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Carbocyclization by Radical Closure onto *O*-Trityl Oximes: Dramatic Effect of Diphenyl Diselenide

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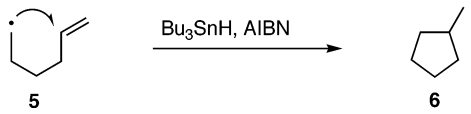
Abstract: *O*-Trityl oximes of 5- and 6-iodoaldehydes undergo radical cyclization to produce oximes when treated in refluxing tetrahydrofuran (THF) with Bu_3SnH, 1,1′-azobis(cyclohexanecarbonitrile), *i*-Pr_2NEt, and diphenyl diselenide (PhSeSePh).

Introduction

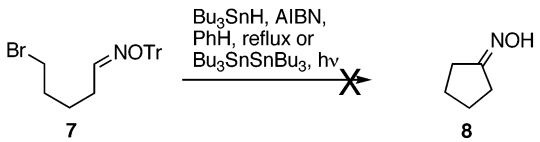
Several years ago, work in this laboratory led to the development of a method for stannane-mediated radical cyclization onto *O*-trityl oxime ethers,[1] as summarized in Scheme 1.[2] This process differs from the classical cyclization of hexenyl radicals (eq 1) in the essential fact that the acceptor



(1)

double bond is preserved in the product (cf. **4** of Scheme 1 and **6** of eq 1). Attempts were made[3] in the initial study to extend the chemistry of Scheme 1 to the more useful case of *carbocyclization*, in which the cyclizing chain does not contain a heteroatom. However, it was found that carbocyclization, unlike the formation of lactones, is not general; it worked in a few cases, though not in others. We have now reexamined such reactions and have identified specific conditions under which the all-carbon process is indeed general, and we report here details of this synthetic method. The products of the reactions are oximes of cyclic ketones and so should serve as precursors to the corresponding amines and ketones.

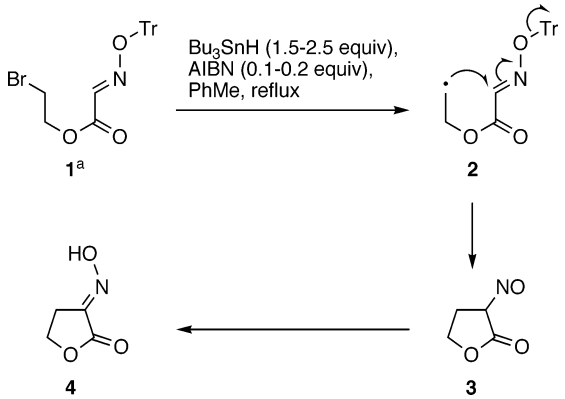
Initial Attempts To Extend the *O*-Trityl Oxime Cyclization to Carbocycles. Initial attempts to effect carbocyclization along the lines of eq 2 were unpromising, as the desired oxime did



(2)

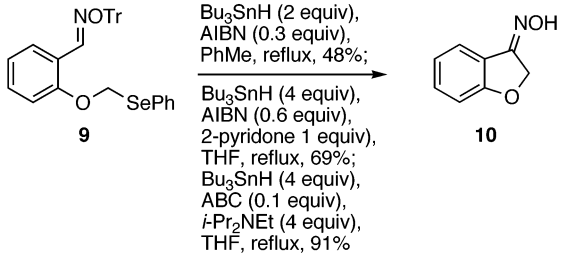
not appear to be formed. Therefore we examined a potentially less demanding case—the ether **9** (eq 3)—chosen because it was known[4] that 5-exo cyclization with oxygen in the chain is faster

Scheme 1[a]



[a] Oxime geometries are arbitrary.

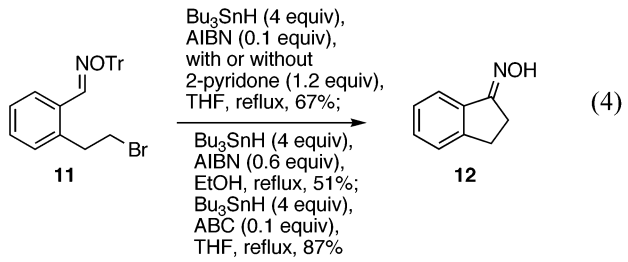
than that of the corresponding all-carbon system. We also expected tautomerization of the intermediate nitroso compound to be facilitated by the adjacent aromatic ring. In the event, a modest yield (48%) of the desired oxime **10** was obtained (eq 3), and the yield was improved (69%) by using tetrahydrofuran



(3)

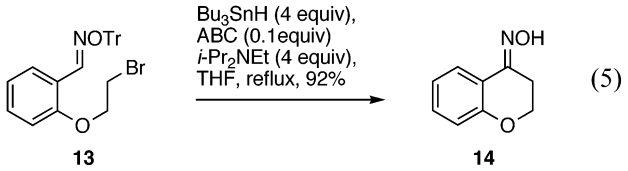
(THF) as solvent in the presence of 2-pyridone—an additive that was introduced in the expectation that it might facilitate (through hydrogen bonding) tautomerization of the intermediate nitroso compound to the oxime. Repetition of the experiment in THF, but with *i*-Pr_2NEt instead of 2-pyridone, and ABC [1,1′-azobis(cyclohexanecarbonitrile)[5]] instead of AIBN (2,2′-azobisisobutyronitrile), raised the yield to 91%.

(1) Clive, D. L. J.; Subedi, R. *Chem. Commun.* **2000**, 237−238.
(2) For evidence of the intermediacy of nitroso compounds in such reactions, see Bella, A. F.; Slawin, A. M. Z.; Walton, J. C. *J. Org. Chem.* **2004**, *69*, 5926−5933.
(3) Subedi, R. Ph.D. Thesis, University of Alberta, Canada, 2002.
(4) Beckwith, A. L. J.; Blair, I.; Phillipou, G. *J. Am. Chem. Soc.* **1974**, *96*, 1613−1614.
(5) ABC (trade name V-40) has a longer half-life than AIBN: Yoshikai, K.; Hayama, T.; Nishimura, K.; Yamada, K.; Tomioka, K. *J. Org. Chem.* **2005**, *70*, 681−685.



The all-carbon system **11** was examined next under several different conditions, some of which are shown in eq 4. Compound **7** was also cyclized by treatment with Bu_3SnH (2 equiv) and AIBN (0.3 equiv) but in THF as solvent; with this procedure, cyclopentanone oxime was isolated in 41% yield.

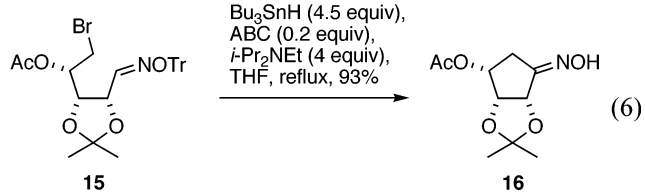
At this point, we examined the possibility of carrying out a 6-exo trigonal cyclization and we found it convenient to use compound **13** (eq 5); while the resulting ring does contain a heteroatom, its location would not facilitate tautomerization of the intermediate nitroso compound (cf. **3**) to any significant extent. A large number of different conditions were tried (Table 1); those shown in eq 5 gave the highest yield. In all our cyclization studies we have used the standard method of simultaneous slow addition of stannane and initiator (by double syringe pump) and have kept initial concentrations of the substrate at ca. 0.02 M.

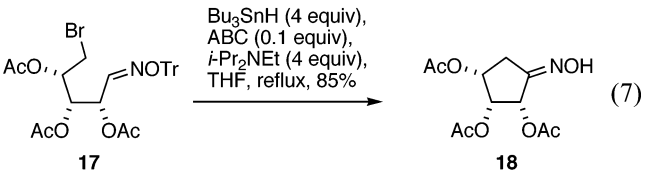


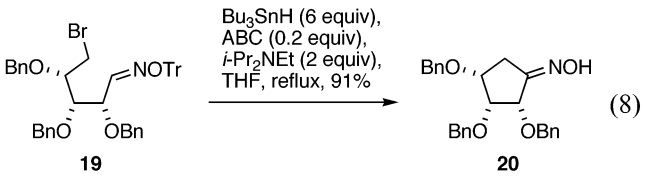
The experiments summarized in Table 1 cover a range of solvent dielectric constants and boiling points, the presence or absence of Lewis acids (which might coordinate to the oxime nitrogen), and the presence or absence of additives (*N*-methylpyrrolidinone, 2-pyridone, pyridine, Hünig's base), which, together with solvent polarity, might facilitate tautomerization[6] of the intermediate *C*-nitroso compound. The observations summarized in Table 1 suggested that the most promising conditions are the use of THF as a solvent, *i*-Pr_2NEt as base, and ABC as initiator. When the THF−Hünig's base−ABC procedure was applied to **7**, the yield was 41%, the same value as that obtained with AIBN in THF without added base (see above). We assume that the base does indeed facilitate tautomerization of an intermediate nitroso compound to the oxime, but the reason for the solvent effect (THF versus PhMe, entries i and iii) is not clear. The ethereal solvents examined [THF, 1,2-dimethoxyethane (DME), dioxane, tetrahydropyran] all have the potential for generating radicals by loss of hydrogens α to oxygen,[7] and it is known[8] that the use of benzene (and presumably toluene) as a solvent for radical reactions can result in homolytic addition to the solvent; the resulting cyclohexadienyl radicals do not propagate the desired chain reaction. While such interference may occur in the present case, it is unlikely to be the only solvent effect since a few of our *O*-trityl oximes do cyclize in an aromatic solvent (**9**, 48% in PhMe; **13**, 43% in PhMe; **15**, 74% in PhH).

Evaluation of First-Generation Conditions: Use of THF, Hünig's Base, and 1,1′-Azobis(cyclohexanecarbonitrile). Although the result with **7** was poor (41% in THF, as stated earlier), we decided to examine a number of other substrates under the conditions that worked best with **13**, and we chose several carbohydrate-derived oximes; these would lead to optically pure cyclopentanone derivatives bearing a variety of functional groups.

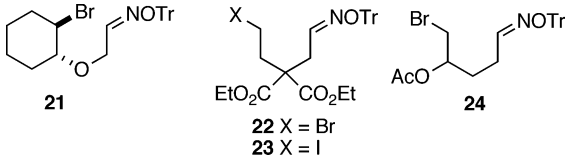
Oxime **15** cyclized efficiently (eq 6), but it appears to be an inherently favorable case, as the simple use of AIBN in PhH without added base gave a yield of 74%. The related, but more flexible, oxime **17** also cyclized in good yield (eq 7), as did the corresponding perbenzylated compound **19** (eq 8), again with an excess of stannane to ensure consumption of the starting material.







Under the conditions used for the reactions shown in eqs 6−8, the oximes **21**[9]−**24** gave little, if any, of the desired cyclization products. In the case of **22** and **23**, the presence of geminal disubstitution had been expected to facilitate ring closure but, evidently, other factors were at work.



When equimolar amounts of **21** and **17** were subjected to our standard conditions [Bu_3SnH (4 equiv), ABC (0.2 equiv), THF, and *i*-Pr_2NEt], the former was largely recovered (65%), while the latter gave the normal cyclization product (76%), and so we conclude that the failure of some compounds to cyclize is not due to contamination by adventitious radical inhibitors. The *O*-benzyl oxime corresponding to **21** cyclized normally (no base, Bu_3SnH, ABC, THF, 61%) to the expected[10] *O*-benzylhydroxylamine.

(6) (a) Donaruma, L. G. *J. Org. Chem.* **1958**, *23*, 1338−1340. (b) Di Giacomo, A. *J. Org. Chem.* **1965**, *30*, 2614−2617.
(7) Cf. Yoshimitsu, T.; Tsunoda, M.; Nagaoka, H. *J. Chem. Soc. Chem. Commun*. **1999**, 1745−1746.
(8) Beckwith, A. L. J.; Bowry, V. W.; Bowman, W. R.; Mann, E.; Parr, J.; Storey, J. M. D. *Angew. Chem., Int. Ed*. **2004**, **43**, 95−98.

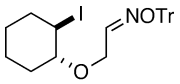
(9) While the desired cyclization product from **21** would have a heteroatom in the newly formed ring, the location of the heteroatom would not (greatly) facilitate tautomerization of the intermediate nitroso compound.

Table 1. Radical Cyclization of **13**

	Bu_3SnH equiv	initiator (equiv)	additive (equiv)	solvent	temp	yield of **14**, %
i	4	AIBN (0.4)		PhMe	reflux	43[a]
ii	4	AIBN (0.4)	2-pyridone (1.3)	THF	reflux	71[a]
iii	4	AIBN (0.4)		THF	reflux	71[a]
iv	4	AIBN (0.8)	*N*-methylpyrrolidinone (1.5)	THF	reflux	69[a]
v	4	AIBN (0.6)		MeCN	reflux	52[a]
vi	4	AIBN (0.63)		DME	reflux	67[a]
vii	4	AIBN (0.6)	pyridine (1.4)	THF	reflux	54[a,b]
viii	2	AIBN (0.2)	$BF_3{\cdot}Et_2O$ (4)	THF	reflux	*c*
ix	4	AIBN (0.6)	$Ti(OPr\text{-}i)_4$ (4)	THF	reflux	39[a]
x	1.5	Et_3B (1.3), air		PhH	room temp	*d*
xi	2	Et_3B (2.5), air	$BF_3{\cdot}Et_2O$ (3)	THF	room temp	*e*
xii	4	AIBN (0.6)		dioxane	reflux	45[a]
xiii	4	AIBN (0.6)		tetrahydropyran	reflux	68[a]
xiv	4	AIBN (0.6)		1:1 THF−DMSO	reflux	43[a,f]
xv	4	AIBN (0.1)		2-butanone	reflux	49[a] (61[g])[a]
xvi	4	AIBN (0.1)		EtOAc	reflux	36[a]
xvii	4	ABC (0.1)	pyridine (4)	THF	reflux	86[h]
xviii	4	ABC (0.1)	pyridine (4)	THF	reflux	86[a]
xix	4	ABC (0.1)	*i*-Pr_2NEt (4)	THF	reflux	92[h]
xx	4	AIBN (0.6)	Bu_3SnCl (4)	THF	reflux	68[a]

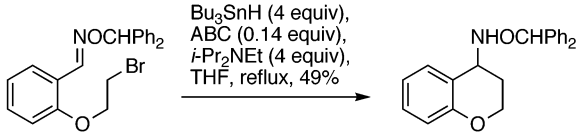
[a] Stannane and initiator were added in two approximately equal portions, as considerable starting material remained after the initial 10-h reflux period. [b] After recrystallization to remove traces of AIBN. [c] No product detected (tlc). [d] Only a trace of product detected (tlc), even after additional Bu_3SnH (1.5 equiv) and Et_3B (1.3 equiv) were added. [e] Mainly starting material recovered. [f] Not corrected for recovered starting material (10%). [g] Based on conversion; 16% of starting material recovered. [h] The excess of reagents was used initially, rather than being added in portions.

Iodide **25** cyclized in THF in 68% yield upon treatment with Bu_3SnH (3 equiv) in the presence of ABC (2 equiv) and *i*-Pr_2-NEt (4 equiv); the yield was somewhat lowered (57%) by using lesser amounts of stannane (1.2 equiv) and ABC (1 equiv).



25

The effect of replacing Bu_3SnH by two other reducing agents was examined. Treatment of **21** with $(Me_3Si)_3SiH$[11] and ABC, with or without *i*-Pr_2NEt, in refluxing THF led to recovery (93−98%) of the starting bromide; and the same bromide was again recovered (82%) when it was exposed to the action of *N*-ethylpiperidine hypophosphite[12] [$C_8H_{15}N{\cdot}H_3PO_2$] and AIBN in refluxing THF. A mixture of **21** and its corresponding *O*-benzyl oxime was treated with *N*-ethylpiperidine hypophosphite and ABC (0.6 equiv) in refluxing THF; only the benzyl oxime appeared to cyclize (27% yield).



26 **27** (9)

A control experiment in which the *O*-trityl oxime of benzaldehyde[13] was treated with Bu_3SnH, AIBN, and *i*-Pr_2NEt in refluxing THF showed that the carbon−nitrogen double bond is not reduced, as the starting oxime was recovered (95%).

Suspecting that formation of a persistent radical ($Ph_3C\bullet$) might be involved in the failure of some compounds to cyclize, we subjected the *O*-benzhydryl oxime **26** to our cyclization conditions but obtained the hydroxylamine **27** (eq 9), indicating that $Ph_2CH\bullet$ is not a sufficiently good radical leaving group.

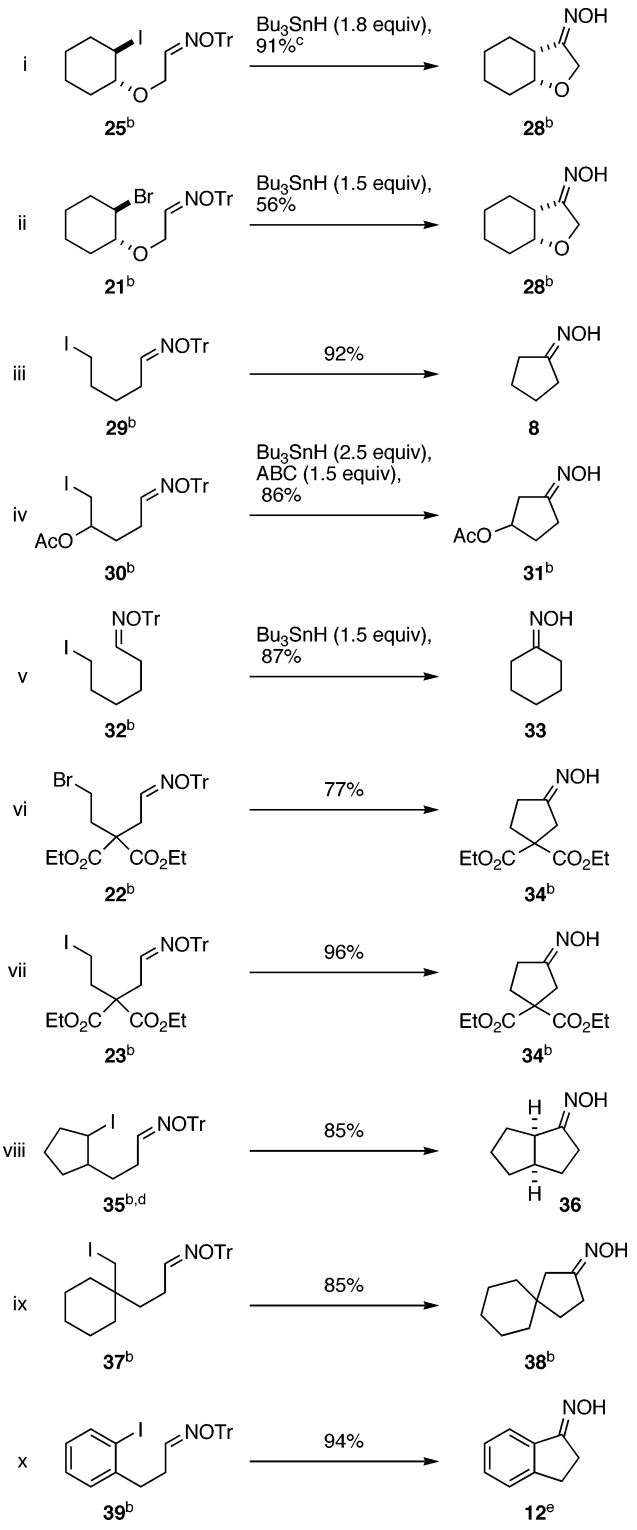
Second-Generation General Conditions: Effect of Diphenyl Diselenide on the Cyclization. As our attempt to incorporate the release of less persistent species than triphenylmethyl radicals was unsuccessful, we decided to examine the effect of generating PhSeH in the reaction mixture,[14] our expectation being that the selenol would rapidly capture triphenylmethyl radicals. To this end, iodide **25** (Table 2, entry i) was cyclized in the presence of PhSeSePh.[14] When this experiment was conducted in PhH [with AIBN (0.1 equiv) and no base] the yield was 38%, but in THF [with ABC (1 equiv) and *i*-Pr_2NEt (4 equiv)] the yield rose to 91%. These conditions were found to be general—even bromide **21** cyclized—and were applied to all the examples listed in Table 2. In a test experiment with **25**, it was established that there is no advantage to using more than 1 equiv of ABC (Table 2, entry 1, footnote *c*).

If our assumption is correct that buildup of a persistent radical prevents chain propagation, and hence cyclization, then the beneficial effect produced by the presence of PhSeSePh (which leads to PhSeH on reaction with Bu_3SnH) is easily understandable. Benzeneselenol has a much greater reactivity (several orders of magnitude) toward carbon radicals compared to the reactivity of Bu_3SnH;[15] consequently, even persistent radicals are reduced,[14] and the resulting phenylselenyl radicals rapidly generate stannyl radicals from Bu_3SnH to re-form PhSeH. In this way, the buildup of persistent radicals (which react slowly with stannanes) is suppressed by the presence of small quantities of PhSeSePh, and so chain propagation is not disrupted.

The iodo ester **23** was used for five additional experiments, whose outcome is listed in Table 3, together with the result (entry i) for our optimum conditions. The tabulated observations confirm the superiority of the conditions (see Table 2, entry i)

(10) Review: Fallis, A. G.; Brinza, I. M. *Tetrahedron* **1997**, *52*, 17543−17594.
(11) Chatgilialoglu, C. *Organosilanes in Radical Chemistry*; Wiley: Chichester, U.K., 2004.
(12) Cf Graham, S. R.; Murphy, J. A.; Kennedy, A. R. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3071−3073.
(13) Lutz, W. B. *J. Org. Chem.* **1971**, *36*, 3835−3837.
(14) Crich, D.; Hwang, J.-T. *J. Org. Chem.* **1998**, *63*, 2765−2770 and references cited therein.
(15) (a) Chatgilialoglu, C.; Ingold, K. U.; Scaiano, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 7739−7742. (b) Newcomb, M.; Choi, S.-Y.; Horner, J. H. *J. Org. Chem.* **1999**, *64*, 1225−1231.

Table 2. Cyclization of *O*-Trityloximes[a]



[a] Except for the differences indicated, the following conditions were used: Bu_3SnH (1.2 equiv), ABC (1 equiv), PhSeSePh (0.2 equiv), *i*-Pr_2NEt (4 equiv), THF, reflux. [b] Mixture of geometric isomers. [c] 89% with 2 equiv of ABC. [d] Relative stereochemistry not established. [e] (*E*) isomer.

identified by the experiments with **25**. While the use of diphenyl diselenide (cf. entries i and vi) is a key factor (as described above), there is clearly a significant dependence on the solvent (cf. entries i and iii), with THF being an effective choice, and on the quantity of initiator, with 1 equiv being needed (cf. entries i and v); the presence of Hünig's base (cf. entries i and ii) is also helpful.

Table 3. Optimization Studies on Cyclization of **23**

entry	solvent	*i*-Pr_2NEt equiv	PhSeSePh equiv	initiator (equiv)	yield of **27**, %
i	THF	4	0.2	ABC (1)	96
ii	THF	none	0.2	ABC (1)	71
iii	PhH	4	0.2	ABC (1)	63
iv	THF	4	0.2	AIBN (1)	83
v	THF	4	0.2	ABC (0.1)	59
vi	THF	4	none	ABC (1)	56

Preparation of Starting *O*-Trityl Oximes. The *O*-trityl oxime ethers used in this work are easily prepared (see Supporting Information for schemes and experimental details) from the corresponding aldehydes, which are themselves readily available. The aldehydes react in high yield (usually >90%) with $TrONH_2$[13] in THF (at 65 °C) or CH_2Cl_2 (room temperature or reflux); those aldehydes required for the preparation of **7**,[16] **9**,[17] **11**,[18] **13**,[19] **29**,[20−22] **32**,[20−22] and **39**[23] were made by the literature methods cited, while **15**, **17**, and **19** were prepared by straightforward routes from known carbohydrates.

Conclusions

Our experiments aimed at extending the process of Scheme 1 to carbocycles allowed us to identify a set of conditions that is general, as well as high-yielding. The results summarized in Table 2 clearly establish that radical cyclization of iodo *O*-trityl oximes in the presence of PhSeSePh and Hünig's base, with THF as a solvent, and 1,1′-azobis(cyclohexanecarbonitrile) as initiator constitutes an efficient route to five- and six-membered carbocycles, independent of the substitution pattern. The method is applicable to flexible chains as well as to those that are rigidified by the presence of rings; carbohydrates represent a very convenient source of the oximes that undergo cyclization. A useful feature of the reaction is that the products contain the original carbonyl group in the form of its oxime and so should be amenable to a number of synthetic transformations.

Experimental Section

General Procedure for Preparing *O*-(Triphenylmethyl)oximes. $TrONH_2$[13] (1.0 equiv) was added to a stirred solution of the aldehyde (1.0 equiv) in dry THF, and the mixture was heated at 65 °C for 12 h under N_2, cooled, and evaporated to give a residue that was processed as described for the individual experiments. In some experiments $CH_2Cl_2$was used, either at room temperature or at reflux.

General Procedure for Radical Cyclization in the Absence of Diphenyl Diselenide (Procedure A). The substrate and base were placed in a round-bottomed flask equipped with a Teflon-coated stirring bar and a reflux condenser sealed with a rubber septum. The system was flushed with argon, and dry solvent was injected into the flask.

(16) Kelkar, S. V.; Joshi, G. S.; Reddy, G. B.; Kulkarni, G. H. *Synth. Commun.* **1989**, *19*, 1369−1379.
(17) Clive, D. L. J.; Yang, W.; MacDonald, A. C.; Wang, Z.; Cantin, M. *J. Org. Chem.* **2001**, *66*, 1966−1983.
(18) Page, P. C. B.; Rassias, G. A.; Barros, D.; Bethell, D.; Schilling, M. B. *J. Chem. Soc., Perkin Trans. 1* **2000**, *19*, 3325−3334.
(19) Kirmse, W.; Hömberger, G. *J. Am. Chem. Soc.* **1991**, *113*, 3925−3934.
(20) Barluenga, J.; González-Bobes, F.; Murguía, M. C.; Ananthoju, S. R.; González, J. M. *Chem.−Eur. J.* **2004**, *10*, 4206−4213.
(21) Buijs, W.; van Elburg, P.; van der Gen, A. *Synth. Commun.* **1983**, *13*, 387−392.
(22) We used HI (cf. ref 16) to make the parent iodo alcohol, instead of P_2I_4 (ref 21). For oxidation to the iodo aldehyde (ref 20) we used PDC.
(23) Gibson, S. E. (née Thomas); Guillo, N.; Middleton, R. J.; Thuilliez, A.; Tozer, M. J. *J. Chem. Soc., Perkin Trans.* **1997**, *1*, 447−455.

The solution was heated to reflux, and solutions of Bu_3SnH and initiator in the corresponding solvent were injected simultaneously by syringe pump over 10 h. Refluxing was continued for an arbitrary period of 2 h after the addition. The mixture was cooled, and the solvent was evaporated to give a residue that was processed as described for the individual experiments.

General Procedure for Radical Cyclization in the Presence of Diphenyl Diselenide (Procedure B). The substrate and PhSeSePh (ca 0.2 mol/mol of substrate) were placed in a round-bottomed flask with a condenser fused on. The flask contained a Teflon-coated stirring bar and was sealed with a rubber septum. Dry THF and Hünig's base (ca 4 mol/mol of substrate) were injected and the solution was purged with Ar via a long needle (dipping into the solvent) for 0.5 h. (We found that yields were lower if oxygen was present.) The solution was heated at 95 °C (oil bath), and solutions of Bu_3SnH (ca 1.2 mol/mol of substrate) and ABC (ca 1 mol/mol of substrate), each in dry THF, were injected simultaneously by syringe pump over 10 h (Ar atmosphere). Refluxing was continued for an arbitrary period of 2 h after the addition. The mixture was cooled and the solvent was evaporated to give a residue that was processed as described for the individual experiments.

2,3-Dihydro-1*H*-inden-1-one Oxime (12) (from 39). General procedure B for radical cyclization was followed, with **39** (44.0 mg, 0.085 mmol), PhSeSePh (5.3 mg, 0.017 mmol), and Hünig's base (0.059 mL, 0.34 mmol) in dry THF (10 mL); Bu_3SnH (0.027 mL, 0.10 mmol) in THF (3 mL); and ABC (21.0 mg, 0.086 mmol) in THF (3 mL). After evaporation of the solvent, flash chromatography of the residue over silica gel (2 × 30 cm), with elution by 30% EtOAc−hexane, gave **12**[24,25] (12.0 mg, 94%) as a single isomer, identical to material made from **11**.

Acetic Acid [*R*-(1α,2α,3α)]-2,3-Diacetoxy-4-(hydroxyimino)cyclopentyl Ester (18). General procedure A for radical cyclization was followed, with **17** (131 mg, 0.219 mmol) in THF (15 mL), Bu_3SnH (256 mg, 0.879 mmol) in THF (5 mL), ABC (6 mg, 0.02 mmol) in THF (5 mL), and *i*-Pr_2NEt (114 mg, 0.879 mmol). Flash chromatography of the residue over silica gel (1.7 × 20 cm), with elution by 50% EtOAc−hexane, gave **18** (50.1 mg, 85%) as a foam, which was a mixture of *Z* and *E* isomers: Fourier transform infrared (FTIR) (CH_2Cl_2 cast) 3396, 2936, 1750, 1429 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.01−2.05 (3 s, 9H), 2.70−2.79 (m, 1H), 2.97 (apparent dd, J = 15.0, 7.5 Hz, 1H), 5.22−5.34 (m, 1.2H), 5.49 (t, J = 4.5 Hz, 0.85H), 5.68 (dd, J = 5.0, 2.0 Hz, 0.82H), 6.02−6.08 (m, 0.21H), 8.61−9.18 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 20.2 (q), 20.3 (q), 20.4 (q), 20.5 (q), 20.6 (q), 20.7 (q), 30.1 (t), 33.0 (t), 65.2 (d), 68.7 (d), 69.9 (d), 70.0 (d), 71.0 (d), 71.4 (d), 156.0 (s), 169.7 (s), 169.8 (s), 170.0 (s); exact mass *m*/*z* calcd for $C_{11}H_{15}NO_7$ 273.0848, found 273.0849.

Acetic Acid 3-(Hydroxyimino)cyclopentyl Ester (31). General procedure B for radical cyclization was followed, with **30** (440 mg, 0.835 mmol), PhSeSePh (52.1 mg, 0.1669 mmol), and Hünig's base (0.58 mL, 3.33 mmol) in THF (25 mL); Bu_3SnH (0.56 mL, 2.08 mmol) in THF (10 mL); and ABC (0.304 g, 1.244 mmol) in THF (10 mL). After evaporation of the solvent, flash chromatography of the residue over silica gel (1.5 × 30 cm), with elution by 30% EtOAc−hexane, gave **31** (112 mg, 86%) as a mixture of *Z* and *E* isomers: FTIR (CH_2Cl_2, cast) 3254, 2978, 1737, 1234 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.88−2.07 (m, 5H), 2.38−2.83 (m, 4H), 5.22−5.33 (m, 1H), 8.58−8.62 (two overlapping br s, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 21.1 (q), 24.5 (t), 27.7 (t), 30.2 (t), 30.7 (t), 33.9 (t), 37.0 (t), 73.8 (d), 163.4 (s), 163.8 (s), 170.49 (s), 170.53 (s); exact mass (electrospray) *m*/*z* calcd for $C_7H_{11}NNaO_3$ 180.06311, found 180.06286.

3-(Hydroxyimino)cyclopentane-1,1-dicarboxylic Acid Diethyl Ester (34) (from 23). General procedure B for radical cyclization was followed with **23** (280 mg, 0.457 mmol), PhSeSePh (28.0 mg, 0.0897 mmol), and Hünig's base (0.32 mL, 1.837 mmol) in THF (30 mL); Bu_3SnH (0.15 mL, 0.5576 mmol) in THF (10 mL); and ABC (120 mg, 0.4911 mmol) in THF (10 mL). After evaporation of the solvent, flash chromatography of the residue over silica gel (2 × 20 cm), with elution by 30% EtOAc−hexane, gave **34** (106.7 mg, 96%) as a mixture (ca. 1:1) of *Z* and *E* isomers (^1H NMR): FTIR (CH_2Cl_2cast) 3254, 2983, 1731, 1368 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.18−1.255 (overlapping t, 6H), 2.31 (q, J = 7.8 Hz, 2H), 2.51 (t, J = 7.9 Hz, 1H), 2.60 (t, J = 8.1 Hz, 1H), 2.97 (s, 1H), 3.08 (s, 1H), 4.10−4.22 (overlapping q, 4H), 8.78−8.90 (two overlapping br s, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 13.8 (q), 25.7 (t), 28.9 (t), 31.6 (t), 32.0 (t), 34.7 (t), 37.8 (t), 58.5 (s), 58.6 (s), 61.7 (t), 162.6 (s), 162.8 (s), 170.6 (s), 170.8 (s); exact mass (electrospray) *m*/*z* calcd for $C_{11}H_{18}NO_5$ (M + H) 244.11795, found 244.11828.

***cis*-Hexahydropentalen-1(2*H*)-one Oxime (36).** General procedure B for radical cyclization was followed, with **35** (376.7 mg, 0.797 mmol), PhSeSePh (49.7 mg, 0.159 mmol), and Hünig's base (0.56 mL, 3.215 mmol) in dry THF (30 mL); Bu_3SnH (0.257 mL, 0.955 mmol) in THF (9 mL); and ABC (190 mg, 0.778 mmol) in THF (9 mL). After evaporation of the solvent, flash chromatography of the residue over silica gel (2 × 30 cm), with elution by 30% EtOAc−hexane, gave **36** (0.0936 g, 85%) as an oil, which was a mixture of *Z* and *E* isomers (^1H NMR): FTIR (CH_2Cl_2,cast) 3244 2949, 2867, 1661 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.25−2.70 (m, 11H), 2.92 (ddd, J = 8.7, 8.7, 4.6 Hz, 0.85H), 3.20 (ddd, J = 9.1, 9.1, 5.1 Hz, 0.13H), 9.0 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 26.2 (t), 26.7 (t), 27.1 (t), 28.9 (t), 29.3 (t), 30.0 (t), 30.9 (t), 32.4 (t), 32.5 (t), 32.8 (t), 43.10 (d), 43.14 (d), 43.7 (d), 46.8 (d), 170.7 (s); exact mass *m*/*z* calcd for $C_8H_{13}NO$ 139.09972, found 139.09970.

Spiro[4.5]decan-2-one Oxime (38).[26] General procedure B for radical cyclization was followed, with **37** (330 mg, 0.61 mmol), PhSeSePh (38 mg, 0.12 mmol), and Hünig's base (0.43 mL, 2.47 mmol) in dry THF (30 mL); Bu_3SnH (0.20 mL, 0.74 mmol) in THF (10 mL); and ABC (150 mg, 0.61 mmol) in THF (10 mL). After evaporation of the solvent, flash chromatography of the residue over silica gel (2 × 30 cm), with elution by 30% EtOAc−hexane, gave **38**[26] (88 mg, 85%) as an oil that was a mixture of *Z* and *E* isomers (^1H NMR): FTIR (CH_2Cl_2 cast) 3239, 3126, 2924, 2855 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.25−1.70 (m, 12H), 2.24 (s, 0.7H), 2.35 (s, 1.2H), 2.44 (t, J = 7.7 Hz, 1H), 2.51 (t, J = 7.6 Hz, 1H), 8.30 and 8.35 (two overlapping br s, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 23.23 (t), 23.25 (t), 25.0 (t), 26.19 (t), 26.23 (t), 28.4 (t), 35.7 (t), 36.4 (t), 37.1 (t), 38.9 (t), 41.5 (t/s), 41.8 (t/s), 42.3 (t/s), 166.7 (s), 167.0 (s); exact mass *m*/*z* calcd for $C_{10}H_{17}NO$ 167.13101, found 167.13098.

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Supporting Information Available: Experimental procedures for **7**−**11**, **12** (from **11**), **13**−**17**, **19**−**27, 30**, **32**−**33**, **34** (from **22**), **35**, **37**, **39**, **41**−**45**, **47**, **49**, **51**, **53, 54**, **56**−**58**, **60**−**62**, *trans*-2-[(2-bromocyclohexyl)oxy]acetaldehyde *O*-(phenylmethyl)-oxime, and *O*-benzyl-*N*-[(3aα,7aα)octahydrobenzofuran-3-yl]-hydroxylamine; NMR spectra of all new compounds except one isomer of **32**, **39**, and **43**−**45**, which were used crude; and X-ray data for **12**. This material is available free of charge via the Internet at http://pubs.acs.org.

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