Stereospecific Lewis Acid-Promoted Reactions of Styrenyl Systems with 2-Alkoxy-(6-alkyl)-1,4-benzoquinones: Scope, Limitations, and Synthetic Applications

Thomas A. Engler,* Keith D. Combrink, Michael A. Letavic, Kenneth O. Lynch, Jr., and James E. Ray

Department of Chemistry, University of Kansas, Lawrence, Kansas 66045

Received June 23, 1994®

Titanium(IV)-promoted reactions of various (*E*)-1-propenylbenzenes with 2-methoxy- and 2-methoxy-6-methyl-1,4-benzoquinones produce trans 2-aryl-6-methoxy-3-(and 4-di)methyl-2,3-dihydro-5-benzofuranols (**10**–**12**), *rel*-(1*S*,6*R*,7*R*,8*R*)-3-methoxy-8-aryl-7-(and 1-di)methylbicyclo[4.2.0]oct-3-ene-2,5-diones (2 + 2 cycloadducts, **13**–**15**) and/or *rel*-(1*R*,5*R*,6*R*,7*R*)-7-aryl-3-hydroxy-6-(and 4)-methylbicyclo[3.2.1]oct-3-ene-2,8-diones (5 + 2 cycloadducts, **16/17**). In many cases, each of the three products can be obtained selectively in good yield by control of reaction conditions and/or by choice of substituents on the quinone or the propenylbenzene. The dihydrobenzofurans are formed stereoselectively, whereas the formation of the bicyclo[4.2.0] systems are stereospecific processes. Thus, reactions of (*Z*)-1-propenylbenzenes afford *rel*-(1*R*,6*S*,7*R*,8*R*)-8-aryl-3-methoxy-7-methylbicyclo-[4.2.0]oct-3-ene-2,5-diones (**24, 25**). No bicyclo[3.2.1]systems are found in reactions of the (*Z*)-propenylbenzenes. The products all apparently result from a thermally allowed $2\pi + 4\pi$ (2 + 5) cycloaddition of the propenylbenzene with a 2-methoxy-4-oxo-2,5-cyclohexadienyl carbocation intermediate (**26**) formed by coordination of the Ti(IV) to the C-1 carbonyl oxygen of the quinone. In the cycloaddition, the aryl ring of the propenylbenzene occupies an endo position with respect to the pentadienyl carbocation moiety of **26** and the bicyclo[3.2.1] carbocation product of the cycloaddition (**28/29**) either undergoes dealkylation or rearrangment to yield the observed products. Treatment of the bicylo[4.2.0] systems with protic acid effects their rearrangement to the dihydrobenzofuranols. Reactions of 2-propenylbenzenes and arylcycloalkenes with the quinones regioselectively give dihydrobenzofuranols **43**–**45** and **49**–**54**, respectively; a 2 + 2 cycloadduct is found in low yield in only one case. The 7-aryl-3-hydroxy-6-methylbicyclo[3.2.1]oct-3-ene-2,8-diones are produced exclusively in reactions of 2-((4-methoxybenzyl)oxy)-1,4-benzoquinones with various propenylbenzenes. Application of these reactions to the synthesis of (±)-obtusafuran, (±)-liliflol-B, (±)-kadsurenone, and (±) denudatin are reported.

Introduction

In a series of communications, we have reported that Lewis acid-promoted reactions of (*E*)-propenylbenzenes with 2-alkoxy- and 2-alkoxy-6-alkyl-1,4-benzoquinones produce up to three different products of formal cycloaddition: the 3-alkyl-2-aryl-2,3-dihydrobenzofuranols **1** (3 + 2 cycloadducts), the 8-aryl-7-methylbicyclo[4.2.0]oct-3-ene-2,5-diones **2** (2 + 2 cycloadducts), and the 7-aryl-6-methylbicyclo[3.2.1]oct-3-ene-2,8-diones **3** (5 + 2 cycloadducts).[1] A noteworthy feature of these reactions is that in many cases any one of the three products can be formed selectively and in good yield by proper choice of substituents on the propenylbenzene or the quinone and/or by careful control of the reaction conditions. These Lewis acid-promoted reactions are quite different from the thermal reactions in which products of initial Diels–Alder reaction are found.[2] The formation of the dihydrobenzofuranols have precedent in the reactions of benzoquinones with electron rich alkenes such as enamines, enols, enol ethers,[3] thioenol ethers[4] and allylsilanes and -stannanes[5] to give indole and/or benzofuran derivatives. Bicyclic products similar to **3** have been reported in thermal reactions of hydroxyquinones[6] and in a few acid-catalyzed reactions of styrenes with alkoxyquinones.[7] Products of 2 + 2 cycloaddition of quinones with alkenes and alkynes occur in some photochemical reac-

® Abstract published in *Advance ACS Abstracts,* September 15, 1994.

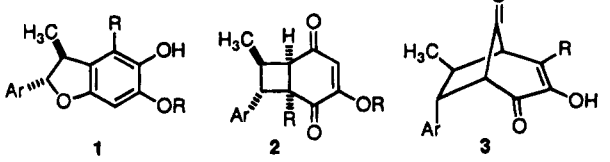
(1) (a) Engler, T. A.; Combrink, K. D.; Ray, J. E. *J. Am. Chem. Soc.* **1988**, *110* , 7931. (b) Engler, T. A.; Combrink, K. D.; Takusagawa, F. *J. Chem. Soc., Chem. Commun.* **1989**, 1573. (c) Engler, T. A.; Letavic, M. A.; Combrink, K. D.; Takusagawa, F. *J. Org. Chem.* **1990**, *55*, 5810. (d) Engler, T. A.; Letavic, M. A.; Reddy, J. P. *J. Am. Chem. Soc.* **1991**, *113*, 5068.

(2) (a) Lora-Tamayo, M. *Tetrahedron* **1958**, *4*, 17. (b) Inouye, Y.; Kakisawa, H. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 563. (c) Manning, W. B. *Tetrahedron Lett.* **1981**, *22*, 1571. (d) Manning, W. B.; Wilbur, D. J. *J. Org. Chem.* **1980**, *45*, 733. (e) Manning, W. B. *Tetrahedron Lett.* **1979**, *20*, 1661. (f) Kelly, T. R.; Magee, J. A.; Weibel, F. R. *J. Am. Chem. Soc.* **1980**, *102*, 798. (g) Rosen, B. I.; Weber, W. P. *J. Org. Chem.* **1977**, *42*, 3463. (h) Kita, Y.; Okunaka, R.; Honda, T.; Shindo, M.; Tamura, O. *Tetrahedron Lett.* **1989**, *30*, 3995. (i) Kita, Y.; Yasuda, H.; Tamura, O; Tamura, Y. *Ibid.* **1984**, *25*, 1813. (j) Willmore, N. D.; Liu, L.; Katz, T. J. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1093. (k) Blatter, K.; Schlüter, A.-D. *Macromolecules* **1989**, *22*, 3506. (l) Tanga, M. J.; Reist E. J. *J. Heterocycl. Chem.* **1991**, *28*, 29. (m) Zhang, Z.-r.; Flachsmann, F.; Moghaddam, F. M.; Rüedi, P. *Tetrahedron Lett.* **1994**, *35*, 2153. (n) Willmore, N. D.; Hoic, D. A.; Katz, T. J. *J. Org. Chem.* **1994**, *59*, 1889. For a protic acid-promoted Diels–Alder reaction of a quinone and a styrene, see: (o) Liu, L.; Katz, T. J. *Tetrahedron Lett.* **1990**, *31*, 3983. For reviews, see: (p) Wagner-Jauregg, T. *Synthesis* **1980**, 769. (q) Onishchenko, A. S. In *Diene Synthesis*, Israel Progam for Scientific Translations; Daniel Davey & Co.: New York, 1964; pp 493–522.

(3) For reviews, see (a) Finley, K. T. In *The Chemistry of the Quinonoid Compounds*, Vol. 2, Part 1; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1988; pp 537–718. (b) Finley, K. T. In *The Chemistry of the Quinonoid Compounds*, Part 2; Patai, S., Ed.; Wiley: New York, 1974; pp 877–1144. (c) Perlmutter, P. *Conjugate Addition Reactions in Organic Synthesis*, Pergamon: New York, 1992; pp 322–330. See also: (d) Brimble, M. A.; Phythian, S. J. *Tetrahedron Lett.* **1993**, *34*, 5813 and earlier reports from this laboratory. (e) Kraus, G. A.; Wu, Y. *Ibid.* **1991**, *32*, 3803. (f) Aso, M.; Hayakawa, K.; Kanematsu, K. *J. Org. Chem.* **1989**, *54*, 5597.

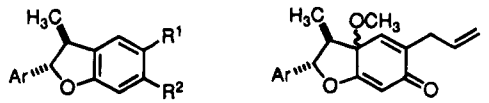
0022-3263/94/1959-6567$04.50/0

tions, although oxetane formation is observed with benzoquinone.[8]



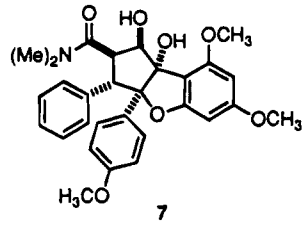
1 2 3

Due to the wide variety of biologically active natural products that incorporate 7-arylbicyclo[3.2.1]octane, and 3-alkyl-2-aryl-2,3-dihydrobenzofuran or benzofuranoid substructures,[9] we undertook a detailed study of the Lewis acid-catalyzed reactions of various propenylbenzenes with substituted 1,4-benzoquinones. Herein we report the details of this study which included reactions of 1,4-benzoquinone and various 2-alkoxy and 2-alkoxy-6-methyl analogs with (*E*)- and (*Z*)-1-propenylbenzenes, 2-propenylbenzenes, and 1-arylcycloalkenes. The application of these reactions to the synthesis of the natural products (±)-obtusafuran (**4**),[10] (±)-liliflol-B (**5**),[11] (±)-kadsurenone (**6a**),[12] and (±)-denudatin B (**6b**)[9,12b,c] are also reported as well as the results of a model study toward the synthesis of (±)-rocaglamide (**7**).[13]



4, R^1=OH, R^2=OCH_3
Ar=C_6H_5
5, R^1=allyl, R^2=OH
Ar=C_6H_3-3,4-$(OCH_3)_2$

6a, α-OCH_3,
Ar=C_6H_3-3,4-$(OCH_3)_2$
6b, β-OCH_3,
Ar=C_6H_3-3,4-$(OCH_3)_2$

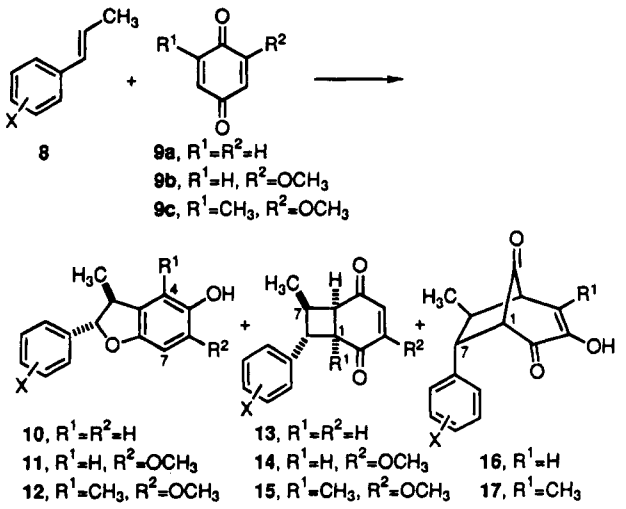


7

Results and Discussion

Reactions of 1,4-Benzoquinone, 2-Alkoxy-1,4-benzoquinones, and 2-Alkoxy-6-methyl-1,4-benzoquinones with (*E*)- and (*Z*)-Propenyl benzenes. The results of titanium(IV)-promoted reactions of various (*E*)-propenylbenzenes **8** with 1,4-benzoquinone and 2-methoxy- and 2-methoxy-6-methyl-1,4-benzoquinones are summarized in Scheme 1 and Table 1. The ratios of the products formed in reactions of 1,4-benzoquinone (**9a**) and 2-methoxy-1,4-benzoquinone (**9b**) are influenced significantly by the nature of the substituents on the propenylbenzene and in some cases on the nature of the Ti(IV). Reactions of propenylbenzenes possessing good electron-donating substituents on the aromatic ring gave mainly the dihydrobenzofurans **10/11**, whereas reactions of propenylbenzenes lacking substituents gave about equal amounts of the dihydrobenzofurans and the bicyclo[4.2.0]octenediones **13/14**; the bicyclo[3.2.1]octenediones **16** were found only in trace amounts, if at all, in reactions of **9b**. In reactions of quinone **9b** with the 4-methyl- and 2-methyl-1-propenylbenzenes (**8d/e**), the ratio of products

Scheme 1



8 **9a**, R^1=R^2=H
9b, R^1=H, R^2=OCH_3
9c, R^1=CH_3, R^2=OCH_3

10, R^1=R^2=H
11, R^1=H, R^2=OCH_3
12, R^1=CH_3, R^2=OCH_3
13, R^1=R^2=H
14, R^1=H, R^2=OCH_3
15, R^1=CH_3, R^2=OCH_3
16, R^1=H
17, R^1=CH_3

For **8** and **10-17**; **a**, X=4-OCH_3; **b**, X=2-OCH_3; **c**, X=3,4-$(OCH_3)_2$; **d**, X=4-CH_3; **e**, X=2-CH_3; **f**, X=H; **g**, X=4-Cl; **h**, X=3,4-(OCH_2O).

(4) Danishefsky, S.; McKee, R.; Singh, R. K. *J. Org. Chem.* **1976**, *41*, 2934.

(5) For a review: Fleming, I.; Dunoguès, J.; Smithers, R. *Org. React.* **1989**, *37*, 57–575. See also: (b) Hosomi, A.; Sakurai, H. *Tetrahedron Lett.* **1977**, *18*, 4041. (c) Ipaktschi, J.; Heydari, A. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 313. (d) Naruta, Y.; Uno, H.; Maruyama, K. *Tetrahedron Lett.* **1981**, *22*, 5221. (e) Takuwa, A.; Soga, O.; Mishima, T.; Maruyama, K. *J. Org. Chem.* **1987**, *52*, 1261.

(6) An early example is the perezone to pipitzol rearrangement which has been shown to be a concerted cycloaddition under thermal conditions: (a) Joseph-Nathan, P.; Mendoza, V.; García, E. *Tetrahedron* **1977**, *33*, 1573. With Lewis acid catalysis, this reaction proceeds through a stepwise mechanism. (b) Sánchez, I. H.; Yáñez, R.; Enríquez, R.; Joseph-Nathan, P. *J. Org. Chem.* **1981**, *46*, 2818. See also: (c) Sánchez, I. H.; Basurto, F.; Joseph-Nathan, P. *J. Nat. Prod.* **1984**, *47*, 382. (d) Sánchez, I. H.; Larraza, M. I.; Basurto, F.; Yañez, R.; Avila, S.; Tovar, R.; Joseph-Nathan, P. *Tetrahedron* **1985**, *41*, 2355. (e) Ishibashi, M.; Tsuyuki, T.; Takahashi, T. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 2357. (f) McGregor, H. H., Jr. Ph.D. Dissertation, Harvard University, 1971. (g) Hienuki, Y.; Tsuji, T.; Nishida, S. *Tetrahedron Lett.* **1981**, *22*, 867.

(7) (a) Mamont, P. *Bull. Soc. Chim. Fr.* **1970**, 1557; (b) **1970**, 1564; (c) **1970**, 1568. See also: (d) Sexmero Cuadrado, M. J.; de la Torre, M. C.; Lin, L.-Z.; Cordell, G. A.; Rodríguez, B.; Perales, A. *J. Org. Chem.* **1992**, *57*, 4722. For an alternate reaction pathway under Lewis acid catalysis, see: (e) Garst, M. E.; Frazier, J. D. *Ibid.* **1987**, *52*, 446.

(8) For reviews, see: (a) Maruyama, K.; Osuka, A. In *The Chemistry of the Quinonoid Compounds*, Vol. 2, Part 1; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1988; pp 759–878. (b) Bruce, J. M. *Quart. Rev.* **1967**, *21*, 405. For recent references, see: (c) Ciufolini, M. A.; Rivera-Fortin, M. A.; Zuzukin, V.; Whitmire, K. H. *J. Am. Chem. Soc.* **1994**, *116*, 1272. (d) Fehnel, E. A.; Brokaw, F. C. *J. Org. Chem.* **1980**, *45*, 578. There have been a few reports of thermal 2 + 2 cycloaddition products in reactions of quinones, see: (e) Shvedov, V. I., Grinev, A. N. *Zh. Org. Khim. (Engl. Transl.)* **1965**, *1*, 613.

(9) For reviews, see: (a) Ward, R. S. *Nat. Prod. Rep.* **1993** *10*, 1, and preceding reports in this series. (b) Gottlieb, O. R.; Yoshida, M. In *Natural Products of Woody Plants I*; Rowe J. W., Ed.; Springer-Verlag: New York, 1989; pp 439–511. For reviews of syntheses of neolignans and lignans, see: (c) Ward, R. S. *Chem. Soc. Rev.* **1982**, *11*, 75. (d) Ward, R. S. *Tetrahedron* **1990**, *46*, 5029.

(10) (a) Gregson, M.; Ollis, W. D.; Redman, B. T.; Sutherland, I. O.; Dietrichs, H. H. *J. Chem. Soc., Chem. Commun.* **1968**, 1394. (b) Jurd, L.; Manners, G.; Stevens, K. *Ibid.* **1972**, 992. (c) Jurd, L.; Stevens, K.; Manners, G. *Tetrahedron* **1973**, *29*, 2347. (d) Gregson, M.; Ollis, W. D.; Redman, B. T.; Sutherland, I. O.; Dietrichs, H. H.; Gottlieb, O. R. *Phytochemistry* **1978**, *17*, 1395.

(11) Iida, T.; Ito, K. *Phytochemistry* **1983**, *22*, 763. See also refs 12b/c, 15g, and (b) Wang, S.; Gates, B. D.; Swenton, J. S. *J. Org. Chem.* **1991**, *56*, 1979.

(12) (a) Shen, T.-Y.; Hwang, S.-B.; Chang, M. N.; Doebber, T. W.; Lam, M.-H. T.; Wu, M. S.; Wang, X.; Han, G. Q.; Li, R. Z. *Proc. Natl. Acad. Sci. U.S.A.* **1985**, *82*, 672. (b) Ponpipom, M. M.; Yue, B. Z.; Bugianesi, R. L.; Brooker, D. R.; Chang, M. N.; Shen, T. Y. *Tetrahedron Lett.* **1986**, *27*, 309. (c) Ponpipom, M. M.; Bugianesi, R. L.; Brooker, D. R.; Yue, B.-Z.; Hwang, S.-B.; Shen, T.-Y. *J. Med. Chem.* **1987**, *30*, 136.

(13) For previous syntheses, see: (a) Trost, B. M.; Greenspan, P. D.; Yang, B. V.; Saulnier, M. G. *J. Am. Chem. Soc.* **1990**, *112*, 9022. b) Davey, A. E.; Schaeffer, M. J.; Taylor, R. J. K. *J. Chem. Soc., Chem. Commun.* **1991**, 1137. For other synthetic approaches, see: (c) Kraus, G. A.; Sy, J. O. *J. Org. Chem.* **1989**, *54*, 77. (d) Feldman, K. S.; Burns, C. J. *Ibid.* **1991**, *56*, 4601.

Table 1. Ti(IV)-Promoted Reactions of (*E*)-1-Propenylbenzenes with 1,4-Benzoquinone, 2-Methoxy-1,4-benzoquinone, and 2-Methoxy-6-methyl-1,4-benzoquinone

entry	propenylbenzene, X	quinone	R^1	R^2	$TiCl_4$:$Ti(OiPr)_4$ [equiv of Ti(IV)]	method[a]	temp (°C)	time (h)	yields (%)		
									10	**13**	
1	**8a**, 4-OCH_3	**9a**	H	H	1.8:1 (1.2)	A	−78	0.12	68		
2	**8c**, 3,4-$(OCH_3)_2$	**9a**	H	H	2:1 (0.8)	B	−78	1	67	10	
3	**8d**, 4-CH_3	**9a**	H	H	3:1 (1.0)	B	−78	5	37	20	
									11	**14**	**16**
4	**8a**, 4-OCH_3	**9b**	H	OCH_3	1:0 (1.0)		−78	0.25	46		
5	**8a**, 4-OCH_3	**9b**	H	OCH_3	1.5:1 (0.8)	B	−78	5	72	12	
6	**8a**, 4-OCH_3	**9b**	H	OCH_3	1.4:1 (1.1)	A	−78	0.25	65	16	
7	**8b**, 2-OCH_3	**9b**	H	OCH_3	1:0 (1.0)		−78	0.75	75		
8	**8c**, 3,4-$(OCH_3)_2$	**9b**	H	OCH_3	1:0 (1.2)		−78	0.5	61		
9	**8c**, 3,4-$(OCH_3)_2$	**9b**	H	OCH_3	2:1 (2.0)	A	−78	1	69	14	
10	**8c**, 3,4-$(OCH_3)_2$	**9b**	H	OCH_3	2:1 (1.1)	A	−78 → 0	1	57		
11	**8c**, 3,4-$(OCH_3)_2$	**9b**	H	OCH_3	1.6:1 (0.8)	B	−78	5	60	23	
12	**8c**, 3,4-$(OCH_3)_2$	**9b**	H	OCH_3	1:1 (1.2)	A	−78	1.5	48	27	
13	**8c**, 3,4-$(OCH_3)_2$	**9b**	H	OCH_3	1:1 (1.0)	B	−40	1.5	58		
14	**8c**, 4-CH_3	**9b**	H	OCH_3	1:0 (1.0)		−78	0.5	64	19	
15	**8d**, 4-CH_3	**9b**	H	OCH_3	4:1 (1.0)	A	−94	2	52	29	
16	**8d**, 4-CH_3	**9b**	H	OCH_3	3:1 (1.0)	B	−78	2	27	39	
17	**8d**, 4-CH_3	**9b**	H	OCH_3	2:1 (1.0)	A	−78	3	36	49	
18	**8e**, 2-CH_3	**9b**	H	OCH_3	1:0 (1.0)		−78	1	27	38	
19	**8e**, 2-CH_3	**9b**	H	OCH_3	2:1 (1.0)	B	−78	2	10	60	13
20	**8f**, H	**9b**	H	OCH_3	1:0 (1.0)		−94	1	28	40	
21	**8f**, H	**9b**	H	OCH_3	1:0 (1.1)		−78	1	41	43	
22	**8f**, H	**9b**	H	OCH_3	1:0 (1.0)		−40	2	30	32	
23	**8f**, H	**9b**	H	OCH_3	4:1 (1.0)	A	−94	1	26	32	
24	**8f**, H	**9b**	H	OCH_3	3:1 (1.0)	B	−78	0.5	27	20	
25	**8f**, H	**9b**	H	OCH_3	2:1 (1.1)	A	−78	2	32	29	
26	**8f**, H	**9b**	H	OCH_3	2:1 (1.0)	B	−78	0.5	25	27	
27	**8g**, 4-Cl	**9b**	H	OCH_3	1:0 (1.0)		−78	0.3	23−43	11−28	
28	**8g**, 4-Cl	**9b**	H	OCH_3	3:1 (1.0)	A	−78	1	28	24	
29	**8h**, 3,4-(OCH_2O)	**9b**	H	OCH_3	2:1 (1.0)	A	−78	3	56	29	
									12	**15**	**17**
30	**8a**, 4-OCH_3	**9c**	CH_3	OCH_3	1:0 (1.0)		−78	0.5	53		
31	**8a**, 4-OCH_3	**9c**	CH_3	OCH_3	2:1 (1.0)	B	−78	2	75		
32	**8a**, 4-OCH_3	**9c**	CH_3	OCH_3	1:1 (1.0)	A	−78	0.5	66		
33	**8c**, 3,4-$(OCH_3)_2$	**9c**	CH_3	OCH_3	1:1 (1.0)	B	−78	0.5	90		
34	**8d**, 4-CH_3	**9c**	CH_3	OCH_3	1:0 (1.0)		−78	4	72		
35	**8d**, 4-CH_3	**9c**	CH_3	OCH_3	4:1 (1.0)	A	−78	1	28	23	
36	**8d**, 4-CH_3	**9c**	CH_3	OCH_3	3:1 (1.0)	A	−90	2	16	54	3
37	**8d**, 4-CH_3	**9c**	CH_3	OCH_3	3:1 (1.0)	B	−70	1.5	20	48	3
38	**8d**, 4-CH_3	**9c**	CH_3	OCH_3	3:1 (1.0)	A	−40	2	60		
39	**8d**, 4-CH_3	**9c**	CH_3	OCH_3	2:1 (1.0)	A	−90	4	11	51	8
40	**8d**, 4-CH_3	**9c**	CH_3	OCH_3	2:1 (1.0)	A or B	−78	6	9−13	33−37	16−21
41	**8d**, 4-CH_3	**9c**	CH_3	OCH_3	2:1 (1.0)	B	−40	2	62	10	
42	**8e**, 2-CH_3	**9c**	CH_3	OCH_3	1:0 (1.0)		−78	4	42	7	37
43	**9e**, 2-CH_3	**9c**	CH_3	OCH_3	2:1 (1.0)	B	−78	2	2	32	44
44	**8f**, H	**9c**	CH_3	OCH_3	1:0 (1.0)		−78	24	23	22	18
45	**8f**, H	**9c**	CH_3	OCH_3	3:1 (1.0)	A or B	−78	4−16	3−10	3−18	38−51
46	**8g**, 4-Cl	**9c**	CH_3	OCH_3	3:1 (1.0)	A or B	−55	8−36	2−10	8−10	23−27
									18	**19**	
47	indene	**9b**	H	OCH_3	1:0 (1.0)		−78	0.5	54		
48	indene	**9b**	H	OCH_3	2:1 (1.0)	A	−78	0.5		85	
									20	**21**	**22**
49	indene	**9c**	CH_3	OCH_3	1:0 (1.0)		−78	3	38		
50	indene	**9c**	CH_3	OCH_3	2:1 (1.0)	A	−78	3	3−9	19−22	32−36

[a] A: $TiCl_4$ and $Ti(OiPr)_4$ were mixed in CH_2Cl_2 at 0 °C or room temperature prior to addition to a solution of the quinone in CH_2Cl_2 at −78 °C. B: $Ti(OiPr)_4$ and/or $TiCl_4$ were added sequentially to a solution of the quinone in CH_2Cl_2 at −78 °C.

was also influenced by the nature of the Ti(IV) used as promoter. In the former case, $TiCl_4$ gave mainly the dihydrobenzofuran **11d** whereas mixtures of $TiCl_4$ and $Ti(OiPr)_4$ gave more of the cyclobutane product **14d**.[14] With 2-methyl-1-propenylbenzene (**8e**), the cyclobutane **14e** was always the major product found, particularly with mixtures of $TiCl_4$:$Ti(OiPr)_4$ as promoter; however, relatively more of the dihydrobenzofuran **11e** was found with $TiCl_4$. Reaction temperature did not have a dramatic influence on these reactions. Thus, in general, the stronger Lewis acid $TiCl_4$ gave more of the dihydrobenzofuran products than the milder Lewis acid composed of mixtures of $TiCl_4$ and $Ti(OiPr)_4$. A particularly dramatic example of this trend was observed in reactions of indene with **9b**. Use of $TiCl_4$ as promoter gave only dihydrobenzofuran **18** in 54% yield whereas use of a 2:1 mixture of $TiCl_4$:$Ti(OiPr)_4$ gave only cyclobutane **19** in 85% yield. The influence of the method for preparation of the mixed Ti(IV)-promoter on the ratio of products

(14) Preformed mixtures of $TiCl_4$ and $Ti(OiPr)_4$ have been reported to be superior to $TiCl_4$ in a number of reactions, presumably to suppress side reactions promoted by the more powerful Lewis acid. For examples, see: (a) Mukaiyama, T. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 817. (b) Mukaiyama, T. *Org. React.* **1982**, *28*, 203. (c) Johnson, W. S.; Crackett, P. H.; Elliott, J. D.; Jagodzinski, J. J.; Lindell, S. D.; Natarajan, S. *Tetrahedron Lett.* **1984**, *25*, 3951. (d) Engler, T. A.; Letavic, M. A.; Lynch, K. O., Jr.; Takusagawa, F. *J. Org. Chem.* **1994**, *59*, 1179. See also: (e) Denmark, S. E.; Almstead, N. G. *J. Am. Chem. Soc.* **1991**, *113*, 8089. (f) Denmark, S. E.; Almstead, N. G. *J. Org. Chem.* **1991**, *56*, 6485; (g) **1991**, *56*, 6458.

Table 2. Reactions of (*E*)-1-Propenylbenzenes with Quinones Promoted by Lewis Acids Other Than Ti(IV)[a]

entry	propylbenzene, X	quinone R¹	quinone R²	Lewis acid (equiv)	temp (°C)	product (% yield)
1	**8a**, 4-OCH_3	**9b** H,	OCH_3	$BF_3{\cdot}Et_2O$ (1.0)	−78	**11a** (30)
2	**8c**, 3,4-$(OCH_3)_2$	**9b** H,	OCH_3	$SnCl_4$ (1.0)	−78	**11c** (52)
3	**8c**, 3,4-$(OCH_3)_2$	**9b** H,	OCH_3	$BF_3{\cdot}Et_2O$ (1.0)	−78	**11c** (43)
4	**8f**, H	**9b** H,	OCH_3	$ZrCl_4$ (1.0)	−78	**11f** (28)
5	**8a**, 4-OCH_3	**9c** CH_3	OCH_3	$ZrCl_4$ (1.0)	−78	**12a** (50)
6	indene	**9b** H,	OCH_3	$ZrCl_4$ (1.5)	−78	**18** (56)

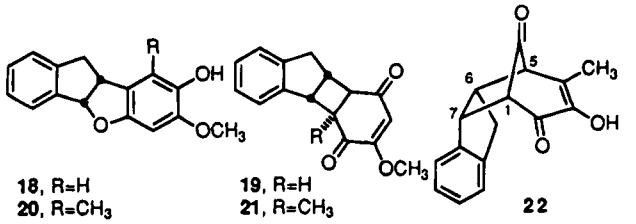
[a] All reactions were conducted in CH_2Cl_2.

Table 3. Ti(IV)-Promoted Reactions of (*Z*)-1-Propenylbenzenes with 2-Methoxy-1,4-benzoquinones

entry	propenylbenzene, X	quinone	R¹	R²	$TiCl_4$:$Ti(OiPr)_4$ [equiv of Ti(IV)]	method	temp (°C)	time (h)	yields (%) 11	24
1	**23c**, 3,4-$(OCH_3)_2$	**9b**	H	OCH_3	1:1.1 (1.0)	A	−78	1.5	22	39
2	**23d**, 4-CH_3	**9b**	H	OCH_3	4:1 (1.0)	A	−78	1	*a*	31
3	**23f**, H	**9b**	H	OCH_3	1:0 (1.1)		−78	1		39
									12	**25**
4	**23c**, 3,4-$(OCH_3)_2$	**9c**	CH_3	OCH_3	2:1 (1.4)	B	−78	7	52[b]	
5	**23d**, 4-CH_3	**9c**	CH_3	OCH_3	4:1 (1.0)	A	−78	1	59[c]	
6	**23f**, H	**9c**	CH_3	OCH_3	4:1 (1.0)	B	−78	4	8−11[d]	24
										36
7	**23c**, 3,4-$(OCH_3)_2$	**32a**	H	OCH_2Ph	1.8:1 (1.2)	B	−78	9		49

[a] Complex mixtures. [b] As a 7:1 ratio of trans:cis isomers. [c] As a 10:1 ratio of trans:cis isomers. [d] As a 7:1 ratio of trans:cis isomers.

found was also examined in several cases. One method involved premixing the $TiCl_4$ and $Ti(OiPr)_4$ at 0 °C or room temperature for 15 min to 1 h prior to addition to the quinone at −78 °C. A second method involved sequential addition of $Ti(OiPr)_4$ and $TiCl_4$ to the quinone at −78 °C and stirring the mixture for 15−30 min prior to addition of the propenylbenzene. Although in a few cases the latter method gave more of the cyclobutane products than the former, for most reactions the two methods gave similar results.



18, R=H
20, R=CH_3

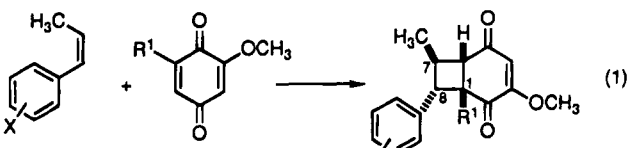
19, R=H
21, R=CH_3

22

Reactions of 2-methoxy-6-methyl-1,4-benzoquinone (**9c**) with propenylbenzenes possessing strong electron-donating groups on the aromatic ring again gave mainly dihydrobenzofurans **12**. 4-Methyl-(*E*)-propenylbenzene (**8d**) gave the dihydrobenzofuran **12d** with $TiCl_4$ as promoter or upon warming reactions utilizing mixtures of $TiCl_4$ and $Ti(OiPr)_4$ to −40 °C; however, at low temperatures, reactions employing the milder Lewis acid made from 2 or 3:1 mixtures of $TiCl_4$:$Ti(OiPr)_4$ gave the cyclobutane **15d** as the major product. Significant quantities of the 5 + 2 adduct **17d** were also found in the latter reactions. In contrast, reactions of propenylbenzenes **8e−g** gave the bicyclo[3.2.1]octenediones **17e−g** as the major products particularly with the milder $TiCl_4$:$Ti(OiPr)_4$ Lewis acid as promoter. Indene gave **20−22** and again the ratios varied with the nature of the Ti(IV). With $TiCl_4$, **20** was the only product isolated whereas with a 2:1 mixture of $TiCl_4$:$Ti(OiPr)_4$, products **20−22** were found with the latter as the major product.

Reactions of some of the propenylbenzenes with quinones utilizing Lewis acids other than Ti(IV) as promoters were also examined briefly (Table 2). In all cases, only dihydrobenzofuran products were found and the yields were lower than those found in the Ti(IV)-promoted reactions. Similarly, reaction of quinone **9c** with indene promoted by $ZrCl_4$ gave only **20** in 56% yield.

A particularly interesting aspect of the formation of cyclobutane adducts **13−15** and bicyclic adducts **16/17** from (*E*)-propenylbenzenes **8** is that although four new stereogenic centers are formed in the reaction, only one diastereomer of each was isolated. The only source of stereochemistry in the reactants is in the carbon−carbon double bond of the propenylbenzene. Thus, Ti(IV)-promoted reactions of (*Z*)-propenylbenzenes **23** with quinones **9b/c** were examined (eq 1 and Table 3). In



(1)

23
(X as in **8**)

9b/c

24, R^1=H
25, R^1=CH_3

general, these reactions were slower, not as clean as reactions of the (*E*)-propenylbenzenes, and produced lower yields of the major isolable products. However, reactions of quinone **9b** gave mainly cyclobutane products **24**; dihydrobenzofurans **11** were also observed, but generally as part of a complex mixture with other unidentified products. With **9c**, reactions with the electron rich propenylbenzenes **23c/d** gave dihydrobenzofuranols **12**, whereas reaction with **23f** gave cyclobutane **25f** as the major product.

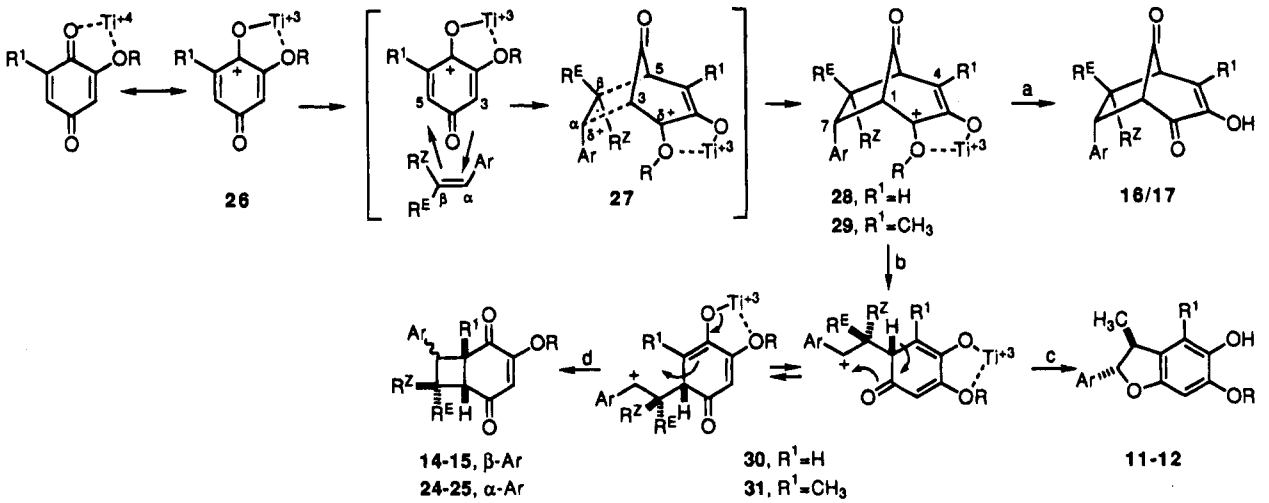
The cyclobutane products **24/25** found in reactions of the (*Z*)-propenylbenzenes were diastereomers of the cyclobutanes produced in the reactions of the (*E*)-propenylbenzenes.[15] Thus, the formation of cyclobutanes **14/15** and **24/25** are diastereospecific processes, and the extent of stereospecificity is remarkable. The diastereospecificity of reactions of **9b** was determined by HPLC analysis of the crude reaction mixtures obtained after standard workup. Cyclobutanes **14** and **24** were obtained stereochemically pure by column chromatography followed by recrystallization. The identity of the signals observed in the HPLC studies were then confirmed by

Table 4. Diastereomeric Ratios of Cyclobutane Adducts Formed in Reactions of 8 and 23 with 9b and 32a (See Tables 1 and 3 for Percent Yields)

entry	propenylbenzenes (trans:cis)[a]	quinone	catalyst ratio $TiCl_4$:$Ti(OiPr)_4$	ratio[c] **14:24**
1	**8a**, X = 4-OMe (14:1)	**9b**	1.6:1 [0.83][b]	>19:1[d]
2	**8c**, X = 3,4-$(OMe)_2$ (14:1)	**9b**	1.67:1 [1.0]	>50:1
3	**8d**, X = 4-Me (8:1)	**9b**	2:1 [1.0]	50:1
4	**8d**, X = 4-Me (8:1)	**9b**	1:0 [1.0]	>19:1[d]
5	**8f**, X = H (64:1)	**9b**	3:1 [1.0]	>50:1
6	**8f**, X = H (64:1)	**9b**	1:0 [1.0]	>50:1
7	**8g**, X = 4-Cl (9:1)	**9b**	3:1 [1.0]	22:1
8	**8g**, X = 4-Cl (9:1)	**9b**	1:0 [1.0]	>50:1
9	**23c**, X = 3,4-$(OMe)_2$ (1:22)	**9b**	1:1.1 [1.0]	1:25
10	**23d**, X = 4-Me (1:19)	**9b**	4:1 [1.0]	1:13
11	**23f**, X = H (1:51)	**9b**	1:0 [1.0]	1:25
				35:36
12	**8c**, X = 3,4-$(OMe)_2$ (14:1)	**32a**	1:1 [1.0]	16:1
13	**23c**, X = 3,4-$(OMe)_2$ (1:22)	**32a**	1.8:1 [1.0]	1:34

[a] The trans:cis ratio was determined by capillary VPC. [b] Total equiv of Ti(IV). [c] Determined by HPLC. [d] An HPLC ratio was not determined; however, only isomer **14** was evident by 300 MHz ^1H NMR.

Scheme 2



coinjection of the purified cyclobutane adduct with the crude reaction mixtures. The results are shown in Table 4. These experiments revealed that small amounts of cyclobutanes **24** were present in reactions of (*E*)-alkenes **8** and also that minor amounts of cyclobutanes **14** were present in reactions of (*Z*)-alkenes **23**. Thus, the formations of **14** and **24** from **8** and **23**, respectively, were highly diastereospecific processes, although not completely. In the chromatographic traces from some of the reactions of the (*Z*)-alkenes, other small signals were observed with retention times similar to those of the cyclobutanes **14** and **24**. However, the amounts of these unidentified compounds were less than the minor cyclobutane of the mixture. Unfortunately, no 5 + 2 products were isolated from reactions of the (*Z*)-propenylbenzenes and at this time the formation of bicyclic adducts **16/17** from (*E*)-propenylbenzenes **8** can only be described as stereoselective.

A mechanism that is consistent with the results detailed above involves coordination of the Ti(IV) to the C-1 carbonyl and the C-2 methoxy oxygens of the quinones to give a complex that can be represented as **26** (Scheme 2). Thermally allowed $4\pi + 2\pi$ cycloaddition of the pentadienyl carbocation moiety of **26** with the propenylbenzene then yields the bicyclo[3.2.1]octenyl carbocations **28/29**.[7,16] The preference for the aromatic ring to occupy an endo position with respect to the pentadienyl moiety in the cycloaddition has been observed previously in reactions of propenylbenzenes and styrenes with cations similar to **26** formed in solvolysis of quinone monoketals[16a] and *p*-quinol ethers[16c,17] and in thermal reactions of hydroxy quinones.[6f] The regioselectivity of the cycloaddition is rationalized by an asynchronous transition state in which carbon–carbon bond formation between the nucleophilic C-β of the propenylbenzene with the most electron deficient C-5 atom of the Ti(IV)–quinone complex is more advanced than bond formation between C-α of the propenylbenzene and C-3 of the

(15) The propenylbenzenes used in these experiments were actually mixtures of geometrical isomers in which one isomer was predominant. The (*E*):(*Z*) ratios were determined by vapor phase chromatography and are included in Table 4. It is apparent that the ratio of the cyclobutanes formed in the cycloaddition reactions were relatively insensitive to the (*E*):(*Z*) ratio of the propenylbenzenes. For example, an 8:1 (*E*):(*Z*) ratio of 4-methyl-1-propenylbenzene (**8d**) gave a 50:1 mixture of **14d:24d** (entry 4, X = Me), whereas a 1:19 (*E*):(*Z*) ratio of the alkene (i.e., **23d**) gave a 1:13 mixture of the two cyclobutanes. In general, reactions of (*E*)-propenylbenzenes gave very high ratios of **14:24**. Reactions with the (*Z*)-isomers **23** were somewhat less stereospecific; however, the ratios of **14:24** were still quite good, in the range of 1:20 for most propenylbenzenes (entries 10–14, Table 4). If the (*E*)- and (*Z*)-isomers were equally reactive, then the ratio of cyclobutane adducts **14:24** should reflect the (*E*):(*Z*) ratio of the alkene used. That the (*E*)-isomers were more reactive was indicated by the fact that a less reactive Lewis acid was necessary for their reactions than was required for reactions of the (*Z*)-isomers. For example, reaction of 2-(benzyloxy)-1,4-benzoquinone (**32a**, *vide infra*) with (*E*)-3,4-dimethoxy-1-propenylbenzene (**8c**) occurred with a 1:1 mixture of $TiCl_4$:$Ti(OiPr)_4$, whereas the (*Z*)-isomer **23c** required a 1.8:1 mixture of $TiCl_4$:$Ti(OiPr)_4$. As a result, the small amount of the (*Z*)-isomer present in the (*E*)-propenylbenzenes was probably not sufficiently reactive, under the reaction conditions, to form significant amounts of the minor cyclobutane adducts **24**. On the other hand, minor amounts of the (*E*)-isomer present in the (*Z*)-propenylbenzenes may have, under the reaction conditions, resulted in some of the minor cyclobutane adduct **14** which probably accounts for the lower diastereomeric ratios of the cyclobutane adducts **14/24** found in these reactions.

complex. The result is a buildup of partial positive charge at C-α and C-2 in the transition state **27** which can be stabilized by the aromatic ring and the quinone alkoxy substituent, respectively. Two reaction paths are available to **28/29**. Dealkylation provides the bicyclo-[3.2.1] systems **16/17** (path a). Alternatively, cleavage of the C-1/C-7 bond gives benzylic cations **30/31** (path b), which can be represented as the two conformers shown. Carbon–oxygen bond formation between the carbocation and the carbonyl oxygen in **30/31** and loss of a proton results in dihydrobenzofurans **11–12** (path c), whereas carbon–carbon bond formation between the carbocation center and the titanium enolate moiety gives **14–15** (path d). In path c, the aryl and methyl groups end up trans in the dihydrobenzofurans due to steric factors. In path d, it is not surprising that a cis ring fusion is formed in the product (a trans-fused bicyclo-[4.2.0]octenyl system with four sp^2-hybridized carbons in the six-membered ring would be highly strained) and the aryl and methyl groups on the cyclobutane are again trans due to steric factors. This mechanism also readily accounts for the diastereospecific formation of cyclobutanes **24/25** from (*Z*)-propenylbenzenes **23**. In addition, the more complex reaction mixtures and lower yields obtained in reactions of the (*Z*)-propenylbenzenes are not surprising. With an initial 5 + 2 cycloaddition to give **28/29**, steric factors associated with placing both the R^2-methyl and the aryl group in an endo orientation would be expected to render this process of higher energy, and alternative reaction modes may compete.[18]

The higher yields of the 5 + 2 products **17** observed in reactions of **9c** in comparison to reactions of **9b** and the effects of the substituents on the propenylbenzenes on the ratio of **11/12:14/15:16/17** found is consistent with the bicyclic carbocation intermediates **28/29** occurring at a divergent point in the reaction manifold. Cation **29** would be expected to be longer lived than **28** due to stabilization by the C-4 methyl. Thus, in reactions involving **29** compared to those involving **28**, path a may compete with path b more effectively, resulting in more of **17.** Path b leading to benzylic carbocations **30/31** and then to the dihydrobenzofuran and cyclobutane products predominates in reactions of both quinones **9b** and **9c** with propenylbenzenes possessing electron-donating groups on the aromatic ring due to the ability of these groups to stabilize carbocations **30/31** and increase the rate of path b. Lack of electron-donating groups on the propenylbenzene results in a slower rate of path b relative to path a, and the latter again competes more effectively in these cases (compare entries 30–35 with 45 and 46). The differences in yields of the bicyclo[3.2.1]-octene products **17** found in reactions of **9c** with the *o*-methyl-substituted propenylbenzene **8e** versus the *p*-methyl-substituted propenylbenzene **8d** are particularly instructive. Using the reaction involving **31f** (from the unsubstituted propenylbenzene **8f**) as a reference, the introduction of a *p*-methyl substituent on the aromatic ring (i.e., **31d**) stabilizes the carbocation center and results in a faster rate of its formation from **29d** via path b relative to the rate of path a to **17** which would be expected to be similar for both intermediates **29d/f**. Thus, relatively small amounts of dealkylation product **17d** are found in reactions of **8d** compared to those of **8f**. However, an *o*-methyl substituent on the aromatic ring of **31** would inhibit resonance stabilization of the benzylic carbocation center.[19] As a result, the formation of **31e** from **29e** by path b is slower relative to the dealkylation to **17e** via path a, and more of the latter product is found in reactions of **8e** (entries 42/43).

Focusing on the postulate that intermediates **28/29** are at a divergent point in the reaction manifold, we reasoned that further pertubation of the system resulting in an increase in the rate of path a relative to path b in Scheme 2 may result in a greater, and perhaps selective, formation of the 5 + 2 products **16/17**. Since benzyl groups, and *p*-methoxybenzyl groups in particular, would be expected to be more easily displaced than methyl groups, in either an S_N1 or S_N2 mechanism, reactions of quinones **32–33** were studied. The quinones were prepared by Fremy's salt oxidation of the corresponding 2-(aryl-methoxy)phenols.[20] The results of the Ti(IV)-promoted reactions of these quinones with various propenylbenzenes are presented in Table 5. Reactions of **32a** with propenylbenzenes bearing strong electron donating alkoxy groups again give major amounts of dihydrobenzofuran and cyclobutane products **34/35**. However, more neutral systems give significant amounts of **16**, and in reactions of **32b** and **33a/b**, the 5 + 2 products **16/17** are formed exclusively.[21] In fact, the highest yield of a 5 + 2 cycloaddition product resulted from a combination of increasing the rate of path a and decreasing the rate of path b in the mechanism shown in Scheme 2. Thus, reaction of the *o*-methyl-substituted propenylbenzene **8e** with aryloxy quinone **33b** gave **17e** in 88% isolated yield. An experimental difficulty encountered in these reactions was the sensitivity of some of the products to silica gel. Compounds **16f** and **17d–f** could be isolated and characterized after rapid flash chromatography; however, isolation of **16d** and **16e** was problematic. In fact, compound **16d** was never obtained in pure form. Simi-

(16) For leading references to the research from several groups on reactions of similar pentadienylcarbocations with alkenes, including styrenyl systems, see: (a) Büchi, G.; Mak, C.-P. *J. Am. Chem. Soc.* **1977**, *99*, 8073. (b) Büchi, G.; Chu, P.-S. *Tetrahedron* **1981**, *37*, 4509. (c) Mortlock, S. V.; Seckington, J. K.; Thomas, E. J. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2305. (d) Angle, S. R.; Turnbull, K. D. *J. Org. Chem.* **1993**, *58*, 5360. (e) Shizuri, Y.; Shigemori, H.; Suyama, K.; Nakamura, K.; Okuno, Y.; Ohkubo, M.; Yamamura, S. In *Studies in Natural Products Chemistry*, Vol. 8; Atta-ur-Rahman, Ed.; Elsevier: Amsterdam, 1991; pp 159–173. (f) Yamamura, S.; Shizuri, Y.; Shigemori, H.; Okuno, Y.; Ohkubo, M. *Tetrahedron* **1991**, *47*, 635. (g) Gates, B. D.; Dalidowicz, P.; Tebben, A.; Wang, S.; Swenton, J. S. *J. Org. Chem.* **1992**, *57*, 2135.

(17) See also refs 16e–g.

(18) (a) There are other mechanistic rationale. For example, the products can be explained via a Diels–Alder reaction of the styrene with the quinone in which the quinone would be expected to adopt an endo orientation. The Diels–Alder adduct could then undergo Ti(IV)-mediated fragmentation to benzylic carbocations **30/31**. However, we think this is unlikely since Diels–Alder reactions of styrenes with quinones are known to give phenanthrenediols or -diones,[2] even with acid catalysis in which fragmentation might be expected.[2n] Alternatively, Swenton[16g] has suggested that π-stacking interactions may be operative in nonconcerted reactions as well as concerted ones and simple alkylation of the quinone–Ti(IV) complex by the styrene may preferentially give benzylic cations **30/31** directly without proceeding through **28/29**. Intermediates **30/31** may then close to any one of the three products. There may be little difference between the cycloaddition mechanism and an alkylation process since in a cycloaddition process, an asynchronous transition state in which C-β/C-5 bond formation is further advanced than C-α/C-3 would be expected due to the higher electrophilicity of C-5 in comparison to C-3 in complex **26**. However, in an alkylation process, it is not clear why path c in Scheme 2 predominates in reactions of benzyloxy quinones **33a/b** or why higher yields of bicyclic adducts **16/17** are found in reactions of **8e**. For studies designed to explore the nature of this π-stacking interaction, see: (b) Cozzi, F.; Cinquini, M.; Annunziata, R.; Dwyer, T.; Siegel, J. S. *J. Am. Chem. Soc.* **1992**, *114*, 5729. (c) Cozzi, F.; Cinquini, M.; Annuziata, R.; Siegel, J. S. *Ibid.* **1993**, *115*, 5330. See also: (d) Hunter, C. A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1584 and references cited therein.

(19) Sera, A.; Takeuchi, S.; Tachikawa, N.; Maruyama, K. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1112.

(20) Zimmer, H.; Lankin, D. C.; Horgan, S. W. *Chem. Rev.* **1971**, *71*, 229.

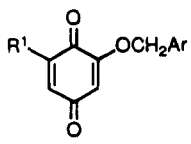
(21) *p*-Methoxybenzyl chloride could be detected in these reactions.

Table 5. Ti(IV)-Promoted Reactions of 2-(Arylmethoxy)-1,4-benzoquinones with Propenylbenzenes

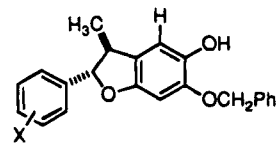
entry	propenylbenzene	quinone R¹	quinone Ar	$TiCl_4$:$Ti(OiPr)_4$ [equiv of Ti(IV)]	temp (°C)	% yield 34	% yield 35	% yield 16/17
1	**8c**, 3,4-$(OCH_3)_2$	**32a** H	Ph	1:1 (1.0)	−70	60	22	
2	**8f**, H	**32a** H	Ph	4:1 (1.1)	−78	29	7	21
3	**8f**, H	**32b** CH_3	Ph	2:1 (1.2)	−78 to rt			54
4	**8d**, 4-CH_3	**33a** H	C_6H_4-4-OCH_3	1:1 (1.0)	−78 to 10			44[a]
5	**8e**, 2-CH_3	**33a** H	C_6H_4-4-OCH_3	1:1 (1.0)	−78 to rt			46
6	**8f**, H	**33a** H	C_6H_4-4-OCH_3	1:1 (1.0)	−78 to rt			59
7	**8d**, 4-CH_3	**33b** CH_3	C_6H_4-4-OCH_3	1:1 (1.0)	−78 to −20			67
8	**8e**, 2-CH_3	**33b** CH_3	C_6H_4-4-OCH_3	1:1 (1.0)	−78 to −20			88
9	**8f**, H	**33b** CH_3	C_6H_4-4-OCH_3	1:1 (1.0)	−78 to rt			76
								22
10	indene	**33b** CH_3	C_6H_4-4-OCH_3	1:1 (1.0)	−78 to 0			63

[a] Crude yield (see text).

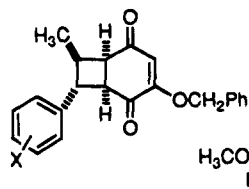
larly, NMR examination of the crude reaction mixtures from reactions of **33b** with propenylbenzenes **8a** and **8c** indicated that 5 + 2 adducts were formed; however, they were not stable and attempts at isolation were not fruitful. In agreement with our mechanistic hypothesis, reactions of (*Z*)-propenylbenzene **23c** and indene with 2-(benzyloxy)-1,4-benzoquinone gave cyclobutane **36** and bicyclic adduct **22**, respectively, in 49 and 63% yields. Unfortunately, reactions of quinone **33b** with (*Z*)-propenylbenzenes failed to produce 5 + 2 adducts; only intractables were found due probably to debenzylation of the quinone before cycloaddition could occur.



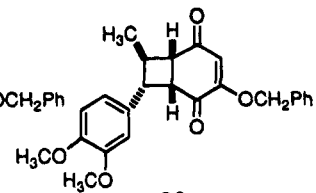
32a, R^1=H, Ar=C_6H_5
32b, R^1=CH_3, Ar=C_6H_5
33a, R^1=H, Ar=C_6H_4-4-OCH_3
33b, R^1=CH_3, Ar=C_6H_4-4-OCH_3



34a, X=3,4-$(OCH_3)_2$
34b, X=H



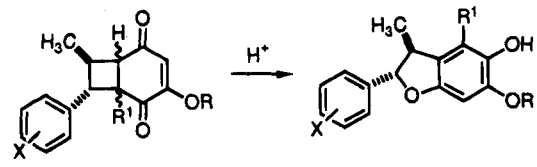
35a, X=3,4-$(OCH_3)_2$
35b, X=H



36

Evidence that the cyclobutanes and the dihydrobenzofurans arise from a common reaction manifold is provided by protic acid-catalyzed rearrangement of the former to the latter at room temperature or above (Table 6). The results of these experiments and a careful examination of the data in Table 1 suggest that, for reasons that are not yet entirely clear, cyclobutanes **13**−**15** and **19/21** formed from benzylic cations **30/31** are products of kinetic control, being preferred at low temperature, whereas the dihydrobenzofurans **10**−**12** and **18/20** are products of thermodynamic control. For reactions involving the same propenylbenzene and quinone, the larger amounts of cyclobutane products found in reactions promoted by mixtures of $Ti(OiPr)_4$ and $TiCl_4$ in comparison to reactions promoted by $TiCl_4$, which give predominately dihydrobenzofurans, are consistent with this postulate and result from the high affinity of Ti(IV) for oxygen ligands. Intermediate **37**, involved in the $TiCl_4$-promoted reactions, has mainly chloride ligands on the Ti(IV) and may be expected to have a tight Ti−O bond and a relatively nonnucleophilic titanium enolate moiety.

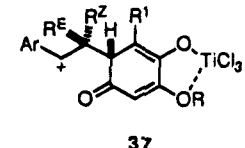
Table 6. Acid-Catalyzed Rearrangement of Bicyclo[4.2.0]octenediones to Dihydrobenzofurans



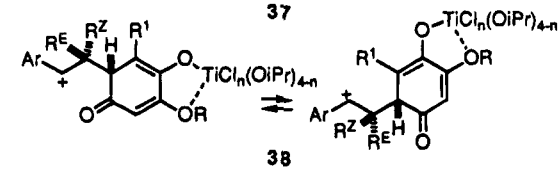
entry	cyclobutane	product	% yield (trans/cis)[b]
1	**14d**	**11d**	91 (16:1)
2	**14e**	**11e**	84 (8.4:1)
3	**14f**	**11f**	100 (10:1)
4	**14g**	**11g**	92 (10:1)
5	**15d**	**12d**	74 (6:1)
6	**19**	**18**	78 (>20:1)[c]
7	**35a**	**34a**	85 (>20:1)[c]
8	**24f**	**11f**	98 (10:1)
9	**36**	**34a**	51 (>20:1)[c]

[a] All reactions were done with H_2SO_4 in CH_2Cl_2 at room temperature. [b] By ^1H NMR. [c] Only one isomer observed by ^1H NMR.

As a result, formation of **10**−**12** is found. In contrast, intermediate **38**, involved in reactions promoted by mixtures of $TiCl_4$ and $Ti(OiPr)_4$, would be expected to have a number of isopropoxide ligands on the titanium, and thus a more nucleophilic titanium enolate moiety, resulting in a kinetic preference for the cyclobutane products. The exact number of isopropoxide ligands on the Ti(IV) in such an intermediate is not clear.



37



38

The structural assignments of the products are supported by chemical and spectroscopic data. The substitution pattern in dihydrobenzofurans **11** was apparent from ^1H-NMR in which H-4 and H-7 appeared as two singlets at ~6.7 and ~6.5 ppm, respectively. In dihydrobenzofuran **12**, the H-7 signal also appears at ~ 6.4 ppm. The trans stereochemistry at C-2 and C-3 was also apparent from ^1H-NMR. The C-3 methyl signals appear at ~1.36 ppm; in the corresponding cis isomers, these signals appear upfield (~0.7 ppm) due to shielding by the C-2

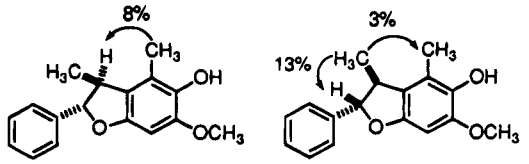


Figure 1. Summary of selected $^1H-^1H$ NOE data accumulated for **12f**.

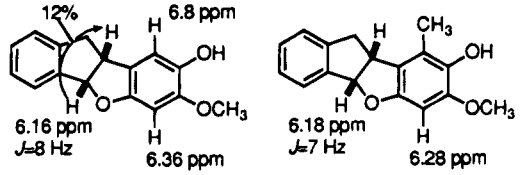
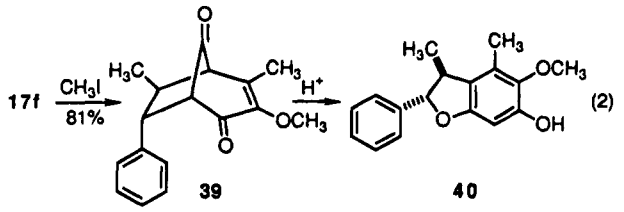


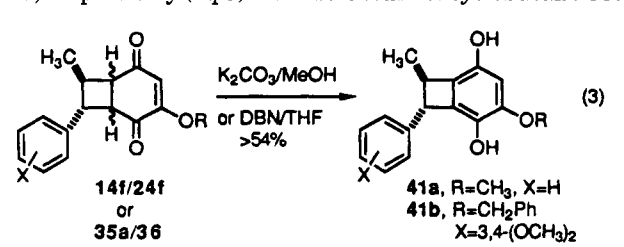
Figure 2. Summary of selected ^1H-NMR and $^1H-^1H$ NOE data accumulated for **18** and **20**.

aryl group.[22] Results of $^1H-^1H$ NOE experiments on **12f** are also supportive of the substitution pattern and the trans stereochemistry (Figure 1). The substitution pattern and cis ring juncture in indene adduct **18** were similarly established by NMR (Figure 2).

In the bicyclo[3.2.1] adducts **16** and **17**, the endo and exo orientations of the aryl and methyl groups, respectively, were indicated by $J_{H\text{-}1/H\text{-}7} = 6-8$ Hz and the lack of an observable coupling between H-5 and H-6. A W coupling between H-1 and H-5 (~2 Hz) was also observed. In the indene adduct **22**, coupling constants of 8–9 Hz between both H-1/H-7 and H-5/H-6 were again indicative of an endo aryl group. Methylation of **17f** to **39** (81%) followed by protic acid-promoted rearrangement[23] gave a 6:1 mixture of trans and cis dihydrobenzofurans **40** that were clearly different than **12** (eq 2). Finally, single crystal X-ray analysis of **17f** firmly established its structure and spectral comparison of it with the other bicyclo[3.2.1] adducts support the structures shown.



The isomeric cyclobutanes **14** and **24**, formed from the (*E*)- and (*Z*)-propenylbenzenes, respectively, were identified as stereoisomers and not constitutional isomers (i.e., a regioisomer with C-4 methoxy group) on the basis of the following rearrangement reactions. Treatment of isomeric cyclobutanes **14f** or **24f** and cyclobutanes **35a** or **36** with protic acid gave identical dihydrobenzofurans **11f** and **34a**, respectively (Table 6). Similarly, base-promoted rearrangements of either **14f** or **24f** and of either **35a** or **36** gave the same hydroquinones **41a** and **41b**, respectively (eq 3). The structure of cyclobutane **35a**



was further established by single crystal X-ray analysis, which clearly showed a cis ring fusion and trans Ar and CH_3 groups on the cyclobutane ring. Results of $^1H-^1H$

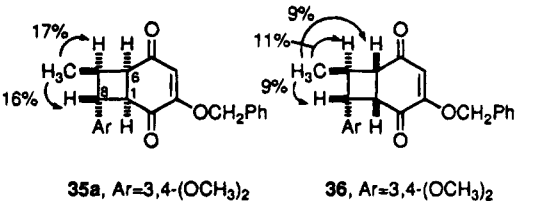


Figure 3. Summary of $^1H-^1H$ NOE data accumulated for **35a** and **36**.

decoupling and NOE experiments (Figure 3) were also consistent with this structure. The four methine signals in **35a** were clearly observed as a multiplet and three doublets of doublets. Irradiation of the H-7 multiplet resulted in collapse of the dd's from H-6 and H-8. Only the H-1 signal was unaffected. Then, irradiation of the C-7 methyl group resulted in enhancement of H-7 and only one other methine signal which was identified as H-8. The spectra of other cyclobutane products **14** from (*E*)-propenylbenzenes were similar to those of **35a**.

With results of the acid- and base-promoted rearrangements of **14f/35a** and **24f/36**, and the results of the X-ray and spectral analysis of **35a** in hand, the structure of the isomeric cyclobutane **36** was deduced from the following ^1H-NMR data. The C-7 methyl signal in **35a** appears at ~1.18 ppm. That the Ar and CH_3 groups in **36** were also trans was inferred from the chemical shift of the C-7 methyl signal at 1.35 ppm; if the methyl and Ar groups were cis, the methyl signal would be expected to be upfield from that in **35a**, due to shielding by the Ar group, not downfield. A trans ring fusion was considered unlikely due to expected ring strain in such a system. Again, the four methine signals in **36** were clearly identifiable as a multiplet and three doublets of doublets in the $^1H-$NMR spectrum. Selective decoupling experiments established the position of the H-1 signal and an $^1H-^1H$ NOE experiment in which irradiation of the C-7 methyl group produced enhancements of the H-6, H-7, and H-8 methine signals clearly indicated the stereochemistry of the four stereogenic centers (Figure 3). The NOE results are consistent only with the substitution pattern and stereochemistry shown.

The structures of the cyclobutane products **15** and **25** from 2-methoxy-6-methyl-1,4-benzoquinone (**9c**) were identified on the basis of acid-catalyzed rearrangement of **15d** to the dihydrobenzofuran **12d** (Table 6), which established the position of the OCH_3 group, and by NMR. In **15**, the appearance of the three methine signals as two doublets and a multiplet is consistent only with the methyl groups at C-1 and C-7 and the phenyl group at C-8. The relative stereochemistry in **15f** and **25f** was determined by the following $^1H-^1H$ NOE experiments. Irradiation of the C-1 methyl singlet in **15f** resulted in enhancements of H-6 proton and the *ortho* protons of the phenyl group while irradiation of the C-7 methyl doublet resulted in enhancements of the signals from both H-7 and H-8 (Figure 4). In isomer **25f**, irradiation of the C-1 methyl singlet resulted in enhancements of the H-6 and H-8 signals, respectively, and irradiation of the C-7

(22) (a) See references cited in refs 1a and 10a. (b) Coupling constants between H-2 and H-3 of 2,3-disubstituted-2,3-dihydrobenzofurans are nearly the same in both the trans and cis isomers, see references cited in the above and (c) Letavic, M. A. Ph.D. Dissertation, University of Kansas, 1992. (d) Lima, O. A.; Gottlieb, O. R.; Magalhães, M. T. *Phytochemistry* **1972**, *11*, 2031. See also: (e) Nakajima, K.; Taguchi, H.; Endo, T.; Yosioka, I. *Chem. Pharm. Bull.* **1978**, *26*, 3050. (f) Engler, T. A.; Draney, B. W.; Gfesser, G. A. *Tetrahedron Lett.* **1994**, *35*, 1661. (g) Wenkert, E.; Gottlieb, H. E.; Gottlieb, O. R.; Pereira, M. O. da S.; Formiga, M. D. *Phytochemistry* **1976**, *15*, 1547.

(23) Büchi, G.; Chu, P.-S. *J. Org. Chem.* **1978**, *43*, 3717.

Table 7. Ti(IV)-Promoted Reactions of α-Methylstyrenes and 1-Arylcycloalkenes with 1,4-Benzoquinones

entry	styrene or cycloalkene, X	quinone	R^1	R^2	$TiCl_4$:$Ti(OiPr)_4$ [equiv of Ti(IV)]	method[a]	temp (°C)	time (h)	% yield
1	**42a**, OCH_3	**9a**	H	H	3:1 (1.1)	A	−78 to −40	9	**43a** (50)
2	**42a**, OCH_3	**9b**	H	OCH_3	3:1 (1.0)	B	−78	2	**44a** (54)
3	**42b**, H	**9b**	H	OCH_3	3:1 (1.0)	A	−78 to 0	5	**44b** (60)
4	**42a**, OCH_3	**9c**	CH_3	OCH_3	3:1 (1.0)	A	−78 to −35	20	**45a** (55)
5	**45b**, H	**9c**	CH_3	OCH_3	2:1 (1.1)	A	−78 to rt	36	**45b** (54)
6	**46a**, OCH_3, 1	**9b**	H	OCH_3	1:1 (1.0)	A	−78	1	**49a** (79)
7	**47a**, OCH_3, 2	**9b**	H	OCH_3	2:1 (1.0)	A	−78	4.3	**50a** (67)
8	**48a**, OCH_3, 3	**9b**	H	OCH_3	2:1 (1.0)	A	−78	4.5	**51a** (53)
9	**46b**, H, 1	**9b**	H	OCH_3	2:1 (1.0)	A	−78	0.75	**49b** (43)
10	**47b**, H, 2	**9b**	H	OCH_3	4:1 (1.0)	A	−78	2.5	**50b** (71)
11	**48b**, H, 3	**9b**	H	OCH_3	2:1 (1.0)	A	−78	1	**51b** (62) **56b** (14)
12	**46a**, OCH_3, 1	**9c**	CH_3	OCH_3	3:1 (1.0)	A	−78 to rt	12	**52a** (63)
13	**47a**, OCH_3, 2	**9c**	CH_3	OCH_3	2:1 (1.0)	A	−78 to rt	23	**53a** (70)
14	**48a**, OCH_3, 3	**9c**	CH_3	OCH_3	4:1 (1.0)	A	−78	2	**54a** (89)
15	**46b**, H, 1	**9c**	CH_3	OCH_3	2:1 (1.0)	A	−78 to rt	12	**52b** (75)
16	**47b**, H, 2	**9c**	CH_3	OCH_3	4:1 (1.0)	A	−78 to rt	18	**53b** (66)
17	**48b**, H, 3	**9c**	CH_3	OCH_3	3:1 (1.0)	A	−78	4	**54b** (92)

[a] See Table 1. [b] 44% starting quinone was recovered. [c] 10% starting quinone was recovered.

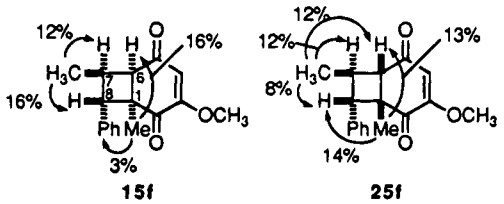


Figure 4. Summary of $^1H-^1H$ NOE data accumulated for **15f** and **25f**.

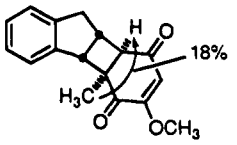


Figure 5. Summary of $^1H-^1H$ NOE data accumulated for **21**.

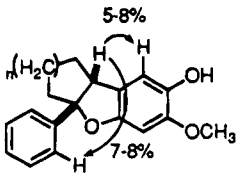
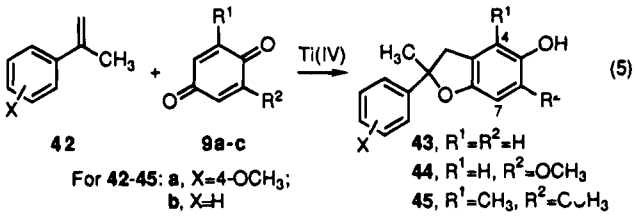
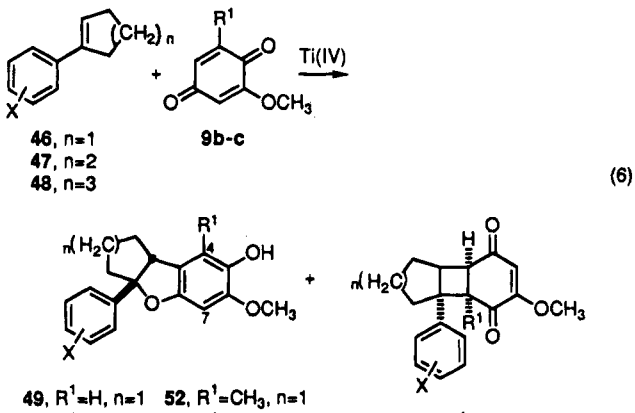


Figure 6. Summary of $^1H-^1H$ NOE data accumulated for **49b**–**50b**.



(5)



(6)

methyl doublet resulted in enhancements of the signals from H-6, H-7, and also H-8. The structures shown are consistent with this data. In the indene adduct **21**, irradiation of the methyl signal at 1.08 ppm showed enhancement of only the signal for H-8a (Figure 5).

Reactions of 1,4-Benzoquinones with α-Methylstyrenes and 1-Arylcycloalkenes. Titanium(IV)-promoted reactions of α-methylstyrenes **42** and 1-arylcycloalkenes **46**–**48** with quinones **9** produced mainly dihydrobenzofurans (eqs 5 and 6 and Table 7). In only one case was a cyclobutane product isolated in low yield (entry 11). The regioselectivity of the reactions to form **44** and **49**–**51** was again indicated by the ^1H-NMR spectra in which H-7 and H-4 were observed as two singlets at 6.42–6.53 and 6.58–6.71 ppm, respectively. Similarly, H-7 appears at 6.32–6.42 ppm in **45** and **52**–**54**. The substitution pattern and the stereochemistry of the ring fusions in **49b**, **50b** and **51a** were confirmed by $^1H-^1H$ NOE experiments (Figure 6).

Reactions of 4-((methoxybenzyl)oxy)quinone **33b** were again used to access products of 5 + 2 cycloaddition from both phenylcycloalkenes and α-methylstyrene. Reaction with phenylcycloheptene **48b** gave **57** in 55% yield (eq 7). In reactions of phenylcyclopentene (**46b**), promotion by 2 equiv of a 2:1 mixture of $TiCl_4$:$Ti(OiPr)_4$ at −78 °C to −20 °C gave only the *o*-quinone **59** in 66% yield. However, with 1 equiv of the Ti(IV) mixture as promoter at −78 °C, **59** was isolated in 43% yield along with a small amount (4%) of bicyclic adduct **58.** The *o*-quinone presumably results from oxidation of the corresponding catechol[24] on SiO_2 chromatography or perhaps by the Lewis acid–quinone complex (vide infra). Reaction of quinone **33b** with α-methylstyrene (**42b**) under similar conditions gave 5 + 2 adduct **60** in 36% yield (eq 8). The endo orientation of the aryl moieties in **57**/**58** and **60** is indicated by the lack of an observable $J_{H\text{-}5/H\text{-}6}$ in the former and $J_{H\text{-}5/H\text{-}6\alpha}$ in the latter; $J_{H\text{-}5/H\text{-}6\beta}$ in **60** is ~6.8

(24) Bruce, J. M. In *Rodd's Chemistry of Carbon Compounds*, 2nd ed.; Coffey, S., Ed.; 1974; Vol. III, Part B, pp 13–15.

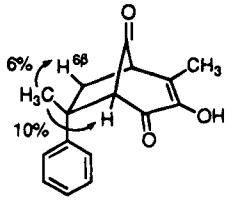
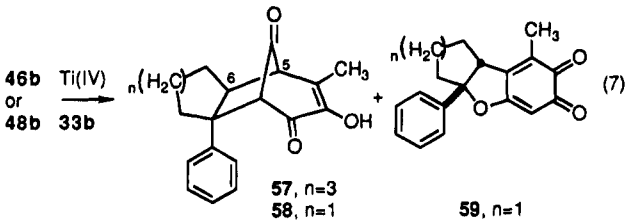
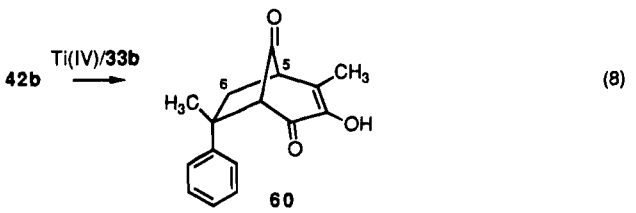


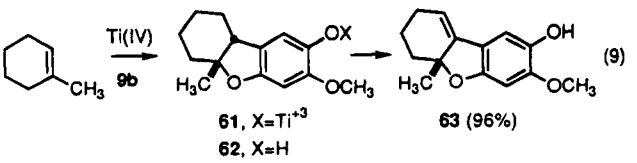
Figure 7. $^1H-^1H$ NOE data accumulated on **60**.

Hz. The signal for H-6β in **60** is indentified from an $^1H-^1H$ NOE experiment (Figure 7).

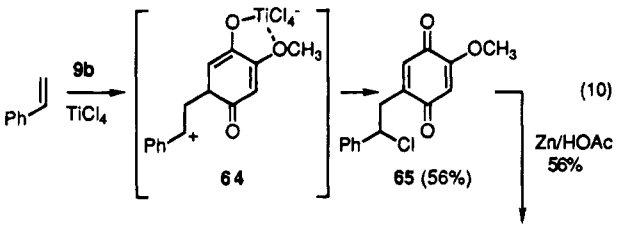


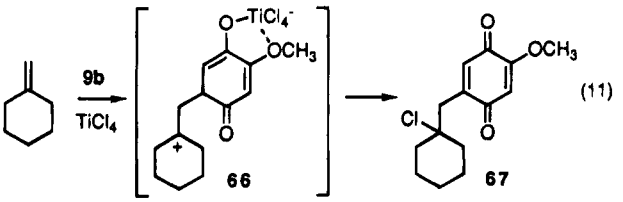


Reactions of 1,4-Benzoquinones with Non-styrenylalkenes. A limited number of Ti(IV)-promoted reactions of 2-methoxy-1,4-benzoquinone with styrene and non-styrenylalkenes were also examined. Treatment of quinone **9b** with $TiCl_4$ at −78 °C followed by addition of 1-methylcyclohexene and warming to room temperature yielded **63**, which is an unexpected oxidized derivative of the anticipated product **62** (eq 9). Apparently, intermediate **61** is oxidized under the reaction conditions. Evidence that the oxidant in the conversion of **61** to **63** was the $TiCl_4$:**9b** complex[25] was provided by treatment of **62** (formed by hydrogenation of **63**) with quinone **9b** and $TiCl_4$ at −78 °C followed by warming to room temperature which produced **63** in 48% yield. Assuming that 2 equiv of the quinone−Ti(IV) complex was required in the original reaction with methylcyclohexene, the yield of **63** is, in fact, 96%. That the **9b**:$TiCl_4$ complex is an effective oxidant is noteworthy in that it may be useful in other transformations (for example, ketone to enone, diarylethanes to stilbenes, aromatization reactions, etc.) and may have advantages over other more common quinone oxidants such as DDQ, chloranil, etc.[25]

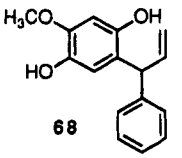


Titanium(IV)-promoted reaction of styrene with quinone **9b** gave the alkylated quinone **65** in 56% yield (eq 10). Similarly, methylenecyclohexane gave **67** in 35% yield (eq 11). Both **65** and **67** are produced by reaction of chloride ion with the presumed intermediate carbocations **64** and **66**, respectively, followed by oxidation of the resultant intermediates, either in situ by the $TiCl_4$−quinone complex or upon exposure to air on workup and chromatography. Treatment of **65** with Zn/HOAc yielded 6-methoxy-2-phenyl-2,3-dihydrobenzofuran-5-ol (56%); however, similar reactions with **67** failed to produce a dihydrobenzofuran.



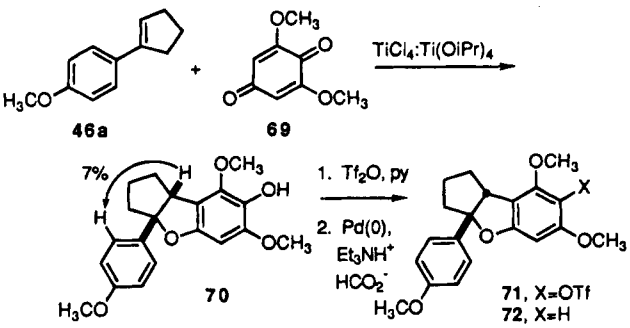


Synthetic Applications. (+)-Obtusafuran (**11f**) is a plant natural product.[10] Its racemate has also been reported as an artifact from the distillation of the oily extracts from the same source via thermal rearrangement of obtusaquinol **68**.[10c] As described above, a direct synthesis of (±)-**11f** was effected through the Ti(IV)-promoted reaction of propenylbenzene **8f** with quinone **9b**. Cyclobutane **14f** was also produced and treatment of it with protic acid produced a 12:1 mixture of **11f** and its cis isomer in quantitative yield. Recrystallization of this mixture produced pure **11f**.



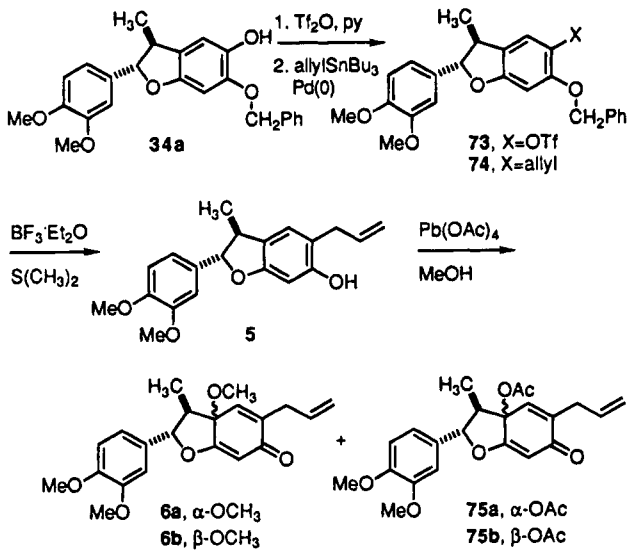
Rocaglamide (**7**) is a naturally occurring antileukemic agent possessing a densely substituted 2-aryl-2,3-dihydrobenzofuran moiety.[13] A model study for a synthetic approach to (±)-**7** was designed using a quinone−arylcycloalkene reaction as a key step (Scheme 3). Thus, addition of 1-(4-methoxyphenyl)cyclopentene (**46a**) to a complex formed from 2,6-dimethoxy-1,4-benzoquinone (**69**)[26] and a 3:1 mixture of $TiCl_4$ and $Ti(OiPr)_4$ generated dihydrobenzofuran **70** in 58% yield; the cis ring fusion was confirmed by an $^1H-^1H$ NOE experiment. Removal of the phenolic OH was accomplished by conversion to

Scheme 3



(25) (a) Becker, H.-D.; Turner, A. B., in ref 3a, p 1351. See also: (b) Engler, T. A.; Reddy, J. P. *J. Org. Chem.* **1991**, *56*, 6491.
(26) Teuber, H.-J.; Rau, W. *Chem. Ber.* **1953**, *86*, 1036.

Scheme 4



triflate **71** followed by a Pd(0)-catalyzed triethylammonium formate reduction[27] to give **72**. The formation of **72** offers a potential strategy for the synthesis of (±)-rocaglamide that we are currently exploring.

Neolignans are defined as naturally occurring dimers of propenylbenzenes connected through atoms other than C-8/C-8′. More than 43 different structural types of neolignans have been identified. Many are highly oxidized and display powerful and diverse biological activity.[9] Liliflol B (**5**), kadsurenone (**6a**), and denudatin B (**6b**) are representatives of one class of neolignan natural products. Kadsurenone in particular has attracted considerable attention as a potent platelet-activating factor antagonist.[12] As a synthetic approach to **5**–**6**, the Ti(IV)-promoted reactions of 2-(benzyloxy)-1,4-benzoquinone (**32a**) with styrene **8c** were designed to produce a 2-aryl-2,3-dihydrobenzofuran product with differentially substituted oxygen substituents which could be selectively manipulated (Scheme 4). As described above, these experiments produce dihydrobenzofuran **34a** and cyclobutane **35a** in 60 and 24% yields, respectively, and the latter rearranged to the former in quantitative yield upon treatment with H_2SO_4. Formation of the triflate **73** followed by Stille coupling with allyltributyltin gave **74** in 90% overall yield. It is noteworthy that in the latter reaction, the allylic double bond did not migrate into conjugation.[28] Debenzylation of **74** with $BF_3{\cdot}Et_2O$ and dimethyl sulfide[29] gave racemic liliflol B (**5**), which has been converted to (±)-kadsurenone (**6a**) in 10% yield upon treatment with methanolic lead(IV) acetate.[12b,c] Denudatin B (**6b**) and a mixture of the epimeric acetates **75** were also found in 19 and 48% yields, respectively. We, and others,[12c] have been unsuccessful in attempts to improve the oxidation of **5** to **6a/b** by reaction with $Pb(O_2CPh)_4$, $Pb(O_2CCF_3)_4$, $Pb[O_2C(2,6\text{-}Cl_2)C_6H_3]$, $Pb(OTf)_4$, or $PhI(OAc)_2$. Electrochemical oxidation of **5** has been reported to yield **6a/b**.[30]

Finally, syntheses of biologically active pterocarpans have recently been reported utilizing the methodology described herein.[31] In addition, preliminary studies on the development of enantioselective reactions of this type utilizing chiral Ti(IV)-complexes have been encouraging.[1d]

Conclusions

Lewis acid-promoted reactions of various styrenyl systems with 2-alkoxy-1,4-benzoquinones provide efficient routes to highly substituted 2-aryl-2,3-dihydrobenzofurans, 8-arylbicyclo[4.2.0]oct-3-ene-2,5-diones, or 7-arylbicyclo[3.2.1]oct-3-ene-2,8-diones and derivatives. In most cases, these products can be accessed regio- and stereoselectively depending upon reaction conditions and/or choice of substituents on either the quinone or styrene.

Experimental Section

General. All compounds were prepared as racemic mixtures. All reactions were conducted in flame- or oven-dried glassware under an atmosphere of dry N_2 or argon with magnetic stirring unless otherwise noted. All solvents were distilled under N_2 or vacuum from the drying agents indicated: CH_2Cl_2, CH_3CN, and DMSO from CaH_2; benzene and toluene from CaH_2 or sodium benzophenone ketyl; Et_2O and THF from sodium benzophenone ketyl; acetone from $CaSO_4$ or K_2CO_3; CF_3CH_2OH from $CaCl_2$; MeOH from Mg; DMF from BaO and then KOH; pyridine from KOH; EtOAc from K_2CO_3. Hexanes were fractionally distilled. $TiCl_4$, $SnCl_4$, and $BF_3{\cdot}Et_2O$ were distilled from CaH_2. $Ti(OiPr)_4$ and $ZrCl_4$ were purchased from Aldrich and used as received. Trifluoromethanesulfonic anhydride was distilled from P_2O_5. Iodomethane was filtered through neutral alumina before use. All other reagents were purchased from commerical vendors and used as received. NMR spectra were recorded on samples dissolved in $CDCl_3$ and chemical shifts are reported in δ (ppm) relative to Me_4Si or residual $CHCl_3$ as internal standards unless stated otherwise. Coupling constants (J) are reported in hertz. Carbon multiplicities were determined by either attached proton test (APT), single frequency off-resonance decoupling (SFORD), or HETCOR experiments. HRMS refers to high-resolution mass spectrometry. Melting and boiling points are uncorrected. All reactions were monitored by thin-layer chromatography (TLC) on precoated 0.25 mm silica gel plates with a fluorescent indicator (Merck Kieselgel 60 F_{254}); visualization was effected with a UV lamp or by staining with p-anisaldehyde/H_2SO_4 or phosphomolybdic acid. Chromatography refers to flash chromatography on silica gel.

2-Methoxy-1,4-benzoquinone and 2-methoxy-6-methyl-1,4-benzoquinone were prepared by Fremy's salt oxidation[20] of 2-methoxyphenol and 2-methoxy-6-methylphenol by the method of Kanematsu.[32] Similarly prepared were 2-(benzyloxy)-1,4-benzoquinone[33] and 2,6-dimethoxy-1,4-benzoquinone[26] from 2-(benzyloxy)phenol and 2,6-dimethoxyphenol, respectively. Quinones **32b** and **33a/b** were prepared by alkylation of catechol and 3-methylcatechol, respectively, followed by Fremy's salt oxidation. Full experimental procedures for the preparation of all quinones are given in the supplementary material. Similarly, propenylbenzenes and alkenes not com-

(27) Saá, J. M.; Dopico, M.; Martorell, G.; García-Raso, A. *J. Org. Chem.* **1990**, *55*, 991 and references cited therein.

(28) Several other reports indicate that double bond isomerization can be prevented. (a) Scott, W. J.; McMurry, J. E. *Acc. Chem. Res.* **1988**, *21*, 47. (b) Tilley, J. W.; Sarabu, R.; Wagner, R.; Mulkerins, K. *J. Org. Chem.* **1990**, *55*, 906. (c) Martorell, G.; García-Raso, A.; Saá, J. M. *Tetrahedron Lett.* **1990**, *31*, 2357. (d) Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585. (e) Saá, J. M.; Martorell, G.; García-Raso, A. *J. Org. Chem.* **1992**, *57*, 678. (f) For a review, see: Ritter, K. *Synthesis* **1993**, 735.

(29) Fuji, K.; Kawabata, T.; Fujita, E. *Chem. Pharm. Bull.* **1980**, *28*, 3662.

(30) Chang, M. N.; Brooker, D. R.; Bugianesi, R. L.; Doebber, T. W.; Ponpipom, M. M.; Wu, M. S.; Yue, B.-Z.; Springer, J.; Hwang, S. B.; Han, G. Q.; Lam, M. T.; Shen, T. Y. *Abstracts of the IUPAC Symposium on Organic Chemistry of Medicinal Natural Products*, Shanghai, 1985, C-33 (see Whiting, D. A. *Nat. Prod. Rep.* **1987**, *4*, 499).

(31) (a) Engler, T. A.; Reddy, J. P.; Combrink, K. D.; Vander Velde, D. *J. Org. Chem.* **1990**, *55*, 1248. (b) Engler, T. A.; Lynch, K. O., Jr.; Reddy, J. P.; Gregory, G. S. *Bioorg. Med. Chem. Lett.* **1993**, *3*, 1229.

(32) Hayakawa, K.; Ueyama, K.; Kanematsu, K. *J. Org. Chem.* **1985**, *50*, 1963.

(33) Ishii, H.; Ohtake, R.; Ohida, H.; Mitsui, H.; Ikeda, N. *J. Pharm. Soc. Jpn.* **1970**, *90*, 1283.

mercially available were prepared by standard techniques and full experimental details appear in the supplementary material.

Reactions of 1,4-Benzoquinones with Propenylbenzenes and Alkenes: General Method A. $TiCl_4$ was added to a solution of $Ti(OiPr)_4$ in CH_2Cl_2 at 0 °C. The mixture was stirred for 15 min, and then an aliquot was transferred via syringe or cannula to a solution of the quinone in CH_2Cl_2 at −78 °C followed, after 15 to 30 min, by the propenylbenzene/alkene. When the reaction was complete (TLC), the mixture was poured into saturated aqueous $NaHCO_3$ and the aqueous layer extracted three times with CH_2Cl_2. The extracts were combined, dried ($MgSO_4$), and concentrated and the residue chromatographed with EtOAc/hexanes as eluent to afford the products.

General Method B. $Ti(OiPr)_4$ and $TiCl_4$ were added sequentially to a solution of the quinone in CH_2Cl_2 at −78 °C. The mixture was stirred for 15 min and the propenylbenzene/alkene added. Upon completion of the reaction (TLC), the mixture was worked up as described in method A.

General Method C. $TiCl_4$ was added to a solution of $Ti(OiPr)_4$ in CH_2Cl_2 at room temperature. After 15 min, an aliquot of this mixture was added slowly to a solution of the quinone in CH_2Cl_2 at −78 °C followed, after 15 min, by the propenylbenzene. The reaction mixture was stirred at −78 °C for the time indicated, solid $NaHCO_3$ (1−2 g) and iPrOH (5−10 mL) were added, and the mixture was diluted with water, filtered through Celite, and then extracted three times with CH_2Cl_2. The extracts were combined, dried (Na_2SO_4), and concentrated and the residue chromatographed on silica gel with EtOAc/hexanes as eluent.

General Method D. Exactly as described in method C, except after addition of the propenylbenzene, the reaction mixture was stirred at −78 °C for the time indicated and then allowed to warm to −20 °C or room temperature.

General Method E. $TiCl_4$ was added to a solution of $Ti(OiPr)_4$ in CH_2Cl_2 at room temperature. After 10−15 min, the mixture was cooled to −78 °C and a solution of the quinone in CH_2Cl_2 added dropwise followed after 15−20 min by a solution of the propenylbenzene in CH_2Cl_2. The reaction was stirred at the temperature indicated and then solid $NaHCO_3$ (1 g), iPrOH (3 mL), and H_2O (25 mL) were added. The mixture was filtered through Celite and then extracted with CH_2Cl_2 three times. The extracts were combined, dried (Na_2SO_4), and concentrated and the residue chromatographed on silica gel with EtOAc/hexanes as eluent.

Reaction of 9a with 8a. According to method A, an aliquot [1.4 mL, 0.53 mmol of Ti(IV)] of a solution of $TiCl_4$ (0.114 mL, 1.04 mmol) and $Ti(OiPr)_4$ (0.176 mL, 0.59 mmol) in CH_2Cl_2 (4 mL) was added to a solution of quinone **9a** (50 mg, 0.46 mmol) in CH_2Cl_2 (10 mL) followed by a solution of **8a** (0.1 mL, 0.67 mmol) in CH_2Cl_2 (1 mL). The reaction was complete in 5 min and gave dihydrobenzofuran **10a** (81 mg, 68%) as a yellow oil: R_f (30% EtOAc/hexanes) 0.57; ^{1}H NMR (300 MHz) 1.34 (d, J = 7, 3H), 3.38 (dq, J = 7, 9, 1H), 3.80 (s, 3H), 4.77 (s, 1H), 5.04 (d, J = 9, 1H), 6.6−6.7 (m, 3H), 6.90 (d, J = 8, 2H), 7.35 (d, J = 8, 2H); ^{13}C NMR (75 MHz) 17.6, 45.6, 55.4, 92.6, 109.5, 111.1, 114.0, 114.4, 127.7, 132.7, 133.3, 150.0, 153.2, 159.7; HRMS m/z 256.1101 (calcd for $C_{16}H_{16}O_3$, 256.1099).

Reaction of 9a with 8c. According to method B, $Ti(OiPr)_4$ (0.216 mL, 0.73 mmol) and $TiCl_4$ (0.158 mL, 1.45 mmol) were added to a solution of quinone **9a** (300 mg, 2.78 mmol) in CH_2Cl_2 (15 mL) followed by a solution of propenylbenzene **8c** (0.6 mL, 3.56 mmol) in CH_2Cl_2 (1 mL). The reaction was complete in 1 h and gave dihydrobenzofuran **10c** (534 mg, 67%) and cyclobutane **13c** (80 mg, 10%).

Data for **10c:** white prisms, mp 106.5−107 °C (40% EtOAc/hexanes); R_f (50% EtOAc/hexanes) 0.41; ^{1}H NMR (300 MHz) 1.33 (d, J = 7, 3H), 3.38 (dq, J = 7, 1H), 3.85 (s, 6H), 4.98 (s, 1H) 5.02 (d, J = 9, 1H), 6.6−6.7 (m, 3H), 6.8−6.9 (m, 3H), ^{13}C NMR (75 MHz) 17.3, 45.5, 55.8 (2 C), 92.8, 109.1, 109.4, 110.9, 111.0, 114.3, 118.9, 132.9, 133.1, 149.0, 149.1, 150.2, 152.8. Anal. Calcd for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.50; 6.45.

Data for **13c:** yellow needles, mp 110−113 °C (40% EtOAc/hexanes; R_f (50% EtOAc/hexanes) 0.36; ^{1}H NMR (300 MHz) 1.19 (d, J = 7, 3H), 3.05 (ddq, J = 9, 10, 7, 1H), 3.35 (dd, J = 9, 9, 1H), 3.43 (dd, J = 9, 9, 1H), 3.46 (dd, J = 9, 9, 1H), 3.88 (s, 3H), 3.91 (s, 3H), 6.8−6.9 (m, 5H); ^{13}C NMR (75 MHz) 17.4, 39.3, 43.8, 47.9 52.7, 55.9 (2 C), 109.7, 111.2, 118.2, 133.7, 140.8, 142.4, 148.2, 149.1, 197.6, 198.0; HRMS m/z 286.1208 (calcd for $C_{17}H_{18}O_4$, 286.1205).

Reaction of 9a with 8d. According to method B, $Ti(OiPr)_4$ (0.208 mL, 0.70 mmol) and $TiCl_4$ (0.229 mL, 2.10 mmol) were added to a solution of quinone **9a** (300 mg, 2.78 mmol) in CH_2Cl_2 (15 mL) followed by a solution of propenylbenzene **8d** (0.6 mL, 4.17 mmol) in CH_2Cl_2 (1 mL). The reaction was complete in 5 h and gave dihydrobenzofuran **10d** (155 mg, 23%) and a 1.4:1 mixture of **10d** and **13d**, respectively, (225 mg, 33%). Pure cyclobutane **13d** was obtained by preparative HPLC [10% iPrOH/hexanes, 2 mL/min, t_R (**13d**) = 8.44 min; t_R (**10d**) = 5.9 min].

Data for **10d**: a yellow oil; R_f (30% EtOAc/hexanes) 0.43; ^{1}H NMR (300 MHz) 1.28 (d, J = 7, 3H), 2.31 (s, 3H), 3.31 (dq, J = 9, 7, 1H), 5.06 (d, J = 9, 1H), 5.75 (br s, 1H), 6.5−6.7 (m, 2H), 7.14 (d, J = 7, 2H), 7.28 (d, J = 7, 2H); ^{13}C NMR (75 MHz) 17.5, 21.1, 45.6, 92.7, 109.5, 111.3, 114.6, 126.2, 129.3, 133.1, 137.5, 138.0, 150.0, 152.8; HRMS m/z 240.1150 (calcd for $C_{16}H_{16}O_2$, 240.1150).

Data for **13d**: R_f (30% EtOAc/hexanes) 0.41; ^{1}H NMR (300 MHz) 1.18 (d, J = 7, 3H), 2.34 (s, 3H), 3.03 (ddq, J = 10, 10, 7, 1H) 3.37 (dd, J = 9, 9, 1H), 3.42 (m, 1H), 6.82 (dd, J = 10, 10, 2H), 7.14 (s, 4H); ^{13}C NMR (75 MHz) 17.4, 21.0, 39.3, 43.9, 47.6, 52.6, 126.2, 129.4, 138.0, 140.8, 142.4, 197.5, 198.0; HRMS m/z 240.1156 (calcd for $C_{16}H_{16}O_2$, 240.1150).

Reaction of 9b with 8a. According to method B, $Ti(OiPr)_4$ (0.14 mL, 0.47 mmol) and $TiCl_4$ (0.08 mL, 0.73 mmol) were added to a solution of quinone **9b** (200 mg, 1.45 mmol) in CH_2Cl_2 (10 mL) followed by propenylbenzene **8a** (0.3 mL, 2.0 mmol). The reaction was complete in 5 h and gave dihydrobenzofuran **11a** (300 mg, 72%) and cyclobutane **14a** (50.3 mg, 12%).

Data for **11a**: a white solid, mp 120−121 °C (iPrOH/hexanes); R_f (50% EtOAc/hexanes) 0.57; ^{1}H NMR (300 MHz) 1.35 (d, J = 7, 3H), 3.46 (dq, J = 9, 8, 1H), 3.82 (s, 3H), 3.85 (s, 3H), 5.06 (d, J = 9, 1H), 5.31 (s, 1H, exchanges with D_2O) 6.48 (s, 1H), 6.73 (s, 1H), 6.90 (d, J = 8, 2H), 7.35 (d, J = 8, 2H); ^{13}C NMR (75 MHz) 18.1, 45.4, 55.3, 56.2, 92.8, 94.2, 109.4, 114.0, 123.0, 127.6, 132.8, 139.8, 146.2, 152.3, 159.6. Anal. Calcd for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.10; H, 6.47.

Data for **14a**: a yellow oil; R_f (50% EtOAc/hexanes) 0.31; ^{1}H NMR (300 MHz) 1.17 (d, J = 7, 3H), 3.00 (ddq, J = 10, 11, 7, 1H), 3.23−3.31 (m, 1H), 3.40−3.50 (m, 2H), 3.79 (s, 3H), 3.84 (s, 3H), 6.08 (s, 1H), 6.87 (d, J = 7, 2H), 7.21 (d, J = 7, 2H); ^{13}C NMR (75 MHz) 17.5, 39.5, 43.4, 48.0, 52.7, 55.3, 56.3, 113.0, 114.0, 127.4, 133.4, 158.7, 162.6, 192.6, 197.5; HRMS m/z 286.1199 (calcd for $C_{17}H_{18}O_4$, 286.1205).

Reaction of 9b with 8b. According to method B, $TiCl_4$ (0.032 mL, 0.29 mmol) was added to a solution of quinone **9b** (40 mg, 0.29 mmol) in CH_2Cl_2 (2 mL) followed by propenylbenzene **8b** (0.057 mL, 0.38 mmol). The reaction was complete in 45 min and gave dihydrobenzofuran **11b** (62 mg, 75%) as a tan solid, mp 112−114 °C (EtOH): R_f (30% EtOAc/hexanes) 0.37; ^{1}H NMR (300 MHz) 1.39 (d, J = 7, 3H), 3.33 (dq, J = 6, 7, 1H), 3.85 (s, 3H), 3.86 (s, 3H), 5.27 (s, 1H), 5.59 (d, J = 6, 1H), 6.53 (s, 1H), 6.70 (s, 1H), 6.8−7.0 (m, 2H), 7.2−7.4 (m, 2H); ^{13}C NMR (75 MHz) 20.1, 45.2, 55.3, 56.1, 87.1, 94.0, 109.7, 110.4, 120.5, 123.2, 126.1, 128.6, 130.0, 139.7, 146.1, 152.4, 156.5. Anal. Calcd for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.12; H, 6.33.

Reaction of 9b with 8c. According to method B, $Ti(OiPr)_4$ (0.084 mL, 0.28 mmol) and $TiCl_4$ (0.048 mL, 0.44 mmol) were added to a solution of quinone **9b** (120 mg, 0.87 mmol) in CH_2Cl_2 (10 mL) followed by a solution of propenylbenzene **8c** (0.16 mL, 0.96 mmol) in CH_2Cl_2 (1.5 mL). The reaction was complete in 5 h and gave dihydrobenzofuran **11c** (164 mg, 60%) and cyclobutane **14c** (62 mg, 23%).

Data for **11c**: white needles, mp 146−146.5 °C (EtOH); R_f (30% EtOAc/hexanes) 0.18; R_f (50% EtOAc/hexanes) 0.39; ^{1}H NMR (300 MHz) 1.35 (d, J = 7, 3H), 3.40 (dq, J = 9, 7, 1H), 3.86 (s, 3H), 3.88 (s, 3H), 3.89 (s, 3H), 5.03 (d, J = 9, 1H), 5.28 (s, exchanges with D_2O, 1H), 6.49 (s, 1H), 6.73 (s, 1H), 6.85−6.90 (m, 1H), 6.90−7.0 (m, 2H); ^{13}C NMR (300 MHz) 17.9, 45.4

56.0 (2 C), 56.2, 93.0, 94.2, 109.2, 109.5, 110.9, 118.9, 123.0, 133.1, 139.9, 146.2, 149.0, 149.2 152.3. Anal. Calcd for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37. Found: C, 68.39; H, 6.58.

Data for **14c**: white needles, mp 138–138.6 °C (50% EtOAc/hexanes); R_f (50% EtOAc/hexanes) 0.13; HPLC (10% iPrOH/hexanes, 2.5 mL/min) t_R 10.43 min; ^{1}H NMR (300 MHz) 1.21 (d, J = 7, 3H), 3.05 (ddq, J = 10, 10, 7, 1H), 3.34 (dd, J = 10, 10, 1H), 3.43 (dd, J = 10, 10, 1H), 3.50 (dd, J = 9, 9, 1H), 3.86 (s, 3H), 3.88 (s, 3H), 3.90 (s, 3H), 6.18 (s, 1H), 6.8–6.9 (m, 3H); ^{13}C NMR (75 MHz) 17.2, 38.4, 44.0, 47.8, 52.7, 55.9 (2 C), 56.3, 109.8, 111.2, 115.0, 118.2, 133.5, 148.2, 149.1, 161.8, 192.1, 197.0. Anal. Calcd for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37. Found: C, 68.46; H, 6.27.

Reaction of 9b with 8d. According to method A, an aliquot [2.3 mL, 1.45 mmol Ti(IV)] of a solution of $Ti(OiPr)_4$ (0.286 mL, 0.97 mmol) and $TiCl_4$ (0.205 mL, 1.87 mmol) in CH_2Cl_2 (4mL) was added to a solution of quinone **9b** (200 mg, 1.45 mmol) in CH_2Cl_2 (15 mL) followed by a solution of propenylbenzene **8d** (0.25 mL, 1.55 mmol) in CH_2Cl_2 (1 mL). The reaction was complete in 3 h and gave dihydrobenzofuran **11d** (140 mg, 36%) and cyclobutane **14d** (193 mg, 49%).

Data for **11d**: mp 122.5–124.5 °C (20% EtOAc/hexanes); R_f (30% EtOAc/hexanes) 0.40; ^{1}H NMR (300 MHz) 1.35 (d, J = 7, 3H), 2.37 (s, 3H), 3.37 (dq, J = 9, 7, 1H), 3.87 (s, 3H), 5.08 (d, J = 9, 1H), 5.23 (s, 1H), 6.50 (s, 1H), 6.73 (s, 1H), 7.20 (d, J = 8, 2H), 7.31 (d, J = 8, 2H); ^{13}C NMR (75 MHz) 18.4, 21.3, 45.6, 56.3, 92.9, 94.2, 109.5, 123.1, 126.1, 129.4, 138.0, 139.9, 146.3, 152.5 (one quaternary carbon was not observed). Anal. Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.69; H, 6.87.

Data for **14d**: mp 97–98.2 °C (30% EtOAc/hexanes); R_f (50% EtOAc/hexanes) 0.38; HPLC (4% iPrOH/hexanes, 2.0 mL/min) t_R 1.07 min; ^{1}H NMR (300 MHz) 1.19 (d, J = 7, 3H), 2.34 (s, 3H), 3.03 (ddq, J = 10, 10, 7, 1H), 3.36 (dd, J = 10, 10, 1H), 3.42 (dd, J = 10, 10, 1H), 3.53 (dd, J = 9, 9, 1H), 3.86 (s, 3H), 6.18 (s, 1H), 7.16 (s, 4H); ^{13}C NMR (75 MHz) 17.1, 21.0, 38.5, 44.1, 47.5, 52.7, 56.3, 114.9, 126.3, 129.4, 136.9, 137.8, 161.8, 192.0, 197.0. Anal. Calcd for $C_{17}C_{18}O_3$: C, 75.52; H, 6.72. Found: C, 75.58; H, 6.59.

In another experiment according to method C, $TiCl_4$ (0.11 mL, 1.0 mmol) was added to a solution of quinone **9b** (142 mg, 1.03 mmol) in CH_2Cl_2 (10 mL) followed by propenylbenzene **8d** (0.20 mL). The reaction was complete in 30 min and gave dihydrobenzofuran **11d** (175 mg, 60%) and cyclobutane **14d** (57 mg, 21%).

Reaction of 9b with 8e. According to method B, $Ti(OiPr)_4$ (0.214 mL, 0.72 mmol) and $TiCl_4$ (0.16 mL, 1.46 mmol) were added to a solution of quinone **9b** (300 mg, 2.17 mmol) in CH_2Cl_2 (20 mL) followed by a solution of propenylbenzene **8e** (0.375 mL, 2.55 mmol) in CH_2Cl_2 (1 mL). The reaction was complete in 2 h and gave dihydrobenzofuran **11e** (56 mg, 10%), bicyclo[3.2.1] adduct **16e** (69 mg, 13%), and cyclobutane **14e** (355 mg, 60%).

Data for **11e**: white plates, mp 130–131 °C (20% EtOAc/hexanes); R_f (30% EtOAc/hexanes) 0.59; ^{1}H NMR (300 MHz) 1.39 (d, J = 7, 3H), 2.41 (s, 3H), 3.42 (dq, J = 7, 7, 1H), 3.88 (s, 3H), 5.26 (s, 1H), 5.40 (d, J = 7, 1H), 6.50 (s, 1H), 6.72 (s, 1H), 7.2–7.3 (m, 3H), 7.3–7.4 (m, 1H); ^{13}C NMR (75 MHz) 19.3, 19.5, 44.9, 56.2, 90.0, 94.1, 109.6, 122.8, 126.1, 126.2, 127.8, 130.7, 135.3, 138.9, 139.9, 146.3, 152.4; HRMS m/z 270.1256 (calcd for $C_{17}H_{18}O_3$, 270.1255).

Data for **16e**: white needles, mp 171–172 °C (20% EtOAc/hexanes); R_f (30% EtOAc/hexanes) 0.55; ^{1}H NMR (300 MHz) 1.25 (d, J = 7, 3H), 2.39 (s, 3H), 2.72 (dq, J = 5, 7, 1H), 3.08 (dd, J = 2, 8, 1H), 3.46 (dd, J = 6, 6, 1H), 3.86 (dd, J = 2, 7, 1H), 5.86 (s, 1H), 6.74 (d, J = 8, 1H), 6.85–6.95 (m, 1H), 7.1–7.2 (m, 3H); ^{13}C NMR (75 MHz) 20.0, 21.6, 41.6, 45.1, 54.3, 67.1, 119.1, 126.5, 126.7, 127.4, 130.8, 136.1, 137.1, 150.1, 191.6, 199.6; HRMS m/z 256.1101 (calcd for $C_{16}H_{16}O_3$, 256.1099).

Data **14e**: white needles, mp 150–151 °C (30% EtOAc/hexanes); R_f (30% EtOAc/hexanes) 0.29; ^{1}H NMR (300 MHz) 1.14 (d, J = 7, 3H), 2.22 (s, 3H), 3.08 (m, 1H), 3.4–3.5 (m, 2H), 3.6–3.7 (m, 1H), 3.85 (s, 3H), 6.19 (s, 1H), 7.1–7.2 (m, 2H), 7.2–7.3 (m, 1H), 7.40 (d, J = 7, 1H); ^{13}C NMR (75 MHz) 17.0 (q), 19.8 (q), 38.7 (d), 43.8 (d), 47.9 (d), 49.7 (d), 56.3 (q), 114.8 (d), 125.4 (d), 126.5 (d), 127.0 (d), 130.4 (d), 136.1 (s), 138.3 (s), 162.0 (s), 192.2 (s), 197.0 (s). Anal. Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.58; H, 6.77.

In another experiment according to method C, $TiCl_4$ (0.11 mL, 1.0 mmol) was added to a solution of quinone **9b** (136 mg, 0.99 mmol) in CH_2Cl_2 (10 mL) followed by propenylbenzene **8e** (0.25 mL, 1.45 mmol). The reaction was complete in 1 h and gave dihydrobenzofuran **11e** (73 mg, 27%) and cyclobutane **14e** (100 mg, 38%).

Reaction of 9b with 8f. According to method B, $Ti(OiPr)_4$ (0.144 mL, 0.487 mmol) and $TiCl_4$(0.105 mL, 0.96 mmol) were added to a solution of quinone **9b** (200 mg, 1.45 mmol) in CH_2Cl_2 (10 mL) at −78 °C followed by a solution of propenylbenzene **8f** (0.30 mL, 2.3 mmol). The reaction was complete in 30 min and gave dihydrobenzofuran **11f** (95 mg, 25%) and cyclobutane **14f** (100 mg, 27%).

Data for **11f**: white needles, mp 120–121 °C (EtOAc/hexanes); R_f (30% EtOAc/hexanes) 0.36; ^{1}H NMR (300 MHz)[22b] 1.37 (d, J = 7, 3H), 3.40 (dq, J = 7, 9, 1H), 3.87 (s, 3H), 5.11 (d, J = 9, 1H), 5.30 (s, 1H), 6.50 (s, 1H), 6.73 (s, 1H), 7.25–7.45 (m, 5H); ^{13}C NMR (75 MHz) (APT) 18.6 (q), 45.9 (d), 56.4 (q), 93.0 (d), 94.4 (d), 109.7 (d), 123.0 (s), 126.2 (d), 128.4 (d), 128.8 (d), 140.1 (s), 141.2 (s), 146.4 (s), 152.6 (s); HRMS m/z 256.1088 (calcd for $C_{16}H_{16}O_3$, 256.1099).

Data for **14f**: white needles, mp 117–118 °C (iPrOH); R_f (30% EtOAc/hexanes) 0.11; HPLC (4% iPrOH/hexanes, 2.5 mL/min) t_R 4.2 min; ^{1}H NMR (300 MHz) 1.20 (d, J = 7, 3H), 3.04 (ddq, J = 10, 10, 7, 1H), 3.40 (dd, J = 10, 10, 1H), 3.43 (dd, J = 10, 10, 1H), 3.56 (dd, J = 10, 10, 1H), 3.84 (s, 3H), 6.18 (s, 1H), 7.2–7.4 (m, 5H); ^{13}C NMR (75 MHz, SFORD) 17.2 (q), 38.3 (d), 44.0 (d), 47.2 (d), 52.7 (d), 56.3 (q), 114.8 (d), 126.3 (d), 127.1 (d), 128.6 (d), 140.8 (s), 161.8 (s), 192.0 (s), 196.9 (s). Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.72; H, 6.40.

In another experiment according to method C, $TiCl_4$ (0.13 mL, 1.18 mmol) was added to a solution of quinone **9b** (139 mg, 1.01 mmol) in CH_2Cl_2 (20 mL) at −78 °C followed by propenylbenzene **8f** (0.21 mL, 1.6 mmol). The reaction was complete in 1 h and gave dihydrobenzofuran **11f** (106 mg, 41%) and cyclobutane **14f** (111 mg, 43%).

In a third experiment according to method C, a solution of $TiCl_4$ (0.11 mL, 1.00 mmol) in CH_2Cl_2 (4 mL) was added to a solution of quinone **9b** (141 mg, 1.02 mmol) in CH_2Cl_2 (15 mL) cooled to −94 °C followed by propenylbenzene **8f** (0.180 mL, 1.39 mmol). The reaction was complete in 1 h and gave dihydrobenzofuran **11f** (73 mg, 28%) and cyclobutane **14f** (106 mg, 40%).

Reaction of 9b with 8g. According to method A, an aliquot [2.1 mL, 0.72 mmol Ti(IV)] of a solution of $Ti(OiPr)_4$ (0.107 mL, 0.36 mmol) and $TiCl_4$ (0.118 mL, 1.08 mmol) in CH_2Cl_2 (4mL) was added to a solution of quinone **9b** (100 mg, 0.72 mmol) in CH_2Cl_2 (5mL) followed by a solution of propenylbenzene **8g** (0.125 mL, 1.08 mmol) in CH_2Cl_2 (1 mL). The reaction was complete in 30 min and gave dihydrobenzofuran **11g** (58 mg, 28%) and cyclobutane **14g** (51 mg, 24%).

Data for **11g**: white needles, mp 100–101 °C (20% EtOAc/hexanes); R_f (50% EtOAc/hexanes) 0.60; ^{1}H NMR (300 MHz) 1.37 (d, J = 7, 3H), 3.33 (dq, J = 8, 7, 1H), 3.87 (s, 3H), 5.08 (d, J = 8, 1H), 5.29 (s, 1H, exchanges with D_2O), 6.49 (s, 1H), 6.72 (s, 1H), 7.35 (s, 4H); ^{13}C NMR (75 MHz) 18.4, 45.8, 56.2, 91.9, 94.2, 109.5, 122.5, 127.3, 128.7, 133.9, 139.6, 140.0, 146.3, 152.2. Anal. Calcd for $C_{16}H_{15}O_3Cl$: C, 66.10; H, 5.20. Found: C, 66.29; H, 5.18.

Data for **14g**: white needles, mp 140.5–141.2 °C (iPrOH); R_f (50% EtOAc/hexanes) 0.26; HPLC (4% iPrOH/hexanes, 2 mL/min) t_R 17 min; ^{1}H NMR (300 MHz) 1.13 (d, J = 7, 3H), 2.96 (ddq, J = 10, 10, 7, 1H), 3.29 (dd, J = 10, 10, 1H), 3.35 (dd, J = 10, 10, 1H), 3.46 (dd, J = 10, 10, 1H), 3.79 (s, 3H), 6.12 (s, 1H), 7.12 (d, J = 8, 2H), 7.21 (d, J = 8, 2H); ^{13}C NMR (75 MHz) 17.2, 38.5, 44.0, 47.2, 52.1, 56.4, 115.0, 127.8, 128.8, 133.0, 139.3, 161.7, 191.8, 196.6. Anal. Calcd for $C_{16}H_{15}O_3$-Cl: C, 66.10; H, 5.20. Found: C, 66.00; H, 5.25.

In another experiment according to method B, $TiCl_4$ (0.23 mL, 2.1 mmol) was added to a solution of quinone **9b** (300 mg, 2.17 mmol) in CH_2Cl_2 (15 mL) followed by a solution of propenylbenzene **8g** (0.4 mL, 2.9 mmol) in CH_2Cl_2 (1 mL). The reaction was complete in 20 min and gave dihydrobenzofuran **11g** (198 mg, 31%) and cyclobutane **14g** (129 mg, 20%).

Reaction of 9b with 8h. According to method E, $TiCl_4$ (0.053 mL, 0.483 mmol) was added to a solution of $Ti(OiPr)_4$ (0.072 mL, 0.244 mmol) in CH_2Cl_2 (3 mL) at 0 °C and the mixture cooled to −78 °C. A solution of quinone **9b** (101 mg, 0.73 mmol) in CH_2Cl_2 (3 mL) was added followed by propenylbenzene **8h** (0.20 mL, 1.38 mmol). The reaction was complete in 0.5 h and gave dihydrobenzofuran **11h** (123 mg, 56%) and cyclobutane **14h** (64 mg, 29%) .

Data for **11h**: a white solid, mp 134−135 °C (EtOAc/hexanes); R_f (50% EtOAc/hexanes) 0.48; ^1H NMR (500 MHz) 6.91 (d, J = 1.6, 1H), 6.86 (dd, J = 1.6, 8.0, 1H), 6.79 (d, J = 7.9, 1H), 6.71 (s, 1H), 6.47 (s, 1H), 5.95 (s, 2H), 5.29−5.28 (m, 1H), 5.01 (d, J = 8.6, 1H), 3.85 (s, 3H), 3.33 (dq, J = 6.8, 8.6, 1H), 1.34 (d, J = 6.8, 3H); ^{13}C NMR (125 MHz) 152.2, 147.9, 147.5, 146.2, 139.9, 134.7, 122.8, 119.8, 109.4, 108.1, 106.5, 101.1, 94.1, 92.8, 56.2, 45.5, 18.2; HRMS m/z 300.0999 (calcd for $C_{17}H_{16}O_5$, 300.0998).

Data for **14h**: a white solid, mp 144−146 °C (EtOAc/hexanes); R_f (50% EtOAc/hexanes) 0.24; ^1H NMR (500 MHz) 6.47 (d, J = 6.3, 1H), 6.73 (s, 1H), 6.68−6.66 (m, 1H), 6.14 (s, 1H), 5.93 (s, 2H), 3.83 (s, 3H), 3.45 (dd, J = 8.0, 8.6, 1H), 3.38 (dd, J = 8.1, 10.4, 1H), 3.27 (dd, J = 8.6, 8.6, 1H), 2.94 (m, 1H), 1.16 (d, J = 7.0, 3H); ^{13}C NMR (125 MHz) 196.9, 191.8, 161.8, 148.0, 146.8, 134.6, 119.7, 114.9, 108.3, 106.8, 101.1, 56.3, 52.9, 47.8, 43.9, 38.7, 17.0; HRMS m/z (M + 1) 301.1077 [calcd for $C_{17}H_{17}O_5$ (M + 1), 301.1076].

Reaction of 9c with 8a. According to method B, $Ti(OiPr)_4$ (0.025 mL, 0.085 mmol) and $TiCl_4$ (0.019 mL, 0.17 mmol) were added to a solution of quinone **9c** (40 mg, 0.26 mmol) in CH_2Cl_2 (5 mL) followed by propenylbenzene **8a** (0.10 mL, 0.67 mmol). The reaction was complete in 2 h and gave dihydrobenzofuran **12a** (59 mg, 75%) as a tan solid which was recrystallized from 30% EtOAc/hexanes to give colorless needles, mp 129−130 °C: R_f (30% EtOAc/hexanes) 0.45; ^1H NMR (300 MHz) 1.39 (d, J = 7, 3H), 2.19 (s, 3H), 3.36 (dq, J = 5, 7, 1H), 3.78 (s, 3H), 3.83 (s, 3H), 5.11 (d, J = 5, 1H), 5.31 (s, 1H), 6.36 (s, 1H), 6.85 (d, J = 9, 2H), 7.25 (d, J = 9, 2H); ^{13}C NMR (75 MHz) 11.9, 20.0, 45.2, 55.2, 56.1, 91.4, 91.5, 113.9, 120.2, 121.5, 126.9, 134.2, 137.8, 146.0, 151.6, 159.3. Anal. Calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 72.19; H, 6.77.

Reaction of 9c with 8c. According to method B, $Ti(OiPr)_4$ (0.196 mL, 0.66 mmol) and $TiCl_4$ (0.072 mL, 0.66 mmol) were added to a solution of quinone **9c** (200 mg, 1.32 mmol) in CH_2Cl_2 (10 mL) followed by a solution of propenylbenzene **8c** (0.4 mL, 2.37 mmol) in CH_2Cl_2 (1 mL). The reaction was complete in 30 min and gave dihydrobenzofuran **12c** (394 mg, 90%). Recrystallization from 30% EtOAc/hexanes furnished a colorless solid, mp 157−158.5 °C: R_f (30% EtOAc/hexanes) 0.28; ^1H NMR (300 MHz) 1.43 (d, J = 7, 3H), 2.21 (s, 3H), 3.42 (dq, J = 6, 7, 1H), 3.86 (s, 3H), 3.87 (s, 3H), 3.88 (s, 3H), 5.11 (d, J = 5, 1H), 5.33 (broad s, 1H), 6.39 (s, 1H), 6.8−6.9 (m, 3H); ^{13}C NMR (75 MHz) 12.0, 19.9, 45.3, 55.8, 55.9 (2 C), 56.2, 91.5, 91.8, 108.8, 111.0, 118.1, 120.2, 121.5, 134.5, 137.9, 146.0, 148.8, 149.2, 151.6. Anal. Calcd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 69.08; H, 6.81.

Reaction of 9c with 8d. According to method B, $Ti(OiPr)_4$ (0.196 mL, 0.66 mmol) and $TiCl_4$ (0.143 mL, 1.30 mmol) were added to a solution of quinone **9c** (300 mg, 1.97 mmol) in CH_2Cl_2 (15 mL) followed by a solution of propenylbenzene **8d** (0.45 mL, 2.8 mmol) in CH_2Cl_2 (1 mL). The reaction was complete in 5.5 h and gave dihydrobenzofuran **12d** (50 mg, 9%), bicyclic adduct **17d** (100 mg, 19%), starting quinone **9c** (62 mg, 21%), and cyclobutane **15d** (184 mg, 33%).

Data for **12d**: colorless needles, mp 111−112 °C (20% EtOAc/hexanes); R_f (50% EtOAc/hexanes) 0.69; ^1H NMR (300 MHz) 1.43 (d, J = 7, 3H), 2.19 (s, 3H), 2.34 (s, 3H), 3.38 (dq, J = 5, 7, 1H), 3.86 (s, 3H), 5.16 (d, J = 5, 1H), 5.30 (s, 1H), 6.40 (s, 1H), 7.14 (d, J = 7, 2H), 7.23 (d, J = 7, 2H); ^{13}C NMR (75 MHz) 12.0, 20.2, 21.1, 45.4, 56.2, 91.5, 120.2, 121.5, 125.4, 129.0, 129.2, 137.6, 137.9, 139.3, 146.0, 151.7. Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.37; H, 7.14.

Data for **17d**: a white solid, mp 140−141 °C (10% EtOAc/hexanes); R_f (30% EtOAc/hexanes) 0.52; ^1H NMR (300 MHz) 1.26 (d, J = 7, 3H), 2.20 (s, 3H), 2.30 (s, 3H), 2.47 (dq, J = 6, 7, 1H), 2.86 (d, J = 2, 1 H), 3.18 (dd, J = 6, 7, 1H), 3.76 (d, J = 2, 7, 1H), 5.88 (s, 1H), 6.91 (d, J = 8, 2H), 7.10 (d, J = 8, 2H); ^{13}C NMR (75 MHz) 16.3, 20.9, 21.6, 42.1, 49.9, 60.8, 69.0, 128.1, 129.4, 133.6, 134.7, 137.2, 145.9, 190.5, 199.4. Anal. Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.61; H, 6.76.

Data for **15d**: colorless needles, mp 106−107 °C (20% EtOAc/hexanes); R_f (50% EtOAc/hexanes) 0.43; ^1H NMR (300 MHz) 1.08 (s, 3H), 1.18 (d, J = 7, 3H), 2.34 (s, 3H), 3.01 (d, J = 11, 1H), 3.32 (ddq, J = 10, 11, 7, 1H), 3.50 (d, J = 10, 1H), 6.19 (s, 1H), 6.19 (s, 1H), 7.00 (d, J = 8, 2H), 7.15 (d, J = 8, 2H); ^{13}C NMR (75 MHz) 16.7, 17.1, 32.4, 47.8, 50.9, 53.6, 56.4, 114.3, 127.3, 129.0, 133.8, 136.7, 161.7, 194.9, 197.1. Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.28; H, 7.33.

In another experiment according to method C, $TiCl_4$ (0.11 mL, 1.0 mmol) was added to a solution of quinone **9c** (150 mg, 0.99 mmol) in CH_2Cl_2 (10 mL) followed by propenylbenzene **8d** (0.20 mL). The reaction was complete in 4 h and gave dihydrobenzofuran **12d** (202 mg, 72%).

In a third experiment according to method A, a solution of $Ti(OiPr)_4$ (0.147 mL, 0.50 mmol) and $TiCl_4$ (0.16 mL, 1.46 mmol) in CH_2Cl_2 (5 mL) was added slowly to a solution of quinone **9c** (300 mg, 1.97 mmol) in CH_2Cl_2 (25 mL) at −90 °C followed by a solution of propenylbenzene **8d** (0.45 mL, 3.1 mmol) in CH_2Cl_2 (1 mL). The reaction was complete in 2 h and gave dihydrobenzofuran **12d** (69 mg, 12%), a 1.3:1 mixture of **12d** and **17d** (35 mg, 4% **12d**, 3% **17d**), and cyclobutane **15d** (302 mg, 54%).

Reaction of 9c with 8e. According to method B, $Ti(OiPr)_4$ (0.197 mL, 0.66 mmol) and $TiCl_4$ (0.144 mL, 1.31 mmol) were added to a solution of quinone **9c** (300 mg, 1.97 mmol) in CH_2Cl_2 (20 mL) followed by a solution of propenylbenzene **8e** (0.45 mL, 3.13 mmol) in CH_2Cl_2 (1mL). The reaction was complete in 2 h and gave dihydrobenzofuran **12e** (14 mg, 2%), bicyclic adduct **17e** (236 mg, 44%), and cyclobutane **15e** (180 mg, 32%)

Data for **12e**: colorless solid, mp 147−148 °C (20% EtOAc/hexanes); R_f (30% EtOAc/hexanes) 0.53; ^1H NMR (300 MHz) 1.45 (d, J = 7, 3H), 2.16 (s, 3H), 2.4 (s, 3H), 3.32 (dq, J = 4, 7, 1H), 3.88 (s, 3H), 5.28 (s, 1H), 5.45 (d, J = 4, 1H), 6.44 (s, 1H), 7.1−7.3 (m, 3H); ^{13}C NMR (75 MHz) 12.0, 19.6, 20.6, 44.5, 56.2, 88.8, 91.4, 120.2, 121.4, 125.0, 126.1, 127.4, 130.6, 134.4, 138.0, 140.3, 146.1, 151.7. Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.24; H, 7.11.

Data for **17e**: colorless needles, mp 139−140 °C (20% EtOAc/hexanes); R_f (30% EtOAc/hexanes) 0.40; ^1H NMR (300 MHz) 1.22 (d, J = 7, 3H), 2.18 (s, 3H), 2.36 (s, 3H), 2.61 (dq, J = 6, 7, 1H), 2.86 (d, J = 2, 1H), 3.43 (dd, J = 6, 6, 1H), 3.76 (dd, J = 2, 7, 1H), 5.96 (s, 1H), 6.7−6.8 (m, 1H), 7.1−7.2 (m, 3H); ^{13}C NMR (75 MHz) (APT) 16.2 (q), 19.9 (q), 21.8 (q), 41.2 (d), 45.9 (d), 60.8 (d), 66.7 (d), 126.3 (d), 126.5 (d), 127.2 (d), 130.5 (d), 132.8 (s), 136.1 (s), 137.0 (s), 146.1 (s), 190.2 (s), 199.7 (s). Anal. Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.46; H, 6.70.

Data for **15e**: colorless needles, mp 161−162 °C (30% EtOAc/hexanes); R_f (30% EtOAc/hexanes) 0.16; ^1H NMR (300 MHz) 1.04 (s, 3H), 1.10 (d, J = 7, 3H), 2.11 (s, 3H), 3.02 (d, J = 11, 1H), 3.45 (ddq, J = 10, 11, 7, 1H), 3.83 (d, J = 10, 1H), 3.88 (s, 3H), 6.19 (s, 1H), 7.1−7.3 (m, 4H); ^{13}C NMR (75 MMHz) (APT) 16.4 (q), 17.0 (q), 19.7 (q), 32.3 (d), 48.4 (s), 51.1 (d), 51.3 (d), 56.4 (q), 113.8 (d), 125.6 (d), 126.9 (d), 127.1 (d), 130.5 (d), 134.4 (s), 137.4 (s), 162.2 (s), 196.0 (s), 196.8 (s). Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.33; H, 7.18.

In another experiment according to method C, $TiCl_4$ (0.11 mL, 1.0 mmol) was added to a solution of quinone **9c** (155 mg, 1.02 mmol) in CH_2Cl_2 (10 mL) followed by propenylbenzene **8e** (0.20 mL). The reaction was complete in 4 h and gave dihydrobenzofuran, **12e** (121 mg, 42%), bicyclic adduct **17e** (102 mg, 37%), and cyclobutane **15e** (19 mg, 7%).

Reaction of 9c with 8f. According to method B, $Ti(OiPr)_4$ (0.144 mL, 0.49 mmol) and $TiCl_4$ (0.165 mL, 1.5 mmol) were added to a solution of quinone **9c** (300 mg, 1.97 mmol) in CH_2Cl_2 (15 mL) followed by a solution of propenylbenzene **8f** (0.6 mL, 4.6 mmol) in CH_2Cl_2 (1 mL). The reaction was complete in 8.5 h and gave dihydrobenzofuran **12f** (47.9 mg, 10%), bicyclic adduct **17f** (206 mg, 41%), starting quinone **9c** (96 mg, 32%), and cyclobutane **15f** (90.4 mg, 18%).

Data for **12f**: a white solid, mp 168–169 °C (hexanes); R_f (30% EtOAc/hexanes) 0.46; ^{1}H NMR (300 MHz) 1.43 (d, J = 7, 3H), 2.18 (s, 3H), 3.39 (dq, J = 5, 7, 1H), 3.86 (s, 3H), 5.19 (d, J = 5, 1H), 5.30 (s, 1H), 6.40 (s, 1H), 7.33 (s, 5H); ^{13}C NMR (75 MHz) 12.0, 20.3, 45.5, 56.2, 91.5 (2 C), 120.2, 121.3, 125.4, 127.8, 128.5, 128.6, 137.9, 142.3, 146.0, 151.7; HRMS m/z 270.1251 (calcd for $C_{17}H_{18}O_3$, 270.1256).

Data for **17f**: white prisms, mp 113–114 °C (10% EtOAc/hexanes); R_f (50% EtOAc/hexanes) 0.64; R_f (30% EtOAc/hexane) 0.45; ^{1}H NMR (300 MHz) 1.27 (d, J = 7, 3H), 2.21 (s, 3H), 2.50 (dq, J = 6, 7, 1H), 2.87 (d, J = 2, 1H), 3.21 (dd, J = 7, 6, 1H), 3.77 (dd, J = 2, 7, 1H), 5.92 (s, 1H), 7.0–7.1 (m, 2H), 7.2–7.4 (m, 3H); ^{13}C NMR (75 MHz) (SFORD) 16.4 (q), 21.7 (q), 42.0 (d), 50.3 (d), 60.9 (d), 68.9 (d), 127.6 (d) 128.2 (d), 128.8 (d), 133.5 (s), 137.8 (s), 146.0 (s), 190.4 (s), 199.2 (s). Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.75; H, 6.54.

Data for **15f**: white needles, mp 130–131 °C (30% EtOAc/hexanes); R_f (30% EtOAc/hexanes) 0.17; ^{1}H NMR (300 MHz) 1.07 (s, 3H), 1.17 (d, J = 7, 3H), 3.01 (d, J = 11, 1H), 3.34 (ddq, J = 10, 11, 7, 1H), 3.52 (d, J = 10, 1H), 3.87 (s, 3H), 6.18 (s, 1H), 7.09 (d, J = 7, 2H), 7.24–7.40 (m, 3H); ^{13}C NMR (75 MHz) 16.7, 17.2, 32.3, 47.8, 50.9, 53.7, 56.4, 114.3, 127.1, 127.3, 128.4, 137.0, 161.6, 194.9, 197.0; HRMS m/z 270.1244 (calcd for $C_{17}H_{18}O_3$, 270.1256).

Reaction of 9c with 8g. According to method A, a solution of Ti(OiPr)$_4$ (0.146 mL, 0.49 mmol) and $TiCl_4$ (0.160 mL, 1.46 mmol) in CH_2Cl_2 (5 mL) was added to a solution of quinone **9c** (300 mg, 1.97 mmol) in CH_2Cl_2 (20 mL) followed by a solution of propenylbenzene **8g** (0.45 mL, 3.23 mmol) in CH_2Cl_2 (1 mL). The reaction was stirred at −55 °C and was complete in 22 h. Chromatography gave dihydrobenzofuran **12g** (37 mg, 6%), bicyclic adduct **17g** (150 mg, 25%), starting quinone **9c** (84 mg, 28%), and cyclobutane **15b** (58 mg, 10%).

Data for **12g**: colorless plates, mp 86–89 °C (hexanes); R_f (30% EtOAc/hexanes) 0.47; ^{1}H NMR (300 MHz) 1.42 (d, J = 7, 3H), 2.17 (s, 3H), 3.32 (dq, J = 5, 7, 1H), 3.86 (s, 3H), 5.15 (d, J = 5, 1H), 5.29 (s, 1H), 6.39 (s, 1H), 7.2–7.35 (m, 4H); ^{13}C NMR (75 MHz) 12.0, 20.3, 45.6, 56.2, 90.7, 91.6, 120.3, 121.1, 126.8, 128.7, 133.6, 138.1, 140.9, 146.1, 151.5; HRMS m/z 304.0874 (calcd for $C_{17}H_{17}O_3Cl$, 304.0866).

Data for **17g**: colorless needles, mp 128–129 °C (20% EtOAc/hexanes); R_f (30% EtOAc/hexanes) 0.44; ^{1}H NMR (300 MHz) 1.27 (d, J = 7, 3H), 2.20 (s, 3H), 2.43 (dq, J = 6, 7, 1H), 2.87 (d J = 2, 1H), 3.18 (dd, J = 6, 1H), 3.76 (dd, J = 2, 7, 1H), 5.89 (s, 1H), 6.96 (d, J = 8, 2H), 7.27 (d, J = 8, 2H); ^{13}C NMR (75 MHz) 16.4, 21.7, 42.3, 49.6, 60.8, 68.7, 129.0, 129.5, 133.6, 133.9, 136.3, 146.0, 190.2, 198.8. Anal. Calcd for $C_{16}H_{15}O_3Cl$: C, 66.10; H, 5.20. Found: C, 66.15; H, 5.34.

Data for **15g**: a yellow oil; R_f (30% EtOAc/hexanes) 0.30; ^{1}H NMR (300 MHz) 1.08 (s, 3H), 1.17 (d, J = 7, 3H), 3.02 (d, J = 11, 1H), 3.28 (ddq, J = 10, 11, 7, 1H), 3.48 (d, J = 10, 1H), 3.88 (s, 3H), 6.19 (s, 1H), 7.04 (d, J = 8, 2H), 7.31 (d, J = 8, 2H); ^{13}C NMR (75 MHz) 17.0, 17.4, 32.6, 47.7, 50.9, 53.2, 56.5, 114.5, 128.6, 128.8, 133.1, 135.6, 161.6, 194.8, 196.7; HRMS m/z 304.0868 (calcd for $C_{17}H_{17}O_3Cl$, 304.0866).

Reactions of 9b with Indene. According to method B, $TiCl_4$ (0.158 mL, 1.45 mmol) was added to a solution of quinone **9b** (200 mg, 1.45 mmol) in CH_2Cl_2 (15 mL). The reaction was complete in 30 min and gave dihydrobenzofuran **18** (198 mg, 54%) as a white solid, mp 164–165 °C; R_f (50% EtOAc/hexanes) 0.57; ^{1}H NMR (300 MHz) 3.15 (d, J = 16, 1H), 3.46 (dd, J = 8, 16, 1H), 3.78 (s, 3H), 4.25 (dd, J = 8, 8, 1H), 5.20 (s, 1H, exchanges with D_2O), 6.16 (d, J = 8, 1H), 6.36 (s, 1H), 6.80 (s, 1H), 7.2–7.3 (m, 3H), 7.5–7.6 (m, 1H); ^{13}C NMR (75 MHz) 39.0, 45.0, 56.1, 90.9, 94.3, 110.1, 121.6, 125.2, 125.8, 127.2, 129.2, 139.9, 141.0, 142.3, 146.6, 152.1. Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.63; H, 5.57.

In another experiment according to method A, an aliquot [2.3 mL, 1.4 mmol Ti(IV)] of a solution of Ti(OiPr)$_4$ (0.285 mL, 0.96 mmol) and $TiCl_4$ (0.210 mL, 1.92 mmol) in CH_2Cl_2 (4 mL) was added to a solution of quinone **9b** (200 mg, 1.45 mmol) in CH_2Cl_2 (10 mL) followed by a solution of indene (0.26 mL, 2.2 mmol) in CH_2Cl_2 (1 mL). The reaction was complete in 30 min and gave cyclobutane **19** (312 mg, 85%) as white needles, mp 144.5–145.5 °C (iPrOH): R_f (50% EtOAc/hexanes) 0.27; ^{1}H NMR (300 MHz) 3.1–3.4 (m, 5H), 3.87 (s, 3H), 3.9–4.1 (m, 2H), 6.13 (s, 1H), 7.3–7.4 (m, 3H), 7.4–7.5 (m, 1H); ^{13}C NMR (75 MHz) 39.3, 43.6, 48.3, 49.6. 49.8, 56.4, 113.9, 125.3, 125.6, 127.5, 127.6, 142.6, 143.5, 162.8, 193.3, 197.7. Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.56; H, 5.44.

Reaction of 9c with Indene. According to method A, a solution of Ti(OiPr)$_4$ (0.327 mL, 1.11 mmol) and $TiCl_4$ (0.24 mL, 2.19 mmol) in CH_2Cl_2 (5 mL) was added slowly to a solution of quinone **9c** (500 mg, 3.29 mmol) in CH_2Cl_2 (35 mL) followed by a solution of indene (0.575 mL, 4.9 mmol) in CH_2Cl_2 (1 mL). The reaction was complete in 3 h and gave dihydrobenzofuran **20** (82 mg, 9%), bicyclic adduct **22** (300 mg, 36%), starting quinone **9c** (96 mg, 19%), and cyclobutane **21** (166 mg, 19%).

Data for **20**: mp 194–195 °C (10% EtOAc/hexanes); R_f (30% EtOAc/hexanes) 0.62; ^{1}H NMR (300 MHz) 2.26 (s, 3H), 3.16 (dd, J = 15, 3, 1H), 3.53 (dd, J = 9, 15, 1H), 3.78 (s, 1H), 4.32 (ddd, J = 3, 7, 7, 1H), 5.27 (s, 1H), 6.18 (d, J = 7, 1H), 6.28 (s, 1H), 7.2–7.32 (m, 3H), 7.54–7.6 (m, 1H); ^{13}C NMR (75 MHz) 12.4, 38.9, 44.4, 56.1, 91.0, 91.6, 119.9, 121.1, 125.2, 125.8, 127.1, 129.2, 137.8, 140.8, 142.7, 146.1, 151.3; HRMS m/z 268.1092 (calcd for $C_{17}H_{16}O_3$, 268.1099).

Data for **22**: mp 183.5–185 °C (10% EtOAc/hexanes); R_f (30% EtOAc/hexanes) 0.56; ^{1}H NMR (300 MHz) 2.09 (s, 3H), 2.80 (dd, J = 3, 17, 1H), 3.22 (dd, J = 10, 17, 1H), 3.32 (dd, J = 2, 8, 1H), 3.36 (dddd, J = 3, 8, 9, 10, 1H), 3.96 (dd, J = 2, 8, 1H), 4.26 (dd, J = 9, 9, 1H), 5.57 (s, 1H), 7.1 (s, 4H); ^{13}C NMR (75 MHz) 18.5, 33.7, 38.7, 46.8, 57.3, 64.4, 124.4, 125.8, 126.9, 127.6, 129.1, 139.1, 143.9, 147.4, 190.3, 199.3. Anal. Calcd for $C_{16}H_{14}O_3$: C 75.57; H 5.55. Found: C 75.43; H 5.54.

Data for **21**: mp 142–143 °C (30% EtOAc/hexanes); R_f (30% EtOAc/hexanes) 0.30; ^{1}H NMR (300 MHz) 1.08 (s, 3H), 2.74 (d, J = 6, 1H), 3.05–3.25 (m, 3H), 3.86 (s, 3H), 3.96 (d, J = 6, 1H), 6.09 (s, 1H), 7.25–7.4 (m, 4H); ^{13}C NMR (75 MHz) 21.8, 39.2, 41.1, 51.0, 52.2, 56.0, 56.4, 113.3, 125.9, 126.8, 127.1, 127.9, 139.9, 143.9, 162.0, 197.6, 198.3. Anal Calcd for $C_{17}H_{16}O_3$: C, 76.10, H, 6.01. Found: C, 76.22; H, 5.64.

Reaction of 9b with 23c. According to method A, an aliquot [2.2 mL, 1.45 mmol Ti(IV)] of a soution of Ti(OiPr)$_4$ (0.476 mL, 1.61 mmol) and $TiCl_4$ (0.158 mL, 1.44 mmol) in CH_2Cl_2 (4 mL) was added to a solution of quinone **9b** (100 mg, 0.72 mmol) in CH_2Cl_2 (5 mL) followed by a solution of propenylbenzene **23c** (0.13 mL, 0.94 mmol) in CH_2Cl_2 (1 mL). The reaction was complete in 1.5 h and gave dihydrobenzofuran **11c** (51 mg, 22%) as white needles, mp 146–146.6 °C (30% EtOAc/hexanes), and cyclobutane **24c** (90.8 mg, 39%).

Data for **24c**: white needles, mp 189–190 °C (EtOAc, CH_2Cl_2, and hexanes); R_f (50% EtOAc/hexanes) 0.10; HPLC t_R (10% iPrOH/hexanes, 2.5 mL/min) 15.9 min; ^{1}H NMR (300 MHz) 1.37 (d, J = 6, 3H), 3.03 (ddq, J = 11, 11, 6, 1H), 3.06 (dd, J = 11, 11, 1H), 3.62 (dd, J = 11, 11, 1H), 3.76 (s, 3H); 3.76 (dd, J = 11, 11, 1H), 3.85 (s, 3H), 3.86 (s, 3H), 6.05 (s, 1H), 6.6–6.65 (m, 2H), 6.78–6.82 (m, 1H); ^{13}C NMR (75 MHz) 20.3, 42.1, 45.7, 47.6, 50.0, 55.7 (2 C), 56.2, 110.9, 111.7, 112.9, 119.8, 129.9, 148.1, 148.7, 163.0, 191.4, 197.7. Anal. Calcd for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37. Found: C, 68.08; H, 6.20.

Reaction of 9b with 23d. According to method A, a solution of Ti(OiPr)$_4$ (0.042 mL, 0.14 mmol) and $TiCl_4$ (0.063 mL, 0.57 mmol) in CH_2Cl_2 (4mL) was added to a solution of quinone **9b** (100 mg, 0.72 mmol) in CH_2Cl_2 (6 mL) followed by a solution of propenylbenzene **23d** (0.143 mL, 1.08 mmol) in CH_2Cl_2 (1 mL). The reaction was complete in 1 h and gave cyclobutane **24d** (61 mg, 31%) as white needles, mp 119.5–121 °C (30% EtOAc/hexanes): R_f (50% EtOAc/hexanes) 0.35; HPLC (4% iPrOH/hexanes, 2.0 mL/min) t_R 16.65; ^{1}H NMR (300 MHz) 1.34 (d, J = 6, 3H), 2.30 (s, 3H), 3.0–3.2 (m, 2H), 3.62 (dd J = 9, 10, 1H), 3.72 (m, 1H), 3.75 (s, 3H), 6.04 (s, 1H), 6.97 (d, J = 8, 2H), 7.11 (d, J = 8, 2H); ^{13}C NMR (300 MHz) 20.2, 21.0, 42.0, 45.8, 47.6, 49.9, 56.2, 117.8, 127.9, 129.1, 134.1, 136.9, 163.0, 191.3, 197.7. Anal. Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.80; H, 6.70.

Reaction of 9b with 23f. According to method B, $TiCl_4$ (0.087 mL, 0.79 mmol) was added to a solution of quinone **9b** (100 mg, 0.72 mmol) in CH_2Cl_2 (10 mL) followed by propenylbenzene **23f** (0.2 mL, 1.5 mmol). The reaction was complete in 15 min and gave cyclobutane **24f** (73 mg, 39%) as white needles, mp 142–142.7 °C (iPrOH): R_f (50%EtOAc/hexanes) 0.28; HPLC (4% iPrOH/hexanes, 2.5 mL/min) t_R 17.8 min; ^{1}H

NMR (300 MHz) 1.35 (d, J = 6, 3H), 3.00–3.15 (m, 2H), 3.6–3.7 (m, 1H), 3.6–3.7 (dd, J = 7, 11, 1H), 3.75 (s, 3H), 3.7–3.8 (m, 1H), 6.04 (s, 1H), 7.09 (d, J = 8, 2H), 7.2–7.3 (m, 3H); ^{13}C NMR (75 MHz) 20.3, 41.9, 45.8, 47.7, 50.1, 56.2, 112.8, 127.3, 128.0, 128.5, 137.2, 163.0, 191.2, 197.7. Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 75.00; H, 6.31.

Reaction of 9c with 23c. According to method B, $Ti(OiPr)_4$ (0.14 mL, 0.47 mmol) and $TiCl_4$ (0.091 mL, 0.83 mmol) were added to a solution of quinone **9c** (200 mg, 1.32 mmol) in CH_2Cl_2 (10 mL) followed by a solution of propenylbenzene **23c** (0.30 mL, 1.78 mmol) in CH_2Cl_2 (1 mL). Starting quinone **9c** still remained after 4 h and additional $TiCl_4$ (0.02 and 0.04 mL, 0.18 and 0.36 mol) was added in two portions over 1 h. Workup and chromatography gave a 7:1 mixture of **12c** and its cis isomer (173 mg, 52%). Recrystallization (30% EtOAc/hexanes) gave pure **12c** as a white solid, mp 157–158.5 °C. ^{1}H NMR signals consistent with the cis isomer are (300 MHz) 0.75 (d, J = 7, 3H), 5.70 (d, J = 7, 1H).

Reaction of 9c with 23d. According to method A, an aliquot [2.0 mL, 0.64 mmol Ti(IV)] of a solution of $Ti(OiPr)_4$ (0.077 mL, 0.26 mmol) and $TiCl_4$ (0.12 mL, 1.1 mmol) in CH_2Cl_2 (4 mL) was added to a solution of quinone **9c** (100 mg, 0.66 mmol) in CH_2Cl_2 (5 mL) followed by a solution of propenylbenzene **23d** (0.15 mL, 0.93 mmol) in CH_2Cl_2 (1 mL). The reaction was complete in 1 h and gave a 10:1 mixture of **12d** and its cis isomer (112 mg, 59%). ^{1}H NMR signals consistent with the cis isomer are (300 MHz) 0.73 (d, J = 7, 3H), 5.67 (d, J = 7, 1H).

Reaction of 9c with 23f. According to method B, $Ti(OiPr)_4$ (0.076 mL, 0.26 mmol) and $TiCl_4$ (0.116 mL, 1.06 mmol) were added to a solution of quinone **9c** (200 mg, 1.32 mmol) in CH_2Cl_2 (10 mL) followed by a solution of propenylbenzene **23f** (0.30 mL, 2.3 mmol) in CH_2Cl_2 (1 mL). The reaction was complete in 4h and gave, in order of elution, a 7:1 mixture of dihydrobenzofuran **12f** and its cis isomer (41 mg, 11%) as a yellow oil, and cyclobutane **25f** (85 mg, 24%).

Data for **25f**: a colorless solid, mp 128.5–130 °C (20% EtOAc/hexanes); R_f (30% EtOAc/hexanes) 0.16; ^{1}H NMR (300 MHz) 1.31 (d, J = 6, 3H), 1.56 (s, 3H), 2.78 (d, J = 8, 1H), 2.85 (ddq, J = 8, 10, 6, 1H), 3.15 (d, J = 10, 1H), 3.75 (s, 3H), 6.01 (s, 1H), 7.05 (d, J = 7, 2H), 7.2–7.4 (m 3H); ^{13}C NMR (75 MHz) 20.2, 27.0, 39.1, 51.8, 56.0, 56.3, 58.3, 112.1, 127.3, 127.7, 128.4, 137.2, 162.2, 194.0, 197.6. Anal. Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.82; H, 67.68.

Reaction of 32a with 8c. According to method D, an aliquot [2 mL, 0.5 mmol Ti(IV)] of a solution of $Ti(OiPr)_4$ (0.150 mL, 0.51 mmol) and $TiCl_4$ (0.055 mL, 0.50 mmol) in CH_2Cl_2 (4 mL) was added to a solution of quinone **32a** (100 mg, 0.47 mmol) in CH_2Cl_2 (5 mL) followed by a solution of propenylbenzene **8c** (0.127 mL, 0.75 mmol) in CH_2Cl_2 (1 mL). The reaction was complete in 7 h and gave dihydrobenzofuran **34a** (113 mg, 60%) and cyclobutane **35a** (40 mg, 22%).

Data for **34a**: white needles, mp 130.5–131.5 °C (EtOAc/hexanes); R_f (30% EtOAc/hexanes) 0.25; ^{1}H NMR (300 MHz) 1.35 (d, J = 7, 3H), 3.40 (dq, J = 10, 7, 1H), 3.87 (s, 3H), 3.89 (s, 3H), 5.03 (d, J = 10, 1H), 5.08 (s, 2H), 5.37 (s, 1H, D_2O exchange), 6.56 (s, 1H), 6.76 (s, 1H), 6.86–6.97 (m, 3H), 7.35–7.42 (m, 5H); ^{13}C NMR (75 MHz) (APT) 17.8 (q), 45.3 (d), 55.8 (q), 55.9 (q), 71.5 (t), 93.1 (d), 95.6 (d), 109.1 (d), 109.6 (d), 110.9 (d), 118.9 (d), 123.6 (s), 127.8 (d), 128.3 (d), 128.7 (d), 133.0 (s), 136.3 (s), 140.2 (s), 145.3 (s), 149.1 (s), 149.2 (s), 152.2 (s). Anal. Calcd for $C_{24}H_{24}O_5$: C, 73.45; H, 6.16. Found: C, 73.10; H, 6.18.

Data for **35a:** yellow needles, mp 84–85 °C (MeOH); R_f (50% EtOAc/hexanes) 0.25; HPLC (4% iPrOH/hexanes, 2.0 mL/min) t_R 10 min; ^{1}H NMR (500 MHz) 1.18 (d, J = 7, 3H), 3.00 (m, 1H), 3.35 (dd, J = 9, 9, 1H), 3.40 (dd, J = 8, 8, 1H), 3.50 (dd, J = 9, 8, 1H), 3.86 (s, 3H), 3.89 (s, 3H), 5.05 (d, J = 12, 1H), 5.10 (d, J = 12, 1H), 6.23 (s, 1H), 6.79–6.18 (m, 3H), 7.37–7.41 (m, 5H); ^{1}H NMR (C_6D_6, 300 MHz) 1.16 (d, J = 7, 3H), 2.65 (m, 1H), 2.90 (m, 1H), 3.10–3.20 (m, 2H), 3.42 (s, 3H), 3.50 (s, 3H), 4.30 (d, J = 12, 1H), 4.38 (d, J = 12, 1H), 5.95 (s, 1H), 6.55–6.70 (m, 3H), 7.00–7.23 (m, 5H); ^{13}C NMR (75 MHz) (APT) 17.1 (q), 38.3 (s), 43.8 (d), 47.6 (d), 52.4 (d), 55.8 (q), 55.9 (q), 71.0 (t), 109.7 (d), 111.1 (d), 116.0 (d), 118.1 (d), 127.6 (d), 128.7 (d), 128.8 (d), 133.6 (s), 133.9 (s), 148.1 (s), 149.0 (s), 160.7 (s), 191.8 (s), 197.0 (s). Anal. Calcd for $C_{24}H_{24}O_5$: C, 73.45; H, 6.16. Found: C, 73.18; H, 6.10.

Reaction of 32a with 8f. According to method D, a solution of $Ti(OiPr)_4$ (0.06 mL, 0.02 mmol) and $TiCl_4$ (0.087 mL, 0.79 mmol) in CH_2Cl_2 (5 mL) was added to a solution of quinone **32a** (188 mg, 0.88 mmol) in CH_2Cl_2 (15 mL) followed by propenylbenzene **8f** (0.18 mL, 1.39 mmol). The reaction was stirred for 6 h at −78 °C and then allowed to warm to room temperature. Workup and chromatography gave dihydrobenzofuran **34b** (83 mg, 29%), bicyclic adduct **16f** (45 mg, 21%), and cyclobutane **35b** (21 mg, 7%).

Data for **34b**: a yellow oil; R_f (30% EtOAc/hexanes) 0.57; ^{1}H NMR (300 MHz) 1.36 (d, J = 7, 1H), 3.37 (dq, J = 7, 8, 1H), 5.06 (s, 2H), 5.10 (d, J = 8, 1H), 5.31 (s, 1H), 6.55 (s, 1H), 6.73 (s, 1H), 7.25–7.45 (m, 5H); ^{13}C NMR (75 MHz) 18.3, 45.7, 71.5, 92.8, 95.6, 109.7, 123.5, 126.0, 127.8, 128.2, 128.4, 128.6, 128.8, 136.4, 140.2, 141.0, 145.4, 152.3; HRMS m/z 332.1417 (calcd for $C_{22}H_{20}O_3$, 332.1412).

Data for **16f**: a yellow oil that solidified on standing, mp 160.5–162 °C; R_f (30% EtOAc/hexanes) 0.36; ^{1}H NMR (300 MHz) 1.28 (d, J = 7, 3H), 2.59 (dq, J = 6, 7, 1H), 3.07 (dd, J = 2, 8, 1H), 3.25 (dd, J = 6, 6, 1H), 3.88 (dd, J = 2, 7, 1H), 5.91 (s, 1H), 6.76 (d, J = 8, 1H), 7.05–7.10 (m, 2H), 7.2–7.35 (m, 3H); ^{13}C NMR (75 MHz) 21.4, 42.3, 49.3, 54.2, 69.3, 119.7, 127.7, 128.3, 128.9, 137.8, 149.9 191.6, 199.2; HRMS m/z 242.0954 (calcd for $C_{15}H_{14}O_3$, 242.0943).

Data for **35b**: a yellow film; ^{1}H NMR (300 MHz) 1.19 (d, J = 6, 3H), 3.02 (m, 1H), 3.4 (m, 2H), 3.56 (m, 1H), 5.06 (AB quartet, 2H), 6.23 (s, 1H), 7.25–7.40 (m, 10H); because of the low yield, and its similarity of other compounds prepared in this study, this compound was identified only by ^{1}H NMR.

Reaction of 32a with 23c. According to method B, $Ti(OiPr)_4$ (0.061 mL, 0.21 mmol) and $TiCl_4$ (0.031 mL, 0.37 mmol) were added to a solution of quinone **32a** (100 mg, 0.47 mmol) in CH_2Cl_2 (5mL) followed by propenylbenzene **23c** (0.10 mL, 0.74 mmol). After 9 h, the reaction was worked up as described in method C and gave cyclobutane **36** (90 mg, 49%) as a white solid, mp 157–157.5 °C (EtOAc/hexanes): R_f (30% EtOAc/hexanes) 0.09; R_f (50% EtOAc/hexanes) 0.24; HPLC (4% iPrOH/hexanes, 2 mL/min) t_R 15 min; ^{1}H NMR (500 MHz) 1.35 (d, J = 6, 3H), 2.99 (ddq, J = 8, 11, 7, 1H), 3.03 (dd, J = 8, 8, 1H), 3.60 (dd, J = 11, 11, 1H), 3.76 (dd, J = 11, 11, 1H), 3.81 (s, 3H), 3.85 (s, 3H), 5.00 (d, J = 14, 16, 2H), 6.06 (s, 1H), 6.61 (m, 2H), 6.7–6.8 (m, 2H), 7.2–7.4 (m, 5H); ^{1}H NMR (C_6D_6, 300 MHz) 1.13 (d, J = 6, 3H), 2.69 (dd, J = 8, 8, 1H), 2.94 (ddq, J = 8, 10, 7, 1H), 3.14 (dd, J = 10, 10, 1H), 3.25 (dd, J = 11, 11, 1H), 3.38 (s, 3H), 3.52 (s, 3H), 4.28 (s, 2H), 5.87 (s, 1H), 6.9–7.2 (m, 3H), 7.16 (s, 5H); ^{13}C NMR (75 MHz) 20.4, 41.7, 45.6, 47.4, 49.9, 55.7 (2 C), 70.7, 110.9, 111.7, 114.2, 119.8, 127.2, 128.6, 128.7, 129.9, 133.9, 148.1, 148.7, 161.9, 191.2, 197.8. Anal. Calcd for $C_{24}H_{24}O_5$: C, 73.44; H, 6.17. Found: C, 73.44; H, 6.19.

Reaction of 33a with 8d. According to method D, a solution of $Ti(OiPr)_4$ (0.15 mL, 0.51 mmol) and $TiCl_4$ (0.5 mL, 0.46 mmol) in CH_2Cl_2 (3 mL) was added to a solution of quinone **33a** (248 mg, 1.02 mmol) in CH_2Cl_2 (15 mL) followed by propenylbenzene **8d** (266 mg, 2.02 mmol). The mixture was stirred for 20 h at −78 °C and then allowed to warm to 10 °C. Workup gave **16d** as a yellow semisolid which degraded rapidly on SiO_2 chromatography. Compound **16d** was identified by ^{1}H NMR of the material (116 mg, 44%) obtained by rapid flash chromatography with 20% and then 35% EtOAc/hexanes as eluents: ^{1}H NMR (500 MHz) 1.15 (d, J = 6, 3H), 2.20 (s, 3H), 2.45 (dq, J = 6, 8, 1H), 2.95 (dd, J = 8, 2, 1H), 3.11 (dd, J = 8, 8, 1H), 3.74 (dd, J = 8, 2, 1H), 6.02 (br s, 1H), 6.65 (d, J = 8, 1H), 6.85 (d, J = 8, 1H), 6.99 (d, J = 8, 1H).

Reaction of 33a with 8e. According to method D, a solution of $TiCl_4$ (0.055 mL, 0.51 mmol) and $Ti(OiPr)_4$ (0.15 mL, 0.51 mmol) in CH_2Cl_2 (3 mL) was added to a solution of quinone **33a** (243 mg, 1.0 mmol) in CH_2Cl_2 (15 mL) followed by propenylbenzene **8e** (223 mg, 1.69 mmol). The mixture was stirred for 20 h at −78 °C and then allowed to warm to 10 °C. Workup and chromatography afforded **16e** (117 mg, 46%) as a white solid, mp 199–201 °C (EtOAc/hexanes); R_f (30% EtOAc/hexanes): 0.55; ^{1}H NMR (500 MHz) 1.25 (d, J = 7, 3H), 2.39 (s, 3H), 2.71 (dq, J = 7, 6, 1H), 3.08 (dd, J = 8, 2, 1H), 3.46 (dd, J = 7, 6, 1H), 3.86 (dd, J = 8, 2, 1H), 5.84 (s, 1H),

6.74 (d, J = 8, 1H), 6.88 (m, 1H), 7.10–7.19 (m, 3H); ^{13}C NMR (125 MHz) 20.0, 21.6, 41.6, 45.1, 54.2, 67.0, 119.1, 126.4, 126.7, 127.4, 130.7, 136.0, 137.1, 150.1, 191.6, 199.6. Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.70; H, 6.25.

Reaction of 33a with 8f. According to method D, a solution of Ti(OiPr)$_4$ (0.15 mL, 0.50 mmol) and $TiCl_4$ (0.055 mL, 0.50 mmol) in CH_2Cl_2 (3mL) was added to quinone **33a** (250 mg, 1.02 mmol) in CH_2Cl_2 (15 mL) followed by propenylbenzene **8f** (0.18 mmol, 1.39 mmol). The mixture was stirred for 10 h at −78 °C and then allowed to warm to room temperature. Workup and chromatography afforded **16f** (146 mg, 59%) as a white solid, mp 160.5–162 °C.

Reaction of 33b with 8d. According to method D, a solution of Ti(OiPr)$_4$ (0.15 mL, 0.50 mmol) and $TiCl_4$ (0.055 mL, 0.50 mmol) in CH_2Cl_2 (5 mL) was added to a solution of quinone **33b** (263 mg, 1.02 mmol) followed by propenylbenzene **8d** (256 mg, 1.94 mmol). The mixture was stirred for 1 h at −78 °C and then allowed to warm to −20 °C. Workup and chromatography gave **17d** (105 mg, 67%) as a white solid.

Reaction of 33b with 8e. In a manner exactly analogous to the reaction of **33b** with **8d**, reaction of **33b** (262 mg, 1.01 mmol) with **8e** (193 mg, 1.46 mmol) gave **17e** (329 mg, 88%) as a white solid.

Reaction of 33b with 8f. According to method D, a solution of Ti(OiPr)$_4$ (0.15 mL, 0.51 mmol) and $TiCl_4$ (0.055 mL, 0.50 mmol) in CH_2Cl_2 (4 mL) was added to a solution of quinone **33b** (256 mg, 0.99 mmol) in CH_2Cl_2 (15 mL) followed by propenylbenzene **8f** (0.18 mL, 1.39 mmol). The reaction was stirred for 12 h at −78 °C and then allowed to warm to room temperature. Workup and chromatography gave **17f** (194 mg, 76%).

Reaction of 33b with Indene. According to method D, a solution of Ti(OiPr)$_4$ (0.15 mL, 0.50 mmol) and $TiCl_4$ (0.055 mL, 0.5 mmol) in CH_2Cl_2 (4 mL) was added to a solution of quinone **33b** (259 mg, 1.00 mmol) in CH_2Cl_2 (15 mL) followed by indene (0.14 mL, 1.20 mmol). The mixture was stirred for 3 h at −78 °C and then allowed to warm to 0 °C. Workup and chromatography gave **22** (161 mg, 63%) as a white solid.

Reaction of 9a with 42a. According to method D, a solution of Ti(OiPr)$_4$ (0.074 mL, 0.25 mmol) and $TiCl_4$ (0.082 mL, 0.75 mmol) in CH_2Cl_2 (1 mL) was added to a solution of quinone **9a** (110 mg, 1.02 mmol) in CH_2Cl_2 (4 mL) followed by a solution of the propenylbenzene **42a** (164 mg, 1.1 mmol) in CH_2Cl_2 (1 mL). The reaction was allowed to warm to −40 °C over 9 h and gave dihydrobenzofuran **43a** (132 mg, 50%) as a colorless solid, mp 108–110 °C (Et_2O/hexanes): R_f (30% EtOAc/hexanes) 0.30; ^{1}H NMR (300 MHz) 7.37 (d, J = 8.8, 2H), 6.86 (d, J = 8.8, 2H), 6.71–6.57 (m, 3H), 5.11 (bs, 1H), 3.78 (s, 3H), 3.30 (ABq, J = 15.6, $\Delta\nu$ = 30.6, 2H), 1.73 (s, 3H); ^{13}C NMR (75 MHz) 158.5, 152.8, 149.6, 138.8, 127.7, 125.7, 114.3, 113.6, 112.4, 109.4, 89.0, 55.2, 45.0, 29.0; HRMS m/z 256.1101 (calcd for $C_{16}H_{16}O_3$, 256.1098).

Reaction of 9b with 42a. According to method B, Ti(OiPr)$_4$ (0.075 mL, 0.25 mmol) and $TiCl_4$ (0.082 mL, 0.75 mmol) were added to a solution of quinone **9b** (139 mg, 1.0 mmol) in CH_2Cl_2 (7 mL) followed by propenylbenzene **42a** (222 mg, 1.50 mmol). The reaction was complete in 2 h and gave dihydrobenzofuran **44a** (153 mg, 54%) as a colorless solid, mp 114–115 °C (Et_2O/hexanes): R_f (50% EtOAc/hexanes) 0.47; ^{1}H NMR (300 MHz) 7.37 (d, J = 9.0, 2H), 6.86 (d, J = 8.7, 2H), 6.71 (s, 1H), 6.49 (s, 1H), 5.25 (s, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 3.28 (ABq, J = 15.0, $\Delta\nu$ = 26.8, 2H), 1.72 (s, 3H); ^{13}C NMR (75 MHz) 158.5, 152.1, 146.2, 139.6, 139.0, 125.7, 117.3, 113.6, 110.7, 94.2, 89.3, 56.1, 55.2, 44.8, 29.0. Anal. Calcd for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.44; H, 6.52.

Reaction of 9b with 42b. According to method B, Ti(OiPr)$_4$ (0.075 mL, 0.25 mmol) and $TiCl_4$ (0.082 mL, 0.75 mmol) were added to a solution of quinone **9b** (138 mg, 1.0 mmol) in CH_2Cl_2 (7 mL) followed by propenylbenzene **42b** (0.20 mL, 1.54 mmol). The reaction mixture was stirred 4 h at −78 °C, allowed to warm to 0 °C, and stirred for 5 h. Workup and chromatography gave dihydrobenzofuran **44b** (154 mg, 60%) as a clear oil: R_f (50% EtOAc/hexanes) 0.67; ^{1}H NMR (300 MHz) 7.46 (d, J = 7.3, 2H), 7.34 (apparent t, J = 7.3, 7.4, 2H), 7.24 (apparent t, J = 7.4, 1H), 6.71 (s, 1H), 6.52 (s, 1H), 5.19 (s, 1H), 3.86 (s, 3H), 3.32 (ABq, J = 15.2, $\Delta\nu$ = 23.0, 2H), 1.74 (s, 3H); ^{13}C NMR (75 MHz) 152.2, 146.9, 146.2, 139.6, 128.3, 127.0, 124.5, 117.2, 110.7, 94.2, 89.5, 56.2, 44.8, 29.2; HRMS m/z 256.1100 (calcd for $C_{16}H_{16}O_3$, 256.1098).

Reaction of 9c with 42a. According to method D, a solution of Ti(OiPr)$_4$ (0.074 mL, 0.25 mmol) and $TiCl_4$ (0.084 mL, 0.75 mmol) in CH_2Cl_2 (1 mL) was added to a solution of quinone **9c** (153 mg, 1.01 mmol) in CH_2Cl_2 (4 mL) followed by a solution of propenylbenzene **42a** (168 mg, 1.13 mmol) in CH_2Cl_2 (1 mL). The reaction mixture was allowed to warm to −35 °C over 20 h and gave dihydrobenzofuran **45a** (168 mg, 55%) and starting quinone **9c** (11 mg, 7%).

Data for **45a**: a white solid, mp 117–118 °C (EtOAc/hexanes); R_f (30% EtOAc/hexanes) 0.40; ^{1}H NMR (300 MHz) 7.40 (d, J = 8.8, 2H), 6.88 (d, J = 8.8, 2H), 6.40 (s, 1H), 5.33 (s, 1H), 3.84 (s, 3H), 3.79 (s, 3H), 3.26 (ABq, J = 15.5, $\Delta\nu$ = 21.2, 2H), 2.13 (s, 3H), 1.75 (s, 3H); ^{13}C NMR (75 MHz), 158.5, 151.0, 145.9, 139.3, 137.5, 125.7, 120.2, 117.1, 113.6, 91.5, 88.7, 56.2, 55.2, 44.0, 29.2, 12.6. Anal. Calcd for $C_{18}H_{20}O_4$: C, 71.97; H, 6.72. Found: C, 71.71, H, 6.90.

Reaction of 9c with 42b. According to method D, a solution of Ti(OiPr)$_4$ (0.110 mL, 0.37 mmol) and $TiCl_4$ (0.080 mL, 0.73 mmol) in CH_2Cl_2 (2 mL) was added to a solution of quinone **9c** (154 mg, 1.01 mmol) in CH_2Cl_2 (5 mL) followed by propenylbenzene **42b** (0.195 mL, 1.50 mmol). The mixture was allowed to warm to room temperature over 36 h and gave dihydrobenzofuran **45b** (149 mg, 54%) as a colorless oil: R_f (EtOAc/hexanes) 0.49; ^{1}H NMR (300 MHz) 7.51–7.25 (m, 5H), 6.42 (s, 1H), 5.29 (s, 1H), 3.86 (s, 3H), 3.30 (ABq, J = 15.5, $\Delta\nu$ = 18.8, 2H), 2.13 (s, 3H), 1.78 (s, 3H); ^{13}C NMR (75 MHz) 151.0, 147.2, 145.9, 137.6, 128.3, 126.9, 124.4, 120.2, 117.0, 91.6, 88.9, 56.2, 44.0, 29.3 12.6; HRMS m/z 270.1262 (calcd for $C_{17}H_{18}O_3$, 270.1256).

Reaction of 33b with 42b. According to method C, a solution of Ti(OiPr)$_4$ (0.110 mL, 0.37 mmol) and $TiCl_4$ (0.080 mL, 0.73 mmol) in CH_2Cl_2 (2 mL) was added to a solution of quinone **33b** (225 mg, 0.87 mmol) in CH_2Cl_2 (4 mL) followed by propenylbenzene **42b** (0.195 mL, 1.50 mmol). The reaction was complete in 45 min and gave bicyclic adduct **60** (80 mg, 36%) as a pale yellow oil. Crystallization from EtOAc/hexanes afforded colorless needles, mp 156–157 °C: R_f (30% EtOAc/hexanes) 0.41; ^{1}H NMR (500 MHz) 7.32–7.18 (m, 5H), 5.70 (s, 1H), 3.74 (d, J = 1.9, 1H), 3.24 (dd, J = 1.9, 6.8, 1H), 2.53 (d, J = 13.0, 1H), 2.40 (dd, J = 6.8, 13.0, 1H), 2.11 (s, 3H), 1.48 (s, 3H); ^{13}C NMR (125 MHz) 199.6, 190.2, 145.4, 143.9, 135.2, 128.5, 126.8, 126.7, 73.3, 53.3, 43.9, 40.9, 33.9, 16.3. Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.97; H, 6.30. Found: C, 74.50; 6.40.

Reaction of 9b with 46a. According to method E, to a solution of Ti(OiPr)$_4$ (0.15 mL, 0.51 mmol) and $TiCl_4$ (0.050 mL, 0.46 mmol) in CH_2Cl_2 (2 mL) at −78 °C was added a solution of quinone **9b** (138 mg, 1.0 mmol) in CH_2Cl_2 (1.5 mL) followed by a solution of arylcyclopentene **46a** (193 mg, 1.10 mmol) in CH_2Cl_2 (0.5 mL). The reaction was complete in 1 h at −78 °C. Workup and chromatography gave dihydrobenzofuran **49a** (247 mg, 79%) as a colorless oil that crystallized from EtOAc/hexanes to afford a white solid, mp 74–75 °C: R_f (30% EtOAc/hexanes) 0.33; ^{1}H NMR (500 MHz) 7.35 (d, J = 8.8, 2H), 6.85 (d, J = 8.8, 2H), 6.66 (s, 1H), 6.42 (s, 1H), 5.16 (s, 1H), 3.83 (s, 3H), 3.77 (s, 3H), 3.70 (d, J = 8.6, 1H), 2.35 (dd, J = 5.8, 13.6, 1H), 2.12–2.01 (m, 2H), 1.89–1.81 (m, 2H), 1.70 (apparent nonet, J = 6.1, 1H); ^{13}C NMR (125 MHz) 158.7, 153.0, 146.2, 139.6, 137.4, 125.9, 121.9, 113.6, 110.2, 100.2, 93.2, 56.1, 55.3, 55.1, 42.5, 36.1, 25.1; HRMS m/z 312.1349 (calcd for $C_{19}H_{20}O_4$, 312.1362).

Reaction of 9b with 46b. According to method C, a solution of Ti(OiPr)$_4$ (0.10 mL, 0.34 mmol) and $TiCl_4$ (0.073 mL, 0.67 mmol) was added to a solution of quinone **9b** (140 mg, 1.01 mmol) in CH_2Cl_2 (2 mL) followed by a solution of phenylcyclopentene **46b** (157 mg, 1.09 mmol) in CH_2Cl_2 (0.5 mL). The reaction was complete in 45 min and gave dihydrobenzofuran **49b** (121 mg, 43%) as a clear oil and starting quinone **9b** (39 mg, 28%). Crystallization of **49b** from EtOAc/hexanes afforded a white solid, mp 72–73 °C: R_f (30% EtOAc/hexanes) 0.37; ^{1}H NMR (500 MHz) 7.45 (d, J = 7.3, 2H), 7.33 (t, J = 7.3, 2H), 7.24 (t, J = 7.3, 1H), 6.67 (s, 1H), 6.46 (s, 1H), 5.17 (s, 1H), 3.85 (s, 3H), 3.74 (d, J = 8.6, 1H), 2.38 (dd, J = 5.9, 13.7, 1H), 2.18–2.05 (m, 2H), 1.93–1.84 (m, 2H), 1.74 (apparent nonet, J = 6.3, 1H); ^{13}C NMR (125 MHz) 153.0,

146.2, 145.4, 139.7, 128.3, 127.0, 124.6, 121.8, 110.2, 100.3, 93.2, 56.1, 55.5, 43.0, 36.2, 25.3. Anal Calcd for $C_{18}H_{18}O_3$: C, 76.56; H, 6.44. Found: C, 76.78; H, 6.46.

Reaction of 9b with 47a. According to method C, a solution of $Ti(OiPr)_4$ (0.10 mL, 0.34 mmol) and $TiCl_4$ (0.080 mL, 0.73 mmol) in CH_2Cl_2 (1 mL) was added to a solution of quinone **9b** (138 mg, 1.0 mmol) in CH_2Cl_2 (2 mL) followed by arylcyclohexene **47a** (209 mg, 1.11 mmol). The reaction was complete in 4.3 h and gave dihydrobenzofuran **50a** (219 mg, 67%) as a colorless oil: R_f (30% EtOAc/hexanes) 0.34; ^1H NMR (300 MHz) 7.44 (d, J = 8.8, 2H), 6.85 (d, J = 8.8, 2H), 6.67 (s, 1H), 6.49 (s, 1H), 5.23 (s, 1H), 3.82 (s, 3H), 3.77 (t, J = 5.6, 1H), 2.08–1.41 (m, 8H); ^{13}C NMR (75 MHz) 158.6, 151.6, 145.9, 139.5, 138.1, 126.6, 123.3, 113.4, 109.6, 94.8, 90.8, 56.1, 55.2, 46.9, 35.2, 27.6, 21.0, 20.4; HRMS m/z 326.1512 (calcd for $C_{20}H_{22}O_4$, 326.1518).

Reaction of 9b with 47b. According to method B, $Ti(OiPr)_4$ (0.06 mL, 0.22 mmol) and $TiCl_4$ (0.09 mL, 0.82 mmol) were added to a solution of quinone **9b** (138 mg, 1.00 mmol) in CH_2Cl_2 (5 mL) followed by phenylcyclohexene (0.25 mL, 1.57 mmol). The reaction was complete in 2.5 h and was worked up as described in method C to give dihydrobenzofuran **50b** (210 mg, 71%) as a colorless oil: R_f (30% EtOAc/hexanes) 0.44; ^1H NMR (500 MHz) 7.53 (d, J = 7.3, 2H), 7.33 (t, J = 7.3, 2H), 7.24 (t, J = 7.3, 1H), 6.68 (s, 1H), 6.53 (s, 1H), 5.22 (s, 1H), 3.85 (s, 3H), 3.53 (t, J = 5.6, 1H), 2.10–1.98 (m, 3H), 1.85–1.76 (m, 1H), 1.67–1.47 (m, 4H); ^{13}C NMR (125 MHz) 151.7, 146.4, 146.0, 139.6, 128.1, 127.0, 125.3, 123.2, 109.6, 94.7, 91.0, 56.2, 46.9, 35.2, 27.9, 20.7, 20.3; HRMS m/z 296.1428 (calcd for $C_{19}H_{20}O_3$, 296.1411).

Reaction of 9b with 48a. According to method C, a solution of $Ti(OiPr)_4$ (0.10 mL, 0.34 mmol) and $TiCl_4$ (0.073 mL, 0.67 mmol) in CH_2Cl_2 (1 mL) was added to a solution of quinone **9b** (139 mg, 1.0 mmol) in CH_2Cl_2 (2mL) followed by a solution of arylcycloheptene **48a** (245 mg, 1.21 mmol) in CH_2Cl_2 (0.5 mL). The reaction was complete in 4.5 h and gave dihydrobenzofuran **51a** (181 mg, 53%) as a clear colorless oil. Crystallization from EtOAc/hexanes afforded a white solid, mp 115–116 °C: R_f (30% EtOAc/hexanes) 0.27; ^1H NMR (500 MHz) 7.37 (d, J = 8.8, 2H), 6.82 (d, J = 8.8, 2H), 6.58 (s, 1H), 6.48 (s, 1H), 5.14 (s, 1H), 3.84 (s, 3H), 3.75 (s, 3H), 3.68 (dd, J = 3.2, 6.3, 1H), 2.18–1.90 (m, 5H), 1.65–1.50 (m, 3H), 1.48–1.37 (m, 2H); ^{13}C NMR (500 MHz) 158.3, 151.5, 146.2, 141.6, 139.5, 125.3, 121.4, 113.5, 109.9, 105.6, 94.6, 93.3, 56.1, 55.2, 53.5, 41.0, 32.5, 31.2, 26.1, 23.9; HRMS m/z 340.1659 (calcd for $C_{21}H_{24}O_4$, 340.1675).

Reaction of 9b with 48b. According to method C, a solution of $TiCl_4$ (0.08 mL, 0.67 mmol) and $Ti(OiPr)_4$ (0.10 mL, 0.33 mmol) in CH_2Cl_2 (1 mL) was added to a solution of quinone **9b** (138 mg, 1.0 mmol) in CH_2Cl_2 (2mL) at −78 °C followed by a solution of phenylcycloheptene **48b** (188 mg, 1.09 mmol) in CH_2Cl_2 (1 mL). The reaction was complete in 1 h and gave dihydrobenzofuran **51b** (191 mg, 62%) and cyclobutane **56b** (42 mg, 14%).

Data for **51b**: *a colorless oil*; R_f (30% EtOAc/hexanes) 0.40; ^1H NMR (500 MHz) 7.46 (d, J = 7.5, 2H), 7.30 (t, J = 7.5, 2H), 7.20 (t, J = 7.5, 1H), 6.59 (s, 1H), 6.52 (s, 1H), 5.16 (s, 1H), 3.86 (s, 3H), 3.72 (dd, J = 3.2, 5.9, 1H), 2.16–1.96 (m, 3H), 1.67–1.56 (m, 3H), 1.42–1.30 (m, 3H); ^{13}C NMR (125 MHz) 151.6, 149.7, 146.2, 139.6, 128.2, 126.7, 124.0, 121.1, 109.9, 94.6, 93.3, 56.1, 53.5, 41.0, 32.5, 31.3, 25.8, 24.0; HRMS m/z 310.1559 (calcd for $C_{20}H_{22}O_3$, 310.1569).

Data for **56b**: a white solid, mp 133–135 °C (EtOAc/hexanes); R_f (30% EtOAc/hexanes) 0.14; ^1H NMR (500 MHz) 7.48 (apparent d, J = 7.3, 2H), 7.38 (apparent t, J = 7.6, 2H), 7.22 (apparent t, J = 7.3, 1H), 6.14 (s, 1H), 3.85 (s, 3H), 3.67 (d, J = 9.5, 1H), 3.51–3.42 (m, 2H), 2.10–2.03 (m, 2H), 1.97–1.89 (m, 1H), 1.79–1.65 (m, 3H), 1.45–1.23 (m, 2H), 1.17–1.06 (m, 1H), 0.91–0.82 (m, 1H); ^{13}C NMR (75 MHz) 198.2, 192.8, 162.9, 148.7, 128.2, 127.3, 126.1, 115.0, 56.4, 53.6, 51.8, 43.9, 40.8, 37.0, 31.1, 30.5, 28.2, 24.6; HRMS m/z 310.1559 (calcd for $C_{20}H_{22}O_3$, 310.1569).

Reaction of 9c with 46a. According to method D, a solution of $Ti(OiPr)_4$ (0.07 mL, 0.24 mmol) and $TiCl_4$ (0.08 mL, 0.73 mmol) in CH_2Cl_2 (1 mL) was added to a solution of quinone **9c** (153 mg, 1.0 mmol) in CH_2Cl_2 (2 mL) followed by a solution of 1-arylcyclopentene **46a** (152 mg, 0.87 mmol) in CH_2Cl_2 (0.5 mL). The reaction was allowed to warm to room temperature overnight and gave dihydrobenzofuran **52a** (178 mg, 63%) as a white solid, mp 160–161 °C: R_f (30% EtOAc/hexanes) 0.44; ^1H NMR (500 MHz) 7.35 (d, J = 8.7, 2H), 6.84 (d, J = 8.7, 2H), 6.32 (s, 1H), 5.21 (s, 1H), 3.82 (s, 3H), 3.76 (s, 3H), 3.67 (d, J = 8.8, 1H), 2.34 (dd, J = 5.5, 13.2, 1H), 2.13 (s, 3H), 2.11–2.03 (m, 2H), 1.89–1.83 (m, 2H), 1.79–1.68 (m, 1H); ^{13}C NMR (125 MHz) 158.6, 152.1, 145.9, 137.7, 137.5, 125.8, 121.3, 119.8, 113.6, 99.9, 90.7, 56.1, 55.3, 54.4, 42.4, 34.7, 25.3, 12.0; HRMS m/z 326.1518 (calcd for $C_{20}H_{22}O_4$, 326.1518).

Reaction of 9c with 46b. According to method E, a solution of $Ti(OiPr)_4$ (0.10 mL, 0.33 mmol) and $TiCl_4$ (0.073 mmol, 0.67 mmol) in CH_2Cl_2 (2 mL) was cooled to −78 °C and a solution of quinone **9c** (152 mg, 1.0 mmol) in CH_2Cl_2 (1.5 mL) added followed by a solution of phenylcyclopentene **46b** (164 mg, 1.14 mmol) in CH_2Cl_2 (0.5 mL). The mixture was stirred at −78 °C and then allowed to warm to room temperature. Workup and chromatography gave dihydrobenzofuran **52b** (222 mg, 75%) as a white solid, mp 94–95 °C (EtOAc/hexanes): R_f (30% EtOAc/hexanes) 0.54; ^1H NMR (500 MHz) 7.46 (d, J = 7.3, 2H), 7.33 (t, J = 7.5, 2H), 7.23 (t, J = 7.3, 1H), 6.36 (s, 1H), 5.22 (s, 1H), 3.84 (s, 3H), 3.71 (d, J = 8.5, 1H), 2.38 (dd, J = 5.8, 13.5, 1H), 2.14 (s, 3H), 2.19–2.08 (m, 2H), 1.92–1.87 (m, 2H), 1.77 (apparent nonet, J = 6.1, 1H); ^{13}C NMR (125 MHz) 152.1, 146.0, 145.5, 137.7, 128.3, 127.0, 124.6, 121.2, 119.8, 100.0, 90.7, 56.1, 54.8, 42.9, 34.8, 25.4, 12.0. Anal. Calcd for $C_{19}H_{20}O_3$: C, 76.99; H, 6.82. Found: C, 76.89; H, 6.83.

Reaction of 9c with 47a. According to method D, a solution of $Ti(OiPr)_4$ (0.10 mL, 0.33 mmol) and $TiCl_4$ (0.073 mL, 0.67 mmol) in CH_2Cl_2 (1 mL) was added to a solution of quinone **9c** (153 mg, 1.0 mmol) in CH_2Cl_2 (2 mL) followed by a solution of arylcyclohexene **47a** (211 mg, 1.12 mmol) in CH_2Cl_2 (0.5 mL). The mixture was allowed to warm to room temperature over 23 h and gave dihydrobenzofuran **53a** (239 mg, 70%) as a colorless oil. Crystallization from EtOAc/hexanes affored a white solid, mp 130–131 °C: R_f (30% EtOAc/hexanes) 0.43; ^1H NMR (500 MHz) 7.44 (d, J = 8.8, 2H), 6.86 (d, J = 8.8, 2H), 6.50 (s, 1H), 5.18 (s, 1H), 3.85 (s, 3H), 3.79 (s, 3H), 3.52 (t, J = 5.5, 1H), 2.05 −1.92 (m, 3H), 1.86–1.79 (m, 1H), 1.63–1.56 (m, 1H), 1.57 (s, 3H), 1.53–1.42 (m, 3H); ^{13}C NMR (125 MHz) 158.6, 151.6, 145.9, 139.5, 138.1, 126.6, 123.3, 113.5, 109.6, 94.8, 90.9, 56.2, 55.2, 46.9, 35.2, 27.6, 21.0, 20.5. Anal. Calcd for $C_{21}H_{24}O_4$: C, 74.08; H, 7.12. Found: C, 74.09; H, 7.30.

Reaction of 9c with 47b. According to method D, a solution of $Ti(OiPr)_4$ (0.059 mL, 0.2 mmol) and $TiCl_4$ (0.088 mL, 0.80 mmol) in CH_2Cl_2 (1 mL) was added to a solution of quinone **9c** (152 mg, 1.0 mmol) in CH_2Cl_2 (2 mL) followed by phenylcyclohexene (0.318 mL, 2.0 mmol). The mixture was allowed to warm to room temperature over 18 h and gave dihydrobenzofuran **53b** (206 mg, 66%) as a colorless oil: R_f (30% EtOAc/hexanes) 0.29; ^1H NMR (300 MHz) 7.44 (d, J = 7.1, 2H), 7.26 (t, J = 7.4, 2H), 7.16 (t, J = 7.1, 1H), 6.44 (s,-1H), 5.23 (s, 1H), 3.81 (s, 3H), 3.38–3.33 (m, 1H), 2.08 (s, 3H), 2.23–2.05 (m, 2H), 1.94–1.84 (m, 2H), 1.70–1.61 (m, 2H), 1.42–1.33 (m, 2H); ^{13}C NMR (75 MHz) 150.7, 147.9, 145.4, 137.7, 127.9, 126.6, 124.9, 123.9, 119.7, 92.1, 90.2, 56.1, 46.2, 36.0, 29.2, 21.1, 20.8, 12.0; HRMS m/z 310.1562 (calcd for $C_{20}H_{22}O_3$, 310.1569).

Reaction of 9c with 48a. According to method C, a solution of $Ti(OiPr)_4$ (0.06 mL, 0.20 mmol) and $TiCl_4$ (0.09 mL, 0.8 mmol) in CH_2Cl_2 (1 mL) was added to a solution of quinone **9c** (153 mg, 1.0 mmol) in CH_2Cl_2 (2 mL) followed by arylcycloheptene **48a** (243 mg, 1.20 mmol). The reaction was complete in 2 h and gave dihydrobenzofuran **54a** (317 mg, 89%) as a clear oil. Crystallization from EtOAc/hexanes afforded white needles, mp 101–103 °C: R_f (30% EtOAc/hexanes) 0.36; ^1H NMR (500 MHz) 7.40 (d, J = 8.8, 2H), 6.83 (d, J = 8.8, 2H), 6.37 (s, 1H), 5.19 (s, 1H), 3.84 (s, 3H), 3.76 (s, 3H), 3.63 (dd, J = 3.0, 7.2, 1H), 2.17–2.15 (m, 4H), 2.10 (s, 3H), 2.08–2.02 (m, 1H), 1.86–1.72 (m, 5H); ^{13}C NMR (125 MHz) 158.3, 150.6, 145.9, 137.6, 125.5, 120.0, 113.4, 94.0, 91.0, 56.1, 55.2, 53.1, 40.4, 31.2, 30.9, 26.6, 23.6, 12.0. Anal. Calcd for $C_{22}H_{26}O_4$: C, 74.54; H, 7.41. Found: C, 74.30; H, 7.80.

Reaction of 9c with 48b. According to method E, to a solution of $Ti(OiPr)_4$ (0.08 mL, 0.27 mmol) and $TiCl_4$ (0.08 mL,

0.73 mmol) in CH_2Cl_2 (2 mL) at −78 °C was added a solution of quinone **9c** (152 mg, 1.0 mmol) in CH_2Cl_2 (1.5 mL) followed by a solution of phenylcycloheptene **48b** (194 mg, 1.13 mmol) in CH_2Cl_2 (0.5 mL). The reaction was complete in 4 h at −78 °C and gave dihydrobenzofuran **54b** (300 mg, 92%) as a colorless oil: R_f (30% EtOAc/hexanes) 0.38; ^{1}H NMR (300 MHz) 7.47 (d, J = 7.3, 2H), 7.29 (t, J = 7.3, 2H), 7.18 (t, J = 7.3, 1H), 6.40 (s, 1H), 5.25 (s, 1H), 3.82 (s, 3H), 3.67 (dd, J = 3.0, 6.5, 1H), 2.10 (s, 3H), 2.23−2.13 (m, 4H), 1.97−1.85 (m, 1H), 1.76−1.34 (m, 5H); ^{13}C NMR (75 MHz) 150.6, 149.4, 145.8, 137.6, 128.1, 126.6, 124.1, 120.3, 120.0, 94.0, 90.9, 56.0 53.2, 40.3, 31.2, 31.0, 26.2, 23.7, 11.9; HRMS m/z 324.1732 (calcd for $C_{21}H_{24}O_3$, 324.1725).

Reaction of 33b with 46b. According to method C, a solution of $Ti(OiPr)_4$ (0.20 mL, 0.68 mmol) and $TiCl_4$ (0.15 mL, 1.37 mmol) in CH_2Cl_2 (2 mL) was added to a solution of quinone **33b** (226 mg, 0.88 mmol) in CH_2Cl_2 (6 mL) followed by a solution of phenylcyclopentene (**46b**, 183 mg, 1.26 mmol) in CH_2Cl_2 (1 mL). The mixture was stirred for 2 h at −78 °C, warmed to −20 °C over 3 h, and gave *o*-quinone **59** (162 mg, 66%) as a bright red solid, mp 133−134 °C (EtOAc/hexanes): R_f (30% EtOAc/hexanes) 0.18; ^{1}H NMR (300 MHz) 7.45−7.30 (m, 5H), 5.87 (s, 1H), 3.64 (d, J = 9.9, 1H), 2.54 (dd, J = 5.8, 14.1, 1H), 2.42−2.29 (m, 1H), 2.22−2.13 (m, 1H), 2.09−1.98 (m, 2H), 1.99 (s, 3H), 1.89−1.74 (m, 1H); ^{13}C NMR (75 MHz) 179.6, 177.6, 171.6, 151.1, 141.5, 133.8, 128.8, 128.2, 124.4, 105.0, 98.8, 52.3, 41.7, 34.0, 25.3, 12.2; HRMS m/z 282.1252[34] (calcd for $C_{18}H_{18}O_3$, 282.1256).

In another experiment according to method C, a solution of $Ti(OiPr)_4$ (0.11 mL, 0.37 mmol) and $TiCl_4$ (0.08 mL, 0.74 mmol) in CH_2Cl_2 (1 mL) was added to a solution of quinone **33b** (246 mg, 0.95 mmol) in CH_2Cl_2 (5 mL) followed by a solution of phenylcyclopentene (**46b**, 171 mg, 1.19 mmol) in CH_2Cl_2 (0.5 mL). The reaction was complete in 1 h and gave bicyclic adduct **58** (11 mg, 4%) and *o*-quinone **59** (114 mg, 43%).

Data for **58**: a colorless film; ^{1}H NMR (500 MHz) 7.03−7.16 (m, 5H), 5.51 (s, 1H), 3.81 (d, J = 1.8, 1H), 3.13 (dd, J = 4.3, 8.3, 1H), 2.93 (d, J = 1.8, 1H), 2.22−2.10 (m, 3H), 2.11 (s, 3H), 1.75−1.61 (m, 3H); ^{13}C NMR (125 MHz) 201.3, 190.2, 144.9, 143.3, 132.4, 128.4, 127.1, 126.8, 73.9, 61.5, 57.0, 48.9, 44.1, 34.0, 25.8, 16.2; HRMS m/z 283.1338 (M + 1) [calcd for $C_{18}H_{19}O_3$ (M + 1), 283.1334].

Reaction of 33b with 48b. According to method C, a solution of $TiCl_4$ (0.08 mL, 0.73 mmol) and $Ti(OiPr)_4$ (0.11 mL, 0.37 mmol) in CH_2Cl_2 (2 mL) was added to a solution of quinone **33b** (224 mg, 0.95 mmol) in CH_2Cl_2 (5 mL) at −78 °C folowed by phenylcycloheptene **48b** (217 mg, 1.26 mmol). The reaction was complete in 0.5 h and gave bicyclic adduct **57** (151 mg, 51%) as a white solid, mp 181−182 °C (EtOAc/hexanes): R_f (30% EtOAc/hexanes) 0.49; ^{1}H NMR (500 MHz) 7.32 (apparent t, J = 7.3, 2H), 7.26−7.24 (m, 2H), 7.19 (apparent t, J = 7.3, 1H), 5.46 (s, 1H), 3.69 (d, J = 2.4, 1H), 3.04 (dd, J = 4.5, 12.5, 1H), 2.80 (d, J = 2.3, 1H), 2.14−2.00 (m, 3H), 2.08 (s, 3H), 1.91−1.83 (m, 1H), 1.75−1.68 (m, 1H), 1.59−1.55 (m, 1H), 1.54−1.46 (m, 1H), 1.41−1.35 (m, 1H), 1.26−1.18 (m, 1H), 0.95−0.89 (m, 1H); ^{13}C NMR (125 MHz) 199.4, 190.2, 144.7, 142.2, 132.8, 128.2, 126.5, 77.4, 62.8, 51.9, 46.6, 40.6, 35.0, 29.7, 27.5, 24.6, 16.2. Anal. Calcd for $C_{20}H_{22}O_3$: C, 77.38; H, 7.16. Found: C, 77.30; H, 7.40.

Reaction of 9b with 1-Methylcyclohexene. $TiCl_4$ (0.083 mL, 0.29 mmol) was added to a solution of quinone **9b** (40 mg, 0.29 mmol) in CH_2Cl_2 (2 mL) at −78 °C and the mixture stirred for 1 h. 1-Methylcyclohexene (0.083 mL, 0.7 mmol) was added dropwise and the mixture allowed to warm to room temperature over 12 h. The mixture was poured into saturated ammonium chloride and the aqueous layer separated and extracted with CH_2Cl_2. The extracts were combined, washed with water, dried (Na_2SO_4), and concentrated. Chromatography of the residue gave **63** (32.5 mg, 48.3%, in fact 96.6% based on quinone **9b**) as a yellow oil: R_f (3:7 EtOAc/hexanes) 0.37; ^{1}H NMR (300 MHz) 6.88 (s, 1H), 6.44 (s, 1H), 5.61 (t, 1H, J = 4), 5.27 (br s, 1H), 3.85 (s, 3H), 2.4−1.1 (m, 6H), 1.38 (s, 3H); ^{13}C NMR (75 MHz) 153.8, 147.6, 142.0, 139.9, 117.8, 114.4, 106.2, 95.0, 87.0, 56.1, 33.0, 24.7, 23.6, 19.0; HRMS m/z 232.1099 (calcd for $C_{14}H_{16}O_3$, 232.1099).

A mixture of compound **63** (25 mg, 0.107 mmol) and 10% Pd/C (10 mg) in EtOAc (3 mL) was placed under an atmosphere (via balloon) of H_2 for 2 h. Filtration of the mixture through Celite, concentration, and chromatography of the residue gave **62** (20 mg, 79%) as an oil: R_f (3:7 EtOAc: hexanes) 0.42; ^{1}H NMR (300 MHz) 6.69 (s, 1H), 6.40 (s, 1H), 5.25 (br s, 1H), 3.83 (s, 3H), 3.05 (dd, 1H, J = 5.5), 1.9−1.2 (m, 8H), 1.48 (s, 3H); ^{13}C NMR (75 MHz) 151.8, 145.8, 139.3, 123.5, 109.5, 95.00, 88.70, 56.2, 46.9, 33.8, 26.0, 25.5, 21.8, 20.8; HRMS m/z 234.1261 (calcd for $C_{14}H_{18}O_3$, 234.1256). The stereochemistry of the ring juncture was confirmed by an ^{1}H−^{1}H NOE experiment; irradiation of the angular CH_3 gave an 8% enhancement of the angular methine signal.

$TiCl_4$ (0.009 mL, 0.082 mmol) was added to a solution of quinone **9b** (12 mg, 0.085 mmol) in CH_2Cl_2 (0.8 mL) at −78 °C followed after 1 h by a solution of **62** (20 mg, 0.085 mmol) in CH_2Cl_2 (0.5 mL). The mixture was allowed to warm to room temperature over 10 h and saturated aqueous ammonium chloride added. The mixture was extracted with CH_2Cl_2, and the extracts were washed with water, dried (Na_2SO_4), and concentrated. Chromatography of the residue gave compound **63** (18.5 mg, 93%) as a yellow oil.

Reaction of 9b with Styrene. According to method B, $TiCl_4$ (0.08 mL, 0.73 mmol) was added to a solution of quinone **9b** (100 mg, 0.73 mmol) in CH_2Cl_2 (5 mL) followed by styrene (0.252 mL, 2.2 mmol). The reaction was complete in 3 h and gave quinone **65** (113 mg, 56%) as a yellow solid, mp 138−139 °C (50% CH_2Cl_2/hexanes): R_f (30% EtOAc/hexanes) 0.29; ^{1}H NMR (300 MHz) 3.09 (dd, J = 9, 14, 1H), 3.20 (dd, J = 5, 14, 1H) 3.83 (s, 3H), 5.13 (dd, J = 5, 9, 1H), 5.94 (s, 1H), 6.55 (s, 1H), 7.2−7.5 (m, 5H); ^{13}C NMR (75 MHz) 40.4, 56.3, 60.7, 107.6, 126.8, 128.7, 128.8, 133.3, 140.6, 145.0, 158.8, 181.8, 186.9; HRMS m/z 276.0567 (calcd for $C_{15}H_{13}O_3Cl$, 276.0552).

Acetic acid (2.5 mL) was added to a mixture of zinc dust (22 mg, 0.34 mmol) and quinone **65** (32 mg, 0.114 mmol) in dry THF (0.5 mL) and the mixture stirred for 1 h at room temperature. Saturated aqueous $NaHCO_3$ was added, and the aqueous layer was separated and extracted with CH_2Cl_2 (3 × 50 mL). The organic extracts were combined, dried (Na_2SO_4), and concentrated. Chromatography of the residue gave 6-methoxy-2-phenyl-2,3-dihydrobenzofuran-5-ol (16 mg, 56%) as tan needles, mp 109−110 °C (CH_2Cl_2/hexanes): R_f (30% EtOAc/hexanes) 0.28; ^{1}H NMR ($CDCl_3$/DMSO-d_6, 300 MHz) 3.24 (d, J = 7, 2H), 3.77 (s, 3H), 5.26 (dd, J = 7, 7, 1H), 6.45 (s, 1H), 6.52 (s, 1H), 7.2−7.4 (m, 5H); ^{13}C NMR ($CDCl_3$/CD_3COCD_3, 75 MHz) 40.7, 55.7, 62.9, 99.9, 114.0, 116.8, 126.9, 127.9, 128.2, 138.5, 141.6, 145.7, 147.6; HRMS m/z 242.0937 (calcd for $C_{15}H_{14}O_3$, 242.0942).

Reaction of 9b with Methylenecyclohexane. According to method B, $TiCl_4$ (0.08 mL, 0.73 mmol) was added to a solution of quinone **9b** (100 mg, 0.72 mmol) in CH_2Cl_2 (10 mL) at −40 °C followed by methylenecyclohexane (0.25 mL, 2.2 mmol). The mixture was warmed to −20 °C and stirred 20 h. Workup and chromatography gave quinone **67** (59 mg, 35%) as a yellow solid, mp 105−107 °C (30% EtOAc/hexanes): R_f (30% EtOAc/hexanes) 0.36; ^{1}H NMR (300 MHz) 1.55−1.90 (m, 10H), 2.93 (s, 2H), 3.83 (s, 3H), 5.96 (s, 1H), 6.84 (s, 1H); ^{13}C NMR (75 MHz) 22.0, 25.0, 40.0, 42.4, 56.3, 74.6, 107.5, 134.8, 144.5, 158.5, 181.4, 187.3; HRMS m/z 268.0873 (calcd for $C_{14}H_{17}O_3Cl$, 268.0865).

Rearrangement Reactions of the Cyclobutanes. A. Base-Promoted Rearrangements of 14f/24f and 35a/36. A solution of cyclobutane **14f** (92 mg, 0.36 mmol) in CH_3OH (2 mL) under N_2 was treated with a solution of K_2CO_3 (150 mg) in CH_3OH/H_2O (2:1, 3 mL). The mixture was stirred for 2 h at room temperature, poured into saturated aqueous NH_4Cl, and extracted with CH_2Cl_2 (3 × 25 mL). The extracts were dried (Na_2SO_4) and concentrated. Chromatography of the residue with 40% EtOAc/hexanes as eluent gave hydroquinone **41a** (50 mg, 54%) as a yellow oil: R_f (50% EtOAc/hexanes) 0.49; ^{1}H NMR (300 MHz) 1.54 (d, J = 6.8, 3H), 3.28 (dq, J = 6.8, 2.2, 1H), 3.79 (s, 3H), 4.10 (d, J = 2.2, 1H), 4.80 (br s, 1H), 5.28 (br s, 1H), 6.34 (s, 1H), 7.18−7.25 (m, 2H), 7.25−7.35 (m, 3H); ^{13}C NMR (75 MHz) 18.8, 46.3, 53.5, 56.3, 100.3, 123.5,

(34) Budzikiewicz, H.; Djerassi, C.; Williams, D. H. *Mass Spectrometry of Organic Compounds*; Holden-Day: San Francisco, 1967; p 118.

126.4, 126.8, 128.2, 128.4, 134.9, 141.6, 143.4, 146.9; HRMS m/z 256.1101 (calcd for $C_{16}H_{16}O_3$, 256.1099).

In a similar manner, treatment of **24f** (60 mg) with K_2CO_3/MeOH (33 mg in 4 mL) gave **41a** (41 mg, 68%).

DBN (0.5 mL, 4.1 mmol) was added to a solution of cyclobutane **35a** (51.5 mg, 0.131 mmol) in THF (2 mL) at room temperature. After 5 h, the dark green mixture was poured into saturated aqueous NH_4Cl (15 mL) and extracted with CH_2Cl_2 (4 × 10 mL). The combined extracts were washed with water (20 mL) and saturated NaCl (20 mL), dried (Na_2SO_4), filtered, and concentrated. Chromatography (40% EtOAc/hexanes) of the residue afforded hydroquinone **41b** (33 mg, 64%) as a yellow oil which crystallized from CH_2Cl_2 as yellow needles, mp 142–143 °C; R_f (40% EtOAc/hexanes) 0.27; ^{1}H NMR (300 MHz) 1.53 (d, J = 7, 3H), 3.27 (dq, J = 2, 7, 1H) 3.82 (s, 3H), 3.83 (s, 3H), 4.06 (d, J = 2, H), 4.80 (b s, D_2O exchange), 5.00 (s, 2H), 5.30 (s, D_2O exchange), 6.40 (s, 1H), 6.75–6.90 (m, 3H), 7.32–7.40 (m, 5H); ^{13}C NMR (75 MHz) 18.6, 46.2, 53.2, 55.8, 55.9, 71.7, 101.7, 110.5, 111.2, 118.7, 124.1, 127.8, 128.3, 128.5, 128.7, 134.4, 135.2, 136.5, 143.4, 146.0, 147.5, 148.9; IR (CCl_4) 3610, 3560, 3450; HRMS m/z 392.1630 (calcd for $C_{24}H_{24}O_5$, 392.1622).

In an identical manner, treatment of **36** (23 mg, 0.059 mmol) with DBN (0.004 mL, 0.032 mmol) produced **41b** (22.6 mg, 98%).

B. Acid-Catalyzed Rearrangements. Reactions of **14d–g**, **15d, 19, 24f, 35a**, and **36** were conducted in a similar manner, and one representative experimental procedure is given. Thus, a solution of **35a** (71 mg, 0.18 mmol) in CH_2Cl_2 (5 mL) was treated with four drops of concentrated H_2SO_4. The reaction was stirred for 5 min at room temperature and poured into saturated aqueous $NaHCO_3$ (10 mL), and the resultant mixture was extracted with CH_2Cl_2 (3 × 30 mL). The combined extracts were washed with water and saturated aqueous NaCl, dried ($NaSO_4$), and concentrated. Chromatography of the residue with 30% EtOAc/hexanes as eluant gave **34a** (60 mg, 85%) as previously identified.

The cis isomers of the dihydrobenzofuran products **11d–g** and **12d** were identified by ^{1}H NMR (300 MHz) signals at 0.67–0.75 (d, J = 7, 3H) and 5.67–5.9 (d, J = 8–9, 1H).

Rearrangement of 39 to 40. An acetone solution (20 mL) of **17f** (395 mg, 1.5 mmol), K_2CO_3 (0.4 g, 3.0 mmol), and CH_3I (2 mL, 30.9 mmol) was stirred at room temperature overnight. The reaction mixture was poured into saturated aqueous $NaHCO_3$ and the aqueous layer separated and extracted with ether (3 × 50 mL). The ether layers were combined, dried (Na_2SO_4), and concentrated to give **39** (328 mg, 81%) as an oil which crystallized from ether/hexanes as white needles, mp 112.5–113 °C: R_f (30% EtOAc/hexanes) 0.38; ^{1}H NMR (300 MHz) 1.24 (d, J = 7, 3H), 2.15 (s, 3H), 2.57 (dq, J =6, 7, 1H) 2.83 (d, J = 2, 1H), 3.23 (dd, J = 6, 6, 1H), 3.53 (s, 3H), 3.70 (dd, J = 2.7, 1H), 7.09 (d, J = 8, 2H), 7.2–7.4 (m, 3H); ^{13}C NMR (75 MHz) 16.8, 21.6, 40.8, 49.7, 59.3, 60.7, 70.8, 127.2, 128.1, 128.4, 137.5, 147.4, 150.3, 190.2, 199.5; HRMS m/z 270.1264 (calcd for $C_{19}H_{24}O_4$, 270.1255).

A solution of **39** (80 mg, 0.296 mmol), concentrated H_2SO_4 (0.016 mL, 0.30 mmol), and glacial acetic acid (0.169 mL, 2.95 mmol) was stirred for 24 h at room temperature and then poured into saturated aqueous $NaHCO_3$. The aqueous layer was separated and extracted with CH_2Cl_2 (3 × 50 mL). The extracts were dried (Na_2SO_4) and concentrated. Chromatography of the residue with 20% EtOAc/hexanes and 30% EtOAc/hexanes as eluents gave a 6:1 mixture (23 mg, 29%) of **40** and its cis isomer and recovered **39** (32 mg, 40%).

Data for **40**: a yellow oil; R_f (30% EtOAc) 0.46; ^{1}H NMR (500 MHz) 1.42 (d, J = 7, 3H), 2.20 (s, 3H), 3.34 (dq, J = 5, 7, 1H), 3.73 (s, 3H), 5.19 (d, J = 5, 1H), 5.64 (s, 1H), 6.41 (s, 1H), 7.34 (s, 5H); ^{13}C NMR (75 MHz) 12.4, 20.0, 45.4, 61.1, 91.8, 95.0, 121.3, 125.4, 126.2, 127.9, 128.6, 139.6, 142.0, 148.9, 155.4; HRMS m/z 270.1256 (calcd for $C_{17}H_{18}O_3$, 270.1256). Additional signals consistent with the cis isomer of **40** are ^{1}H NMR (300 MHz) 0.70 (d, J = 7, 3H), 5.70 (d, J = 8, 1H).

Rocaglamide Model Study: Synthesis of Dihydrobenzofuran 70. $TiCl_4$ (0.88 mL, 8.03 mmol) was added dropwise to a solution of $(TiOiPr)_4$ (1.18 mL, 3.99 mmol) in CH_2Cl_2 (5 mL) at 0 °C. After 5 min, the mixture was added to a solution of 2,6-dimethoxy-1,4-benzoquinone (**69**, 1.01 g, 6.00 mmol) in CH_2Cl_2 (10 mL) at −78 °C followed by a solution of arylcyclopentene **46a** (1.05 g, 6.01 mmol) in CH_2Cl_2 (3mL). After 1.5 h, solid $NaHCO_3$ (3.5 g) and 2-propanol (6 mL) were added, the mixture was diluted with water (30 mL) and filtered through Celite. The aqueous layer was separated and extracted with CH_2Cl_2 (3 × 45 mL), and the combined extracts were washed with brine (100 mL), dried (Na_2SO_4), and concentrated. Chromatography of the residue with 20% EtOAc/hexanes as eluent furnished dihydrobenzofuran **70** as a tan solid (1.20 g, 58%), mp 114–115 °C (white needles from EtOAc/hexanes): R_f (30% EtOAc/hexanes) 0.28; ^{1}H NMR (300 MHz) 7.37 (d, J = 8.8, 2H), 6.87 (d, J = 8.8, 2H), 6.24 (s, 1H), 5.08 (s, 1H), 3.93 (s, 3H), 3.85 (buried d, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 2.36 (dd, J = 5.8, 14, 1H), 2.21–1.96 (m, 3H), 1.92–1.83 (m, 1H), 1.75 (apparent nonet, J = 6.2, 1H); ^{13}C NMR (75 MHz) 158.7, 152.9, 147.5, 143.2, 137.2, 131.5, 125.8, 113.6, 113.1, 100.2, 88.7, 59.9, 56.3, 55.2, 53.8, 42.4, 35.1, 25.1. Anal. Calcd for $C_{20}H_{22}O_5$: C, 70.15; H, 6.49. Found: C, 69.95; H, 6.49.

Synthesis of Triflate 71. Pyridine (0.35 mL, 4.38 mmol) was added to a solution of dihydrobenzofuran **70** (506 mg, 1.48 mmol) in CH_2Cl_2 (4 mL) at −78 °C. The mixture was stirred for 30 min, and trifluoromethanesulfonic anhydride (0.49 mL, 2.92 mmol) was added dropwise. The reaction mixture was stirred for 1 h at −78 °C; the dry ice bath was then removed and the mixture stirred an additional 1 h. Cold aqueous 10% HCl (20 mL) was added, and the aqueous layer was separated and extracted with CH_2Cl_2 (2 × 30 mL). The organic extracts were combined, washed with saturated aqueous $NaHCO_3$ (40 mL), water (50 mL), and brine (50 mL), and dried (Na_2SO_4). Concentration and chromatography (10% and then 20% EtOAc/hexanes) afforded the triflate as a clear, colorless oil. The product crystallized upon refrigeration to give **71** as a white solid (679 mg, 97%), mp 84–86 °C (EtOAc/hexanes): R_f (30% EtOAc/hexanes) 0.49; ^{1}H NMR (300 MHz) 7.36 (d, J = 8.7, 2H), 6.89 (d, J = 8.7, 2H), 6.23 (s, 1H), 3.93 (buried d, 1H), 3.92 (s, 3H), 3.84 (s, 3H), 3.80 (s, 3H), 2.39 (dd, J = 5.8, 13.6, 1H), 2.21–1.96 (m, 3H), 1.95–1.84 (m, 1H), 1.74 (apparent nonet, J = 6.2, 1H); ^{13}C NMR (300 MHz) 160.2, 158.9, 152.7, 149.2, 136.2, 125.7, 124.6, 118.7 (q, J = 319), 113.8, 112.1, 101.5, 88.8, 59.7, 56.2, 55.3, 53.7, 42.4, 35.2, 25.1; HRMS m/z 474.0965 (calcd for $C_{21}H_{21}F_3O_7S$, 474.0960).

Synthesis of 72. To a solution of triflate **71** (679 mg, 1.43 mmol) in DMF (5 mL) under argon were added palladium(II) acetate trimer (207 mg, 0.31 mmol), 1,1′-bis(diphenylphosphino)ferrocene (411 mg, 0.75 mmol), Et_3N (3.99 mL, 28.6 mmol), and 98–100% formic acid (1.08 mL, 28.6 mmol). The reaction mixture was heated to 78–80 °C for 15 h, cooled to room temperature, and diluted with EtOAc (30 mL) and water (40 mL). The aqueous layer was separated and extracted with EtOAc (8 × 30 mL). The organic extracts were combined, washed with saturated aqueous NH_4Cl (100 mL), water (100 mL), and brine (100 mL), dried (Na_2SO_4), and concentrated. Chromatography of the residue (10% and then 20% EtOAc/hexanes) afforded **72** as a clear, colorless oil (389 mg, 83%): R_f (30% EtOAc/hexanes) 0.53; ^{1}H NMR (500 MHz) 7.37 (d, J = 8.8, 2H), 6.85 (d, J = 8.8, 2H), 6.08 (d, J = 1.8, 1H), 5.99 (d, J =1.9, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 3.76 (s, 3H), 2.38 (dd, J = 5.7, 13.6, 1H), 2.08–1.97 (m, 3H), 1.87–1.82 (m, 1H), 1.76–1.66 (apparent nonet, J = 6.2, 1H) [a proton doublet is buried under the methoxy group signals]; ^{13}C NMR (125 MHz) 161.6, 161.5, 158.6, 156.4, 137.2, 125.8, 113.6, 109.8, 101.2, 91.0, 85.5, 55.4, 55.3, 55.2, 52.5, 42.4, 34.2, 25.2; HRMS m/z 326.1515 (calcd for $C_{20}H_{22}O_4$, 326.1517).

Preparation of (±)-Kadsurenone: Synthesis of Triflate 73. Pyridine (0.62 mL, 7.67 mmol) was added to a solution of dihydrobenzofuran **34a** (1.0 g, 2.55 mmol) in CH_2Cl_2 (10 mL) at −78 °C, and the mixture was stirred for 30 min. Trifluoromethanesulfonic anhydride (0.60 mL, 3.57 mmol) was added dropwise, and the yellow mixture was stirred at −78 °C for 1 h and then warmed to room temperature. The reaction mixture was poured into cold 10% aqueous HCl (25 mL), the layers were separated, and the acid layer was extracted with CH_2Cl_2 (2 × 20 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (20 mL), water (2 × 20 mL), and brine (20 mL) and dried (Na_2SO_4). Concentration of the solution and chromatography of the residue (30%

EtOAc/hexanes) gave **73** (1.29 g, 96%) as a clear oil: R_f (30% EtOAc/hexanes) 0.31 (UV active, deep red under *p*-anisaldehyde stain); ^{1}H NMR (300 MHz), 1.38 (d, J = 7, 3H), 3.41 (m, 1H), 3.88 (s, 3H)), 3.89 (s, 3H), 5.12 (d, J = 10, 1H), 5.14 (s, 2H), 6.59 (s, 1H), 6.86–6.96 (m, 3H), 7.30–7.42 (m, 5H); ^{13}C NMR (75 MHz) 17.4 (q), 44.5 (d), 55.8 (q) 71.1 (t), 77.1 (q), 93.9 (d), 96.7 (d), 108.9 (d), 110.8 (d), 117.2 (d), 118.8 (d), 123.7 (s), 127.1 (d), 128.0 (d), 128.4 (d), 131.8 (s), 132.7 (s), 135.5 (s), 149.1, 149.2, 150.8, 158.8 (CF_3 is buried); HRMS m/z 524.1116 (calcd for $C_{25}H_{23}F_3O_7S$, 524.1115).

Synthesis of Dihydrobenzofuran 74. A dry 10-mL flask was charged with triflate **73** (413 mg, 0.788 mmol), allyltri-*n*-butylstannane (0.30 mL, 0.972 mmol) and DMF (2 mL). LiCl (125 mg, 2.95 mmol) and $Pd(PPh_3)_4$ (25 mg, 0.022 mmol) were added, and the mixture was heated to 100 °C. After 2 h, the mixture was cooled and poured into a mixture of 10% aqueous NH_4OH (25 mL) and ether/benzene (1:1, 50 mL). The layers were separated, and the aqueous phase was extracted with Et_2O/benzene (1:1, 4 × 25 mL). The combined extracts were washed with water (4 × 25 mL) and brine (2 × 25 mL), dried (Na_2SO_4), and concentrated. Chromatography (25% EtOAc/hexanes) yielded **74** (320 mg, 98%) as a pale oil. Crystallization from EtOH gave white needles, mp 90–92 °C: R_f (25% EtOAc/hexanes) 0.33 (UV active, purple under *p*-anisaldehyde stain); ^{1}H NMR (300 MHz) 1.36 (d, J = 7, 3H), 3.40 (m, 3H), 3.86 (s, 3H), 3.89 (s, 3H), 5.00–5.10 (m, 2H), 5.50 (s, 2H), 5.55 (d, J = 9, 1H), 6.01 (m, 1H), 6.51 (s, 1H), 6.86–6.95 (m, 4H), 7.25–7.45 (m, 5H); ^{13}C NMR (75 MHz) 18.3 (q), 34.8 (t), 45.4 (d), 56.3 (q), 70.7 (t), 93.8 (d), 95.5 (d), 109.6 (d), 111.4 (d), 115.5 (t), 119.3 (d), 121.4 (s), 123.8 (s), 124.6 (d), 127.5 (d), 128.2 (d), 129.0 (d), 133.5 (s), 137.7 (s), 138.0 (d), 149.5 (s), 149.7 (s), 157.0 (s), 159.0 (s). Anal. Calcd for $C_{27}H_{28}O_4$: C, 77.86; H, 6.78. Found: C, 77.59; H, 6.84.

Debenzylation of 74. $BF_3{\cdot}Et_2O$ (0.4 mL, 3.25 mmol) was added dropwise over 5 min to a solution of **112** (340 mg, 0.817 mmol) in CH_2Cl_2 (2mL) and SMe_2 (2 mL). After stirring at room temperature for 4 h, the reaction mixture was treated with additional $BF_3{\cdot}Et_2O$ (0.2 mL, 1.63 mmol) and stirred for another 6 h. Water (5 mL) was added, the mixture was stirred 20 min, and the two layers were separated. The water layer was extracted with CH_2Cl_2 (3 × 15 mL), and the combined organic layers were washed with water (10 mL) and saturated aqueous $NaHCO_3$ (10 mL), dried (Na_2SO_4), and concentrated. Chromatography (25% EtOAc/hexanes) gave dihydrobenzofuranol **5** (179 mg, 67%) as a clear oil which solidified on standing. Recrystallization from MeOH gave white needles, mp 101–102.5 °C (lit.[12b,c] mp 98–99 °C): R_f (30% EtOAc/hexanes) 0.23; ^{1}H NMR (300 MHz)[35] 1.36 (d, J = 7, 3H), 3.36 (m, 1H), 3.40 (d, J = 6, 2H), 3.88 (s, 3H), 3.89 (s, 3H), 4.97 (s, 1H), 5.05 (d, J = 9, 1H), 5.11–5.21 (m, 2H), 6.01 (m, 1H), 6.39 (s, 1H), 6.84–6.96 (m, 4H); ^{13}C NMR (75 MHz) 17.9, 35.0, 44.9, 55.8, 55.9, 93.4, 98.0, 109.2, 110.9, 116.1, 117.2, 118.9, 124.1, 124.6, 133.0, 137.0, 149.0, 149.2, 154.3, 158.9; HRMS m/z 326.1515 (calcd for $C_{20}H_{22}O_4$, 326.1517).

Oxidation of 5.[12b,c] A solution of **5** (30 mg, 0.092 mmol) in anhydrous CH_3OH (2 mL) was added to a flask containing lead(IV) acetate (58 mg, 0.131 mmol). The solution immediately became yellow. After 7.5 h, the CH_3OH was removed under vacuum, and the residue was taken up in ether (30 mL) and washed with water (3 × 10 mL) and saturated aqueous $NaHCO_3$ (10 mL). The mixture was dried (Na_2SO_4) and concentrated. Chromatography (25–50% EtOAc/hexanes) gave three fractions: (1) R_f (30% EtOAc/hexanes) 0.36, 6.2 mg (19%), (±)-denudatin-B (**6b**); (2) R_f (30% EtOAc/hexanes) 0.31, 3.3 mg (10%) (±)-kadsurenone (**6a**); and (3) R_f (50%EtOAc hexanes) 0.23, 17 mg (48%), a mixture of acetoxy epimers **75a/b**: all were identified by comparison of their ^{1}H NMR to spectra those previously reported.[35]

Acknowledgment. Financial support for this research was provided by the National Institutes of Health [GM37003, GM39820, GM07775 (as a predoctoral fellowship to M.A.L.)], the National Science Foundation (CHE-9116576), the Petroleum Research Fund, administered by the American Chemical Society, and the University of Kansas General Research Fund and Biomedical Sciences Support Grant. We thank Dr. Jayachandra Reddy for results of initial experiments involving **8h**, Dr. Sriram Naganathan for initial experiments with methylcyclohexene and styrene, Mr. Bradley Andersh for initial experiments with the α-methylstyrenes and arylcycloalkenes, Dr. Fusao Takusagawa for X-ray structure determinations, Dr. David Vander Velde for help with the NOE experiments, and Dr. Mitree Ponpipom for copies of ^{1}H spectra. T.A.E. also acknowledges an Alfred P. Sloan Foundation Fellowship and an Eli Lilly Granteeship.

Supplementary Material Available: Experimental details for the preparation of propenylbenzenes **8b,d–g, 23c/d,f, 42a,** and **46–48** and quinones **9b/c, 32, 33,** and **69**; IR, mass, and selected UV spectral data on new compounds; ^{1}H and ^{13}C NMR spectra of all new compounds for which C,H,N elemental analyses were not obtained; ORTEP drawings of **17f** and **35a** (108 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information. The authors have deposited the crystallographic data and atomic coordinates for **17f** and **35a** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

(35) We thank Dr. M. Ponpipom for providing spectra of **5, 6a/b,** and **75a/b.**