NMR spectrometers (QE-300 and GN-300) which made this study possible. The support of the University-Industry Program of Puerto Rico as well as the NSF-EPSCoR and NIH-MBRS Programs (Grant No. RR08102) is gratefully acknowledged.

Supplementary Material Available: Tables III and IV listing complete, assigned ^{13}C NMR spectra for compounds **1-10**, **13c**, and **14** (2 pages). Ordering information is given on any current masthead page.

Oxygenation of Substituted Vinylcyclopropanes: Preparative and Mechanistic Studies

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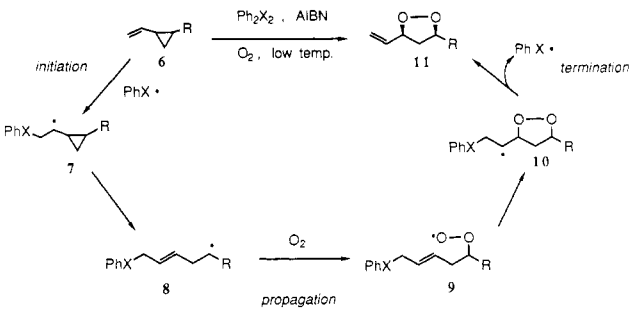
Abstract: 1-Vinylcyclopropanes bearing phenyl, vinyl, or ester substituents at C(2) of the cyclopropyl ring or alkyl groups at C(1) of the vinyl moiety were subjected to phenylthio or phenylseleno radical catalyzed oxygenation to furnish the corresponding substituted 1,2-dioxolane products. A self-consistent hypothesis was developed which describes the gross features of this multistep transformation. The mechanistic basis for stereochemical issues, including 1,2 relative asymmetric induction upon oxygen addition and stereochemistry upon cyclization of a putative 5-hexenylperoxy radical, were probed through substituent effects and deuterium-labeling studies. Reduction of the 1,2-dioxolane products afforded functionalized 1,3-diol derivatives.

Regio- and stereoselectivity in the preparation of 1,2- or 1,3-diol subunits has enabled the efficient construction of many polyoxygenated natural products. High levels of selectivity in the synthesis of diol subunits has been achieved, inter alia, through transition-metal-mediated epoxidation[1a] or osmylation[1b] technology or chelation-controlled nucleophilic addition to α-alkoxy aldehydes.[1c] Methods for the elaboration of the 1,3-diol subunit rely on either carbon-carbon bond formation,[2] carbon-hydrogen bond formation,[3] or carbon-oxygen bond formation[4] as key steps. Implementation of carbon-carbon bond forming methodology, usually in the guise of aldol (or aldol-like) condensations, has led to remarkable advances in relative and absolute control of product stereochemistry.[3a-f] Stereochemical control in carbon-oxygen bond forming strategies often depends upon hydroxyl-assisted addition of an oxygen atom equivalent to the olefinic component of homoallylic alcohols.[4b,d,f,h] In contrast, formal addition of dioxygen or a dioxygen equivalent to a hydrocarbon precursor has scarcely been investigated as a means to synthesize 1,3-diols or derivatives. However, a few reports of multistep electrophilic addition of hydrogen peroxide to cyclopropanes[5] or of direct addition of molecular oxygen across the carbon-carbon bond of uniquely activated cyclopropanes[6] (for example, imbedded in the semibulvalene framework[7]) suggested that this strategy may be a valuable complement to the more established approaches mentioned above.

Scheme I



We felt that the advantages associated with *direct oxygenation* of cyclopropane rings to form 1,3-diol derivatives in the form of dioxolane rings, including efficiency in C-O bond construction and the potential for regio- and stereochemical control (vide infra), provided strong impetus for the development of this process as a general synthetic method. Furthermore, many polyoxygenated target molecules contain repetitive 1,3-diol subunits (i.e., polyene and macrolide antibiotics), and so extension of monocyclopropane oxidation to encompass polycyclopropane precursors, thus affording poly-1,3-diol derivatives, would greatly increase the scope of this chemistry.

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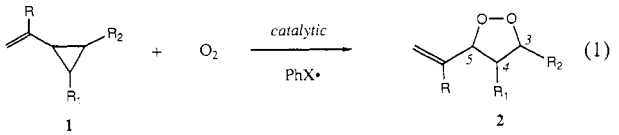
We recognized that the great wealth of available physical data describing the reactions of carbon radicals, particularly cyclopropylcarbinyl and homoallylic species, with molecular oxygen could serve as the basis for developing this process.[8] Seminal contributions by Beckwith,[9] Porter,[10] and Mihelich[11] documented that homoallylic carbon radicals, when generated in the presence of molecular oxygen, rapidly react to furnish 5-hexenylperoxy radicals, which then undergo intramolecular cyclization to produce 1,2-dioxolanylcarbinyl radicals (Scheme I, **9** → **10**). Furthermore, Russian workers demonstrated the intermediacy of phenylthiomethyl-substituted homoallylic radicals in the reversible addition of phenylthio radical to substituted vinylcyclopropanes (cf. Scheme I, **8**).[12] Taken together, these observations provide a paradigm for the addition of molecular oxygen across the carbon–carbon bond of substituted vinyl cyclopropanes to yield 1,3-diol derivatives.

Preliminary experiments indicated that the desired reaction (eq 1) was feasible. Thus, phenylthio radical efficiently catalyzed



(1)

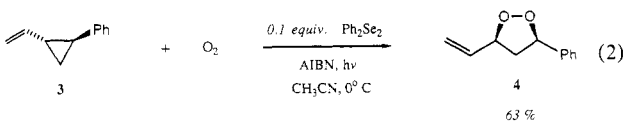
1 2

addition of molecular oxygen to the vinylcyclopropanes **1** to furnish the dioxolane products **2**.[4a] Furthermore, serial oxygenation of polycyclopropanes through a sequence of free-radical intermediates, proved possible, as a consequence of the chain-reaction nature of this process (vide infra).

In this paper, we expand our initial disclosure of this chemistry by describing the oxygenation of vinylcyclopropanes **1** bearing a range of common substituents. These new species **1** help define the scope and limitations of this formal [3-atom + 2-atom] addition process. Furthermore, analysis of the stereochemical and regiochemical outcome of the addition as a function of substituents R, R_1, and R_2 provides the basis for refining our mechanistic description of this complex transformation.

Results and Discussion

(1) Monocyclopropane Oxygenations. Initial attempts to add oxygen to vinylcyclopropanes focused on the simple species *trans*-1-phenyl-2-vinylcyclopropane (**3**) (eq 2). A range of ex-

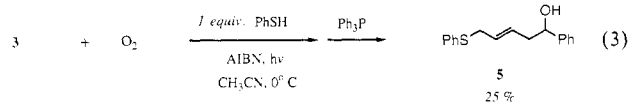


(2)

3 4

63 %

perimental variables were examined, including solvent, radical source, and temperature. In all cases where dioxolane **4** was detected, strictly syn stereochemistry was observed. This particular oxygenation reaction proved remarkably insensitive to solvent (hexane, benzene, ethyl acetate, acetonitrile, methanol, trifluoroethanol) and temperature (−78 to 35 °C), although the product dioxolane **4** had diminished stability in hydroxylic solvents or at temperatures exceeding 35 °C. Prospecting among the group IVB and VIB elements for radical sources (Ph_2Se_2, Ph_2S_2, 4,4′-dipyridyl disulfide, 2,2′-dipyridyl disulfide, bis-(2-phenylphenyl)disulfide,[13] 4,4′-bis(dimethylamino)diphenyl disulfide,[14] t-Bu_2S_2, n-Bu_2S_2, PhSH, t-BuSH, Bu_3SnH, Ph_6Sn_2) led to the observation that while tin-based radical sources and alkyl sulfur species were not effective, almost all of the aromatic chalcogen radical precursors performed with equal facility. However, thiols typically resulted in lower yields of dioxolane product relative to their disulfide counterparts, presumably as a consequence of the readily abstractable hydrogen atom. In these instances, substantial amounts of the homoallylic alcohol **5** were isolated following triphenylphosphine reduction of the crude reaction solution (eq 3).



(3)

5

25 %

Thus, convenience and cost dictated that the commercially available Ph_2Se_2 or Ph_2S_2 serve as the source of chalcogen radical, which can be generated through reaction with α-isobutyronitrile radical (AIBN, sunlamp irradiation). Omission of any of the ingredients necessary to form the chalcogen radical resulted in complete recovery of the starting vinylcyclopropane **3**. A balloon filled with oxygen placed over the reaction solution sufficed as the oxygen source in these transformations.

On the basis of (1) the results of related mechanistic studies from our laboratory,[4a,15] (2) the obtention of alcohol **5** from the thiophenol-mediated process, and (3) known absolute rate constants from the work of others,[16–18] the mechanistic picture of this transformation shown in Scheme I emerged. *Initiation* of this free-radical chain process occurs when chalcogen radical adds to the vinyl appendage of **6**.[16] While oxygen addition to the cyclopropylcarbinyl radical **7** could, in principle, compete with its isomerization to the homoallylic radical **8**, in fact no products corresponding to oxygenation of this radical were detected.[17] The homoallylic radical **8** is the first carbon radical long-lived enough to trap molecular oxygen,[17b] and the substituted 5-hexenylperoxy radical **9** results. In the absence of a suitable hydrogen donor, this radical suffers facile intramolecular cyclization to furnish the dioxolanylcarbinyl radical **10**. In the presence of thiophenol, hydrogen abstraction competes with the intramolecular cyclization of **10** and the homoallylic alcohol (e.g. **5**, following reduction with Ph_3P) is formed. The stereochemistry of the dioxolane product is set during this cyclization reaction, and this will be discussed in greater detail along with Scheme III. The dioxolanylcarbinyl radical **10** could, in principle, trap a second molecule of oxygen, but no such products are observed. Rather, ejection of the chalcogen radical occurs more rapidly[18] and constitutes the *termination* event of this chain sequence. Key features of this mechanistic proposal include the following: (1) The transformation is catalytic (1–10 mol %) in chalcogen radical source and (2) while several carbon radicals are present in solution during reaction, only the homoallylic radical **8** does not suffer rapid unimolecular rearrangement and, hence, can participate in bimolecular reaction with oxygen.

Once these reliable experimental conditions were established, several monosubstituted vinylcyclopropanes were examined in an effort to define clearly the scope and limitations of this oxygenation

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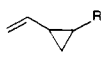
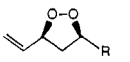
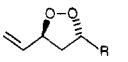
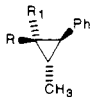
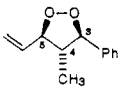
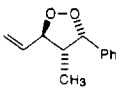
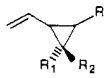
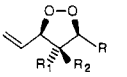
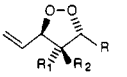
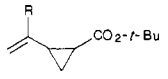
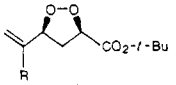
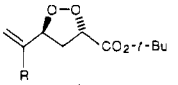
(16) The rate constant for phenylthio radical addition to styrene is 1.2×10^9 L m^{-1} s^{-1}, and to 1-butene is 7×10^6 L m^{-1} s^{-1} at 25 °C: Sivertz, C. *J. Phys. Chem.* **1959**, *63*, 34.

(17) (a) Cyclopropyl carbinyl radicals isomerize to homoallylic radicals with a rate constant $\geq 10^8$ s^{-1} at 25 °C. See ref 8 and references sited therein. (b) Benzyl radical combines with molecular oxygen with a rate constant of $\sim 3 \times 10^9$ L m^{-1} s^{-1} at 25 °C: Maillard, B.; Ingold, K. U.; Scaiano, J. C. *J. Am. Chem. Soc.* **1983**, *105*, 5095. (c) Under our reaction conditions, oxygen concentration is ca. 8 mM: See ref 17b.

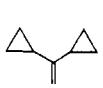
(18) The rate constant for ejection of phenylthio radical from a β-phenylthio alkyl radical is $\sim 2 \times 10^8$ L m^{-1} s^{-1} at 25 °C: Wagner, P. J.; Sedon, J. H.; Lindstrom, M. J. *J. Am. Chem. Soc.* **1978**, *100*, 2579.

Table I. Oxygenation of Monocyclopropanes

entry	vinylcyclopropane	condtn[a]	dioxolane (prod. ratio)			% yield[b]
						
a	**13**: R = CO_2-*t*-Bu	a	**20a**	(1:1.8)	**20b**	41
b	**14a**: R = CH=$CHCO_2Me$	b	**21a**	(>95:<5)[c]	**21b**	88
						
c	**15**: R = H, R_1 = CH=CH_2	c	**22**	(2.8:1)	**22b**	73
d	**16**: R = CH=CH_2, R_1 = H	c		(2.8:1)		63
						
e	**14b**: R = CH=$CHCO_2Me$, R_1 = CH_3, R_2 = H	d	**23a**	(6.5:1)	**23b)**	55
f	**14c**: R = CH=$CHCO_2Me$, R_1 = R_2 = CH_3	b	**24a**	(>95:<5)[c]	**24b**	73
g	**17**: R = Ph, R_1 = R_2 = CH_3	a	**25a**	(>95:<5)[c]	**25b**	63
						
h	**18**: R = CH_3	a	**26a**	(1:1.7)	**26b**	53
i	**19**: R = *t*-Bu	a	**27a**	(1:1)	**27b**	52

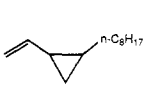
[a] Conditions: (a) 0.2 equiv of Ph_2Se_2, 0.1 equiv of AIBN, CH_3CN, 0 °C; (b) 0.15 equiv of Ph_2Se_2, 0.08 equiv of AIBN, CH_3CN, 0 °C; (c) 1.0 equiv of Ph_2Se_2, 0.1 equiv of AIBN, CH_3OH, −50 °C; (d) 0.04 equiv of Ph_2Se_2, 0.02 equiv of AIBN, hexane, 0 °C. [b] All yields refer to chromatographically purified material. [c] No minor isomer was observed. This ratio is an estimate of ^1H NMR detection limits.

reaction. Initial experiments with the hydrogen-substituted vinylcyclopropanes **12a** and **12b**[19] or the alkylated species **12c** did



12a

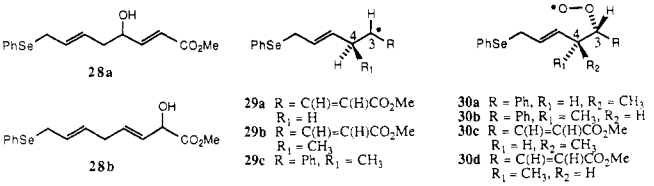
12b



12c

not lead to isolation of any oxygenated products. However, placing a radical-stabilizing substituent on that carbon which eventually combines with oxygen led to more encouraging results. Thus, the ester-substituted vinylcyclopropane **13** (Table I, entry a) combined with molecular oxygen to provide the dioxolane products **20b** and **20a** in modest yield as a mixture of 1.8:1 anti:syn diastereomers. Resubmission of a purified sample of the anti species **20b** to reaction conditions did not lead to any equilibration of dioxolane stereochemistry. This surprising reversal in stereoselectivity relative to the phenyl vinyl case underscores the dependence of 5-hexenylperoxy conformation upon a subtle interplay of both steric and electronic factors. These ester substituted dioxolanes (as well as analogues **26** and **27**) proved to be quite prone to decomposition upon purification by SiO_2 chromatography. Examination of the crude ^1H NMR spectrum of this reaction mixture indicated that the chemical yield of **20a/b** is actually 66% (vs anisole as an internal standard).

The divinylcyclopropane **14a**, used as a 85:15 trans:cis mixture, underwent smooth oxygenation to afford the divinyldioxolane **21a** in very good yield (88%). As with the phenyl-substituted cyclopropane **3**, the dioxolane product was formed with complete syn stereoselectivity. This particular example raises an interesting regiochemical issue—the homoallylic radical generated upon cyclopropane cleavage (cf. **8**, Scheme I) is itself allylic, and so oxygen addition might, in principle, occur both α and γ to the ester moiety. Only the product of γ oxygenation was observed. A priori, the regiochemistry of oxygenation may be rationalized by invoking either kinetic or thermodynamic control. Much precedent exists for regiochemical equilibration of pentadienyl[20a] and allylic[9b,20b] peroxy radicals under reaction conditions similar to those we used. It is conceivable, therefore, that for radical **29a**



the observed regioselectivity is a consequence of a slower 5-hexenylperoxy radical cyclization from a γ-oxygenated species after equilibrium is rapidly established between γ- and α-peroxy radicals. Evidence in support of this hypothesis might be obtained by trapping a putative α-oxygenated intermediate. Toward this end, the cyclopropyl diene **14a** was subjected to oxygenation conditions, although 1 equiv of selenophenol, bearing a readily abstractable hydrogen, was used as the radical source. After PPh_3 workup of the crude reaction solution, both the γ-hydroxy diene **28a** (56% by ^1H NMR vs internal standard, 8% isolated) and the α-hydroxy regioisomer **28b** (19% by ^1H NMR vs internal standard, 4% isolated) were formed. Obtention of products resulting from α-oxygenation of radical **29a** when selenophenol was employed, in contrast to formation of exclusively γ-oxygenated products under diphenyl diselenide catalysis, suggests that the regiochemistry of oxygenation is under thermodynamic control, as discussed above. Furthermore, resubmission of dioxolane **21a** to reaction conditions in the presence of 2 equiv of selenophenol, followed by PPh_3 workup, did not furnish the hydroxy selenide products **28a/b**. This result suggests that the peroxy radical intermediate corresponding to **30c** (R_1 = R_2 = H) is not regenerated from the product dioxolane under our experimental conditions.

The experiments with monosubstituted vinylcyclopropanes **3**, **12a–c**, **13**, and **14a** help define the minimum structural and functional requirements for successful oxygenation of vinylcyclopropane substrates. With these studies as a foundation, the oxygenation of various alkylated derivatives of the prototype 1-vinyl-2-substituted-cyclopropane was explored. Use of the 1-vinyl-2-methyl-3'-substituted-cyclopropanes **15/16** and **14b** probes the question of relative asymmetric induction upon oxygen addition to the intermediate homoallylic radicals **29b** and **29c**. In addition, the potential for regioisomeric cyclopropane cleavage exists. However, no products which might have resulted from

(19) Bicyclo[3.1.0]hexan-1-yl radicals undergo stereoelectronically controlled cleavage of the exocyclic bond to yield cyclopent-1-entyl-3-methyl radicals: Friedrich, E. C.; Holmstead, R. L. *J. Org. Chem.* **1971**, *36*, 971.

(20) (a) Porter, N. A.; Lehman, L. S.; Weber, B. A.; Smith, K. J. *J. Am. Chem. Soc.* **1981**, *103*, 6447. (b) Concerted rearrangement of allylic peroxy radicals, rather than dissociation/recombination, is suggested by Porter and Wujek: Porter, N. A.; Wujek, J. S. *J. Org. Chem.* **1987**, *52*, 5085.

scission of the methyl-bearing cyclopropane bond were observed, presumably reflecting the greater radical-stabilizing capabilities of the vinyl or phenyl moieties in the alternate scission mode.

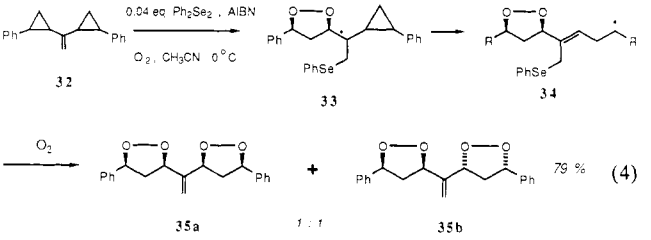
It has been observed previously that addition of oxygen to acyclic secondary carbon radicals bearing an adjacent stereogenic center generally proceeds with minimal stereoselectivity (1:1 to 1.5 to 1).[10] However, methylvinylcyclopropanes **15**/**16** and **14b** produced dioxolane products with anti C(3)–C(4) stereochemistry (set upon oxygen addition to the homoallylic radicals **29b**/**c**) which exceeded these expectations. For the phenyl substituted species **15** and **16**, product yields and cyclization stereoselectivity were responsive to solvent and temperature (Table I, entries c and d). Optimization of these variables (methanol, −50 °C) led to formation of a 2.8:1 mixture of syn to anti dioxolanes **22a**:**22b**. The major syn dioxolane features anti C(3)–C(4) stereochemistry, consistent with oxygen addition to the face of radical **29c** opposite the methyl substituent to yield intermediate **30a**. Interestingly, the minor isomeric peroxy radical **30b**, which arises from the diastereomeric addition mode, cyclizes to give the anti dioxolane **22b**. Note that similar yields and identical stereoisomer ratios resulted when either of the stereoisomeric vinylcyclopropanes **15** or **16** were oxygenated, in accord with the mechanistic scheme described earlier (Scheme I). For the methyl divinyl substrate **14b**, oxygenation in hexane at 0 °C afforded the syn and anti dioxolanes **23a** and **23b** in a 6.5:1 ratio. As in the phenyl series, oxygenation occurs with a significant preference for anti C(3)–C(4) stereochemistry. The major C(3)–C(4) *anti*-peroxy radical **30c** cyclizes to afford the syn dioxolane **23a**, while the minor C(3)–C(4) *syn*-peroxy radical isomer **30d** again leads exclusively to the anti dioxolane **23b**. In a control experiment, a stereochemically pure sample of dioxolane **23a** could be recovered unchanged after resubmission to the reaction conditions.

Analysis of the stereoselectivity of these reactions is complicated by the possible incursion of reversibility both upon both oxygen addition to the radicals **29a–c** and upon cyclization of the derived 5-hexenylperoxy radicals **30c**/**d**. Recovery of alcohol **28b** from the selenophenol-mediated oxygenation of the demethyl analogue **14a** suggests that oxygen addition to radical **29b**, derived from cyclopropane **14b**, may be rapid and reversible. In contrast, the failure to (1) detect stereochemical equilibration of **23a** or (2) trap a peroxy radical derived from dioxolane **21a** with selenophenol, upon resubmission to the reaction conditions, argues against reversibility in the 5-hexenylperoxy cyclization. Rather, these results, taken together, are consistent with a scenerio in which both diastereomeric 5-hexenylperoxy radicals **30c** and **30d** are in facile equilibrium, and product dioxolane stereoselectivity then would depend only on the relative rates of cyclization for each species. An analysis of the steric and stereoelectronic features which should influence the relative rates of cyclization of these peroxy compounds **30c** and **30d** is discussed below. Reversible oxygenation of benzylic radicals in systems similar to ours has been detected,[21] although direct evidence for this process in the case of radical **29a** has not been obtained. To the extent that (1) thermodynamic considerations dominate C(3)–C(4) stereoselectivity upon oxygen addition to radicals **29a–c** and (2) the steric interactions which influence the relative rates of cyclization of the diastereomeric 5-hexenylperoxy radicals **30a**/**b** and **30c**/**d** also are reflected in the product dioxolanes, diastereoselectivity might be correlated with product stability. In fact, molecular mechanics minimization[22] of the product dioxolanes **22a**/**b** and **23a**/**b** provided data consistent with this contention. Thus, in the phenyl series, **22b** possesses 0.6 kcal/mol more strain energy than **22a** (at −50 °C, 3.9:1 ratio **22a**:**22b** predicted), while in the unsaturated ester series, **23b** is calculated to be 1.1 kcal/mol more strained than **23a** (at 0 °C, 7.6:1 ratio **23a**:**23b** predicted).[23]

The obtention of the unexpected anti dioxolane products **22b** and **23b**, in comparison with the strict syn stereochemistry seen for the demethyl analogues **3** and **14a**, led to refinements in our working hypothesis for rationalizing dioxolane stereochemistry (vide infra). In order to further probe these mechanistic subtleties, oxygenation of the dimethylated analogues **14c** and **17** was explored (Table I, entries f and g). Oxygen addition to both the phenyl dimethyl species **17** and the vinyl carbomethoxy dimethyl analogues **14c** occurs with complete syn stereochemistry. In both cases, the yields are quite high, and there is no evidence of products resulting from alternate regioisomeric cyclopropane cleavage modes. Thus, the dimethyl species undergo oxygenation with the same syn stereochemical results seen in both the demethyl cases **3** and **14a** and also in the major isomer of the monomethyl analogues **15**, **16**, and **14b**.

Oxygenation of the propenylcyclopropyl ester **18** and the neopentenyl ester **19** (entries h and i) demonstrates that (1) alkyl substituents at C(1) of the vinyl appendage are tolerated and (2) no obvious empirical correlation between steric bulk at this position and product stereochemistry exists. The propenyl species **18** underwent oxygenation with stereochemical control similar to that observed with the parent vinylcyclopropane **13**, while the neopentenyl congener exhibited no preference for either product stereochemistry upon oxygen addition. Thus, oxygenation of the propenyl ester **18** resulted in a 53% yield of the anti and syn dioxolanes **26b** and **26a** (1.7:1). As in the vinyl case, examination of the crude ^{1}H NMR spectrum of this reaction mixture indicated that the yield of dioxolane product was actually 70%. In a similar manner, the neopentenyl cyclopropyl ester **19** underwent oxygenation under standard conditions to afford both syn and anti dioxolanes **27a**/**b** in 52% isolated yield (84% ^{1}H NMR yield). Attempted oxygen addition to 1-phenyl-2-(α-styryl)cyclopropane under the above conditions did not lead to dioxolane products.

(2) Polycyclopropane Oxygenations. The potential for effecting serial oxygenation of an appropriately linked polycyclopropane system was realized for substrates **32**, **36**, and **40**. Thus, under phenylseleno radical catalysis, the 1,1-bis(cyclopropyl)ethylene derivative **32** combines with two molecules of molecular oxygen to yield equal amounts of two diastereomeric bis-dioxolanes **35a** and **35b** (eq 4). Presumably this reaction follows the usual



(4)

mechanistic course (Scheme I) up to the point where the dioxolanyl carbinyl radical **33** is formed. This species could, in principle, eject the phenylseleno radical and deliver the monooxygenated product. However, competitive cyclopropyl carbinyl ring opening to produce the homoallylic radical **34** intervenes and, following a second oxygenation sequence, yields the bis-dioxolane products. Deuterium labeling studies detailed below allow the qualitative assessment that the rate of the cleavage pathway is faster than the termination option. Of course, reversibility of the termination path might serve to funnel any monodioxolane formed back to the bis-dioxolane products **35a** and **35b**. Each dioxolane ring is formed with complete syn stereoselectivity in accord with oxygenation of the parent species **3**. Lack of *interring* stereochemical control can be understood by noting that the stereochemistry of the second dioxolane ring is set upon oxygen addition to homoallylic radical **34** under the (negligible) influence of a now quite remote stereogenic center. In any event, this transformation forms four new carbon–oxygen bonds in a repeating 1,3-diol pattern

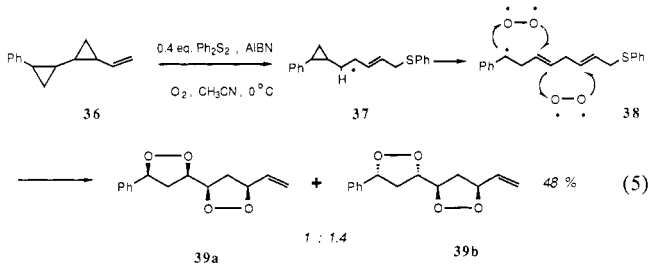
(21) (a) Howard, J. A.; Chenier, J. H. B.; Yamada, T. *Can. J. Chem.* **1982**, *60*, 2566. (b) Baignee, A.; Chenier, J. H. B.; Howard, J. A. *Can. J. Chem.* **1983**, *61*, 2037. (c) Howard, J. A.; Bennett, J. E.; Brunton, G. *Can. J. Chem.* **1981**, *59*, 2253.

(22) PC Model developed by Serena Software was used. Initial geometries included all combinations of 120° rotomers about the two exocyclic groups and all C–O–O–C dihedral angles between ~60° and +60° (15° increments).

(23) While it would be unjustified to draw mechanistic conclusions based on these calculations, examination of other dioxolane systems prepared in this study bears out this empirical correlation between diastereoselectivity and product stability.

reminiscent of several natural-product structures. Furthermore, while six stereoisomers can in principle be formed, only two were detected.

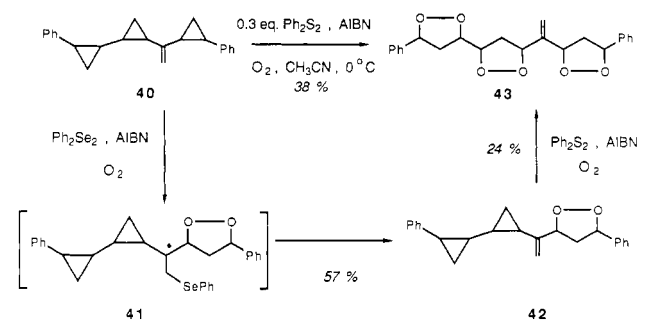
The linear bis-cyclopropane substrate **36** undergoes serial bis-oxygenation under phenylthio, but *not* phenylseleno, radical catalysis, to furnish the bis-dioxolanes **39b** and **39a** as a 1.4:1 mixture of diastereomers (eq 5). While complete intraring syn



(5)

stereochemistry obtains, there is only a modest level of interring selectivity for the anti isomer **39b**. Note that the magnitude of this stereochemical preference, while in accord with much precedent,[10] remains substantially lower than that reported for the vinylmethylcyclopropanes **15**/**16** and **14b** discussed earlier. As in the previous example, the intermediate radical **37** formed upon phenylthio radical addition to **36** is confronted with two options. In this case, cyclopropylcarbinyl ring opening to afford the homo 1,4-dienylic radical **38** must compete effectively with direct bimolecular oxygenation, as the products of monooxygenation are not detected. The dienyl radical **38** can then sequentially combine with two molecules of oxygen to deliver the dioxolane products.

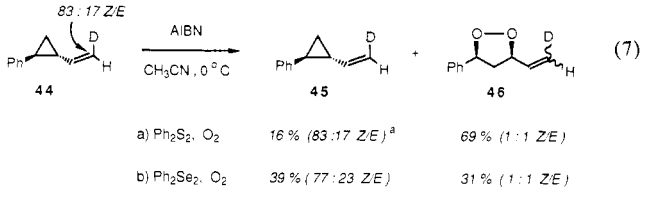
Oxygenation of the tris-cyclopropane **40** (eq 6) proved to be more complicated than either of the bis-cyclopropanes **32** or **36**.



(6)

Under selenium radical catalysis, only the monooxygenated product **42** was obtained. However, sulfur radical catalysis smoothly afforded the triple oxygenation product **43** as a mixture of five separable (HPLC) diastereomers. Resubmission of monodioxolane **42** to the standard reaction conditions with *sulfur* radical catalysis also led to complete oxygenation and isolation of the tris-dioxolane **43**. The differing reactivity of sulfur and selenium radicals in catalyzing these oxygenations, suggested in the comparison of **32** with **36** and clearly identified in the chemistry of **40**, were explored through oxygenation studies of the deuterium labeled substrates **44** and **47** discussed below. Overall, this last transformation encompasses a four component condensation which results in the regiospecific introduction of six new carbon–oxygen bonds. If all the dioxolane rings were formed with strictly syn stereochemistry, only four stereoisomers would result. As five diastereomers are formed, at least one compound has an anti disposition of a dioxolane ring. The basis for this erosion of stereochemical control is not apparent at present. Nevertheless, successful realization of this chain oxygenation sequence requires the faithful execution of 11 distinct propagation steps between phenylthio radical addition (initiation) and ejection (termination) from the hydrocarbon substrate, and thus demonstrates the feasibility of utilizing these serial reaction processes to effect complex chemical transformations.

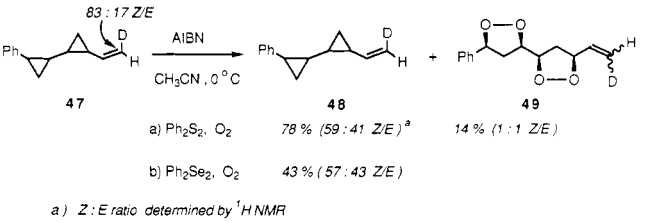
(3) Deuterium-Labeling Experiments. Although the bulk of the experimental evidence accumulated to date suggests that the oxygenation process transpires as indicated in Scheme I and eq 4 and 5, several points remain unresolved. For example, the failure of phenylselenyl radical to effect either oxygenation of **36** or oxygenation of two of the three cyclopropyl rings of **40**, while phenylthio radical performed satisfactorily in this regard, is not readily accommodated by the aforementioned mechanistic description. Oxygenation of the deuterium labeled substrates **44** and **47** was explored in order to refine the mechanistic model and account for these observations. Upon oxygenation mediated by both phenylthio and phenylseleno radicals, the location of the deuterium atom was determined in product dioxolane and, more importantly, in unreacted starting material recovered at partial conversion. Oxygenation of the deuterated (83:17 *Z*:*E*) 1-phenyl-2-vinylcyclopropane **44** under either sulfur or selenium radical catalysis led to recovery of the expected dioxolane **46** with complete equilibration of the olefin geometry (eq 7). Further-



(7)

more, in both cases, recovered starting material exhibited *retention* of olefin geometry.

While oxygenation results with the monocyclopropane **44** using either chalcogen were essentially indistinguishable, reaction of the bis-cyclopropane homologue **47** did, in fact, lead to a divergence of behavior between sulfur and selenium catalysis (eq 8).

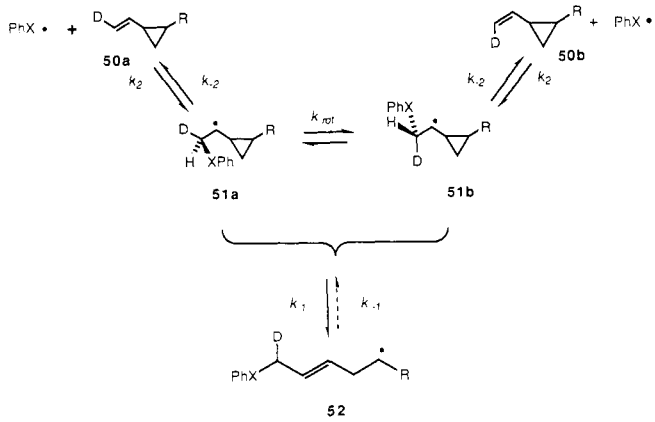


(8)

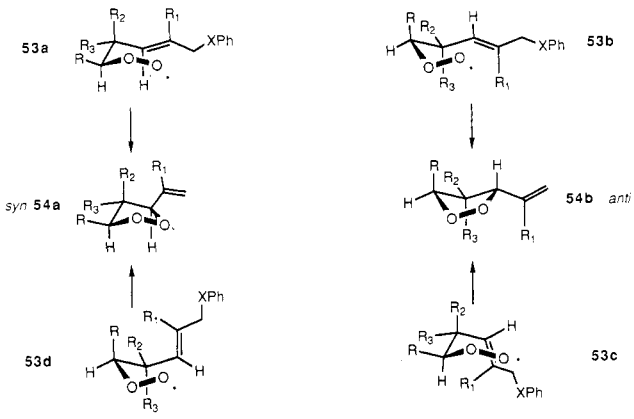
Phenylthio radical mediated oxygenation of the (predominately) *Z* deutereovinyl species **47** afforded the bis-dioxolanes **49** as a 1:1 mixture of olefin isomers. Recovered starting material **48** from this reaction was almost totally equilibrated (59:41 *Z*:*E*). Although the bis-cyclopropane **47** does not undergo oxygenation with phenylseleno radical (cf. eq 5), recovered starting material from reaction under oxygenation conditions is almost completely scrambled (57:43 *Z*:*E*, eq 8)!

These observations can be rationalized by the mechanistic hypothesis described below (Scheme II). When the cyclopropyl ring is substituted with a particularly good radical-stabilizing group such as a phenyl ring (i.e. **44**), cyclopropylcarbinyl ring opening is faster than the bond rotation–chalcogen radical ejection[18] process which leads to deuterium scrambling, for both sulfur and selenium. Thus, oxygenation proceeds smoothly and recovered starting material is not scrambled ($k_1 > k_{rot}$, k_{-2} processes for R = Ph, X = S or Se). However, when the cyclopropyl ring is substituted by a much less effective radical stabilizing group, such as a cyclopropyl ring (i.e., **47**), the difference between sulfur and selenium becomes manifest. Both phenylthio and phenylseleno radical competently generate the cyclopropylcarbinyl radical **51**. In the case of sulfur, ring opening is probably on the same order of magnitude as phenylthio radical ejection, and so oxygenation occurs competively with scrambling of olefin geometry ($k_1 \approx k_{rot}$, k_{-2} processes for R = 2-phenylcyclopropyl, X = S). However, with selenium, ring opening must be much slower than ejection of the phenylselenyl radical, as oxygenation does not occur, but scrambling of olefin geometry is complete (k_{rot}, k_{-2} processes > k_1 for R = 2-phenylcyclopropyl, X = Se). Thus, selenium radical is only effective for the oxygenation of those cyclopropyl substrates

Scheme II



Scheme III



that are substituted with a particularly good radical stabilizing group (e.g. phenyl, vinyl)—less reactive substrates require the less readily ejected phenylthio radical.

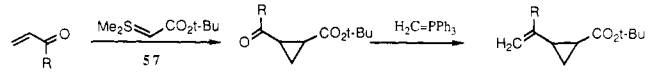
(4) Stereochemistry of Dioxolane Formation. Since equilibration studies with dioxolanes **20b** and **23a** and a trapping experiment with dioxolane **21a** provided no evidence for reversal of the 5-hexenylperoxy radical cyclization, we suspect that cyclization stereoselectivity is under kinetic control. A satisfactory model based on both extensive experimental studies[24] and theoretical calculations[25] has been developed for rationalizing the kinetically determined stereochemical consequences of substituted 5-hexenyl radical cyclizations. We believe that the bulk of our experimental results can be accommodated by adapting this model to the 5-hexenylperoxy radical cyclization central to this study. Thus, consideration of the relative energetics of the four transition states, approximated by the conformers **53a–d** shown in Scheme III, should allow interpretation of the experimental results. The syn dioxolane product **54a** can result from cyclization through either the chairlike transition state **53a** featuring a pseudoequatorial substituent R or a boatlike transition state **53d** with pseudoaxial R. Consideration of relative energies of the relevant steric interactions leads inevitably to the conclusion that conformer **53a** provides the lower energy pathway to syn dioxolane. For vinylcyclopropanes, **3**, **14a–c**, and **15–17** oxygenation produces the syn dioxolane as either the major or the exclusive product. Thus, preferential cyclization through the equatorial chair conformer **53a** provides a consistent (but not compelling) rationalization for the observed selectivity.

Upon oxygen addition to homoallylic radicals **29b/c**, the major isomers **30a/c** (R = Ph or $CH{=}CHCO_2Me$, $R_1 = R_2 = H$, R_3 = CH_3 in Scheme III) experience no further untoward steric interactions and therefore cyclize through conformer **53a** to furnish the syn dioxolane product. The minor isomers **30b/d** (R = Ph or $CH{=}CHCO_2Me$, $R_1 = R_3 = H$, $R_2 = CH_3$ in Scheme III) now contain a destabilizing $A^{1,3}$ interaction between $R_2 = CH_3$ and R_1 = H. This interaction can be alleviated through rotation about the allylic bond to deliver the boatlike conformer **53c**, leading to the anti dioxolane **54b**. While conformer **53b** could, in principle, participate in this reaction, placing a phenyl substituent (R) in an axial position makes this possibility less attractive than the alternative **53c**.

The corresponding *gem*-dimethyl species **14c** and **17** both suffer from this interaction in the equatorial chair conformer **53a** (R = Ph or $CH{=}CHCO_2Me$, $R_2 = R_3 = CH_3$, R_1 = H in Scheme III). However, in these cases, the alternative boat conformer **53c** should also experience a destabilizing (R ↔ R_2) 1,2 eclipsing interaction which would raise its energy accordingly. A priori, prediction of which of these two competing steric interactions would dominate is difficult—however, only the products arising from the chairlike precursor **53a** are detected, and so the accompanying steric interactions must be less severe.

The anti dioxolanes **20b**, **26b**, and **27b** derived from the ester-substituted cyclopropanes **13**, **18**, and **19**, respectively, can result from cyclization through either conformer **53b** or **53c**. The accumulated experimental evidence to date contraindicates cyclization through boatlike conformer **53c**, as no relationship between steric bulk of the substituent R_1 (R_1 = H, CH_3, *t*-Bu) and product stereochemistry was observed. The limited data do not, however, reveal a compelling basis for the apparent preference for the axial ester conformer **53b** over the equatorial conformer **53a**.

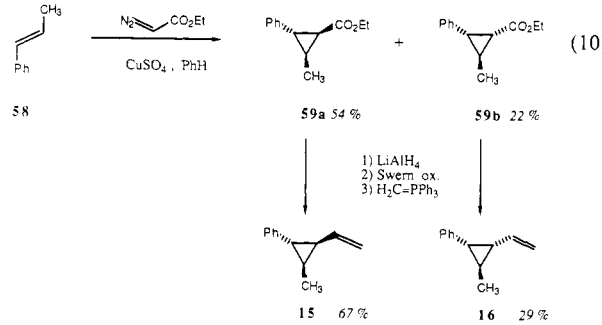
(5) Monocyclopropane Synthesis. The mono and multiple vinylcyclopropanes examined in this study were used as mixtures of cis and trans isomers, unless otherwise noted. Syntheses of the phenyl[26]-substituted cyclopropane **3** and the propenyl *tert*-butyl cyclopropyl ester **18**[27] have been reported. The *tert*-butyl esters **13** and **19** were prepared via the aldehydes **56a** and **56b**, respectively, which in turn were derived from cyclopropanation of the unsaturated carbonyls with sulfonium ylide **57**[28] (eq 9).



55a R = H 56a 55 % 13 55 %
55b R = t-Bu 56b 77 % 19 27%

(9)

Copper-catalyzed decomposition of ethyl diazoacetate in the presence of (*E*)-2-methylstyrene **58** led to the corresponding cyclopropyl esters **59a** and **59b**, respectively (eq 10). The ester



58 59a 54 % 59b 22 %

15 67 % 16 29 %

(10)

moieties could be converted to the requisite vinyl appendages by a routine series of transformations. The divinyl-substituted cyclopropanes **14a–c** were prepared from the cyclopropylmethanol precursors **60a–c**,[29–31] respectively, via Swern oxidation followed

(24) (a) Beckwith, A. L. J.; Easton, C. J.; Serelis, A. K. *J. Chem. Soc., Chem. Commun.* **1980**, 482. (b) Beckwith, A. L. J.; Lawrence, T.; Serelis, A. K. *Ibid.* 484 and references cited therein.

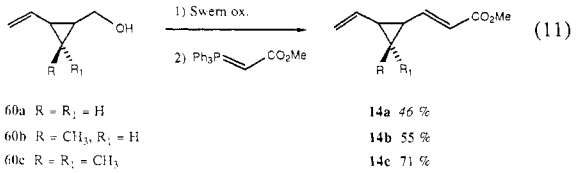
(25) (a) Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1987**, *52*, 959. (b) Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron Lett.* **1985**, *26*, 373. (c) Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925.

(26) Goh, S. H.; Closs, L. E.; Closs, G. L. *J. Org. Chem.* **1969**, *34*, 25.

(27) Demonceau, A.; Noels, A. F.; Anciaux, A. J.; Hubert, A. J.; Teyessie, P. *Bull. Soc. Chim. Belg.* **1984**, *93*, 949.

(28) Ger. Patent 2,949,269; *Chem. Abstr.* **1981**, *95*, 150427.

by in situ Wittig homologation to the unsaturated ester (eq 11).[32]

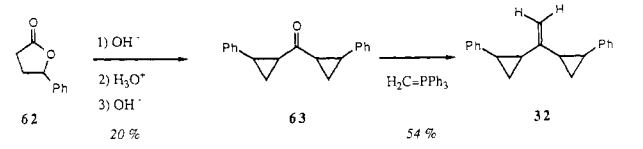


(11)

60a R = R1 = H — 14a 46 %
60b R = CH3, R1 = H — 14b 55 %
60c R = R1 = CH3 — 14c 71 %

The analogous phenyldimethylvinylcyclopropane **17** was formed by Wittig methylenation of the known 2,2-dimethyl-3-phenylcyclopropanecarboxaldehyde (**61**).[33]

(6) Polycyclopropane Synthesis. The syntheses of the biscyclopropanes **32** and **36**, and the tris-cyclopropane **40** are shown in eq 12–14. In all cases, the cyclopropane products were isolated



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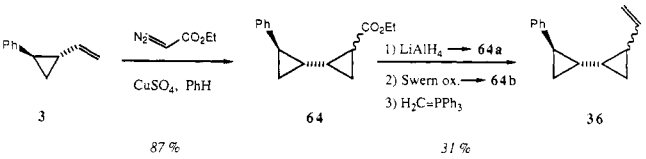
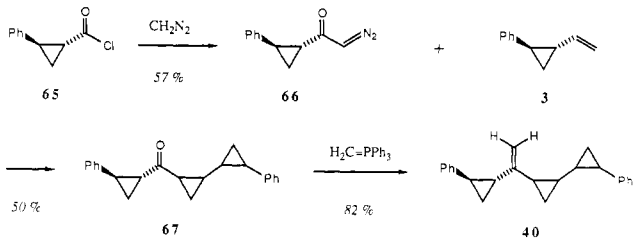


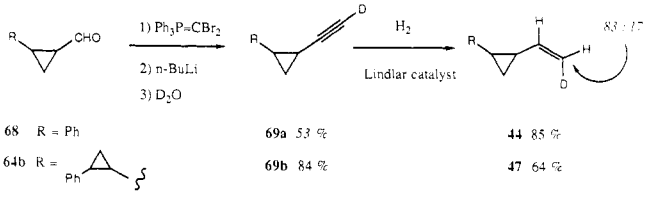
(13)



(14)

as complex mixtures of diastereomers and were used as such in all subsequent transformations. The preparation of the dicyclopropyl ketone **63** follows established procedures.[34]

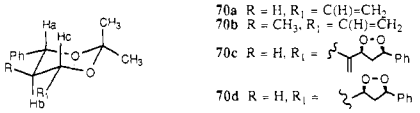
The deuterated vinylcyclopropanes **44** and **47** were prepared from the corresponding aldehydes **68** and **64b**, respectively, via the deuteroacetylenes **69a** and **69b** (eq 15).[35] Lindlar hydro-



(15)

genation provided the alkenes as 83:17 *Z*:*E* mixtures. This ratio was insensitive to solvent (ether, hexane, ethyl acetate) although it did vary with different batches of catalyst. The cyclopropylalkenes with the highest *Z*:*E* ratio (83:17) were used in the subsequent oxygenation studies.

(7) Stereochemical Elucidation of the Product Dioxolanes. The structure and stereochemistry of the bis-dioxolanes **35b** and **39a** were unambiguously established by X-ray crystallographic analysis.[4a] The stereochemistry of dioxolanes **4**, **22a**, **35a**, and **39b** was determined by analysis of the coupling constants of the derived acetonides ($LiAlH_4$, $(CH_3)_2C(OCH_3)_2$/PPTS). For the acetonides **70a–d**, coupling constants characteristic of trans diaxial



hydrogens on a cyclohexane ring were observed (i.e., **70a–d**, $J_{ab} \simeq J_{bc}$ = 10–12 Hz—see the Experimental Section for specific cases). The acetonide derived from dioxolane **22b** exhibited J_{ab} = 7.0 Hz, and J_{bc} = 8.0 Hz. The relative stereochemistry between H_a, H_b, and H_c in the acetonide could be assigned as shown only after DNOE studies on the parent dioxolane **22b**. Note that, in our original communication of these results,[4a] the stereochemistry of dioxolane **22b** was misassigned.

The stereochemistry of the remaining dioxolanes **20b**, **21a**, **23a**, **23b**, **24a**, **25a**, **26a**, **26b**, and **27b** were determined by a combination of homonuclear decoupling and DNOE techniques. Both syn and anti 1,2-dioxolanes invariably displayed substantial (>-10%) NOEs between the C(3), C(4), and C(5) protons of the dioxolane ring. Numerical values for the NOEs are given in the supplementary material.

Conclusion

The chalcogen radical catalyzed addition of molecular oxygen across the carbon–carbon bond of suitably substituted vinylcyclopropanes affords 1,3-diol derivatives in the form of 1,2-dioxolane rings. Permissible cyclopropane substituents include phenyl, ester, and vinyl ester moieties, while alkyl substitution at C(1) of the olefinic appendage is tolerated. The starting mono- and polycyclopropane substrates are readily available via standard cyclopropanation methodology. Stereoselectivity upon oxygen addition is generally high and favors the syn disposition of substituents. One notable exception to this generalization is seen with ester substituted cyclopropanes, where a slight preference for anti dioxolane stereochemistry is observed. The addition of two or three molecules of oxygen to bis- and tris-cyclopropyl substrates occurs with near complete intraring syn selectivity but with negligible interring stereochemical control. Several of the product dioxolanes feature both oxygenation patterns and peripheral functionality which may prove useful in the efficient, stereoselective synthesis of mono- and poly-1,3-diol containing natural products. Efforts in this direction are under way and will be reported in due course.

Experimental Section

Gas–liquid chromatography (GLC) was performed with a capillary cross-linked methyl silicone column (25 m; i.d. 0.20 mm; film thickness 0.33 mm) and a flame-ionization detector. Liquid (flash)[36] chromatography was carried out with 32–63-μm silica gel (Woelm-Pharma) and the indicated solvent. Analytical thin-layer chromatography was performed with precoated silica gel (60 F_{254}) plates (E. Merck). High-pressure liquid chromatography (HPLC) was performed on a Waters 6000A semi-preparative instrument equipped with an R-400 refractometer and 440 UV detector, using a ZORBAX-SIL™ silica gel column (25 cm × 20 mm, Du Pont).

Thiophenol-Mediated Oxygenation of *t*-1-Phenyl-2-vinylcyclopropane (3). A solution of AIBN (12 mg, 0.075 mmol) in 10 mL of hexane was added via a motor-driven syringe to a 0 °C solution of cyclopropane **3** (108 mg, 0.75 mmol) and thiophenol (154 μL, 1.5 mmol) in 30 mL of hexane under a balloon of O_2 with concomitant sunlamp irradiation. After ca. 3 mL of the AIBN solution was added, TLC indicated complete consumption of cyclopropane. At this time, the O_2 balloon was removed, the flask was purged with N_2, and PPh_3 was added (197 mg, 0.75 mmol). After 20 min, the reaction solution was concentrated in vacuo and the crude product was purified by flash chromatography with 25% ether/hexane to yield 50 mg of (*E*)-1-(phenylthio)-5-phenylpent-2-en-5-ol (**5**) as a colorless oil (25%): IR (CCl_4) 3599 (OH) cm^{-1}; ^1H NMR (360

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MHz, $CDCl_3$) δ 7.29 (m, 10 H, ArH), 5.56 (m, 1 H, $PhSCH_2CH$=), 5.42 (m, 1 H, $PhCH(OH)CH_2CH$=), 4.54 (dd, J = 6.6, 6.0 Hz, 1 H, $CH(OH)$), 3.49 (d, J = 7.0 Hz, 2 H, $PhSCH_2$), 2.39 (m, 2 H, $PhCH(OH)CH_2$); homonuclear-decoupling experiments indicated that the olefinic protons had a 15.2 Hz coupling constant; ^{13}C NMR (90 MHz, $CDCl_3$) δ 143.6, 135.6, 130.3, 129.3, 129.2, 128.8, 128.3, 127.4, 126.4, 125.7, 73.3, 42.3, 36.4; MS m/z (relative intensity) 270 (M^+, 2), 164 (M^+ - PhCHO, 1), 110 (M^+ - $C_{10}H_{10}O$, 100); HRMS calcd for $C_{17}H_{18}OS$ 270.1079, found 270.1074.

Selenophenol-Mediated Oxygenation of Methyl 3-(2-Ethenylcyclopropyl)propenoate (14a). A solution of AIBN (17 mg, 0.1 mmol) in 10 mL of hexane was added via a motor-driven syringe to a −40 °C solution of cyclopropane **14a** (153 mg, 1.0 mmol) and selenophenol (215 μL, 2.0 mmol) in 40 mL of hexane under a balloon of O_2, with concomitant sunlamp irradiation. After ca. 3.4 mL of the AIBN solution was added, TLC indicated that the starting cyclopropane was completely consumed, and PPh_3 was added (525 mg, 2.0 mmol). After 4 h, the reaction solution was concentrated in vacuo and the residue was purified by flash chromatography with 25% ether/hexane as eluent to yield 26 mg (8%) of γ-alcohol **28a** and 14 mg (4%) of α-alcohol **28b** as colorless oils. Examination of the ^1H NMR spectrum of the reaction solution prior to chromatography revealed that 56% of **28a** and 19% of **28b** were formed (vs PhCHO as an added internal standard).

(*E*,*E*)-Methyl 4-hydroxy-8-(phenylseleno)octa-2,6-dienoate (28a): IR (CCl_4) 1745 (C=O), 3587 (OH) cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.4 (m, 5 H, ArH), 6.83 (dd, J = 15.7, 4.4 Hz, 1 H, CH=$CHCO_2Me$), 5.94 (dd, J = 15.8, 1.8 Hz, 1 H, CH=$CHCO_2Me$), 5.70(ddd, J = 15.2, 7.7, 6.5 Hz, 1 H, $PhSeCH_2CH$=CH), 5.23 (dt, J = 14.8, 7.4 Hz, 1 H, $PhSeCH_2CH$=CH), 4.13 (m, 1 H, $CHOH$), 3.74 (s, 3 H, OCH_3), 3.49 (d, J = 7.6 Hz, 2 H, $PhSeCH_2$), 2.30 (m, 1 H, CHH), 2.17 (m, 1 H, CHH); ^{13}C NMR (90 MHz, $CDCl_3$) δ 166.8, 149.1, 133.9, 131.4, 129.6, 129.1, 127.5, 126.7, 120.1, 69.8, 51.6, 39.5, 29.7; MS m/z (relative intensity) 326 (M^+, 100), 168 (M^+ - PhSeH, 19); HRMS calcd for $C_{15}H_{18}SeO_3$ 326.0421, found 326.0432.

(*E*,*E*)-Methyl 2-hydroxy-8-(phenylseleno)octa-3,6-dienoate (28b): IR (CCl_4) 1738 (C=O), 3565 (OH) cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.3 (m, 5 H, ArH), 5.80 (dtd, J = 15.3, 6.4, 1.4 Hz, 1 H, CH=$CHCO_2Me$), 5.61 (dd, J = 15.2, 7.6 Hz, 1 H, CH=$CHCO_2Me$), 5.39 (m, 2 H, CH=CH), 4.60 (m, 1 H, $CHOH$), 3.80 (s, 3 H, OCH_3), 3.50 (dd, J = 7.6, 0.8 Hz, 2 H, $PhSeCH_2$), 2.74 (dd, J = 6.3, 5.7 Hz, 2 H, CH_2); MS m/z (relative intensity) 326 (M^+, 27), 168 (M^+ - PhSeH, 13); HRMS calcd for $C_{15}H_{18}SeO_3$ 326.0421, found 326.0413.

General Procedure for the Oxygenation of Vinylcyclopropanes. A solution of phenyl disulfide or phenyl diselenide (35 mM) and AIBN (17 mM) in the indicated solvent was added dropwise via a motor-driven syringe to a stirring solution of the vinylcyclopropane substrate (12 mM) in the indicated solvent with concomitant sunlamp irradiation. The reaction flask was capped with a balloon filled with oxygen, and was held at the indicated (internal) temperature by immersion in an externally cooled 2-propanol bath. Reaction progress was monitored by TLC, and when starting material was consumed, the reaction solution was concentrated in vacuo, and pure product dioxolanes were isolated by flash chromatography and, if necessary, HPLC.

c-3-Ethenyl-5-phenyl-1,2-dioxolane (4): ^1H NMR (200 MHz, $CDCl_3$) δ 7.4 (m, 5 H), 5.91 (ddd, J = 17.3, 10.2, 7.3 Hz, 1 H, CH=CH_2), 5.4 (m, 3 H, CH=CH_2, $PhC(O)H$), 4.85 (q, J = 7.2 Hz, 1 H, $C(O)HCH$=CH_2), 3.22 (dt, J = 12.3, 7.3 Hz, 1 H, CHH), 2.46 (dt, J = 12.2, 7.3 Hz, 1 H, CHH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.6, 135.0, 128.6, 128.2, 126.5, 118.9, 82.9, 82.7, 49.2; MS m/z (relative intensity (CI)) 176 (M^+, 12), 159 (M^+ - OH, 50); HRMS calcd for $C_{11}H_{12}O_2$ 176.0839, found 176.0843.

1,1-Dimethylethyl c-4-ethenyl-2,3-dioxolanecarboxylate (20a): IR ($CDCl_3$) 1765 (C=O) cm^{-1}; ^1H NMR (360 MHz, C_6D_6) δ 5.65 (ddd, J = 17.2, 10.3, 7.6 Hz, 1 H, CH=CH_2), 5.02 (dd, J = 17.9, 1.4 Hz, 1 H, CH=CHH), 4.89 (dd, J = 10.2, 1.5 Hz, 1 H, CH=CHH), 4.34 (q, J = 6.9 Hz, 1 H, $CH(O)C$=CH_2), 4.32 (dd, J = 8.7, 4.3 Hz, 1 H, $CH(O)CO_2t$-Bu), 2.52 (ddd, J = 11.2, 7.0, 4.2 Hz, 1 H, CHH), 2.30 (ddd, J = 12.2, 8.6, 7.7 Hz, 1 H, CHH), 1.32 (s, 9 H, CO_2t-Bu); ^{13}C NMR (90 MHz, $CDCl_3$) δ 169.3, 132.8, 120.7, 82.4, 82.0, 78.8, 44.3, 27.9; MS m/z (relative intensity) 200 (M^+, 0.2), 99 (M^+ - CO_2t-Bu, 3); HRMS calcd for $C_5H_7O_2$ (M^+ - CO_2t-Bu) 99.0446, found 99.0441.

1,1-Dimethylethyl t-4-ethenyl-2,3-dioxolanecarboxylate (20b): IR ($CDCl_3$) 1752 (C=O) cm^{-1}; ^1H NMR (360 MHz, C_6D_6) δ 5.55 (ddd, J = 17.3, 10.4, 6.9 Hz, 1 H, CH=CH_2), 4.98 (dd, J = 17.2, 1.2 Hz, 1 H, CH=CHH), 4.86 (dd, J = 10.4, 1.3 Hz, 1 H, CH=CHH), 4.51 (q, J = 6.7 Hz, 1 H, $CH(O)CH$=CH_2), 4.35 (dd, J = 8.5, 3.9 Hz, 1 H, $CH(O)CO_2t$-Bu), 2.77 (ddd, J = 11.2, 7.4, 3.8 Hz, 1 H, CHH), 2.04 (ddd, J = 12.2, 8.5, 5.6 Hz, 1 H, CHH), 1.32 (s, 9 H, CO_2t-Bu); ^{13}C NMR (90 MHz, $CDCl_3$) δ 169.0, 134.6, 118.9, 82.5, 80.8, 78.4, 44.6, 28.0; MS m/z (relative intensity) 101 (M^+ - $C_5H_7O_2$, 2), 99 (M^+ - CO_2t-Bu, 4%); HRMS calcd for $C_5H_7O_2$ (M^+ - CO_2t-Bu) 99.0446, found 99.0450.

(*E*)-Methyl 3-(c-4-ethenyl-2,3-dioxolanyl)propenoate (21a): IR (CCl_4) 1741 (C=O) cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 6.87 (ddd, J = 15.8, 7.3, 6.2 Hz, 1 H, CH=$CHCO_2Me$), 6.06 (ddd, J = 15.7, 8.5, 1.3 Hz, 1 H, CH=$CHCO_2Me$), 5.79 (ddd, J = 17.4, 10.0, 7.2 Hz, 1 H, CH=CH_2), 5.35 (dd, J = 17.2, 1.0 Hz, 1 H, CH=CHH), 5.27 (dd, J = 10.3, 1.0 Hz, 1 H, CH=CHH), 4.91 (ddd, J = 8.0, 6.0, 1.2 Hz, 1 H, $CH(O)CH$=$CHCO_2Me$), 4.73 (q, J = 7.4 Hz, 1 H, $CH(O)CH$=CH_2), 3.05 (ddd, J = 12.2, 7.9, 7.5 Hz, 1 H, CHH), 2.24 (ddd, J = 12.5, 7.0, 5.8 Hz, 1 H, CHH); ^{13}C NMR (90 MHz, $CDCl_3$) δ 166.2, 144.5, 133.7, 122.1, 120.0, 82.4, 79.6, 51.7, 46.7; MS m/z (relative intensity) 184 (M^+, 5), 113 (M^+ - C_4H_7O); HRMS calcd for $C_9H_{12}O_4$ 184.0736, found 184.0742.

c-5-Ethenyl-t-4-methyl-r-3-phenyl-1,2-dioxolane (22a): ^1H NMR (200 MHz, $CDCl_3$) δ 7.4 (m, 5 H), 5.85 (ddd, J = 17.3, 10.1, 7.7 Hz, 1 H, CH=CH_2), 5.4 (m, 2 H, CH=CH_2), 4.80 (d, J = 8.2 Hz, 1 H, PhCHO), 4.39 (t, J = 8.0 Hz, 1 H, $OCHCH$=CH_2), 2.6 (m, 1 H, CCH_3H), 1.16 (d, J = 6.7 Hz, 3 H, CCH_3H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 137.3, 133.5, 128.7, 128.5, 126.7, 120.2, 89.8, 76.4, 57.6, 13.2; MS m/z (relative intensity (CI)), 191 (M^+ + 1, 5); HRMS calcd for $C_{12}H_{14}O_2$ 190.0994, found 190.0984.

t-5-Ethenyl-c-4-methyl-r-3-phenyl-1,2-dioxolane (22b): ^1H NMR (200 MHz, $CDCl_3$) δ 7.4 (m, 5 H), 5.79 (ddd, J = 17.5, 10.0, 7.6, Hz, 1 H, CH=CH_2), 5.4 (m, 3 H, CH=CH_2, PhCHO), 4.29 (t, J = 7.91 Hz, 1 H, $OCHCH$=CH_2), 2.91 (sextet, J = 7.5 Hz, 1 H, CCH_3H), 0.73 (d, J = 7.2 Hz, 3 H, CCH_3H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 136.8, 133.2, 128.3, 127.9, 126.8, 120.6, 88.1, 85.6, 52.8, 12.7; MS m/z (relative intensity (CI)) 191 (M^+ + 1, 5), 190 (M^+, 8); HRMS calcd for $C_{12}H_{14}O_2$ 190.0994, found 190.0995.

(*E*)-Methyl 3-r-(c-4-ethenyl-t-5-methyl-2,3-dioxolanyl)propenoate (23a): IR (CCl_4) 1747 (C=O) cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 6.86 (dd, J = 15.8, 6.7 Hz, 1 H, CH=$CHCO_2Me$), 6.05 (dd, J = 15.9, 1.1 Hz, 1 H, CH=$CHCO_2Me$), 5.72 (ddd, J = 17.3, 10.3, 7.8 Hz, 1 H, CH=CH_2), 5.38 (d, J = 17.1 Hz, 1 H, =CHH), 5.32 (d, J = 10.4 Hz, 1 H, =CHH), 4.41 (t, J = 7.1 Hz, 1 H, $CH(O)CH$=$CHCO_2Me$), 4.26 (t, J = 7.9 Hz, 1 H, $CH(O)CH$=CH_2), 3.75 (s, 3 H, OCH_3), 2.45 (q, J = 7.3 Hz, 1 H, CCH_3H), 1.17 (d, J = 6.8 Hz, 3 H, CCH_3H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 166.1, 143.2, 132.5, 122.8, 121.0, 89.7, 86.7, 55.3, 51.8, 13.6; MS m/z (relative intensity) 198 (M^+, 10), 113 (M^+ - C_4H_5O, 54); HRMS calcd for $C_{10}H_{14}O_4$ 198.0892, found 198.0883.

(*E*)-Methyl 3-r-(t-4-ethenyl-c-5-methyl-2,3-dioxolanyl)propenoate (23b): IR (CCl_4) 1748 (C=O) cm^{-1}; ^{1}NMR (360 MHz, $CDCl_3$) δ 6.86 (dd, J = 15.8, 5.9 Hz, 1 H, CH=$CHCO_2Me$), 6.13 (dd, J = 15.8, 1.4 Hz, 1 H, CH=$CHCO_2Me$), 5.75 (ddd, J = 17.2, 10.2, 7.6 Hz, 1 H, CH=CH_2), 5.38 (dd, J = 17.1, 1.0 Hz, 1 H, =CHH), 5.33 (d, J = 10.5 Hz, 1 H, =CHH), 4.93 (td, J = 7.5, 1.2 Hz, 1 H, $CH(O)CH$=$CHCO_2Me$), 4.17 (t, J = 7.8 Hz, 1 H, $CH(O)CH$=CH_2), 3.76 (s, 3 H, OCH_3), 2.84 (q, J = 7.7 Hz, 1 H, CCH_3H), 1.05 (d, J = 7.1 Hz, 3 H, CCH_3H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 166.1, 141.7, 132.9, 123.6, 120.8, 88.0, 82.3, 52.3, 51.8, 11.9, MS m/z (relative intensity) 195 (M^+, 5), 113 (M^+ - $C_4H_5O_2$, 53); HRMS calcd for $C_{10}H_{14}O_4$ 198.0892, found 198.0916.

(*E*)-Methyl 3-(5,5-dimethyl-c-4-ethenyl-2,3-dioxolanyl)propenoate (24a): IR (CCl_4) 1747 (C=O) cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 6.86 (dd, J = 15.8, 6.4 Hz, 1 H, CH=$CHCO_2Me$), 6.13 (dd, J = 15.9, 1.5 Hz, 1 H, CH=$CHCO_2Me$), 5.76 (ddd, J = 17.6, 9.9, 7.7 Hz, 1 H, CH=CH_2), 5.44 (m, 2 H, =CH_2), 4.57 (dd, J = 6.4, 1.4 Hz, 1 H, $CH(O)CH$=$CHCO_2Me$), 4.42 (dd, J = 7.2, 0.6 Hz, 1 H, $CHOCH$=CH_2), 3.84 (s, 3 H, OCH_3), 1.20 (s, 3 H, CCH_3CH_3), 1.01 (s, 3 H, CCH_3CH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 165.9, 140.4, 129.9, 124.0, 121.7, 91.3, 88.2, 55.1, 51.8, 22.1, 16.8; MS m/z (relative intensity) 212 (M^+, 1), 113 (M^+ - $C_6H_{11}O$, 9); HRMS calcd for $C_{11}H_{16}O_4$ 212.1049, found 212.1028.

4,4-Dimethyl-c-5-ethenyl-3-phenyl-1,2-dioxolane (25a): ^1H NMR (360 MHz, $CDCl_3$) δ 7.34 (M, 5 H, ArH), 5.75 (ddd, J = 17.3, 10.3, 7.9 Hz, 1 H, CH=CH_2), 5.40 (dd, J = 17.2, 1.4 Hz, 1 H, =CHH), 5.38 (dd, J = 10.3, 1.4 Hz, 1 H, =CHH), 5.00 (s, 1 H, $PhCHO$), 4.48 (d, J = 7.9 Hz, 1 H, $CH(O)CH$=CH_2), 1.11 (s, 3 H, CCH_3CH_3), 0.69 (s, 3 H, CCH_3CH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 134.8, 130.7, 128.2, 126.7, 121.3, 91.3, 54.3, 21.8, 16.7; MS m/z (relative intensity) 204 (M^+, 2), 106 (M^+ - PhCHO, 9); HRMS calcd for $C_{13}H_{16}O_2$ 204.1150, found 204.1150.

1,1-Dimethylethyl c-4-(2-prop-1-enyl)-2,3-dioxolanecarboxylate (26a): IR ($CDCl_3$) 1752 (C=O) cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 5.10 (s, 1 H, =CHH), 4.98 (d, J = 1.2 Hz, 1 H, =CHH), 4.67 (m, 2 H, $CH(O)CH_2CH(O)$), 2.98 (m, 1 H, CHH), 2.70 (m, 1 H, CHH), 1.74 (s, 3 H, CH_2=CCH_3), 1.50 (s, 9 H, t-Bu); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.4, 139.5, 115.6, 83.9, 82.3, 78.7, 42.8, 28.0, 17.3; MS m/z (relative intensity) 113 (M^+ - CO_2t-Bu, 4), 101 (M^+ - CCO_2t-Bu, 3); HRMS

calcd for $C_6H_9O_2$ ($M^+ - CO_2t$-Bu) 113.0603, found 113.0622.

1,1-Dimethylethyl *t*-4-(2-prop-1-enyl)-2,3-dioxolanecarboxylate (26b): IR ($CDCl_3$) 1749 (C=O) cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 5.05 (s, 1 H, =C*H*H), 4.93 (d, J = 1.2 Hz, 1 H, =CH*H*), 4.72 (t, J = 6.8 Hz, 1 H, OC*H*CH_2), 4.67 (dd, J = 8.5, 3.9 Hz, 1 H, OC*H*CH_2), 2.95 (m, 1 H, C*H*H), 2.73 (m, 1 H, CH*H*), 1.76 (s, 3 H, CH_2=CCH_3), 1.49 (s, 9 H, t-Bu); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.0, 141.5, 113.7, 82.6, 82.5, 78.5, 43.0, 28.0, 17.7; MS m/z (relative intensity) 113 ($M^+ - CO_2t$-Bu, 2), 101 ($M^+ - CCO_2t$-Bu, 2); HRMS calcd for $C_6H_9O_2$ ($M^+ - CO_2t$-Bu) 113.0603, found 113.0589.

1,1-Dimethylethyl *c*-4-(3,3-dimethylbut-1-en-2-yl)-2,3-dioxolanecarboxylate (27a): IR ($CDCl_3$) 1748 (C=O) cm^{-1}; ^1H NMR (360 MHz, C_6D_6) δ 5.50 (s, 1 H, =C*H*H), 5.02 (s, 1 H, =CH*H*), 4.52 (t, J = 7.8 Hz, 1 H, C*H*(O)Ct-Bu=CH_2), 4.40 (dd, J = 9.0, 4.3 Hz, 1 H, C*H*(O)CO_2t-Bu), 2.63 (ddd, J = 12.2, 8.2, 4.3 Hz, 1 H, C*H*H), 2.52 (ddd, J = 12.1, 9.0, 7.3 Hz, 1 H, CH*H*), 1.39 (s, 9 H, CO_2t-Bu), 0.91 (S, 9 H, t-Bu); ^{13}C NMR (90 MHz, $CDCl_3$), δ 169.9, 152.7, 109.6, 82.2, 79.1, 78.9, 47.0, 35.3, 28.9, 28.0; MS m/z (relative intensity) 256 (M^+, 0.08), 155 ($M^+ - CO_2t$-Bu, 1); HRMS calcd for $C_9H_{15}O_2$ ($M^+ - CO_2t$-Bu) 155.1073, found 155.1026.

1,1-Dimethylethyl *t*-4-(3,3-dimethylbut-1-en-2-yl)-2,3-dioxolanecarboxylate (27b): IR ($CDCl_3$) 1751 (C=O) cm^{-1}; ^1H NMR (360 MHz, C_6D_6) δ 5.28 (s, 1 H, =C*H*H), 4.98 (s, 1 H, =CH*H*), 4.80 (t, J = 7.1 Hz, 1 H, C*H*(O)Ct-Bu=CH_2), 4.55 (dd, J = 8.6, 4.0 Hz, 1 H, C*H*(O)CO_2t-Bu), 2.90 (ddd, J = 11.3, 7.0, 4.1 Hz, 1 H, C*H*H), 2.32 (ddd, J = 12.1, 8.6, 7.3 Hz, 1 H, CH*H*), 1.36 (s, 9 H, CO_2t-Bu), 0.92 (s, 9 H, t-Bu); ^{13}C NMR (90 MHz, $CDCl_3$) δ 168.9, 154.0, 109.3, 82.5, 79.1, 78.3, 46.9, 35.3, 29.1, 27.9; MS m/z (relative intensity) 256 (M^+, 0.1), 155 ($M^+ - CO_2t$-Bu, 2); HRMS calcd for $C_{10}H_{16}O_4$ ($M^+ - t$-Bu) 200.1049, found 200.1037.

35a: ^1H NMR (200 MHz, $CDCl_3$) δ 7.4 (m, 10 H, ArH), 5.40 (s, 2 H, =CH_2), 5.30 (t, J = 7.5 Hz, 2 H, PhCHO), 5.01 (t, J = 7.4 Hz, 1 H, OC*H*C=CH_2), 3.29 (dt, J = 12.4, 7.4 Hz, 2 H, C*H*H), 2.61 (dt, J = 12.4, 7.5 Hz, 2 H, CH*H*); ^{13}C NMR (90 MHz, $CDCl_3$) δ 144.2, 137.7, 128.7, 128.4, 126.6, 114.7, 83.1, 81.4, 49.1; MS m/z (relative intensity (CI)) 325 (M^+ + 1, 12); HRMS calcd for $C_{20}H_{20}O_4$ 324.1361, found 324.1353.

35b: ^1H NMR (200 MHz, $CDCl_3$) δ 7.4 (m, 10 H, ArH), 5.45 (s, 2 H, =CH_2), 5.31 (t, J = 7.6 Hz, 2 H, PhCHO), 4.96 (t, J = 7.2 Hz, 2 H, OC*H*C=CH_2), 3.25 (dt, J = 12.2, 7.4 Hz, 2 H, C*H*H), 2.66 (ddd, J = 11.9, 7.6, 7.1 Hz, CH*H*); ^{13}C NMR (90 MHz, $CDCl_3$) δ 144.5, 137.8, 128.7, 128.4, 126.7, 113.8, 83.2, 81.3, 48.6; MS m/z (relative intensity (CI)) 325 (M^+ + 1, 21); HRMS calcd for $C_{20}H_{20}O_4$ 324.1361, found 324.1378.

39a: ^1H NMR (360 MHz, $CDCl_3$) δ 7.2 (m, 5 H, ArH), 5.77 (ddd, J = 17.4, 10.5, 7.4 Hz, 1 H, C*H*=CH_2), 5.37 (d, J = 17.3 Hz, 1 H, CH=C*H*H), 5.28 (d, J = 10.3 Hz, 1 H, CH=CH*H*), 5.24 (t, J = 7.6 Hz, 1 H, PhCHO), 4.6 (m, 3 H), 3.11 (dt, J = 12.7, 7.4 Hz, 1 H, C*H*H), 2.87 (dt, J = 12.2, 7.4 Hz, 1 H, CH*H*), 2.30 (ddd, J = 13.6, 7.5, 4.6 Hz, 1 H, C′*H*H), 2.06 (ddd, J = 13.1, 7.9, 5.1 Hz, 1 H, C′H*H*); MS m/z (relative intensity) 249 (M^+ + 1, 35); HRMS calcd for $C_{14}H_{16}O_4$ 248.1049, found 248.1052.

39b: ^1H NMR (360 MHz, $CDCl_3$) δ 7.2 (m, 5 H, ArH), 5.79 (ddd, J = 17.3, 10.3, 7.9 Hz, 1 H, C*H*=CH_2), 5.38 (d, J = 17.0 Hz, 1 H, CH=C*H*H), 5.3 (m, 2 H, CH=CHH_2, PhCHO), 4.68 (m, 1 H), 4.5 (m, 3 H), 3.17 (dt, J = 12.6, 7.4 Hz, 1 H, C*H*H), 2.98 (dt, J = 12.6, 7.4 Hz, 1 H, CH*H*), 2.8 (m, 1 H), 2.41 (ddd, J = 12.0, 7.5, 4.4 Hz, 1 H, C′*H*H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 135.4, 133.5, 128.9, 128.8, 128.5, 120.7, 83.6, 82.4, 82.2, 81.7, 45.9, 44.3; MS m/z (relative intensity (CI)) 249 (M^+ + 1, 30); HRMS calcd for $C_{14}H_{16}O_4$ 248.1049, found 248.1060.

42: ^1H NMR (200 MHz, $CDCl_3$) δ 7.4, (m, 10 H, ArH), 5.35 (t, J = 7.5 Hz, 1 H, PhCHO), 5.02 (d, J = 2.9 Hz, 1 H, =C*H*H), 4.94 (t, J = 7.4 Hz, 1 H, OC*H*C=CH_2), 4.71 (d, J = 2.4 Hz, 1 H, =CH*H*), 3.2 (m, 1 H), 2.7 (m, 1 H), 1.7–0.5 (m, 8 H); MS m/z (relative intensity (CI)) 333 (M^+ + 1, 2); HRMS calcd for $C_{16}H_{18}O$ (M^+ - PhCHO) 226.1357, found 226.1355.

43: ^1H NMR (200 MHz, $CDCl_3$) δ 7.3 (m, 10 H, ArH), 5.5–5.3 (m, 4 H), 5.1–4.7 (m, 2 H), 4.6–4.4 (m, 2 H), 3.3–2.8 (m, 3 H), 2.5 (m, 2 H), 2.3 (m, 1 H); MS m/z (relative intensity (CI)) 397 (M^+ + 1, 6); HRMS calcd for $C_9H_{12}O_9$ (M^+ - 2PhCHO) 184.0736, found 184.0351.

General Procedure for Acetonide Formation from 1,2-Dioxolanes. A solution of dioxolane (0.1 M) in ether was added to a suspension of $LiAlH_4$ (0.5 equiv per O–O bond) in an equal volume of ether. After TLC indicated the complete consumption of dioxolane (5 min), the product alcohol was recovered following the standard Fieser[37] workup. 2,2-Dimethoxypropane (10 equiv) and pyridinium p-toluenesulfonate (0.11 equiv) were added to a solution of the crude alcohol in CH_2Cl_2 (0.05 M) and stirred at room temperature until TLC indicated the absence of starting material (1–10 h). The reaction solution was washed with an equal volume of ice-cold 1 M H_3PO_4, saturated $NaHCO_3$, and brine, dried with Na_2SO_4, filtered, and concentrated in vacuo, and the crude product was purified by flash chromatography to provide the product acetonide.

***c*-2,2-Dimethyl-6-ethenyl-4-phenyl-1,3-dioxane (70a)**: ^1H NMR (360 MHz, $CDCl_3$) δ 7.4 (m, 5 H, ArH), 5.85 (ddd, J = 17.2, 10.4, 5.7 Hz, 1 H, C*H*=CH_2), 5.29 (dt, J = 17.2, 1.0 Hz, 1 H, CH=C*H*H), 5.15 (dt, J = 10.5, 1.5 Hz, 1 H, CH=CH*H*), 4.93 (dd, J = 11.5, 2.8 Hz, 1 H, PhCHO), 4.51 (ddd, J = 11.4, 5.7, 2.7 Hz, 1 H, OC*H*CH=CH_2), 1.82 (dt, J = 13.1, 2.7 Hz, 1 H, C*H*H), 1.60 (m, 4 H, CH_3, CH*H*), 1.54 (s, 3 H, CH_3); ^{13}C NMR (90 HMz, $CDCl_3$) δ 142.1, 138.4, 128.4, 127.6, 125.9, 115.6, 99.2, 71.3, 70.3, 38.9, 30.2, 19.7; MS m/z (relative intensity) 218 (M^+, 2), 203 ($M^+ - CH_3$, 72); HRMS calcd for $C_{14}H_{18}O_2$ 218.1307, found 218.1304.

2,2-Dimethyl-*c*-6-ethenyl-*t*-5-methyl-*r*-4-phenyl-1,3-dioxane (70b): ^1H NMR (200 MHz, $CDCl_3$) δ 7.3 (m, 5 H, ArH), 5.73 (ddd, J = 17.3, 10.2, 7.3 Hz, 1 H, C*H*=CH_2), 5.29 (dd, J = 17.8, 0.6 Hz, 1 H, CH=C*H*H), 5.15 (d, J = 10.4 Hz, 1 H, CH=CH*H*), 4.39 (d, J = 10.3 Hz, 1 H, PhCHO), 4.01 (dd, J = 10.1, 7.4 Hz, 1 H, OC*H*CH=CH_2), 1.5 (m, 4 H, CCH_3H, CH_3), 1.44 (s, 3 H, C′H_3), 0.54 (d, J = 6.7 Hz, 3 H, CCH_3H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 140.1, 136.7, 128.1, 127.8, 127.3, 118.0, 98.5, 76.7, 76.1, 39.8, 29.9, 19.4, 12.0; MS m/z (relative intensity) 217 ($M^+ - CH_3$, 10), 174 ($M^+ - (CH_3)_2C$=O); HRMS calcd for $C_{14}H_{17}O_2$ ($M^+ - CH_3$) 217.1228, found 217.1228.

70c: ^1H NMR (200 MHz, $CDCl_3$) δ 7.4 (m, 10 H, ArH), 5.28 (s, 2 H, C=CH_2), 4.97 (dd, J = 11.5, 2.6 Hz, 2 H, PhCHO), 4.67 (dd, J = 11.2, 2.0 Hz, 2 H, OC*H*CH=CH_2), 1.92 (dt, J = 13.0, 2.6 Hz, 2 H, C*H*H), 1.73 (t, J = 11.5 Hz, 2 H, CH*H*), 1.61 (s, 6 H, CH_3), 1.54 (s, 6 H, C′H_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 149.1, 142.3, 128.5, 127.6, 126.0, 112.0, 99.3, 71.6, 69.1, 38.7, 30.3, 19.7; MS m/z (relative intensity) 408 (M^+, 0.2), 393 ($M^+ - CH_3$, 8); HRMS calcd for $C_{26}H_{32}O_4$ 408.2300, found 408.2302.

70d: ^1H NMR (360 MHz, $CDCl_3$) δ 7.4 (m, 5 H, ArH), 5.84 (ddd, J = 17.2, 10.3, 5.8 Hz, 1 H, C*H*=CH_2), 5.28 (dt, J = 17.3, 1.3 Hz, 1 H, CH=C*H*H), 5.14 (dt, J = 10.4, 1.1 Hz, 1 H, CH=CH*H*), 4.90 (dd, J = 11.8, 2.5 Hz, 1 H, PhCHO), 4.36 (ddd, J = 11.6, 5.8, 2.2 Hz, 1 H, OC*H*CH=CH_2), 3.8 (ddd, J = 11, 8, 2.5 Hz, 1 H, PhCH(O)CH_2C*H*O), 3.7 (ddd, J = 10, 8, 2 Hz, 1 H, OC*H*CH_2CH(O)CH=CH_2), 4.13 (dt, J = 13.2, 2.4 Hz, 1 H, C*H*H), 1.91 (dt, J = 13.1, 2.6 Hz, 1 H, CH*H*), 1.57 (s, 3 H, CH_3), 1.54 (s, 3 H, C′H_3), 1.42 (s, 3 H, C″H_3), 1.39 (s, 3 H, C‴H_3); MS m/z (relative intensity) 317 ($M^+ - CH_3$, 85%), 259 ($M^+ - CH_3$, $(CH_3)_2C$=O).

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Supplementary Material Available: Synthesis and spectral data for **14a–c**, **15–17**, **19**, **32**, **36**, **40**, **44**, **56b**, **59a/b**, **60b**, **63**, **64**, **64a/b**, **66**, **67**, and **69a/b** and DNOE data for **20b**, **21a**, **22a/b**, **23a/b**, **24a**, **25a**, **26a/b**, and **27a/b** (15 pages). Ordering information is given on any current masthead page.

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