1-Alkenylcycloalkoxy Radical Chemistry. A Two-Carbon Ring Expansion Methodology[1]

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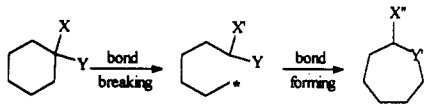
The exploitation of alkoxy radicals derived from 1-ethenylcycloalkanols for use in a two-carbon ring expansion protocol was proposed. Direct one-pot alkoxy radical-mediated fragmentation–cyclization was not feasible since the reactive intermediate was quenched by iodine in the reaction mixture. However, via the use of iodo epoxides **3**, the tandem fragmentation–cyclization sequence could be accomplished. This afforded ring-expanded products via an endo mode of cyclization, although in one example product from an exo mode of cyclization was also isolated. This methodology was shown to be valid for large ring compounds as well. The intermediary of iodo epoxides **3** also afforded improved yields as compared to the direct cyclization of iodo enones **4**. These results are the first examples of radical cyclization to medium-sized carbocycles.

Over the past 10 years, a resurgence in free-radical chemistry has occurred.[2] The use of carbon-centered radicals has primarily focused on synthetic applications as witnessed by the large number of synthetic approaches in which the key step was based on radical chemistry. To a much lesser extent, a concurrent interest in alkoxy radicals can be noted,[2d,3-10] however, in the past few years this interest has increased.[11] In our ongoing process to develop new methods for the generation of medium-sized carbocycles, we began a study in which an alkoxy radical plays a pivotal role in a ring expansion protocol.

Two requirements need to be addressed for any ring expansion methodology.[12] One must first provide for a bond fragmentation reaction, and second, this must be followed by a bond-forming reaction such that the pre-existing ring is enlarged (see reaction 1). The functional



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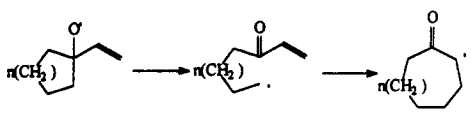
groups (X and Y in reaction 1) present in the molecule must serve as the site of initiation and termination for this sequence of events and are varied in nature.[12] We became interested to see if an alkoxy radical could be used to initiate this process. The proposed ring expansion reaction sequence is as follows. It has been previously shown that a potential reactive manifold for an alkoxy radical is to undergo β-scission.[2d,3-10] This would be our bond fragmentation reaction. The result of β-scission is the conversion of the alkoxy substituent to a carbonyl moiety and the bond that was ruptured to a carbon radical. If the initial alcohol was substituted by an olefin, then β-scission would produce an enone and a carbon radical (see reaction 2). This intermediate is ideally set up for



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the radical to proceed through a Michael-like reaction to close the ring, our bond-forming reaction. The addition of radicals to enones is well documented, and Porter[13] has shown that macrocyclization of radicals with enones is a facile process.

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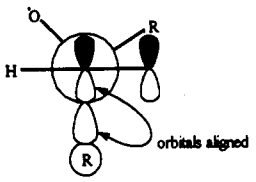
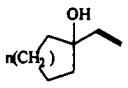


Figure 1.

It is interesting to speculate whether the fragmentation and the cyclization are concerted/synchronous[14] events. Molecular mechanics calculations[15] show that the lowest energy rotamer for the olefin–cycloalkanol bond has the carbon alkoxy–radical bond ideally aligned with the p orbitals of the olefin for the olefin to stabilize the carbon radical as it is formed or as a result of the close proximity of the reactive functional groups for the two steps to be synchronous (see Figure 1). This may provide a bypass for the entropic and enthalpic factors[16] which normally hinder cyclizations to medium-sized carbocycles. We now present our work directed toward this ring expansion methodology.

Results and Discussion

In order to systematically study the scope and limitations of this premise, a homologous series of allylic alcohols 1



a n=0 d n=3
b n=1 e n=4
c n=2 f n=8

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were constructed from the corresponding ketones via addition of vinylmagnesium bromide.[17] With the allylic alcohols in hand, various methods for the generation of alkoxy radicals were investigated. Our first attempt to generate the requisite alkoxy radical was via the hypochlorite,[18] however, all methods resulted in recovery of starting material or products analogous to those of Johnson.[19] Next we looked at the generation of the corresponding nitrite ester in order to carry out a Barton-like reaction[20] to generate the radical. Here decomposition of the starting material was witnessed. The use of lead tetraacetate is known to generate alkoxy radicals,[21] however, in our systems this resulted in decomposition as well. The conditions of Macdonald,[10] mercuric oxide–iodine in refluxing carbon tetrachloride, were also attempted but did not afford the desired ring-expanded products. However, iodo epoxides 3 and iodo enones 4 were isolated from these reaction conditions, and these results are summarized in Table I. The low yields may partially reflect the photochemical or thermal instability of these products. If left standing at room temperature on the bench for several days or in the freezer for several weeks, the oils decompose to a tarry mixture. Molecular mechanics calculations[15] of iodo epoxides 3 (see Table II) provide some insight into the chemistry occurring in this reaction. Iodo epoxide **3a** has the greatest strain energy and the highest heat of formation. This may explain why experimentally this compound was not observed. Moreover, only iodo enone **4a** was isolated. The relief of ring strain presumably facilitates the β-scission process. As the strain energy and the heat of formation decrease in magnitude, the formation of iodo epoxides 3 becomes energetically more favorable and is observed experimentally as the major product. The cross-over point appears to be between **3b**/**4b** and **3c**/**4c**.

Table I. Product Distribution from Reaction of 1 with Mercuric Oxide–Iodine

		product yield[a] (%)	
reactant	solvent	3	4
1a	CCl_4	0[b]	24
	PhMe	[c]	[c]
1b	CCl_4	7	47
	PhMe	5	30
1c	CCl_4	41	11
	PhMe	8	38
1d	CCl_4	41	16
	PhMe	14	37
1e	CCl_4	30	1
	PhMe	4	37
1f	CCl_4	50	17
	PhMe	8	36

[a] Isolated, chromatographically pure material. [b] Product could not be found in reaction mixture. [c] Reaction not carried out.

Table II. Molecular Mechanics Calculations of Strain Energy and Heats of Formation[a]

compd	strain energy	heat of formation
3a	48.19	7.74
3b	26.08	-20.12
3c	18.75	-33.21
3d	24.30	-33.42
3e	28.90	-35.19
3f	28.75	-57.73

[a] MMX force field.[15]

It has been established for chlorine[22] and for bromine[23] that reactions 3 and 4 occur with mercuric oxide. It would

$$HgO + 2X_2 \rightleftharpoons X_2O + HgX \quad (3)$$

$$X_2O \rightleftharpoons XO^{\bullet} + X^{\bullet} \quad (4)$$

therefore be plausible to expect the same reactions to hold true for iodine. This being the case, the hypoiodite radical must be the reactive species which generates alkoxy radicals 2. Alternatively, it is possible that an ionic mechanism is reponsible for the formation of the iodo epoxides; however, we feel the experimental evidence does not support this mode of action. For example, the use of hypochlorite has been shown to proceed through an ionic mechanism[19] and in those cases a one-carbon ring expansion was observed. Our use of hypochlorite afforded similar results (vide supra). More directly, subjecting **1d**,

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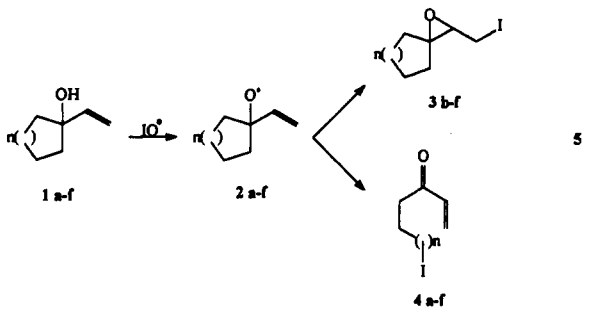
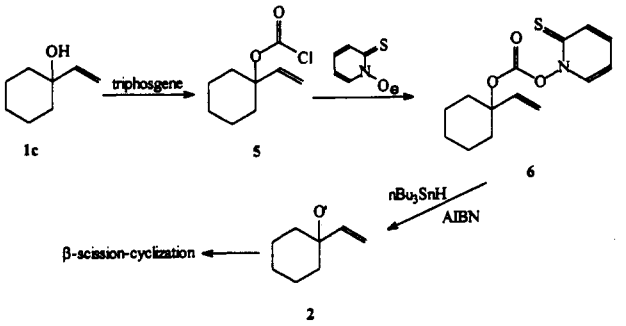
for example, to the standard ionic conditions (I_2, K_2CO_3) for 24 h at room temperature followed by heating to 70 °C for an additional 24 h resulted in a 92% yield of recovered **1d**. Furthermore, exposing **1d** to the standard oxymercuration–demercuration conditions ($Hg(OAc)_2/NaBH_4$) did not result in any epoxide formation. On the basis of the forgoing discussion and the observation that β-scission does indeed occur (vide infra), we feel that a radical mechanism as outlined in reaction 5 is in operation in



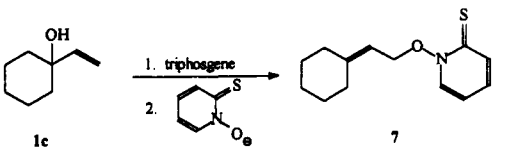
these systems. In refluxing carbon tetrachloride, the alkoxy radical cyclizes onto the adjacent olefin and the resulting carbon radical is trapped by iodine thus affording iodo epoxides **3**. A minor pathway in this system is the desired β-scission to generate the enone and the carbon radical; however, under these reaction conditions trapping of the radical by iodine is faster than cyclization thus affording iodo enones **4**. At the outset we had some reservations about complications that might arise due to the olefin since there had been limited examples of alkoxy radicals being generated adjacent to an olefin.[11] *These results do indicate that β-scission α to an olefin is feasible.*

In order to optimize the β-scission pathway we investigated various reaction conditions. The parameters initially studied were reaction concentration and the rate of iodine addition. Both proved to have little or no effect on the product distribution. Since a preequilibrium of mercuric oxide–iodine is required to generate the reactive species and the standard procedure is to add the iodine to a mixture of the alcohol and mercuric oxide, heating the mercuric oxide with iodine prior to addition of alcohols **1** also was examined. Again this had no beneficial effect. A solvent effect, however, was observed for this reaction. The use of toluene inverted the product distribution as witnessed by the fact that iodo enones **4** were now the major product (see Table I). It appeared that these conditions for alkoxy radical generation favored the β-scission pathway. We initially thought the higher temperatures were causing iodo epoxides **3** to fragment back to alkoxy radicals **2** and this subsequently underwent the β-scission. Treatment of **3** either thermally or resubmitting to the reaction conditions results in recovery of starting material or in decomposition with longer reaction times. This shows that the products of the reaction are not in equilibrium with each other and lie on distinct reaction pathways. If the higher temperatures associated with refluxing toluene were favoring the β-scission pathway, then even higher temperatures may improve the yields of these products. To this end the reactions were also carried out in refluxing xylenes. Here a similar product distribution was observed, iodo enones **4** were the major product; however, the isolated yields were slightly lower. This would tend to support the observation of the thermal instability of these products. As with the use of carbon tetrachloride, the radical intermediates were trapped by iodine, thus short-circuiting our desired reaction sequence.

Barton,[24] Newcomb,[25] and Beckwith[26] have shown it is possible to generate oxygen-centered radicals by tin hydride reduction of derivatives of 2-thiopyridine *N*-oxide. Ideally, formation of the oxygen alkyl derivative of 2-thiopyridine *N*-oxide would result in the generation of the required alkoxy radical for our studies; however, there is no facile manner for preparing this derivative. The standard method is to use the 2-thiopyridine *N*-oxide as a nucleophile in a displacement reaction, and this is not possible in our compounds. Alternatively, the carbonate



esters of 2-thiopyridine *N*-oxide have been prepared, but in the published systems (primary and secondary alkoxy derivatives) the alkoxycarbonyl radicals do not decarboxylate to the corresponding alkoxy radicals. Since it was easier for us to prepare these derivatives, this avenue was explored. It was hoped that the tertiary nature of our alcohols would facilitate the decarboxylation. For our systems, treating **1c**, for example, with triphosgene[27] should afford the corresponding chloroformate **5**, and subsequent exposure to the sodium salt of 2-thiopyridine *N*-oxide would produce carbonate **6**. Tin hydride reduction of **6** would then provide **2** free of competing iodine which should give us access to the desired ring expansion. This did not occur and the result of this chemistry was **7**, the product of a net S_N2' reaction. Newcomb[25] has noted similar rearrangements in allylic systems.



Since it appeared that a one-pot ring expansion sequence was not going to be possible under these conditions, we turned to the reaction product **3** in order to affect a net ring expansion sequence. Others[28] have shown that a radical adjacent to an epoxide results in C–O bond cleavage provided the epoxide is not substituted by an olefin or an aryl substituent. Therefore, treatment of iodo epoxides

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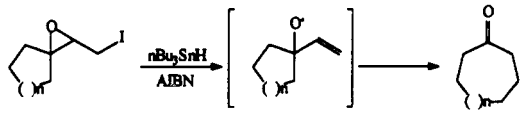
Table III. Product Distribution from *n*-Bu_3SnH/AIBN Reduction Reaction

	product yield[a] (%)		
iodo substrate	8	9	10
3b	9	20	0[b]
4b	16	16	0[b]
3c	23	0[b]	5
4c	21	0[b]	11
3d	20	0[b]	16
4d	12	0[b]	10
3e	0[b,c]	0[b,c]	0[b,c]
4e	12	0[b]	6
3f	47	0[b]	15
4f	52	0[b]	0[b]

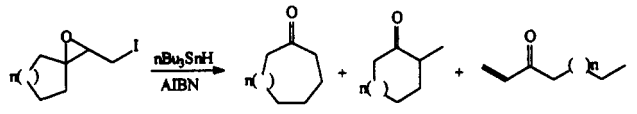
[a] Isolated, chromatographically pure material. [b] Product could not be found in reaction mixture. [c] Alternate reaction manifold (see text).

3 under standard conditions should provide the desired alkoxy radical **2** which could then proceed through the



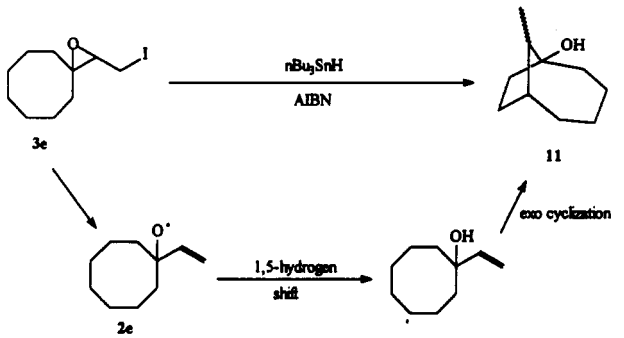
3 **2**

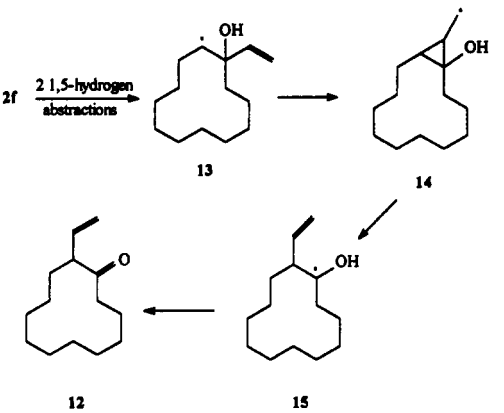
β-scission–cyclization sequence to the ring-expanded product (vide supra). In order to make this a viable methodology, a more efficient preparation of the iodo epoxides would need to be developed. It was at this time that we began investigating the use of iodobenzene diacetate[4,29] in conjunction with iodine as a method of generating the desired alkoxy radicals. Although these radicals were indeed formed, β-scission was not the major reaction pathway and this resulted in a rapid and facile preparation of iodo epoxides **3**. Our work on this chemistry has recently been reported.[30] Thus, iodo epoxides **3** were treated with tri-*n*-butyltin hydride/AIBN to generate the desired alkoxy radicals **2** as outlined. The product of a two-carbon ring expansion **8** is the expected result. Two other products, in principle, are possible. The carbon-



3 **8** **9** **10**

centered radical could add exo to the olefin to give **9**, while the propensity for the radical is to add in an endo fashion to the enone system there are examples of exo addition in similar systems,[31] or this radical could be reduced to afford **10**. The results of these reactions are summarized in Table III. As can be seen, we indeed were able to isolate ring-expanded products, and this validates the concept of an alkoxy radical-mediated fragmentation–cyclization sequence for a net two-carbon ring expansion. For **3b**, in addition to the expected endo cyclization to afford cycloheptanone **8b**, product **9b** derived from an exo cyclization was also isolated. This stands in contrast to work by Yamakawa[32] in which radical cyclization to afford 7-membered rings proceeded exclusively via an endo mode of cyclization. In the cases of **3c** and **3d** the major product was the one from endo cyclization to the corresponding two-atom expanded medium-sized cycloalkanone. Accompanying these products were varying amounts of reduction product **10** of the intermediate carbon-centered radical. The results from **3e** were very surprising. Apparently in this case, β-scission is unfavored when compared to an intramolecular 1,5-hydrogen abstraction. The resultant radical then cyclizes onto the olefin providing the bicyclic product **11** as a 2:1 mixture by NMR in 39% yield. When the reduction was carried out on **3f**, the major product isolated was **8f**, while compound **12** was obtained in 15% yield as the only other product isolated. In this reaction, the products arise from initial formation of alkoxy radical **2f**. The desired β-scission–cyclization sequence to afford **8f** gives rise to the major product. In the case of compound **12**, presumably there exists a conformation from which two intramolecular 1,5-hydrogen abstractions could occur to afford **13**. Compound **13** then undergoes a cyclopropylcarbinyl–homo allyl rearrangement via **14** to **15**. Hydrogen atom abstraction then produces **12**.





The low yields for the formation of the medium-sized rings may be a reflection of the detrimental entropic and enthalpic factors associated with the formation of these systems,[16] they may be a result of the volatility of these products, or they may be a combination of both. For the large-ring compound **3f**, the greater molecular weight should have reduced the complications associated with volatility and the effects controlling medium-sized ring formation should no longer be a problem. In this case the yields are good considering the number of steps occurring in the reaction. Although we cannot directly comment on the ability of this methodology to overcome the detrimental

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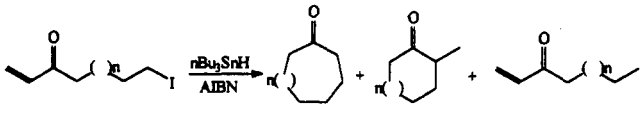
factors associated with medium-sized ring formation, we can say that as a result of volatility of the compounds involved our yields provide a low-end estimate for the cyclization and perhaps the actual yields are higher than reported. *These results are the first examples of radical cyclization to afford medium-sized carbocycles.*[33]

For comparative purposes, iodo enones **4** were also submitted to the reduction conditions. These results are reported in Table III. Noteworthy is the fact that smaller



4 **8** **9** **10**

amounts of reduction products were observed via the epoxide route than from the enone route. This may be an indication of a slight degree of synchronicity in the bond breaking–bond making reactions involved in this process. Due to the close proximity of the incipient carbon-centered radical to the newly formed enone, cyclization to the medium-sized ring is facilitated, while reduction becomes competitive in the cyclization of the iodo enones where all degrees of freedom of the chain are present.

Summary

We have shown that the generation of alkoxy radicals adjacent to a sensitive functional group (e.g., olefins) is possible. Once formed, the alkoxy radical could undergo either cyclization to form iodo epoxides **3** or β-scission to form iodo enones **4**. Both of these compounds could serve as precursors for radical reactions; however, epoxides **3** were superior to enones **4** in terms of the relative yields of cyclized product to reduction. These reactions constitute the first examples of radical cyclizations to afford medium-sized carbocycles.[33] With an improved procedure for the formation of iodo epoxides,[30] this protocol is a viable alternative for the construction of medium-sized ring. Presently, we are studying the affect of substitution on this process and the use of functionalized Grignard reagents in order to obtain fused bicyclic compounds. This work will be published in due course.

Experimental Section

General Procedures and Materials. High-resolution mass spectra (HRMS) were performed at 35 eV. All experiments were carried out under a positive pressure of argon in a dry flask equipped with rubber septa for introduction of reagents by syringe. All solvents used for chromatography were distilled prior to use. Reactions were monitored by TLC using E. Merck precoated silica gel 60 F-250 (0.25-mm thickness) aluminum-backed plates. The plates were visualized by immersion in *p*-anisaldehyde solution and warming on a hotplate. E. Merck silica gel 60 (70–230 mesh) was used for column chromatography. All solvents were reagent grade, and anhydrous solvents were dried prior to use as follows: methylene chloride was distilled from CaH_2; ether, THF, and benzene were distilled from benzophenone ketyl, while toluene and xylenes were distilled from sodium. Compounds obtained from commercial sources were used directly as received. Products **1**,[17] **4e**,[13c] **4f**,[13c] **8**, **9**, **10c**,[34] **10d**,[35] and **10e**[13c] are all known compounds, and the spectral data agree with those reported.

General Procedure for Mercuric Oxide–Iodine Reactions. Method A. Iodine (1.65 mmol) in 30 mL of CCl_4 was added via cannula over 20–30 min to a refluxing suspension of yellow HgO (1.65 mmol) and alcohol **1** (1.5 mmol) in 15 mL of CCl_4. The reaction was refluxed for an additional 60 min and cooled to rt over 30 min. The suspension was filtered, the filtrate washed with saturated sodium thiosulfate (2 × 20 mL), and the aqueous phase back-extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were dried (Na_2SO_4) and filtered and the solvent removed in vacuo. The residue was purified by chromatography (30 g of silica gel, ethyl acetate:hexanes = 1:19) to afford iodo epoxides **3** and iodo enones **4** as pale yellow oils which decomposed at rt over several days or over several weeks at −30 °C in a freezer.

Method B. The forgoing procedure was modified by the use of toluene as solvent. Also, a 90–120-min addition time for the toluene solution of iodine was required.

Reaction of Alcohol 1a. Exposure of **1a** (42 mg, 0.43 mmol) to HgO (100 mg, 0.46 mmol) and iodine (120 mg, 0.47 mmol) according to method A afforded 23 mg of **4a** (24%).

6-Iodohex-1-en-3-one (4a): IR (film) 1696, 1687, 1615 cm^{-1}; ^{1}H NMR δ 6.31 (dd, 1 H, J = 17.5, 10.0 Hz), 6.29 (dd, 1 H, J = 19.6, 3.8 Hz), 5.85 (dd, 1 H, J = 17.5, 3.8 Hz), 3.22 (t, 2 H, J = 7.5 Hz), 2.73 (t, 2 H, J = 7.5 Hz), 2.12 (quintet, 2 H, J = 7.5 Hz); ^{13}C NMR δ 199.45, 136.58, 128.68, 39.62, 27.01, 6.30; HRMS C_6H_9IO calcd 223.9698, found 223.9697.

Reaction of Alcohol 1b. Exposure of **1b** (600 mg, 5.4 mmol) to HgO (1.3 g, 5.9 mmol) and iodine (1.5 g, 5.9 mmol) according to method A afforded 90 mg of **3b** (7%) and 600 mg of **4b** (47%). Alternatively, exposure of **1b** (1.0 g, 8.9 mmol) to HgO (2.1 g, 9.7 mmol) and iodine (2.5 g, 9.8 mmol) according to method B afforded 110 mg of **3b** (5%) and 630 mg of **4b** (30%).

2-(Iodomethyl)-1-oxaspiro[2.4]heptane (3b): IR (film) 1172, 847, 608 cm^{-1}; ^{1}H NMR δ 3.30 (m, 2 H), 2.88 (m, 1 H), 1.81 (m, 4 H), 1.68 (m, 4 H); ^{13}C NMR δ 60.92, 33.13, 27.96, 24.81, 3.69; HRMS $C_7H_{11}IO$ calcd 237.9854, found 237.9855. **7-Iodohept-1-en-3-one (4b):** IR (film) 1696, 1687, 1615 cm^{-1}; ^{1}H NMR δ 6.31 (dd, 1 H, J = 17.5, 10.0 Hz), 6.18 (dd, 1 H, J = 18.5, 2.5 Hz), 5.80 (dd, 1 H, J = 10.0, 2.5 Hz), 3.15 (t, 2 H, J = 8.8 Hz), 2.58 (t, 2 H, J = 7.0 Hz), 1.75 (m, 4 H); ^{13}C NMR δ 200.55, 136.57, 128.42, 38.11, 32.69, 24.54, 5.94; HRMS $C_7H_{11}IO$ calcd 237.9854, found 237.9860.

Reaction of Alcohol 1c. Exposure of **1c** (180 mg, 1.4 mmol) to HgO (300 mg, 1.4 mmol) and iodine (390 mg, 1.5 mmol) according to method A afforded 145 mg of **3c** (41%) and 39 mg of **4c** (11%). Alternatively, exposure of **1c** (500 mg, 4.0 mmol) to HgO (940 mg, 4.3 mmol) and iodine (1.11 g, 4.4 mmol) according to method B afforded 80 mg of **3c** (8%) and 380 mg of **4c** (38%). **2-(Iodomethyl)-1-oxaspiro[2.5]octane (3c):** IR (film) 1248, 839, 608 cm^{-1}; ^{1}H NMR δ 3.55 (dd, 1 H, J = 8.6, 5.0 Hz), 3.10 (AB portion of ABC system, 2 H, J_{ab} = 8.6, J_{ac} = 5.0, J_{bc} = 8.6, $\Delta\nu_{ab}$ = 18.8 Hz), 1.64 (m, 10 H); ^{13}C NMR δ 64.14, 36.89, 30.43, 29.07, 28.94, 24.59, 24.16, 2.59; HRMS $C_8H_{13}IO$ calcd 252.0010, found 252.0009.

8-Iodooct-1-en-3-one (4c): IR (film) 1696, 1680, 1616 cm^{-1}; ^{1}H NMR δ 6.38 (dd, 1 H, J = 18.4, 10.5 Hz), 6.21 (dd, 1 H, J = 18.4, 2.6 Hz), 5.85 (dd, 1 H, J = 10.5, 2.6 Hz), 3.20 (t, 2 H, J = 7.9 Hz), 2.61 (t, 2 H, J = 7.9 Hz), 1.86 (quintet, 2 H, J = 7.9 Hz), 1.65 (quintet, 2 H, J = 7.9 Hz), 1.42 (quintet, 2 H, J = 7.9 Hz); ^{13}C NMR δ 201.11, 137.03, 128.55, 39.47, 33.48, 30.25, 22.91, 6.89; HRMS $C_8H_{13}IO$ calcd 252.0010, found 252.0005.

Reaction of Alcohol 1d. Exposure of **1d** (200 mg, 1.4 mmol) to HgO (340 mg, 1.6 mmol) and iodine (400 mg, 1.6 mmol) according to method A afforded 156 mg of **3d** (41%) and 61 mg of **4d** (16%). Alternatively, exposure of **1d** (500 mg, 3.6 mmol) to HgO (850 mg, 3.9 mmol) and iodine (1.0 g, 3.9 mmol) according to method B afforded 132 mg of **3d** (14%) and 350 mg of **4d** (37%). **2-(Iodomethyl)-1-oxaspiro[2.6]nonane (3d):** IR (film) 1256, 856, 845, 608 cm^{-1}; ^{1}H NMR δ 3.32 (dd, 1 H, J = 8.3, 5.0 Hz), 3.00 (AB portion of ABC system, 2 H, J_{ab} = 8.3, J_{ac} = 5.0, J_{bc} = 8.3, $\Delta\nu_{ab}$ = 17.9 Hz), 1.60 (m, 12 H); ^{13}C NMR δ 64.09, 36.84, 30.40, 29.03, 28.90, 24.56, 24.13, 2.59; HRMS $C_9H_{15}IO$ calcd 266.0167, found 266.0169.

9-Iodonon-1-en-3-one (4d): IR (film) 1694, 1670, 1608 cm^{-1}; ^{1}H NMR δ 6.34 (dd, 1 H, J = 17.5, 10.0 Hz), 6.18 (dd, 1 H, J = 17.5, 2.5 Hz), 5.78 (dd, 1 H, J = 10.0, 2.5 Hz), 3.15 (t, 2 H, J = 7.5 Hz), 2.55 (t, 2 H, J = 7.5 Hz), 1.79 (quintet 2 H, J = 7.5 Hz),

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1.70 (quintet, 2 H, J = 7.5 Hz), 1.35 (m, 4 H); ^{13}C NMR δ 201.60, 137.08, 128.47, 39.63, 33.46, 30.46, 28.28, 23.84, 7.19; HRMS $C_9H_{15}IO$ calcd M+1 267.0245, found 267.0127.

Reaction of Alcohol 1e. Exposure of **1e** (200 mg, 1.3 mmol) to HgO (300 mg, 1.4 mmol) and iodine (360 mg, 1.4 mmol) according to method A afforded 104 mg of **3e** (30%) and 4 mg of **4e** (1%). Alternatively, exposure of **1e** (200 mg, 1.3 mmol) to HgO (300 mg, 1.4 mmol) and iodine (360 mg, 1.4 mmol) according to method B afforded 15 mg of **3e** (4%) and 136 mg of **4e** (37%). **2-(Iodomethyl)-1-oxaspiro[2.7]decane (3e):** IR (film) 1171, 732, 610 cm^{-1}; ^{1}H NMR δ 3.31 (m, 1 H), 3.11 (m, 2 H), 1.64 (m, 14 H); ^{13}C NMR δ 64.74, 35.56, 28.85, 28.76, 26.72, 26.21, 24.92, 23.76, 23.34, 2.76; HRMS $C_{10}H_{17}IO$ calcd 280.0323, found 280.0280.

Reaction of Alcohol 1f. Exposure of **1f** (490 mg, 2.3 mmol) to HgO (550 mg, 2.5 mmol) and iodine (650 mg, 2.5 mmol) according to method A afforded 374 mg of **3f** (50%) and 125 mg of **4f** (17%). Alternatively, exposure of **1f** (490 mg, 2.3 mmol) to HgO (550 mg, 2.5 mmol) and iodine (650 mg, 2.5 mmol) according to method B afforded 53 mg of **3f** (8%) and 238 mg of **4f** (36%). **2-(Iodomethyl)-1-oxaspiro[2.11]tetradecane (3f):** IR (film) 2930, 2856, 1471, 1444, 1345, 1245, 1171, 949, 888, 721 cm^{-1}; ^{1}H NMR δ 3.32 (dd, 1 H, J = 13.3, 9.5 Hz), 3.07 (m, 2 H), 1.70–1.15 (m, 22 H); ^{13}C NMR δ 67.50, 63.43, 31.52, 25.98, 25.86, 25.66, 25.47, 22.52, 22.27, 22.20, 20.66, 20.61, 2.60; HRMS calcd for $C_{14}H_{25}IO$ (M^+ – I) 209.1905, found 209.1912.

General Procedure for n-Bu$_3$SnH/AIBN Reduction Reactions. To a solution of either iodo epoxides **3** or iodo enones **4** (0.50 mmol) in 240 mL of benzene containing AIBN (0.13 mmol) at reflux was added a solution of nBu$_3$SnH (0.6 mmol) in 45 mL of benzene by syringe pump over 3 h. The reaction was cooled to rt, and the solvent was removed in vacuo. Tin byproducts were removed as follows. The residue was partitioned between 10 mL of ether and 10 mL of a 10% aqueous KF solution and vigorously stirred for 24 h. The two phases were separated, the aqueous phase was extracted with ether (4×), and the combined organic phases were dried (Na_2SO_4). The drying agent was removed by filtration and the solvent by rotary evaporation. The crude mixture was purified by column chromatography (35 g of silica gel, ether:pentane = 1.33) followed by bulb-to-bulb distillation. Known products were confirmed by comparing IR, ^{1}H and ^{13}C NMR, and HRMS of purified products with reported data.

Reduction of 3b and 4b. Reduction of **3b** (100 mg, 0.42 mmol) with n-Bu$_3$SnH (150 mg, 0.52 mmol) and AIBN (17 mg, 0.10 mmol) according to the general procedure afforded 4 mg of **8b** (9%) and 9 mg of **9b** (20%), while reduction of **4b** (50 mg, 0.21 mmol) with n-Bu$_3$SnH (73 mg, 0.25 mmol) and AIBN (9 mg, 0.06 mmol) according to the general procedure afforded 4 mg of **8b** (16%) and 4 mg of **9b** (16%).

Reduction of 3c and 4c. Reduction of **3c** (140 mg, 0.56 mmol) with n-Bu$_3$SnH (190 mg, 0.65 mmol) and AIBN (16 mg, 0.10 mmol) according to the general procedure afforded 16 mg of **8c** (23%) and 4 mg of **10c** (5%), while reduction of **4c** (150 mg, 0.60 mmol) with n-Bu$_3$SnH (210 mg, 0.72 mmol) and AIBN (24 mg, 0.15 mmol) according to the general procedure afforded 16 mg of **8c** (21%) and 8 mg of **10c** (11%).

Reduction of 3d and 4d. Reduction of **3d** (150 mg, 0.56 mmol) with n-Bu$_3$SnH (200 mg, 0.69 mmol) and AIBN (16 mg, 0.10 mmol) according to the general procedure afforded 16 mg of **8d** (20%) and 13 mg of **10d** (16%), while reduction of **4d** (150 mg, 0.56 mmol) with n-Bu$_3$SnH (200 mg, 0.69 mmol) and AIBN (16 mg, 0.10 mmol) according to the general procedure afforded 10 mg of **8d** (12%) and 8 mg of **10d** (10%).

Reduction of 3e and 4e. Reduction of **3e** (1.0 g, 3.6 mmol) with n-Bu$_3$SnH (1.2 g, 4.3 mmol) and AIBN (147 mg, 0.90 mmol) according to the general procedure afforded 214 mg of **11** (39%), while reduction of **4e** (130 mg, 0.46 mmol) with n-Bu$_3$SnH (160 mg, 0.55 mmol) and AIBN (19 mg, 0.12 mmol) according to the general procedure afforded 10 mg of **8e** (12%) and 4 mg of **10e** (6%). **1-Hydroxy-9-methylbicyclo[4.2.1]nonane (11):** IR (CCl_4) 3611, 3550–3280, 2915, 2870, 1458, 1075, 1041, 992, 967, 908 cm^{-1}; ^{1}H NMR δ 2.20 (m, 1 H), 2.12–1.98 (m, 3 H), 1.93–1.83 (m, 3 H), 1.82–1.24 (m, 23 H), 1.05 (d, 3 H, J = 7.2 Hz), 1.04 (d, 3 H, J = 7.2 Hz); ^{13}C NMR δ 82.63, 71.46, 48.14, 42.90, 41.89, 39.55, 38.98, 38.75, 37.99, 32.81, 32.73, 30.92, 29.16, 24.89, 23.59, 23.56, 22.88, 22.35, 13.06, 9.25; HRMS calcd for $C_{10}H_{18}O$ 154.1358, found 154.1348.

Reduction of 3f and 4f. Reduction of **3f** (375 mg, 1.1 mmol) with n-Bu$_3$SnH (390 mg, 1.3 mmol) and AIBN (45 mg, 0.27 mmol) according to the general procedure afforded 109 mg of **8f** (47%) and 35 mg of **12** (15%), while reduction of **4f** (190 mg, 0.56 mmol) with n-Bu$_3$SnH (197 mg, 0.68 mmol) and AIBN (23 mg, 0.14 mmol) according to the general procedure afforded 62 mg of **8f** (52%). **2-Ethenylcyclododecanone (12):** IR (CCl_4) 2933, 2867, 2850, 1712, 1635, 1471, 1450, 1136, 1000, 925 cm^{-1}; ^{1}H NMR δ 5.80 (ddd, 1 H, J = 17.3, 10.0, 8.3 Hz), 5.14 (ddd, 1 H, J = 17.2, 1.4, 1.4 Hz), 5.10 (ddd, 1 H, J = 10.3, 1.5, 1.5 Hz), 3.37 (ddd, 1 H, J = 11.4, 8.1, 3.3 Hz), 2.50 (AB portion of ABMX, 2 H, J_{AB} = 15.7, J_{AM} = 6.9, J_{AX} = 3.7, J_{BM} = 9.9, J_{BX} = 3.7, $\Delta\nu_{AB}$ = 28.7 Hz), 1.88 (m, 2 H), 1.70–1.10 (m, 16 H); ^{13}C NMR δ 212.36, 136.90, 116.73, 55.84, 38.29, 30.24, 25.43, 24.91, 24.63, 24.50, 24.22, 23.17, 22.28, 22.22; HRMS calcd for $C_{14}H_{24}O$ 208.1827, found 208.1830.

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Supplementary Material Available: ^{1}H NMR spectra for all compounds (16 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.