mass calcd for $C_{19}H_{20}O_4$ 312.1361, found 312.1364.

2,3-Dimethoxy-5-(2-propenyl)-2,5-cyclohexadiene-1,4-dione, 48a. A solution of 96.3 mg (0.463 mmol) of **46a** and 5 mL of freshly distilled *p*-xylene was heated and then refluxed for 17 min in a dry 25-mL pear-shaped flask under an atmosphere of nitrogen. The initially colorless solution became red during the thermolysis. The reaction mixture was allowed to cool to room temperature and the solvent was removed in vacuo at 65 °C. The product was purified by flash column chromatography (6:1 hexanes/ethyl acetate) to yield 58.0 mg (0.279 mmol) of **48a** as a red liquid. This represents a 60% yield from **46a**: IR (neat) 2950 (m), 1660 (s), 1605 (s), 1456 (m), 1390 (m), 1060 (m); ^{1}H NMR ($CDCl_3$) 6.40 (t, 1 H, J = 1.6 Hz), 5.78 (m, 1 H), 5.20 (m, 2 H), 4.03 (s, 3 H), 4.00 (s, 3 H), 3.18 (dd, 2 H, J = 1.4, 6.8 Hz); ^{13}C NMR ($CDCl_3$) δ 184.37, 184.01, 146.10, 145.19, 144.96, 132.80, 131.08, 119.28, 61.49, 61.40, 32.89; MS, *m/e* (relative intensity) EI 208 (100), 193 (47), 163 (35), 109 (35), 109 (32), 94 (28), CI 209 (100); exact mass calcd for $C_{11}H_{12}O_4$ 208.0735, found 208.0728.

2,3-Dimethoxy-5-(phenylmethyl)-6-(2-propenyl)-2,5-cyclohexadiene-1,4-dione, 48b. Compound **48b**: red oil; 0.13 g (0.44 mmol); 76% yield; IR (neat) 3300 (w), 3063 (m), 2951 (s), 2845 (m), 1663 (s), 1611 (s), 1496 (m), 1455 (s), 1270 (s), 1144 (s), 740 (s), 696 (s); ^{1}H NMR ($CDCl_3$) δ 7.15-7.35 (m, 5 H), 5.63-5.80 (m, 1 H), 5.06 (m, 1 H), 5.05-4.95 (m, 1 H), 4.00 (s, 3 H), 3.99 (s, 3 H), 3.87 (s, 2 H), 3.30 (dt, 2 H, J_t = 1.41 Hz, J_d = 4.90 Hz); MS, *m/e* (relative intensity) EI 298 (50), 283 (16), 207 (48), 165 (21), 128 (27), 115 (45), 91 (100), 65 (20), CI 299 (100); exact mass calcd for $C_{18}H_{18}O_4$ 298.1205, found 298.1200.

Anal. Calcd for $C_{18}H_{18}O_4$: C, 72.48; H, 6.08. Found: C, 72.24; H, 5.83.

2,3-Dimethoxy-5-(phenylmethyl)-6-(1-methyl-2-propenyl)-2,5-cyclohexadiene-1,4-dione, 48c. Compound **48c**: orange oil; 35 mg (0.11 mmol); 54% yield; IR (neat) 2950 (m), 1655 (s), 1607 (s), 1455 (s), 1265 (s); ^{1}H NMR ($CDCl_3$) δ 7.35-7.10 (m, 5 H), 6.08 (ddd, 1 H, J_{cis} = 10.18 Hz, J_{trans} = 17.19 Hz, J = 7.08 Hz), 4.95 (ddd, 1 H, J_{gem} = $J_{allylic}$ = 1.25 Hz, J_{cis} = 10.18 Hz), 4.85 (ddd, 1 H, J_{gem} = $J_{allylic}$ = 1.25 Hz, J_{trans} = 17.19 Hz), 4.00 (s, 3 H), 3.94 (s, 3 H), 3.72 (m, 1 H), 1.27 (d, 3 H, J = 7.06 Hz); MS, *m/e* (relative intensity) EI 312 (33), 265 (10), 207 (53), 189 (24), 165 (21), 115 (51), 91 (100), 77 (44), CI 313 (100), 237 (10); exact mass calcd for $C_{19}H_{20}O_4$ 312.1361, found 312.1338.

3,4-Dimethoxy-5-(3-phenyl-1-propynyl)-2(5*H*)-furanone, 61a. A solution of 0.25 g (0.97 mmol) of **9l** and 450 mL of freshly distilled THF was cooled to 0 °C in a photochemical reaction vessel under an atmosphere of nitrogen. The photochemical reaction vessel was fitted with a quartz immersion well and then the solution was photolyzed through the quartz immersion well with a 450-W, medium-pressure photochemical immersion lamp for 2 h at 0 °C. The initially colorless THF solution became light yellow during the photolysis. Solvent removal under reduced pressure yielded **61a** (0.13 g, 0.50 mmol) as a white solid (mp 73.5-74.0 °C) after flash column chromatography (5:1 hexanes/ethyl acetate) and recrystallization from ethyl ether. This represents a 52% yield from **9l**: IR (KBr) 2960, 2243, 1786, 1695, 1347, 1121, 1050 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.32 (m, 5 H), 5.30 (t, 1 H, J = 2.1 Hz), 4.16 (s, 3 H), 3.86 (s, 3 H), 3.68 (d, 2 H, J = 2.1 Hz); ^{13}C NMR ($CDCl_3$) δ 168.3, 156.4, 135.5, 128.8, 128.1, 127.1, 122.2, 87.4, 74.1, 65.4, 60.4, 59.8, 25.3; MS, *m/e* (relative intensity) EI 258 (50), 128 (53), 115 (100), 87 (38), CI 259 (100); exact mass calcd for $C_{15}H_{14}O_4$ 258.0892, found 258.0893.

3,4-Dimethoxy-4-(phenylethynyl)-2(5*H*)furanone, 61b. Compound **61b**: yellow oil; 62 mg, (0.25 mmol); 28% yield; IR (neat) 2963 (m), 2229 (m), 1780 (s), 1690 (s), 1344 (s); ^{1}H NMR ($CDCl_3$) δ 7.50-7.30 (m, 5 H), 5.47 (s, 1 H), 4.19 (s, 3 H), 3.88 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 168.2, 156.2, 132.1, 129.5, 128.5, 122.2, 121.3, 88.3, 80.4, 65.5, 60.4, 59.7; MS, *m/e* (relative intensity) EI 244 (6), 142 (52), 129 (62), 114 (100), 87 (42), CI 245 (100), 171 (2); exact mass calcd for $C_{14}H_{12}O_4$ 244.0735, found 244.0740.

3,4-Dimethoxy-4-(1-hexynyl)-2(5*H*)-furanone, 61c. Compound **61c**: yellow oil; 110 mg, (0.49 mmol); 50% yield; IR (neat) 2951 (s), 2240 (m), 1779 (s), 1690 (s), 1346 (s); ^{1}H NMR ($CDCl_3$) δ 5.23 (t, 1 H, J = 2.0 Hz), 4.15 (s, 3 H), 3.85 (s, 3 H), 2.24 (td, 2 H, J_t = 7.0 Hz, J_d = 2.0 Hz), 1.60-1.30 (m, 4 H), 0.91 (t, 3 H, J = 7.3 Hz); MS, *m/e* (relative intensity) EI 224 (15), 115 (100), 87 (89), CI 225 (100), 167 (2); exact mass calcd for $C_{12}H_{16}O_4$ 224.1048, found 224.1059.

Acknowledgment. We thank the National Institutes of Health (CA-11890 and GM-36312) for financial support of this work. We also thank Dr. Joseph W. Ziller and Catherine A. Moore, UCI, for accomplishing the X-ray structure of **21** and for technical assistance in obtaining mass spectra.

Synthesis of Isoarnebifuranone, Nanaomycin, and Deoxyfrenolicin. Structure Elucidation of Arnebifuranone

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Contribution from the Department of Chemistry, University of California, Irvine, California 92717. *Received June 24, 1988*

Abstract: The synthesis of isoarnebifuranone is reported. This compound was established to have the *E* stereochemistry, which had previously been suggested for the natural product arnebifuranone. On the basis of a comparison of the spectral properties of the natural and synthetic products, arnebifuranone was shown to actually be the *Z* isomer. Also described is a new synthesis of naphthoquinones which involves the thermal rearrangement of alkynyl-substituted benzocyclobutenones. The reaction was employed as a key step in the synthesis of 2-(1-hydroxyethyl)- and 2-(1-hydroxybutyl)-8-methoxy-3-(2-propenyl)-1,4-naphthoquinones, which constitutes a formal synthesis of the natural isochroman-1,4-naphthoquinones nanaomycin and deoxyfrenolicin.

The rearrangement of 4-alkynylcyclobutenones to 1,4-benzoquinones described in the preceding paper has wide synthetic scope and can be utilized as a key step in the construction of quinones having a variety of substitution patterns.[1] Its utility is further illustrated here by specific syntheses related to selected targets in the natural products arena—arnebifuranone (**2**), nanaomycin D (**3**), and deoxyfrenolicin (**4**). Arnebifuranone is a natural benzoquinone reported to have *E* stereochemistry at the stereogenic alkene site.[2] However, this compound, **1**, *now referred to as isoarnebifuranone*, was prepared as outlined in Scheme III and

(1) Foland, L. D.; Karlsson, J. O.; Perri, S. T.; Schwabe, R.; Xu, S. L.; Patil, S.; Moore, H. W. *J. Am. Chem. Soc.*, the preceding paper in this issue. Also see for preliminary accounts: Karlsson, J. O.; Nguyen, N. V.; Foland, L. D.; Moore, H. W. *J. Am. Chem. Soc.* **1985**, *107*, 3392. Perri, S. T.; Foland, L. D.; Decker, O. H. W.; Moore, H. W. *J. Org. Chem.* **1986**, *51*, 3067.

(2) Xin-Sheng, Y.; Ebizuka, Y.; Noguchi, H.; Kiuchi, F.; Seto, H.; Sankawa, U. *Tetrahedron Lett.* **1984**, 5541.

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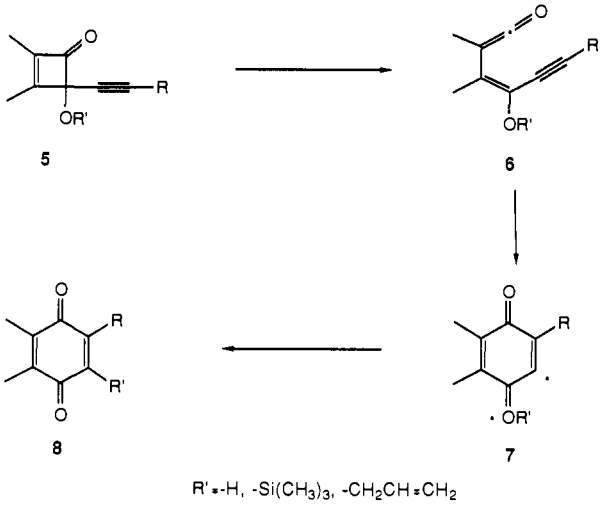
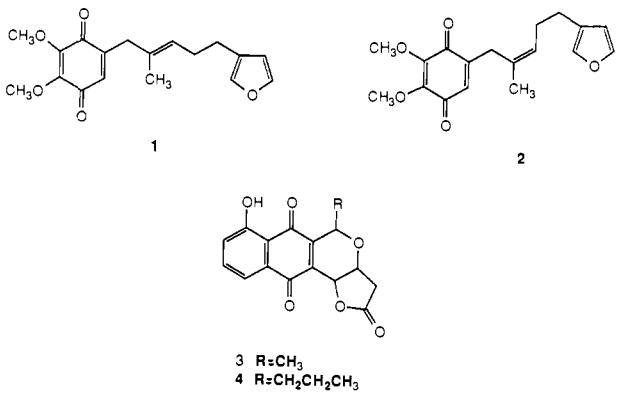
Scheme I



shown to actually be stereoisomeric with the natural product. As a result, the natural product is now reassigned as having the thermodynamically less stable *Z* configuration, **2**.



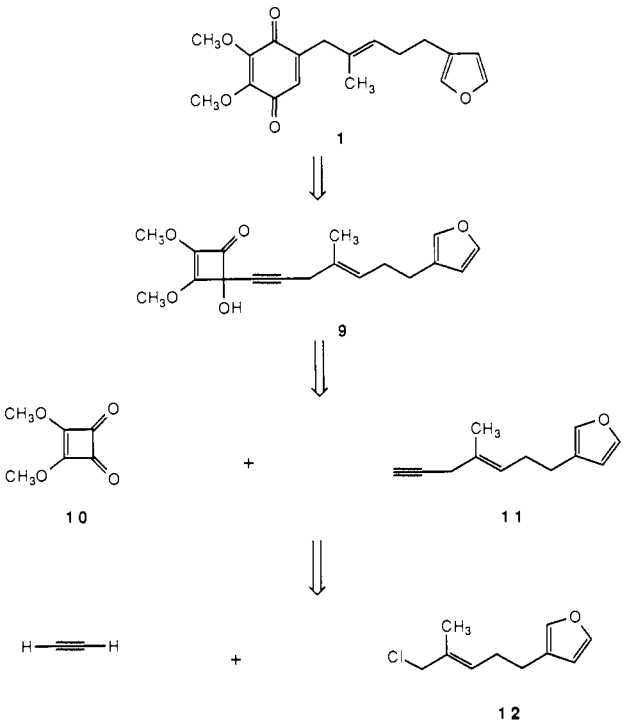
Formal syntheses of the natural isochroman-1,4-naphthoquinones nanaomycin-D (**3**) and deoxyfrenolicin (**4**) are also reported here. In addition to providing efficient pathways to the natural products, the methodology provides a potentially general route to variously substituted naphthoquinones, many of which could function as bioreductive alkylating agents.

Results and Discussion

1. Synthesis of Isoarnebifuranone. Arnebifuranone, along with coenzyme Q, methylpedicin, amorphaquinone, (3*S*)-abruquinone A, B, and C, (*R*)-3,4-dimethoxydalbergione, and arbeinol, is a naturally occurring 2,3-dimethoxy-1,4-benzoquinone.[3] Furthermore, arnebifuranone, des-*O*-methyllasiodiplodin, shikonofuran, arnebinol, and arnebinone have been isolated from the roots of *Arnebia euchroma* (Royle) Johnst., which has been given the Japanese name "Man Shikon" and has been used as a pain killer in the Chinese culture.[4] The pharmacological activity of this plant may, at least in part, be due to the natural products listed above since they have been established as inhibitors of prostaglandin biosynthesis.[5]

As noted, the synthesis of isoarnebifuranone (**1**) rests on a new convergent benzoquinone synthesis of significant generality and versatility. This is summarized in Scheme I, which shows the thermal rearrangement of 4-alkynyl-4-hydroxy(or trimethylsilyloxy

Scheme II



or allyloxy)cyclobutenones **5** to benzoquinones **8**, a transformation involving the proposed ketenes **6** and diradical intermediates **7**, which leads to products via migration of the R′ substituent (R′ = H, $Si(CH_3)_3$, $CH_2CH{=}CH_2$).

A retrosynthetic analysis of the isoarnebifuranone structure **1**, which takes advantage of the above rearrangement, is outlined in Scheme II. Disconnection through the quinone nucleus reveals a 4-alkynyl-4-hydroxycyclobutenone, **9**. This alcohol could be prepared from the monoalkynylation of dimethyl squarate, **10**, with the lithium acetylide of **11**, followed by a protic workup. The preparation of the previously unknown terminal alkyne **11** is envisaged to come from the addition of lithium acetylide, or its synthetic equivalent, to the known allylic chloride **12**, the preparation of which has been reported in four steps in 20% overall yield from β-myrcene.[6]

The synthesis of **1** initiates from 3-(2-bromoethyl)furan, **13**, which upon conversion to the corresponding Grignard reagent and treatment with 2-methylpropenal gave **14** in 75% yield (Scheme III).[7] Treatment of **14** with $SOCl_2$ in hexane gave the allylic chloride **12** in 65% isolated yield as the major isomer of a 7:1 mixture of regioisomers. Treatment of **12** with the Grignard reagent obtained from (trimethylsilyl)ethyne under copper-catalyzed conditions and subsequent deprotection gave the previously unknown alkyne **11** in 76% yield as a colorless liquid. This was converted to its lithium salt and added to dimethyl squarate in THF at −78 °C to give the adduct **9** as a colorless oil. Finally, thermolysis of **9** in refluxing *p*-xylene (138 °C) for 2 h gave isoarnebifuranone (**1**) as an orange oil in 86% isolated yield.

Critical evidence for the *E* stereochemistry for the alkene group of **1** comes from NOE experiments. Specifically, irradiation at the alkene proton absorption at 5.27 ppm resulted in an enhancement of the 3.07 ppm absorption, a peak due to the methylene group adjacent to the quinone nucleus. Additional evidence is given below.

Comparison of the spectroscopic data of the synthetic material to the analogous data reported for naturally occurring arnebifuranone clearly showed them to be different compounds (see Table I). The spectral data for the synthetic compound and the NOE experiment described above are consistent with the proposed

(3) Thomson, R. H. *Naturally Occurring Quinones III*; Chapmann and Hall: London, 1987. Thomson, R. H. *Naturally Occurring Quinones*; Academic: New York, 1976.

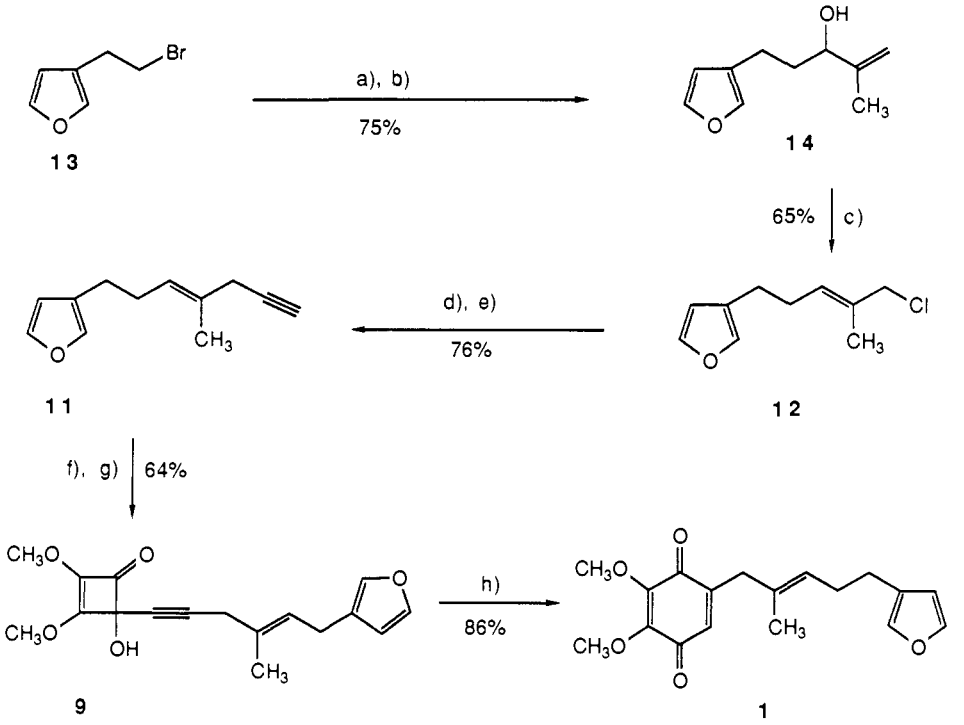
(4) *Encyclopedia of Chinese Nateria Melica* (*Zhon Yao Dai Zi Ten*); Su, J., Ed.; p 2342; *Zhon Yao Zhi*, Chinese Academy of Medicinal Sciences, Ed.; People's Hygenic Publisher: 1979; Vol. 1, p 569.

(5) Kruchi, F.; Shibuya, M.; Sankawa, U. *Chem. Pharm. Bull.* **1982**, *30*, 754. Kruchi, F.; Shibuya, M.; Sankawa, U. *Ibid.* **1982**, *30*, 2279.

(6) Kondo, K.; Matsumoto, M. *Tetrahedron Lett.* **1976**, 391.

(7) For an independent synthesis of **14**, see: Tanis, S. P.; Harrinton, P. M. *J. Org. Chem.* **1985**, *50*, 3988.

Scheme III



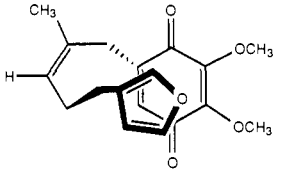
a) Mg, $(C_2H_5)_2O$ b) $CH_2=C(CH_3)CHO$ c) $SOCl_2$, Hexanes

d) Li_2CuCl_4 MgBr—≡—TMS e) $AgNO_3$, KCN f) BuLi g) Dimethyl Squarate, NH_4Cl

h) p-Xylene, 138°

structure **1** for isoarnebifuranone and **2** for the natural product. For example, an observation to support these structural assignments is based on ^{13}C NMR spectral data of both compounds. Specifically, the upfield signal of the methyl group on the stereogenic alkene moiety of arnebifuranone (**2**) (23.4 ppm) relative to the analogous methyl group signal of isoarnebifuranone (**1**) (16.5 ppm) as well as the greater downfield shift of the methylene carbon adjacent to the quinone nucleus of **1** (38.1 ppm) relative to that of **2** (30.7 ppm) are anticipated on the basis of steric-compression shifts.[8] The ^1H NMR signal for the olefinic proton appears as a triplet at 5.27 ppm for the synthetic material and as a triplet at 5.46 ppm in the naturally occurring compound.

The difference in the n–π^* transition of the quinone chromophore in arnebifuranone (404 nm) and isoarnebifuranone (390 nm) is of particular interest since, in the absence of nonconjugated interacting chromophores, the UV spectra of these two isomers should be identical. The bathochromic shift of 14 nm may be due to the interaction of the furan and quinone rings, which is possible for the *Z* but not the *E* isomer (see structure **15**).



15

Finally, personal communications with Professor Sankawa revealed that the naturally occurring quinone is quite unstable.[9] For example, it was pointed out that even after purification of arnebifuranone to a homogeneous compound, it gradually isomerizes to isoarnebifuranone. This was evidenced by the fact that the "extra signals" in both the ^1H and ^{13}C NMR spectra of the isomerized mixture corresponded exactly to the signals observed for the synthetic compound.

Table I. Comparison of Arnebifuranone and Isoarnebifuranone

arnebifuranone		isoarnebifuranone	
UV (Ethanol)			
212, 266, 404		264 (1.06×10^4), 390 (7.90×10^2)	
Exact Mass Calcd			
$C_{13}H_{15}O_4$ 235.0970 (fragment)		$C_{18}H_{20}O_5$ 316.1311	
Found 235.0951		Found 316.1300	
^1H NMR ($CDCl_3$, ppm)			
7.33 (dd, 1 H)		7.35 (t, 1 H)	
7.20 (br s, 1 H)		7.20 (br s, 1 H)	
6.25 (br d, 1 H)		6.28 (t, 1 H)	
6.24 (t, 1 H)		6.26 (br s, 1 H)	
5.46 (br t, 1 H)		**5.27** (br t, 1 H)	
4.02 (s, 3 H)		4.03 (s, 3 H)	
4.00 (s, 3 H)		3.99 (s, 3 H)	
3.10 (d, 2 H)		3.07 (br s, 2 H)	
2.46 (br t, 2 H)		2.48 (t, 2 H)	
2.21 (dt, 2 H)		2.28 (q, 2 H)	
1.65 (d, 3 H)		1.56 (br s, 3 H)	
^{13}C NMR ($CDCl_3$, ppm)			
23.4	130.0	**16.5**	130.9
24.7	130.3	24.9	131.1
28.6	130.3	28.8	139.1
30.7	130.8	**38.1**	143.0
61.0	138.8	61.4	144.9
61.0	142.6	61.5	145.2
110.8	145.0	111.2	146.2
124.3	184.0	124.7	184.3
128.8	184.2	129.2	184.6

2. Synthesis of Nanaomycin and Deoxyfrenolicin. Nanaomycin D (**3**) and deoxyfrenolicin (**4**) are members of an important family of naturally occurring isochroman-1,4-naphthoquinones (approximately 45) which show biological activity as antibiotics and antimycotics and, in some cases, show antineoplastic activity.[10,11]

(8) For a discussion of compression shifts in ^{13}C NMR spectroscopy, see: Levy, G. C.; Nelson, G. L. *Carbon-13 Nuclear Magnetic Resonance for Organic Chemists*; Wiley-Interscience: New York, 1972.

(9) We are grateful to Professor U. Sankawa, Faculty of Pharmaceutical Sciences, University of Tokyo, for providing an authentic sample of arnebifuranone as well as copies of its ^1H NMR spectrum.

Scheme IV

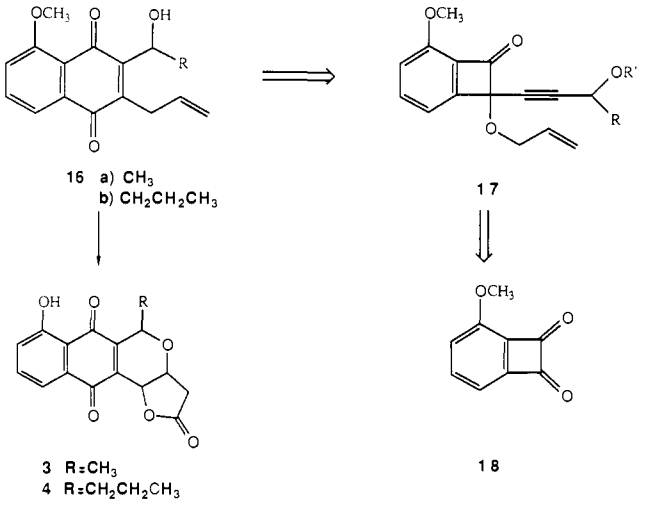


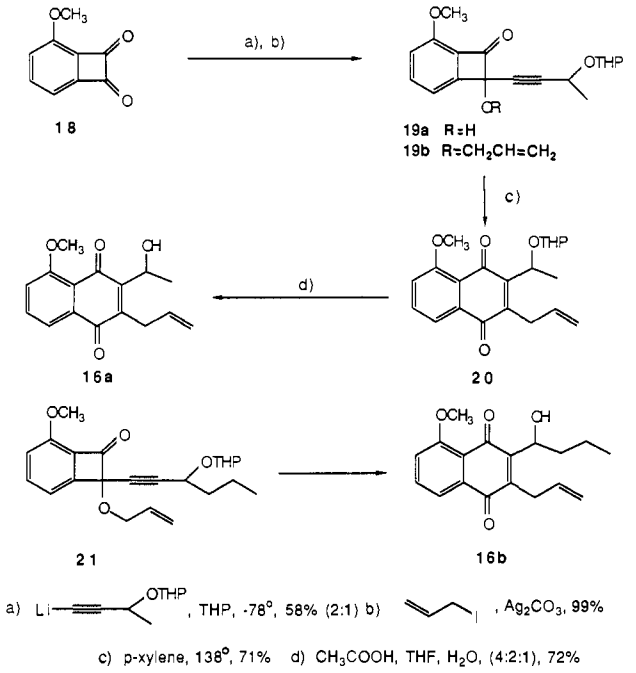
Table II. Alkynylation of 3-Methoxybenzocyclobutenone

R	conditions	yield, %	ratio A:B
H	THF, −78 °C	83	2:1
CH_3	THF, −78 °C	85	3:1
$CH_2CH_2CH_3$	THF, −78 °C	85	4:1
H	1:1 THF/Et_2O, −100 °C	52	95:5
CH_3	1:1 THF/Et_2O, −100 °C	54	95:5
$CH_2CH_2CH_3$	1:1 THF/Et_2O, −100 °C	58	95:5

Their mode of biological action has not yet been established but is often viewed as involving bioreductive alkylation since they have structural features deemed necessary to allow them to function as precursors to electrophilic quinone methides subsequent to an in vivo reduction.[12,13]

As a further illustration of the synthetic utility of the quinone/cyclobutenone rearrangement, the regiospecific syntheses of the naphthoquinones **16a** and **16b** are reported here. Since these compounds have previously been employed as key synthetic precursors to the biologically important quinones nanaomycin D (**3**) and deoxyfrenolicin (**4**), the synthesis reported here constitutes a formal synthesis of the natural products.[14-16] In this regard, new chemistry is also presented in the form of a potentially general

Scheme V



naphthoquinone synthesis which was employed as the key step in the construction of **16a,b**.[17]

The results reported above for the isoarnebifuranone synthesis and those in the preceding paper suggested the retrosynthetic approach to **16a** depicted in Scheme IV. That is, conversion of **18** to the benzocyclobutenones **17** would give a compound expected to rearrange with allyl group migration to the naphthoquinone **16** upon thermolysis. This came to fruition.

When **18** was treated with the lithium salt of 3-(tetrahydropyranyloxy)propyne 2:1 mixture of diastereomers) at −78 °C in THF, **19a** (yellow oil) and its regioisomer were obtained in 85% yield in a respective ratio of 3:1 (Scheme V); furthermore each regioisomer was formed as a 2:1 mixture of diastereomers. Upon further experimentation with **18** and other lithium acetylides it was found that regioselectivities of approximately 95:5 were obtained at −100 °C in a mixed solvent of THF/diethyl ether (1:1).[18] However, these conditions also resulted in a sacrifice in yields (Table II).

The allyl ether **19b** was formed in >95% yield as a yellow oil by treating **19a** with an excess of allyl iodide and Ag_2CO_3 in dioxane.[19] Thermolysis of this ether in refluxing *p*-xylene (138 °C) gave the naphthoquinone **20** as a yellow oil (71%). Removal of the THP protecting group with 4:2:1 $CH_3COOH/THF/H_2O$ gave **16a** (73%), whose spectral data correlated with those reported in the literature.[14] Synthesis of **16b**, the precursor of deoxyfrenolicin, was accomplished by a procedure analogous to that described above. That is, alkynylation of **18** with the lithium salt of 3-(tetrahydropyranyloxy)hexyne gave a mixture of two diastereomeric benzocyclobutenones contaminated with only 2% of the corresponding regioisomers (Table II). The major product was conveniently purified by flash chromatography (ethyl acetate/hexane, silica gel), but the diastereomers were not easily separated. Allylation of the major product gave **21**, which was converted to **16b** by the method reported above.

The overall syntheses of **16a,b** are reasonably efficient. Quinone **16a** was obtained in 28% yield from **18**, and **16b** was obtained in 22% yield. The dione **18** was obtained in 31% yield from

(10) See, for example: Hayashi, M.; Unemoto, T.; Minami-Kakinuma, S.; Tanaka, H.; Omura, S. *J. Antibiot.* **1982**, *35*, 1078. Marumo, H.; Kitaura, K.; Mirimoto, M.; Tanaka, H.; Omura, S. *Ibid.* **1980**, *33*, 885.

(11) Watanabe, S.; Shimizu, H. *J. Antibiot.* **1985**, *38*, 1447. Chang, C. J.; Floss, H. G.; Soong, P.; Gang, C. T. *J. Antibiot.* **1975**, *28*, 156.

(12) Moore, H. W. *Science* **1977**, *197*, 527.

(13) Moore, H. W.; Czerniak, R. *Med. Res. Rev.* **1981**, *1*, 289.

(14) Semmelhack, M. F.; Keller, L.; Sato, T.; Spiess, E. J. *J. Org. Chem.* **1985**, *50*, 5566. Semmelhack, M. F.; Bozell, J. J.; Keller, L.; Sato, T.; Spiess, E. J.; Wulff, W.; Zask, A. *Tetrahedron* **1985**, *24*, 5803.

(15) For total synthesis efforts, see: (a) Reference 1. (b) Naruta, Y.; Uno, H.; Maruyama, K. *Chem. Lett.* **1982**, 609. (c) Kometani, T.; Takechi, Y.; Yoshii, E. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1197. (d) Ichihara, A.; Ubukata, M.; Oikawa, H.; Murakami, K.; Sakamura, S. *Tetrahedron Lett.* **1980**, 4469. (e) Kraus, G. A.; Roth, B. *J. Org. Chem.* **1978**, *43*, 4923. (f) Li, T.; Ellison, R. H. *J. Am. Chem. Soc.* **1978**, *100*, 6263. (g) Pyrek, J. S.; Achmatowica, O., Jr.; Zamojski, A. *Tetrahedron* **1977**, *33*, 673. (h) South, M. S.; Liebeskind, L. *J. Am. Chem. Soc.* **1984**, *106*, 4181. (i) Giles, R. G. F.; Green, I. R.; Hugo, V. I.; Mitchell, P. R. K. *J. Chem. Soc., Chem. Commun.* **1983**, 51. (j) Semmelhack, M. F.; Zask, A. *J. Am. Chem. Soc.* **1985**, *107*, 2034.

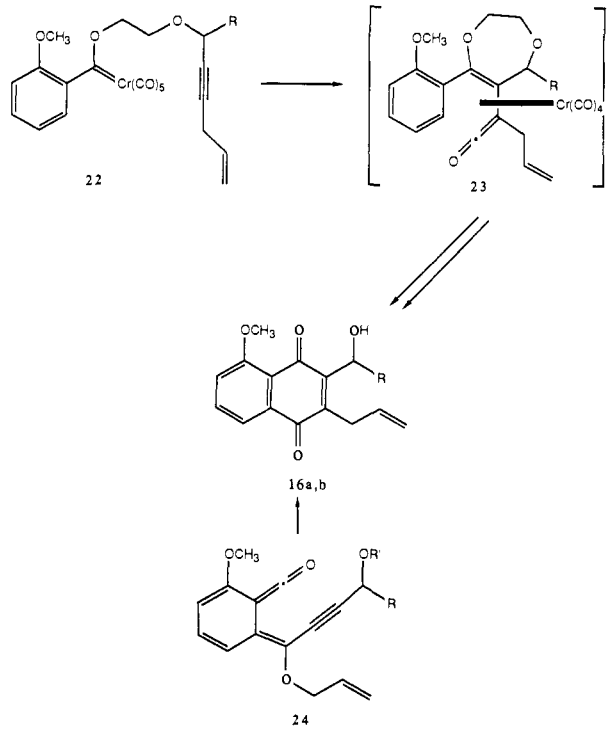
(16) Deoxyfrenolicin (**4**) is a degradation product of the natural epoxy naphthoquinone frenolicin: Ellestad, G. Z.; Kuntsmann, M. P.; Whaley, H. A.; Patterson, E. L. *J. Am. Chem. Soc.* **1968**, *90*, 1325.

(17) For a preliminary account of this work, see: Decker, O. H. W.; Moore, H. W. *J. Org. Chem.* **1987**, *52*, 1174.

(18) For other examples of the regioselective addition of organometallic reagents to cyclobutenediones and benzocyclobutenediones, see: Perri, S. T.; Foland, L. D.; Decker, O. H. W.; Moore, H. W. *J. Org. Chem.* **1986**, *51*, 3067. Liebeskind, L. S.; Jewell, C. F.; Iyer, S. *Ibid.* **1986**, *51*, 3066.

(19) Bernady, K. F.; Floyd, M. B.; Poletto, J. F.; Weiss, M. J. *J. Org. Chem.* **1979**, *44*, 1438.

Scheme VI



2-bromoanisole.[20] The brevity and simplicity of these syntheses recommend the overall approach as a viable method for the preparation of naphthoquinones of specific substitution patterns.

In conclusion, the significant points to arise from this study include the following: (1) the structure of the natural benzoquinone arnebifuranone has been reassigned as structure **2**, (2) alkynylbenzocyclobutenones ring expand to naphthoquinones and this was utilized in a formal synthesis of the natural isochroman-1,4-naphthoquinones nanaomycin (**3**) and deoxyfrenolicin (**4**), and (3) finally, a comparison of the synthesis of **16a,b** as outlined here to the related aryl carbene method is in order.[14] As noted earlier, the regiochemical outcome of the former is controlled in the initial alkynylation step of **18** (Scheme V). The latter (Scheme VI) requires the tethered aryl carbene complex **22**. Interestingly, both methods involve a conjugated ketene intermediate, respectively, **23** and **24**. The unique feature of the carbene method is the generation of **23** from the carbene complex **22**. The latter is also unique in that **24** ring closes and suffers allyl migration to give the naphthoquinones **16a,b** directly.

Experimental Section

(*E*)-4-[7-(3-Furanyl)-4-methyl-4-hepten-1-ynyl]-2,3-dimethoxy-4-hydroxy-2-cyclobuten-1-one, 9. A solution of 0.144 g (0.825 mmol) of **11** and 5 mL of freshly distilled THF was delivered to a dry 25-mL round-bottom flask and stirred under an atmosphere of nitrogen in a dry ice/acetone bath. A 0.54-mL (0.87 mmol) portion of a 1.60 M *n*-BuLi solution was introduced dropwise via a syringe and the resulting light yellow solution was stirred for 45 min. This solution was then transferred under a positive pressure of nitrogen, via a cannula, to a solution of 123 mg (0.866 mmol) of dimethyl squarate in 10 mL of freshly distilled THF that was also under an atmosphere of nitrogen in a dry ice/acetone bath. The resulting light yellow solution was stirred for 30 min in the cold bath and then quenched with 10 mL of 10% ammonium chloride and 20 mL of ether. The aqueous layer was separated and extracted with 2 × 10 mL of ether, and the combined organic layers were dried with 20 mL of brine and $MgSO_4$. Removal of the solvent in vacuo yielded a light yellow oil. Column chromatography of this oil (3:1 hexanes/ethyl acetate) yielded 168 mg (0.531 mmol) of **9** as a clear oil. This represents a 64% yield from dimethyl squarate. **9**: IR ($CHCl_3$) 3390 (br m), 2970 (m), 2242 (w), 1790 (s), 1645 (s), 1355 (s), 1047 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.34 (t, J = 1.5 Hz, 1 H), 7.22 (d, J = 0.5 Hz, 1 H), 6.28 (d, J = 0.6 Hz, 1 H), 5.40 (t, J = 7.0 Hz, 1 H), 4.18 (s, 3 H), 3.97 (s, 3 H), 2.95 (brs, 2 H), 2.93 (s, 1 H), 2.47 (t, J = 7.2 Hz, 2 H), 2.27 (q, J = 6.8 Hz, 2 H), 1.64 (s, 3 H); mass spectrum, m/e (relative intensity) EI 316 (1), 235 (12), 221 (37), 135 (30), 81 (100), CI 317 (100), 299 (97), 285 (39), 183 (19), 135 (18), 81 (3); exact mass calcd for $C_{18}H_{20}O_5$ 316.1311, found 316.1323.

(*E*)-3-(4-Methyl-7-(trimethylsilyl)-3-hepten-6-ynyl)furan. A solution of 0.28 g (2.84 mmol) of (trimethylsilyl)acetylene and 2 mL of freshly distilled THF was delivered to a dry 25-mL round-bottom flash fitted with a condenser and was stirred under an atmosphere of nitrogen at room temperature. A 0.76-mL portion (2.27 mmol) of a 3.0 M ethylmagnesium bromide solution was introduced dropwise via a syringe. The solution was then heated for 30 min at 38–40 °C. The reaction mixture was allowed to cool to room temperature and then a 1.1-mL portion (0.11 mmol) of a 0.1 M dilithium tetrachlorocuprate solution was added dropwise from a syringe. The colorless solution was stirred for 10 min at room temperature and then a solution of 0.210 g (1.14 mmol) of **13** and 2 mL of freshly distilled THF was added rapidly from a syringe. The reaction mixture was then heated at 38–42 °C for 5.25 h and then cooled to room temperature. The reaction mixture was quenched with 30 mL of ether and 10 mL of saturated ammonium chloride. The aqueous layer was separated and then extracted with 2 × 5 mL of ether. The combined organic layers were dried with 2 × 10 mL of brine and $MgSO_4$. Solvent removal in vacuo yielded a oil that was purified by flash column chromatography (hexanes) on silica to yield 0.237 g (0.963 mmol) of the title compound as a colorless oil: 84% yield; IR (neat) 2975 (m), 2183 (m), 1258 (m), 1032 (m), 849 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.34 (t, J = 1.5 Hz, 1 H), 7.22 (s, 1 H), 6.28 (s, 1 H), 5.46 (t, J = 7.0 Hz, 1 H), 2.92 (s, 2 H), 2.48 (t, J = 7.3 Hz, 2 H), 2.29 (q, J = 7.6 Hz, 2 H), 1.65 (s, 3 H), 0.16 (s, 9 H); mass spectrum, m/e (relative intensity) EI 231 (5), 149 (11), 135 (15), 81 (45), 73 (100), CI 303 (64), 289 (1), 247 (100), 191 (26), 173 (24), 135 (45), 73 (62); exact mass calcd for $C_{15}H_{22}OSi$ 246.1440, found 246.1430.

(*E*)-3-(4-Methyl-3-hepten-6-ynyl)furan, 11. A solution of 0.220 g (0.891 mmol) of the above described trimethylsilyl-protected alkyne and 1.8 mL of ethanol was treated with a solution of 0.39 g (2.32 mmol) of silver nitrate dissolved in 2.3 mL of ethanol and 1.1 mL of water at room temperature. A white, gluey precipitate formed and the reaction mixture was stirred for 10 min. A solution of 0.73 g (11.1 mmol) of potassium cyanide in 1.1 mL of water was added in one portion and the homogeneous reaction mixture was stirred for 15 min. The reaction mixture was then poured onto 10 mL of water and 30 mL of pentane. The aqueous layer was separated and extracted with 2 × 10 mL of pentane. The combined organic layers were dried with 2 × 15 mL of brine and $MgSO_4$. Solvent removal in vacuo yielded a colorless oil that was purified by flash column chromatography (hexanes) to yield 0.138 g (0.792 mmol) of **11** as a colorless oil: 89% yield; IR (neat) 3317 (s), 2940 (m), 2126 (w), 1508 (m), 1030 (s), 878 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.34 (t, J = 1.3 Hz, 1 H), 7.27 (s, 1 H), 6.28 (s, 1 H), 5.47 (t, J = 7.0 Hz, 1 H), 2.88 (brs, 2 H), 2.48 (t, J = 7.1 Hz, 2 H), 2.30 (q, J = 6.9, 2 H), 2.11 (t, J = 2.8 Hz, 1 H), 1.67 (s, 3 H); mass spectrum, m/e (relative intensity) EI 174 (2), 131 (11), 81 (100), 77 (56), CI 231 (100), 217 (4), 175 (68), 135 (74), 81 (26); exact mass calcd for $C_{12}H_{14}O$ 174.1045, found 174.1044.

(*E*)-3-(5-Chloro-4-methyl-3-pentenyl)furan (12) and 3-(3-Chloro-4-methyl-4-pentenyl)furan. A solution of 0.59 g (3.55 mmol) of **14** and 10 mL of dry hexanes was treated with 0.42 mL (0.68 g, 5.68 mmol) of thionyl chloride. The reaction mixture was stirred at room temperature for 18 h under an atmosphere of nitrogen. The reaction mixture was then poured onto 150 mL of ether and then was washed with 40 mL of saturated $NaHCO_3$ and 40 mL of water and then was dried with 40 mL of brine and $MgSO_4$. Removal of the solvent in vacuo yielded a pale yellow oil. ^1H NMR examination of this oil revealed it to be a 7:1 ratio of two allylic chlorides. The two allylic chlorides were purified by flash column chromatography (hexanes) on silica gel to yield 0.425 g (2.23 mmol) of **12** as the major product: 65% yield; IR (neat) 3155 (w), 2940 (s), 1508 (m), 1448 (s), 1273 (s), 1030 (s), 878 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (s, 1 H), 7.21 (s, 1 H), 6.27 (s, 1 H), 5.56 (t, J = 6.9 Hz, 1 H), 4.01 (s, 2 H), 2.49 (t, J = 7.4 Hz, 2 H), 2.30 (m, 2 H), 1.72 (s, 3 H); mass spectrum, m/e (relative intensity) EI 186 (0.5), 184 (2.0), 149 (16), 81 (100), CI 187 (4), 185 (17), 149 (100), 117 (35). 3-(3-Chloro-4-methyl-4-pentenyl)furan: clear oil; 48 mg (0.26 mmol); 7% yield; IR (neat) 3160 (w), 3096 (w), 2963 (s), 1650 (w), 1508 (m), 1452 (m), 1172 (s), 1030 (s), 878 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.37 (t, J = 1.6 Hz, 1 H), 7.24 (m, 1 H), 6.28 (d, J = 1.6 Hz, 1 H), 5.01 (s, 1 H), 4.91 (t, J = 0.6 Hz, 1 H), 4.36 (dd, J = 6.4 Hz, J = 8.2 Hz, 1 H), 2.55 (m, 2 H), 2.08 (m, 2 H), 1.82 (brs, 3 H); mass spectrum, m/e (relative intensity) EI 186 (0.12), 184 (0.94), 149 (46), 81 (100), CI 187 (3.3), 185 (12), 149 (100).

3-(3-Hydroxy-4-methyl-4-pentenyl)furan, 14. A suspension of 0.23 g (9.71 mmol) of freshly sanded magnesium ribbon, cut into $^1/_8$ in. strips,

(20) Stevens, R. V.; Bisacchi, G. S. *J. Org. Chem.* **1982**, *47*, 2396.

and 5 mL of freshly distilled THF and one crystal of iodine was delivered to a dry three-neck 100-mL round-bottom flask fitted with a septum, a glass stopper, and a reflux condenser. A solution of 1.70 g (9.71 mmol) of 3-(2-bromoethyl)furan and 35 mL of freshly distilled THF was prepared and approximately 15% of this solution was added to the magnesium suspension. Once the Grignard began to form the balance of the alkyl bromide solution was added at 0.35 mL/min via a syringe pump. After the addition, the resulting brown suspension was stirred for 3 h until most of the magnesium ribbon disappeared. The reaction mixture was cooled to 0 °C with an ice bath. A solution of 0.45 g (6.47 mmol) of methacrolein in 30 mL of freshly distilled THF, also at 0 °C, was transferred to the Grignard solution via a cannula. The resulting light yellow solution was maintained at 0 °C and stirred for 30 min. The solution was then poured onto 40 mL of 1 M HCl and then diluted with 100 mL of ether. The organic layer was separated and washed with 3 × 40 mL of saturated $NaHCO_3$ and 40 mL of water and then dried with 40 mL of brine and $MgSO_4$. Solvent removal yielded a light yellow oil that was purified by flash column chromatography (6:1 hexanes/ethyl acetate) to yield 0.81 g (4.87 mmol) of **14** as a colorless oil: 75% yield; IR (neat) 3700–3200 (br m), 3078 (w), 2950 (m), 1653 (w), 1508 (m), 1453 (m), 1028 (m), 878 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.36 (t, J = 1.5 Hz, 1 H), 7.23 (t, J = 1.2 Hz, 1 H), 6.29 (s, 1 H), 4.96 (5-line multiplet, 1 H), 4.87 (t, J = 1.4 Hz, 1 H), 4.09 (brt, J = 6.6 Hz, 1 H), 2.49 (8-line multiplet, 2 H), 1.81 (AB quartet, J = 7.42 Hz, 2 H), 1.74 (s, 3 H), 1.54 (brs, 1 H); mass spectrum, m/e (relative intensity) EI 166 (0.84), 148 (13), 82 (55), 81 (39), 40 (100); CI 167 (2), 149 (100).

(*E*)-5-[5-(3-Furanyl)-2-methyl-2-pentenyl]-2,3-dimethoxy-2,5-cyclohexadiene-1,4-dione (Isoarnebifuranone), 1. A solution of 114.3 mg (0.361 mmol) of **9** and 8 mL of freshly distilled *p*-xylene was delivered to a dry 25-mL round-bottom flask and stirred under an atmosphere of nitrogen at room temperature. The colorless solution was heated and then refluxed for 20 min under nitrogen, during which time the solution became orange. The solvent was removed in vacuo at 70 °C. The resulting red oil was purified by column chromatography (4:1 hexanes/ethyl acetate) to yield 97.8 mg (0.309 mmol) of **1** as a red-orange oil: 86% yield; UV–vis (EtOH) 264 nm (ϵ = 10600), I = 390 nm (ϵ = 790); IR (neat) 3250 (w), 2959 (s), 1667 (s), 1610 (s), 1456 (m), 876 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (t, J = 1.7 Hz, 1 H), 7.20 (s, 1 H), 6.28 (t, J = 1.5 Hz, 1 H), 6.26 (s, 1 H), 5.27 (t, J = 7.0 Hz, 1 H), 4.03 (s, 3 H), 3.99 (s, 3 H), 3.07 (s, 2 H), 2.48 (t, J = 7.8 Hz, 2 H), 2.28 (q, J = 7.5 Hz, 2 H), 1.56 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 184.6, 184.3, 146.2, 145.2, 144.9, 143.0, 130.1, 131.1, 130.9, 129.2, 124.7, 111.2, 61.5, 61.4, 38.1, 28.8, 24.9, 16.5; mass spectrum, m/e (relative intensity) EI 316 (12), 235 (18), 182 (40), 134 (48), 81 (100), CI 317 (100), 183 (51); exact mass calcd for $C_{18}H_{20}O_5$ 316.1311, found 316.1300.

5-Hydroxy-1-methoxy-5-[3-(tetrahydropyran-2-yloxy)butynyl]benzocyclobuten-6-one, 19a. To a solution of 3-((tetrahydro-2*H*-pyran-2-yl)-oxy)but-1-yne (0.523 g, 3.39 mmol) in 1:1 THF/diethyl ether (16 mL) at −78 °C and under argon was added *n*-butyllithium in hexane solution (2.00 mL of a 1.62 M solution, 3.24 mmol). The solution was warmed to 0 °C for 10 min, cooled to −78 °C, and cannulated slowly into a stirred (−100 °C) suspension of 1-methoxybenzocyclobutenedione (**18**) (0.502 g, 3.08 mmol) in 1:1 THF/diethyl ether (16 mL). The mixture was stirred for 90 min and then quenched at −100 °C by the addition of a pH 7 aqueous phosphate buffer solution. The mixture was extracted with diethyl ether. The organic phase was washed with brine, and the solvent was removed in vacuo. The resulting yellow oil was shown by ^1H NMR analysis to be primarily a mixture of **19a** and its diastereomer. Chromatography of the crude product on silica gel gave 0.526 g (1.66 mmol), on the major isomer **19a** (54%): IR (CCl_4) 3330, 1777, 1605, 1580, 1465, 1375, 1170, 1025, 975 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.46 (d, J = 7 Hz, 3 H), 1.47–1.88 (m, 6 H), 3.43–3.53 (m, 1 H), 3.72–3.83 (m, 1 H), 4.16 (s, 3 H), 4.59 (q, J = 7 Hz, 1 H), 4.83–4.94 (m, 1 H), 6.96 (d, J = 9 Hz, 1 H), 7.28 (d, J = 8 Hz, 1 H), 7.57 (dd, J = 9 Hz, 1 H); mass spectrum, m/e (relative intensity) EI 316 (1, M^+), 259 (3), 232 (45), 215 (65), 214 (100), 85 (95); exact mass calcd for $C_{18}H_{20}O_5$ 316.1311, found 316.1294.

When this reaction was accomplished at −78 °C in THF, **19a** and its regioisomer were formed as a 3:1 mixture in 85% yield. Here the minor diastereomer of **19a** was also isolated and observed to have the following spectral properties: IR (CCl_4) 3350, 1775, 1602, 1568, 1481, 1175, 1125, 1020, 975 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.43 (d, J = 7 Hz, 3 H), 1.45–1.85 (m, 6 H), 3.43–3.55 (m, 1 H), 3.89–4.00 (m, 1 H), 4.14 (s, 3 H), 4.47 (q, J = 7 Hz, 1 H), 4.76–4.80 (m, 1 H), 6.94 (d, J = 9 Hz, 1 H), 7.27 (d, J = 7 Hz, 1 H), 7.56 (dd, J = 9, 8 Hz, 1 H); exact mass calcd for $C_{18}H_{20}O_5$ 316.1311, found 316.1296.

1-Methoxy-5-(2-propenyloxy)-5-[3-(tetrahydropyran-2-yloxy)butyn-1-yl]benzocyclobuten-6-one, 19b. A mixture of excess Ag_2CO_3 and a solution of the major diastereomer of **19a** (1.31 g, 4.14 mmol) and allyl iodide (6.26 g, 37.3 mmol) in 1,4-dioxane (21 mL) was stirred at room temperature for 15 h under an atmosphere of argon. Petroleum ether (low boiling, 80 mL) was then added and the mixture was filtered through Celite. Evaporation at reduced pressure yielded pure **19b** as a light yellow oil (1.47 g, 4.12 mmol, >95% yield): IR (CCl_4) 3075, 1775, 1600, 1565, 1480, 1275, 1115, 1025, 975, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.48 (d, J = 7 Hz, 3 H), 1.40–1.90 (m, 6 H), 3.46–3.56 (m, 1 H), 3.71–3.86 (m, 1 H), 4.17 (s, 3 H), 4.38 (d, J = 6 Hz, 2 H), 4.65 (q, J = 7 Hz, 1 H), 4.75–4.83 (m, 1 H), 5.21 (d, J = 11 Hz, 1 H), 5.32 (d, J = 18 Hz, 1 H), 5.97 (ddt, J = 18, 11, 6 Hz, 1 H), 6.97 (d, J = 8 Hz, 1 H), 7.24 (d, J = 8 Hz, 1 H), 7.56 (dd, J = 8, 8 Hz, 1 H); mass spectrum, m/e (relative intensity) EI 356 (0.7, M^+), 272 (27), 254 (33), 239 (26), 231 (23), 203 (23), 135 (18), 85 (100); exact mass calcd for $C_{21}H_{24}O_5$ 356.1623, found 356.1642.

When the minor diastereomer of **19a** was subjected to the above reaction conditions, it gave the diastereomer of **19b**: light yellow oil (0.34 g, 9.54 mmol, >95% yield; IR (CCl_4) 3075, 1775, 1600, 1565, 1480, 1280, 1120, 1025, 980, 920 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.47 (t, J = 7 Hz, 3 H), 1.39–1.90 (m, 6 H), 3.38–3.55 (m, 1 H), 3.87–4.00 (m, 1 H), 4.15 (s, 3 H), 4.41 (d, J = 6 Hz, 2 H), 4.52 (q, J = 7 Hz, 1 H), 4.75–4.82 (m, 1 H), 5.19 (d, J = 11 Hz, 1 H), 5.32 (d, J = 17 Hz, 1 H), 5.98 (ddt, J = 17, 11, 6 Hz, 1 H), 6.95 (d, J = 8 Hz, 1 H), 7.24 (d, J = 8 Hz, 1 H), 7.55 (dd, J = 8, 8 Hz, 1 H); mass spectrum, m/e (relative intensity) EI 356 (M^+, 0.7), 272 (23), 254 (33), 239 (26), 231 (23), 203 (23), 135 (18), 85 (10); exact mass calcd for $C_{21}H_{24}O_5$ 356.1623, found 272.1048 (fragment).

5-Methoxy-2-(2-propenyl)-3-[1-(tetrahydropyran-2-yloxy)ethyl]-1,4-naphthalenedione, 20. A solution of the major diastereomer of **19b** (0.95 g, 2.67 mmol) in *p*-xylene (135 mL) was heated at reflux under argon for 1 h. The solution was cooled, evaporatively concentrated at 60 °C, and chromatographed (4:1 hexanes/ethyl acetate, silica gel) to yield **21** as a light yellow oil (0.67 g, 1.88 mmol, 71% yield): IR (CCl_4) 1725, 1655, 1585, 1275, 1253, 980, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.55 (d, J = 7 Hz, 3 H), 1.45–1.90 (m, 6 H), 3.47–3.56 (m, 1 H), 3.60 (dd, J = 15, 6 Hz, 1 H), 3.77 (dd, J = 15, 6 Hz, 1 H), 3.86–3.97 (m, 1 H), 3.99 (s, 3 H), 4.50 (dd, J = 4, 3 Hz, 1 H), 5.05 (dd, J = 11, 2 Hz, 1 H), 5.08 (dd, J = 17, 2 1 H), 5.45 (q, J = 7 Hz, 1 H), 5.60 (ddd, J = 17, 11, 6 Hz, 1 H), 7.28 (d, J = 8 Hz, 1 H), 7.65 (d, J = 8 Hz, 1 H), 7.72 (d, J = 8 Hz, 1 H); mass spectrum, m/e (relative intensity) CI 357 (M + 1, (3.5)), 273 (55), 233 (21), 103 (15), 85 (100); exact mass calcd for $C_{21}H_{24}O_5$ 356.1623, found 356.1660.

When the minor diastereomer of **19b** was subjected to the above conditions a compound diastereomeric to the above product was obtained in 74% yield (0.25 g, 0.70 mmol) as a yellow oil: IR (CCl_4) 1730, 1660, 1588, 1275, 1265, 980, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.48 (d, J = 7 Hz, 3 H), 1.40–1.80 (m, 6 H), 3.30–3.40 (m, 1 H), 3.62 (dd, J = 14, 7 Hz, 1 H), 3.59–3.70 (m, 1 H), 3.78 (dd, J = 14, 7 Hz, 1 H), 4.00 (s, 3 H), 4.75 (dd, J = 5, 3 Hz, 1 H), 5.07 (dd, J = 11, 2 Hz, 1 H), 5.13 (dd, J = 17, 2 Hz, 1 H), 5.32 (q, J = 7 Hz, 1 H), 5.95 (ddd, J = 17, 11, 7 Hz, 1 H), 7.27 (d, J = 8 Hz, 1 H), 7.63 (d, J = 8 Hz, 1 H), 7.72 (d, J = 8 Hz, 1 H); mass spectrum, m/e (relative intensity) EI 356 (M^+, 0.25), 315 (10), 272 (33), 254 (29), 239 (19), 215 (8), 85 (100); exact mass calcd for $C_{21}H_{24}O_5$ 356.1623, found 356.1622.

3-(1-Hydroxyethyl)-5-methoxy-2-(2-propenyl)-1,4-naphthalenedione, 16a. A solution of the major diastereomer of **20** (0.535 g, 1.50 mmol) in 3:1:1 acetic acid/THF/H_2O (15 mL) was heated under argon at 50 °C for 6 h. The solution was cooled to room temperature, concentrated at reduced pressure, evaporated from methanol (2 × 15 mL), and then chromatographed (7:3 hexanes/ethyl acetate, silica gel) to yield **16a** as an yellow brown solid (0.275 g, 1.01 mmol, 67% yield) after recrystallization: mp 76–78 °C (lit.[14] mp 76–78 °C); IR (CCl_4) 3530, 3070, 3005, 2970, 2925, 2830, 1660, 1650, 1615, 1585, 1470, 1450, 1270, 1065, 970, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.60 (d, J = 7 Hz, 3 H), 3.40 (brd, J = 6 Hz, 2 H), 3.98 (d, J = 10 Hz, 1 H), 4.03 (s, 3 H), 4.91 (dq, J = 10, 7 Hz, 1 H), 5.10 (d, J = 10 Hz, 1 H), 5.12 (d, J = 18 Hz, 1 H), 5.84 (ddt, J = 18, 10, 6 Hz, 1 H), 7.30 (dd, J = 9, 2 Hz, 1 H), 7.67 (dd, J = 9, 8 Hz, 1 H), 7.75 (dd, J = 8, 2 Hz, 1 H).

A similar hydrolysis of the minor diastereomer of **20** also gave **16a** in 72% yield.

5-Hydroxy-1-methoxy-5-[3-(tetrahydropyran-2-yloxy)hexyn-1-yl]-benzocyclobuten-6-one. This compound was prepared as a mixture of diastereomers in analogy to the synthesis of **19a** and showed the following properties. Diastereomer 1 (major isomer): oil; IR (CCl_4) 3350, 1775, 1605, 1570, 1480, 1435, 1280, 1115, 1015 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.94 (t, J = 7 Hz, 3 H), 1.40–1.78 (m, 10 H), 3.45–3.57 (m, 1 H), 3.72–3.83 (m, 1 H), 4.14 (s, 3 H), 4.48 (dd, J = 7, 7 Hz, 1 H), 4.93 (brd, J = 4 Hz, 1 H), 6.95 (d, J = 9 Hz, 1 H), 7.26 (d, J = 8 Hz, 1 H), 7.57 (dd, J = 9, 8 Hz, 1 H); mass spectrum EI, m/e (relative intensity) 260 (4), 242 (12), 227 (14), 213 (58), 203 (11), 189 (11), 135 (16), 85 (100); CI 345 (0.1, M + 1), 327 (4.5), 261 (3), 243 (39), 103 (15), 85 (100). Diastereomer 2: oil; IR (CCl_4) 3350, 1775, 1600, 1565, 1480, 1440,

1275, 1115, 1015 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.91 (t, J = 7 Hz, 3 H), 1.34-1.88 (m, 10 H), 2.45 (s, 1 H), 3.44-3.56 (m, 1 H), 3.92-4.02 (m, 1 H), 4.15 (s, 3 H), 4.29 (dd, J = 7, 7 Hz, 1 H), 4.75 (brd, J = 7 Hz, 1 H), 6.94 (d, J = 9 Hz, 1 H), 7.27 (d, J = 8 Hz, 1 H), 7.55 (dd, J = 9, 8 Hz, 1 H); mass spectrum, m/e (relative intensity) EI 344 (M^+, 1), 260 (35), 242 (40), 227 (25), 213 (90), 85 (100); exact mass calcd for $C_{20}H_{24}O_5$ 344.1628, found 344.1623.

1-Methoxy-5-(2-propenyloxy)-5-[3-(tetrahydropyran-2-yloxy)hexyn-1-yl]benzocyclobuten-6-one, 21. Two diastereomers of the title compound were obtained when **16** was allylated by using the procedure described for the synthesis of **19b**. Diastereomer 1 (major): light yellow oil (0.27 g, 0.70 mmol), 73% yield); IR (CCl_4) 3075, 3015, 1775, 1600, 1565, 1480, 1435, 1275, 1115, 1020, 980, 920 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.94 (t, J = 7 Hz, 3 H), 1.43-1.88 (m, 10 H), 3.46-3.56 (m, 1 H), 3.72-3.83 (m, 1 H), 4.15 (s, 3 H), 4.38 (brd, J = 6 Hz, 2 H), 4.52 (dd, J = 7, 7 Hz, 1 H), 4.87-4.95 (m, 1 H), 5.20 (dd, J = 11, 2 Hz, 1 H), 5.32 (dd, J = 18, 2 Hz, 1 H), 5.97 (ddd, J = 18, 11, 7 Hz, 1 H), 6.96 (d, J = 8 Hz, 1 H), 7.24 (d, J = 8 Hz, 1 H), 7.56 (dd, J = 8, 8 Hz, 1 H); mass spectrum, m/e (relative intensity) EI 384 (M^+, 1), 300 (25), 259 (45), 203 (45), 85 (100); exact mass calcd for $C_{23}H_{28}O_5$ 384.1936, found 384.1943. Diastereomer 2 (minor): light yellow oil; IR (CCl_4) 3075, 3015, 1775, 1605, 1570, 1485, 1435, 1280, 1120, 1020, 920 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.92 (t, J = 7 Hz, 3 H), 1.38-1.90 (m, 10 H), 3.44-3.55 (m, 1 H), 3.88-4.01 (m, 1 H), 4.13 (s, 3 H), 4.34 (dd, J = 8, 8 Hz, 1 H), 4.41 (d, J = 7 Hz, 2 H), 4.76 (dd, J = 11, 2 Hz, 1 H), 5.19 (dd, J = 11, 2 Hz, 1 H), 5.31 (dd, J = 18, 2 Hz, 1 H), 5.98 (ddd, J = 18, 11, 7 Hz, 1 H), 6.94 (d, J = 9 Hz, 1 H), 7.23 (d, J = 8 Hz, 1 H), 7.54 (dd, J = 9, 8 Hz, 1 H); mass spectrum, m/e (relative intensity) EI 384 (M^+, 8), 300 (6), 259 (35), 203 (40), 85 (100); exact mass calcd for $C_{23}H_{28}O_5$ 384.1936, found 384.1934.

5-Methoxy-2-(2-propenyl)-3-[1-(tetrahydropyran-2-yloxy)butyl]-naphthalene-1,4-dione. When the major diastereomer (0.206 g, 0.54 mmol) of the above was subjected to thermolysis in refluxing p-xylene for 3 h, the title compound was obtained as a light yellow oil in 74% yield after chromatographic purification on silica gel with 4:1 hexanes/ethyl acetate as the eluting solvent: IR (CCl_4) 3070, 1660, 1585, 1275, 1255, 1067, 1030, 965, 905 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.97 (t, J = 7 Hz, 3 H), 1.30-1.90 (m, 10 H), 3.47-3.58 (m, 1 H), 3.59 (dd, J = 14, 6 Hz, 1 H), 3.76 (dd, J = 14, 6 Hz, 1 H), 3.84-3.94 (m, 1 H), 3.99 (s, 3 H), 4.45-4.51 (m, 1 H), 5.06 (d, J = 11 Hz, 1 H), 5.07 (d, J = 17 Hz, 1 H), 5.89 (dddd, J = 17, 11, 6, 6 Hz, 1 H), 7.27 (d, J = 9 Hz, 1 H), 7.64 (dd, J = 9, 8 Hz, 1 H); mass spectrum, m/e (relative intensity) EI 384 (M^+, 8), 343 (10), 300 (35), 282 (25), 257 (23), 239 (15), 85 (100); exact mass calcd for $C_{23}H_{28}O_5$ 384.1938, found 384.1952. Thermolysis of the minor diastereomer of the cyclobutenone gave an isomer of the above naphthoquinone in 55% yield.

3-(1-Hydroxybutyl)-5-methoxy-2-(2-propenyl)-1,4-naphthalenedione, 16b. The above major diastereomer (0.134 g, 35 mmol) was hydrolyzed as described for the conversion of **20** to **16a**. This gave the naphthoquinone **16b** in 51% yield as a yellow oil after chromatography on silica gel with hexanes/ethyl acetate as the eluting solvent (7:3). In a similar fashion the minor diastereomer was converted to **16b** in 64% yield: IR (CCl_4) 3550, 3070, 2965, 2885, 2840, 1650, 1620, 1590, 1470, 1280, 1075, 975, 910 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.95 (t, J = 7 Hz, 3 H), 1.32-1.50 (m, 1 H), 1.56-1.70 (m, 2 H), 1.97-2.04 (m, 1 H), 3.36 (dd, J = 14, 6 Hz, 1 H), 3.43 (dd, J = 14, 6 Hz, 1 H), 3.77 (d, J = 11 Hz, 1 H), 4.02 (s, 3 H), 4.72 (ddd, J = 11, 10, 4 Hz, 1 H), 5.10 (dd, J = 11, 2 Hz, 1 H), 5.13 (dd, J = 18, 2, Hz, 1 H), 5.83 (dddd, J = 18, 11, 6, 6 Hz, 1 H), 7.29 (d, J = 8 Hz, 1 H), 7.67 (dd, J = 8, 8 Hz, 1 H), 7.75 (d, J = 8 Hz, 1 H). These data are in excellent agreement with those reported for the known compound.[14]

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Photochemical Rearrangements of Molecules Having Quenchers on a Chain. Mechanistic and Exploratory Organic Photochemistry[1,2]

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Abstract: The photochemistry of 4,4-diphenylcyclohexenones bearing substituents at C-6 was investigated. The C-6 substituents utilized were 4-(β-naphthyl)butyl, β-naphthylmethyl, biphenylylmethyl, methyl, and propyl. There was an interesting kinetic preference for formation of that C-3 substituted *trans*-5,6-diphenylbicyclo[3.1.0]hexan-2-one stereoisomer with the 3-endo alkyl configuration. This stereoselectivity was understood on the basis of the geometry of the partially phenyl-migrated species. The naphthylbutyl enone had a direct irradiation quantum yield that was essentially that (0.048) of the unsubstituted 4,4-diphenylcyclohexenone as well as the methyl and propyl enones. In contrast, the naphthylmethyl enone efficiency was markedly depressed (0.0059). In both naphthylalkyl enones, singlet excitation was distributed with facility from naphthyl to enone with triplet excitation being then engendered by intersystem crossing at the locus of the carbon groups. In contrast, enone to naphthyl triplet energy transfer occurred in the naphthylmethyl but not the naphthylbutyl enone. The efficiency of the biphenylylmethyl enone is also reported (0.033). In sensitized runs the naphthyl moiety was able to intercept sensitizer species and prevent reaction to varying extents. In the naphthylbutyl case, approximately half of the sensitizer triplets were intercepted and quenched. In the naphthylmethyl case, interception was more efficient ($\geq$75%). Moreover in this case, T_1, with the naphthyl group excited, was able to afford to the extent of 24% the reactive T_2 in which the enone moiety was excited. Finally, in an approach to placing triplet enone reaction rate determination on a firmer basis, a viscosity-dependent Stern-Volmer treatment was employed.

Two and a half decades ago we reported a photochemical reaction in which a 4-aryl-substituted cyclohexenone rearranged to a 6-arylbicyclo[3.1.0]hexan-2-one.[3a] Subsequently we found the rearrangement to proceed via the enone triplet excited state

(1) This is Paper 154 of our photochemical series and Paper 214 of the general series.

(2) For Paper 153 see: Zimmerman, H. E.; Nuss, J. M.; Tantillo, A. W. *J. Org. Chem.* **1988**, *53*, 3792-3803.

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