5.31 (s, 2 H), 4.33 (q, J = 7 Hz, 2 H), 1.52 (t, J = 7 Hz, 3 H); IR 2220 (m), 1595 (m), 1440 (s), 1150 (s); MS, m/e 285 (EI); exact mass calcd for $C_{16}H_{11}ClNO_2$ 285.0556, found 285.0553.

2-Chloro-4-cyano-3-ethoxy-1-hydroxydibenzofuran (37). A solution of 0.25 g (0.70 mmol) of **33d** and 0.10 mL (0.77 mmol) of trimethylsilyl chloride in 75 mL of dry CCl_4 was added dropwise to 300 mL of refluxing CCl_4. The solution was heated at reflux for 1.5 h and then concentrated. The residue was absorbed on to silica gel and subjected to flash chromatography (1:1 hexanes/ethyl acetate) to give 0.15 g (76%) of off-white crystals (37): mp 214-215 °C; ^1H NMR 8.06 (d, J = 6 Hz, 1 H), 7.62 (d, J = 6 Hz, 1 H), 7.38-7.51 (m, 2 H), 6.63 (br s, 1 H), 4.43 (q, J = 6 Hz, 2 H), 1.54 (t, J = 6 Hz, 3 H); IR 3340 (br), 2240 (m), 1600 (s), 1450 (m), 1200 (m), 1165 (s); MS, m/e 287 (EI); exact mass calcd for $C_{15}H_{10}ClNO_3$ 287.03491, found 287.0340.

Acknowledgment. We thank the National Institutes of Health (CA-11890) for financial support of this work.

Synthesis of Alkynyl Quinones and Related Compounds

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A general synthetic route to alkynyl-substituted 1,4- and 1,2-benzoquinones is presented. This involves the 1,2-addition of lithium acetylides to a variety of alkoxy quinones followed by hydrolysis of the 3-hydroxy enol ether moiety of the resulting quinols. The use of these quinols and alkynyl quinones in the synthesis of various aromatic phenols and potential bioreductive alkylating agents is also presented.

Previously we reported a new method for the synthesis of 2,5-dialkylated-1,4-benzoquinones.[1] This involves treating a 2,5-dialkoxy-1,4-benzoquinone with 1 equiv of a lithium acetylide followed by a second equivalent of the same or a different lithium reagent and subsequent hydrolysis of the resulting adduct. At this time we report an expansion of this work that further illustrates the general synthetic scope.[2] Specifically, this methodology is shown to provide a simple and efficient procedure for the construction of a variety of alkynylated benzoquinones from readily available haloalkoxy quinones.[3] Such products are of interest since, as a class of compounds, alkynyl quinones have received very little attention[4] and its members represent useful precursors to a variety of other quinones and aromatic systems by taking advantage of the synthetically versatile alkyne moiety.[5] Our specific interest in developing synthetic routes to these quinones stems from their potential utility as precursors to bioreductive alkylating agents,[6] to 3-azido-4-alkynyl-1,2-benzoquinones, which are easily converted to cyanophenols,[7] to 2,5-dialkynyl-3,6-diazido-1,4-benzoquinones, which give (alkynylcyano)ketenes upon thermolysis,[8] and to polyalkynyl quinones, which might show unusual electronic properties. Outlined below are the details of this study.

Synthesis of Alkynyl Quinones. In general, the methodology described here rests on a well-known carbonyl transposition sequence involving initial 1,2-addition of an organometallic reagent to the carbonyl group of 3-alkoxy enones. Subsequent acid hydrolyses of the resulting adducts results in 3-substituted enones. A particularly useful example of this reaction sequence as it applies to synthetic routes to substitued quinones is given in Scheme I. Here, 4,5-dimethoxy-1,2-benzoquinone (1)[9] was treated with a variety of lithium acetylides to give excellent yields (70-95%) of the corresponding 6-alkynyl-6-hydroxy-3,4-

Table I. Atomic Parameters for 1,2-Bis(phenylethynyl)-4,5-dimethoxy-3,5-cyclohexadiene-1,2-diol (2a) with Standard Deviations in Parentheses

atom	x	y	z
C(01)	0.1766 (1)	0.1638 (1)	0.0187 (2)
C(02)	0.2011 (1)	0.1260 (1)	0.1689 (2)
C(03)	0.2158 (1)	0.0476 (1)	0.1543 (2)
C(04)	0.1854 (1)	0.0115 (1)	0.0350 (2)
C(05)	0.1369 (1)	0.0469 (1)	-0.0878 (2)
C(06)	0.1300 (1)	0.1177 (1)	-0.0933 (2)
C(07)	0.1509 (1)	0.2351 (1)	0.0351 (2)
C(08)	0.1361 (1)	0.2949 (1)	0.0506 (2)
C(09)	0.1197 (1)	0.3679 (1)	0.0689 (2)
C(10)	0.0812 (2)	0.3827 (2)	0.1461 (4)
C(11)	0.0677 (2)	0.4557 (3)	0.1639 (5)
C(12)	0.0930 (2)	0.5099 (2)	0.1076 (5)
C(13)	0.1306 (2)	0.4948 (2)	0.0359 (4)
C(14)	0.1441 (1)	0.4241 (1)	0.0149 (3)
C(15)	0.2587 (1)	0.1628 (1)	0.2608 (3)
C(16)	0.3072 (1)	0.1910 (1)	0.3268 (3)
C(17)	0.3665 (1)	0.2253 (1)	0.3995 (3)
C(18)	0.3763 (1)	0.2681 (2)	0.5197 (3)
C(19)	0.4328 (1)	0.3030 (2)	0.5822 (4)
C(20)	0.4779 (1)	0.2949 (2)	0.5288 (3)
C(21)	0.4713 (1)	0.2517 (2)	0.4106 (3)
C(22)	0.4147 (1)	0.2172 (1)	0.3455 (3)
C(23)	0.2402 (1)	-0.0971 (1)	0.1235 (3)
C(24)	0.0651 (1)	0.0267 (2)	-0.3259 (3)
O(01)	0.2277 (1)	0.1744 (1)	-0.0316 (2)
O(02)	0.1519 (1)	0.1336 (1)	0.2256 (2)
O(03)	0.1939 (1)	-0.0590 (1)	0.0089 (2)
O(04)	0.1028 (1)	-0.0016 (1)	-0.1881 (2)

(1) Moore, H. W.; Sing, Y. L.; Sidhu, R. S. *J. Org. Chem.* **1980**, *45*, 5057.
(2) Part of this work has appeared in preliminary form. See: Moore, H. W.; West, K. F. *J. Org. Chem.* **1982**, *47*, 3591.
(3) Most of the halo alkoxy quinones used here have only recently become available from methods developed in our laboratory. Wriede, U.; Fernandez, M.; Moore, H. W. *J. Org. Chem.*, in press.
(4) Shvartsberg, M. S.; Romanov, V. S.; Bel'chenko, O. I.; Schastnev, P. V.; Moroz, A. A. *Izv. Akad. Nauk. SSSR, Ser. Khim.* **1985**, *4*, 842.
(5) *The Chemistry of the Carbon-Carbon Triple Bond*; Patai, S., Ed.; Wiley and Sons: New York, 1978, Vol. 1, 2.
(6) Moore, H. W. *Science (Washington, D.C.)* **1977**, *197*, 527. Moore, H. W.; Czerniak, R. *Med. Res. Rev.* **1981**, *1*, 249.
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(9) Itoh, Y.; Kakuta, T.; Herano, M.; Morimoto, T. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 2169. Wanzlick, H.; Janke, Y. *Chem. Ber.* **1968**, *101*, 3744.

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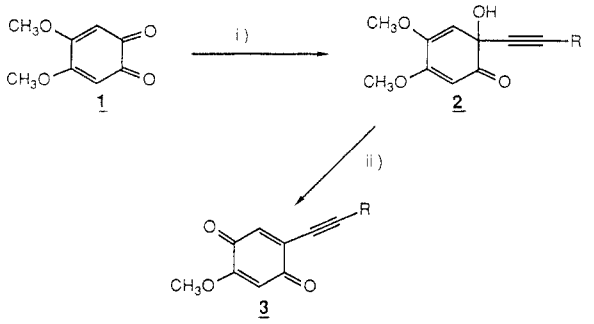
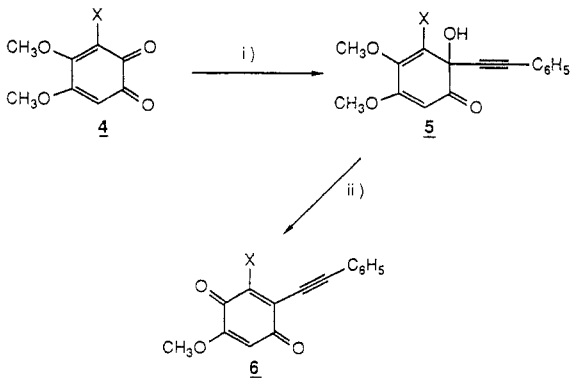
Scheme I



i) Li-C≡CR/ THF/-78°C, NH_4Cl (aq). ii) H_2SO_4 (aq).

	R	%2	%3
a)	$-C_6H_5$	95	97
b)	$-CH_2OCH_2C_6H_5$	95	92
c)	$-CH_2(CH_2)_2CH_3$	94	94
d)	$-CO_2C_2H_5$	92	94
e)	$-(CH_2)_4C{\equiv}CH$	71	85
f)	$-C(CH_3){=}CH_2$	90	94
g)	-H	70	94

Scheme II



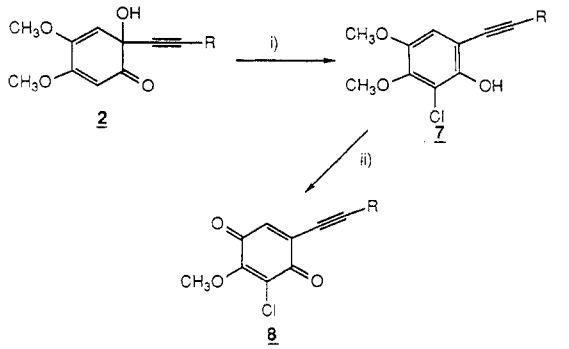
i) Li-C≡CC_6H_5/THF / -78°C . NH_4Cl (aq). ii) $(CF_3CO)_2O$ / H^+

	X	%5	%6
a)	Cl	81	96
b)	Br	97	84

dimethoxy-2,4-cyclohexadienones **2a–g**. Hydrolysis of these adducts with dilute sulfuric acid resulted in their conversion to the corresponding 2-alkynyl-5-methoxy-1,4-benzoquinones **3a–g** in isolated yields of 85–97%.[2]

This reaction sequence was extended to include 4,5-dimethoxy-3-chloro(and bromo)-1,2-benzoquinones **4a,b**[3] (Scheme II). For these quinones, the regioselectivity of the alkynylation step was of key interest. Specifically, would attack of the acetylide carbanions take place at the less hindered C-1 carbonyl or at the more electrophilic C-2 position? The electronic effect was observed to control the reaction in that quinols **5a,b** were obtained in high yields. Hydrolysis of these gave the respective 2-halo-3-(phenylethynyl)-6-methoxy-1,4-benzoquinones **6a,b** in 94% and 84% yields. The regiochemistry of these quinones was established by comparison of the ^1H NMR spectrum of the 2-chloro isomer **6a** with its regioisomer **8a**,

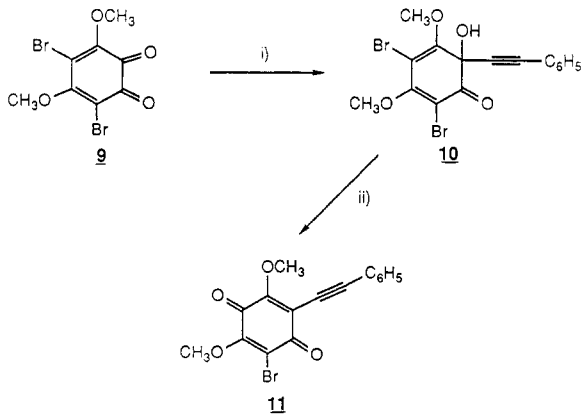
Scheme III



i) $SOCl_2$ / THF / 25°C . ii) $(NH_4)_2Ce(NO_3)_6$ / CH_3CN/ 25°C

	R	%7	%8
a)	$-C_6H_5$	80	89
b)	$-CH_2OCH_2C_6H_5$	83	73
c)	- n-C_4H_9	68	85

Scheme IV

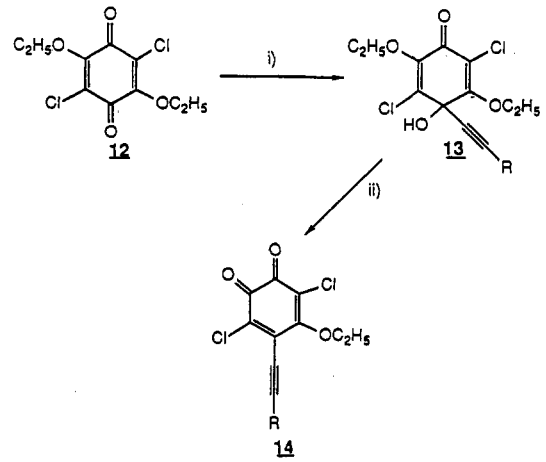


i) Li-C≡CC_6H_5 / THF / -78°C , NH_4Cl (aq). ii) $(CF_3CO)_2O$ / H^+

which was obtained by an independent synthesis. Specifically, this synthesis was accomplished by treating **2a–c** with thionyl chloride, which resulted in an interesting transformation to the chlorophenols **7a–c**. Oxidation of **7a** (CAN) gave **8a** (Scheme III). The chemical shift of the quinoid vinyl proton in **8a** appears at lower field (δ 6.85) than that of **6a** (δ 5.99). This is, of course, expected from the assigned structures since the vinyl proton in **6a** is in direct conjugation with the electron-donating methoxy group and thus would experience the observed up-field shift.

A further instructive example regarding the regiochemistry of alkynylation is given in Scheme IV. Here, 3,5-dibromo-4,6-dimethoxy-1,2-benzoquinone (**9**)[3] was subjected to the reaction sequence outlined above using the lithium salt of phenylacetylene. Attack takes place at the nonvinylogous ester carbonyl (position-1) to give the quinol **10** as evidenced by the fact that hydrolysis of the crude product gave 2-bromo-3,5-dimethoxy-6-(phenylethynyl)-1,4-benzoquinone (**11**) (72%) rather than the dibromoquinone, 2,6-dibromo-5-methoxy-3-(phenylethynyl)-1,4-benzoquinone. It is of no further interest to note that this is a unique example in this study since it illustrates hydrolysis of the β-hydroxyvinyl bromide moiety of **10**. Thus,

Scheme V



i) Li-C≡CR / THF / -78°C , NH_4Cl(aq). ii) $(CF_3CO)_2O$ / H^+

	R	%13	%14
a)	-C_6H_5	78	80
b)	-n-C_4H_9	86	69
c)	-$C(CH_3)=CH_2$	74	85
d)	-C_6H_4-o-OCH_3	80	80
e)	-C_6H_4-o-CH_3	72	77
f)	-$CH=CHC_6H_5$	75	78
g)	-$CH_2CH_2C_6H_5$	76	64
h)	-$C_{10}H_7$(d-naphthyl)	66	83
i)	-$(CH_2)_4C\equiv CH$	57	57
j)	-$CO_2C_2H_5$	68	68
k)	-H	79	79
l)	-CH_2OTHP	97	56

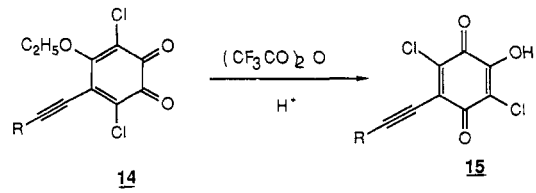
the potential general utility of this structural unit could compliment the β-hydroxy enol ether moiety hydrolysis that was generally employed throughout this investigation.

A particular interest in our laboratory is an investigation of the thermal chemistry of 3-azido-4-alkynyl-1,2-benzoquinones.[7] As a result, synthetic routes to the azido quinone precursors have become an important objective. Ideal precursors are the corresponding 3-chloro-4-alkynyl-1,2-benzoquinones, and outlined in Scheme V is a general route to one such class of compounds. Specifically, treatment of the readily available 2,5-dichloro-3,6-diethoxy-1,4-benzoquinone (**12**) with a variety of lithium acetylides gave the quinols **13a–l** in good to excellent yield. Their subsequent hydrolysis resulted in the corresponding 1,2-benzoquinones **14a–l**. This provides a very convenient route to these compounds, which are now under study as precursor to a variety of highly substituted aromatic molecules as well as to (2-alkynylethenyl)ketenes via the azido quinone thermolyses.[7]

When the quinols **13** were subjected to the above hydrolysis for approximately 3 h, the resulting 1,2-quinones **14** suffered further hydrolysis to give good yields of the 2-alkynyl-3,6-dichloro-5-hydroxy-1,4-benzoquinones **15a–f** (Scheme VI).

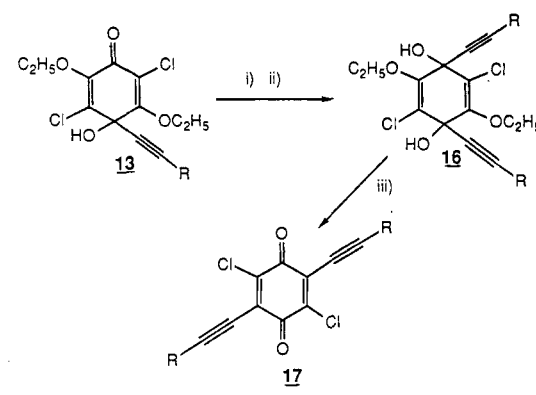
We have previously reported that treatment of the quinone **12** with 2 equiv of the lithium salts of phenylethyne or 1-hexyne give the corresponding diadducts.[1] Subsequent studies in our laboratory have revealed a limitation to this method. Specifically, alkynes that are more bulky than the above often give only the monoadducts **13** or, at best, poor yields of the diadducts. We have now

Scheme VI



	R	%15
a)	-C_6H_5	85
b)	-n-C_4H_9	74
c)	-$C(CH_3)=CH_2$	76
d)	-$(CH_2)_4C\equiv CH$	81
e)	-$CO_2C_2H_5$	75
f)	-H	77

Scheme VII



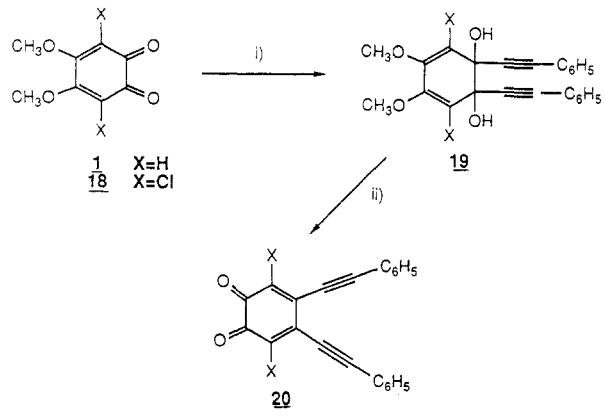
i) NaH / THF ii) Li-C≡CR / THF. iii) $(CF_3CO)_2O$ / H^+

	R	%16	%17
a)	-$CH_2CH_2C_6H_5$	50	73
b)	-$C(CH_3)=CH_2$	93	63
c)	-CH_2OTHP	92	55
d)	-C_6H_4-o-OCH_3	63	83
e)	-C_6H_4-o-CH_3	76	42

found a way to circumvent this limitation by employing the sodium rather than the lithium salt of **13**. Specifically, treatment of **13** with sodium hydride followed by the lithium acetylide reagent give good yields of the diadducts **16a–e** (Scheme VII). These, in turn, are conveniently hydrolyzed to the corresponding 2,5-dichloro-3,6-dialkynyl-1,4-benzoquinones **17a–e**. The reasons for the higher reactivity of the alkoxide of **13** when the sodium counterion is present are not understood. However, it is assumed that this is due to a less aggregated and therefore less sterically congested form of the alkoxide.

The above route to 2,5-dialkynyl-1,4-benzoquinones **17** suggested a strategy for the synthesis of other regioisomers. This was successfully accomplished as outlined in Schemes VIII and IX. The results outlined in Scheme VIII illustrate the dialkynylation of the 1,2-benzoquinones **1** or **18** to give respectively **19a** and **19b**, which upon hydrolysis provides the 4,5-dialkynyl-1,2-benzoquinones **20a,b**, the first examples of dialkynyl-1,2-benzoquinones. It is of interest to note that the alkynylation of **1** can be controlled

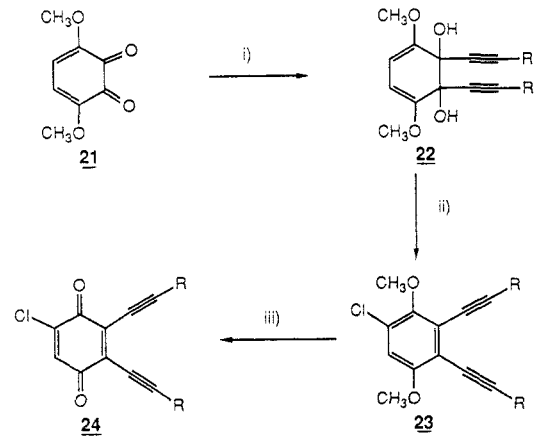
Scheme VIII



i) $Li\text{-}C{\equiv}CC_6H_5$ / THF / -78°C, NH_4Cl (aq). ii) $(CF_3CO)_2O$ / H^+

	X	%19	%20
a)	H	92	90
b)	Cl	78	41

Scheme IX



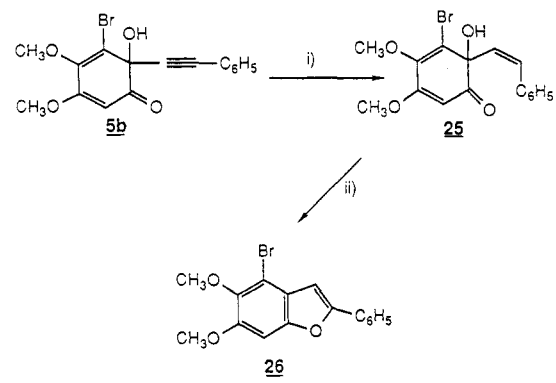
i) $Li\text{-}C{\equiv}CR$ / THF/ -78°C, AcOH/THF. ii) $SOCl_2$ / THF. iii) CAN / CH_3CN

R	%22	%23	%24
a) $-C_6H_5$	86	65	50
b) $-CH_2OCH_2C_6H_5$	84	73	48
c) $-n\text{-}C_4H_9$	92	75	54
d) $-CO_2C_2H_5$	90	60	NR

to give either the mono- or the diadducts, i.e. **2** or **19a**. In comparison, only diadduct **22** could be obtained from 3,6-dimethoxy-1,2-benzoquinone (**21**) when it was treated with lithium acetylides under a variety of conditions (Scheme IX).[10] Also, hydrolysis of **22** under the conditions used above gave only low yields of the corresponding quinones. However, treatment of **22** with thionyl chloride in THF in the presence of pyridine gave the 1,2-di-

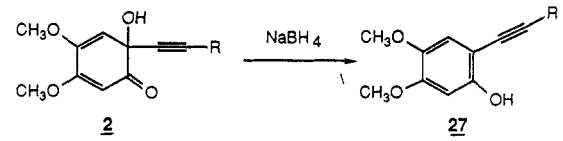
(10) This difference in reactivity is presumably due to the fact that vinylogous ester carbonyl groups have less extended conjugation to the methoxy group in **1** than in **21**. Thus, the former is less reactive and more selective in its reactions with the acetylide anion than the latter. See ref 3 for the synthesis of **21**.

Scheme X



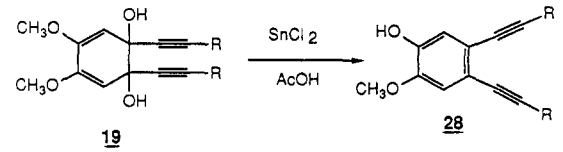
i) Pd / $BaSO_4$ / H_2 / ETOAc. ii) $(CF_3CO)_2O$ / H^+

Scheme XI



R	%27
a) $-C_6H_5$	95
b) $-n\text{-}C_4H_9$	91
c) $-C(CH_3)_2OH$	86

Scheme XII



R	%28
a) $-C_6H_5$	81
b) $-n\text{-}C_4H_9$	79

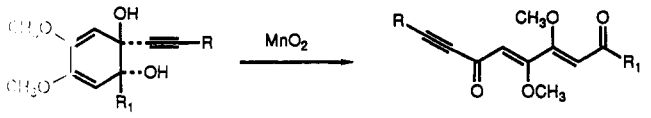
alkynyl-4-chloro-3,6-dimethoxybenzenes **23a–d**. Examples of 2,3-dialkynyl-1,4-benzoquinones **24a–c** were then prepared by treating **23a–c** with ceric ammonium nitrate.

Taken together, the reaction sequences outlined in Schemes I–IX illustrate the scope of the alkynyl quinone synthetic methodology. Some selected examples to illustrate the synthetic utilization of these quinones and their quinol precursors are now presented.

Chemistry of Alkynyl Quinones and Their Quinol Precursors. An unusual result was obtained from a study of the hydrolysis of **25**, a quinol readily obtained from the reduction of the alkyne moiety in **5b** (Scheme X). Specifically, when **25** was subjected to the hydrolytic conditions ($(CF_3CO)_2O/H^+$) normally employed in the preparation of the alkynyl quinones, the benzofuran **26** rather than the expected alkenyl quinone was obtained in excellent yield (88%). The facility of this route to **26** suggests a potentially general route to such heterocyclic compounds.

An established synthetic route to benzofurans employs ring closure of 2-alkynylphenols under basic conditions.[11]

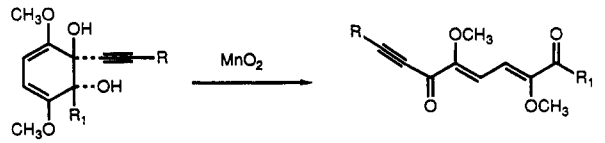
Scheme XIII



19 29

	R	R_1	% Yield
a)	$-C_6H_5$	$-C_6H_5$	87
b)	$-C_4H_9$	$-C_4H_9$	80
c)	-H	-H	83
d)	$-C_4H_9$	$-CH_3$	88

Scheme XIV



22 30

	R	R_1	% Yield
a)	$-C_6H_5$	$-C_6H_5$	84
b)	$-CH_2OCH_2C_6H_5$	$-CH_2OCH_2C_6H_5$	83
c)	$-C_4H_9$	$-C_4H_9$	71
d)	$-CO_2C_2H_5$	$-CO_2C_2H_5$	78
e)	$-CH_2OCH_3$	$-CH_2OCH_3$	67
f)	-H	-H	56

A general synthesis of a variety of such precursors was envisaged to arise via a reductive dehydration of many of the quinols described in this paper. This was successfully accomplished and an illustration of this transformation is given in Scheme XI. Here the quinols **2a–c** were converted in excellent yields to the alkynylphenols **27a–c** upon treatment with sodium borohydride.

Still another route to alkynylphenols was discovered when the cyclohexadienediols **19** were treated with stannous chloride in acetic acid (Scheme XII).[12] This results in the formation of 3,4-dialkynyl-6-methoxyphenols **28a,b**.

An unusual class of highly substituted dienes are available from the diols **19** and **22** upon oxidative cleavage with activated MnO_2 (Schemes XIII and XIV). Specifically, treatment of 4,5-dimethoxy-1,2-benzoquinone (**1**) and 3,6-dimethoxy-1,2-benzoquinone (**21**) with the corresponding lithium reagent(s) in THF at −78 °C gave the respective cyclohexadienediols **19** and **22** in yields ranging from 76% to 92%. The stereochemistry of all of these compounds is assumed to be trans. This is based upon an unambiguous determination of the structure of one example, **19a**, by single-crystal X-ray analysis (Figure 1). Treatment of a methylene chloride solution of the diols **19a–d** and **22a–f** with a large molar excess of activated MnO_2[13] gave the respective enynes **29a–d** and **30a–f** as single stereoisomers. These products show spectral

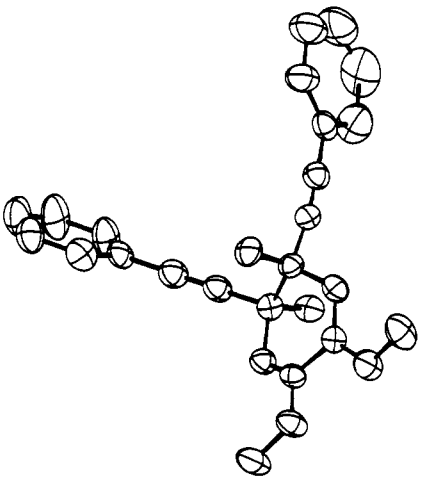
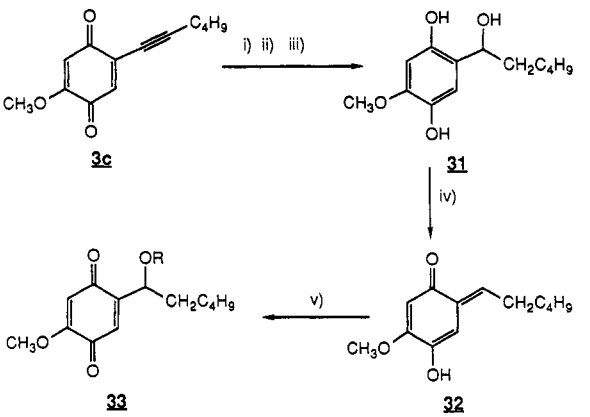


Figure 1. ORTEP view of 1,2-bis(phenylethynyl)-4,5-dimethoxy-3,5-cyclohexadiene-1,2-diol (**19a**).

Scheme XV



i) $Na_2S_2O_4$. ii) H_2SO_4 / H_2O. iii) $NaBH_4$. iv) $FeCl_3$/ ROH
v) ROH / oxidation.

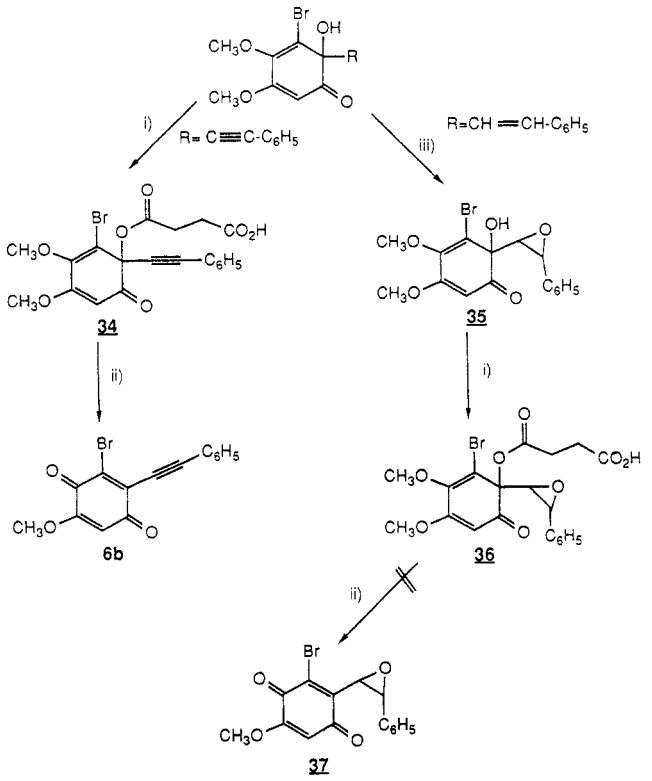
	R	%33
a)	-H	88
b)	$-C_2H_5$	65
c)	$-COCH_3$	85

properties in agreement with their assigned structures. For members of the **19** series, a single methoxy absorption appears in their individual ^1H NMR spectrum in the range of δ 3.75–3.81. The chemical shifts of the vinyl proton on the trisubstituted double bond are also singlet absorptions and appear in the range of δ 5.60–5.86. The chemical shift range for the analogous functionality of members of the regioisomeric series **30** is δ 3.71–3.75 and δ 7.15–7.40, respectively. The *E,E* stereochemistry for both series was not established but is assumed to be as indicated on the basis of the structures of the starting diols.

Finally, we illustrate the utility of alkynyl quinones as synthetic precursors to potential bioreductive alkylating agents.[6] Such agents are pro-drugs, which are assumed to express their biological action as potent alkylating agents, but only upon reductive activation within the hypoxic cells of solid tumors.[14] As this applies to quinones, compounds

(11) Ried, W. *Angew. Chem.* **1964**, *24*, 973.
(12) For analogous conversion of dialkynylcyclohexadienediols to dialkynylbenzenes, see: Rutledge, T. *Acetylenic Compounds*; Reinhold Book Corp.: New York, 1968; p 223; Reid, W.; Wesselborg, K. *Naturwissenschaften* **1959**, *46*, 142.
(13) Fataida, A. *Synthesis* **1976**, 65. See also: Ohloff, G.; Giersch, W. *Angew. Chem., Int. Ed. Engl.* **1973**, 401.
(14) For an excellent review on reductive activation at the hypoxic level of solid tumor, see: Denny, W. A.; Wilson, W. R. *J. Med. Chem.* **1986**, *29*, 879.

Scheme XVI



i) Succinic anhydride. ii) $NaHCO_3$ / H_2O. iii) m-CPBA.

of structural type **33** are reasonable candidates (Scheme XV). That is, reduction of such compounds to the corresponding hydroquinones followed by an elimination of ROH would give a quinone methide, i.e., **32**. Such reactive intermediates could then function as alkylating agents via Michael addition of a biologically important nucleophile (DNA, protein, etc.) to the resulting enone. An example of the synthesis of quinones of the bioreduction alkylation type is outlined in Scheme XV. Here, the alkynyl quinone **3c** was converted to the hydroquinone **31** via dithionite reduction and hydration of the resulting alkynyl hydroquinone. Subsequent borohydride reduction gave **31**, which was converted directly to **33a–c** upon ferric chloride oxidation. The conversion of **31** to **33** is viewed as involving a Lewis acid assisted dehydration to the quinone methide **32**. Michael addition of ROH and subsequent oxidation would then afford the quinones **33a–c**.[15]

Further studies on pro-drug design are outlined in Scheme XVI. The first example is the successful preparation of a water-soluble compound that would undergo facile hydrolysis to give a Michael acceptor. Conceptually, such molecules could take advantage of the reported lower pH of solid tumors[16] to enhance the hydrolysis step and thus provide increased concentrations of the alkylating agent within the confines of the tumor. An example that is chemically consistent with this idea is **34**, which is obtained from **5b** in 76% yield upon treatment with succinic anhydride. At ambient temperature compound **34** is readily soluble in a volume of water containing 1 equiv of sodium bicarbonate. Within the initial 2-min period the quinone **6b** begins to precipitate from solution as orange crystals. After 10 min 71% of **6b** was isolated. Thus, the concept of developing pro-drugs related to **34** is at hand since the aqueous solubility and facile hydrolysis of such compounds is readily obtainable. Indeed, the ease of hydrolysis of **34** suggests a probable need to retard this step in order to obtain good drug distribution.

A potential pro-pro-drug is given by structure **36** (Scheme XVI). Here, in vivo hydrolysis of **36** would give the corresponding epoxy quinones **37**. Bioreduction of this would be expected to readily result in quinone methide formation.[17] As a result, such compounds might show significant selective toxicity to solid tumors since both a site-selective hydrolysis and a bioreduction are needed for activation. Synthesis of **36** was accomplished via *m*-CPBA epoxidation of **5b** to give **35** (26%) followed by succinylation to the target molecule **36** (66%). Interestingly, unlike **34**, this compound was stable for several hours when dissolved in water containing an equivalent of sodium bicarbonate. Thus, its hydrolytic "activation" may be too slow while that of **34** is too rapid. Clearly, additional synthetic design studies as well as biological evaluations are needed, and these are in progress.

In conclusion, we note the following significant points concerning this study: (1) the alkynylation of variously substituted halo alkoxy quinones is a general and usually high-yielding reaction; (2) the resulting quinols are useful precursors to a variety of substituted quinones and aromatic compounds; (3) the potential utilization of these compounds to synthesize a variety of molecules within the freamework of bioreductive alkylating agents is now possible.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary apparatus or a Fisher-Jones apparatus and are uncorrected. Microanalyses were performed by Robertson's Laboratory, Florham Park, NJ. ^1H NMR and ^{13}C NMR spectra were obtained on Varian EM 360, Varian FT-80, or Bruker WM-250 spectrometers. All NMR spectra were run in $CDCl_3$ and are reported relative to the internal standard tetramethylsilane (Me_4Si) as values in parts per million, unless otherwise specified. Coupling constants (J) are apparent unless otherwise stated and are reported by using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Infrared spectra were determined with a Perkin-Elmer 137 spectrometer. The positions of the absorption bands are expressed in cm^{-1} and polystyrene was used as an external reference. Mass spectra were determined on a medium resolution Finnigan 4000 GC/MS quadrupole spectrometer, which was interfaced to a Nova 312 data system. High-resolution mass spectra were run on a VG 7070E-HF mass spectrometer.

Commercial organolithium reagents were titrated according to the method of Whiteside et al.[18] Emmerie–Engel reagent[19] was used as a spot test for hydroquinones. Leuco-methylene blue[20] was freshly prepared and used as a spot test for the quinone moiety.

(15) For examples of the chemistry of quinone methide, see: Wagner, H. V.; Gompper, R. "Quinone Methides" in *The Chemistry of the Quinonoid Compounds*; Patai, S., Ed.; Wiley and Sons: New York, 1974; p 1145. Benson, M.; Jurd, L. *Org. Magn. Reson.* **1984**, *22*(2), 86. Jurd, L.; Wang, R. Y. *Aust. J. Chem.* **1981**, *34*(8), 1633. Jurd, L. *Ibid.* **1980**, *33*, 1603. Jurd, L.; Wang, R. Y. *Ibid.* **1980**, *33*, 137. Jurd, L.; Roitman, J. N. *Tetrahedron* **1979**, *35*, 1567. Jurd, L.; Roitman, J. N. *Ibid.* **1979**, *35*, 1041. Jurd, L.; Roitman, J. N. *Ibid.* **1978**, *34*, 57.

(16) Hinsall, S. M.; Colson, R. H.; Franklin, A.; Watson, B. W.; Bellamy, D. *J. Natl. Cancer Inst.* **1984**, *73*, 463. Jain, R. K.; Shah, S. A.; Finney, P. L. *Ibid.* **1984**, *73*, 429. See also ref 14.

(17) In unpublished work we have prepared epoxy quinones analogous to **34** and have found them to readily give quinone methide products upon reduction.

(18) Whitesides, G.; Casey, C.; Krieger, J. *J. Am. Chem. Soc.* **1971**, *93*, 1379.

(19) Quaife, M.; Harris, P. *J. Biol. Chem.* **1944**, *156*, 499.

(20) Lin, B.; Page, A.; Wong, E.; Ciale, P.; Shank, C.; Folkers, K. *J. Biol. Chem.* **1959**, *81*, 4007.

3,4-Dimethoxy-6-hydroxy-6-(phenylethynyl)-2,4-cyclohexadienone (2a). The following experimental procedure for the synthesis of **2a** is representative of that used for the preparation of all quinols reported in this manuscript. As a result, the details are given only for this one example. A solution of 729 mg (7.14 mmol) of phenylacetylene in 75 mL of dry THF, under an argon atmosphere, was stirred at −78 °C while 4.56 mL of *n*-butyllithium (1.5 M in hexane) was added dropwise. The solution was stirred for 30 min and then transferred slowly dropwise, via cannula, to a rapidly stirred suspension of 1.00 g (5.95 mmol) of 4,5-dimethoxy-1,2-benzoquinone (**1**), in 400 mL of dry THF at −78 °C. The stirring was continued at −78 °C for 1 h and the reaction quenched with 200 mL of 2 M aqueous ammonium chloride. The organic layer was removed and the aqueous layer washed twice with 50 mL of dichloromethane. The organic layers were combined, dried, and concentrated. The residue was absorbed onto silica gel and subjected to flash chromatography (1:1 hexane/ethyl acetate) to give the product as a white solid (95%), which was recrystallized from diisopropyl ether: mp 125–126 °C; ^{1}H NMR 3.84 (s, 3 H), 3.90 (s, 3 H), 3.95 (br s, 1 H), 5.52 (s, 2 H), 7.35 (m, 5 H); IR 3460 (s), 3307 (s), 2205 (s), 1661 (s), 1583 (s), 751 (s), 683 (s); MS, *m/e* 271 (CI).

Anal. Calcd for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 71.19; H, 5.32.

6-[3-(Benzyloxy)-1-propynyl]-3,4-dimethoxy-6-hydroxy-2,4-cyclohexadienone (2b): cream-colored solid (95%, diisopropyl ether); mp 125.5–126.5 °C; ^{1}H NMR 3.70 (s, 3 H), 3.83 (s, 3 H), 4.10 (s, 1 H), 4.14 (s, 2 H), 4.53 (s, 2 H), 5.45 (s, 1 H), 5.50 (s, 1 H), 7.30 (s, 5 H); IR 3375 (s), 1640 (s), 1580 (s), 730 (s), 688 (s); MS, *m/e* 314 (EI).

Anal. Calcd for $C_{18}H_{18}O_5$: C, 68.79; H, 5.77. Found: C, 68.94; H, 6.01.

3,4-Dimethoxy-6-hexynyl-6-hydroxy-2,4-cyclohexadienone (2c): white solid (94%, diisopropyl ether); mp 83–84 °C; ^{1}H NMR 0.86 (m, 3 H), 1.41 (m, 6 H), 2.15 (m, 2 H), 3.73 (s, 4 H), 3.87 (s, 3 H), 5.44 (s, 1 H), 5.48 (s, 1 H); IR 3435 (s), 2205 (s), 1650 (s), 1582 (s).

Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.09; H, 7.05.

6-(Carbethoxyethynyl)-3,4-dimethoxy-6-hydroxy-2,4-cyclohexadienone (2d): white solid (92%, diisopropyl ether); mp 102–103 °C; ^{1}H NMR 1.30 (t, J = 7 Hz, 3 H), 3.76 (s, 3 H), 3.97 (s, 1 H), 4.23 (q, J = 7 Hz, 2 H), 5.43 (s, 1 H), 5.55 (s, 1 H); IR 3450 (s), 2215 (s), 1720 (s), 1659 (s), 1580 (s); MS, *m/e* 267 (CI).

Anal. Calcd for $C_{13}H_{14}O_6$: C, 58.64; H, 5.30. Found: C, 58.72; H, 5.29.

3,4-Dimethoxy-6-hydroxy-6-(1-octa-1,7-diynyl)-2,4-cyclohexadienone (2e): white solid (71%, aqueous ethanol); mp 114.8–115.2 °C; ^{1}H NMR 1.16 (m, 4 H), 2.01 (t, J = 4 Hz, 1 H), 2.27 (m, 4 H), 3.81 (s, 4 H), 3.95 (s, 3 H), 5.53 (s, 1 H), 5.56 (s, 1 H); IR 3330 (br), 3270 (s), 1582 (s); MS, *m/e* 275 (CI).

Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 70.22; H, 6.79.

2,4-Dimethoxy-6-hydroxy-6-(3-methylbutenynyl)-2,4-cyclohexadienone (2f): white solid (90%, diisopropyl ether); mp 123.5–124 °C; ^{1}H NMR 1.67 (t, J = 1 Hz, 3 H), 3.57 (s, 3 H), 3.67 (s, 1 H), 3.71 (s, 3 H), 5.13 (m, 2 H), 5.29 (s, 1 H), 5.33 (s, 1 H); IR 3202 (s), 2208 (w), 1650 (s), 1580 (s); MS, *m/e* 235 (CI).

Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02. Found: C, 66.55; H, 6.07.

3,4-Dimethoxy-6-ethynyl-6-hydroxy-2,4-cyclohexadienone (2g): white solid (70%, diethyl ether); mp 133–134 °C; ^{1}H NMR 2.54 (s, 1 H), 3.74 (s, 3 H), 3.88 (s, 3 H), 4.08 (br s, 1 H), 5.46 (s, 1 H), 5.53 (s, 1 H); IR 3450 (s), 3271 (s), 1642 (s), 1582 (s); MS, *m/e* 195 (CI).

Anal. Calcd for $C_{10}H_{10}O_4$: C, 61.92; H, 5.38. Found: C, 61.85; H, 5.38.

5-Methoxy-2-(phenylethynyl)-2,5-cyclohexadiene-1,4-dione (3a). The following procedure is representative of the hydrolysis of the quinols **2** to the quinones **3**. A solution of 1.00 g (3.70 mmol) of 3,4-dimethoxy-6-hydroxy-6-(phenylethynyl)-2,4-cyclohexadienone (**2a**) in 50 mL of ethyl acetate was stirred with 6 drops of 50% aqueous sulfuric acid for 1 h. The solution was washed with two 50-mL portions of 2% aqueous sodium bicarbonate. The organic layers were separated and the aqueous layers combined and washed with 50 mL of dichloromethane. The organic layers were combined and dried with anhydrous magnesium sulfate. The product was then absorbed onto silica gel. Flash chromatography (1:1 hexane/ethyl acetate) gave a yellow solid (97%), which was recrystallized from ethyl acetate: mp 171.0–171.8 °C; ^{1}H NMR 3.85 (s, 3 H), 5.98 (s, 1 H), 6.90 (s, 1 H), 7.45 (m, 5 H); IR 2205 (m), 1668 (s), 1650 (s), 1620 (m), 1582 (s), 764 (s), 685 (s); MS, *m/e* 238 (EI).

Anal. Calcd for $C_{15}H_{10}O_3$: C, 75.62; H, 4.23. Found: C, 75.57; H, 4.44.

2-[3-(Benzyloxy)-1-propynyl]-5-methoxy-2,5-cyclohexadiene-1,4-dione (3b): yellow solid (92%, ethyl acetate); mp 90.0–91.4 °C; ^{1}H NMR 3.83 (s, 3 H), 4.42 (d, J = 0.6 Hz, 2 H), 4.66 (s, 2 H), 6.82 (t, J = 0.6 Hz, 1 H), 7.35 (m, 5 H); IR 2213 (m), 1670 (s), 1645 (s), 1622 (s), 1597 (s), 750 (s), 690 (s); MS, *m/e* 177 (CI), 176 (EI) (M − PhCHO).

Anal. Calcd for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00. Found: C, 72.55; H, 5.27.

2-(1-Hexynyl)-5-methoxy-2,5-cyclohexadiene-1,4-dione (3c): yellow solid (94%, ethyl acetate); mp 90.0–91.5 °C; ^{1}H NMR 0.94 (m, 3 H), 1.50 (m, 4 H), 2.50 (t, J = 7.45 Hz, 2 H), 3.83 (s, 3 H), 5.93 (s, 1 H), 6.76 (s, 1 H); IR 2211 (m), 1663 (s), 1645 (s), 1623 (s), 1588 (s); MS, *m/e* 219 (CI).

Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.70; H, 6.66.

2-Carbethoxy-5-methoxy-2,5-cyclohexadiene-1,4-dione (3d): yellow oil (94%, decomposition on SiO_2); ^{1}H NMR 1.35 (t, J = 7 Hz, 3 H), 3.87 (s, 3 H), 4.30 (q, J = 7 Hz, 2 H), 6.02 (s, 1 H), 7.01 (s, 1 H); IR 2220 (m), 2100 (m), 1715 (s), 1682 (s), 1660 (s), 1624 (s), 1590 (s); MS, *m/e* 237 (CI), 236 (EI) (hydroquinone).

5-Methoxy-2-(1,7-octadiynyl)-2,5-cyclohexadiene-1,4-dione (3e): yellow solid (85%, methanol); mp 105–106 °C; ^{1}H NMR 1.80 (m, 4 H), 2.03 (t, 1 H), 2.31 (m, 1 H), 2.61 (m, 2 H), 3.88 (s, 3 H), 5.98 (s, 1 H), 6.82 (s, 1 H); IR 3250 (s), 2221 (m), 1663 (s), 1645 (s), 1624 (s), 1589 (s); MS, *m/e* 243 (CI).

Anal. Calcd for $C_{15}H_{14}O_3$: C, 74.36; H, 5.83. Found: C, 74.07; H, 5.79.

2-(2-Methylbutenynyl)-5-methoxy-2,5-cyclohexadiene-1,4-dione (3f): yellow solid (94%, hexane/ethyl acetate) which decomposes within a few days (The quinone is reasonably stable when kept in solution at 0°.); ^{1}H NMR 1.98 (m, 3 H), 3.83 (s, 3 H), 5.46 (m, 1 H), 5.54 (m, 1 H), 5.94 (s, 1 H), 6.80 (s, 1 H); IR 2198 (m), 1667 (s), 1623 (s), 1610 (s), 1575 (s); MS, *m/e* 202 (EI).

2-Ethynyl-5-methoxy-2,5-cyclohexadiene-1,4-dione (3g): yellow solid (94%, acetone/chloroform) (The compound was unstable and thus satisfactory elemental analyses could not be obtained.); ^{1}H NMR 3.82 (d, J = 0.6 Hz, 1 H), 3.93 (s, 3 H), 6.07 (s, 1 H), 6.07 (s, 1 H), 7.00 (d, J = 0.6 Hz, 1 H); IR 3240 (s), 2100 (m), 1670 (s), 1643 (s), 1622 (m), 1584 (s); MS, *m/e* 162 (EI).

3-Chloro-2-hydroxy-4,5-dimethoxy-2-(phenylethynyl)-3,5-cyclohexadienone (5a): yellow solid (81%, hexane/ethyl acetate); mp 111–112 °C; ^{1}H NMR 3.78 (s, 3 H), 3.86 (s, 3 H), 4.62 (br s, 1 H), 5.60 (s, 1 H), 7.22–7.41 (m, 5 H); IR 3310, 2205, 1670, 1565; MS (CI), *m/e* (relative intensity) 305/307 (M^+ + 1, 72.8/39.2).

Anal. Calcd for $C_{16}H_{13}ClO_4$: C, 63.06; H, 4.30. Found: C, 63.29; H, 4.42.

5-Bromo-6-hydroxy-4,5-dimethoxy-6-(phenylethynyl)-2,4-cyclohexadienone (5b): yellow solid (97%, hexane/ethyl acetate); mp 99–100 °C; ^{1}H NMR 3.78 (s, 3 H), 3.88 (s, 3 H), 4.58 (br s, 1 H), 5.68 (s, 1 H), 7.27–7.44 (m, 5 H); IR 3380, 2230, 1670, 1580; MS (CI), *m/e* (relative intensity) 349/351 (M^+ + 1, 25.6/30.3).

Anal. Calcd for $C_{16}H_{13}BrO_4$: C, 55.04; H, 3.75. Found: C, 55.10; H, 3.83.

3-Chloro-5-methoxy-2-(phenylethynyl)-2,5-cyclohexadiene-1,4-dione (6a). Hydrolysis of **5a** was accomplished by treating a toluene solution of the quinol with trifluoroacetic anhydride/trifluoroacetic acid (2/1) and heating at 65 °C for 1 h; orange solid (96%); mp 178–179 °C dec; ^{1}H NMR 3.86 (s, 3 H), 5.99 (s, 1 H), 7.35–7.49 (m, 3 H), 7.55–7.70 (m, 2 H); IR 2191, 1672, 1643, 1551; MS, *m/e* (relative intensity) (CI) 273/275 (M^+ + 1 100/83.3).

Anal. Calcd for $C_{15}H_9ClO_3$: C, 66.07; H, 3.33. Found: C, 65.89; H, 3.51.

3-Bromo-5-methoxy-2-(phenylethynyl)-2,5-cyclohexadiene-1,4-dione (6b): orange solid (84%); mp 187–188 °C; ^{1}H NMR 3.87 (s, 3 H), 6.00 (s, 1 H), 7.39–7.44 (m, 3 H), 7.64–7.67 (m, 2 H); IR 2200, 1690, 1565.

Anal. Calcd for $C_{15}H_9BrO_3$: C, 56.81; H, 2.86. Found: C, 56.67; H, 2.86.

2-Chloro-3,4-dimethoxy-6-(phenylethynyl)phenol (7a). The following procedure is representative of that used for the conversion of **2a–c** to the chlorophenols **7a–c**. A solution containing 3.4 mmol of **2a** in 50 mL of dry THF was treated with 3.7 mmol of pyridine and 3.7 mmol of thionyl chloride. After 2 h, the mixture was filtered through a bed of Celite and the solvent removed in vacuo. The residue was passed through a flash column (silica gel, hexanes–ethyl acetate, 7:3). Evaporation of the solvent yielded a colorless oil, which when triturated with diisopropyl ether gave 0.77 g (80%) of white crystals: mp 83–84 °C; ^{1}H NMR 3.85 (s, 3 H), 3.92 (s, 3 H), 5.76 (s, 1 H), 6.92 (s, 1 H), 7.45 (m, 5 H); IR 3542 (s), 2960 (w), 1500 (s), 1490 (s), 1365 (s), 1260 (s), 1120 (s), 1050 (s).

Anal. Calcd for $C_{16}H_{13}ClO_3$: C, 66.56; H, 4.53. Found: C, 66.46; H, 4.80.

6-[3-(Benzyloxy)-1-propynyl]-2-chloro-3,4-dimethoxyphenol (7b): colorless oil, 0.06 g (83%); ^{1}H NMR 3.90 (s, 3 H), 4.45 (s, 2 H), 4.68 (s, 2 H), 5.78 (s, 1 H), 6.83 (s, 1 H), 7.32 (m, 5 H); IR 3475 (br), 2980 (s), 2118 (w); exact mass calcd for $C_{18}H_{17}ClO_4$ 332.08152, found 332.0820.

2-Chloro-6-hexynyl-3,4-dimethoxyphenol (7c): colorless oil, 0.51 g (68%); ^{1}H NMR 0.95 (t, J = 7.5 Hz, 3 H), 1.55 (m, 4 H), 2.48 (t, J = 7.5 Hz, 2 H), 3.81 (s, 3 H), 3.87 (s, 3 H), 6.79 (s, 1 H); IR 3555 (s), 2975 (w), 2112 (w); exact mass calcd for $C_{14}H_{17}ClO_3$ 268.08661, found 268.0896.

2-Chloro-3-methoxy-6-(phenylethynyl)-2,5-cyclohexadiene-1,4-dione (8a). The following represents a typical procedure for the conversion of **7a–c** to **8a–c**. A solution of 0.7 mmol of **7a** in 5 mL of acetonitrile was treated with 1.4 mmol of ceric ammonium nitrate (CAN) dissolved in 2 mL of water. After 15 min, the mixture was diluted with 50 mL of water. The aqueous solution thus formed was extracted twice with dichloromethane (30 mL), the organic layers were combined and dried over $MgSO_4$, and the solvent was removed to yield orange solids that were recrystallized from diisopropyl ether to afford 0.16 g (89%) of orange crystals; mp 121–122 °C; ^{1}H NMR 4.26 (s, 3 H), 6.85 (s, 1 H), 7.4 (m, 3 H), 7.6 (m, 2 H); IR 2220 (s), 1670 (s), 1660 (s).

Anal. Calcd for $C_{15}H_9ClO_3$: C, 66.07; H, 3.32. Found: C, 65.97; H, 3.17.

2-Chloro-3-methoxy-6-[3-(benzyloxy)-1-propynyl]-2,5-cyclohexadiene-1,4-dione (8b): yellow oil, 0.20 g (85%); ^{1}H NMR 3.85 (s, 3 H), 4.45 (s, 2 H), 4.66 (s, 2 H), 6.80 (s, 1 H), 7.35 (m, 5 H); IR 2221 (m), 1675 (s), 1665 (s), 1611 (s), 1597 (s); exact mass calcd for $C_{17}H_{13}ClO_4$ 316.05021, found 316.05211.

2-Chloro-3-methoxy-6-hexynyl-2,5-cyclohexadiene-1,4-dione (8c): orange oil, 0.17 g (73%); ^{1}H NMR 0.94 (t, J = 7.2 Hz, 3 H), 1.45 (m, 4 H), 2.52 (t, J = 7.0 Hz, 2 H), 4.22 (s, 3 H), 6.71 (s, 1 H); IR 2215 (m), 1670 (s), 1660 (s), 1580 (s), 1210 (s), 1160 (s); exact mass calcd for $C_{13}H_{13}ClO_3$ 252.05531, found 252.05528.

6-Bromo-3,5-dimethoxy-2-(phenylethynyl)-2,4-cyclohexadiene-1,4-dione (11). The alkynylation of **9** was accomplished by the general procedure outlined above. However, because of the instability of the resulting quinol **10**, it was immediately hydrolyzed [$(CF_3CO)_2O/H^+$] to **11**: purple crystals (72%); mp 115.5–116 °C; ^{1}H NMR 4.15 (s, 3 H), 4.39 (s, 3 H), 7.30–7.55 (m, 5 H); IR 2210, 1690, 1665.

Anal. Calcd for $C_{16}H_{11}BrO_4$: C, 55.36; H, 3.19. Found: C, 55.34; H, 3.29.

2,5-Dichloro-3,6-diethoxy-4-(phenylethynyl)-4-hydroxy-2,5-cyclohexadienone (13a). The alkynyl derivatives **13a–l** were prepared according to the general procedures given for the synthesis of **2a–g**. **13a**: yellow solid (78%, hexane/dichloromethane); mp 104–106 °C; ^{1}H NMR 7.33–7.48 (m, 5 H), 4.72–4.84 (m, 2 H), 4.13–4.19 (m, 2 H), 3.76 (s, 1 H), 1.49 (t, J = 7 Hz, 3 H), 1.37 (t, J = 7 Hz, 3 H); IR 3400 (b), 3060 (w), 2980 (s), 2937 (m), 2900 (m), 2100 (s), 1665 (s), 1600 (s).

Anal. Calcd for $C_{18}H_{16}Cl_2O_4$: C, 58.87; H, 4.39. Found: C, 59.04; H, 4.41.

2,5-Dichloro-3,6-diethoxy-4-hexynyl-4-hydroxy-2,5-cyclohexadienone (13b): white solid (86%, hexane/dichloromethane); mp 107–109 °C; ^{1}H NMR 4.58–4.80 (m, 2 H), 4.03–4.24 (m, 2 H), 3.39 (s, 1 H), 2.25 (t, J = 7 Hz, 2 H), 1.33–1.70 (m, 10 H), 0.91 (t, J = 7 Hz, 3 H); IR 3508 (s), 2978 (s), 2956 (s), 2880 (m), 2220 (m), 1678 (s), 1611 (s).

Anal. Calcd for $C_{16}H_{20}Cl_2O_4$: C, 55.34; H, 5.80. Found: C, 55.55; H, 5.77.

2,5-Dichloro-3,6-diethoxy-4-hydroxy-4-(3-methylbutenynyl)-2,5-cyclohexadienone (13c): yellow solid (78%, 1.95 g, hexane/dichloromethane); mp 104–15 °C; ^{1}H NMR 5.37–5.42 (m, 2 H), 4.61–4.79 (m, 2 H), 4.10–4.19 (m, 2 H), 3.57 (s, 1 H), 1.88–1.89 (m, 3 H), 1.47 (t, J = 7 Hz, 3 H), 1.37 (t, J = 7 Hz, 3 H); IR 3580 (br), 2982 (m), 2930 (w), 2900 (w), 2100 (w), 1672 (s), 1610 (s).

Anal. Calcd for $C_{15}H_{16}Cl_2O_4$: C, 62.55; H, 4.00. Found: C, 62.53; H, 4.11.

2,5-Dichloro-3,6-diethoxy-4-hydroxy-4-[(2-methoxyphenyl)ethynyl]-2,5-cyclohexadien-1-one (13d): white crystals (80%, 12.28 g); mp 111–112 °C; ^{1}H NMR 7.62–7.41 (m, 2 H), 6.86–6.94 (m, 2 H), 4.87 (d, q, J = 9, 6 Hz, 1 H), 4.72 (d, q, J = 9, 6 Hz, 1 H), 4.19 (d, q, J = 9, 6 Hz, 1 H), 4.12 (d, q, J = 9, 6 Hz, 1 H), 3.84 (s, 3 H), 1.49 (t, J = 6 Hz, 3 H), 1.37 (t, J = 6 Hz, 3 H); IR 3340 (br), 2230 (m), 1640 (s), 1570 (s), 1260 (s), 1120 (s); MS, m/e 396 (EI); exact mass calcd for $C_{19}H_{18}Cl_2O_5$ 396.0531, found 396.0520.

2,5-Dichloro-3,6-diethoxy-4-hydroxy-4-[(2-methylphenyl)ethynyl]-2,5-cyclohexadien-1-one (13e): white crystals (72%, 4.64 g); mp 105–107 °C; ^{1}H NMR 7.40 (d, J = 7 Hz, 1 H), 7.12–7.31 (m, 3 H), 4.80 (d, q, J = 9, 7 Hz, 1 H), 4.71 (d, q, J = 9, 7 Hz, 1 H), 4.20 (d, q, J = 9, 7 Hz, 1 H), 4.13 (d, q, J = 9, 7 Hz, 1 H), 3.53 (s, 1 H), 2.42 (s, 3 H), 1.50 (t, J = 7 Hz, 3 H), 1.38 (t, J = 7 Hz, 3 H); IR 3320 (br), 2240 (m), 1660 (s), 1600 (s), 1270 (s); MS, m/e 381 (CI); exact mass calcd for $C_{19}H_{18}Cl_2O_4$ 380.05819, found 380.0562.

2,5-Dichloro-3,6-diethoxy-4-hydroxy-4-(4-phenyl-3-buten-1-ynyl)-2,5-cyclohexadien-1-one (13f): yellow crystals (75%, 5.56 g); mp 98–99.5 °C; ^{1}H NMR 7.34 (br s, 5 H), 7.05 (d, J = 16 Hz, 1 H), 6.13 (d, J = 16 Hz, 1 H), 4.73 (q, J = 7 Hz, 2 H), 4.18 (q, J = 7 Hz, 2 H), 3.54 (s, 1 H), 1.48 (t, J = 7 Hz, 3 H), 1.37 (t, J = 7 Hz, 3 H); IR 3560 (w), 2200 (w), 1670 (s), 1600 (s), 1270 (m), 1020 (m); MS, m/e 393 (CI); exact mass calcd for $C_{20}H_{18}Cl_2O_4$ 392.05819, found 392.05725.

2,5-Dichloro-3,6-diethoxy-4-hydroxy-4-(4-phenylbut-1-ynyl)-2,5-cyclohexadien-1-one (13g): yellow crystals (76%, 11.4 g); mp 82–83 °C; ^{1}H NMR 7.17–7.30 (m, 5 H), 4.51–4.64 (m, 2 H), 4.03–4.19 (m, 2 H), 3.58 (br s, 1 H), 2.82 (t, J = 6 Hz, 2 H), 2.55 (t, J = 6 Hz, 2 H), 1.37 (t, J = 6 Hz, 3 H), 1.35 (t, J = 6 Hz, 3 H); IR 3340 (br), 3040 (w), 2240 (m), 1650 (s), 1580 (s), 1280 (s); MS, m/e 395 (CI); exact mass calcd for $C_{20}H_{20}Cl_2O_4$ 394.07384, found 394.0731.

2,5-Dichloro-3,6-diethoxy-4-hydroxy-4-(1-naphthylethynyl)-2,5-cyclohexadien-1-one (13h): gold crystals (66%, 13.5 g); mp 130–131.5 °C; ^{1}H NMR 8.23–8.50 (m, 1 H), 7.40–7.92 (m, 6 H), 4.81 (q, J = 7 Hz, 2 H), 4.21 (q, J = 7 Hz, 2 H), 3.69 (br s, 1 H), 1.51 (t, J = 7 Hz, 3 H), 1.38 (t, J = 7 Hz, 3 H); IR 3550 (w), 2980 (w), 1670 (s), 1600 (s), 1235 (m), 1020 (s); MS, m/e 416 (EI); exact mass calcd for $C_{22}H_{18}Cl_2O_4$ 416.0582, found 416.0602.

2,5-Dichloro-3,6-diethoxy-4-hydroxy-4-(1-octa-1,7-diynyl)-2,5-cyclohexadienone (13i): white solid (79%, 2.21 g, hexane/dichloromethane); ^{1}H NMR 4.48–4.82 (m, 2 H), 3.86–4.25 (m, 2 H), 3.35 (s, 1 H), 2.05–2.35 (m, 4 H), 1.81–1.92 (m, 1 H), 1.25–1.95 (m, 10 H); IR 3580 (br), 3307 (s), 2980 (s), 2940 (s), 2860 (w), 2100 (m), 1670 (s), 1607 (s).

Anal. Calcd for $C_{18}H_{20}Cl_2O_4$: C, 58.23; H, 5.43. Found: C, 57.93; H, 5.57.

4-(Carbethoxyethynyl)-2,5-dichloro-3,6-diethoxy-4-hydroxy-2,5-cyclohexadienone (13j): white solid (76%, 2.1 g, hexane/dichloromethane); mp 86–87 °C; ^{1}H NMR 4.64–4.67 (m, 2 H), 4.15–4.31 (m, 4 H), 3.70 (s, 1 H), 1.48 (t, J = 7 Hz, 3 H), 1.29–1.40 (m, 6 H); IR 3582 (br), 2990 (m), 2986 (m), 2100 (m), 1754 (s), 1672 (s), 1601 (s).

Anal. Calcd for $C_{15}H_{16}Cl_2O_6$: C, 49.60; H, 4.44. Found: C, 49.46; H, 4.55.

2,5-Dichloro-3,6-diethoxy-4-ethynyl-4-hydroxy-2,5-cyclohexadienone (13k): white solid (87%, 1.92 g, hexane/dichloromethane); ^1H NMR 4.50–4.86 (m, 2 H), 3.96–4.31 (m, 2 H), 3.48 (s, 1 H), 2.15 (s, 1 H), 1.25–1.70 (m, 6 H); ^{13}C NMR 175.56, 163.94, 145.26, 134.88, 112.84, 78.60, 75.22, 70.87, 69.23, 68.46, 15.33, 15.24; IR 3585 (br), 3309 (s), 2990 (m), 2940 (w), 2250 (m), 1679 (s), 1615 (s); exact mass calcd for $C_{12}H_{12}Cl_2O_4$ 290.0796, found 290.0783.

2,5-Dichloro-3,6-diethoxy-4-hydroxy-4-[3-[(tetrahydropyran-2-yl)oxy]prop-1-ynyl]-2,5-cyclohexadien-1-one (13l): orange oil (97%, 15.0 g); ^1H NMR 4.63–4.80 (m, 4 H), 4.32 (s, 2 H), 4.06–4.20 (m, 2 H), 3.76–3.86 (m, 1 H), 3.52–3.54 (m, 1 H), 1.53–1.82 (m, 6 H), 1.48 (t, J = 7 Hz, 3 H), 1.37 (t, J = 7 Hz, 3 H); IR 3580 (m), 3320 (br), 2980 (s), 1680 (s), 1610 (s), 1030 (s); MS, m/e 405 (CI); exact mass calcd for $C_{18}H_{22}Cl_2O_6$ 404.0793, found 404.0789.

3,6-Dichloro-4-ethoxy-5-(phenylethynyl)-3,5-cyclohexadiene-1,2-dione (14a). The following is a representative procedure used for the hydrolysis of the quinols **13** to the quinones **14**. Into a stirred solution of 0.10 g (0.27 mmol) of 2,5-dichloro-3,6-diethoxy-4-(phenylethynyl)-4-hydroxy-2,5-cyclohexadienone (**13a**) in 20 mL of dry diethyl ether were added 1 mL of trifluoroacetic anhydride and 1 drop of concentrated sulfuric acid at room temperature, under an atmosphere of argon. The solution immediately turned from colorless to red. After being stirred for 3 min, the solution was placed in an ice bath for 1 h and then filtered. The red solid residue was recrystallized from ether/petroleum ether to afford 0.7 g (80%) of a red solid: mp 143–145 °C; ^1H NMR 7.43–7.62 (m, 5 H), 4.68 (q, J = 7 Hz, 2 H), 1.56 (t, J = 7 Hz, 3 H); IR 3080 (w), 2180 (s), 1675 (s), 1580 (m), 1525 (m).

Anal. Calcd for $C_{16}H_{10}Cl_2O_3$: C, 59.83; H, 3.14. Found: C, 59.57; H, 3.25.

3,6-Dichloro-4-ethoxy-5-hexynyl-3,5-cyclohexadiene-1,2-dione (14b): red solid (69%, 120 mg, diethyl ether/petroleum ether); mp 58–59 °C; ^1H NMR 4.61 (q, J = 7 Hz, 2 H), 2.63 (t, J = 7 Hz, 2 H), 1.45–1.72 (m, 7 H), 0.96 (t, J = 7 Hz, 3 H); IR 2960 (m), 2918 (m), 2200 (m), 1676 (s), 1585 (w), 1530 (m).

Anal. Calcd for $C_{14}H_{14}Cl_2O_3$: C, 55.83; H, 4.69. Found: C, 55.75; H, 4.71.

3,6-Dichloro-4-ethoxy-5-(3-methylbutenynyl)-3,5-cyclohexadiene-1,2-dione (14c): red solid (85%, 70 mg, hexane/diethyl ether); mp 103–104 °C; ^1H NMR 5.50–5.70 (m, 2 H), 4.45–4.75 (q, J = 7 Hz, 2 H), 2.05–2.13 (m, 3 H), 1.51 (t, J = 7 Hz, 3 H); IR 2980 (m), 2921 (w), 2168 (s), 1678 (s), 1578 (s), 1528 (s); MS, m/e 284 (EI); exact mass calcd for $C_{13}H_{10}Cl_2O_3$ 284.00067, found 284.0003.

3,6-Dichloro-4-ethoxy-5-[(2-methoxyphenyl)ethynyl]-3,5-cyclohexadiene-1,2-dione (14d): red crystals (80%, 0.72 g); mp 114 °C dec; ^1H NMR 7.43–7.53 (m, 2 H), 6.92–7.01 (m, 2 H), 4.65 (q, J = 6 Hz, 2 H), 3.91 (s, 3 H), 1.56 (t, J = 6 Hz, 3 H); IR 2160 (s), 1670 (s), 1255 (s); MS, m/e 352 (EI) (hydroquinone); exact mass calcd for $C_{17}H_{12}Cl_2O_4$, 350.0112, found 350.0086.

3,6-Dichloro-4-ethoxy-5-[(2-methylphenyl)ethynyl]-3,5-cyclohexadiene-1,2-dione (14e): red crystals (77%, 0.34 g); mp 155 °C dec; ^1H NMR 7.25–7.59 (m, 4 H), 4.70 (q, J = 7 Hz, 2 H), 2.56 (s, 3 H), 1.56 (t, J = 7 Hz, 3 H); IR 2170 (s), 1670 (s), 1580 (m), 1525 (s), 1255 (s); MS, m/e 335 (CI) (hydroquinone); exact mass calcd for $C_{17}H_{12}Cl_2O_3$ 334.01633, found 334.0169.

3,6-Dichloro-4-ethoxy-5-(4-phenyl-3-buten-1-ynyl)-3,5-cyclohexadiene-1,2-dione (14f): red crystals (78%, 0.68 g); mp 142 °C dec; ^1H NMR 7.39–7.51 (m, 5 H), 7.29 (d, J = 16 Hz, 1 H), 6.54 (d, J = 15 Hz, 1 H), 4.65 (q, J = 7 Hz, 2 H), 1.55 (t, J = 7 Hz, 3 H); IR 3020 (w), 2160 (s), 1670 (s), 1515 (m), 1310 (s), 1300 (m), 1190 (m); MS, m/e 347 (CI); exact mass calcd for $C_{18}H_{12}Cl_2O_3$ 346.0163, found 346.0164.

3,6-Dichloro-4-ethoxy-5-(4-phenylbut-1-ynyl)-3,5-cyclohexadiene-1,2-dione (14g): red crystals (64%, 0.28 g); mp 91–92 °C; ^1H NMR 7.24–7.35 (m, 5 H), 4.49 (q, J = 6 Hz, 2 H), 2.90–3.02 (m, 4 H), 1.39 (t, J = 6 Hz, 3 H); IR 2190 (s), 1670 (s), 1585 (m), 1545 (s), 1300 (s); MS, m/e 349 (CI); exact mass calcd for $C_{18}H_{14}Cl_2O_3$ 348.0320, found 348.03017.

3,6-Dichloro-4-ethoxy-5-(1-naphthylethynyl)-3,5-cyclohexadiene-1,2-dione (14h): red crystals (84%, 1.49 g); mp 96 °C dec; ^1H NMR 8.42–8.46 (m, 1 H), 7.87–8.04 (m, 3 H), 7.51–7.68 (m, 3 H), 4.76 (q, J = 7 Hz, 2 H), 1.62 (t, J = 7 Hz, 3 H); IR 2160 (m), 1660 (s), 1520 (m), 1315 (m), 1270 (s), 1240 (m), 1000 (m); MS, m/e 370 (EI); exact mass calcd for $C_{20}H_{12}Cl_2O_3$ 370.0163, found 370.0155.

3,6-Dichloro-4-ethoxy-5-(1-octa-1,7-diynyl)-3,5-cyclohexadiene-1,2-dione (14i): red solid (57%, 50 mg, hexane/diethyl ether); mp 68–69 °C; ^1H NMR 4.36–4.75 (q, J = 7 Hz, 2 H), 2.52–2.76 (m, 2 H), 2.12–2.42 (m, 2 H), 1.85–1.97 (m, 1 H), 1.65–1.87 (m, 4 H), 1.51 (t, J = 7 Hz, 3 H); IR 3306 (s), 2983 (w), 2950 (m), 2900 (w), 2202 (s), 1680 (s), 1588 (m); MS, m/e 325 (CI).

5-(Carbethoxyethynyl)-3,6-dichloro-4-ethoxy-3,5-cyclohexadiene-1,2-dione (14j): red solid (68%, 60 mg, hexane/diethyl ether); mp 67–69 °C; ^1H NMR 4.52–4.81 (t, J = 7 Hz, 2 H), 4.21–4.48 (t, J = 7 Hz, 2 H), 1.26–1.63 (m, 6 H); IR 6985 (m), 2940 (w), 2900 (w), 2205 (w), 1715 (s), 1682 (s), 1580 (m), 1541 (m).

Anal. Calcd for $C_{13}H_{10}Cl_2O_5$: C, 49.24; H, 3.18. Found: C, 49.14; H, 3.15.

3,6-Dichloro-4-ethoxy-4-ethynyl-3,5-cyclohexadiene-1,2-dione (14k): red solid (79%, 70 mg, diethyl ether/petroleum ether); ^1H NMR 4.66 (q, J = 7 Hz, 2 H), 4.29 (s, 1 H), 1.50 (t, J = 7 Hz, 3 H); MS, m/e 244 (EI), 245 (CI).

3,6-Dichloro-4-ethoxy-5-[3-[(tetrahydropyran-2-yl)oxy]-prop-1-ynyl]-3,5-cyclohexadiene-1,2-dione (14l): red crystals (56%, 0.49 g); mp 78–79.5 C; ^1H NMR 4.91 (m, 1 H), 4.63 (q, J = 6 Hz, 2 H), 4.62 (s, 2 H), 3.82–3.89 (m, 1 H), 3.55–3.61 (m, 1 H), 1.52–1.81 (m, 6 H), 1.49 (t, J = 6 Hz, 3 H); IR 2920 (s), 2860 (s), 2200 (s), 1670 (s), 1585 (m); MS, m/e 101 (CI) (2-tetrahydropyranyloxy).

2,5-Dichloro-6-hydroxy-3-(phenylethynyl)-2,5-cyclohexadiene-1,4-dione (15a). The following is a representative procedure used for the synthesis of the hydroxy quinones **15a–f**. Into a stirred solution of 0.10 g (0.27 mmol) of 2,5-dichloro-3,6-diethoxy-4-(phenylethynyl)-4-hydroxy-2,4-cyclohexadienone (**14a**) in 20 mL of dry ethyl acetate were added 1 mL of trifluoroacetic anhydride (Aldrich) and 1 drop of concentrated sulfuric acid at room temperature, under an atmosphere of argon. The solution gradually turned from colorless to red in color. After stirring for 3 h, 10 mL of water was added. The organic layer was washed twice with 10-mL portions of distilled water, once with 10 mL of saturated brine solution, dried over anhydrous magnesium sulfate, and then concentrated. The red oily residue was triturated with diisopropyl ether/hexane to afford 0.07 g (85%) of a dark pink solid: mp 200–203 °C; ^1H NMR 7.25–7.73 (m, 5 H), 6.01 (br s, 1 H); IR 3295 (br), 2180 (s), 1645 (s), 1551 (s); MS, m/e 292 (EI), 293 (CI).

Anal. Calcd for $C_{14}H_6Cl_2O_3$: C, 57.37; H, 2.06. Found: C, 57.49; H, 2.22.

2,5-Dichloro-3-hexynyl-6-hydroxy-2,5-cyclohexadiene-1,4-dione (15b): orange solid (74%, 0.11 g, diisopropyl ether); mp 160 °C dec; ^1H NMR 6.03 (br s, 1 H), 2.56 (t, J = 7 Hz, 2 H), 1.48–1.69 (m, 4 H), 1.03 (t, J = 7 Hz, 3 H); IR 3423 (br), 2982 (s), 2940 (s), 2209 (s), 1671 (s), 1570 (s); MS, m/e 272 (EI), 273 (CI).

Anal. Calcd for $C_{12}H_{10}Cl_2O_3$: C, 52.77; H, 3.69. Found: C, 52.86; H, 3.72.

2,5-Dichloro-6-hydroxy-3-(3-methylbutenynyl)-2,5-cyclohexadiene-1,4-dione (15c): orange solid (76%, 0.12 g, diisopropyl ether); mp 178 °C dec; ^1H NMR 5.49–5.54 (m, 2 H), 5.12 (br s, 1 H), 2.03 (m, 3 H); IR 3422 (s), 2997 (w), 2923 (w), 2185 (s), 1673 (s), 1565 (s); MS, m/e 256 (EI), 257 (CI).

2,5-Dichloro-6-hydroxy-3-(1-octa-1,7-diynyl)-2,5-cyclohexadiene-1,4-dione (15d): orange solid (81%, 0.07 g, diisopropyl ether/hexane); mp 108–109 °C; ^1H NMR 5.95 (br s, 1 H), 2.66 (t, J = 7 Hz, 2 H), 2.20–2.30 (m, 2 H), 1.97 (t, J = 2.6 Hz, 1 H), 1.70–1.84 (m, 4 H); IR 3320 (s), 2975 (m), 2860 (w), 2210 (s), 1672 (s), 1571 (s); MS, m/e 296 (EI), 297 (CI).

Anal. Calcd for $C_{14}H_{10}Cl_2O_3$: C, 56.59; H, 3.39. Found: C, 56.79; H, 3.60.

3-(Carbethoxyethynyl)-2,5-dichloro-6-hydroxy-2,5-cyclohexadiene-1,4-dione (15e): yellow solid (75%, 0.06 g, diisopropyl ether/hexane); mp 125–127 °C; ^1H NMR 4.41 (br s, 1 H), 4.31 (q, J = 7 Hz, 2 H), 1.42 (t, J = 7 Hz, 3 H); IR (3430 (m), 2982 (w), 2208 (w), 1718 (s), 1680 (s), 1575 (m); MS, m/e (288 (EI), 289 (CI).

2,5-Dichloro-3-ethynyl-6-hydroxy-2,5-cyclohexadiene-1,4-dione (15f): orange solid (77%, 0.11 g); mp 205 °C dec; ^1H NMR

6.11 (br s, 1 H), 3.96 (s, 1 H); IR 3401 (br), 2210 (m), 1670 (s), 1570 (s); MS, *m/e* 216 (EI), 217.

General Procedure for the Preparation of the Dialkynyl Adduct of 2,5-Dichloro-3,6-diethoxy-2,5-cyclohexadiene-1,4-dione. The following experimental procedure for the synthesis of **16c** is representative of that used for the preparation of **16a–e**. A solution of 5.0 g (0.012 mol) of **13** in 250 mL of dry THF, under an argon atmosphere, was stirred at 0 °C while 0.48 g (0.017 mol) of sodium hydride was added. To the solution was added dropwise, via cannula, [3-[(tetrahydropyran-2-yl)oxy]prop-1-yl]lithium, which had been prepared from the addition of 14.7 mL (1.55 M in hexanes) of *n*-butyllithium to a solution of 3.36 g (0.024 mol) of 3-[(tetrahydropyran-2-yl)oxy]prop-1-yne in 75 mL of dry THF at −78 °C. After the addition was completed, the solution was stirred for 1 h at −78 °C before being quenched with 150 mL of 2 M aqueous ammonium chloride. The organic layer was washed twice with water, dried over anhydrous magnesium sulfate, and concentrated. The residue was absorbed on to silica gel and subjected to flash chromatography (3:2 hexanes/ethyl acetate) to give 6.14 g (92%) of **16c** as white crystals.

2,5-Dichloro-3,6-diethoxy-1,4-dihydroxy-1,4-bis(4-phenylbut-1-ynyl)-2,5-cyclohexadiene (16a): yellow crystals (50%, 2.0 g); mp 88.5–89.5 °C; ^{1}H NMR 7.18–7.31 (m, 10 H), 4.25 (d, q, *J* = 9, 6 Hz, 2 H), 4.12 (d, q, *J* = 9, 6 Hz, 2 H), 2.91 (s, 2 H), 2.81 (t, *J* = 9 Hz, 2 H), 2.52 (t, *J* = 9 Hz, 2 H), 1.35 (t, *J* = 6 Hz, 6 H); IR 3500 (s), 3440 (s), 3040 (w), 2220 (m), 1240 (s), 1030 (s); MS, *m/e* 488 (CI neg. ion) (M − HCl).

2,5-Dichloro-3,6-diethoxy-1,4-dihydroxy-1,4-bis(3-methyl-3-buten-1-ynyl)-2,5-cyclohexadiene (16b): tan crystals (93%, 3.35 g); mp 129–131 °C; ^{1}H NMR 5.35 (s, 2 H), 5.31 (s, 2 H), 4.26 (d, q, *J* = 9, 6 Hz, 2 H), 4.43 (d, q, *J* = 9, 6 Hz, 2 H), 3.15 (s, 2 H), 1.88 (s, 6 H), 1.42 (t, *J* = 6 Hz, 6 H); IR 3540 (s), 3440 (br), 2980 (s), 2210 (m), 1610 (m), 1575 (m), 1210 (s), 1015 (s); MS, *m/e* 350 (CI neg. ion) (M − EtOH).

2,5-Dichloro-3,6-diethoxy-1,4-dihydroxy-1,4-bis[3-[(tetrahydropyran-2-yl)oxy]prop-1-ynyl]-2,5-cyclohexadiene (16c): white crystals (92%, 6.14 g); mp 138–140 °C; ^{1}H NMR 4.80 (s, 2 H), 4.24–4.40 (m, 8 H), 3.78–3.84 (m, 2 H), 3.50–3.55 (m, 2 H), 3.19 (s, 2 H), 1.51–1.81 (m, 12 H), 1.40 (t, *J* = 6 Hz, 6 H); IR 3380 (br), 2960 (s), 1220 (s), 1015 (s); MS, *m/e* 508 (CI neg. ion) (M − EtOH).

2,5-Dichloro-3,6-diethoxy-1,4-dihydroxy-1,4-bis[(2-methoxyphenyl)ethynyl]-2,5-cyclohexadiene (16d): light yellow crystals (63%, 2.53 g); mp 127 °C dec; ^{1}H NMR 7.40 (d, *J* = 6 Hz, 2 H), 7.28–7.34 (m, 2 H), 6.84–6.92 (m, 4 H), 4.42–4.53 (m, 4 H), 3.84 (s, 6 H), 3.32 (s, 2 H), 1.45 (t, *J* = 6 Hz, 6 H); IR 3380 (s), 2210 (m), 1590 (m), 1490 (m), 1230 (s), 1005 (s); MS, *m/e* 526 (CI neg. ion) (M − 2).

2,5-Dichloro-3,6-diethoxy-1,4-dihydroxy-1,4-bis[(2-methylphenyl)ethynyl]-2,5-cyclohexadiene (16e): yellow crystals (76%, 2.96 g); mp 114 °C dec; ^{1}H NMR 7.40 (d, *J* = 6 Hz, 2 H), 7.11–7.28 (m, 6 H), 4.47 (d, q, *J* = 9, 6 Hz, 2 H), 4.38 (d, q, *J* = 9, 6 Hz, 2 H), 3.21 (s, 2 H), 2.45 (s, 6 H), 1.45 (t, *J* = 6 Hz, 6 H); IR 3460 (s), 3060 (w), 2980 (m), 2210 (s), 1590 (s), 1480 (m), 1220 (s), 1010 (s); MS, *m/e* 450 (CI neg. ion) (M − EtOH).

2,5-Dichloro-3,6-bis(4-phenylbut-1-ynyl)-2,5-cyclohexadiene-1,4-dione (17a). Hydrolyses of **16a–c** were accomplished by employing the procedures used to prepare the quinones **3** or **14**: orange crystals (73%, 0.15 g); mp 126 °C dec; ^{1}H NMR 7.22–7.30 (m, 10 H), 2.97 (t, *J* = 7 Hz, 4 H), 2.88 (t, *J* = 7 Hz, 4 H); IR 3020 (w), 2940 (w), 2205 (s), 1675 (s), 1555 (m), 1390 (w), 1190 (s), 745 (s); MS, *m/e* 435 (CI) (hydroquinone); exact mass calcd. for $C_{26}H_{18}Cl_2O_2$ 432.06837, found 432.0656.

2,5-Dichloro-3,6-bis(3-methyl-3-buten-1-ynyl)-2,5-cyclohexadiene-1,4-dione (17b): red crystals (63%, 0.24 g); mp 100 °C dec; ^{1}H NMR 5.67 (s, 2 H), 5.56 (s 2 H), 2.04 (s, 6 H); IR 2190 (s), 1675 (s), 1545 (s), 1240 (s), 1180 (s); MS, *m/e* 304 (EI); exact mass calcd for $C_{16}H_{10}Cl_2O_2$ 304.00577, found 304.0042.

2,5-Dichloro-3,6-bis[3-[(tetrahydropyran-2-yl)oxy]prop-1-ynyl]-2,5-cyclohexadiene-1,4-dione (17c): yellow oil (55%, 0.32 g); ^{1}H NMR 4.93–4.95 (m, 2 H), 4.60 (s, 2 H), 3.83–3.91 (m, 2 H), 3.55–3.61 (m, 2 H), 1.53–1.86 (m, 12 H); IR 2930 (s), 2220 (m), 1670 (s), 1560 (s), 1190 (s), 1115 (s), 1020 (s); MS, *m/e* 452 (CI neg. ion).

2,5-Dichloro-3,6-bis[(2-methoxyphenyl)ethynyl]-2,5-cyclohexadiene-1,4-dione (17d): red solid (83%, 0.17 g); mp 235 °C dec; ^{1}H NMR 7.59 (d, *J* = 6 Hz, 2 H), 7.40–7.46 (m, 2 H), 6.93–7.01 (m, 4 H), 3.95 (s, 6 H); IR 2170 (s), 1670 (s), 1595 (w), 1550 (s), 1275 (m), 1210 (s), 1145 (m); MS, *m/e* 436 (EI); exact mass calcd for $C_{24}H_{14}Cl_2O_4$ 436.0260, found 436.0289.

2,5-Dichloro-3,6-bis[(2-methylphenyl)ethynyl]-2,5-cyclohexadiene-1,4-dione (17e): red crystals (42%, 0.34 g); mp 219–221 °C; ^{1}H NMR 7.20–7.63 (m, 8 H), 2.59 (s, 6 H); IR 2180 (s), 1670 (s), 1550 (s); MS, *m/e* 407 (CI) (hydroquinone); exact mass calcd for $C_{24}H_{14}Cl_2O_2$ 404.03707, found 404.0356.

1,4-Dichloro-2,3-dimethoxy-5,6-dihydroxy-5,6-bis(phenylethynyl)-1,3-cyclohexadiene (19b): colorless crystals (78%, 1.72 g, ethyl acetate); mp 119–120 °C; ^{1}H NMR 3.52 (br s, 2 H), 3.80 (s, 6 H), 7.21–7.53 (m, 10 H); IR 3489, 2224, 1591.

Anal. Calcd for $C_{24}H_{18}Cl_2O_4$: C, 65.32; H, 4.11. Found: C, 65.24; H, 4.15.

4,5-Bis(phenylethynyl)-3,5-cyclohexadiene-1,2-dione (20a). A solution of 500 mg of **19a**[10] in 100 mL of ethyl acetate was stirred with 4 drops of 50% aqueous sulfuric acid. After 45 min the solution was washed with water, and the solvent was removed after drying. The resulting yellow oil was not purified further because of its instability. However, by HPLC and ^{1}H NMR analysis, it appeared to be >90% **19a**: yellow oil; ^{1}H NMR 7.0–7.5 (m, 12 H); MS (CI), *m/e* 309.

1,4-Dichloro-2,3-bis(phenylethynyl)-1,3-cyclohexadiene-5,6-dione (20b): black crystals (41%, 310 mg); mp >250 °C; ^{1}H NMR 7.32–7.64 (m, 10 H); IR 2177, 1674, 1600, 1559; MS (CI), *m/e* (relative intensity) 377/379/381 (M^+ + 1, 9.6/11.3/8.0).

The quinone decomposed upon attempted purification.

2,3-Bis(phenylethynyl)-5-chloro-1,4-dimethoxybenzene (23a). The following is a representative procedure used for the preparation of the phenols **23**. A solution containing 1.35 mmol of **22a** in 50 mL of THF was treated with 2.70 mmol of pyridine and 1.35 mmol of thionyl chloride. After 12 h the mixture was filtered through a bed of Celite and the solvent removed in vacuo. The residue was recrystallized from methanol to give **23a** in 65% yield: mp 150–151 °C; ^{1}H NMR 3.90 (s, 3 H), 3.98 (s, 3 H), 6.89 (s, 1 H), 7.37 (m, 10 H); IR 2320, 1560, 1480.

Anal. Calcd for $C_{24}H_{17}ClO_2$: C, 77.31; H, 4.59. Found: C, 77.48; H, 4.68.

2,3-Bis[3-(benzyloxy)-1-propynyl]-5-chloro-1,4-dimethoxybenzene (23b): colorless oil, 73% yield; ^{1}H NMR 7.30 (m, 10 H), 6.87 (s, 1 H), 4.68 (s, 4 H), 4.44 (s, 2 H), 4.42 (s, 2 H), 3.89 (s, 3 H), 3.84 (s, 3 H); IR 2220 (m), 1575 (m), 1470 (s), 1410 (s), 1320 (s), 1080 (s); MS, *m/e* 460 (EI); exact mass calcd for $C_{28}H_{25}ClO_4$ 460.1441, found 460.1472.

2,3-Dihexynyl-5-chloro-1,4-dimethoxybenzene (23c): colorless oil, 75% yield; ^{1}H NMR 6.78 (s, 1 H), 3.87 (s, 3 H), 3.81 (s, 3 H), 2.51 (m, 4 H), 1.67 (m, 8 H), 0.93 (m, 6 H); IR 2960 (s), 2240 (w), 1572 (m), 1475 (s), 1412 (s), 1410 (s); exact mass calcd for $C_{20}H_{25}ClO_2$ 332.15430, found 332.1550.

2,3-Bis(carbethoxyethynyl)-5-chloro-1,4-dimethoxybenzene (23d): white crystals, 63% yield; mp 138–139 °C; ^{1}H NMR 7.0 (s, 1 H), 4.30 (m, 4 H), 3.93 (s, 3 H), 3.88 (s, 3 H), 1.41 (m, 6 H); IR 3000 (m), 2220 (s), 1715 (s), 1570 (m), 1485 (s), 1420 (s), 1250 (s).

Anal. Calcd for $C_{18}H_{17}ClO_6$: C, 59.27; H, 4.69. Found: C, 59.25; H, 4.74.

2,3-Bis(phenylethynyl)-5-chloro-2,5-cyclohexadiene-1,4-dione (24a). The following is a representative procedure used for the syntheses of quinones **24a–d**. One equivalent of **23a** in 10 mL of acetonitrile was treated with 2 equiv of cerric ammonium nitrate (CAN) in 5 mL of distilled water. After 45 min, water was added and the resulting mixture was extracted with dichloromethane (3 × 20 mL). The organic solution was dried and the solvent removed in vacuo. The residue was then purified by PTLC (hexane/ethyl acetate, 9:1) to give 0.13 g of **23a** (50%) as red crystals: mp 108 °C dec; ^{1}H NMR 7.07 (s, 1 H), 7.42 (m, 10 H); IR 2205 (m), 1685 (s), 1660 (s), 1560 (m), 1130 (s); exact mass calcd for $C_{22}H_{11}ClO_2$ 342.04474, found 342.0428.

2,3-Bis[3-(benzyloxy)-1-propynyl]-5-chloro-2,5-cyclohexadiene-1,4-dione (24b): yellow oil, 0.14 g, 60% yield; ^{1}H NMR 7.33 (s, 10 H), 6.88 (s, 1 H), 4.55 (s, 4 H), 4.33 (s, 4 H); IR 2220 (m), 1678 (s), 1669 (s), 1565 (s), 1425 (s); exact mass calcd for $C_{26}H_{19}ClO_4$ 430.0970, found 430.0959.

2,3-Dihexynyl-5-chloro-2,5-cyclohexadiene-1,4-dione (24c): yellow oil, 0.16 g, 54% yield; ^{1}H NMR 6.92 (s, 1 H), 2.45 (m, 4 H), 1.44 (m, 8 H), 0.92 (m, 6 H); IR 2215 (m), 1685 (s), 1665 (s), 1570 (s), 1470 (s); exact mass calcd for $C_{18}H_{19}ClO_2$ 302.10727, found 302.10897.

3-Bromo-2-hydroxy-4,5-dimethoxy-2-(phenylethenyl)-3,5-cyclohexadienone (25). A solution containing 2 g (5.7 mmol) of **5b** in 200 mL of ethyl acetate was treated with 0.4 g of Pd/$BaSO_4$ (20%) and 0.2 mL of quinoline.[21] The reaction mixture was kept under a slight pressure of hydrogen. After 3 h the catalyst and solvent were removed. The residue was purified by flash chromatography on silica gel (ethyl acetate/hexane, 4:6) to yield 1.26 g (61%) of **25** after recrystallization from diethyl ether: mp 101–102 °C; ^{1}H NMR 3.59 (s, 3 H), 3.70 (s, 3 H), 3.84 (br s, 1 H), 5.26 (s, 1 H), 5.67 (d, 1 H, J = 12.0 Hz), 6.72 (d, 1 H, J = 12.0 Hz), 7.21 (s, 5 H); MS (CI), m/e (relative intensity) 351/353 (M^+ + 1, 100/99.2).

Anal. Calcd for $C_{16}H_{15}BrO_4$: C, 54.72; H, 4.27. Found: C, 54.71; H, 4.25.

3-Bromo-4,5-dimethoxy-1-phenylbenzo[*b*]furan (26). Hydrolysis of 0.7 g (2 mmol) of **25** using CF_3CO_2O/H_2SO_4 gave 0.59 g (88%) of **26** after flash chromatography on silica gel (ethyl acetate/hexane, 4:6): mp 76–77 °C; ^{1}H NMR 3.88 (s, 3 H), 3.94 (s, 3 H), 6.97 (d, 1 H, J = 0.7 Hz), 7.06 (d, 1 H, J = 0.7 Hz), 7.31–7.47 (m, 3 H), 7.79–7.83 (m, 2 H); MS (CI), m/e (relative intensity) 333/335 (M^+ + 1, 99.0/100).

Anal. Calcd for $C_{16}H_{13}BrO_3$: C, 57.68; H, 3.93. Found: C, 57.90; H, 3.88.

4,5-Dimethoxy-2-(phenylethynyl)phenol (27a). The following procedure is representative of that used for the synthesis of the alkynylphenols **26a–c**. A solution of 210 mg (0.775 mmol) of 3,4-dimethoxy-6-hydroxy-6-(phenylethynyl)-2,4-cyclohexadienone (**2a**) in absolute ethanol was stirred with 59 mg (1.55 mmol) of sodium borohydride. Afterl h 50 mL of 1 M HCl was added and most of the ethanol was removed under reduced pressure. The aqueous solution was washed with dichloromethane, and the organic layers were combined and dried with anhydrous magnesium sulfate. Removal of the solvent gave an oil, which was purified by preparative thin layer chromatography to give 186 mg (95%) of an oily solid: ^{1}H NMR 7.30 (m, 5 H), 6.82 (s, 1 H), 6.51 (s, 1 H), 3.81 (s, 3 H), 3.80 (s, 3 H); IR 3533 (s), 1623 (s), 1600 (m); exact mass calcd for $C_{16}H_{14}O_3$ 254.0943, found 254.0943.

4,5-Dimethoxy-2-hexynylphenol (27b): pale yellow oil (91%, 426 mg, flash chromatography); ^{1}H NMR 6.76 (s, 1 H), 6.50 (s, 1 H), 5.56 (s, 1 H), 3.84 (s, 3 H), 3.80 (s, 3 H), 2.46 (t, 2 H), 1.52 (m, 4 H), 0.95 (t, 3 H); IR 3464 (br), 2961 (s), 2942 (s), 1624 (s), 1141 (s); exact mass calcd for $C_{14}H_{18}O_3$ 234.1256, found 234.1255.

4,5-Dimethoxy-2-(3-hydroxy-3-methyl-1-butynyl)phenol (27c): white solid (86%, 626 mg, diisopropyl ether); mp 137–138 °C; ^{1}H NMR 6.76 (s, 1 H), 6.51 (s, 1 H), 5.68 (br s, 1 H), 3.85 (s, 3 H), 3.81 (s, 3 H), 2.25 (br s, 1 H), 1.64 (s, 6 H); IR 3603 (br), 3059 (m), 2299 (w), 1514 (s).

Anal. Calcd for $C_{13}H_{16}O_4$: 66.09; H, 6.83. Found: C, 66.32; H, 6.69.

4,5-Bis(phenylethynyl)-2-methoxyphenol (28a). This is a representative procedure used for the preparation of the phenols **28a,b**. A solution of 185 mg (.497 mmol) of 1,2-bis(phenylethynyl)-4,5-dimethoxy-3,5-cyclohexadiene-1,2-diol (**19a**)[10] in 5 mL of methanol was added dropwise to a solution of 0.03 g (1.14 mmol) stannous chloride, in 10 mL 50% aqueous acetic acid. The solution was stirred at room temperature for 45 min and then at 50–60 °C. After 2 h, 50 mL of water and 2 mL of concentrated HCl were added and the mixture was extracted with dichloromethane. The organic layers were combined and dried with a large amount of anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. Preparative thin layer chromatography gave 130 mg (81%) of a pale yellow oil: ^{1}H NMR 7.40 (m, 10 H), 7.08 (s, 1 H), 6.98 (s, 1 H), 5.72 (br s, 1 H), 3.84 (s, 3 H); IR 3529 (br), 3060 (m), 2940 (m), 2204 (w), 1599 (s), 748 (s), 652 (s); exact mass calcd for $C_{23}H_{16}O_2$ 324.1150, found 324.1153.

4,5-Dihexynyl-2-methoxyphenol (28b): pale yellow oil (77%, 132 mg, PTLC); ^{1}H NMR 6.91 (s, 1 H), 6.83 (s, 1 H), 5.52 (br s, 1 H), 3.86 (s, 3 H), 2.44 (m, 4 H), 1.58 (m, 8 H), 0.94 (m, 6 H); IR 3500 (br), 2960 (s), 2939 (s), 2221 (w); exact mass calcd for $C_{19}H_{24}O_2$ 284.1776, found 284.1775.

General Procedure for the Synthesis of the Dienes 29 and 30. Solutions of diols **19** or **22** (1 mmol) in 75 mL of methylene chloride were stirred with 46.0 mmol of activated manganese dioxide. In most cases TLC showed the reaction to be complete in 30 min. After filtration through a bed of Celite, the solvent was removed in vacuo to give the corresponding dienes. Chromatography and recrystallization from diisopropyl ether afforded the corresponding dienes **29** and **30** in pure form.

5,6-Dimethoxy-1,10-diphenyl-4,6-decadiene-1,9-diyne-3,8-dione (29a): colorless oil; yield 87%; ^{1}H NMR 7.42 (m, 5 H), 5.86 (s, 1 H), 3.78 (s, 3 H); IR 2978 (m), 2186 (s), 1650–1550 (br, centered about 1605), 1396 (s); exact mass calcd for $C_{24}H_{18}O_4$ 370.1205, found 370.1205.

9,10-Dimethoxyoctadeca-8,10-diene-5,13-diyne-7,12-dione (29b): white solid; yield 80%; mp 48–50 °C; ^{1}H NMR 5.69 (s, 1 H), 3.78 (s, 3 H), 2.34 (m, 2 H), 1.50 (m, 4 H), 0.91 (s, 3 H); IR 2937 (s), 2202 (s), 1660–1540 (br, centered about 1590).

Anal. Calcd for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.76; H, 7.63.

5,6-Dimethoxydeca-4,6-diene-1,9-diyne-3,8-dione (29c): colorless oil, yield 83%; ^{1}H NMR 5.75 (s, 2 H), 3.81 (s, 3 H), 3.18 (s, 1 H); IR 2203 (m), 1650–1550 (br, centered about 1605); MS, m/e 219 (CI); exact mass calcd for the fragment $C_9H_9O_3$ 165.0552, found 165.0548.

4,5-Dimethoxy-3,5-tridecadien-8-yne-2,7-dione (29d): colorless oil, yield 89%; ^{1}H NMR 5.69 (s, 1 H), 5.63 (s, 1 H), 3.79 (s, 3 H), 2.75 (s, 3 H), 2.33 (m, 2 H), 2.15 (s, 3 H), 1.50 (m, 4 H), 0.91 (m, 3 H); IR 2943 (s), 2212 (s), 1732 (s), 1694 (s), 1670–1580 (br, centered about 1620); MS, m/e 265 (CI); exact mass calcd for $C_{15}H_{20}O_4$ 265.1361, found 265.1360.

5-Methoxy-2-(1-oxohexyl)-1,4-benzenediol. A solution of 1.00 g (4.85 mmol) of 2-hexynyl-5-methoxy-2,5-cyclohexadiene-1,4-dione (**3e**) in ether was shaken in a separatory funnel with aqueous sodium dithionite for 5 min. The ether layer was then separated and most of the solvent removed and replaced with 250 mL of ethanol. The mixture was stirred while 50 mL of concentrated sulfuric acid in 200 mL of water was added in one portion. Enough acetone was added to make the mixture homogeneous (approximately 50 mL). The yellow mercuric oxide (100 mg) was added and the solution was heated at 70 °C (bath temperature) for 1.5 h. The cooled mixture was concentrated in vacuo. Dichloromethane was added to the aqueous layer and extracted thoroughly. After drying, the solvent was removed and the residue was recrystallized from methanol to give 850 mg (78%) of a white solid: mp 92–93 °C; NMR 12.62 (s, 1 H), 7.26 (s, 1 H), 6.4 (s, 1 H), 5.25 (s, 1 H), 3.92 (s, 1 H); IR 3561 (s), 2935 (s), 2862 (m), 1632 (s), 1593 (s), 1505 (s), 1446 (s), 1387 (s).

Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.80; H, 7.72.

4,7-Dimethoxy-1,10-diphenyl-4,6-decadiene-1,9-diyne-3,6-dione (30a): yellow crystals; mp 119–120 °C; yield 84%; ^{1}H NMR 7.48 (m, 5 H), 7.25 (s, 1 H), 3.65 (s, 3 H); IR 2220 (s), 1630 (s), 1550 (m), 1340 (s), 1075 (s); MS, m/e 371 (CI), 370 (EI).

Anal. Calcd for $C_{24}H_{18}O_4$: C, 77.82; H, 4.89. Found: C, 77.94; H, 4.76.

1,12-Bis(benzyloxy)-5,8-dimethoxydeca-5,7-diene-2,10-diyne-4,9-dione (30b): yellow crystals; mp 88–89 °C; yield 83%; ^{1}H NMR 7.35 (s, 5 H), 7.29 (s, 1 H), 4.66 (s, 2 H), 4.38 (s, 2 H), 3.75 (s, 3 H); IR 2918 (m), 2220 (s), 1648 (s), 1555 (m), 1455 (m), 1350 (s), 1180 (s); MS, m/e 459 (CI), 458 (EI).

Anal. Calcd for $C_{28}H_{26}O_6$: C, 73.35; H, 5.71. Found: C, 73.25; H, 5.82.

8,11-Dimethoxyoctadeca-8,10-diene-5,13-diyne-7,12-dione (30c): yellow crystals; mp 70–71 °C; yield 71%; ^{1}H NMR 7.15 (s, 1 H), 3.17 (s, 3 H), 2.31 (t, J = 5.6 Hz, 2 H), 1.55 (m, 4 H), 0.81 (m, 6 H); IR 2960 (m), 2945 (m), 2220 (s), 1628 (s), 1535 (m), 1340 (s), 1182 (s); MS, m/e 331 (CI), 330 (EI).

Anal. Calcd for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.61; H, 8.05.

1,10-Dicarbethoxy-4,7-dimethoxydeca-4,6-diene-1,9-diyne-3,8-dione (30d): yellow solid; mp 96–98 °C; yield 78%; ^{1}H NMR 7.15 (s, 1 H), 4.15 (q, J = 8 Hz, 2 H), 3.65 (s, 3 H), 1.25 (t, J = 8 Hz, 3 H); IR 3000 (m), 2220 (s), 1715 (s), 1660 (s), 1240 (s);

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MS, *m/e* 363 (CI), 362 (EI); exact mass calcd for $C_{18}H_{18}O_8$ 362.10013, found 362.0995.

1,4,8,12-Tetramethoxydeca-5,7-diene-2,10-diyne-4,9-dione (30e): yellow crystals; mp 106–107 °C; yield 67%; ^{1}H NMR 7.22 (s, 1 H), 4.31 (s, 2 H), 3.72 (s, 3 H), 3.4 (s, 3 H); IR 2230 (s), 1655 (s), 1560 (s), 1385 (m), 1350 (s), 1200 (s), 1148 (m), 1020 (s); MS, *m/e* 307 (CI), 306 (EI).

Anal. Calcd for $C_{16}H_{18}O_6$: C, 62.74; H, 5.92. Found: C, 62.54; H, 5.88.

4,7-Dimethoxydeca-4,6-diene-1,9-diyne-3,8-dione (30f): yellow crystals; mp 148–149 °C; yield 56%; ^{1}H NMR 7.41 (s, 1 H), 3.75 (s, 3 H), 3.35 (s, 1 H); IR 3220 (m), 2070 (s), 1635 (s), 1540 (m), 1340 (s), 1115 (s); MS, *m/e* 219 (CI), 218 (EI).

Anal. Calcd for $C_{12}H_{10}O_4$: C, 66.05; H, 4.62. Found: C, 66.14; H, 4.71.

General Procedure for the Synthesis of Diols 19 and 22. A solution of 2.1 equiv of the alkyne in 75 mL of dry THF under an argon atmosphere was stirred at −78 °C while 2.15 equiv of *n*-butyllithium (2.2 M in hexanes) was added dropwise. The solution was stirred for 30 min and then transferred dropwise, via cannula, to a suspension of 1.0 g (1.0 equiv) of orthoquinones **1** or **21** in 400 mL of dry THF at −78 °C. After 1.5 h the reaction was quenched with acetic acid or NH_4Cl. The solvent was evaporated and the residue absorbed onto silica gel. Flash chromatography (hexanes/ethyl acetate, 1:1) gave the purified diols **19a–d** and **22a–e**.

1,2-Bis(phenylethynyl)-4,5-dimethoxy-3,5-cyclohexadiene-1,2-diol (19a): white crystals; 92% yield; mp 171–172 °C; ^{1}H NMR 7.40 (m, 5 H), 5.14 (s, 1 H), 3.72 (s, 1 H), 2.95 (s, 1 H); IR 3552 (br), 3060 (w), 2225 (w), 1624 (s), 1399 (s), 1230 (s).

Anal. Calcd for $C_{24}H_{20}O_4$: C, 77.40; H, 5.41. Found: C, 77.57; H, 5.46.

1,2-Dihexynyl-4,5-dimethoxy-3,5-cyclohexadiene-1,2-diol (19b): white crystals; 90% yield; mp 81–82 °C; ^{1}H NMR 4.79 (s, 1 H), 3.67 (s, 3 H), 2.72 (s, 1 H), 2.29 (m, 2 H), 1.50 (m, 2 H), 0.93 (s, 3 H); IR 3544 (br), 2966 (s), 2942 (s), 2229 (s), 1626 (s), 1400 (s).

Anal. Calcd for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49. Found: C, 72.29; H, 8.51.

1,2-Diethynyl-4,5-dimethoxy-3,5-cyclohexadiene-1,2-diol (19c): white crystals; mp 178–180 °C dec; 76% yield; ^{1}H NMR 4.96 (s, 1 H), 3.64 (s, 3 H), 2.70 (s, 1 H), 2.58 (s, 1 H); IR 3510 (s), 3397 (s), 3274 (s), 1664 (s).

Anal. Calcd for $C_{12}H_{12}O_4$: C, 65.45; H, 5.49. Found: C, 65.49; H, 5.44.

4,5-Dimethoxy-1-hexynyl-2-methyl-3,5-cyclohexadiene-1,2-diol (19d): white solid; mp 109–111 °C; 82% yield; ^{1}H NMR 4.98 (S, 1 H), 4.79 (S, 1 H), 3.66 (S, 3 H), 3.64 (s, 3 H), 2.66 (m, 2 H), 1.46 (m, 7 H), 0.91 (m, 3 H); IR 3487 (s), 3408 (s), 2941 (s), 2215 (w), 1627 (s), 1400 (s).

Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.65; H, 8.32. Found: C, 67.89; H, 8.49.

1,2-Bis(phenylethynyl)-3,6-dimethoxy-3,5-cyclohexadiene-1,2-diol (22a): white crystals; mp 139–140 °C; 86%; ^{1}H NMR 7.3 (m, 5 H), 5.04 (s, 1 H), 3.74 (s, 3 H), 3.22 (s, 1 H); IR 3460 (s), 2220 (w), 1655 (m), 1634 (m), 1485 (s), 1320 (s), 1230 (s).

Anal. Calcd for $C_{24}H_{20}O_4$: C, 77.40; H, 5.41. Found: C, 77.48; H, 5.47.

1,2-Bis[3-(benzyloxy)-1-propynyl]-3,6-dimethoxy-3,5-cyclohexadiene-1,2-diol (22b): colorless oil; 84% yield; ^{1}H NMR 7.31 (s, 5 H), 5.28 (s, 1 H), 4.99 (s, 1 H), 4.58 (s, 2 H), 4.20 (s, 2 H), 3.67 (s, 3 H); IR 3250 (br), 2218 (w), 1670 (m), 1460 (m), 1360 (s), 1255 (s), 1050 (s). Exact mass calcd for $C_{28}H_{28}O_6$ 460.1878, found 460.1862.

1,2-Dihexynyl-3,6-dimethoxy-3,5-cyclohexadiene-1,2-diol (22c): light yellow oil: 92% yield; ^{1}H NMR 4.96 (s, 1 H), 3.67 (s, 3 H), 2.20 (t, J = 7.0 Hz, 2 H), 1.44 (m, 4 H), 0.90 (t, J = 7.2 Hz, 3 H); IR 3520 (s), 2220 (w), 1652 (m), 1460 (s), 1240 (s), 1075 (s); exact mass calcd for $C_{20}H_{28}O_4$ 332.19800, found 332.19856.

1,2-Bis(carbethoxyethynyl)-3,6-dimethyl-3,5-cyclohexadiene-1,2-diol (22d): white crystals; mp 165 °C dec; 90% yield; ^{1}H NMR 5.0 (s, 1 H), 4.15 (q, J = 6.4 Hz, 2 H), 3.65 (s, 3 H), 1.64 (br s, 1 H), 1.25 (t, 3 H); IR 3480 (s), 2240 (s), 1690 (s), 1470 (m), 1250 (s), 1138 (s), 1050 (s).

Anal. Calcd for $C_{18}H_{20}O_8$: C, 59.34; H, 5.53. Found: C, 59.31; H, 5.59.

1,2-Bis(3-methoxy-1-propynyl)-3,6-dimethoxy-3,5-cyclohexadiene-1,2-diol (22e): light yellow oil; 55% yield; ^{1}H NMR 4.97 (s, 1 H), 4.15 (s, 2 H), 3.70 (s, 3 H), 3.35 (s, 3 H), 3.19 (s, 1 H); IR 3450 (br), 2960 (m), 2050 (w), 1610 (m), 1520 (m), 1270 (s), 1120 (s); exact mass calcd for $C_{16}H_{20}O_6$ 308.1256, found 308.1245.

1,2-Diethynyl-3,6-dimethoxy-3,5-cyclohexadiene-1,2-diol (22f): white crystals; mp 178–179 °C; 64% yield; ^{1}H NMR 5.01 (s, 1 H), 3.73 (s, 3 H), 3.21 (s, 1 H), 2.48 (s, 1 H); IR 3490 (s), 3240 (s), 2094 (w), 1660 (m), 1210 (s), 1030 (s).

Anal. Calcd for $C_{12}H_{12}O_4$: C, 65.45; H, 5.49. Found: C, 65.38; H, 5.36.

5-Methoxy-2-(1-hydroxyhexyl)-1,4-benzenediol (31). A solution of 1.00 g (4.85 mmol) of 2-hexynyl-5-methoxy-2,5-cyclohexadiene-1,4-dione (**3c**) in ether was shaken in a separatory funnel with aqueous sodium dithionite for 5 min. The ether layer was separated with most of the solvent removed on a rotovap and replaced with 250 mL of methanol. About half of this volume was removed on the rotovap and replaced with more methanol. This process was repeated 3 times and serves to remove most of the residual ether. The mixture was stirred while 50 mL of concentrated sulfuric acid in 200 mL of water was added in one portion. Enough acetone was added to make the mixture homogeneous (approximately 50 mL). Yellow mercuric oxide (100 mg) was added and the solution was heated at 70 °C (bath temperature) for 1.5 h. The cooled mixture was then placed on the rotovap to remove most of the methanol acetone. Dichloromethane was added to the aqueous layer and extracted thoroughly. Drying and removal of the solvent gave a solid, which was recrystallized from methanol to give 850 mg (78%) of a white solid: mp 92–93 °C; ^{1}H NMR 12.62 (s, 1 H), 7.26 (s, 1 H), 6.44 (s, 1 H), 5.25 (s, 1 H), 3.92 (s, 1 H); IR 3561 (s), 2935 (s), 2862 (m), 1632 (s), 1593 (s), 1505 (s), 1446 (s), 1387 (s).

Anal. Calcd for $C_{13}H_{20}O_4$: C, 65.53; H, 7.61. Found: C, 65.80; H, 7.72.

2-(1-Hydroxyhexyl)-5-methoxy-2,5-cyclohexadiene-1,4-dione (33a). A solution of 1.00 g (4.20 mmol) in 77 mL dry THF refluxed with 500 mg (12.9 mmol) of sodium borohydride. After about 45 min, the solution turned milky and TLC showed the reaction to be complete. The mixture was cooled, ether was added, and the solution was washed rapidly with 1 M HCl and then with 2% aqueous bicarbonate. This ether solution was treated slowly dropwise with a solution of aqueous ferric chloride (100 mL of a saturated solution). The organic layer was removed, washed thoroughly with water, and dried, and the product was isolated, via flash chromatography (6:4 hexane/ethyl acetate), to give 880 mg (88%) of a yellow solid: ^{1}H NMR 6.68 (d, J = 1 Hz, 1 H), 5.89 (s, 1 H), 4.63 (m, 1 H), 3.83 (s, 3 H), 2.53 (m, 1 H), 1.50 (m, 6 H), 0.90 (m, 3 H); IR 3560 (s), 2958 (s), 1679 (s), 1650 (s), 1604 (s); MS, *m/e* 224 (EI).

Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.73; H, 7.81.

2-(1-Ethoxyhexyl)-5-methoxy-2,5-cyclohexadiene-1,4-dione (33b). An etheral solution of 500 mg (2.10 mmol) of the hydroquinone **31** was stirred in 200 mL of ethanol, while a solution of ferric chloride (50 mL of a saturated solution) containing 200 mL of ethanol was added dropwise. The solution was stirred for 1 h and the organic layer was separated and dried. Removal of the solvent and flash chromatography (6:4 hexane/ethyl acetate) gave 363 mg (65%) of the desired product **33b**, as well as 101 mg (18%) of 2-(1-hydroxyhexyl)-5-methoxy-2,5-cyclohexadiene-1,4-dione (**33a**). The best product ratios of **33b**:**33a** obtained are on the order of 5:1 regardless of whether the reaction is allowed to stir overnight or worked up immediately: ^{1}H NMR 6.71 (d, J = 1.1 Hz, 1 H), 5.91 (s, 1 H), 4.39 (m, 1 H), 3.83 (s, 3 H), 3.42 (m, 2 H), 2.40 (m, 8 H), 0.88 (m, 3 H); IR 2965 (s), 1685 (s), 1659 (s), 1613 (s); exact mass calcd for $C_{15}H_{22}O_4$ 266.1518, found 266.1530.

2-(1-Acetoxyhexyl)-5-methoxy-2,5-cyclohexadiene-1,4-dione (33c). A solution of 20.0 mg (0.084 mmol) of 2-(1-hydroxyhexyl)-5-methoxy-2,5-cyclohexadiene-1,4-dione (**33a**) in 2 mL of pyridine and 2 mL of acetic anhydride was stirred overnight. Methanol (5 mL) was added and the mixture was stirred for 15 min. Dichloromethane (50 mL) was added and extracted thoroughly with 1 M HCl. The organic layer was removed and dried and the product was isolated, via preparative thin layer chromatography, to give 20 mg (85%) as a yellow oil: ^{1}H NMR 6.54 (d, J = 1 Hz, 1 H), 5.91 (s, 1 H), 5.70 (m, 1 H), 3.82 (s, 3 H), 2.10

(s, 1 H), 1.65 (m, 2 H), 1.30 (m, 6 H), 0.87 (m, 3 H); IR 1745 (s), 1680 (s), 1652 (s), 1609 (s); MS, *m/e* 281 (CI); exact mass calcd for $C_{15}H_{20}O_5$ 280.1311, found 280.1311.

5-Bromo-3,4-dimethoxy-6-(phenylethynyl)-1-oxocyclohexa-2,4-dien-6-yl Succinate (34). Treatment of **4b** (1.3 g, 3.7 mmol) with the lithium salt of phenylacetylene was accomplished as described above at −78 °C in THF. The reaction was quenched by the addition of 0.75 g (7.5 mmol) of succinic anhydride and 2.5 mL of HMPA at −78 °C. The mixture was allowed to warm to ambient temperature and the THF was then removed in vacuo. To the residue were added 50 mL of water and 5 mL of concentrated hydrochloric acid. Immediately, this was extracted several times with diethyl ether. After removal of the solvent the residue was purified by flash column chromatography (ethyl acetate/hexane, 6:4) to give 1.71 g (76%) of **32** as pale orange crystals: mp 118–120 °C; ^{1}H NMR 2.76 (m, 4 H), 3.76 (s, 3 H), 3.87 (s, 3 H), 5.67 (s, 1 H), 7.26–7.34 (m, 5 H), 8.69 (br s, 1 H); IR 3500–2400, 2235, 1770, 1730.

Anal. Calcd for $C_{20}H_{17}BrO_7$: C, 53.47; H, 3.81. Found: C, 53.21; H, 3.80.

Hydrolysis of 34. A mixture containing 0.9 g (2 mmol) of **34** and 0.18 g (2.1 mmol) of sodium bicarbonate in 100 mL of water was stirred at ambient temperature. After 2 min, orange crystals of the quinone **6b** began to precipitate. After 10 min, the mixture was extracted with diethyl ether to give 0.45 g (71%) of **6b** after flash chromatography.

3-Bromo-2-hydroxy-4,5-dimethoxy-2-(2-phenyloxiran-1-yl)-3,5-cyclohexadien-1-one (35). A solution of 1.77 g (5 mmol) of **25** and 2.0 g (10.3 mmol) of *m*-chloroperbenzoic acid in 50 mL of dichloromethane was stirred at ambient temperature for 12 h. The reaction mixture was then washed with aqueous sodium bicarbonate. The organic layer was dried ($MgSO_4$) and concentrated, and the residue was subjected to flash column chromatography (ethyl acetate/hexane, 6:4) to give 0.48 g (26%) of **35** as colorless crystals: mp 128–129 °C; ^{1}H NMR 3.52 (s, 3 H), 3.59 (s, 1 H), 3.66 (d, 1 H, J = 4.21 Hz), 3.69 (s, 3 H), 4.08 (d, 1 H, J = 4.2 Hz), 4.81 (s, 1 H), 7.28 (s, 5 H); IR 3390, 1680, 1660, 1590; MS (CI), *m/e* (relative intensity) 367/369 (M^+ + 1, 21.5/22.0).

Anal. Calcd for $C_{16}H_{15}BrO_5$: C, 52.33; H, 4.12. Found: C, 52.16; H, 4.15.

3-Bromo-4,5-dimethoxy-2-(2-phenyloxiran-1-yl)-1-oxocyclohexa-3,5-dienyl Succinate (36). A solution of 0.25 g (0.68 mmol) of **35** in 30 mL of anhydrous THF was treated with 40 mg (0.83 mmol) of sodium hydride at 0 °C. Succinic anhydride, 80 mg (0.8 mmol), in 15 mL of THF was then added. After 3 days under nitrogen 1 mL of concentrated hydrochloric acid, 50 mL of water, and 50 mL of dichloromethane were added. The resulting mixture was extracted with dichloromethane, and the organic solution was dried ($MgSO_4$) and concentrated in vacuo. The residue was subjected to flash chromatography (ethyl acetate/hexane, 6:4) to give 0.21 g (66%) of **36** as colorless crystals: mp 178–179 °C; ^{1}H NMR (Me_2SO-d_6) 2.45 (m, 4 H), 3.49 (s, 3 H), 3.59 (s, 3 H), 3.72 (d, 1 H, J = 4.0 Hz), 3.84 (d, 1 H, J = 4.0 Hz), 4.93 (s, 1 H), 7.12 (br s, 1 H), 7.25–7.31 (m, 5 H); IR 3440, 1750, 1670, 1645, 1575; MS (CI), *m/e* (relative intensity) 367/369 [(M^+ + 1) − HO_2C − $(CH_2)_2CO_2H$, 6.8/7.6].

This compound slowly decomposed upon standing. As a result, satisfactory C, H analysis was not obtained.

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Oxidative Coupling of Carboxylic Acid Dianions: The Total Synthesis of (±)-Hinokinin and (±)-Fomentaric Acid[1]

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The oxidative coupling of carboxylic acid dianion derivatives provides the key intermediates needed for efficient syntheses of the symmetrical lignan hinokinin (**9**) and the unsymmetrical fungal metabolite fomentaric acid (**22**). Racemic hinokinin (**9**), a target chosen to test the facility of dianion oxidative coupling in the presence of electron-rich aromatic rings, is prepared in an overall conversion of 61% from 3,4-(methylenedioxy)hydrocinnamic acid. Racemic fomentaric acid (**22**), a trisubstituted succinic acid derivative, results from a straightforward two-step sequence that proceeds in an overall yield of 40% from eicosanoic acid. Preliminary studies demonstrate the utility of oxidative coupling in the synthesis of novel surfactant prototypes.

Valuable, but underutilized, methodology for the formation of carbon–carbon bonds involves the oxidative coupling of electron-rich systems.[2] The suitability of numerous carbanionic species to serve as substrates for oxidation makes accessible an almost unlimited variety of products.[3] In essence, coupling reactions provide an inherently convergent strategy for the assembly of complex molecular targets.[4]

Oxidative coupling reactions may be conveniently subdivided (Scheme I) into three separate classes: type I,[5] type II,[5] and type III.[6] This classification is based upon the similarity or difference of groups attached to the coupling carbons. The focus of this paper is on the application of type I and type II coupling to the synthesis of selected natural products.

Carboxylic acid dianions are easily prepared, versatile, strongly nucleophilic intermediates.[7] Building upon initial studies published by Ivanoff[8] and by Morton,[9] carboxylic acid dianions have been shown to exhibit considerable

(1) Dedicated to Prof. George Büchi on the occasion of his 65th birthday.

(2) See, for instance: (a) Eglinton, G.; McCrae, W. *Adv. Org. Chem.* **1963**, *4*, 225. (b) Cadiot, P.; Chodkiewicz, W. In *Acetylenes*; Viehe, H. G., Ed.; Marcell Dekker, Inc.: New York, 1969; pp 597–647. (c) Taylor, W. L.; Battersby, A. R., Eds. *Oxidative Coupling of Phenols*; Marcell Dekker: New York, 1967. (d) Hampton, K. G.; Christie, J. J. *J. Org. Chem.* **1975**, *40*, 3887. (e), Paquette, L. A.; Snow, R. A.; Muthard, J. L.; Cynkowski, T. *J. Am. Chem. Soc.* **1978**, *100*, 1600. (f) Frazier, R. H., Jr.; Harlow, R. L. *J. Org. Chem.* **1980**, *45*, 5408. (g) Kobayashi, Y.; Taguchi, T.; Morikawa, T. *Tetrahedron Lett.* **1978**, 3555. (h) Ito, Y.; Konoike, T.; Saegusa, T. *J. Am. Chem. Soc.* **1975**, *97*, 649. (i) Ito, Y.; Konoike, T.; Harada, T.; Saegusa, T. *Ibid.* **1977**, *99*, 1487. (j) Kaiser, E. M. *J. Am. Chem. Soc.* **1967**, *89*, 3659. (h) Kauffmann, T. *Angew Chem. Int. Ed. Engl.* **1974**, *13*, 291. (l) Maryanoff, C. A.; Maryanoff, B. E.; Tang, R.; Mislow, K. *J. Am. Chem. Soc.* **1973**, *95*, 5839. (m) Vijh, A. K.; Conway, B. E. *Chem. Rev.* **1967**, *67*, 623. (n) Weedon, B. C. L. *Q. Rev. Chem. Soc.* **1952**, *6* 380. (o) Weedon, B. C. L. *Adv. Org. Chem.* **1960**, *1*, 1. (p) Kofron, W. G.; Hauser, C. R. *J. Org. Chem.* **1970**, *35*, 2085. (q) Rathke, M. W.; Lindert, A. *J. Am. Chem. Soc.* **1971**, *93*, 4605. (r) Brocksom, T. J.; Petragnani, N.; Rodriques, R.; LaScala Teixeira, H. *Synthesis* **1975**, 396. (s) Chung, S. K.; Dunn, L. B., Jr. *J. Org. Chem.* **1983**, *48*, 1125. (t) Kobayashi, Y.; Taguchi, T.; Morikawa, T.; Tokuno, E.; Sekiguchi, S. *Chem. Pharm. Bull.* **1980**, *28*, 262.

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