Annelation Reactions of 4-Alkynylcyclobutenones. Formation of Methylenebenzofurans

Simon L. Xu, Meng Taing, and Harold W. Moore*

Department of Chemistry, University of California, Irvine, California 92717

Received April 4, 1991

Thermolysis of a number of 4-alkynyl-4-(propargyloxy)cyclobutenones is reported. These studies show a remarkable rearrangement to methylenebenzofurans accompanied by remote alkene formation. The mechanism and scope of the reactions are discussed.

Introduction

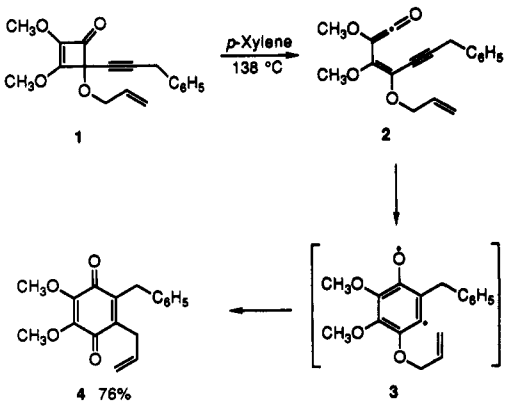
A number of examples of an unusual rearrangement of 4-alkynyl-4-(propargyloxy)cyclobutenones to methylenebenzofurans are described in this paper, e.g., **16a–21**, Scheme V. These transformations embrace both an annelation step and formation of a remotely placed alkene moiety. They add to a growing number of synthetically useful ring expansions of cyclobutenones that include formation of 1,4-benzo- and 1,4-naphthoquinones,[1,2] hydroquinones,[3-8] chlorophenols,[9] 2-alkylidene-1,3-cyclopentenediones,[2,10,11] and bicyclo[3.2.0]heptenones.[12]

The rearrangements outlined here are envisaged to involve the intermediacy of conjugated ketenes and diradicals such as **17** and **18**. Analogies are found in the mechanistic pathway associated with the thermal rearrangements of 4-alkynyl-4-hydroxycyclobutenones to quinones.[2,13] As an illustration, 4-(3-phenylpropynyl)-4-(allyloxy)-2,3-dimethoxycyclobutenone (**1**) was shown to give the corresponding (alkynylethenyl)ketene **2** and thus the diradical **3** upon thermolysis in refluxing *p*-xylene; intramolecular addition of the ring-based radical center of **3** to the allylic double bond initiates allyl group migration resulting in the benzoquinone **4** (Scheme I).[2]

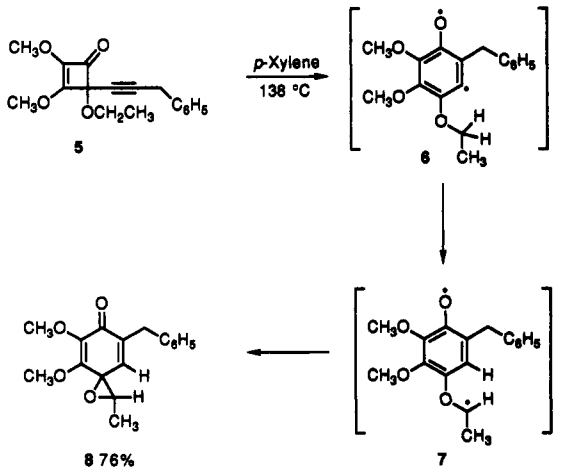
A variant of the above stems from the thermolysis of 4-(3-phenylpropynyl)-4-ethoxy-2,3-dimethoxycyclobutenone (**5**) (Scheme II).[2] Here, the diradical intermediate **6** gives **7** upon intramolecular H-atom abstraction from the methylene group of the ethoxy substituent. Diradical **7** then proceeds to the spiroepoxide **8** upon intramolecular radical recombination.

Still another interesting example comes from for the thermolysis of 4-chlorocyclobutenone **9** (Scheme III). In this case, the ring-based radical center of **10** abstracts a hydrogen atom from the terminal methyl of the butyl substituent to generate **11**; ring closure then provides the observed products **12** and **13** (Scheme II).[9]

Scheme I



Scheme II



Results and Discussion

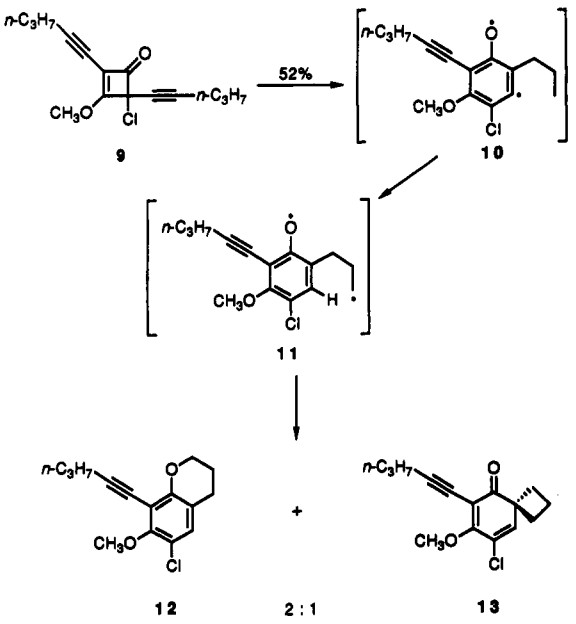
The cyclobutenones **15a–h** were synthesized in excellent yields by addition of the appropriate lithium acetylides to dimethyl squarate (**14**).[2] These, in turn, were converted to the cyclobutenones **16a–h** upon treatment with propargyl iodides in the presence of silver(I) oxide and potassium carbonate at ambient temperature in acetonitrile (Scheme IV).[13,14]

(1) Karlsson, J. O.; Nguyen, N. V.; Foland, L. D.; Moore, H. W. *J. Am. Chem. Soc.* **1985**, *107*, 3392.
(2) Foland, L. D.; Karlsson, J. O.; Perri, S. T.; Schwabe, R.; Xu, S. L.; Patil, S.; Moore, H. W. *J. Am. Chem. Soc.* **1989**, *111*, 975. Foland, L. D.; Decker, O. H. W.; Moore, H. W. *J. Am. Chem. Soc.* **1989**, *111*(3), 989–95. Also: Gayo, L.; Moore, H. W. Unpublished results.
(3) Liebeskind, L. S.; Iyer, S.; Jewell, C. F. *J. Org. Chem.* **1986**, *51*(15), 3065–7.
(4) Reed, M. W.; Moore, H. W. *J. Org. Chem.* **1988**, *53*(18), 4166–71.
(5) Moore, H. W.; Perri, S. T. *J. Org. Chem.* **1988**, *53*(5), 996–1003.
(6) Perri, S. T.; Moore, H. W. *Tetrahedron Lett.* **1987**, *28*(39), 4507–10.
(7) Perri, S. T.; Foland, L. D.; Decker, O. H. W.; Moore, H. W. *J. Org. Chem.* **1986**, *51*(15), 3067–8. Perri, S. T.; Moore, H. W. *J. Am. Chem. Soc.* **1990**, *112*(5), 1897–905.
(8) Perri, S. T.; Dyke, H. J.; Moore, H. W. *J. Org. Chem.* **1989**, *54*(9), 2032–4.
(9) Xu, S. L.; Moore, H. W. *J. Org. Chem.* **1989**, *54*(17), 4024–6, and unpublished results.
(10) Mitchell, D.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1990**, *112*(1), 291–6.
(11) Liebeskind, L. S.; Mitchell, D.; Foster, B. S. *J. Am. Chem. Soc.* **1987**, *109*(25), 7908–10.
(12) Xu, S. L.; Moore, H. W. *J. Org. Chem.* **1989**, *54*(26), 6018–21.
(13) For allylation of hydroxycyclobutenones, see: Foland, L. D.; Decker, O. H. W.; Moore, H. W. *J. Am. Chem. Soc.* **1989**, *111*, 989.

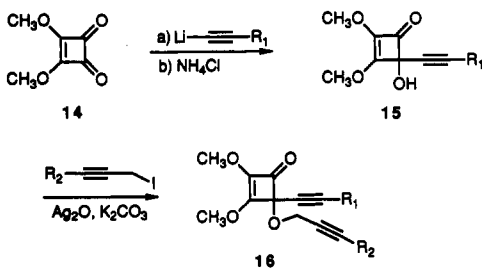
(14) The required propargyl iodides were prepared from commercially available propargyl alcohols. Treatment of the alcohols with tosyl chloride and sodium hydroxide generated the corresponding tosylates, and these were converted to the bromides and then to the propargyl iodide (Finkelstein reaction). Although the propargyl iodides were found to decompose easily in air at ambient temperature, they can be stabilized by addition of copper wire. Propargyl iodides have also been reported from the cleavage of methyl propargyl ether with acetyl iodide, see: Kunau, W. H. *Chem. Phys. Lipids* **1971**, *7*, 108.

0022-3263/91/1956-6104$02.50/0

Scheme III



Scheme IV



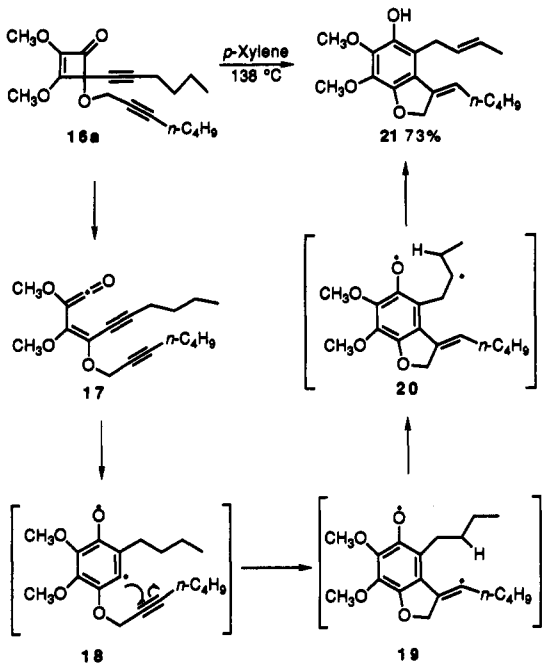
	R_1	R_2	% 15	%16
a	-n-C_4H_9	n-C_4H_9	89*	76
b	-n-C_4H_9	n-C_3H_7	89*	85
c	-n-C_3H_7	n-C_3H_7	92	88
d	-C_2H_5	n-C_3H_7	90	81**
e	-CH_3	n-C_3H_7	91	73**
f	-$CH_2OC_6H_5$	n-C_3H_7	62	66
g	-$CH_2C_6H_5$	n-C_3H_7	82*	65
h	-$C(CH_3)=CH_2$	n-C_3H_7	76	68

* For experimental details see Ref 2.
** Yields based on recovered starting material

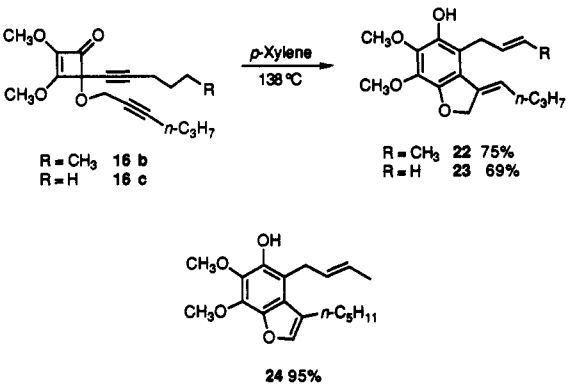
Thermolysis of **16a** in refluxing *p*-xylene led to the methylenebenzofuran **21** in 73% isolated yield (Scheme V). The structure of **21** is based upon its spectral properties and a single-crystal X-ray analysis, the details of which are provided in the supplementary material.

The formation of **21** is envisaged to involve electrocyclic ring opening of **16a** to the conjugated ketene **17** and then to the diradical **18** upon ring closure. Subsequent 5-exo cyclization involving attack of the aryl radical on the propargyloxy triple bond gives the new diradical **19**. The resulting vinyl radical center in **19** abstracts a H-atom from the proximal butyl side chain to give **20**; this then leads to **21** via a second H-atom abstraction involving the phenoxy radical. Interestingly, both proposed H-atom abstractions require seven-membered ring transition states. Although this is a less common process as compared to the six-membered counterpart, it has some experimental and theoretical precedent.[15,16]

Scheme V



Scheme VI



Additional examples of the formation of methylenebenzofurans from 4-alkynyl-4-(propargyloxy)cyclobutenones are presented in Scheme VI. Compound **16b**, differing from **16a** only in the length of the propargyl side chain, gave **22** in 75% isolated yield. Also, **16c** provided **23** (69%) together with a trace amount of the regioisomer having the alkene double bond in conjugation with the aromatic ring.

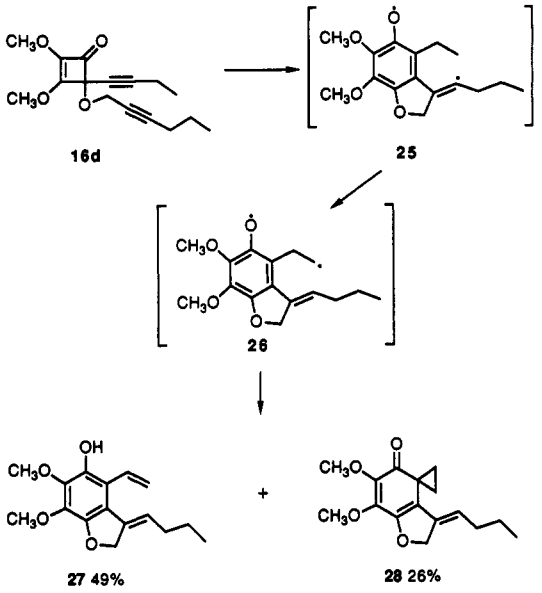
The methylenebenzofurans can be converted to the aromatic benzofurans upon mild acid treatment. For example, when **21** was treated with 1 N HCl in a mixed solvent of methanol and tetrahydrofuran, benzofuran **24** was obtained in 95% yield.

Cyclobutenones having progressively shorter 4-alkynyl substituents were investigated in order to explore further the scope of the diradical initiated annelation reactions. To this end, thermolysis of **16d** represents an interesting variant (Scheme VII). The products realized from the thermolysis of **16d** are the methylenebenzofuran **27** and, surprisingly, the spiro cyclohexadienone **28**. Characteristic structural data for **28** (IR, ^1H and ^{13}C NMR) show the presence of a carbonyl group as well as four methylene carbons. The methylene protons in the cyclopropane ring appear as two sets of doublets of doublets resulting from geminal and trans couplings.

The thermolysis of **16d** is assumed to generate the diradical **25** and the vinyl radical center abstracts a hydrogen

(15) (a) Wagner, P. J.; Kelso, P. A.; Kemppainen, A. E.; Zepp, R. G. *J. Am. Chem. Soc.* **1972**, *94*, 7500. (b) Mihailovic, M. L.; Miloradovic, M. *Tetrahedron* **1966**, *22*, 723.
(16) Dorigo, A. E.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 2197.

Scheme VII



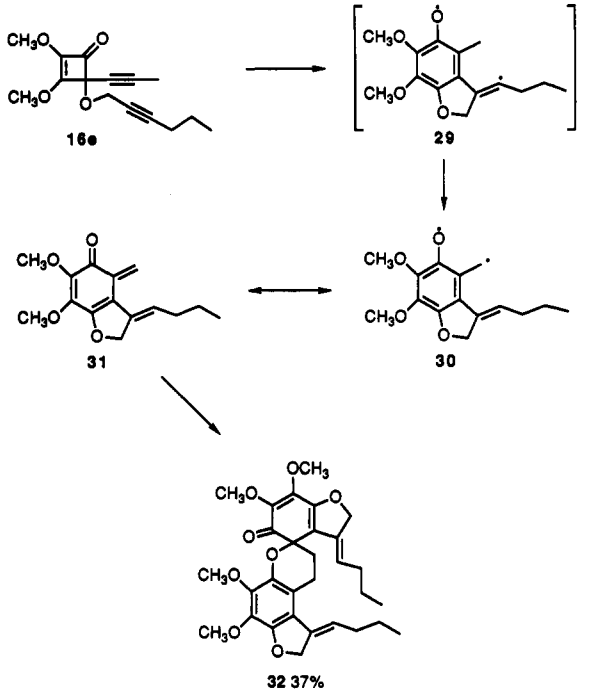
atom from the terminal methyl group of the ethyl side chain to give **26**. The phenoxide radical then abstracts a hydrogen atom from the methylene group though a five-membered ring transition state to give methylenebenzofuran **27**. Intramolecular radical recombination is in competition, thus leading to the spiro compound **28**. Although unusual, its formation is not completely unexpected on the basis of the observation that the similar diradical **11** (Scheme III) gave spiro compound **13**. It is, however, surprising that analogous products were not observed from the thermolysis of **16a–c** or that radical–radical coupling between the oxygen-based center and the carbon-based radical in **26** is apparently noncompetitive.

Formation of **28** is rationalized by assuming that the hydrogen atom abstraction in **25** gives **26**, having an initial conformation of the side chain that entropically favors ring closure to **28**. That the similar diradical **20** (Scheme V) did not give a spiro product may be due to steric effects as well as differences in reactivity, i.e., the primary alkyl radical in **26** should have a shorter lifetime compared to the secondary alkyl radical in **20**.

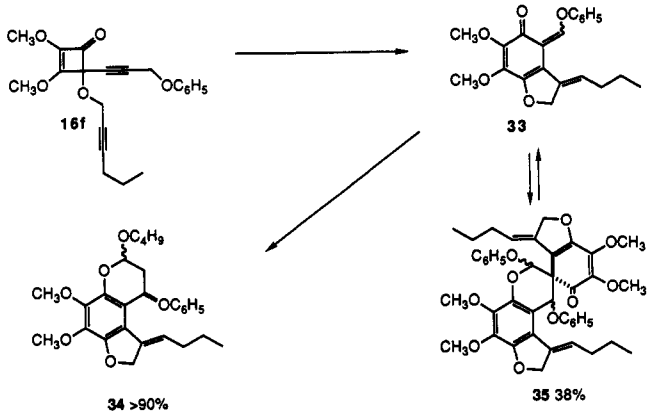
Still another example of the annelation reaction is outlined in Scheme VIII. Here, compound **16e** bears a propynyl group at position-4. Thermolysis of this compound gave the dimer **32**. Presumably, the vinyl radical in **29** abstracts a hydrogen atom from the methyl group to give the quinone methide **30–31**. The transient quinone methide then undergoes self-condensation (Diels–Alder) to provide the dimer **32**.[17]

The structure assignment of **32** is based upon the following characteristic spectral data: the correct molecular weight (525) was obtained from the HRCI mass spectrum;

Scheme VIII



Scheme IX



the IR (1670 cm^{-1}) and ^{13}C NMR spectra (196 ppm) indicate the presence of a carbonyl group; the ^{1}H NMR spectrum shows absorptions for four methoxy groups (3.73, 3.81, 3.94, and 4.19 ppm) and the characteristic coupling patterns expected for the four methylene protons in the cyclohexene ring.

In a comparison study, the thermolysis of **16f** in the presence of butoxyethene was observed to give a high yield of the quinone methide **33** as evidenced by the formation of the hetero-Diels–Alder product, chromanol **34** (>90%), as a 2:1 mixture of diastereomers (Scheme IX).

In the absence of a trap the dimer **35** was realized as an ostensible single yellow diastereomer in 38% isolated yield. The regiochemistry of this dimer is apparent from its ^{1}H NMR spectrum, which shows the two methine proton absorptions as singlets at 5.63 and 6.38 ppm.[18] The correct molecular weight for **35** (708) was obtained by FAB MS. However, high resolution mass spectroscopy showed no peaks above 354, the molecular weight for the quinone methide monomer. The quinone methide/dimer reversibility was further established by the observation that the yellow dimer reverts to the red quinone methide upon

(17) For dimerization and trimerization of quinone methides, see: Dean, F. M.; Matkin, D. A.; Osrabi, M. O. A. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1437. Cavitt, S. B.; Sarrafizadeh, H.; Gardner, P. D. *J. Org. Chem.* **1962**, *27*, 1211. Boldt, M.; Gaudiano, G.; Haddadin, M. J.; Koch, T. H. *J. Am. Chem. Soc.* **1989**, *111*(6), 2283–92. Yamashita, A.; Scahill, T. A.; Chidester, C. G. *Tetrahedron Lett.* **1985**, *26*(9), 1159–62. Zanarotti, A. *J. Chem. Res., Synop.* **1983**, (12), 306–7. Musil, L.; Kouter, B.; Pisova, M.; Soucek, M. *Collect. Czech. Chem. Commun.* **1981**, *46*(5), 1148–59. Lanteri, P.; Longeray, R.; Royer, J. *J. Chem. Res., Synop.* **1981**, (6), 168–9. Hemmingson, J. A. *Tetrahedron Lett.* **1977**, (34), 2967–8. Chauhan, M. S.; Dean, F. M.; McDonald, S.; Robinson, M. S. *J. Chem. Soc., Perkin Trans. 1* **1973**, (4), 359–63. Bolon, D. A. *J. Org. Chem.* **1970**, *35*(3), 715–19. Bavoux, C.; Perrin, M.; Goldmann, H.; Boehmer, V. *J. Chem. Soc., Perkin Trans. 2* **1989**, (12), 2059–63. Soejima, Y. *Kyushu Sangyo Daigaku Kogakubu Kenkyu Hokoku* **1988**, *25*, 59–62.

(18) For an example of this mode of quinone methide dimerization, see: Jurd, L. *Tetrahedron* **1977**, *33*(2) 163.

thermolysis in refluxing toluene. When this was accomplished in the presence of butoxyethene, the chromanol **34** was again observed as a mixture of diastereomers (4:1) in 70% isolated yield.

It is of interest to note that the more electron rich nature of quinone methide **33** as compared to **31** completely inverts the mode of dimerization; the former results in a cycloaddition involving carbon–oxygen bond formation and the latter in carbon–carbon bond formation.

Finally, attempts to extend the rearrangement to include examples where more than one ring would be formed have thus far failed. In this regard, thermolyses of 2,3-dimethoxy-4-(3-phenyl-1-propynyl)-4-(2-hexynyloxy)-2-cyclobuten-1-one (**16g**) and 2,3-dimethoxy-4-(3-methyl-3-buten-1-yn-1-yl)-4-(2-hexynyloxy)-2-cyclobuten-1-one (**16h**) resulted in complex mixtures of products.

Conclusion

Thermolyses of 4-alkynyl-4-(propargyloxy)cyclobutenones were found to result in annelations accompanied by remote functionalization. Although some limitations were observed, the rearrangement is potentially useful for the synthesis of highly substituted benzofurans and for the generation and in situ trapping of *o*-quinone methides.

Experimental Section

General Procedures. All reactions were performed in flame-dried glassware under a positive pressure of argon. Reaction mixtures were stirred magnetically. Air-sensitive solutions were transferred via cannula and were introduced into the reaction vessels through rubber septa. Butyllithium was introduced to the reaction mixture vessels via syringe. Reaction solutions were concentrated on a Buchi rotary evaporator at 15–20 mmHg. Column chromatography was performed by using E. Merck silica gel (230–400 mesh), with hexanes and ethyl acetate as the eluants.

The new compounds reported here were greater than 90% pure as evidenced by NMR analysis. These data as well as the X-ray data for compound **21** are available as supplementary material.

Commercial grade solvents were used without further purification except as indicated below. Tetrahydrofuran was distilled from sodium benzophenone ketyl. Benzene and *p*-xylene were distilled from calcium hydride.

2,3-Dimethoxy-4-hydroxy-4-pentynyl-2-cyclobuten-1-one (15c). A solution of 0.42 mL (4.2 mmol) of 1-pentyne in 25 mL of THF was cooled to −78 °C and 2.42 mL (3.87 mmol) of *n*-butyllithium (1.6 M solution in THF) was then added. The resulting solution was stirred at −78 °C for 30 min and then transferred to second flask containing 0.50 g (3.5 mmol) of dimethyl squarate in 100 mL of THF at −78 °C. The reaction mixture was stirred for 20 min and quenched by being poured into a separatory funnel containing 20 mL of ether and 10 mL of 5% NH_4Cl solution. The organic phase was washed with brine (2 × 10 mL), dried ($MgSO_4$), and concentrated to gave a yellow oil. Purification of this by chromatography (3:1 hexanes/ethyl acetate) gave **15c** (0.68 g, 92%) as a slightly yellow oil: IR (film) 3400, 2970, 2880, 2240, 1780, 1640, 1620, 1470, 1435, 1355, 1345, 1220, 1150, 1140, 1050, 1030, 980, 830, 730 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.95 (t, J = 7.5 Hz, 3 H), 1.53 (q, J = 7.5 Hz, 2 H), 2.22 (t, J = 7.0 Hz, 2 H), 3.53 (s, 1 H), 3.94 (s, 3 H), 4.18 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.4, 20.7, 21.6, 58.5, 59.9, 74.5, 78.5, 90.4, 135.2, 165.1, 181.4; MS (EI) m/z (rel intensity) 210 (2), 195 (19), 167 (27), 153 (6), 139 (46), 135 (21), 124 (28), 107 (38), 96 (69), 77 (100); exact mass calcd for $C_{11}H_{14}O_4$ 210.0892, found 210.0895.

4-Butynyl-4-hydroxy-2,3-dimethoxy-2-cyclobuten-1-one (5d). Dimethyl squarate (0.60 g, 4.2 mmol) and excess 1-butyne gave **15d** (0.75 g, 90%) as a slightly yellow oil: IR ($CHCl_3$) 3550, 3400, 2990, 2960, 2240, 1780, 1660, 1650, 1630, 1470, 1440, 1350, 1040, 990, 910, 830, 810 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.15 (t, J = 7.5 Hz, 3 H), 2.27 (q, J = 7.5 Hz, 2 H), 2.71 (s, 1 H), 3.97 (s, 3 H), 4.19 (s, 3 H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 12.5, 13.2, 58.4, 59.9, 73.7, 78.4, 91.6, 135.1, 165.2, 181.5; MS (EI), m/z (rel intensity) 196 (21), 181 (24), 153 (86), 125 (65), 110 (47), 95 (43), 93 (46), 82 (100), 81 (55), 65 (44), 53 (87); exact mass calcd for $C_{10}H_{12}O_4$ 196.0736, found 196.0728.

2,3-Dimethoxy-4-hydroxy-4-propynyl-2-cyclobuten-1-one (15e). Dimethyl squarate (0.50 g, 3.5 mmol) and excess propyne gave **15e** (0.58 g, 91%) as a white solid: mp 65–67 °C; IR ($CHCl_3$) 3580, 3350, 3000, 2960, 2240, 1780, 1640, 1470, 1430, 1350, 1230, 1160, 1140, 1130, 990, 830 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.86 (s, 3 H), 3.89 (s, 1 H), 3.91 (s, 3 H), 4.16 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 3.7, 58.4, 59.9, 73.5, 78.3, 85.9, 135.0, 165.3, 181.6; MS (EI), m/z (rel intensity) 182 (24), 167 (11), 139 (51), 111 (34), 96 (50), 83 (23), 81 (39), 79 (34), 68 (100), 67 (96), 53 (28), 51 (25); exact mass calcd for $C_9H_{10}O_4$ 180.0578, found 182.0583.

4-Hydroxy-2,3-dimethoxy-4-(3-phenoxypropynyl)-2-cyclobuten-1-one (15f). Dimethyl squarate (0.50 g, 3.5 mmol) and 1-phenoxy-2-propyne (0.52 g, 3.9 mmol) gave **15f** (0.66 g 62%) as a slightly yellow oil: R_f = 0.12; IR (film) 3378, 2953, 2239, 1778, 1641, 1598, 1494, 1470, 1433, 1345, 1214, 1152, 1041 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.01 (s, 1 H), 3.96 (s, 1 H), 4.10 (s, 3 H), 4.76 (s, 2 H), 6.94–7.02 (m, 3 H), 7.27–7.32 (m, 2 H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 55.8, 58.4, 59.9, 78.0, 81.3, 83.9, 114.8, 121.3, 129.2, 135.2, 157.2, 157.2, 164.7, 164.7, 180.4; MS (EI), m/z (rel intensity) 274 (26), 259 (11), 231 (10), 199 (12), 181 (51), 149 (100), 125 (42), 104 (27), 94 (92); exact mass calcd for $C_{15}H_{14}O_5$ 274.0841, found 274.0840.

2,3-Dimethoxy-4-(1-hexynyl)-4-(2-heptynyloxy)-2-cyclobuten-1-one (16a). To a solution of 0.66 g (2.9 mmol) of **15b** in 8 mL of acetonitrile were added 1.0 g (4.5 mmol) of 1-iodo-2-heptyne and 4.4 g (32 mmol) of K_2CO_3. The mixture was stirred at rt under an atmosphere of Ar. To the suspension was added 2.72 g (11.6 mmol) of Ag_2O in 4 portions over a period of 9 h. After 12 h, the orange suspension was filtered through a pad of Celite, washed with ether (20 mL), and concentrated in vacuo. The oil was purified by column chromatography (30:1 hexanes/ethyl acetate) to yield 0.71 g (76%) of **16a** as a clear slightly yellow oil: IR (film) 2970, 2950, 2880, 2240, 1790, 1740, 1650, 1473, 1350, 1150 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, J = 7.5 Hz, 3 H), 0.91 (t, J = 7.5 Hz, 3 H), 1.37–1.55 (m, 8 H), 2.21 (tt, J = 7.5, 2.2 Hz, 2 H), 2.28 (t, J = 7.5 Hz, 2 H), 3.95 (s, 3 H), 4.16 (s, 3 H), 4.37 (dt, J = 14.5, 2.2 Hz, 1 H), 4.45 (dt, J + 14.5, 2.2 Hz, 1 H); MS (CI), m/z 319; MS (EI), m/z (rel intensity) 318 (2), 275 (7), 261 (9), 233 (7), 223 (22), 181 (17), 169 (13), 153 (20), 135 (12), 125 (26), 109 (36), 91 (24), 79 (60), 67 (57), 53 (100); exact mass calcd for $C_{19}H_{26}O_4$ 318.1831, found 318.1831.

4-Hexynyl-4-(2-hexynyloxy)-2,3-dimethoxy-2-cyclobuten-1-one (16b). A solution of 0.30 g (1.3 mmol) of **15b**, 0.42 g (2.0 mmol) of 1-iodo-2-hexyne, 0.78 g (3.4 mmol) of Ag_2O, and 0.93 g (6.7 mmol) of K_2CO_3 in 5 mL of acetonitrile afforded 0.35 g (85%) **16b** as a slightly yellow oil: IR (film) 2960, 2940, 2880, 2242, 2238, 1780, 1660, 1655, 1650, 1470, 1440, 1380, 1350, 1220, 1160, 1120, 1050, 840 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.91 (t, J = 7.3 Hz, 3 H), 0.97 (t, J = 7.3 Hz, 3 H), 1.40 (sextet, J = 7.0 Hz, 2 H), 1.47–1.58 (m, 4 H), 2.19 (t, J = 7.1 Hz, 2 H), 2.29 (t, J = 7.1 Hz, 2 H), 3.95 (s, 3 H), 4.16 (s, 3 H), 4.37 (d, J = 14.4 Hz, 1 H), 4.45 (d, J = 14.7 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.3, 13.4, 18.5, 20.7, 21.7, 21.8, 30.2, 55.3, 58.4, 59.9, 71.8, 75.6, 83.1, 87.0, 92.2, 135.7, 164.1, 179.6; MS (EI), m/z (rel intensity) 223 (11), 181 (11), 169 (8), 153 (15), 125 (23), 109 (34), 91 (26), 79 (86), 67 (42), 53 (100); MS (CI), m/z (rel intensity) 305 (100), 207 (88); exact mass calcd for $C_{18}H_{24}O_4$ 304.1673, found 304.1683.

4-(2-Hexynyloxy)-2,3-dimethoxy-4-pentynyl-2-cyclobuten-1-one (16c). A solution of 0.50 g (2.4 mmol) of **15c**, 0.74 g (3.6 mmol) of 1-iodo-2-hexyne, 0.74 g (3.6 mmol) of Ag_2O, and 1.64 g (11.9 mmol) of K_2CO_3 in 10 mL of acetonitrile afforded 0.61 g (88%) of **16c** as a colorless oil: IR (film) 2980, 2940, 2880, 2240, 1790, 1660, 1650, 1470, 1440, 1350, 1160, 1050, 840 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.97 (t, J = 7.5 Hz, 3 H), 0.99 (t, J = 7.4 Hz, 3 H), 1.49–1.61 (m, 4 H), 2.19 (t, J = 7.0 Hz, 2 H), 2.27 (t, J = 7.0 Hz, 2 H), 3.96 (s, 3 H), 4.17 (s, 3 H), 4.37 (dt, J = 14.6, 2.1 Hz, 1 H), 4.45 (dt, J = 14.6, 2.2 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.26, 20.61, 20.72, 21.54, 21.70, 55.30, 58.33, 59.89, 72.01, 75.57, 83.10, 86.94, 92.04, 135.68, 164.01, 179.51; MS (CI), m/z (rel intensity) 291 (100); exact mass calcd for $C_{17}H_{22}O_4$ 290.1518, found 290.1508.

4-Butynyl-2,3-dimethoxy-4-(2-hexynyloxy)-2-cyclobuten-1-one (16d). A solution of 0.49 g (2.5 mmol) of **15d**, 0.78 g (3.8 mmol) of 1-iodo-2-hexyne, 1.15 g (5.0 mmol) of Ag_2O, and 1.73

g (12.5 mmol) of K_2CO_3 in 5 mL of acetonitrile afforded 0.52 g (81% based on recovering starting material) of **16d** as a colorless oil: IR (film) 2960, 2870, 2230, 1780, 1640, 1470, 1435, 1350, 1220, 1155, 1152, 1050, 840, 810 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.96 (t, J = 7.5 Hz, 3 H), 1.16 (t, J = 7.5 Hz, 3 H), 1.52 (sextet, J = 7.2 Hz, 2 H), 2.19 (tt, J = 7.1, 2.2 Hz, 2 H), 2.30 (q, J = 7.5 Hz, 2 H), 3.95 (s, 3 H), 4.16 (s, 3 H), 4.37 (dt, J = 14.5, 2.2 Hz, 1 H), 4.45 (dt, J = 14.5, 2.2 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.5, 13.3, 13.3, 20.7, 21.8, 55.3, 58.4, 60.0, 71.2, 75.6, 83.1, 87.0, 93.4, 135.7, 146.1, 179.6; MS (CI) m/z (rel intensity) 277 (99); MS (EI), m/z (rel intensity) 247 (4), 233 (5), 195 (100), 167 (32), 139 (25), 109 (26), 93 (28), 81 (36), 53 (49); exact mass calcd for $C_{16}H_{21}O_4^+$ (HRCI) 277.1439, found 277.1431.

2,3-Dimethoxy-4-(2-hexynyloxy)-4-propynyl-2-cyclobuten-1-one (16e). A solution of 0.50 g (2.7 mmol) of **15e**, 0.84 g (4.1 mmol) of 1-iodo-2-hexyne, 1.6 g (6.8 mmol) of Ag_2O, and 1.9 g (14 mmol) of K_2CO_3 in 8 mL of acetonitrile afforded 0.35 g (70% based on recovered starting material) of **16e** as a colorless oil: IR (film) 2960, 2940, 2880, 2240, 1790, 1660, 1650, 1470, 1350, 1160, 1130, 1050, 850 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.95 (t, J = 6.0 Hz, 3 H), 1.52 (sextet, J = 6.0 Hz, 2 H), 1.92 (s, 3 H), 2.18 (tt, J = 7.1, 2.1 Hz, 2 H), 3.94 (s, 3 H), 4.15 (s, 3 H), 4.36 (tt, J = 14.6, 2.1 Hz, 1 H), 4.44 (tt, J = 14.6, 2.1 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 3.89, 13.39, 20.74, 21.82, 55.42, 58.49, 60.07, 71.24, 75.62, 83.20, 87.14, 87.85, 135.84, 164.12, 179.65; MS (CI), m/z (rel intensity) 263 (76), 165 (100); MS (EI), m/z (rel intensity) 247 (4), 233 (5), 219 (6), 181 (43), 125 (32), 79 (32), 67 (100), 53 (35); exact mass calcd for $C_{15}H_{19}O_4^+$ (HRCI) 263.1282, found 263.1276.

2,3-Dimethoxy-4-(2-hexynyloxy)-4-(3-phenoxy-1-propynyl)-2-cyclobuten-1-one (16f). A solution of 0.50 g (1.39 mmol) of **15f**, 0.43 g (2.1 mmol) of 1-iodo-2-hexyne, 1.3 g (5.6 mmol) of Ag_2O, and 2.1 g (15.2 mmol) of K_2CO_3 in 8 mL of acetonitrile afforded 0.32 g (66%) of **16f** as a yellowish oil: R_f = 0.29; IR (film) 2961, 2870, 2238, 1783, 1644, 1598, 1470, 1345, 1214, 1117, 1048, 844, 755, cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.96 (t, J = 7.0 Hz, 3 H), 1.48–1.55 (m, 2 H), 2.14–2.20 (m, 2 H), 3.93 (s, 3 H), 4.05 (s, 3 H), 4.37 (dd, J = 2 Hz, 2 H), 4.76 (s, 2 H), 6.94–6.98 (m, 3 H), 7.0–7.31 (m, 3 H); ^{13}C NMR (300 Hz, $CDCl_3$) δ 13.4, 20.7, 21.8, 55.6, 55.7, 58.5, 60.1, 75.4, 79.3, 83.1, 85.9, 87.4, 114.9, 121.5, 129.4, 136.2, 157.4, 163.3, 178.1; MS (EI), m/z (rel intensity) 354 (66), 325 (21), 297 (14), 279 (12), 261 (38), 217 (47), 189 (59), 159 (57), 115 (63), 94 (100); exact mass calcd for $C_{21}H_{22}O_5$ 354.1467, found 354.1455.

2,3-Dimethoxy-4-(3-phenyl-1-propynyl)-4-(2-hexynyloxy)-2-cyclobuten-1-one (16g). A solution of 0.50 g (1.9 mmol) of **15g** in 9 mL of acetonitrile, 0.61 g (2.9 mmol) of 1-iodo-2-hexyne, and 2.7 g (19 mmol) of K_2CO_3 afforded 0.43 g (65%) of **16g** as a light yellow oil: IR (film) 2960, 2880, 2240, 1790, 1650, 1470, 1440, 1350, 1220, 1050, 840, 730, 690 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.96 (t, J = 7.4 Hz, 3 H), 1.52 (m, 2 H), 2.19 (tt, J = 7.1, 2.1 Hz, 2 H), 3.72 (s, 2 H), 3.96 (s, 3 H), 4.16 (s, 3 H), 4.42 (dt, J = 14.7, 2.1 Hz, 1 H), 4.49 (dt, J = 14.7, 2.1 Hz, 1 H), 7.26–7.33 (m, 5 H); MS (CI), m/z 339 (MH^+); MS (EI), m/z 338; exact mass calcd for $C_{21}H_{22}O_4$ 338.1518, found 338.1509.

2,3-Dimethoxy-4-(3-methyl-3-buten-1-yn-1-yl)-4-(2-hexynyloxy)-2-cyclobuten-1-one (16h). A solution of 0.50 g (2.4 mmol) of **15h**, 0.80 g (3.8 mmol) of 1-iodo-2-hexyne, 3.3 g (24 mmol) of K_2CO_3, and 1.1 g (4.7 mmol) of Ag_2O in 8 mL of acetonitrile afforded 0.47 g (68%) of **16h** as a colorless clear oil: IR (film) 2960, 2870, 2240, 1790, 1660, 1645, 1470, 1435, 1345, 1045 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.97 (t, J = 7.5 Hz, 3 H), 1.54 (m, 2 H), 1.91 (s, 3 H), 2.20 (tt, J = 7.1, 2.2 Hz, 2 H), 3.97 (s, 3 H), 4.17 (s, 3 H), 4.41 (dt, J = 14.5, 2.2 Hz, 1 H), 4.47 (dt, J = 14.5, 2.2 Hz, 1 H), 5.31 (q, J = 1.7 Hz, 1 H), 5.38 (s, 1 H); MS (CI), m/z 289 (MH^+); MS (EI), m/z (rel intensity) 207 (1), 192 (1), 134 (1), 105 (3), 94 (7), 93 (100), 77 (52), 65 (67), 59 (17), 53 (88); exact mass calcd for $C_{17}H_{20}O_4$ 288.1361, found 288.1359.

4-(2-Butenyl)-2,3-dihydro-6,7-dimethoxy-5-hydroxy-3-pentylidenebenzofuran (21). A solution of 219 mg (0.69 mmol) of **16a** in 150 mL of p-xylene was refluxed for 30 min. During this time the initially colorless solution turned orange and then faded to a bright yellow. The reaction solution was allowed to cool to ambient temperature and was then concentrated in vacuo. The resulting yellow oil was purified by column chromatography (30:1 hexanes/ethyl acetate) to give a yellow solid. Recrystallization gave 160 mg (73%) of **21** as slightly yellow crystals: mp 53–54 °C; IR (CCl_4) 3500, 2950, 1750, 1630, 1510, 1420, 1380, 1330, 1200, 1130, 1060 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.92 (t, J = 7.2 Hz, 3 H), 1.41 (m, 4 H), 1.65 (dd, J = 5.9, 1.3 Hz, 2 H), 2.01 (dd, J = 7.2, 7.1 Hz, 2 H), 3.47 (m, 2 H), 3.92 (s, 3 H), 3.94 (s, 3 H), 5.06 (d, J = 3.1 Hz, 2 H), 5.42 (s, 1 H), 5.50 (m, 2 H), 5.77 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 18.1, 22.5, 28.7, 30.2, 31.6, 60.7, 61.6, 74.2, 116.4, 119.9, 120.1, 126.0, 127.4, 135.3, 136.2, 139.4, 141.2, 149.4; MS (CI), m/z 319 (MH^+); MS (EI) m/z (rel intensity) 318 (100), 289 (7), 275 (43), 261 (38), 247 (21), 233 (36), 215 (58), 201 (23), 187 (11), 159 (11), 145 (11), 128 (17), 115 (32), 105 (20), 91 (44), 77 (36), 69 (24), 55 (86); exact mass calcd for $C_{19}H_{26}O_4$ 318.1831, found 318.1808.

4-(2-Butenyl)-2,3-dihydro-6,7-dimethoxy-5-hydroxy-3-butylidenebenzofuran (22). A solution of 120 mg of **16b** in 70 mL of distilled p-xylene was refluxed for 2 h. The colorless solution turned orange and then bright yellow. Removal of the solvent in vacuo gave a yellow oil, which was purified by chromatography (20:1 hexanes/ethyl acetate) to give a light yellow oil, which solidified upon refrigeration. The solid was recrystallized from cold hexanes to yield 85 mg (71%) of **22** as a white solid: mp 52–54 °C; IR ($CHCl_3$) 3430, 2980, 2960, 2880, 1620, 1505, 1460, 1420, 1375, 1330, 1195, 1120, 1050, 960 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.95 (t, J = 7.5 Hz, 3 H), 1.50 (sextet, J = 7.3 Hz, 2 H), 1.65 (dd, J = 6.1, 1.3 Hz, 3 H), 2.00 (qt, J = 7.3, 1.6 Hz, 2 H), 3.46–3.50 (m, 2 H), 3.93 (s, 3 H), 3.95 (s, 3 H), 5.05–5.09 (m, 2 H), 5.43 (s, 1 H), 5.38–5.62 (m, 2 H), 5.74–5.81 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.6, 17.8, 22.4, 28.4, 32.2, 60.4, 61.3, 74.0, 116.1, 119.6, 125.8, 127.1, 135.0, 136.1, 139.1, 140.9, 149.2; MS (EI), m/z (rel intensity) 304 (38), 289 (5), 275 (16), 261 (15), 243 (11), 233 (16), 215 (25), 201 (14), 187 (8), 173 (8), 159 (10), 145 (10), 131 (18), 115 (32), 105 (20), 91 (50), 77 (45), 65 (29), 55 (100); exact mass calcd for $C_{18}H_{24}O_4$ 308.1673, found 308.1679. Anal. Calcd for $C_{18}H_{24}O_4$: C, 71.01; H, 7.95. Found: C, 71.30; H, 8.24.

2,3-Dihydro-6,7-dimethoxy-5-hydroxy-3-butylidene-4-(2-propenyl)benzofuran (23). A solution of 115 mg of **16c** in 60 mL of distilled p-xylene was refluxed for 2 h. The colorless solution turned orange and then bright yellow. Removal of the solvent in vacuo gave a yellow oil, which was purified by chromatography (30:1 hexanes/ethyl acetate) to give 79 mg (69%) of **23** as a slightly yellow oil: IR (film) 3480, 2960, 2940, 2880, 1640, 1620, 1500, 1460, 1420, 1375, 1330, 1200, 1120, 1050, 1030, 1000, 940, 910 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, J = 6.0 Hz, 3 H), 1.49 (sextet, J = 7.3 Hz, 2 H), 1.95–2.03 (m, 2 H), 3.55 (d, J = 6.0 Hz, 2 H), 3.93 (s, 3 H), 3.94 (s, 3 H), 4.97–5.10 (m, 2 H), 5.06 (s, 2 H), 5.45 (s, 1 H), 5.70–5.79 (m, 1 H), 5.90–6.15 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.7, 22.4, 29.6, 32.3, 60.5, 61.3, 74.0, 115.1, 115.1, 119.6, 119.8, 134.7, 135.2, 136.1, 139.2, 141.1, 149.2; MS (EI), m/z (rel intensity) 290 (100), 275 (22), 261 (79), 247 (47), 233 (29), 215 (27), 201 (38), 187 (15), 173 (13), 159 (13), 145 (12), 128 (27), 115 (38), 105 (22), 91 (54), 77 (47), 65 (31), 55 (50); exact mass calcd for $C_{17}H_{22}O_4$ 290.1517, found 290.1508.

4-(2-Butenyl)-6,7-dimethoxy-5-hydroxy-3-pentylbenzofuran (24). To a solution of 5 mL of THF, 1 mL of methanol, and 1 mL of 1 N HCl was added 20 mg of **21**. The solution was stirred at ambient temperature for 6 h and then extracted with 10 mL of ether. The organic phase was washed with water (2 × 2 mL) and brine (1 × 2 mL) and then dried ($MgSO_4$). The solvent was removed in vacuo to give a white solid, which was recrystallized from hexanes to give 19 mg (95%) of **24** as white crystals: mp 67–68 °C; IR (CCl_4) 3540, 2940, 1515, 1415, 1320, 1160 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.92 (t, J = 7.2 Hz, 3 H), 1.40 (m, 4 H), 1.64 (m, 4 H), 2.71 (td, J = 7.5, 0.8 Hz, 2 H), 3.57 (m, 2 H), 3.97 (s, 3 H), 4.13 (s, 3 H), 5.39 (m, 1 H), 5.63 (m, 1 H), 5.67 (s, 1 H), 7.30 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 18.1, 22.7, 25.2, 28.7, 29.5, 31.9, 60.9, 61.8, 112.0, 121.8, 123.4, 125.4, 129.9, 136.0, 136.2, 141.4, 141.8, 142.2; MS (CI), m/z 319 (MH^+); MS (EI), m/z (rel intensity) 318 (100), 303 (12), 287 (4), 275 (6), 262 (16), 247 (18), 233 (13), 215 (14), 207 (7), 201 (12), 187 (5), 173 (5), 159 (5), 145 (8), 128 (6), 115 (10), 105 (5), 91 (11), 77 (8), 69 (4), 55 (13); exact mass calcd for $C_{19}H_{26}O_4$ 318.1831, found 318.1842.

4-Ethenyl-2,3-dihydro-6,7-dimethoxy-5-hydroxy-3-butylidenebenzofuran (27). A solution of 102 mg of **16d** in 70 mL of distilled p-xylene was refluxed for 30 min. The initially colorless solution turned orange and then yellow. Concentration gave a

yellow oil, which upon chromatography (20:1 hexanes/ethyl acetate) gave 50 mg (49%) of **27** as a light yellow oil and 26 mg (25%) of **28** as a yellow solid.

Compound 27: IR (film) 3500, 2970, 2940, 2880, 1615, 1505, 1460, 1410, 1380, 1330, 1240, 1200, 1140, 1110, 1090, 1050, 1000, 940, 920 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, J = 7.5 Hz, 3 H), 1.48 (sextet, J = 6.0 Hz, 2 H), 1.99 (q, J = 6.0 Hz, 2 H), 3.94 (s, 3 H), 3.95 (s, 3 H), 5.05–5.07 (m, 2 H), 5.61 (dd, J = 12.0, 3.0 Hz, 1 H), 5.68 (s, 1 H), 5.84–5.91 (m, 4 H), 6.75 (dd, J = 18.0, 12.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8, 22.4, 32.4, 60.4, 61.3, 73.9, 114.6, 118.9, 120.2, 120.8, 129.7, 136.2, 136.3, 139.3, 141.2, 148.7; MS (EI), m/z (rel intensity) 276 (85), 247 (52), 215 (100), 201 (45), 187 (17), 173 (10), 159 (11), 115 (23), 105 (18), 91 (26), 77 (31), 65 (17), 55 (30); exact mass calcd for $C_{16}H_{20}O_4$ 276.1361, found 276.1368.

Compound 28: (Attempts to recrystallize **28** were unsuccessful because of its instabilty): mp 49–54 °C; IR ($CHCl_3$) 3000, 2960, 2940, 2880, 1620, 1550, 1470, 1425, 1370, 1320, 1270, 1070 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.91 (t, J = 7.5 Hz, 3 H), 1.41 (sextet, J = 7.5 Hz, 2 H), 1.82 (dd, J = 7.9, 3.3 Hz, 2 H), 1.84–1.89 (m, 2 H), 1.95 (dd, J = 7.9, 3.0 Hz, 2 H), 3.77 (s, 3 H), 4.20 (s, 3 H), 4.93–4.98 (m, 1 H), 5.01–5.03 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.7 (CH_3), 22.3 (CH_2), 25.5 (CH_2), 31.5 (C), 32.1 (C), 60.6 (CH_3), 60.7 (CH_3), 74.0 (CH_2), 114.4 (CH), 118.9 (C), 136.8 (C), 138.2 (C), 152.1 (C), 152.2 (C), 193.1 (C); MS (EI), m/z (rel intensity) 276 (100), 261 (12), 247 (86), 234 (35), 216 (39), 201 (11), 188 (12), 187 (11), 177 (11), 161 (9), 145 (8), 131 (10), 117 (17), 115 (19), 105 (22), 103 (16), 91 (33), 79 (19), 78 (15), 77 (37), 65 (19), 55 (20), 53 (14), 51 (17); exact mass calcd for $C_{16}H_{20}O_4$ 276.1361, found 276.1365.

Dimer 32. A solution of 102 mg of **16e** in 65 mL of distilled *p*-xylene was refluxed for 20 min. Removal of the solvent gave an orange oil, which was chromatographed (15:1 hexanes/ethyl acetate) to provide 37 mg (36%) of **32** as a yellow oil: IR ($CHCl_3$) 2960, 2940, 2880, 1670, 1570, 1495, 1460, 1420, 1410, 1370, 1320, 1310, 1130, 1110, 1095, 1070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.85 (t, J = 7.5 Hz, 3 H), 0.94 (t, J = 7.5 Hz, 3 H), 1.35 (sextet, J = 7.4 Hz, 2 H), 1.47 (sextet, J = 7.4, Hz, 2 H), 1.83–2.04 (m, 5 H), 2.34–2.45 (m, 1 H), 2.66–2.78 (m, 1 H), 2.95 (dd, J = 15.6, 4.2 Hz, 1 H), 3.73 (s, 3 H), 3.81 (s, 3 H), 3.94 (s, 3 H), 4.19 (s, 3 H), 5.05–5.15 (m, 4 H), 5.31–5.39 (m, 1 H), 5.59–5.66 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.7 (CH_3), 13.8 (CH_3), 18.5 (CH_2), 22.3 (CH_2), 22.5 (CH_2), 27.4 (CH_2), 32.4 (CH_2), 32.4 (CH_2), 32.4 (CH_2), 32.4 (CH_2), 60.7 (CH_3), 60.8 (CH_3), 61.0 (CH_3), 61.0 (CH_3), 61.4 (CH_3), 74.2 (CH_2), 74.5 (CH_2), 77.5 (C), 111.7 (C), 117.2 (CH), 117.9 (C), 118.3 (C), 119.3 (CH), 135.0 (C), 135.3 (C), 136.5 (C), 137.3 (C), 141.4 (C), 141.6 (C), 149.5 (C), 150.7 (C), 150.9 (C), 196.6 (C); MS (EI), m/z (rel intensity) 263 (100), 221 (21), 129 (11), 115 (18), 91 (33), 73 (34), 60 (33), 55 (37); MS (CI), m/z (rel intensity) 525 (85), 263 (100); exact mass (HRCI) calcd for $C_{30}H_{37}O_8^+$ 525.2486, found 525.2464.

Dimer 35. A sample of cyclobutenone **16f** (88.8 mg, 0.25 mmol) in a round-bottom flask was placed under vacuum for 2 h and the flask was filled with argon. It was then dissolved in 35 mL of freshly distilled toluene and refluxed for 2.5 h. The solution turned from colorless to red during the reflux period. Upon cooling to ambient temperature, the solution became red-yellow. The solvent was removed and the residue chromatographed (SiO_2) using hexanes/ethyl acetate (4:1) to afford **35** as a yellow-red sticky solid, 33.8 mg (38%): R_f = 0.08; IR ($CDCl_3$) 2958, 2933, 2873, 1656, 1597, 1571, 1495, 1461, 1404, 1304, 1214, 1140, 1036 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 0.69 (t, J = 7.3 Hz, 3 H), 0.92 (t, J = 7.3 Hz, 3 H), 1.0–1.16 (m, 2 H), 1.40–1.52 (m, 2 H), 1.72–2.40 (m, 4 H), 3.56 (s, 3 H), 3.72 (s, 3 H), 3.96 (s, 3 H), 4.04 (s, 3 H), 4.92–5.12 (m, 4 H), 5.52–5.58 (m, 1 H), 5.64 (s, 1 H), 5.70–5.76 (m, 1 H), 6.36 (s, 1 H), 6.90–7.28 (m, 10 H); ^{13}C NMR δ 13.5, 13.8, 21.9, 22.4, 32.1, 32.4, 57.7, 60.6, 60.7, 60.7, 61.5, 70.3, 74.1, 77.3, 99.3, 113.0, 114.2, 117.2, 117.5, 118.3, 119.6, 121.4, 122.3, 123.1, 128.8, 129.3, 135.0, 137.2, 137.5, 138.7, 139.8, 142.1, 149.8, 151.6, 153.6, 156.0, 156.6, 189.1; MS (CI), m/z (rel intensity) 615 (3), 614 (8), 522 (15), 521 (32), 520 (40), 354 (35), 278 (7), 277 (5), 263 (6), 262 (32), 93 (100); MS (FB^+) calcd for $C_{42}H_{44}O_{10}$ 708, found 708; exact mass (HRMS-CI) showed peaks corresponding to the quinone methide monomer; calcd for $C_{21}H_{23}O_5^+$ 355.1546, found, 355.1545.

Chromanol 34. Thermolysis (3 h) of **16f** (27.6 mg, 0.078 mmol, 30 mL of THF) as described above except in the presence of butoxyethene (0.5 mL, 3.9 mmol) gave a light yellow final solution. During the thermolysis the color changed from colorless to slightly red and then to light yellow. The product was subjected to flash chromatography to afford a mixture of diastereomers of **34** (34 mg, 98%) as a yellow oil in a ratio of 2:1. Further chromatography gave the purified isomers.

Major product: yield (70%); R_f = 0.32; IR (film) 2931, 2871, 1598, 1494, 1454, 1423, 1367, 1300, 1226, 1141, 1066, 1010 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.67 (t, J = 7.3 Hz, 3 H), 0.85 (t, J = 7.3 Hz, 3 H), 1.11 (ddd, J = 14.42, 7.26, 2.8 Hz, 2 H), 1.24–1.34 (m, 2 H), 1.49–1.59 (m, 2 H), 1.82 (ddd, J = 14.23, 7.12, 2.01 Hz, 2 H), 2.12 (ddd, J = 14.87, 5.08, 3.20 Hz, 1 H), 2.57 (dt, J = 14.84, 1.90 Hz, 1 H), 3.49 (dt, J = 9.54, 6.74 Hz, 1 H), 3.85 (dt, J = 9.55, 6.67 Hz, 1 H), 3.93 (s, 3 H), 3.99 (s, 3 H), 5.07 (d, J = 1.43 Hz, 2 H), 5.32 (t, J = 2.59 Hz, 1 H), 5.42–5.46 (m, 1 H), 5.52 (d, J = 3.91 Hz, 1 H), 6.95–7.29 (m, 3 H), 7.31–7.34 (m, 2 H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 13.4, 13.7, 19.1, 22.0, 29.8, 31.4, 32.2, 60.7, 61.5, 63.3, 68.9, 74.3, 77.4, 95.6, 110.5, 115.6, 120.0, 120.9, 129.5, 135.0, 139.0, 140.0, 142.0, 150.6, 156.2; MS (CI), m/z (rel intensity) 455 (6), 381 (17), 361 (79), 289 (23), 287 (18), 263 (2), 179 (13), 137 (3), 95 (70), 94 (100), 85 (18), 81 (30), 71 (41); exact mass calcd for $C_{27}H_{34}O_6$ 454.2355, found 454.2359.

Minor product: ^1H NMR (500 MHz, $CDCl_3$) δ 0.64 (t, J = 7 Hz, 3 H), 0.92 (t, J = 7 Hz, 3 H), 1.03–1.10 (m, 2 H), 1.37–1.42 (m, 2 H), 1.57–1.64 (m, 2 H), 1.78–1.81 (m, 2 H), 2.02–2.50 (m, 1 H), 2.51 (dt, J = 14.5, 2 Hz, 1 H), 3.61 (dt, J = 9.65, 6.80 Hz, 1 H), 3.92 (s, 3 H), 3.98 (s, 3 H), 4.05 (dt, J = 9.32, 6.56 Hz, 1 H), 5.05–5.09 (m, 2 H), 5.20 (dd, J = 10, 2 Hz, 1 H), 5.30 (m, 1 H), 5.60–5.62 (m, 1 H), 7.0–7.20 (m, 3 H), 7.32–7.35 (m, 2 H); MS (EI), m/z (rel intensity) 454 (6), 362 (31), 287 (100), 277 (6), 244 (16), 231 (12), 217 (8), 210 (8), 187 (5), 159 (6), 131 (9), 115 (14), 103 (10), 94 (61), 91 (14), 77 (17), 65 (30), 57 (47); exact mass calcd for $C_{27}H_{34}O_6$ 454.2355, found 454.2332.

The chromanols **34** were also realized in 70% yield in a ratio of 4:1 when a solution of dimer **35** (33.8 mg, 0.447 mmol) in 30 mL of toluene and butoxyethene (0.60 mL, 47.7 mmol) was refluxed for 3.5 h. The reaction solution changed from yellow to red and finally to light yellow during the reflux period.

Acknowledgment. We thank the National Institutes of Health (GM-36312) for financial support. We also thank Catherine A. Moore for technical support in obtaining high resolution mass spectral data and Dr. J. Ziller for the X-ray structure determinations. Funds for the purchases of the Nicolet R3m/V diffractometer system were made available from the National Science Foundation under Grant CHE 85-14495.

Registry No. **15b**, 118041-72-8; **15c**, 135482-01-8; **15d**, 135482-02-9; **15e**, 135482-03-0; **15f**, 135482-04-1; **15g**, 113976-71-9; **15h**, 135482-11-0; **16a**, 135482-05-2; **16b**, 135512-69-5; **16c**, 135482-06-3; **16d**, 135482-07-4; **16e**, 135482-08-5; **16f**, 135482-09-6; **16g**, 135482-10-9; **16h**, 135482-12-1; **21**, 135482-13-2; **22**, 135482-14-3; **23**, 135482-15-4; **24**, 135482-16-5; **27**, 135482-17-6; **28**, 135482-18-7; **32**, 135482-19-8; **34** (isomer 1), 135482-21-2; **34** (isomer 2), 135558-21-3; **35**, 135482-20-1; dimethyl squarate, 5222-73-1; 1-pentynyllithium, 18643-50-0; 1-butynyllithium, 1119-18-2; 1-propynyllithium, 4529-04-8; (3-phenoxy-1-propynyl)lithium, 85970-86-1; 1-iodo-2-heptyne, 34498-13-0; 1-iodo-2-hexyne, 34498-12-9.

Supplementary Material Available: X-ray data for **21** and NMR data for new compounds (33 pages). Ordering information is given on any current masthead page.