 Hz), isomer at 6.340 (t, $J$ = 1.06 Hz), 4.017 (s, 3 H), isomer at 3.930 (s), 1.980 (d, 2 H, $J$ = 1.08 Hz), 1.929 (s, 3 H), 0.915 (s, 9 H), −0.088 (s, 6 H). Anal. Calcd for $C_{15}H_{24}SiO_3$ ($M_r$ 280.43) C, 64.24; H, 8.63. Found: C, 64.29; H, 8.63.

**Inverse Additions Using $SnCl_4$.** To a solution of the cobalt complex **1** (0.104 g, 0.25 mmol) in 10 mL of dichloroethane under $N_2$ was added 1 equiv of Lewis acid, and the reaction mixture was stirred for 1 h at room temperature. The alkyne was then added, and stirring was continued for 12–48 h. The usual workup then gave a mixture of the regioisomeric quinones whose ratio was determined by $^1H$ NMR.

**Reaction of 1 with 1-Hexyne.** Complex **1** (0.104 g, 0.25 mmol) and 250 μL of 1 M $SnCl_4$ reacted with 58 μL (0.042 g, 0.5 mmol) of 1-hexyne to give after the usual workup 0.036 g (69%) of the quinone regioisomers (7.3:1 ratio by $^1H$ NMR).

**Reaction of 1 with Ethyl Tetrolate.** Complex **1** (0.104 g, 0.25 mmol) and 250 μL of 1 M $SnCl_4$ reacted with 44 μL (0.042 g, 0.375 mmol) of ethyl tetrolate to give after the usual workup 0.037 g (62%) of the quinone regioisomers (12:1 ratio by $^1H$ NMR).

**$AgBF_4$ Reactions. Reaction with Ethyl Tetrolate.** A flame-dried flask was charged with 0.049 g (0.25 mmol) of $AgBF_4$ and 0.104 g (0.25 mmol) of the cobalt complex **1** under $N_2$, and 10 mL of dry, degassed dichloroethane was added. The mixture was stirred for 30 min, and 0.042 g (44 μL, 0.375 mmol, 1.5 eq) of ethyl tetrolate was added via a syringe. Stirring was continued under $N_2$ for 12 h. The usual workup and chromatographic purification gave 0.037 g (62%) of the quinone regioisomers (24:1 ratio by $^1H$ NMR).

**Reaction with 1-Hexyne.** Complex **1** (0.104 g, 0.25 mmol) and 0.049 g (0.25 mmol) of $AgBF_4$ reacted with 0.042 g (58 μL, 0.5 mmol, 2 equiv) of 1-hexyne to give after the usual workup and chromatographic purification 0.035 g (67%) of the quinone regioisomers (11:1 ratio by $^1H$ NMR).

**Reaction with 3-Hexyn-2-one.** Complex **1** (0.104 g, 0.25 mmol) and 0.049 g (0.25 mmol) of $AgBF_4$ reacted with 0.036 g (35 μL, 0.375 mmol, 1.5 equiv) of the alkyne to give after the usual workup and chromatographic purification 0.037 g (62%) of the quinone regioisomers (20:1 ratio by $^1H$ NMR).

**Activation by $BF_3$·$Et_2O$. Reaction with 1-Hexyne.** Complex **1** (0.104 g, 0.25 mmol) reacted with 58 μL (0.042 g, 0.5 mmol, 2 equiv) of 1-hexyne in the presence of 31 μL (0.036 g, 0.25 mmol) of $BF_3$·$Et_2O$ to give aftr the usual workup and chromatographic purification 0.026 g (50%) of the quinone regioisomers (9:1 ratio by $^1H$ NMR).

**Reaction with Ethyl Tetrolate.** Complex **1** (0.104 g, 0.25 mmol) reacted with 0.042 g (44 μL, 0.375 mmol, 1.5 equiv) of ethyl tetrolate in the presence of 31 μL (0.036 g, 0.25 mmol) of $BF_3$·$Et_2O$ to give after the usual workup and chromatographic purification 0.018 g (30%) of the quinone regioisomers (12:1 ratio by $^1H$ NMR).

**Control Reactions. Reaction of 1 with 1-Hexyne.** Complex **1** (0.104 g, 0.25 mmol) reacted with 58 μL (0.042 g, 0.5 mmol) of 1-hexyne at room temperature to give after 72 h, following the usual workup, 0.005 g (10%) of the quinone regioisomers (4:1 ratio by $^1H$ NMR).

**Reaction of 1 with Ethyl Tetrolate.** Complex **1** (0.104 g, 0.25 mmol) reacted with 44 μL (0.042 g, 0.375 mmol) of ethyl tetrolate at room temperature to give after 72 h, following the usual workup, 0.006 g (10%) of the quinone regioisomers (8:1 ratio by $^1H$ NMR).

**Reaction of 3-(*tert*-Butyldimethylsilyl)-1-propyne with 1.** Cobalt complex **1** (0.104 g, 0.25 mmol) was stirred with 0.078 g (0.5 mmol, 2 equiv) of the alkyne in 10 mL of dichloroethane for 72 h. The usual workup gave 0.011 g (16%) of the quinone regioisomers (9:1 ratio by $^1H$ NMR).

The same reaction was also performed in the absence of Lewis acid at 80 °C and gave 63% of the quinone regioisomers in a ratio of 6:1.

**Reaction of (*tert*-Butyldimethylsilyl)-2-butyne with 1.** Cobalt complex **1** (0.104 g, 0.25 mmol) was stirred with 0.063 g (0.375 mmol) of the alkyne in dichloroethane for 72 h to give, after workup, 0.006 g (8%) of the quinone regioisomers (18:1 ratio by $^1H$ NMR).

The same reaction was also performed in the absence of Lewis acid at 80 °C and gave 60% of the quinone regioisomers in a ratio of 8:1.

**Reaction of Ethyl Propynyl Ether with 1.** A flame-dried flask was charged with 0.104 g (0.25 mmol) of the cobalt complex **1** under $N_2$, and 10 mL of dry, degassed dichloroethane was added followed by 0.032 g (38 μL, 0.375 mmol, 1.5 equiv) of ethyl propynyl ether. Stirring was continued under $N_2$ for 72 h. The usual workup and chromatographic purification gave 0.028 g (52%) of the quinone regioisomers (14:1 ratio by $^1H$ NMR): IR ($CH_2Cl_2$, $cm^{-1}$) 2980, 2940, 1650, 1610, 1440, 1375, 1320, 1260, 1115, 1010, 975, 940, 700; $^1H$ NMR (360 MHz, $CDCl_3$, δ) 4.264 (q, 2 H, $J$ = 7.22 Hz), 3.996 (s, 3 H), isomer at 3.955 (s), 1.927 (s, 3 H), 1.917 (s, 3 H), 1.349 (t, 3 H, $J$ = 7.22 Hz).

**Reaction of 1-Methoxy-1-buten-3-yne with 1.** A flame-dried flask was charged with 0.104 g (0.25 mmol) of the cobalt complex **1** under $N_2$, and 10 mL of dry, degassed dichloroethane was added followed by 36 μL (0.033 g, 0.4 mmol, 2 equiv) of the enyne. Stirring was continued under $N_2$ for 72 h. The reaction mixture was poured into saturated $NaHCO_3$ solution and extracted with ether, the combined ether extracts were washed with water, dried, and concentrated to give a reddish yellow gum. Purification by flash chromatography over silica gel gave 0.026 g (50%) of the quinone regioisomers (20:1 ratio by $^1H$ NMR): IR ($CH_2Cl_2$, $cm^{-1}$) 3025, 2940, 2850, 1645, 1620, 1575, 1450, 1410, 1375, 1280, 1210, 1145, 1100, 995, 940, 890; $^1H$ NMR (360 MHz, $CDCl_3$, δ) 7.19 (s, 1 H), 6.60 (dd, 1 H, $J$ = 6.92 Hz, 0.46 Hz), 5.59 (d, 1 H, $J$ = 6.87 Hz), 4.02 (s, 3 H), 3.88 (s, 3 H), isomer at 3.87 (s), 1.95 (s, 3 H), isomer at 1.954 (s). Major isomer mp 70–71 °C; mass spectral $M_r$ calcd for $C_{11}H_{12}O_4$ 208.0736, found 208.0740.

**Confirmation of Regiochemistry. Structure Proof of the Products from Reaction of 1 with Ethyl Tetrolate.** Assignment of structures was based upon conversion of the major isomer to 2,4-dimethyl-3,5,6-(trimethoxybenzyl)alcohol and the minor isomer to 2,5-dimethyl-3,4,6-(trimethoxybenzyl)alcohol which were identical with authentic samples prepared from 2,6-dimethylbenzoquinone and 2,5-dimethylbenzoquinone, respectively.

Cobalt complex **1** (339 mg, 0.82 mmol) and ethyl tetrolate (300 μL, 2.5 mmol) in 5 mL of $(CH_2Cl)_2$ gave a crude mixture of quinone re-

gioisomers after heating in a sealed tube at 80 °C for 6 h. The mixture was dissolved in 2 mL of glacial AcOH and treated with Zn dust (0.1 g, 1.5 mmol) at room temperature. After having been stirred for 5 min the reaction mixture was poured into water (50 mL) and extracted with ether (3 × 30 mL). The combined ether extracts were washed with water, saturated $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated on a rotary evaporator to give a mixture of hydroquinones which was purified by flash chromatography over silica gel (230–400 mesh, hexane/ether, (3:1)) to give 0.088 g of the more polar regioisomer, 2-carbethoxy-3,5-dimethyl-6-methoxyhydroquinone: mp 82–83 °C (hexane); IR ($CCl_4$, $cm^{-1}$) 3634, 1658; $^1H$ NMR (270 MHz, $CDCl_3$, $\delta$) 10.57 (s, 1 H), 4.50 (br s, 1 H), 4.42 (q, 2 H, $J$ = 7.5 Hz), 3.82 (s, 3 H), 2.40 (s, 3 H), 2.22 (s, 3 H), 1.64 (t, 3 H, $J$ = 7.5 Hz); MS (70 eV), $m/e$ (rel intensity) 240 ($M^+$, 38), 195 (25), 194 (100), 166 (42), 165 (35), 151 (18), 83 (13), 67 (24), and 0.021 g of the less polar minor isomer, 2-carbethoxy-3,6-dimethyl-5-methoxyhydroquinone: mp 103–104 °C (hexane); IR ($CCl_4$, $cm^{-1}$), 3565, 1654, 1619; $^1H$ NMR (270 MHz, $CDCl_3$, $\delta$) 11.24 (s, 1 H), 5.45 (s, 1 H), 4.18 (q, 2 H, $J$ = 7.5 Hz), 3.81 (s, 3 H), 2.45 (s, 3 H), 2.19 (s, 3 H), 1.42 (t, 3 H, $J$ = 7.5 Hz); MS (70 eV), $m/e$ (rel intensity) 240 ($M^+$, 68), 195 (47), 194 (100), 193 (18), 166 (67), 165 (47), 151 (19), 123 (20), 83 (18), 67 (44).

**Methylation.** The major isomer from above was dissolved in 1 mL of MeOH under argon and treated with dimethyl sulfate (0.5 mL, excess) followed by aqueous NaOH (0.8 g in 10 mL). After having been stirred at room temperature for 1 h 20 mL of water was added, the product was extracted with ether (3 × 20 mL), and the combined ether extracts were washed with water, dried ($MgSO_4$), and concentrated to obtain a colorless oil. Purification by flash chromatography over silica gel (230–400 mesh, hexane/ether, 95:5) gave 0.026 g (79%) of 2,4-dimethyl-3,5,6-trimethoxyethyl benzoate as a colorless oil: IR (neat, $cm^{-1}$) 1725; $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$) 4.40 (q, 2 H, $J$ = 8 Hz), 3.85 (s, 3 H), 3.81 (s, 3 H), 3.67 (s, 3 H), 2.20 (s, 3 H), 2.18 (s, 3 H), 1.39 (t, 3 H, $J$ = 8 Hz); MS (70 eV), $m/e$ (rel intensity) 268 ($M^+$, 100), 253 (11), 225 (12), 223 (43), 208 (12), 207 (82), 179 (27), 165 (17), 91 (13), 77 (15), 67 (22), 65 (13), 53 (11); mass spectral $M_r$ calcd for $C_{14}H_{20}O_5$ 268.1310, found 268.1327.

**Preparation of 2,4-Dimethyl-3,5,6-trimethoxybenzyl Alcohol.** A solution of the ethyl benzoate as prepared above (0.01 g) in 2 mL of dry THF was refluxed for 45 min in the presence of $LiAlH_4$ (0.006 g) under $N_2$. After having been cooled to room temperature, the reaction mixture was poured onto ice, acidified with 10% HCl, and extracted with ether (3 × 30 mL). The combined ether extracts were washed with water, dried ($MgSO_4$), and concentrated to obtain 0.007 g (87%) of product as a solid: mp 63–64 °C (hexane); IR ($CCl_4$, $cm^{-1}$) 3630, 3490; $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$) 4.71 (br s, 2 H), 3.88 (s, 3 H), 3.80 (s, 3 H), 3.66 (s, 3 H), 2.29 (s, 3 H), 2.20 (s, 3 H), 2.00 (br, 1 H); MS (70 eV), $m/e$ (rel intensity) 226 ($M^+$, 100), 211 (18), 193 (11), 151 (28). Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 64.00; H, 7.83.

**Preparation of Authentic 2,4-Dimethyl-3,5,6-trimethoxybenzyl Alcohol.** 2,6-Dimethylbenzoquinone was prepared according to a literature procedure.[13] It was converted into 1,3-dimethyl-2,4,5-triacetoxybenzene by the procedure of Erdtman.[14] Conversion to the trimethoxybenzene was accomplished by dissolving the triacetoxybenzene (1 g, 3.6 mmol) in MeOH under argon and treating with dimethyl sulfate (5 g, 40 mmol) followed by slow addition of aqueous NaOH (3.4 g in 5 mL) over 15 min. After the addition was complete, stirring was continued for 1 h, then water (50 mL) was added, and the reaction mixture was extracted with ether (3 × 30 mL). The combined ether extracts were washed with water, dried ($MgSO_4$), and concentrated. Purification by flash chromatography over silica gel (230–400 mesh, hexane/ether, 95:5) gave 0.455 g (65%) of product as a colorless oil: IR (neat, NaCl, $cm^{-1}$) 2960, 1590, 1480, 1460, 1330, 1230, 1120, 1090, 1020, 830; $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$) 6.56 (s, 1 H), 3.82 (s, 3 H), 3.78 (s, 3 H), 3.66 (s, 3 H), 2.25 (s, 3 H), 2.21 (s, 3 H); MS (70 eV), $m/e$ (rel intensity) 196 ($M^+$, 100), 181 (81), 153 (31), 138 (24), 77 (13). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.34; H, 8.39.

**Preparation of 2,4-Dimethyl-3,5,6-trimethoxybenzaldehyde.** 1,3-Dimethyl-2,4,5-trimethoxybenzene (0.178 g, 0.9 mmol) was dissolved in 5 mL of dry $CH_2Cl_2$ under argon. After having been cooled to −10 °C, $TiCl_4$ (470 μL, 4.3 mmol) was added followed by dichloromethyl methyl ether (162 μL, 1.8 mmol). After having been stirred at room temperature for 6 h, the reaction mixture was poured into ice and extracted with ether (3 × 30 mL), and the combined ether extracts were washed with water, saturated $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. Purification by radial chromatography (Chromatotron, 2 mm Kieselgel 60 PF254, hexane/ether 95:5) gave 0.184 g (95%) of 2,4-dimethyl-3,5,6-trimethoxybenzaldehyde as a colorless oil: IR (neat, NaCl, $cm^{-1}$) 1675; $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$) 10.5 (s, 1 H), 3.96 (s, 3 H), 3.86 (s, 3 H), 3.67 (s, 3 H), 2.48 (s, 3 H), 2.29 (s, 3 H); MS (70 eV), $m/e$ (rel intensity) 224 ($M^+$, 100), 209 (82), 194 (20), 181 (25), 166 (16), 151 (17), 91 (20), 83 (18), 79 (16), 77 (32); mass spectral $M_r$ calcd for $C_{12}H_{16}O_4$ 224.1049, found 224.1017.

**Preparation of 2,4-Dimethyl-3,5,6-trimethoxybenzyl Alcohol.** To a solution of the benzaldehyde (0.1 g, 0.44 mmol) in 10 mL of dry ether was added $LiAlH_4$ (0.017 g, 0.44 mmol), and the reaction mixture was stirred under argon at room temperature for 3 h. It was then poured onto ice, acidified with 10% HCl, and extracted with ether (3 × 30 mL), and the combined ether extracts were washed with water, dried ($MgSO_4$), and concentrated. Purification by flash chromatography (230–400 mesh, hexane/ether (90:10) gave 0.09 g (90%) of 2,4-dimethyl-3,5,6-trimethoxybenzyl alcohol as colorless crystals: mp 63–64 °C (hexane); IR ($CCl_4$, $cm^{-1}$) 3630, 3490; $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$) 4.71 (br s, 2 H), 3.88 (s, 3 H), 3.80 (s, 3 H), 3.66 (s, 3 H), 2.29 (s, 3 H), 2.20 (s, 3 H), 2.00 (br, 1 H); MS (70 eV), $m/e$ (rel intensity), 226 ($M^+$, 100), 211 (18), 193 (11), 151 (28). This compound was identical in all respects with the major isomer prepared above via the maleoylcobalt complex reaction.

**Preparation of Ethyl 2,5-Dimethyl-3,4,6-trimethoxybenzoate.** The hydroquinone of the minor isomer formed in the maleoylcobalt reaction described above (0.015 g, 0.06 mmol) was methylated by the procedure described earlier to give 0.012 g (75%) of product as a colorless oil: IR (neat, NaCl, $cm^{-1}$) 1725; $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$) 4.39 (q, 2 H, $J$ = 7 Hz), 3.83 (s, 3 H), 3.77 (s, 3 H), 3.74 (s, 3 H), 2.18 (s, 3 H), 2.17 (s, 3 H), 1.39 (t, 3 H, $J$ = 7 Hz); MS (70 eV), $m/e$ (rel intensity) 268 ($M^+$, 100), 253 (29), 223 (59), 207 (73), 193 (14), 179 (32), 165 (15), 77 (20), 67 (25), 65 (15); mass spectral $M_r$ calcd for $C_{14}H_{20}O_5$ 268.1310, found 268.1293.

**Preparation of 2,5-Dimethyl-3,4,6-trimethoxybenzyl Alcohol.** The ethyl benzoate as prepared above (0.012 g) was dissolved in 2 mL of dry THF and refluxed in the presence of 0.01 g of $LiAlH_4$ for 45 min under argon. The reaction mixture was cooled, poured onto ice, acidified with 10% HCl, and extracted with ether (2 × 25 mL). The combined ether extracts were washed with water, dried ($MgSO_4$), and concentrated to obtain 0.008 g (67%) of product as a solid: mp 50–51 °C (hexane); IR ($CCl_4$, $cm^{-1}$) 3620, 3480; $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$) 4.71 (br d, 2 H, $J$ = 5 Hz), 3.84 (s, 3 H), 3.79 (s, 3 H), 3.77 (s, 3 H), 2.30 (s, 3 H), 2.19 (s, 3 H), 1.90 (br t, 1 H, $J$ = 5 Hz); MS (70 eV), $m/e$ (rel intensity) 226 ($M^+$, 100), 211 (35), 151 (11), 128 (21); mass spectral $M_r$ calcd for $C_{12}H_{18}O_4$ 226.1205, found 226.1187.

**Preparation of Authentic 2,5-Dimethyl-3,4,6-trimethoxybenzyl Alcohol.** 2,5-Dimethylbenzoquinone was prepared according to a literature procedure.[13] It was then converted into 1,4-dimethyl-2,3,6-triacetoxybenzene by the procedure of Fieser and Ardao.[15] The triacetoxybenzene (0.81 g, 2.9 mmol) was methylated following the procedure described earlier by using 3 mL of dimethyl sulfate and 2.7 g of NaOH in 3 mL of water. Purification by flash chromatography over silica gel (230–400 mesh, hexane/ether, 95:5) gave 0.425 g (75%) of 1,4-dimethyl-2,3,6-trimethoxybenzene as a colorless oil: IR (neat, NaCl, $cm^{-1}$) 2980, 2920, 2840, 1600, 1580, 1480, 1460, 1400, 1330, 1230, 1220, 1130, 1090, 1030, 990, 920, 845, 830; $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$) 6.40 (s, 1 H), 3.82 (s, 3 H), 3.78 (s, 6 H), 2.24 (s, 3 H), 2.09 (s, 3 H); MS (70 eV), $m/e$ (rel intensity) 196 ($M^+$, 100), 181 (88), 153 (24), 138 (15); mass spectral $M_r$ calcd for $C_{11}H_{16}O_3$ 196.1099, found 196.1132.

**Preparation of 2,5-Dimethyl-3,4,6-trimethoxybenzaldehyde.** The trimethoxybenzene (0.8 g, 4.1 mmol) was formylated by the procedure described earlier by using 2.11 mL (19 mmol) of $TiCl_4$ and 560 μL (6.24 mmol) of dichloromethyl methyl ether. The usual workup and purification by vacuum distillation (110 °C, 0.5 mmHg) gave 0.786 g (90%) of product as a low melting solid: mp 30 °C; IR (neat, NaCl, $cm^{-1}$) 1680; $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$) 10.45 (s, 1 H), 3.94 (s, 3 H), 3.82 (s, 3 H), 3.77 (s, 3 H), 2.49 (s, 3 H), 2.19 (s, 3 H); MS (70 eV), $m/e$ (rel intensity) 224 ($M^+$, 100), 209 (98), 191 (24), 181 (65), 166 (28), 165 (21), 151 (20), 137 (21), 123 (21), 121 (20), 91 (27), 83 (25), 79 (27), 78 (21), 77 (55), 67 (52), 66 (22), 65 (28), 55 (22), 53 (30), 51 (34). Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 63.98; H, 7.15.

**Preparation of 2,5-Dimethyl-3,4,6-trimethoxybenzyl Alcohol.** To a solution of the benzaldehyde (0.1 g, 0.44 mmol) in 10 mL of dry ether was added $LiAlH_4$ (0.017 g, 0.44 mmol), and the reaction mixture was stirred under argon at room temperature for 3 h. It was then poured onto ice, acidified with 10% HCl, and extracted with ether (3 × 30 mL), and the combined ether extracts washed with water, dried ($MgSO_4$), and concentrated. Purification by flash chromatography (230–400 mesh, hexane/ether 90:10) gave 0.09 g (90%) of 2,5-dimethyl-3,4,6-trimethoxybenzyl alcohol as colorless crystals: mp 50–51 °C (hexane); IR ($CCl_4$,

(13) Liotta, D., et al. *J. Org. Chem.* **1983**, *48*, 2932.
(14) Erdtman, H. G. *Chem. Abstr.* **1934**, *28*, 1337.
(15) Fieser, L. F.; Ardao, M. I. *J. Am. Chem. Soc.* **1956**, *78*, 774.

$cm^{-1}$) 3620, 3480; $^1H$ NMR (200 MHz, $CDCl_3$, $\delta$) 4.71 (br d, 2 H, $J$ = 5 Hz), 3.84 (s, 3 H), 3.79 (s, 3 H), 3.77 (s, 3 H), 2.30 (s, 3 H), 2.19 (s, 3 H), 1.90 (br t, 1 H, $J$ = 5 Hz); MS (70 eV), $m/e$ (rel intensity) 226 ($M^+$, 100), 211 (35), 151 (11), 128 (21). This material was identical in all respects with the minor isomer prepared by the maleoylcobalt route described above.

**Proof of Regiochemistry of the Quinones Formed from Propargylsilanes. Methylation of Quinone Mixture from Reaction of Trimethylsilyl-2-butyne with 1.** The mixture of quinones (0.025 g, 0.1 mmol) formed from trimethylsilyl-2-butyne and maleoylcobalt complex **1** was dissolved in 1 mL of glacial acetic acid, and 0.05 g of Zn dust was added to the solution. The bright yellow solution became colorless after stirring for 5 min; it was then poured into water (50 mL) and extracted with ether (3 × 30 mL), and the combined ether extracts washed with water (2 × 50 mL), saturated $NaHCO_3$ solution, and saturated NaCl, dried ($MgSO_4$), and concentrated to obtain a colorless gum (hydroquinone) which was used as such in the next step. The hydroquinone obtained was dissolved in 5 mL of MeOH (degassed) in a three-necked, round-bottomed flask fitted with a reflux condenser, and dimethyl sulfate (1 mL, excess) was added to the solution. The flask was flushed with argon and maintained under a slight flow of argon. A 10% solution of NaOH (0.2 g) was then added dropwise via a syringe with stirring (solution began to reflux gently). The addition was done in 30 min, and the reaction mixture was stirred (ambient temperature) for 2 h, poured into water (100 mL), extracted with ether (3 × 30 mL), washed with water, dried, and concentrated to obtain a gum which was purified by flash chromatography over silica gel (230–400 mesh, hexane/ether 9:1) to give 0.018 g (66%) of the trimethoxy compound. From IR and $^1H$ NMR spectra the major isomer formed in the propargylsilane reactions was identical with 2,4,5-trimethoxy-3,6-((dimethylbenzyl)trimethyl)silane, prepared below.

**Preparation of 2,4-Dimethyl-3,5,6-trimethoxybenzyl Chloride.** 2,4,5-Trimethoxy-1,3-dimethylbenzene (0.588 g, 3 mmol), prepared above, was taken in a flame-dried, 25-mL, round-bottomed flask under $N_2$. Dry $CH_2Cl_2$ (10 mL) was then added via a syringe, and the solution was cooled to −10 °C in an ice bath. Chloromethyl methyl ether (0.486 g, 458 μL, 6 mmol) was added followed by 3 mL (0.783 g, 3 mmol) of 1 M $SnCl_4$ in $CH_2Cl_2$. The reaction mixture was stirred under $N_2$ and slowly warmed to room temperature. After 3 h, when all the starting material had been consumed, the reaction was quenched by pouring into ice and extracted with $CH_2Cl_2$ (3 × 50 mL), the combined extracts were washed with water, dried over anhydrous $MgSO_4$, and concentrated on a rotary evaporator to obtain a colorless gum. Purification by flash chromatography over silica gel (230–400 mesh, hexane/ether, 4:1) to give 0.66 g (90%) of the benzylchloride: IR ($CH_2Cl_2$, $cm^{-1}$) 2930, 2820, 1460, 1400, 1330, 1110, 1090, 1060, 1000, 960, 660, 640, 620; $^1H$ NMR (360 MHz, $CDCl_3$, $\delta$) 4.706 (s, 2 H), 3.906 (s, 3 H), 3.809 (s, 3 H), 3.674 (s, 3 H), 2.31 (s, 3 H), 2.209 (s, 3 H). Anal. Calcd for $C_{12}H_{17}ClO_3$: C, 58.90; H, 7.00. Found: C, 59.00; H, 7.04.

**Preparation of 2,5-Dimethyl-3,4,6-trimethoxybenzyl Chloride.** 2,3,5-Trimethoxy-1,4-dimethylbenzene (0.588 g, 3 mmol) was taken in a flame-dried, 25-mL, round-bottomed flask equipped with a magnetic stirrer bar. Dry $CH_2Cl_2$ (10 mL) was added via a syringe under $N_2$, and the solution was cooled to −10 °C in an ice bath. Chloromethyl methyl ether (458 μL, 0.486 g, 6 mmol) was added to the above solution followed by 3 mL (0.783 g, 3 mmol) of 1 M $SnCl_4$ in $CH_2Cl_2$. The reaction mixture was stirred under $N_2$ and slowly allowed to warm to room temperature, and after 3 h it was quenched by pouring into ice, extracted with $CH_2Cl_2$ (3 × 50 mL), and washed with water, and the combined extracts dried ($MgSO_4$) and concentrated on a rotary evaporator to give a gum. Purification by flash chromatography over silica gel (230–400 mesh, hexane/ether, 4:1) gave 0.674 g of the compound as a colorless solid (92%). Recrystallization from $CH_2Cl_2$/hexanes gave colorless needles: mp 58–59 °C; IR ($CH_2Cl_2$, $cm^{-1}$) 2930, 2850, 2820, 1460, 1400, 1330, 1110, 1090, 1070, 1010, 960, 820, 675, 625; $^1H$ NMR (360 MHz, $CDCl_3$, $\delta$) 4.711 (s, 2 H), 3.835 (s, 3 H), 3.807 (s, 3 H), 3.789 (s, 3 H), 2.317 (s, 3 H), 2.185 (s, 3 H). Anal. Calcd for $C_{12}H_{17}ClO_3$: C, 58.90; H, 7.00. Found: C, 58.98; H, 7.04.

**Preparation of (2,3,5-Trimethoxy-4,6-dimethylbenzyl)trimethylsilane.** Hexamethyldisilane (112 μL, 0.08 g, 0.55 mmol) was taken in a flame-dried, 25-mL, round-bottomed flask, 200 μL of dry HMPA was added to it via a syringe, and the solution was cooled to 0 °C. MeLi (294 μL, 0.011 g, 0.5 mmol, 1.7 M solution in ether) was added, and the solution was stirred under $N_2$ at 0 °C. After 15 min 2 mL of dry THF was added to the reaction flask, and the solution was immediately cooled to −78 °C. A precooled solution (−78 °C) of 2,4-dimethyl-3,5,6-trimethoxybenzyl chloride (0.061 g, 0.25 mmol) in dry THF was cannulated into the above solution of $Me_3SiLi$. The reaction mixture was stirred at −78 °C for 30 min and quenched by adding saturated $NH_4Cl$ solution. After extracting with ether (3 × 30 mL), the combined ether extracts were washed with saturated NaCl solution, dried ($MgSO_4$), and concentrated to obtain a colorless gum which was purified by flash chromatography over silica gel (230–400 mesh, hexane/ether, 9:1) to give product as a colorless oil (0.044 g, 63%): IR (neat, KCl, $cm^{-1}$) 2920, 2810, 1460, 1400, 1330, 1240, 1105, 1080, 1050, 1000, 960, 850, 690, 650; $^1H$ NMR (360 MHz, $CDCl_3$, $\delta$) 3.777 (s, 3 H), 3.754 (3 H), 3.639 (s, 3 H), 2.166 (s, 3 H), 2.10 (s, 3 H), 2.086 (s, 2 H), −0.012 (s, 9 H). Anal. Calcd for $C_{15}H_{26}SiO_3$: C, 63.78; H, 9.28. Found: C, 63.88; H, 9.33.

**Preparation of (2,5-Dimethyl-3,4,6-trimethoxybenzyl)trimethylsilane.** 2,4,5-Trimethoxy-3,6-dimethylbenzyl chloride (0.061 g, 0.25 mmol) was similarly treated with $Me_3SiLi$ generated as above from 112 μL (0.08 g, 0.55 mmol) of hexamethyldisilane and 294 μL (0.011 g, 0.5 mmol) of 1.7 M MeLi to give, after workup and flash chromatography over silica gel (230–400 mesh, hexanes/ether, 9:1), 0.045 g (65%) of product: IR (neat, KCl, $cm^{-1}$) 2940, 2920, 2860, 1455, 1400, 1250, 1110, 1090, 1050, 1010, 900, 845, 690; $^1H$ NMR (360 MHz, $CDCl_3$, $\delta$) 3.803 (s, 3 H), 3.762 (s, 3 H), 3.622 (s, 3 H), 2.174 (s, 3 H), 2.103 (s, 3 H), 2.041 (s, 2 H), −0.018 (s, 9 H). Anal. Calcd for $C_{15}H_{26}SiO_3$: C, 63.78; H, 9.28. Found: C, 63.90; H, 9.33.

**Reactions of Complex 7 in Table II. Activation by $SnCl_4$. Reaction of 1-Hexyne with 7.** Cobalt complex **7** (0.123 g, 0.25 mmol), 57 μL of 1-hexyne (0.041 g, 0.5 mmol), and 250 μL of 1 M $SnCl_4$ (0.25 mmol) after 12 h gave 0.037 g (71%) of the quinone regioisomers (10:1 ratio by $^1H$ NMR).

**Reaction of Ethyl Tetrolate with 7.** Cobalt complex **7** (0.123 g, 0.25 mmol), 44 μL of ethyl tetrolate (0.042 g, 0.375 mmol, 1.5 equiv), and 250 μL of 1 M $SnCl_4$ (0.25 mmol) after 48 h gave 0.045 g (76%) of the quinone regioisomers (18:1 ratio by $^1H$ NMR).

**Reaction of (*tert*-Butyldimethylsilyl)-2-butyne with 7.** Cobalt complex **7** (0.123 g, 0.25 mmol) was stirred with 0.063 g (0.375 mmol) of the alkyne and 250 μL (0.25 mmol) of 1 M $SnCl_4$ in dichloroethane for 48 h to give, after workup, 0.041 g (55%) of the quinone regioisomers (>20:1 ratio by $^1H$ NMR).

**Reaction of 3-(*tert*-Butyldimethylsilyl)-1-propyne with 7.** Cobalt complex **7** (0.123 g, 0.25 mmol) was stirred with 0.078 g (0.5 mmol, 2 equiv) of the alkyne and 250 μL of 1 M $SnCl_4$ (0.25 mmol) in 10 mL of dichloroethane for 48 h. Usual workup gave 0.04 g (57%) of the quinone regioisomers (12:1 ratio by $^1H$ NMR).

**Activation by Zinc Triflate. Reaction with Ethyl Tetrolate.** Cobalt complex **7** (0.123 g, 0.25 mmol), 44 μL of ethyl tetrolate (0.042 g, 0.375 mmol, 1.5 equiv), and 0.091 g (0.25 mmol) of zinc triflate after 48 h gave 0.047 g (79%) of the quinone regioisomers (21:1 ratio by $^1H$ NMR).

**Reaction with 1-Hexyne.** Cobalt complex **7** (0.123 g, 0.25 mmol), 58 μL of ethyl tetrolate (0.042 g, 0.5 mmol, 1.5 equiv), and 0.091 g (0.25 mmol) of zinc triflate after 48 h gave 0.039 g (74%) of the quinone regioisomers (10:1 ratio by $^1H$ NMR).

**Procedures Used in Table III. $SnCl_4$ Reactions of 1 with ω-Aminoalkynes. General Procedure.** A 25-mL, round-bottomed flask was flame dried under $N_2$, cooled, charged with 0.104 g (0.25 mmol) of the dimethylglyoxime complex **1**, and sealed with a septum. The alkyne (1.5 equiv) and 10 mL of dry, $N_2$ saturated dichloroethane were then added via a syringe. The solution was stirred under $N_2$, and (0.25 mL, 0.25 mmol) $SnCl_4$ (1 M solution in $CH_2Cl_2$) was then added via syringe. The reaction mixture was stirred at room temperature under $N_2$ for 12–72 h. It was then poured into a flask containing 25 mL of 10% HCl, stirred for 1 h, and extracted with ether (3 × 25 mL), and the combined ether extracts were washed with (2 × 50 mL) 10% HCl and water, dried (anhydrous $MgSO_4$), and concentrated on a rotary evaporator to give a yellow gum which was usually a mixture of quinone and hydroquinone. The mixture was stirred in a 10% solution of $FeCl_3$ in methanol (10 mL) for 1 h, poured into 50 mL of water, and extracted with ether (3 × 25 mL), and the combined ether extracts were washed with water, dried, and concentrated. The quinone was then purified by flash chromatography on silica gel (230–400 mesh, eluent/hexanes, ether mixture).

**Reaction of 1 with 4-Phthalimido-1-butyne.** Cobalt complex **1** (0.104 g, 0.25 mmol) reacted with 0.05 g (0.25 mmol) of the alkyne in the presence of 250 μL (0.25 mmol) of 1 M $SnCl_4$ in 10 mL of dichloroethane at room temperature to give after 48 h 0.034 g (42%) of the mixture of regioisomeric quinones (7:1 ratio by $^1H$ NMR): IR ($CH_2Cl_2$, $cm^{-1}$) 3050, 2940, 2850, 1770, 1710, 1650, 1610, 1440, 1395, 1210, 1140, 1100, 1005, 980; $^1H$ NMR (360 MHz, $CDCl_3$, $\delta$) 7.84–7.7 (m, 5 H), 6.33 (t, 1 H, $J$ = 1.0 Hz), isomer at 6.37 (t, $J$ = 1.1 Hz), 3.99 (s, 3 H), isomer at 4.04 (s), 3.92 (s, 2 H, $J$ = 6.5 Hz), 2.8 (m, 2 H), 1.97 (s, 3 H), isomer at 1.98 (s).

**Reaction of 1 with *N*-Benzyl-*N*-(carbobenzyloxy)-4-amino-1-butyne.** Cobalt complex **1** (0.104 g, 0.25 mmol) was treated with 0.075 g (0.25 mmol) of the alkyne in the presence of 250 μL of 1 M $SnCl_4$ in 10 mL of dichloroethane to give after 48 h 0.038 g (35%) of the quinone regioisomers: IR ($CH_2Cl_2$, $cm^{-1}$) 2940, 1700, 1650, 1610, 1475, 1420, 1375, 1240, 1210, 1115; $^1H$ NMR (360 MHz, $CDCl_3$, $\delta$) 7.35–7.15 (m,

10 H), 6.322, 6.265, 6.157 (3 s, 1 H), 5.141 (s, 2 H), 4.512, 4.486 (2 s, 2 H), 3.984 (s, 3 H), 3.44 (m, 2 H), 2.64–2.53 (m, 2 H), 1.92, 1.824 (2 s, 3 H).

**Reaction of *N*-Benzyl-*N*-(4-butynyl)trifluoroacetamide with 1.** Cobalt complex **1** (0.104 g, 0.25 mmol), 0.064 g (0.25 mmol) of the alkyne, and 250 μL of 1 M $SnCl_4$ after 48 h gave 0.032 g (33%) of the quinone regioisomers: IR (neat, KCl, $cm^{-1}$) 3060, 2950, 2850, 2250, 1685, 1645, 1610, 1450, 1375, 1320, 1205, 1170, 1145, 905, 650; $^1H$ NMR (360 MHz, $CDCl_3$, δ) 7.4–7.2 (m, 5 H), 6.35, 6.34 (2 t, 1 H, $J$ = 1.05 Hz), 4.73, 4.63 (2 s, 2 H), 4.02, 4.0 (2 s, 3 H), 3.47 (m, 2 H), 2.73–2.59 (m, 2 H), 1.94, 1.92 (2 s, 3 H). Anal. Calcd for $C_{19}H_{18}F_3NO_4$: C, 59.84; H, 4.76; N, 3.68. Found: C, 59.65; H, 4.79; N, 3.60.

**Reaction of *N*-Benzyl-*N*-(4-butynyl)trifluoromethanesulfonamide with 1.** Cobalt complex **1** (0.104 g, 0.25 mmol), 0.147 g (0.5 mmol) of the aminoalkyne, and 250 μL of 1 M $SnCl_4$ (0.25 mmol) after 12 h gave 0.068 g (65%) of the quinone regioisomers (7:1 ratio by $^1H$ NMR): IR ($CH_2Cl_2$, $cm^{-1}$) 3060, 2940, 2840, 1650, 1610, 1190, 1140; $^1H$ NMR (360 MHz, $CDCl_3$, δ) 7.392 (s, 5 H), 6.18 (t, 1 H, $J$ = 1.01 Hz), 4.001 (s, 3 H), isomer at 3.955 (s), 3.497 (br t, 2 H), 2.492 (t, 2 H, $J$ = 7.2 Hz), 1.898 (s, 3 H), isomer at 1.908 (s). Anal. Calcd for $C_{18}H_{18}F_3NO_5S$: C, 51.80; H, 4.35; N, 3.36. Found: C, 51.70; H, 4.37; N, 3.31. The major isomer melts at 88–89 °C.

**Reaction of Ethyl *N*-Benzyl-*N*-(4-butynyl)oxamate with 1.** Cobalt complex **1** (0.104 g, 0.25 mmol), 0.145 g (0.5 mmol) of the aminoalkyne, and 250 μL of 1 M $SnCl_4$ after 48 h gave 0.027 g (30%) of the quinone regioisomers: IR ($CH_2Cl_2$, $cm^{-1}$) 3050, 2920, 1740, 1660, 1610, 1450, 1320, 1205, 1190, 1170, 1150, 890, 800, 690; $^1H$ NMR (360 MHz, $CDCl_3$, δ) 7.32 (m, 5 H), 6.356, 6.271 (2 s, 1 H), 4.659, 4.455 (2 s, 2 H), 4.34–4.30 (m, 2 H), 4.013, 4.002 (2 s, 3 H), 3.463, 3.362 (2 t, 2 H, 7.22 Hz), 2.66, 2.605 (2 t, 2 H, $J$ = 7.22 Hz), 1.930 (s, 3 H), 1.371, 1.314 (2 t, 3 H, $J$ = 7.22 Hz). Anal. Calcd for $C_{21}H_{23}NO_6C$: C, 65.44; N, 6.02; N, 3.64. Found: C, 64.72; H, 5.88; N, 3.58. Although the value for carbon was slightly off in this analysis, the remaining data are in full accord with the proposed structure.

**Thermal Reactions of 1 with ω-Aminoalkynes. General Procedure.** Cobalt complex **1** (0.104 g, 0.25 mmol) was taken in a hard glass reaction vessel, and 3 mL of dry, degassed dichloroethane was added followed by 0.375 mmol of the alkyne. The reaction vessel was sealed and placed in an oil bath maintained at 80 °C. After 8 h the reaction mixture was cooled, poured into 25 mL of 10% HCl, stirred for 30 min, and extracted with ether (3 × 30 mL), and the combined ether extracts were washed with 10% HCl and water, dried ($MgSO_4$), and concentrated to obtain a mixture of quinone and hydroquinone. The mixture was stirred with a 10% methanolic solution of $FeCl_3$ for 1 h, added to 50 mL of water, and extracted with ether (3 × 30 mL), and the ether extracts were washed with water, dried, and concentrated. Purification by flash chromatography over silica gel (230–400 mesh, hexane/ether 90:10) gave the mixture of isomeric quinones.

**Reaction of 1 with 4-Phthalimido-1-butyne.** Cobalt complex **1** (0.104 g, 0.25 mmol) reacted with 0.05 g (0.25 mmol) of the alkyne in 3 mL of dichloroethane at 80 °C to give after 8 h 0.063 g (77%) of the mixture of regioisomeric quinones (3:1 ratio by $^1H$ NMR).

**Reaction of 1 with *N*-Benzyl-*N*-(carbobenzyloxy)-4-amino-1-butyne.** Cobalt complex **1** (0.104 g, 0.25 mmol) reacted with 0.075 g (0.375 mmol) of the alkyne in 3 mL of dichloroethane at 80 °C to give after 8 h 0.083 g (76%) of the mixture of regioisomeric quinones.

**Reaction of *N*-Benzyl-*N*-(4-butynyl)trifluoroacetamide with 1.** Cobalt complex **1** (0.104 g, 0.25 mmol) reacted with 0.096 g (0.375 mmol) of the alkyne and after 8 h gave 0.07 g (72%) of the mixture of regioisomeric quinones.

**Reaction of Ethyl *N*-Benzyl-*N*-(4-butynyl)oxamate with 1.** Cobalt complex **1** (0.104 g, 0.25 mmol) reacted with 0.109 g (0.375 mmol) of the aminoalkyne at 80 °C and after 8 h gave 0.068 g (76%) of the mixture of regioisomeric quinones.

**Synthesis of Isoquinoline Quinone 8, 1,6-Dimethyl-7-methoxy-5,8-dihydroisoquinoline-5,8-dione. Preparation of *N*-Benzyl-*N*-(carbobenzyloxy)-6-amino-3-hexyn-2-one, 9. (a) Reaction of *N*-Benzyl-4-amino-1-butyne with Acetaldehyde.** A 50-mL, flame-dried flask was cooled and charged with 0.575 g (3.62 mmol) of *N*-benzyl-4-amino-1-butyne and 10 mL of dry THF, and the solution was cooled to −78 °C. *n*-BuLi (2.8 mL, 4.4 mmol, 1.2 equiv, 1.7 M solution) was added via a syringe, and the reaction mixture was stirred under $N_2$ at −78 °C for 1 h and then warmed to −30 °C. A precooled (−78 °C) solution of acetaldehyde (0.319 g, 405 μL, 7.24 mmol, 2 equiv) in dry THF was then cannulated into the alkynyllithium solution. The reaction mixture was stirred at −30 °C for 30 min, then quenched with saturated $NH_4Cl$, and extracted with ether (3 × 50 mL), and the combined ether extracts were washed with water, dried, and concentrated to yield a gum. Purification by flash chromatography over silica gel (230–400 mesh, hexane/ether, 1:4) gave 0.493 g (67%) of a colorless oil: IR (neat, KCl, $cm^{-1}$) 3500–3100 (br), 2920, 2240, 1600, 1450, 1370, 1330, 1150 m, 1080, 1010, 890, 740, 700; $^1H$ NMR (360 MHz, $CDCl_3$, δ) 7.32 (m, 5 H), 4.56 (m, 21 H), 3.811 (s, 2 H), 2.77 (t, 2 H, $J$ = 6.48 Hz), 2.433 (m, 2 H), 1.418 (d, 3 H, $J$ = 6.48 Hz), 1.8 (br, 1 H).

**(b) Reaction with Benzyl Chloroformate.** The aminopropargyl alcohol prepared above (1.0 g, 4.94 mmol) was treated with 25 mL of 1% aqueous NaOH and 1.01 g (846 μL, 5.93 mmol, 1.2 equiv) of benzyl chloroformate to give after chromatographic purification 1.531 g (96%) of the N-protected hydroxyalkyne: IR (neat, KCl, $cm^{-1}$) 3440 (br), 2980, 2250, 1690, 1600, 1590, 1480, 1420, 1380, 1240, 1220, 1120, 1080, 740, 700; $^1H$ NMR (360 MHz, $CDCl_3$, δ) 7.3 (m, 10 H, 5.205, 5.169 (d, 2 H), 4.58 (s, 2 H), .48 (br m, 1 H), 3.4 (m, 2 H), 2.4 (m, 2 H), 1.88, 1.74 (br, 1 H), 1.402, 1.383 (d, 3 H, $J$ = 6.98 Hz).

**(c) PDC Oxidation.** The above alcohol (1.27 g, 3.91 mmol) was dissolved in 15 mL of dry $CH_2Cl_2$ in a 25-mL, round-bottomed flask, and 2.21 g (5.87 mmol, 1.5 equiv) of pyridinium dichromate were added to the solution. The reaction was stirred at room temperature for 24 h, monitoring for loss of the starting compound by TLC. It was then poured into 100 mL of petroleum ether and filtered through a pad of Celite. The filtrate was concentrated to obtain a gum which was purified by flash chromatography over silica gel (230–400 mesh, hexane/ether, 3:2) to give 1.023 g (81%) of *N*-benzyl-*N*-(carbobenzyloxy)-6-amino-3-hexyn-2-one, **9**, as a pale yellow oil: IR (neat, KCl, $cm^{-1}$) 3060, 3020, 2940, 2210, 1700, 1670, 1470, 1415, 1360, 1230, 1110, 1020, 980, 730, 700; $^1H$ NMR (360 MHz, $CDCl_3$, δ) 7.38–7.15 (m, 10 H), 5.212, 5.185 (2 s, 2 H), 4.581 (s, 2 H), 3.45 (m, 2 H), 2.612, 2.508 (2 t, 2 H, $J$ = 6.95 Hz, 6.8 Hz), 2.280 (s, 3 H). Anal. Calcd for $C_{21}H_{21}NO_3$ ($M_r$ 335.388) C, 75.20; H, 6.31; N, 4.18. Found: C, 75.26; H, 6.32; N, 4.17.

**Thermal Reaction of *N*-Benzyl-*N*-(carbobenzyloxy)-6-amino-3-hexyn-2-one with 1.** Cobalt complex **1** (0.104 g, 0.25 mmol) reacted with 0.084 g (0.25 mmol) of the aminoalkyne **9** at 80 °C and after 8 h gave 0.098 g (84%) of the mixture of isomeric quinones. The mixture was dissolved in 1 mL of glacial AcOH and 0.05 g of Zn dust added to it. After having been stirred for 5 min, 50 mL of water was added, and the mixture was extracted with ether (3 × 30 mL), washed with combined ether extracts several times with water, dried, and concentrated to obtain a colorless gum. Purification by flash chromatography over silica gel (230–400 mesh, hexane/ether, 60:40) gave 0.070 g (35%) of the more polar major hydroquinone and 0.025 g of the less polar minor hydroquinone. **Major isomer (hydroquinone of 10)**: IR ($CH_2Cl_2$, $cm^{-1}$) 3010, 3480–3100 (br), 2940, 2260, 1665, 1475, 1450, 1415, 1330, 1300, 1240, 1180, 1110, 1050, 910, 650; $^1H$ NMR (360 MHz, $CDCl_3$, δ) 8.283 (s, 1 H), 7.40–7.20 (m, 10 H), 6.334 (s, 1 H), 5.260 (s, 2 H), 4.531 (s, 2 H), 3.751 (s, 3 H), 3.398 (t, 2 H, $J$ = 8.0 Hz), 2.593 (t, 2 H, $J$ = 7.94 Hz), 2.482 (s, 3 H), 2.229 (s, 3 H). **Minor isomer**: IR ($CH_2Cl_2$, $cm^{-1}$) 3480–3100 (br), 3040, 2930, 1700, 1675, 1620, 1575, 1415, 1360, 1300, 1230, 1120, 975; $^1H$ NMR (360 MHz, $CDCl_3$, δ) 13.25 (s, 1 H), 7.4–7.2 (m, 10 H), 5.28, 5.06 (2 s, 2 H), 3.87 (s, 3 H), 3.48–3.41 (m, 2 H), 2.62–2.5 (m, 2 H), 2.41 (s, 3 H), 2.28 (s, 3 H).

Elemental analysis was obtained on the quinone **10**. Anal. Calcd for $C_{27}H_{27}NO_6$: C, 70.26; H, 5.90; N, 3.01. Found: C, 70.27; H, 5.91; N, 3.01.

**$SnCl_4$ Reaction of *N*-Benzyl-*N*-(carbobenzyloxy)-6-amino-3-hexyn-2-one with 7.** Cobalt complex **7** (0.123 g, 0.25 mmol) was reacted with 0.084 g (0.25 mmol) of the aminoalkyne and 250 μL (0.25 mmol) of 1 M $SnCl_4$ under $N_2$ at room temperature. The usual workup after 48 h gave 0.098 g of a yellow oil which showed the presence of unreacted alkyne by IR. The mixture was dissolved in 1 mL of glacial AcOH and 0.05 g of Zn dust added to it. After having been stirred for 5 min, 50 mL of water was added, and the mixture was extracted with ether (3 × 30 mL), and combined ether extracts were washed several times with water, dried, and concentrated to obtain a colorless gum. Purification by flash chromatography over silica gel (230–400 mesh, hexane/ether, 60:40) gave 0.05 g (43%) of the hydroquinone of **10** described above and 0.023 g of the unreacted alkyne.

**Preparation of *N*-Benzyl-*N*-(carbobenzyloxy)-2-[2-acetyl-3,4,6-trimethoxy-5-(methylphenyl)]ethylamine (11).** The major hydroquinone (0.14 g, 0.3 mmol) obtained from the reaction of the cobalt complex **7** with **9** was methylated by treatment with 1 mL (excess) of dimethyl sulfate in 10 mL of methanol in the presence of 15% aqueous NaOH (5 mL) under an argon atmosphere at ambient temperature. Workup and flash chromatography following the usual procedure gave 0.111 g (75%) of **11** as a colorless oil: IR ($CH_2Cl_2$, $cm^{-1}$) 2940 (br), 2870, 1705, 1695, 1490, 1460, 1420, 1400, 1215, 1200, 1160, 1115, 1070, 985, 825, 750, 700; $^1H$ NMR (360 MHz, $CDCl_3$, δ) 7.45–7.20 (m, 10 H), 5.2, 5.19 (2 s, 2 H), 4.49, 4.45 (2 s, 2 H), 3.8–3.4 (m, 9 H), 3.31 (m, 2 H), 2.78–2.6 (m, 2 H), 2.48, 2.33 (2 s, 3 H), 2.18, 2.14 (2 s, 3 H).

**Preparation of 1,6-Dimethyl-7-methoxy-5,8-dihydroisoquinoline-5,8-dione (8). (a) Hydrogenolysis and Cyclization of (11).** The trimethoxy compound **11** (0.1 g, 0.2 mmol) was taken in a hard glass reaction vessel,

and 20 mL of absolute ethanol was added to it. Palladium on carbon (0.005 g of 10% Pd/C) was added to the above solution, and the reaction mixture was hydrogenated in a Parr apparatus (40 psi $H_2$ pressure). After 5 h the reaction mixture was filtered and concentrated to obtain a gum which was passed through a short column of silica gel eluting with hexane/EtOAc (1:1) to give 0.035 g (68%) of the cyclized product **12**: IR ($CH_2Cl_2$, $cm^{-1}$) 2930, 2860, 2800–2500, 1590, 1470, 1410, 1345, 1110, 1075, 920, 860, 810; $^1H$ NMR (360 MHz, $CDCl_3$, $\delta$) 4.29 (q, 1 H, $J$ = 6.7 Hz), 3.81 (s, 3 H), 3.78 (s, 3 H), 3.66 (s, 3 H), 3.15–3.05 (m, 2 H), 2.75–2.6 (m, 2 H), 2.17 (s, 3 H), 1.44 (d, 3 H, $J$ = 6.63 Hz).

**(b) Dehydrogenation of 12.** Tetrahydroisoquinoline **12** (0.025 g, 0.1 mmol) was taken in a 10-mL, round-bottomed flask equipped with a magnetic stirrer bar and a reflux condenser, and 1 mL of decalin was added to it. The mixture was placed in an oil bath maintained at 160 °C, and after 3 h the reaction mixture was cooled, and the product was purified by flash chromatography over a column of silica gel (230–400 mesh, hexane/EtOAc, 10%) to give 0.015 g (60%) of **13**: IR ($CH_2Cl_2$, $cm^{-1}$) 2940, 2860, 1460, 1410, 1330, 980; $^1H$ NMR (360 MHz, $CDCl_3$, $\delta$) 8.3 (d, 1 H, $J$ = 5.95 Hz), 7.65 (d, 1 H, $J$ = 5.92 Hz), 3.94 (s, 3 H), 3.85 (s, 3 H), 3.1 (s, 3 H), 2.4 (s, 3 H); mass spectral $M_r$ calcd for $C_{14}H_{17}NO_3$ 247.1208, found 247.1211.

**Oxidation of 13.** The trimethoxyisoquinoline **13** (0.03 g, 0.12 mmol) and 0.06 g (0.48 mmol) of $Ag_2O$ was taken in a flask containing 1 mL of dioxane. Nitric acid (0.1 mL, 6 M) was added to the mixture, and after having been stirred at room temperature for 15 min, the reaction mixture was diluted with water and extracted with $CHCl_3$. The chloroform extract was washed with water, dried, and concentrated to obtain a yellow solid which was purified by flash chromatography over silica gel (230–400 mesh, hexane/EtOAc, 10%) to give 0.012 g (50%) of the known compound[6] **1,6-dimethyl-7-methoxy-5,8-dihydroisoquinoline-5,8-dione, 8**: mp 188–190 °C; IR ($CH_2Cl_2$, $cm^{-1}$) 2920, 2850, 1670, 1615, 1570, 1400, 1380, 1340, 1300, 1205, 905; $^1H$ NMR (360 MHz, $CDCl_3$, $\delta$) 8.85 (d, 1 H, $J$ = 4.45 Hz), 7.81 (d, 1 H, $J$ = 4.96 Hz), 4.14 (s, 3 H), 2.99 (s, 3 H), 2.08 (s, 3 H).

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**Registry No. 1**, 92421-26-6; **2** (R = Me; R′ = $CO_2Et$), 92421-38-0; **2** (R = $CO_2Et$; R′ = Me), 92421-39-1; **2** (R = Me; R′ = $CO_2Et$, hydroquinone), 107301-78-0; **2** (R = $CO_2Et$; R′ = Me, hydroquinone), 107301-79-1; **2** (R = Et; R′ = COMe), 107301-67-7; **2** (R = COMe; R′ = Et), 107301-68-8; **2** (R = $CH_2SiMe_3$; R′ = Me), 107301-69-9; **2** (R = Me; R′ = $CH_2SiMe_3$), 107301-70-2; **2** (R = $CH_2SiMe_2Bu$-*t*; R′ = Me), 107301-71-3; **2** (R = Me; R′ = $CH_2SiMe_2Bu$-*t*), 107301-72-4; **2** (R = OEt; R′ = Me), 92421-48-2; **2** (R = Me; R′ = OEt), 92421-49-3; **2** (R = R′ = Me, hydroquinone), 107301-80-4; **3** (R = **Bu**), 92421-34-6; **3** (R = $CH_2SiMe_2Bu$-*t*), 107301-73-5; **3** (K = CH=CHOMe-(*Z*)), 107301-75-7; **3** (R = $(CH_2)_2NPhth$), 107301-85-9; **3** (R = $(CH_2)_2NCbz$(**Bn**)), 107301-87-1; **3** (R = $(CH_2)_2NCOCF_3$(Bn)), 107301-89-3; **3** (R = $(CH_2)_2NSO_2CF_3$(Bn)), 107301-91-7; **3** (R = $(CH_2)_2NCOCO_2Et$(Bn)), 107301-93-9; **4** (R = Bu), 92421-35-7; **4** (R = $CH_2SiMe_2Bu$-*t*), 107301-74-6; **4** (R = (*Z*)-CH=CHOMe), 107301-76-8; **4** (R = $(CH_2)_2NPhth$), 107301-86-0; **4** (R = $(CH_2)_2NCbz$(Bn)), 107301-88-2; **4** (R = $(CH_2)_2NCOCF_3$(Bn)), 107301-90-6; **4** (R = $(CH_2)_2NSO_2CF_3$(Bn)), 107301-92-8; **4** (R = $(CH_2)_2NCOCO_2Et$(Bn)), 107301-94-0; **7**, 107302-04-5; **8**, 79664-58-7; **9**, 107301-97-3; **10** (major isomer), 107301-98-4; **10** (minor isomer), 107301-99-5; **10** (major isomer, hydroquinone), 107302-00-1; **10** (minor isomer, hydroquinone), 107302-01-2; **11**, 107302-03-4; **12**, 107302-02-3; **13**, 98498-39-6; MeBrMg, 75-16-1; $ClCo(PPh_3)_3$, 26305-75-9; $Me_3SiC{\equiv}CMe$, 6224-91-5; *t*-$BuMe_2SiCl$, 18162-48-6; *t*-$BuMe_2SiCH_2C{\equiv}CH$, 107301-60-0; $HO(CH_2)_2C{\equiv}CH$, 927-74-2; $HC{\equiv}C(CH_2)_2NPhth$, 14396-90-8; 4-$MeC_6H_4SO_2(CH_2)_2C{\equiv}CH$, 36832-51-6; $PhCH_2NH_2$, 100-46-9; $PhCH_2NH(CH_2)_2C{\equiv}CH$, 107301-61-1; $PhCH_2CO_2Cl$, 501-53-1; $PhCH_2N$(Cbz)$(CH_2)_2C{\equiv}CH$, 107301-62-2; $F_3CCO_2OCF_3$, 407-25-0; $PhCH_2N(COCF_3)(CH_2)_2C{\equiv}CH$, 107301-63-3; $F_3CSO_2N(CH_2Ph)(CH_2)_2C{\equiv}CH$, 107301-64-4; $PhCH_2N(COCO_2Et)(CH_2)_2C{\equiv}CH$, 107301-65-5; $HC{\equiv}C(CH_2)_3CH_3$, 693-02-7; $MeCH_2C{\equiv}CCOMe$, 1679-36-3; $MeOCH{=}CHC{\equiv}CH$, 2798-73-4; $EtOC{\equiv}CMC$, 14273-06-4; *t*-$BuMe_2SiCH_2C{\equiv}CMe$, 107301-66-6; $Cl_2CHOMe$, 4885-02-3; $ClCH_2OMe$, 107-30-2; $Me_3SiSiMe_3$, 1450-14-2; MeCHO, 75-07-0; $Me_3SiC{\equiv}CCH_2SiMeBu$-*t*, 78978-51-5; $PhCH_2NH(CH_2)_2C{\equiv}CCH(OH)Me$, 107301-95-1; $PhCH_2N$(Cbz)$(CH_2)_2C{\equiv}CCH(OH)Me$, 107301-96-2; $Me_3SiCH_2C{\equiv}CMe$, 18825-29-1; squaric acid, 2892-51-5; diethyl squarate, 5231-87-8; 3-hydroxy-4-methylcyclobutenedione, 29769-75-3; 3-methoxy-4-methylcyclobutenedione, 29769-77-5; dimethylglyoxime, 95-45-4; silver trifluoroacetate, 2966-50-9; phthalimide, 85-41-6; triflic anhydride, 358-23-6; ethyloxachloride, 4755-77-5; ethyl tetrolate, 4341-76-8; 2,4-dimethyl-3,5,6-(trimethoxy)benzyl alcohol, 107301-77-9; 2,5-dimethyl-3,4,6-(trimethoxy)benzyl alcohol, 92421-45-9; 2,4-dimethyl-3,5,6-(trimethoxy)ethyl benzoate, 92421-40-4; 1,3-dimethoxy-2,4,5-triacetoxybenzene, 41168-76-7; 1,3-dimethyl-2,4,5-trimethoxybenzene, 92421-42-6; 2,4-dimethyl-3,5,6-trimethoxybenzaldehyde, 92421-43-7; ethyl 2,5-dimethyl-3,4,6-trimethoxybenzoate, 92421-44-8; 2,5-dimethyl-3,4,6-trimethoxybenzyl alcohol, 92421-45-9; 4,4-dimethyl-2,3,6-triacetoxybenzene, 40853-36-9; 1,4-dimethyl-2,3,6-trimethoxybenzene, 92421-46-0; 2,5-dimethyl-3,4,6-trimethoxybenzaldehyde, 92421-47-1; 2,4,5-trimethoxy-3,6-(dimethylbenzyl)trimethyl)silane, 107301-81-5; 2,4-dimethyl-3,5,6-trimethoxybenzyl chloride, 107301-82-6; 2,3,5-trimethoxy-1,4-dimethylbenzene, 92421-46-0; 2,5-dimethyl-3,4,6-(trimethoxy)benzyl chloride, 107301-83-7; 2,3,5-trimethoxy-4,6-dimethylbenzyl(trimethyl)silane, 107301-84-8; chlorobis(triphenylphosphine)maleoylcobalt complex, 92421-25-5; *p*-quinone, 106-51-4; 2-butyne, 503-17-3.

# Mechanisms of Hemin-Catalyzed Epoxidations: Electron Transfer from Alkenes

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**Abstract:** Two rearrangements of alkenes, known to proceed through the intermediacy of the alkene cation radical, have been observed to accompany the hemin-catalyzed epoxidations of these alkenes. Hexamethyl(Dewar benzene) partially rearranged to hexamethylbenzene during its epoxidation using (tetraphenylporphyrinato)iron(III) chloride and *m*-chloroperbenzoic acid, but not with either of the reagents separately. In a similar manner the diene, 1,4,4a,5,8,8a-hexahydro-1,4,5,8-*endo*,*endo*-dimethanonaphthalene, closed to the known "birdcage hydrocarbon" under these conditions. This diene also brought about some N-alkylation of the catalyst during the reaction. These observations are interpreted in terms of an electron transfer from alkene to the high-valent iron intermediate, leading to both rearrangement and epoxidation.

It is generally agreed that an iron(IV) porphyrin cation radical ($Fe^+{=}O$, oxene) is an intermediate in epoxidation and hydroxylation reactions catalyzed by cytochromes P-450 or by model iron(III) porphyrins.[1-5] The first step in the reaction of the oxene

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