Synthesis of 2,3-Dihydrobenzofurans by $Mn(OAc)_3$-Based Oxidative Cycloaddition of 2-Cyclohexenones with Alkenes. Synthesis of (±)-Conocarpan

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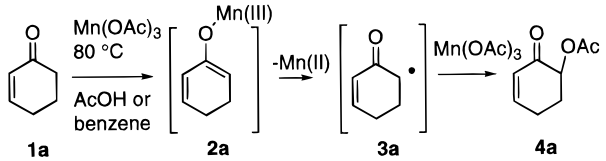
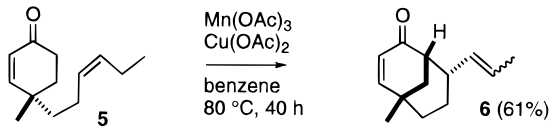
Oxidative cycloaddition of a 2-cyclohexenone or α-tetralone and an alkene with dried $Mn(OAc)_3$ in benzene at 80−140 °C provides a general route to dihydrobenzofurans **15** and dihydronaphthofurans **17**. Although the yields are modest, this one-pot reaction provides simple access to these compounds, which have previously been prepared by multistep routes. Oxidative cycloaddition of 2-cyclohexenones with β-methylstyrenes provides a new route to benzofuranoid neolignans, which was applied to the synthesis of conocarpan (**22**). The formation of 2-acetoxyhexanedioic acids **27** and **47** from acetoxylation of 2-cyclohexenones in HOAc, but not in benzene, opens up a new class of $Mn(OAc)_3$ reactions and explains Watt and Demir's discovery that much higher yields of α′-acetoxy enones are obtained in benzene than in HOAc.

In 1976, Williams and Hunter reported that $Mn(OAc)_3 \cdot 2H_2O$ oxidation of enones in HOAc at reflux affords 6−35% of α′-acetoxy enones.[1,2] In a series of papers initiated in 1984, Watt, Demir, and co-workers reported that using $Mn(OAc)_3$ dried over P_2O_5 in benzene at reflux for 1 h to 2 d improves the yields of α′-acetoxylation to 50−90%.[3] These reactions proceed by kinetic enolization of 2-cyclohexenone (**1a**) to give Mn(III) enolate **2a**, which loses Mn(II) to give α′-keto radical **3a**, which is oxidized by a second equivalent of $Mn(OAc)_3$ to give α′-acetoxy enone **4a**. No explanation was provided for the vastly improved yields obtained in benzene.



We found that intramolecular trapping of the α′-keto radicals obtained from cyclohexenones by suitably situated double bonds is much faster than acetoxylation, affording good yields of bicyclic dienones in favorable cases.[4] For instance, oxidative cyclization of **5** with 5 equiv of $Mn(OAc)_3$ and 1 equiv of $Cu(OAc)_2$ in benzene at reflux for 40 h affords 61% of **6** as a 3.4:1 *E*/*Z* mixture. We therefore decided to examine the intermolecular reactions of cyclohexenones and alkenes.



Results and Discussion

Oxidative Cycloadditions in Benzene. To our surprise, we found that oxidative addition of 2-cyclohexenones **1a**−**e** with methylenecyclohexane (**7a**) in benzene at 80 °C for 3 d using $Mn(OAc)_3$ dried over P_2O_5 in vacuum as described by Watt affords 25−42% of dihydrobenzofurans **15aa**−**ea** and 0−18% of 6-(1-cyclohexenylmethyl)-2-cyclohexenones **12aa**−**ea** (the first letter corresponds to the 2-cyclohexenone (**1a**−**g**) and the second to the alkene **7a**−**c** or **19ab**). Grisan (**15aa**), so named because it contains the griseofulvin skeleton, has been prepared twice by multistep routes[5] and is now available in a single step. No monomeric products are formed from **1a** and 1-octene under these reaction conditions.

The following mechanistic scheme is consistent with these results. Oxidation of cyclohexenone **1** will form α′-keto radical **3**. Addition of radical **3** to methylenecyclohexane (**7a**) will give radical **8**, which is tertiary and is therefore readily oxidized by $Mn(OAc)_3$ to cation **11**.[2] Loss of a proton from cation **11** will give 2-alkenyl-2-cyclohexenone **12**. Cyclization of **11** will give bicyclic cation **10**. Loss of a proton from **10** will give tetrahydrobenzofuran **9** or a double bond position isomer. Electron-rich double bonds are oxidized to radical cations by $Mn(OAc)_3$.[6] Therefore dienyl ether **9** should be oxidized to cation radical **13**, which should lose a proton to give radical **14**. Further oxidation will give a cation that will lose a proton to give dihydrobenzofuran **15**. We confirmed that tetrahydrobenzofurans are oxidized to dihydrobenzofurans **15** by $Mn(OAc)_3$. Birch reduction[7] of 2,3-dihydro-3,3-dimethylbenzofuran (**15ac**)[8] with Li in NH_3, EtOH, and ether provides >90% of 2,3,4,7-tetrahydro-3,3-dimethylbenzofuran. Oxidation of the tetrahydrobenzofuran with $Mn(OAc)_3$ in benzene at 80 °C for 12 h affords **15ac**[6] in good yield, thereby establishing that

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(1) Williams, G. J.; Hunter, N. R. *Can. J. Chem.* **1976**, *54*, 3830.

(2) For reviews of $Mn(OAc)_3$ as an oxidant, see: (a) Snider, B. B. *Chem. Rev.* **1996**, *96*, 339. (b) Melikyan, G. G. In *Organic Reactions*; Paquette, L. A., Ed.; Wiley: New York, 1997; Vol. 49, Chapter 3.

(3) (a) Dunlap, N. K.; Sabol, M. R.; Watt, D. S. *Tetrahedron Lett.* **1984**, *25*, 5839. (b) Demir, A. S.; Jeganathan, A.; Watt, D. S. *J. Org. Chem.* **1989**, *54*, 4020. (c) Demir, A. S.; Jeganathan, A. *Synthesis* **1992**, 235.

(4) Snider, B. B.; Kiselgof, E. Y. *Tetrahedron* **1996**, *52*, 6073.

(5) (a) Antus, S.; Baitz-Gács, E.; Snatzke, G.; Vas, J. *Tetrahedron* **1986**, *42*, 5637. (b) Kaufman, T. S.; Sindelar, R. D. *J. Heterocycl. Chem.* **1989**, *26*, 879.

(6) (a) Fristad, W. E.; Peterson, J. R.; Ernst, A. B.; Urbi, G. B. *Tetrahedron* **1986**, *42*, 3429. (b) Vinogradov, M. G.; Todres, Z. V.; Il'ina, G. P.; Rutavichus, A. I.; Kursanov, D. N.; Nikishin, G. I. *Bull. Acad. Sci. USSR* **1976**, 1278.

(7) Murai, A.; Sato, S.; Masamune, T. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2286.

(8) Shulgin, A. T.; Baker, A. W. *J. Org. Chem.* **1963**, *28*, 2468.

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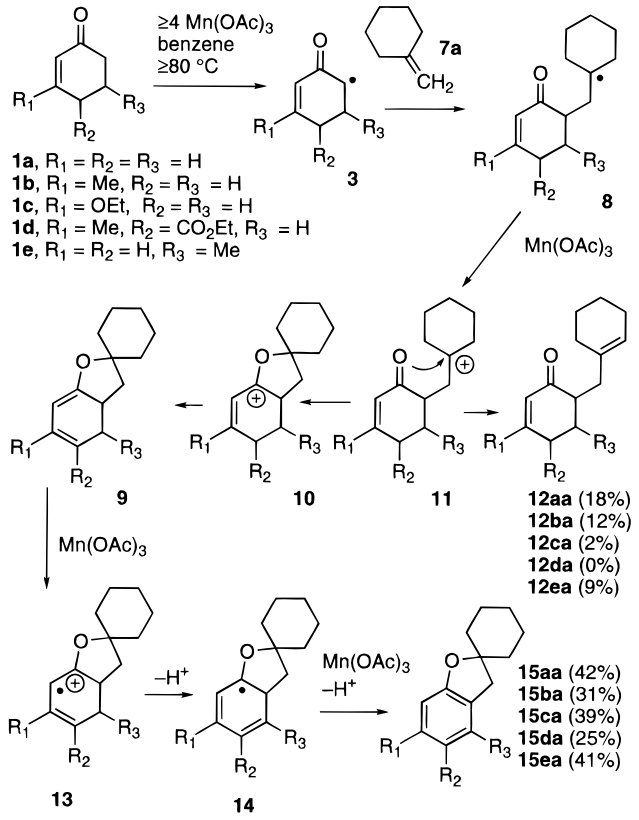
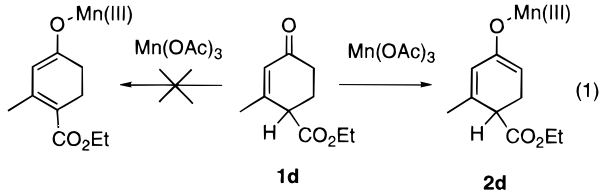


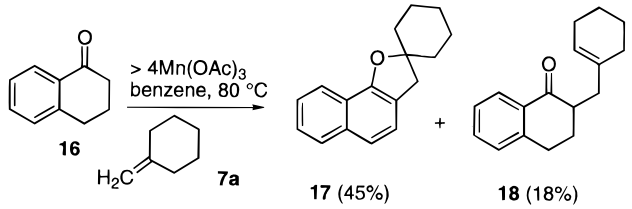
tetrahydrobenzofurans are competent intermediates in the formation of **15** from **1**.

Remarkably, oxidative cycloaddition of Hagemann's ester (**1d**) with **7a** for 3 d affords 25% (50% based on recovered **1d**) of 6-methyldihydrobenzofuran-5-carboxylate **15da** and 0% of alkenyl enone **12da**. The formation of **15da** indicates that loss of the α′-proton occurs despite the fact that the γ-proton is several orders of magnitude more acidic due to the presence of the ester group (see eq 1) and is lost exclusively in all other reactions of **1d**. The selective loss of the α′-proton from **1d** provides clear evidence that Mn(III) enolate **2d** is formed by $Mn(OAc)_3$-assisted kinetic enolization rather than reaction of the enol tautomer with $Mn(OAc)_3$.



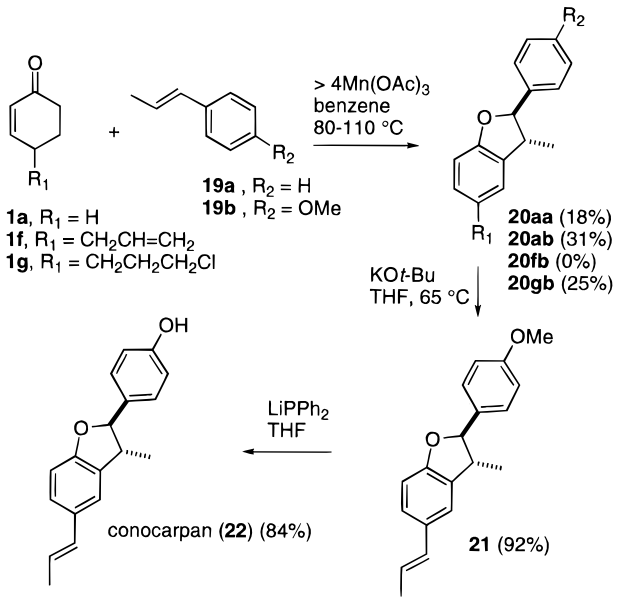
The analogous oxidative cyclization of α-tetralone (**16**) with an alkene should give dihydronaphthofuran **17**. As expected, reaction of α-tetralone (**16**) and methylenecyclohexane (**7a**) in benzene with dried $Mn(OAc)_3$ at 80 °C for 3 d yields the desired dihydronaphthofuran **17a** (45%) and alkenyltetralone **18a** (18%) as the only products, indicating that α-tetralone behaves analogously to cyclohexenones in these oxidative cycloadditions, providing a general route to dihydronaphthofurans.

Synthesis of Dihydrobenzofuran Neolignans. 3-Methyl-2-aryldihydrobenzofuran neolignan natural products possess a wide variety of antibacterial, cytotoxic, antiproliferative, immunosuppressive, and insecticidal activities. For instance, conocarpan (**22**)[9–11] is toxic to the larvae of the European corn borer at 10 μg/mL.[11] These neolignans have been prepared by acid-catalyzed



cycloaddition reactions of styrenes and quinone monoketals, abnormal Claisen rearrangements of phenyl allyl ethers, Lewis acid-catalyzed cycloadditions of benzoquinones with styrenes, oxidative cycloaddition of *p*-methoxyphenols with electron-rich styrenes with PhI(OTFA)$_2$, and Lewis acid-promoted reactions of styrenes with *N*-(phenylsulfonyl)-1,4-benzoquinone monoimines.[12,13]

Oxidative cycloaddition of 2-cyclohexenone (**1a**) with β-methylstyrene (**19a**) in benzene for 3 d at 80 °C affords 18% of the desired 2,3-dihydro-3-methyl-2-phenylbenzofuran (**20aa**)[14] as a 93:7 trans/cis mixture and 2% of cinnamyl acetate. The methyl group in the minor cis isomer of **20aa** is shielded by the phenyl group and resonates at δ 0.81 as compared with δ 1.43 in the major trans isomer of **20aa**; similarly, the methine proton in the minor cis isomer of **20aa** resonates at δ 5.81 as compared with 5.16 in the major trans isomer of **20aa**.[14]



We were concerned about the scope of this reaction with electron-rich β-methylstyrenes because anethole is known to be oxidized to the radical cation by $Mn(OAc)_3$.[6a] Fortunately, oxidative cycloaddition of 2-cyclohexenone (**1a**) with anethole (**19b**) and 4 equiv of dried $Mn(OAc)_3$ in benzene in a sealed tube at 140 °C for 2 d provides

(9) Hayashi, T.; Thomson, R. H. *Phytochemistry* **1975**, *14*, 1085. Oxidative dimerization of *p*-(1*E*)-propenylphenol with $FeCl_3$ affords 20% of conocarpan.

(10) Achenbach, H.; Gross, J.; Dominguez, X. A.; Cano, G.; Verde Star, J.; Del Carmen Brussolo, L.; Muñoz, G.; Salgado, F.; López, L. *Phytochemistry* **1987**, *26*, 1159.

(11) Chauret, D. C.; Bernand, C. B.; Arnason, J. T.; Durst, T.; Krishnamurty, H.; Sanchez-Vindas, P.; Moreno, N.; Roman, L. S.; Poveda, L. *J. Nat. Prod.* **1996**, *59*, 152.

(12) Wang, S.; Gates, B. D.; Swenton, J. S. *J. Org. Chem.* **1991**, *56*, 1979 and references cited therein.

(13) Engler, T. A.; Chai, W. *Tetrahedron Lett.* **1996**, *37*, 6969 and references cited therein.

(14) (a) Schmid, E.; Fráter, Gy.; Hansen, H.-J.; Schmid, H. *Helv. Chim. Acta* **1972**, *55*, 1625. (b) Gregson, M.; Ollis, W. D.; Redman, B. T.; Sutherland, I. O.; Dietrichs, H. H. *J. Chem. Soc., Chem. Commun.* **1968**, 1394. (c) Bowden, B. F.; Ritchie, E.; Taylor, W. C. *Aust. J. Chem.* **1972**, *25*, 2659.

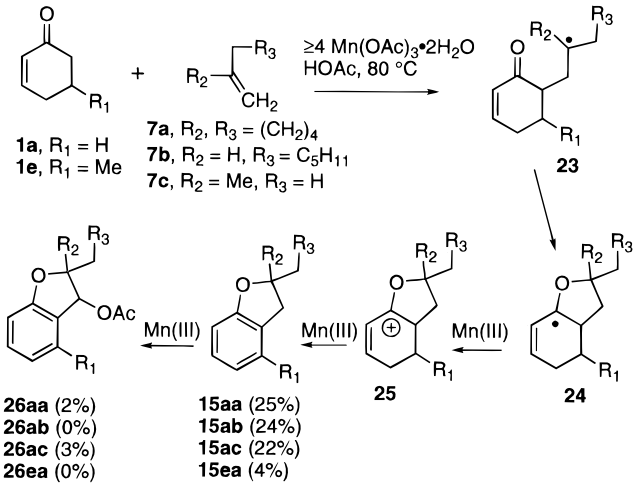
31% of 2,3-dihydro-2-(4-methoxyphenyl)-3-methylbenzofuran (**20ab**) as a 49:1 trans/cis mixture, and only 4% of the cinnamyl acetate, indicating that 2-cyclohexenone is oxidized more rapidly than anethole under these conditions.

We then turned our attention to the preparation of a suitably substituted 2-cyclohexenone for conocarpan synthesis. 4-Allyl-2-cyclohexenone (**1f**)[15] gives a complex mixture of products since addition can occur inter- or intramolecularly to the allyl group.[4] Alkylation of the lithium enolate of 3-ethoxy-2-cyclohexenone with 1-chloro-3-iodopropane in THF containing HMPA followed by LAH reduction of the crude product and hydrolysis with HCl provides 52% of 4-(3-chloropropyl)-2-cyclohexenone (**1g**).[15] Oxidative cycloaddition of **1g** with anethole (**19b**) in benzene at 110 °C for 1.5 d provides 25% of the desired adduct 5-(3-chloropropyl)-2,3-dihydro-2-(4-methoxyphenyl)-3-methylbenzofuran (**20gb**) as a 50:1 trans/cis mixture, 32% of recovered **1g**, and 31% of recovered anethole as the only products. Elimination of HCl from **20gb** with potassium *tert*-butoxide in THF at reflux,[16] followed by evaporation of the THF and further heating to effect conjugation of the double bond,[17] yields 92% of 2,3-dihydro-2-(4-methoxyphenyl)-3-methyl-5-((1*E*)-propenyl)-benzofuran (**21**). Demethylation of **21** with $LiPPh_2$ in THF[18] provides 84% of conocarpan (**22**) with spectral data identical to those reported.[9−11]

Oxidative Cycloadditions in Acetic Acid. Although Watt and Demir obtained much higher yields of α′-acetoxy enones with dried $Mn(OAc)_3$ in benzene than in acetic acid, the reactions are much slower in benzene. Since our intramolecular cyclizations generally proceeded faster and in equally good yield in AcOH, we decided to investigate dihydrobenzofuran formation in AcOH. Oxidation of 2-cyclohexenone (**1a**) as a 0.1−0.2 M solution in HOAc containing 2 equiv of methylenecyclohexane (**7a**) with 4 equiv of $Mn(OAc)_3 \cdot 2H_2O$ at 80 °C for 1 d affords 25% of grisan (**15aa**),[5] 2% of dihydrobenzofuran-3-yl acetate **26aa**, 4% of dihydrobenzofuran-7-yl acetate **33aa**, and traces of 2-(1-cyclohexenylmethyl)-2-cyclohexenone (**38aa**). The yield of **15aa** is much lower in acetic acid than in benzene, no **12aa** is formed, and minor products **26aa**, **33aa**, and **38aa**, which are not formed at all in benzene, are isolated in low yield, indicating that the solvent profoundly influences the course of these radical cyclizations.

The successful oxidative cycloaddition of **1a** with 1-octene (**7b**) in acetic acid, but not in benzene, provides further evidence of significant solvent effects. Oxidation of 2-cyclohexenone (**1a**) with 1.5 equiv of 1-octene (**7b**) and 4 equiv of $Mn(OAc)_3 \cdot 2H_2O$ in AcOH at 80 °C for 1 d affords 24% of 2,3-dihydrobenzofuran (**15ab**), 27% of 6-acetoxy-2-cyclohexenone (**4a**), and a trace of dihydrobenzofuran-7-yl acetate (**33ab**) and 2-(2-octenyl)-2-cyclohexenone (**38ab**). Acetoxy enone **4a** is formed with 1-octene but not with the more nucleophilic methylenecyclohexane (**7a**), which reacts with the electrophilic α′-keto radical **3a** more rapidly than 1-octene does.

Since secondary radicals cannot be oxidized to cations by $Mn(OAc)_3$, the successful oxidative cycloaddition with 1-octene in acetic acid indicates that secondary radical



23ab cyclizes to radical **24ab**, which is then oxidized to cation **25ab**, which reacts to give the dihydrobenzofuran as indicated above for the analogous cation **10**. The conversion of **23** to **25** is well-precedented in the oxidation of secondary γ-carboxy radicals to lactones by $Mn(OAc)_3$.[2] The formation of 6-alkenyl-2-cyclohexenone **12** in much greater yield in benzene than in HOAc is consistent with exclusive oxidation of tertiary radical **8** to cation **11** in benzene, while in HOAc radical **8** (**23**) mainly cyclizes to radical **24** prior to oxidation. The failure to obtain dihydrobenzofuran **15ab** in benzene indicates that either cyclization of radical **23ab** to give radical **24ab** or oxidation of radical **24ab** to provide cation **25ab** does not occur in benzene.

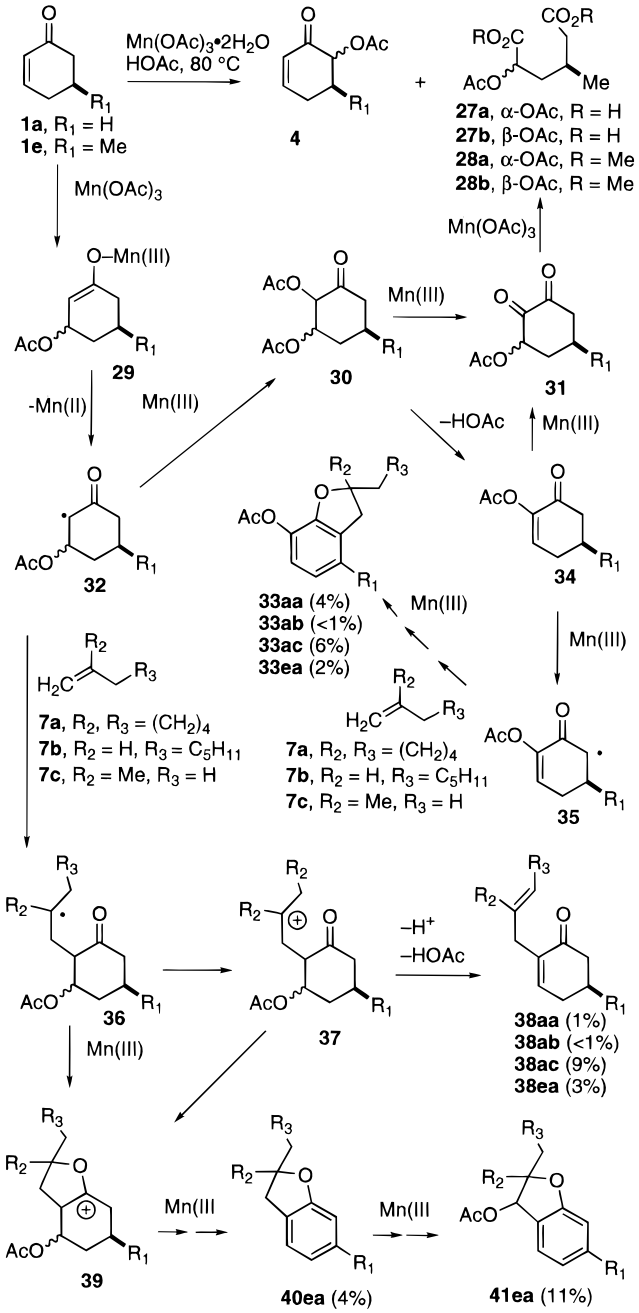
Similar oxidative cycloaddition of 2-cyclohexenone (**1a**) with excess isobutene (**7c**) provides 22% of 2,3-dihydro-2,2-dimethylbenzofuran (**15ac**),[8] 3% of 2,3-dihydro-2,2-dimethylbenzofuran-3-yl acetate (**26ac**),[19] 6% of 2,3-dihydro-2,2-dimethylbenzofuran-7-yl acetate (**33ac**), and 9% of 2-(2-methyl-2-propenyl)-2-cyclohexenone (**38ac**). The structure of **33ac** was confirmed by hydrolysis to the phenol, which is identical to a commercially available sample. Low yields of products are obtained from 1-octene and substituted 2-cyclohexenones **1b**−**e**, and from 2-cyclohexenone (**1a**) and 1-methylcyclohexene. Complex mixtures and polymer are obtained from **7a** and 2-methylcyclopentenone, 3-methylcyclopentenone, mesityl oxide, or 1-acetylcyclohexene, indicating the reaction is synthetically useful only with 2-cyclohexenones that lead to dihydrobenzofurans.

The formation of dihydrobenzofuran-3-yl acetate **26** is easily accounted for by benzylic oxidation of dihydrobenzofuran **15**, which occurs in acetic acid, but not in benzene. As expected, benzylic oxidation of **15aa** with $Mn(OAc)_3 \cdot 2H_2O$ in HOAc at 80 °C for 18 h provides 99% of **26aa**. The mechanism outlined above for the oxidative cycloaddition cannot account for the formation of minor, but significant, amounts of dihydrobenzofuran-7-yl acetate **33** or 2-alkenyl-2-cyclohexenone **38**.

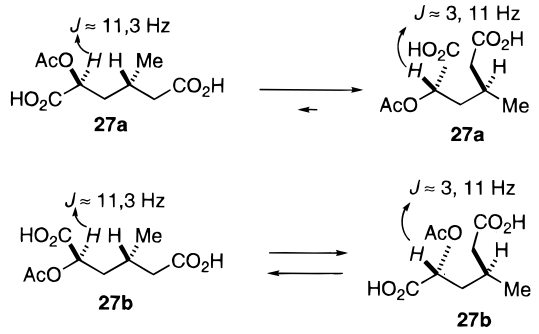
The lack of regioselectivity in the oxidative cycloaddition of 5-methylcyclohexenone (**1e**) with **7a** in acetic acid provides further evidence that the mechanism in acetic acid is much more complicated than in benzene. We obtained an unexpectedly complex mixture of products containing 4% of dihydro-4-methylbenzofuran **15ea**, 2% of dihydro-4-methylbenzofuran-7-yl acetate **33ea**, 3% of **38ea**, along with 4% of dihydro-6-methylbenzofuran **40ea** (**15ba**), which was obtained from 3-methylcyclohexenone

(15) Stork, G.; Danheiser, R. L. *J. Org. Chem.* **1973**, *38*, 1775.
(16) Grethe, G.; Lee, H. T.; Mitt, T.; Uskokovic, M. *Helv. Chim. Acta* **1973**, *56*, 1485.
(17) Thach, L. N.; Hanh, D.-L.; Hiep, N. B.; Radhakrishna, A. S.; Singh, B. B.; Loupy, A. *Synth. Commun.* **1993**, *23*, 1379 and references cited therein.
(18) Ireland, R. E.; Walba, D. M. In *Organic Syntheses*; Noland, W. E., Ed.; Wiley: New York, 1988; Collect. Vol. VI, pp 567−570.
(19) Hurd, C. D.; Dowbenko, R. *J. Am. Chem. Soc.* **1960**, *82*, 3662.

(**1b**) in benzene, and 11% of dihydro-6-methylbenzofuran-3-yl acetate **41ea**. The formation of **40ea** and **41ea** from **1e** indicates that addition of **7a** to **1e** is occurring at both the α- and α′-positions. However, oxidation of 5-methyl-2-cyclohexenone (**1e**) with $Mn(OAc)_3 \cdot 2H_2O$ in HOAc gives 44% of 6-acetoxy-5-methyl-2-cyclohexenone (**4e**) as the only organic soluble product, suggesting incorrectly that enolization at the α′-carbon is the only reaction.



The crucial observation entailed examination of the aqueous layer from the workup of the oxidation of **1e**. Acidification and extraction with EtOAc yields 20% of a 4:1 mixture of 2-acetoxy-4-methylhexanedioic acids (**27a** and **27b**), which was treated with diazomethane to give a 4:1 mixture of dimethyl 2-acetoxy-4-methylhexanedioates (**28a** and **28b**). The stereochemical assignment follows from the absorption of C*H*OAc, which occurs as a dd, $J = 10.5$, 3.5 Hz, in the major isomer and a dd, $J =$ 8.1, 5.5 Hz, in the minor isomer. The more disparate coupling constants of the major diastereomer isomer indicate that it exists in one conformation to a greater extent than the minor diastereomer does. The major diastereomer **27a** should have a single preferred conformation with the larger CO_2H and CH_2CO_2H substituents extended and the smaller acetate and methyl groups offset as shown in the left structure. The minor diastereomer **27b** is a mixture of two conformers so that the two coupling constants are 8.1 and 5.5 Hz. The NMR spectra of the diastereomers of dimethyl 4-(benzyloxy)-2-acetoxyhexanedioate show similar differences.[20] Similarly, oxidation of **1a** affords 22% of **4a** and 21% of 2-acetoxyhexanedioic acid (**47**).



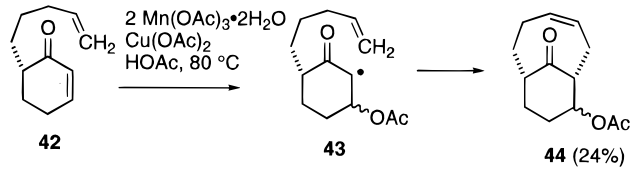
The formation of **27** suggests that **1e** also reacts by conjugate addition of acetate to give Mn(III) enolate **29**. Loss of Mn(II) will give α-keto radical **32**, which can react with $Mn(OAc)_3$ to give 2,3-diacetoxycyclohexanone (**30**). Further oxidation will give acetoxycyclohexanedione (**31**), which will be oxidatively cleaved to give diacid **27**. Alternatively, elimination of an acetate from **30** will give 2-acetoxy-2-cyclohexenone **34**, which could undergo conjugate addition of acetate and oxidation to give 3-acetoxy-1,2-cyclohexanedione **31**. The formation of diacid **27a** as the major diastereomer is consistent with this scheme since conjugate addition of acetate to either **1e** or **34** should occur predominantly by axial attack from the α-face.

Reaction of α-keto radical **32** with **7a** will lead to tertiary radical **36**, which will be oxidized to give cation **37**. Loss of a proton and elimination of the *β*-acetoxy group will give 2-alkenyl-2-cyclohexenone **38ea**. Cyclization of radical **36** and oxidation will give cation **39**, which will lose a proton and HOAc to give a tetrahydrobenzofuran that will be oxidized to dihydro-6-methylbenzofuran **40ea**. Dihydro-4-methylbenzofuran-7-yl acetate **33ea** can be formed by α′-enolization of **34** to give radical **35**, which should react with **7a** to give **33ea** analogously to the conversion of **3** to **15** discussed above. The formation of dihydrobenzofuran-7-yl acetate **33** from 2-cyclohexenone (**1a**) and 5-methyl-2-cyclohexenone (**1e**), but not from 3-substituted 2-cyclohexenones **1b**−**d**, is consistent with this mechanism. (These reactions are described in the Supporting Information.) The substituent on the *β*-carbon of enones **1b**−**d** should retard conjugate addition of acetate so that enolization from the α′-carbon is the exclusive reaction.

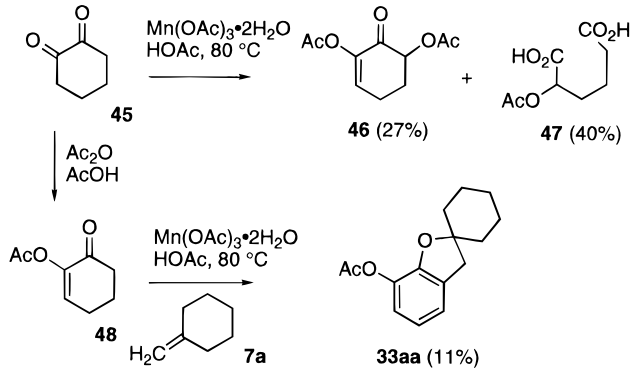
We had observed a single instance of conjugate addition of acetate in our study of oxidative cyclizations of alkenyl cyclohexenones.[4] 6-(4-Pentenyl)-2-cyclohexenone (**42**) affords 24% of 10-acetoxybicyclo[5.3.1]undec-3-en-11-one (**44**) as the major product. The 6-alkyl substituent slows down enolization at the α′-position so that conjugate addition of acetate becomes the major pathway.

We investigated the oxidation of 1,2-cyclohexanedione (**45**) with $Mn(OAc)_3$ as a model for proposed intermediate

(20) Suemune, H.; Matsuno, K.; Uchida, M.; Sakai, K. *Tetrahedron: Asymmetry* **1992**, *3*, 297.



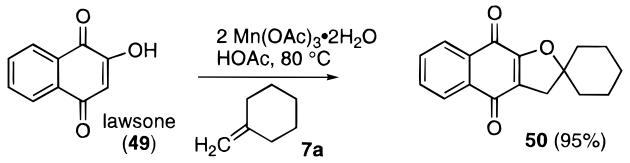
34. As expected, oxidation of **45** with $Mn(OAc)_3 \cdot 2H_2O$ in HOAc at 80 °C for 1 h affords 27% of 2,6-diacetoxy-2-cyclohexenone (**46**), which is analogous to **31**, and 40% of 2-acetoxyhexanedioic acid (**47**). Nikishin and coworkers reported a similar oxidation of **45** with $CuCl_2$ and H_2O_2 that affords 2-chlorohexanedioic acid.[21] Reaction of **45** with Ac_2O in HOAc provides 2-acetoxy-2-cyclohexenone (**48**). Oxidation of **48** and **7a** with $Mn(OAc)_3 \cdot 2H_2O$ in HOAc at 80 °C for 20 h provides 11% of dihydrobenzofuran-7-yl acetate **33aa**, indicating that 2-acetoxy-2-cyclohexenones **34** and **48** are competent intermediates for the formation of **33a**.



The formation of 2-acetoxyhexanedioic acids as significant products from the oxidation of 2-cyclohexenones with $Mn(OAc)_3 \cdot 2H_2O$ in HOAc explains the modest yields of 6-acetoxy-2-cyclohexenones **4** obtained by Williams and Hunter in acetic acid.[1] Higher yields of **4** were obtained by Watt and Demir in benzene because conjugate addition of acetate does not occur in this solvent and no hexanedioic acids are formed.

There are several advantages to carrying out these oxidative cycloadditions in benzene and one benefit to carrying them out in acetic acid. Conjugate addition of acetic acid does not occur in benzene so that no material is converted to diacid, and regioisomers and dihydrobenzofuran-7-yl acetate **33** are not obtained. Benzylic oxidation does not occur as readily in benzene, so that overoxidized products such as dihydrobenzofuran-3-yl acetates **26** and **41** are not obtained. On the other hand, terminal alkenes can be used in acetic acid but not in benzene since secondary radical **23ab** cyclizes to afford **24ab** which is then oxidized to provide **25ab** only in acetic acid.

Oxidative cycloaddition of α-tetralone (**16**) with **7a** and 6 equiv of $Mn(OAc)_3 \cdot 2H_2O$ in HOAc at 80 °C for 15 h affords 19% of 2-acetoxy-α-tetralone, 24% of the naphthofuranone derived from oxidation of **17**, 15% of alkenyltetralone **18**, and 19% of naphthoquinone **50**. Similar products are obtained in comparable yields from isobutene. Dihydronaphthofuran **17** is formed and undergoes rapid benzylic oxidation to give the naphthofuranone since the naphthalene ring is more readily oxidized than a benzene ring.[22]



The formation of naphthoquinone **50** was not expected. We established the structure of the analogue obtained from isobutene by comparison of the ^1H and ^{13}C NMR spectral data with literature data.[23,24] These naphthoquinones are readily available by [3 + 2] photoaddition of 2-hydroxy-1,4-naphthoquinone (lawsone, **49**) with alkynes or with alkenes followed by air oxidation.[23] We thought that α-tetralone **16** might be oxidized by $Mn(OAc)_3 \cdot 2H_2O$ to give **49**, which could undergo oxidative cycloaddition with alkenes to give **50**. As expected, oxidative cycloaddition of **49** with **7a** and 4 equiv of $Mn(OAc)_3 \cdot 2H_2O$ in HOAc at 80 °C for 15 h affords 95% of **50**. Oxidative cycloaddition of lawsone with alkenes thus provides an alternative to the photochemical route developed by Suginome.[23] Oxidative cycloaddition of *β*-tetralone with **7a** in acetic acid provides 20% of **50** as the only isolable product, suggesting that *β*-tetralone is also oxidized to lawsone by $Mn(OAc)_3 \cdot 2H_2O$.

Conclusion. Oxidative cycloaddition of a 2-cyclohexenone or α-tetralone and an alkene with dried $Mn(OAc)_3$ in benzene at 80−140 °C provides a general route to dihydrobenzofurans **15** and dihydronaphthofurans **17**. Although the yields are modest, this one-step reaction provides simple access to these compounds, which have previously been prepared by multistep routes. Oxidative cycloaddition of 2-cyclohexenones with *β*-methylstyrenes provides a new route to benzofuranoid neolignans, which was applied to the synthesis of conocarpan (**22**). The formation of 2-acetoxyhexanedioic acids **27** and **47** from acetoxylation of 2-cyclohexenones in HOAc, but not in benzene, opens up a new class of $Mn(OAc)_3$ reactions and explains Watt and Demir's discovery that much higher yields of α′-acetoxyenones are obtained in benzene than in HOAc.

Experimental Section

General Procedures. NMR spectra were recorded at 300 MHz in $CDCl_3$. Chemical shifts are reported in *δ* (ppm) and coupling constants in hertz. IR spectra are reported in cm^{-1}.

Oxidative Cycloaddition of 2-Cyclohexenone (1a) with Methylenecyclohexane (7a) in Benzene. A solution of **1a** (107 mg, 1.11 mmol), **7a** (213 mg, 2.22 mmol), and $Mn(OAc)_3$ (1.03 g, 4.44 mmol) in 10 mL of benzene was refluxed at 80 °C for 3 d. Saturated $NaHSO_3$ solution was added and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with saturated NaCl solution, dried (Na_2SO_4), and concentrated in vacuo to provide 191 mg of crude product, which was purified by flash chromatography on silica gel (50:1 hexane/EtOAc, then 10:1 hexane/EtOAc) to yield 88 mg (42%) of **15aa**, followed by 37 mg (18%) of **12aa**.

The data for **12aa**: ^1H NMR 6.93 (dddd, 1, J = 10.1, 5.3, 4.4, 0.7), 5.99 (ddd, 1, J = 10.1, 2.1, 2.0), 5.43 (br s, 1), 2.56 (br d, 1, J = 15), 2.47−2.30 (m, 3), 2.10−1.87 (m, 5), 1.71−1.50 (m, 6); ^{13}C NMR 201.8, 149.7, 134.9, 129.4, 123.6, 44.2, 37.6, 27.8, 26.7, 25.3, 24.7, 22.9, 22.4; IR (neat) 1715, 1673, 1443, 1219.

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The data for **15aa**: ^{1}H NMR 7.12 (br d, 1, J = 7.4), 7.09 (br dd, 1, J = 8.0, 7.4), 6.79 (br dd, 1, J = 7.4, 7.4), 6.74 (br d, 1, J = 8.0), 2.96 (s, 2), 1.85−1.40 (m, 10); ^{13}C NMR 158.9, 127.8, 126.8, 125.1, 119.7, 109.5, 88.4, 41.0, 37.2 (2 C), 25.2, 23.1 (2 C); IR (neat) 1597, 1481, 1240, 747. The data are identical to those previously reported.[5]

Oxidative Cycloaddition of 3-Methyl-2-cyclohexenone (1b) with 7a in Benzene. A solution of **1b** (101 mg, 0.92 mmol), **7a** (176 mg, 1.84 mmol), and $Mn(OAc)_3$ (852 mg, 3.67 mmol) in 10 mL of benzene was refluxed at 80 °C for 3 d. Normal workup and flash chromatography on silica gel (50:1 hexane/EtOAc, 10:1 hexane/EtOAc, then 3:1 hexane/EtOAc) gave 58 mg (31%) of **15ba**, followed by 22 mg (12%) of 6-(1-cyclohexenylmethyl)-3-methyl-2-cyclohexenone (**12ba**) and 23 mg (23%) of recovered **1b**.

The data for **12ba**: ^{1}H NMR 5.85 (br dd, 1, J = 2.7, 1.3), 5.42 (br s, 1), 2.54 (br d, 1, J = 14.9), 2.38−2.24 (m, 3), 2.09−1.82 (m, 5), 1.95 (s, 3), 1.68−1.49 (m, 6); ^{13}C NMR 201.7, 161.5, 135.2, 126.2, 123.4, 43.1, 37.7, 29.8, 27.8, 26.6, 25.3, 24.1, 22.9, 22.4; IR (neat) 1669, 1638, 1438, 1379, 1210.

The data for **15ba**: ^{1}H NMR 7.00 (d, 1, J = 7.5), 6.61 (d, 1, J = 7.5), 6.58 (s, 1), 2.92 (s, 2), 2.29 (s, 3), 1.80−1.47 (m, 10); ^{13}C NMR 159.0, 137.9, 124.7, 123.8, 120.4, 110.2, 88.6, 40.7, 37.2, 25.2, 23.1, 21.5; IR (neat) 1622, 1590, 1499, 1448, 1275, 1250, 1032, 946, 796.

Oxidative Cycloaddition of 3-Ethoxy-2-cyclohexenone (1c) with 7b in Benzene. A solution of **1c** (115 mg, 0.82 mmol), **7a** (158 mg, 1.64 mmol), and $Mn(OAc)_3$ (762 mg, 3.38 mmol) in 10 mL of benzene was refluxed at 80 °C for 3 d. Normal workup and flash chromatography on silica gel (50:1 hexane/EtOAc, 15:1 hexane/EtOAc, then 1:1 hexane/EtOAc) gave 74 mg (39%) of 6-ethoxyspiro[benzofuran-2(3*H*),1′-cyclohexane] (**15ca**), followed by 4 mg (2%) of 6-(1-cyclohexenylmethyl)-3-ethoxy-2-cyclohexenone (**12ca**), and 50 mg (43%) of recovered **1c**.

The data for **12ca**: ^{1}H NMR 7.54 (d, 1, J = 8.6), 6.60 (dd, 1, J = 2.2, 8.6), 6.51 (d, 1, J = 2.2), 4.10 (q, 2, J = 7.0), 1.81−1.55 (m, 10), 1.45 (t, 3, J = 7.0); ^{13}C NMR 201.8, 173.6, 167.6, 125.7, 113.0, 111.8, 96.6, 90.6, 64.2, 31.7, 24.6, 21.7, 14.5; IR (neat) 1709, 1613, 1447, 1292, 1179, 1097.

The data for **15ca**: ^{1}H NMR 6.97 (br d, 1, J = 8.5), 6.35 (dd, 1, J = 8.5, 2.0), 6.34 (d, 1, J = 2), 3.97 (q, 2, J = 7.0), 2.89 (s, 2), 1.86−1.45 (m, 10), 1.37 (t, 3, J = 7.0); ^{13}C NMR 160.3, 160.0, 125.4, 118.9, 106.4, 97.0, 89.8, 63.9, 40.7, 37.5, 25.5, 23.4, 15.2; IR (neat) 1621, 1495, 1446, 1294, 1168, 1038, 969, 926.

Oxidative Cycloaddition of Ethyl 2-Methyl-4-oxo-2-cyclohexenecarboxylate (1d) with 7a in Benzene. A solution of **1d** (121 mg, 0.66 mmol), **7a** (128 mg, 1.33 mmol), and $Mn(OAc)_3$ (617 mg, 2.66 mmol) in 10 mL of benzene was refluxed at 80 °C for 3 d. Normal workup and flash chromatography on silica gel (25:1 hexane/EtOAc, then 3:1 hexane/EtOAc) gave 34 mg (25%) of ethyl 6-methylspiro[benzofuran-2(3*H*),1′-cyclohexane]-5-carboxylate (**15da**), followed by 62 mg (51%) of recovered **1c**.

The data for **15da**: ^{1}H NMR 7.77 (s, 1), 6.59 (s, 1), 4.30 (q, 2, J = 7.1), 2.93 (s, 2), 2.56 (s, 3), 1.85−1.70 (m, 4), 1.70−1.60 (m, 2), 1.60−1.45 (m, 4), 1.37 (t, 3, J = 7.1); ^{13}C NMR 167.4, 162.1, 142.4, 128.0, 124.4, 121.2, 112.4, 90.2, 60.1, 40.3, 37.1, 25.1, 23.0, 22.5, 14.4; IR (neat) 1712, 1621, 1583, 1494, 1257.

Oxidative Cycloaddition 5-Methyl-2-cyclohexenone (1e) with 7a in Benzene. A solution of **1e** (92 mg, 0.84 mmol), **7a** (160 mg, 1.66 mmol), and $Mn(OAc)_3$ (770 mg, 3.32 mmol) in 10 mL of benzene was refluxed at 80 °C for 3 d. Normal workup and flash chromatography on silica gel (50:1 hexane/EtOAc, then 15:1 hexane/EtOAc) gave 70 mg (41%) of **15ea**, followed by 18 mg (9%) of 6-(1-cyclohexenylmethyl)-5-methyl-2-cyclohexenone (**12ea**) as a 3:2 trans/cis mixture and 3 mg (3%) of recovered **1e**.

The data for **12ea**: ^{1}H NMR 6.80 (m,1), 5.96 (br d, J = 10.0), 5.46 (br s, 0.6 × 1), 5.41 (br s, 0.4 × 1), 2.60−1.80 (m, 10), 1.70−1.50 (m, 4), 1.05 (d, 0.6 × 3, J = 6.9), 0.92 (d, 0.4 × 3, J = 6.9); ^{13}C NMR (202.1, 202.0), (147.3, 146.9), (135.1, 134.9), (129.2, 128.4), (123.7, 123.3), (51.4, 49.5), (38.1, 37.3), (33.7, 33.3), (31.5, 31.1), (27.97, 27.90), (25.3, 25.3), (22.92, 22.88), (22.43, 22.37), (19.8, 14.2).

The data for **15ea**: ^{1}H NMR 7.00 (dd, 1, J = 7.6. 7.6), 6.62 (d, 1, J = 7.6), 6.58 (d, 1, J = 7.6), 2.87 (s, 2), 2.21 (s, 3), 1.86−1.51 (m, 10); ^{13}C NMR 158.5, 134.9, 127.7, 125.6, 120.7, 106.7, 88.1, 39.9, 37.3, 25.2, 23.1, 18.8; IR (neat) 1614, 1599, 1460, 1275, 1023, 932, 767.

Oxidative Cycloaddition of 16 with 7a in Benzene. A solution of **16** (100 mg, 0.68 mmol), **7a** (132 mg, 1.36 mmol), and $Mn(OAc)_3$ (636 mg, 2.72 mmol) in 10 mL of benzene was refluxed at 80 °C for 3 d. Normal workup and flash chromatography on silica gel (50:1 hexane/EtOAc, then 15:1 hexane/EtOAc) gave 74 mg (45%) of spiro[cyclohexane-1,2′(3′*H*)-naphtho[1,2-*b*]furan] (**17**), followed by 29 mg (18%) of **18** and 26 mg (26%) of recovered **16**.

The data for **17**: ^{1}H NMR 7.97 (m, 1), 7.77 (m, 1), 7.39 (m, 2), 7.32 (d, 1, J = 8.2), 7.28 (d, 1, J = 8.2), 3.12 (s, 2), 1.97−1.48 (m, 10); ^{13}C NMR 154.2, 133.9, 127.8, 125.3, 124.8, 123.3, 121.7, 120.8, 119.3, 119.2, 89.3, 41.9, 37.4, 25.3, 23.0; IR (neat) 3056, 1944, 1814, 1684, 1581, 1516, 1445, 1378.

The data for **18**: ^{1}H NMR 8.03 (d, 1, J = 7.8), 7.46 (dd, 1, J = 7.8, 7.6), 7.30 (dd, 1, J = 7.6, 7.5), 7.24 (d, 1, J = 7.5), 5.47 (s, 1), 3.00−2.93 (m, 2), 2.72−2.58 (m, 2), 2.22−1.47 (m, 11); ^{13}C NMR 200.4, 144.1, 135.1, 133.1, 132.5, 128.7, 127.5, 126.5, 123.7, 45.2, 38.0, 28.1, 27.9, 27.4, 25.3, 23.0, 22.5; IR (neat) 1682, 1600, 741.

Oxidative Cycloaddition of 1a with β-Methylstyrene (19a) in Benzene. A solution of **1a** (105 mg, 1.10 mmol), **19a** (143 mg, 1.21 mmol), and $Mn(OAc)_3$ (1.02 g, 4.40 mmol) in 10 mL of benzene was refluxed at 80 °C for 3 d. Normal workup and flash chromatography on silica gel (50:1 hexane/EtOAc, then 15:1 hexane/EtOAc) gave 69 mg (42%) of unreacted **19a**, followed by 46 mg (18%) of a 93:7 mixture of *trans*-2,3-dihydro-3-methyl-2-phenylbenzofuran (**20aa**) and the cis isomer, and 2% of cinnamyl acetate.

The data for **20aa**: ^{1}H NMR 7.45−7.30 (m, 5), 7.19 (br d, 1, J = 7.4), 7.15 (br dd, 1, J = 8.0, 7.4), 6.92 (br dd, 1, J = 7.4, 7.4), 6.87 (br d, 1, J = 8.0), 5.16 (d, 1, J = 8.7), 3.44 (dq, 1, J = 8.7, 6.8), 1.43 (d, 3, J = 6.8); ^{13}C NMR 159.2, 140.9, 131.9, 128.6 (2 C), 128.24, 128.18, 126.0 (2 C), 123.6, 120.8, 109.5, 92.4, 45.6, 18.1; IR (neat) 1597, 1478, 1432, 750.

Partial data for the cis isomer: ^{1}H NMR 5.81 (d, 1, J = 8.8), 3.70 (m, 1), 0.81 (d, 3, J = 7.2).

Oxidative Cycloaddition of 1a with Anethole (19b) in Benzene. A solution of **1a** (96 mg, 1.00 mmol), anethole (150 mg, 1.01 mmol), $Mn(OAc)_3$ (928 mg, 4.00 mmol), and 8 mL of benzene was stirred in a sealed tube at 140 °C for 2 d. Normal workup and flash chromatography on silica gel (50:1 hexane/EtOAc, then 10:1 hexane/EtOAc) gave 55 mg (37%) of recovered *trans*-anethole, followed by 73 mg (31%) of a 50:1 mixture of *trans*-2,3-dihydro-2-(4-methoxyphenyl)-3-methylbenzofuran (**20ab**) and the cis isomer, and 8 mg (4%) of 3-(4-methoxyphenyl)-2(*E*)-propenyl acetate.

The data for **20ab**: ^{1}H NMR 7.35 (d, 2, J = 8.7), 7.16 (dd, 1, J = 6.9, 6.1), 7.13 (d, 1, J = 6.9), 6.90 (d, 2, J = 8.7), 6.88−6.94 (m, 1), 6.84 (d, 1, J = 8.3), 5.09 (d, 1, J = 8.9), 3.79 (s, 3), 3.43 (dq, 1, J = 8.9, 6.8), 1.39 (d, 3, J = 6.8); ^{13}C NMR 160.0, 159.5, 133.1, 132.4, 128.6, 128.0, 124.0, 121.0, 114.4, 109.8, 92.7, 55.7, 45.7, 18.2; IR (neat) 1614, 1514, 1478, 1376, 1249.

Partial data for the cis isomer: ^{1}H NMR 5.75 (d, 1, J = 8.7), 0.82 (d, 3, J = 8.3).

Preparation of 4-(3-Chloropropyl)-2-cyclohexenone (1g).[15] To a solution of diisopropylamine (0.9 mL, 7.00 mmol) in 5 mL of dry THF at 0 °C under N_2 was added *n*-butyllithium solution (2.5 M in hexane, 2.5 mL, 6.25 mmol). After 15 min at 0 °C, the solution was cooled to −78 °C, and 3-ethoxy-2-cyclohexenone (712 mg, 5.08 mmol) in 2.5 mL of THF was added dropwise over 30 min. The solution was warmed to −40 °C, and HMPA (1.25 g, 6.98 mmol) in THF and then 1-chloro-3-iodopropane (1.43 g, 7.01 mmol) were added. The mixture was warmed to rt over 1.5 h and then stirred at rt for additional 2 h. Saturated NH_4Cl solution was added, and the mixture was extracted with hexane (2 × 10 mL). The combined organic layers were washed with saturated NaCl solution, dried (Na_2SO_4), and concentrated to provide 1.3 g of crude product.

The above product in 10 mL of dry THF was added dropwise to lithium aluminum hydride solution (1.0 M in THF, 4.6 mL, 4.60 mmol) under N_2 at 0 °C. The mixture was warmed to rt and then held at rt for 1 h. Water (0.1 mL, then 5 mL) and then 2 N HCl solution (to adjust the pH to 2) were added. After

20 min of stirring, the solution was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution and NaCl solution and dried (Na_2SO_4). Evaporation followed by flash chromatography on silica gel gave 454 mg (52%) of **1g**: ^{1}H NMR 6.86 (ddd, 1, J = 10.2, 2.7, 1.4), 5.99 (ddd, 1, J = 10.2, 2.4, 0.7), 3.59 (dd, 2, J = 6.5, 6.5), 2.57−2.32 (m, 3), 2.19−2.10 (m, 1), 1.94−1.85 (m, 2), 1.79−1.52 (m, 3); ^{13}C NMR 199.2, 154.0, 129.0, 44.5, 36.6, 35.2, 31.5, 29.6, 28.2; IR (neat) 1678.

Oxidative Cycloaddition 1g with 19b in Benzene. A solution of **1g** (96 mg, 0.56 mmol), *trans*-anethole (83 mg, 0.56 mmol), $Mn(OAc)_3$ (518 mg, 2.23 mmol), and 5 mL of benzene was stirred at 110 °C for 1.5 d. Normal workup and flash chromatography on silica gel (50:1 hexane/EtOAc) gave 26 mg (31%) of recovered anethole, followed by 43 mg (24.5%) of 5-(3-chloropropyl)-2,3-dihydro-2-(4-methoxyphenyl)-3-methylbenzofuran (**20gb**) as a 50:1 trans/cis mixture and 31 mg (32%) of recovered **1g**.

The data for **20gb**: ^{1}H NMR 7.35 (dt, 2, J = 8.6, 1.9), 6.96 (d, 1, J = 7.8), 6.96 (s, 1), 6.91 (dt, 2, J = 8.6, 1.9), 6.76 (d, 1, J = 7.8), 5.08 (d, 1, J = 9.2), 3.81 (s, 3), 3.54 (dd, 2, J = 6.5, 6.5), 3.40 (dq, 1, J = 9.2, 6.8), 2.73 (dd, 2, J = 7.5, 7.5), 2.06 (dddd, 2, J = 6.5, 6.5, 7.5, 7.5), 1.38 (d, 3, J = 6.8); ^{13}C NMR 160.0, 157.9, 133.4, 133.0, 132.6, 128.5, 128.0, 124.0, 114.3, 109.5, 92.9, 55.7, 45.7, 44.7, 34.9, 32.6, 18.0; IR (neat) 1613, 1515, 1487, 1242.

Preparation of *trans*-2,3-Dihydro-2-(4-methoxyphenyl)-3-methyl-5-(1(*E*)-propenyl)benzofuran (21). A solution of **20gb** (16 mg, 0.051 mmol) in 2 mL of dry THF and 1.0 M KO-*t*-Bu in THF (0.12 mL) was refluxed at 67 °C for 4 h. After the THF evaporated, the viscous residue was stirred at 70 °C for an additional 3 h. NaOH solution (1 N, 3 mL) was added, and the solution was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated. Purification of the residue by chromatography on silica gel (50:1 hexane/EtOAc) gave 13 mg (92%) of **21**: ^{1}H NMR 7.35 (dt, 2, J = 8.7, 2.0), 7.14 (s, 1), 7.12 (d, 1, J = 8.1), 6.91 (dt, 2, J = 8.7, 2.0), 6.76 (d, 1, J = 8.1), 6.36 (dd, 1, J = 15.7, 1.5), 6.09 (dq, 1, J = 15.7, 6.6), 5.09 (d, 1, J = 8.8), 3.81 (s, 3), 3.40 (dq, 1, J = 8.8, 6.8), 1.86 (dd, 3, J = 6.6, 1.6), 1.39 (d, 3, J = 6.8); ^{13}C NMR 159.6, 158.3, 132.6, 132.4, 131.2, 130.7, 127.6, 126.3, 123.0, 120.7, 114.0, 109.3, 92.6, 55.3, 45.2, 18.4, 17.8; IR (neat) 1612, 1515, 1486, 1241.

Synthesis of Conocarpan (22). *n*-Butyllithium (2.5 M in hexane, 0.06 mL, 0.15 mmol) was added dropwise to a solution of diphenylphosphine (0.02 mL, 0.12 mmol) in THF (0.2 mL) under N_2 at 0 °C. The solution was stirred at 0 °C for 30 min, and **21** (10 mg, 0.035 mmol) in 0.1 mL of THF was added. The mixture was warmed to rt and stirred at rt for 4 h. NaOH solution (2 N, 5 mL) was added, and the solution was extracted with hexane (3 × 3 mL) which was dried ($MgSO_4$), and concentrated. Flash chromatography of the residue on silica gel (50:1 hexane/EtOAc) gave 0.6 mg (6%) of recovered **21**. The basic aqueous layer was cooled in an ice bath and acidified by 4 N HCl solution to pH = 3−4. The cloudy solution was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were washed with saturated NaCl solution, dried (Na_2SO_4), and concentrated. Flash chromatography of the residue on silica gel provided 7.8 mg (84%) of **22**: ^{1}H NMR 7.30 (dt, 2, J = 8.6, 2.0), 7.14 (s, 1), 7.12 (d, 1, J = 8.3), 6.83 (dt, 2, J = 8.6, 2.0), 6.76 (d, 1, J = 8.3), 6.37 (dd, 1, J = 15.7, 1.6), 6.09 (dq, 1, J = 15.7, 6.6), 5.09 (d, 1, J = 8.8), 4.95 (s, 1, OH), 3.39 (dq, 1, J = 8.8, 6.8), 1.86 (dd, 3, J = 6.6, 1.6), 1.39 (d, 3, J = 6.8); ^{13}C NMR 158.2, 155.6, 132.9, 132.3, 131.2, 130.7, 127.9, 126.3, 123.0, 120.7, 115.4, 109.3, 92.6, 45.2, 18.4, 17.8; IR (neat) 3394 (OH), 1613, 1605, 1516, 1486, 1239.

Oxidative Cycloaddition of 2-Cyclohexenone (1a) with 1-Octene (7b) in HOAc. A solution of **1a** (48 mg, 0.50 mmol), **7b** (84 mg, 0.75 mmol), and $Mn(OAc)_3 \cdot 2H_2O$ (536 mg, 2.00 mmol) in 5 mL of HOAc was stirred under N_2 at 80 °C for 16 h. Water (20 mL) and saturated $NaHSO_3$ solution (10 mL) were added, and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution, dried (Na_2SO_4), and concentrated in vacuo to provide 138 mg of crude product, which was purified by flash chromatography on silica gel (20:1 hexane/EtOAc) to yield 25 mg (24%) of 2,3-dihydro-2-hexylbenzofuran (**15ab**), followed by 1 mg (1%) of a 1:1 mixture of 2,3-dihydro-2-hexylbenzofuran-7-yl acetate (**33ab**) and 2-(2-octenyl)-2-cyclohexenone (**38ab**), and 21 mg (27%) of 6-acetoxy-2-cyclohexen-1-one (**4a**).[25]

The data for **15ab**: ^{1}H NMR 7.14 (br d, 1, J = 7.3), 7.09 (br dd, 1, J = 8.0, 7.4), 6.81 (br dd, 1, J = 7.4, 7.3), 6.76 (br d, 1, J = 8.0), 4.76 (m, 1), 3.26 (dd, 1, J = 15.4, 9.0), 2.85 (dd, 1, J = 15.4, 7.9), 1.85−1.25 (m, 10), 0.89 (t, 3, J = 6.7); ^{13}C NMR 159.6, 127.9, 127.0, 124.9, 120.0, 109.2, 83.4, 36.1, 35.5, 31.8, 29.2, 25.4, 22.6, 14.1; IR (neat) 1599, 1482, 1233, 749.

Oxidation of 5-Methyl-2-cyclohexenone (1e). A solution of **1e** (93 mg, 0.85 mmol) and $Mn(OAc)_3 \cdot 2H_2O$ (679 mg, 2.54 mmol) in 8 mL of HOAc was stirred at 80 °C for 5 h. Workup as described above for the oxidation of **1a** and **7b** in HOAc provided 63 mg (44%) of 6-acetoxy-5-methyl-2-cyclohexenone (**4e**) as a 1:1 trans/cis mixture in the organic layer and 39 mg (20%) of a 4:1 mixture of **27a** and **28b** (2-acetoxy-4-methylhexanedioic acid) in the water layer. Flash chromatography of **4e** gave 5 mg of pure *trans*-**4e** followed by a mixture of isomers.

The data for *trans*-**4e**: ^{1}H NMR 6.95 (ddd, 1, J = 10.1, 6.1, 2.0), 6.06 (dd, 1, J = 10.1, 2.0), 5.11 (d, 1, J = 12.7), 2.58 (ddd, 1, J = 18, 6.2, 3.1), 2.51−2.26 (m, 2), 1.55 (s, 3), 1.11 (d, 3, J = 6.1); ^{13}C NMR 193.8, 170.4, 149.1, 128.3, 79.1, 35.7, 34.4, 20.8, 19.1.

The data for *cis*-**4e**: ^{1}H NMR 6.85 (dddd, 1, J = 10.0, 5.4, 2.7, 1.2), 6.05 (ddd, 1, J = 10.0, 2.7, 2.7), 5.51 (d, 1, J = 3.8), 2.80 (dddd, 1, J = 19.2, 5.4, 2.7, 2.7), 2.63−2.52 (m, 1), 2.36 (br d, 1, J = 19.2); ^{13}C NMR 193.8, 170.4, 147.5, 128.3, 79.1, 33.6, 33.0, 21.1, 13.2.

The data for **27a**: ^{1}H NMR 9.60−9.00 (br s, 2, OH), 5.08 (dd, 1, J = 10.4, 3.4), 2.39 (dd, 1, J = 15.3, 6.3), 2.30 (dd, 1, J = 15.3, 7.2), 2.22−2.00 (m, 1), 2.09 (s, 3), 1.97 (ddd, 1, J = 14.2, 10.4, 4.2), 1.79 (ddd, 1, J = 14.2, 9.5, 3.4), 1.04 (d, 3, J = 6.4); ^{13}C NMR 179.5, 175.9, 170.8, 70.0, 41.4, 37.1, 26.7, 20.8, 18.9; IR (neat) 3471, 1726, 1377, 1232, 1075, 937.

Partial data for **27b**: ^{1}H NMR 5.06 (dd, 1, J = 8.1, 5.5), 1.06 (d, 3, J = 6.5).

Esterification of 27. A solution of diazomethane in ether was added to **27** (39 mg, 0.20 mmol). The mixture was stirred and evaporated to provide 43 mg (99%) of a 4:1 mixture of **28a** and **28b**.

The data for **28a**: ^{1}H NMR 5.06 (dd, 1, J = 10.5, 3.5), 3.75 (s, 3), 3.68 (s, 3), 2.34 (dd, 1, J = 14.8, 6.2), 2.23 (dd, 1, J = 14.8, 7.4), 2.16−2.06 (m, 1), 2.15 (s, 3), 1.92 (ddd, 1, J = 14.2, 10.5, 4.3), 1.71 (ddd, 1, J = 14.2, 9.4, 3.4), 1.00 (d, 3, J = 6.5); ^{13}C NMR 172.7, 170.8, 170.5, 70.3, 52.3, 51.5, 41.5, 37.4, 26.8, 20.6, 18.8; IR (neat) 1732, 1438, 1373, 1224, 1082, 1009.

Partial data for **28b**: ^{1}H NMR 5.03 (dd, 1, J = 8.1, 5.5), 3.75 (s, 3), 3.67 (s, 3), 1.02 (d, 3, J = 6.7).

Oxidative Cycloaddition of 2-Hydroxy-1,4-naphthoquinone (49) with 7a in HOAc. $Mn(OAc)_3 \cdot 2H_2O$ (890 mg, 3.32 mmol), **49** (144 mg, 0.83 mmol), and **7a** (180 mg, 1.87 mmol) were stirred in 8 mL of HOAc at 80 °C for 15 h. Normal workup gave 137 mg (95%) of **50**: mp 189−200 °C; ^{1}H NMR 8.09−8.05 (m, 2), 7.75−7.63 (m, 2), 2.96 (s, 2), 1.89−1.49 (m, 10); ^{13}C NMR 182.7, 178.4, 159.2, 134.0, 133.1, 132.8, 131.6, 126.2, 125.9, 123.3, 94.2, 38.0, 37.0, 24.7, 22.7; IR (KBr) 1682, 1639, 1622, 1593.

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Supporting Information Available: Experimental procedures for other oxidative cycloadditions in HOAc, and ^{1}H and ^{13}C NMR spectra for new compounds (64 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.

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