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FREE RADICAL ANNULATION OF DICHLOROCYCLOBUTANONES WITH SEQUENTIAL RING EXPANSION

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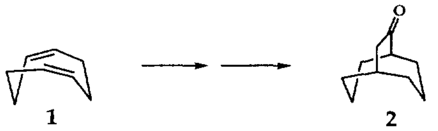
Abstract: *A new synthetic sequence that adds the elements of ketene across the termini of a 1,5-diene is described. Dichlorocyclobutanone adducts from reaction of dichloroketene with 1,5-dienes undergo intramolecular free radical annulation. Lewis acid-promoted ring-opening of the cyclized cyclobutanones then yields novel ring expansion products. Reaction of (R)-carvone provides an unusual example leading to the formation of a tricyclic dione. The carbonyl group of carvone enhances the radical cyclization and influences the ring-opening pathway.*

Introduction

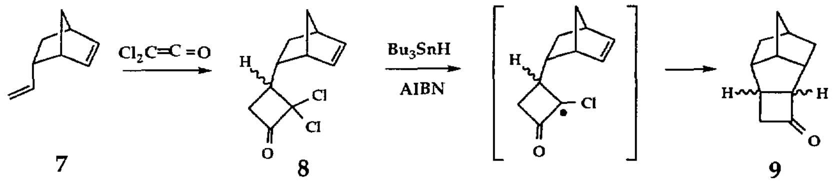
Defined reaction sequences, or synthetic reaction cascades, can lead to useful and even unexpected transformations. We have discovered a new reaction sequence that interpolates the elements of ketene across the double bonds of a 1,5-diene (eq 1).[1,2] The new method is straightforward and efficient. It takes advantage of the ready cycloaddition of dichloroketene to isolated double bonds and draws upon the availability of a broad spectrum of 1,5-dienes developed in the context of the Cope rearrangement.



(1)

Results and Discussion

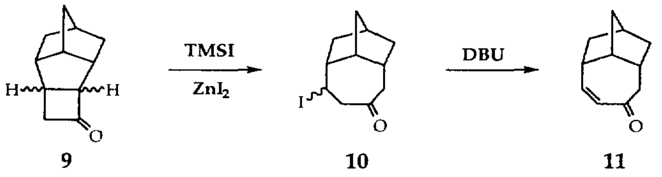
In the first step of the sequence, the 1,5-diene is treated with one equivalent of dichloroketene to form a dichlorocyclobutanone adduct.[3] In the example shown in eq 2, advantage is taken of both the chemoselectivity for the less substituted double bond and the regioselectivity,



(2)

the carbonyl group of the ketene becoming attached to the less substituted end of the double bond. Treatment of the dichloroketene adduct **8**, a mixture of two diastereomers, with tri-*n*-butyltin hydride yields a cyclobutyl radical that undergoes internal addition to the second double bond.[4,5] The radical on the four-membered ring is stabilized by the adjacent carbonyl as well as by the chlorine substitutent.[6] These features make dichlorocyclobutanones much better substrates for fruitful radical generation and double bond addition than ordinary alkyl chlorides. The tin hydride promoted radical addition of the cyclobutanone takes place in the well established 1,5-addition mode.[7] The method thus provides a general way to prepare fused and bridged cyclobutanones. In the example in eq 2, the use of 2.2 equivalents of tin hydride results in production of the tetracyclo$[6.2.1.0^{6,10}0^{2,5}]$undecan-4-one (**9**) as an *exo* and *endo* mixture.

Treatment of **9** with trimethylsilyl iodide leads to cyclobutanone ring opening (eq 3) and yields the corresponding seven-membered ring iodide **10**.[8] The iodide is readily eliminated to



(3)

yield the enone **11**, or the iodide can be reductively removed to provide the corresponding saturated ketone.

In sum, this novel reaction sequence is suitable for the preparation of fused and bridged seven-membered rings. More examples are shown in Table 1. Entries 3 and 4 (Table 1) attest to the potential utility of the method in the preparation of substituted cycloheptanones. The use of allyl vinyl ether **23** (Table 1, entry 5) to prepare the fused tetrahydrofuran **25** shows the versatility of the procedure. Employing the annulation sequence on 2-allylmethylenecyclohexane **26** and the corresponding cycloheptane **29** (Table 1, entries 6 and 7) leads, following dichloroketene addition and subsequent cyclization, to the highly condensed ring systems **28** and **31**.

Use of divinylbenzene **32** (Table 1, entry 8) demonstrates that molecules with double bonds conjugated to an aromatic ring make good substrates. In the radical addition, however,

Table 1. [2 + 2] Cycloaddition and Dichlorocyclobutanone Annulation

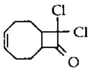
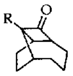
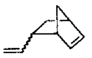
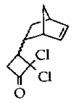
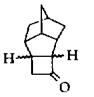
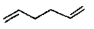
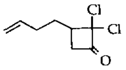
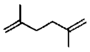
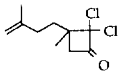
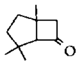
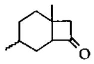
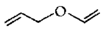
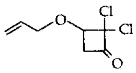
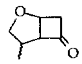
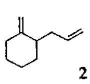
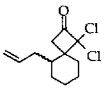
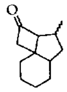
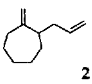
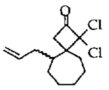
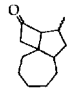
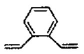
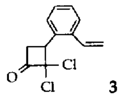
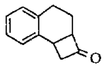
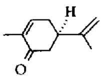
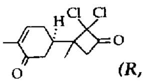
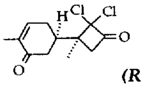
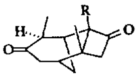
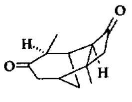
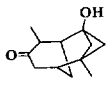
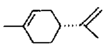
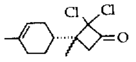
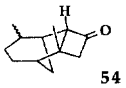
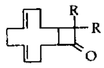
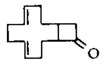
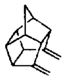
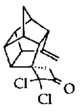
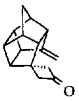
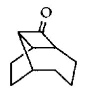
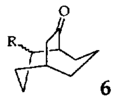
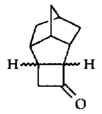
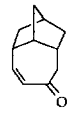
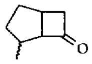
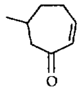
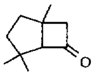
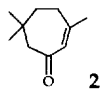
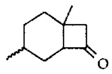
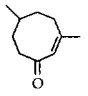
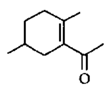
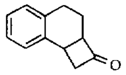
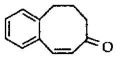
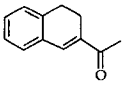
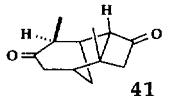
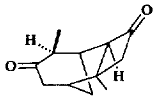
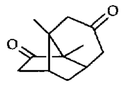
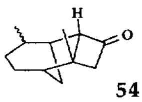
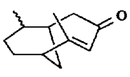
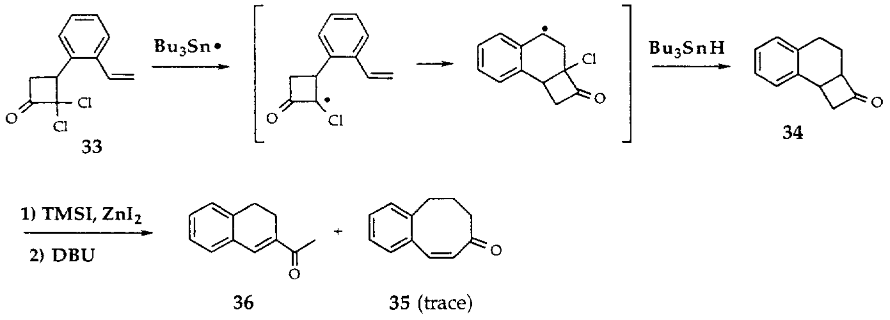
entry	1,5-diene	ketene adduct		cyclization product	
1	 1	 3	85%	 4 5	R=Cl, 91% R=H, 85%
2	 7 (75/25 *endo/exo*)	 8	95% (75/25)	 9	58% (84/16) (based on *endo*)
3	 12	 13	69%	 14	85% (84/16)
4	 16	 17	90%	 18 21% +  19 70%(48/52)	
5	 23	 24	45%	 25	72% (85/15)
6	 26	 27	63% (55/45)	 28	43% (90/10)
7	 29	 30	45% (65/35)	 31	41% (85/15)
8	 32	 33	70%	 34	61%
9	 (*R*)-carvone	 (*R,R*)-37 +  (*R,S*)-37	69% 12%	  45 45~55% +  49 10~20%	40, R=Cl 71% 41, R = H 51%
10	 (*R*)-limonene	 53	95% (55/45)	 54	51% (87/13)
11	 56		57, R=Cl 90% 58, R=Br 50%	 59	93% (from 57)
12	 60	 61	54%	 62	94%

Table 2. TMSI-Promoted Ring-Opening of Cyclobutanones

entry	cyclobutanone	ring-opening
1	 5	 6 R=I, 87% (35/65) 2 R=H, 84%
2	 9	 11 92%
3	 14	 15 90%
4	 18	 20 87%
5	 19	 +  21 40% 22 48%
6	 34	 +  35 trace 36 83%
7	 41 or  45	 52 73%
8	 54 (87:13)	 55 94%

formation of the stabilized benzyl radical (Scheme 1) occurs by 6-*endo* cyclization and is the

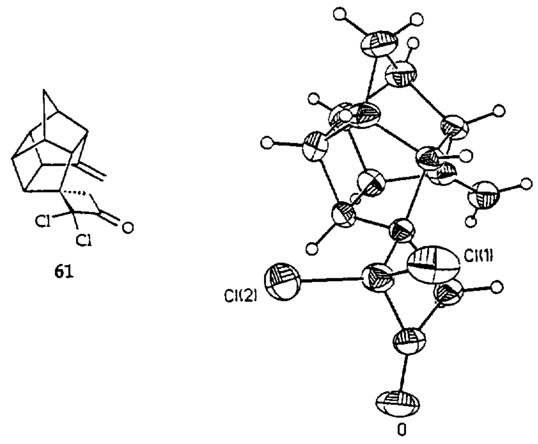
Scheme 1



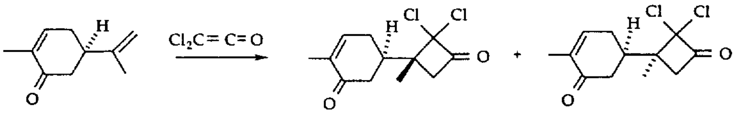
dominant pathway in forming the fused cyclobutanone **34**. Ring-opening of **34** leads mainly to the six-membered product **36** (Table 2, entry 6).

Attempted extension of 1,5-cyclization to *trans,trans,cis*-1,5,9-cyclododecatriene (**56**) (Table 1, entry 11) led to the formation of direct reduction product **59**, even when use was made of the more reactive dibromocyclobutanone **58** as the radical precursor. This result suggests that the conformation of the large ring may not be favorable for cyclization. Application to the highly condensed 1,5-diene **60** (Table 1, entry 12) was not successful, because the chlorines of **61** are *exo*-oriented with respect to the double bond as shown by X-ray crystal structure analysis (Figure 1).

Figure 1. X-Ray Structure of 61



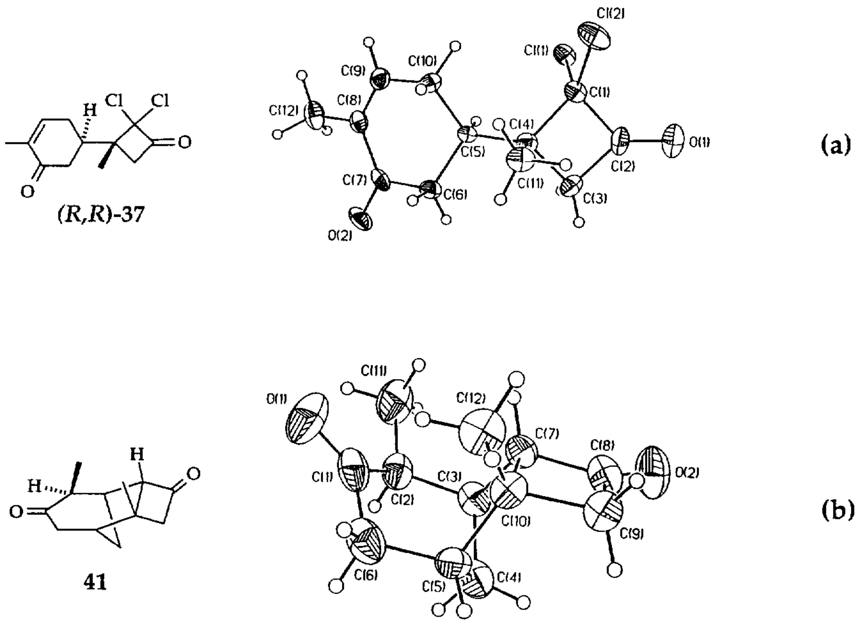
Reaction of (*R*)-carvone provides an especially interesting example.[9] (*R*)-Carvone reacts with dichloroketene to yield a mixture of diastereomeric adducts (*R,R*)-**37** and (*R,S*)-**37** (eq 4).



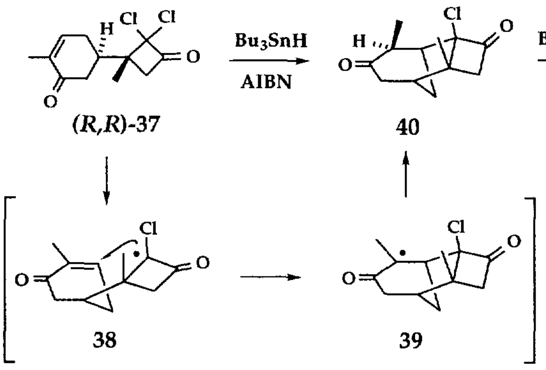
(*R*)-carvone (*R,R*)-**37** (*R,S*)-**37** **(4)**

Isomer (*R,R*)-**37** was isolated from the mixture by crystallization (mp 129-130 °C), and its structure was established by X-ray crystal analysis (Figure 2a). Free radical-promoted annulation of (*R,R*)-**37** is stereospecific (Scheme 2). Treatment of (*R,R*)-**37** with tributyltin hydride yields an initial α-acyl radical **38**. Radical **38** has a sterically favorable transition state for 1,5-*exo* cyclization to the enone double bond yielding a second, stable, α-acyl radical **39**. This step is followed by selective hydrogen transfer to the less hindered face of radical **39** to give the *anti*-annulation product **40** as

Figure 2. X-Ray Structures of (*R,R*)-37 and 41



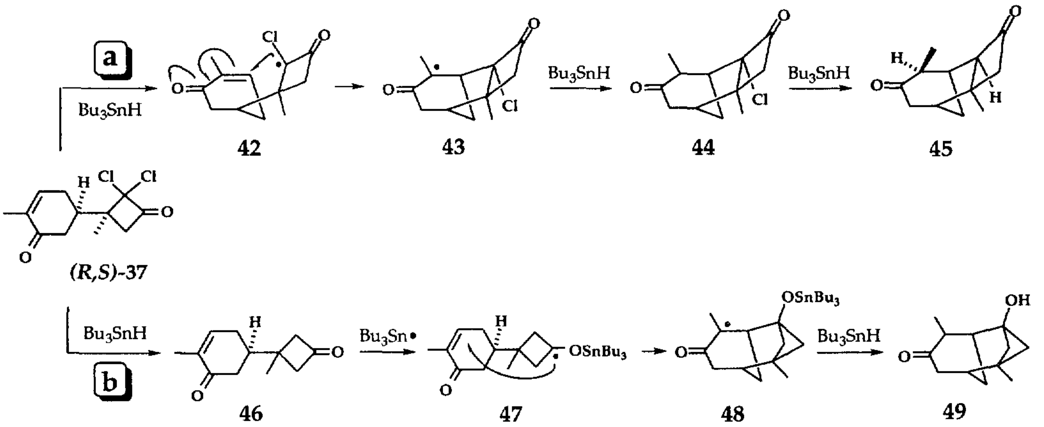
Scheme 2



a single diastereomer. If excess Bu$_3$SnH is employed, the second chlorine can be reductively removed generating **41**. The structure of **41** has also been established by X-ray crystal structure analysis (Figure 2b).

Radical reaction of *(R,S)*-**37** is stereospecific affording *syn*-annulation product **44**, a diastereomer of **40**, together with a small amount of alcohol **49** (Scheme 3). The rate of cyclization of **42** leading to **44** (Scheme 3, path a) is expected to be slower than that of **38** to **39** (Scheme 2). Radical **42** has a less sterically favorable transition state than **38**, because the four-membered ring in **42** is in the *endo* orientation. Of course, cyclization of **42** does benefit from the formation of the stable α-acyl radical **43**, which is reduced to **44** by reaction with tributyltin hydride. Use of a second equivalent of tin hydride yields **45**.

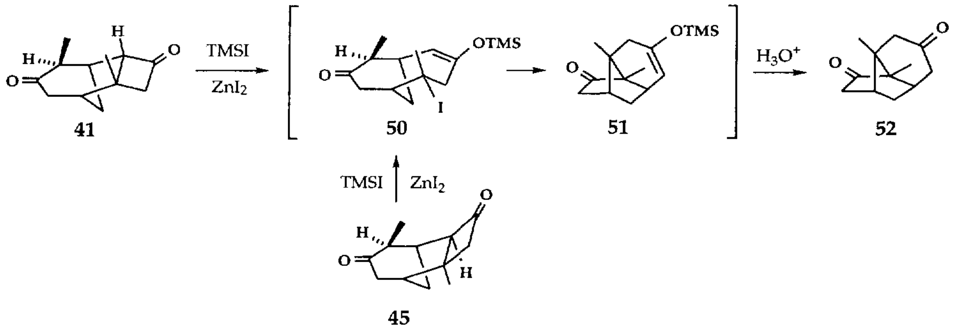
Scheme 3



Alcohol **49** is produced through a competitive process (Scheme 3, path b). The chlorines α to the carbonyl in *(R,S)*-**37** are quite reactive, and are reduced by tributyltin hydride directly. Thus, following reduction of *(R,S)*-**37** to **46**, addition of tributyltin radical yields the O-stannyl ketyl[10] **47**. 1,6-Cyclization of **47** then gives alcohol **49**. Formation of **49** is sensitive to the concentration of tributyltin hydride; more **49** is formed at higher concentrations of the reagent.

Treatment of **41** or **45** with TMSI, leads to a tricyclic dione **52** (Scheme 4), instead of the straightforward ring-opening product (cf. Table 2, entry 8). Thus, the expected ring opening produces the reactive iodide **50**. Enolization and internal alkylation of **50** leads to **51** and may be assisted by trans-silylation. Hydrolytic workup then leads to **52**. The sequence leading to the tricyclic dione **52** may prove to be synthetically useful. For example, the tricyclic sesquiterpenes sativene, copacamphene, and sinularene possess this ring skeleton.[11]

Scheme 4



We also studied the reaction of (*R*)-limonene (Table 1, entry 10). The diastereomeric mixture of dichlorocyclobutanones **53** could not be separated by chromatography. Tributyltin hydride treatment of the adducts gives a mixture of cyclization product **54** and a minor amount of direct reduction product. As expected, treatment of **54** with TMSI-ZnI_2 yielded ring-opening product **55** (Table 2, entry 8).

In summary, a new free radical annulation and Lewis acid-promoted ring expansion sequence has been developed that promises to become a powerful method for assembling fused and bridged ring systems of some complexity.

Experimental Section

Materials and Methods. All reactions were performed under a nitrogen atmosphere. Benzene and diethyl ether were distilled from blue or purple solutions of sodium benzophenone ketyl under nitrogen. Methylene chloride was distilled from CaH_2. Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were obtained on Bruker AC-300, or IBM AF-300 spectrometers (300 MHz for ^{1}H NMR, 75 MHz for ^{13}C NMR). Infrared (IR) spectra were obtained on an IBM IR/32 FTIR or a Mattson Cygnus 100 FTIR spectrometer. Gas chromatography and low resolution mass spectra (GC-MS) were obtained using a Hewlett-Packard gas chromatograph (5890 series II) equipped with a Hewlett-Packard mass spectrometer (5970 series) and a fused silica capillary column with 100% dimethylpolysiloxane (HP-1, Hewlett-Packard). Diastereomer ratios were determined by GC. High-resolution mass spectra were obtained on Varian MAT CH-5DF spectrometer.

Dichloroketene-Olefin Cycloadditions

General Procedure:[3b] A solution of trichloroacetyl chloride (12-15 mmol) in 20 mL of anhydrous ether was added to a suspension of 1,5-diene (10 mmol) and zinc dust (20 mmol) in 50 mL of anhydrous ether over a period of 0.5-2 h. During the addition of the trichloroacetyl chloride, the reaction mixture was irradiated in the water bath of a sonicator (Branson 2200, 117 V-50/60 Hz, 175.5 W) at a bath temperature between 20-30 °C. The sonication was continued for an additional 0.5-3 h after the addition was complete. The reaction mixture was filtered and the filtrate was washed with H_2O, saturated $NaHCO_3$, and brine solution. The ether layer was dried over $MgSO_4$, concentrated, and filtered through a short silica gel column with ether. The resulting crude product was, in most cases, used in the next step of the free radical annulation without further purification.

For preparation and spectral data for dichlorocyclobutanones **3**, **53**, and **57**, see ref. 3b.

5-(2',2'-Dichlorocyclobutan-3'-onyl)bicyclo[2.2.1]hept-2-ene (8) was obtained in 95% yield as a 75:25 diastereomeric mixture of *endo* and *exo* isomers. ^{1}H NMR ($CDCl_3$) δ 0.55-0.65 (m), 0.96-1.04 (m), 1.25-1.62 (m), 1.80-2.15 (m), 2.85-2.60 (m), 2.70-3.00 (m), 3.00-3.35 (m), 5.85-6.37 (m). ^{13}C NMR ($CDCl_3$) δ 29.3 (t, *J*=130 Hz), 30.6 (t, *J*=130 Hz), 40.9, 41.8, 42.0, 42.6, 44.7, 44.8, 46.8, 46.8, 49.0, 49.4, 49.5, 51.2, 87.7 (s), 89.0 (s), 131.9 (d, *J*=172 Hz), 132.8 (d, *J*=171 Hz), 137.8 (d, *J*=172 Hz), 138.6 (d, *J*=166 Hz), 192.2 (s), 192.6 (s). IR (neat) 1810 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 230 (<1, M^+), 188 (1), 160 (2), 117 (2), 91 (8), 77 (13), 66 (100).

2,2-Dichloro-3-(3'-butenyl)cyclobutanone (13) was obtained in 69% yield. ^{1}H NMR ($CDCl_3$) δ 1.71 (m, 1 H), 2.04 (m, 1 H), 2.20 (m, 2 H), 2.78-3.13 (m, 2 H), 3.20-3.50 (m, 1 H), 4.90-5.18 (m, 2 H), 5.81 (m, 1 H). ^{13}C NMR ($CDCl_3$) δ 30.4 (t, *J*=131 Hz), 31.2 (t, *J*=126 Hz), 45.0 (d, *J*=143 Hz), 47.5 (t, *J*=141 Hz), 88.6 (s), 115.9 (t, *J*=154 Hz), 136.7 (d, *J*=151 Hz), 193.4 (s). IR (neat) 1811 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 192 (<1, M^+), 154 (1), 152 (4), 150 (6, M^+-C_2H_2O), 128 (4), 115 (64), 109 (100), 79 (29), 67 (31).

2,2-Dichloro-3-methyl-3-(3-methylbut-3-enyl)cyclobutanone (17) was obtained in 90% yield. ^{1}H NMR ($CDCl_3$) δ 1.39 (s, 3 H), 1.77 (s, 3 H), 1.70-2.28 (m, 4 H), 2.86 (d, *J*=16.8 Hz, 1 H), 3.20 (d, *J*=16.8 Hz, 1 H), 4.74 (br s, 1 H), 4.76 (br s, 1 H). ^{13}C NMR ($CDCl_3$) δ 22.2 (q, *J*=127 Hz), 22.4 (q, *J*=127 Hz), 33.1 (t, *J*=129 Hz), 35.5 (t, *J*=129 Hz), 44.8 (s), 54.0 (t, *J*=141 Hz), 92.4 (s), 110.3 (t, *J*=159 Hz), 144.5 (s), 192.9 (s). IR (neat) 1808 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 220 (<1, M$^+$), 142 (8), 123 (37), 107 (100), 95 (30), 87 (22), 67 (14), 55 (34).

2,2-Dichloro-3-(2'-propenoxy)cyclobutanone (24) was obtained in 45% yield. ^{1}H NMR ($CDCl_3$) δ 3.34 (dd, *J*=18.5, 7.7 Hz, 1 H), 3.47 (dd, *J*=18.5, 7.7 Hz, 1 H), 4.10-4.42 (m, 2 H), 4.45 (t, *J*=7.7 Hz, 1 H), 5.22-5.48 (m, 2 H), 5.96 (m, 1 H). IR (neat) 1811 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 194 (<1, M$^+$), 152 (40), 117 (25), 109 (100), 89 (20), 83 (45), 71 (49), 61 (36).

1,1-Dichloro-5-(2'-propenyl)spiro[3.5]nonan-2-one (27) was obtained in 63% yield as a 55:45 mixture of two isomers. ^{1}H NMR ($CDCl_3$) δ 1.35-2.26 (m, 11 H), 2.78 (d, *J*=17.4 Hz, 1 H), 3.15 (d, *J*=17.4 Hz, 1 H), 5.03-5.16 (m, 2 H), 5.65-5.86 (m, 1 H). IR (neat) 1808 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 246 (<1, M$^+$), 207 (<1), 163 (100), 127 (40), 105 (7), 69 (69), 77 (29). HRMS calcd for $C_7H_9{}^{35}Cl_2$ (M^+-C_5H_7O): 163.0081. Found: 163.0086.

1,1-Dichloro-5-(2'-propenyl)spiro[3.6]decan-2-one (30) was obtained in 45% yield as a 65:35 mixture of two isomers. ^{1}H NMR ($CDCl_3$) δ 1.20-3.40 (m, 15 H), 4.92-5.18 (m, 2 H), 5.70 (m, 1 H). IR (neat) 1808 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 260 (<1, M$^+$), 169 (<1), 151 (10), 133 (21), 109 (90), 91 (38), 81 (41), 67 (100). HRMS calcd for $C_{13}H_{18}{}^{35}Cl_2O$: 260.0735. Found: 260.0735.

2,2-Dichloro-3-(2'-vinylphenyl)cyclobutanone (33) was obtained in 70% yield. ^{1}H NMR ($CDCl_3$) δ 3.66 (dd, *J*=15.6, 10.5 Hz), 1 H), 3.69 (dd, *J*=15.6, 10.5 Hz), 1 H), 4.58 (t, *J*=10.5 Hz, 1 H), 5.49 (d, *J*=10.9 Hz, 1 H), 5.75 (d, *J*=17.1 Hz, 1 H), 7.16-7.70 (m, 5 H). IR (neat) 1811 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 240 (<1, M$^+$), 205 (11, M$^+$-Cl), 163 (100), 141 (27), 128 (93), 115 (37), 102 (9), 89 (11).

(5*R*)-2-Methyl-5-(1'-methyl-2',2'-dichlorocyclobuta-3'-onyl)cyclohex-2-enones (*R,R*-37 and *R,S*-37) were obtained in 81% yield as an 85:15 mixture of two diastereomers. Chromatography of the mixture gave the major isomer ***R,R*-37** as white crystals from 20:1 hexanes-ether, mp. 129-130 °C.

Data for ***R,R*-37:** ^{1}H NMR ($CDCl_3$) δ 1.29 (s, 3 H), 1.80 (br s, 3 H), 2.27-2.43 (m, 3 H), 2.55 (m, 1 H), 2.73 (d, *J*=16.5 Hz, 1 H), 2.83 (m, 1 H), 3.28 (d, *J*=16.5 Hz, 1 H), 6.78 (br d, *J*=5.7 Hz, 1 H). ^{13}C NMR ($CDCl_3$) δ 15.7 (q, *J*=128 Hz), 19.1 (q, *J*=130 Hz), 27.9 (t, *J*=128 Hz), 40.2 (t, *J*=132 Hz), 41.4 (d, *J*=129 Hz), 46.6 (s), 53.7 (t, *J*=145 Hz), 91.9 (s), 135.6 (s), 144.2 (d, *J*=151 Hz), 191.2 (s), 198.4 (s). IR (neat) 1808 (s, C=O), 1674 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 260 (<1, M$^+$), 222 (2), 220 (9), 218 (15, M^+-C_2H_2O), 183 (9), 155 (3), 140 (12), 135 (10), 107 (8), 82 (100), 79 (19). HRMS calcd for

$C_{10}H_{12}{}^{35}Cl_2O$ (M^+-C_2H_2O): 218.0265. Found: 218.0270. X-ray analysis: see supplementary material.[16]

Data for *R,S*-**37**: ^1H NMR ($CDCl_3$) δ 1.31 (s, 3 H), 1.81 (s, 3 H), 2.17-2.53 (m, 3 H), 2.68 (m, 1 H), 2.74 (d, *J*=16.5 Hz, 1 H), 2.88 (m, 1 H), 3.31 (d, *J*=16.5 Hz, 1 H), 6.80 (br d, *J*=5.7 Hz, 1 H). ^{13}C NMR ($CDCl_3$) δ 15.7 (q, *J*=133 Hz), 19.0 (q, *J*=126 Hz), 27.8 (t, *J*=124 Hz), 40.0 (t, *J*=131 Hz), 40.9 (d, *J*=131 Hz), 46.5 (s), 53.3 (t, *J*=138 Hz), 91.9 (s), 135.7 (s), 143.7 (d, *J*=152 Hz), 191.5 (s), 198.2 (s). IR (neat) 1806 (s, C=O), 1673 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 260 (1, M^+), 222 (2), 220 (10), 218 (18, M^+-C_2H_2O), 183 (11), 155 (2), 140 (12), 135 (10), 107 (10), 82 (100), 79 (17). HRMS calcd for $C_{10}H_{12}{}^{35}Cl_2O$ (M^+-C_2H_2O): 218.0265. Found: 218.0253.

14,14-Dibromobicyclo[10.2.0]tetradeca-*trans,trans*-4,8-dien-13-one (58) was obtained in 50% yield after chromatography following reaction of **56** with tribromoacetyl chloride under the general procedure above. ^1H NMR ($CDCl_3$) δ 1.20-2.48 (m, 13 H), 3.04 (m, 1 H), 3.57 (m, 1 H), 5.10-5.50 (m, 4 H). ^{13}C NMR ($CDCl_3$) δ 26.3, 29.0, 30.4, 30.5, 32.1, 32.5, 50.2, 57.0, 66.2, 130.3, 130.5, 131.9, 132.0, 197.2. IR (neat) 3025 (m), 1796 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 360 (1, M^+), 283 and 281 (6, M^+-Br), 265 (4), 199 (23), 145 (20), 109 (100).

Dichlorocyclobutanone 61 was obtained in 54% yield as a solid following chromatography and crystallization from 1:1 hexanes-ether, mp. 102-103 °C. ^1H NMR ($CDCl_3$) δ 1.44 (d, *J*=10.9 Hz, 1 H), 1.81 (d, *J*=10.9 Hz, 1 H), 2.38 (br s, 1 H), 2.68 (br s, 1 H), 2.70-2.90 (m, 3 H), 2.93-3.07 (m, 3 H), 3.37 (d, *J*=18.3 Hz, 1 H), 3.01 (d, *J*=18.3 Hz, 1 H), 4.61 (d, *J*=1.2 Hz, 1 H), 4.73 (d, *J*=1.2 Hz, 1 H). ^{13}C NMR ($CDCl_3$) δ 36.2 (t), 41.4 (d), 41.7 (d), 43.4 (d), 45.8 (d), 46.4 (d), 46.5 (d), 47.1 (t), 49.0 (d) , 53.1 (d), 54.5 (s), 96.2 (s), 105.4 (t), 153.5 (s), 194.1 (s). IR (neat) 1808 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 280 (1, M^+), 247 (5), 245 (15, M^+-Cl), 216 (38), 203 (51), 167 (54), 155 (73), 115 (46), 91 (100). X-ray analysis: see supplementary material.[16]

Free Radical Annulation of Dichlorocyclobutanones

Cyclization of 3. To a solution of 183 mg of **3** (0.84 mmol) in 10 mL of benzene was added 1.2 equiv. of Bu_3SnH (285 μl 1.0 mmol) and 14 mg of AIBN. The mixture was heated to reflux for 4 h. DBU workup[12] followed by flash chromatography on silica gel eluting with 40:1 hexanes-ether afforded 140 mg of **4** (91%). ^1H NMR ($CDCl_3$) δ 1.45-2.52 (10 H), 2.64 (br t, *J*=5.9 Hz, 1 H), 2.90 (br t, *J*=9.4 Hz, 1 H), 3.28 (m, 1 H). ^{13}C NMR ($CDCl_3$) δ 20.0 (t, *J*=123 Hz), 21.6 (t, *J*=132 Hz), 28.8 (t, *J*=131 Hz), 30.6 (t, *J*=131 Hz), 32.9 (t, *J*=134 Hz), 47.1 (d, *J*=145 Hz), 48.1 (d, *J*=139 Hz), 56.7 (d, *J*=142 Hz), 57.6 (s), 203.1 (s). IR (neat) 1790 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 184 (<1, M^+), 149 (5, M^+-Cl), 140 (20), 121 (100), 113 (13), 91 (37), 79 (60). HRMS calcd for $C_{10}H_{13}{}^{35}ClO$: 184.0655. Found: 184.0655.

Treatment of 3.30 g of **3** (15 mmol) with 2.5 equiv. of Bu_3SnH (10.2 mL, 37.5 mmol) and 246 mg of AIBN afforded 1.92 g of **5** (85%). ^1H NMR ($CDCl_3$) δ 1.40-2.12 (10 H), 2.52 (br s, 1 H), 2.79 (m, 1 H), 3.11 (m, 1 H), 3.57 (q, *J*=8.1 Hz, 1 H). ^{13}C NMR ($CDCl_3$) δ 21.1(t, *J*=129 Hz), 22.2 (t, *J*=130 Hz), 29.0 (t, *J*=129 Hz), 31.1 (t, *J*=125 Hz), 35.2 (t, *J*=130 Hz), 35.8 (d, *J*=143 Hz), 37.2 (d, *J*=135 Hz), 61.5 (d, *J*=140 Hz), 70.3 (d, *J*=142 Hz), 210.9 (s). IR (neat) 1770 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 150 (8, M^+), 132 (2), 122 (45), 107 (20), 93 (80), 80 (100), 67 (55). HRMS calcd for $C_{10}H_{14}O$: 150.1045. Found: 150.1036.

Cyclization of 8. Treatment 2.10 g of the *endo* and *exo* mixture of **8** (9.1 mmol, *endo:exo*=75:25) with 2.2 equiv. of Bu_3SnH (5.85 mL, 21.8 mmol) and 149 mg of AIBN afforded 855 mg of cyclization product **9** as an *exo* and *endo* mixture (84/16, 58% yield, based on the *endo* isomer of **8**) and 251 mg of direct reduction product (17%). Data for the major isomer of **9**: ^1H NMR ($CDCl_3$) δ 0.80-0.98 (m, 2 H), 1.49 (br s, 2 H), 1.83 (m, 2 H), 2.10 (br s, 1 H), 2.26-2.35 (m, 2 H), 2.50 (td, *J*=3.7, 18.4 Hz, 1 H), 2.59 (br s, 1 H), 3.00-3.10 (m, 1 H), 3.43 (m, 1 H). ^{13}C NMR ($CDCl_3$) δ 35.6 (d, *J*=145 Hz), 37.2, 38.7 (t, *J*=132 Hz), 39.1, 39.1 (t, *J*=128 Hz), 41.4 (d, *J*=144 Hz), 44.6 (d, *J*=142 Hz), 46.0 (d, *J*=138 Hz), 49.9 (t, *J*=133 Hz), 72.4 (d, *J*=140 Hz), 213.8 (s). IR (neat) 1775 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 162 (11, M^+), 134 (3), 120 (64), 105 (22), 91 (40), 79 (100), 66 (15). HRMS calcd for $C_{11}H_{14}O$: 162.1045. Found: 162.1037.

Cyclization of 13. Treatment of 768 mg of **13** (4.0 mmol) with 2.5 equiv. of Bu_3SnH (2.7 mL, 10 mmol) and 66 mg of AIBN afforded 422 mg (85%) of **14** as an 84:16 mixture of two diastereomers. Data for one of the major diastereomers: ^1H NMR ($CDCl_3$) δ 1.12 (d, *J*=6.9 Hz, 3 H), 1.20-1.98 (4 H), 2.09 (m, 1 H), 2.47 (td, *J*=18.7, 3.7 Hz, 1 H), 2.82 (br s, 1 H), 3.10 (m, 1 H), 3.42 (m, 1 H). ^{13}C NMR ($CDCl_3$) δ 15.4 (q, *J*=128 Hz), 29.4 (d, *J*=146 Hz), 33.0 (t, *J*=130 Hz, two overlapping carbons), 39.3 (d, *J*=126 Hz), 51.6 (t, *J*=130 Hz), 69.1 (d, *J*=140 Hz), 213.2 (s). IR (neat) 1771 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 124 (9, M^+), 109 (1), 96 (12), 81 (35), 67 (100), 55 (13). HRMS calcd for C_5H_7 (M^+-C_3H_5O): 67.0548. Found: 67.0555.[13]

Cyclization of 17. Treatment of 440 mg of **17** (2.0 mmol) with 2.5 equiv. of Bu_3SnH (1.34 mL, 5.0 mmol) and 33 mg of AIBN afforded 63 mg of bicyclo[3.2.0]heptanone **18** (21%) and 213 mg (70%) of bicyclo[4.2.0]heptanone **19** as a 48:52 mixture of two diastereomers.

Data for **18**: ^1H NMR ($CDCl_3$) δ 0.94 (s, 3 H), 1.10 (s, 3 H), 1.43 (s, 3 H), 1.67 (m, 2 H), 1.88 (m, 2 H), 2.58 (br s, 1 H), 2.73 (s, 1 H), 2.74 (br s, 1 H). ^{13}C NMR ($CDCl_3$) δ 24.9 (q, *J*=125 Hz), 26.3 (q, *J*=126 Hz), 27.9 (q, *J*=126 Hz), 38.0 (s), 38.9 (t, *J*=123 Hz), 40.4 (t, *J*=125 Hz), 44.3 (s), 56.9 (t, *J*=137 Hz), 79.3 (d, *J*=138 Hz), 212.7 (s). IR (neat) 1773 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 152 (1, M^+), 124 (8), 109 (15), 95 (100), 83 (14), 67 (19). HRMS calcd for C_7H_{11} (M^+-C_3H_5O): 95.0861. Found: 95.0844.[13]

Data for the diastereomeric mixture of **19**: ^1H NMR ($CDCl_3$) δ 0.86 (d, *J*=6.5 Hz, 3 H for one diastereomer), 0.91 (d, *J*=6.6 Hz, 3 H for the other diastereomer), 1.27 (s, 3 H for one diastereomer), 1.38 (s, 3 H for the other diastereomer), 1.06-2.05 (m), 2.48-3.07 (m); IR (neat) 1778 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 152 (3, M^+), 137 (1), 119 (1), 110 (80), 95 (100), 81 (35), 68 (83); HRMS calcd for C_8H_{14} (M^+-C_2H_2O): 110.1096. Found: 110.1093.

Cyclization of 24. Treatment of 230 mg of **24** (1.18 mmol) with 2.2 equiv. of Bu_3SnH (701 µL, 2.6 mmol) and 19 mg of AIBN afforded 107 mg (72%) of **25** as an 85:15 mixture of two diastereomers. Data for the major diastereomer of **25**: ^1H NMR ($CDCl_3$) δ 1.12 (d, *J*=6.9 Hz, 2 H), 2.40 (m, 1 H), 2.90 (dt, *J*=19.1, 2.8 Hz, 1 H), 3.20 (dt, *J*=19.1, 6.0 Hz, 1H), 3.48 (dd, *J*=10.9, 9.2 Hz, 1 H), 3.68 (m, 1H), 4.16 (dd, *J*=9.2, 7.0 Hz, 1 H), 4.93 (td, *J*=6.0, 2.8 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 11.9 (q, *J*=127 Hz), 37.6 (d, *J*=134 Hz), 53.0 (t, *J*=134 Hz), 69.7 (d, *J*=145 Hz), 70.6 (d, *J*=159 Hz), 73.5 (t, *J*=140 Hz), 209.2 (s). IR (neat) 1777 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 126 (<1, M^+), 111 (<1), 98 (1), 84 (69), 65 (100), 55 (17). HRMS calcd for C_5H_8O (M^+-C_2H_2O): 84.0575. Found 84.0564.

Cyclization of 27. Treatment of 170 mg of **27** (0.69 mmol) with 2.3 equiv. of Bu_3SnH (432 µL, 1.6 mmol) and 11 mg of AIBN afforded 52.8 mg (43%) of **28** as a 90:10 mixture of two diastereomers together with the direct reduction product (43.0 mg, 35%). Data for the major diastereomer of **28**: ^1H NMR ($CDCl_3$) δ 1.00 (d, *J*=6.9 Hz, 3 H), 1.05-1.88 (11 H), 2.20 (m, 1H), 2.42 (dd, *J*=18.1, 5.8 Hz, 1 H), 2.72 (br d, *J*=18.1 Hz, 1 H), 2.94 (m, 1 H). ^{13}C NMR ($CDCl_3$) δ 16.1 (q, *J*=126 Hz), 23.7 (t, *J*=127 Hz), 26.2 (t, *J*=128 Hz), 26.2 (t, *J*=125 Hz), 35.0 (t, *J*=123 Hz), 36.5 (d, *J*= 132 Hz), 37.7 (t, *J*= 131 Hz), 43.2 (s), 48.5 (d, *J*=118 Hz), 51.4 (t, *J*=131 Hz), 70.1 (d, *J*=144 Hz), 211.1 (s). IR (neat) 1773 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 178 (<1, M^+), 163 (1), 150 (5), 136 (72), 121 (100), 107 (22), 93 (62), 79 (58), 67 (31). HRMS calcd for $C_{10}H_{16}$ (M^+-C_2H_2O): 136.1252. Found: 136.1222.

Cyclization of 30. Treatment of 530 mg of **30** (2.0 mmol) with 2.3 equiv. of Bu_3SnH (1.2 mL, 4.5 mmol) and 33 mg of AIBN afforded 157 mg (41%) of **31** as an 85:15 mixture of two diastereomers and direct reduction product (45 mg, 12%). Data for the major diastereomer of **31**: ^1H NMR ($CDCl_3$) δ 1.03 (d, *J*=6.8 Hz, 3 H), 1.20-2.10 (m, 13 H), 2.10 (m, 1 H), 2.58 (dd, *J*=18.0, 5.2 Hz, 1 H), 2.79 (br d, *J*=18.0 Hz, 1 H), 2.94 (m, 1 H). ^{13}C NMR ($CDCl_3$) δ 15.6 (q, *J*=129 Hz), 25.7 (t, *J*=123 Hz), 27.1 (t, *J*=129 Hz), 28.0 (t, *J*=124 Hz), 28.2 (t, *J*=124 Hz), 36.9 (d, *J*=129 Hz), 39.1 (t, *J*=124 Hz), 43.1 (t, *J*=124 Hz), 43.6 (s), 47.3 (d, *J*=128 Hz), 50.0 (t, *J*=124 Hz), 75.5 (d, *J*=140 Hz), 213.2 (s). IR (neat) 1772 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 192(M^+, 2), 164 (5), 150 (50), 135 (100), 121 (17), 107 (35), 93 (50), 79 (40), 67 (30). HRMS calcd for $C_{13}H_{20}O$: 192.1514. Found: 192.1493.

Cyclization of 33. Treatment of 50 mg of **33** (0.20 mmol) with 2.5 equiv. of Bu_3SnH (140 µL, 0.5 mmol) and 3 mg of AIBN afforded 21 mg (61%) of **34**. The ^1H NMR, ^{13}C NMR, IR, and GC-MS spectra of **34** are in good agreement with those of an authentic sample.

Authentic Sample of 34. A solution of trichloroacetyl chloride in 20 mL of ether was added over 1.5 h to a mixture of 5.3 mL of 1,2-dihydronaphthalene (40 mmol) and 5.2 g of zinc dust (80 mmol) in 40 mL of ether, while the reaction mixture was irradiated in an ultrasonic water bath between 20 to 30 °C. The sonication was continued for 30 min after the addition was complete to afford 8.8 g (92%) of the dichlorocyclobutanone adduct. ^{1}H NMR ($CDCl_3$) δ 1.72 (m, 1 H), 2.34 (m, 1 H), 2.52-2.83 (m, 2 H), 4.29 (m, 2 H), 7.08-7.36 (4 H). ^{13}C NMR δ 21.6 (t, *J*=131 Hz), 27.1 (t, *J*=129 Hz), 50.3 (d, *J*=148 Hz), 54.8 (d, *J*=142 Hz), 88.4 (s), 126.6 (d, *J*=161 Hz), 127.9 (d, *J*=157 Hz), 128.0 (d, *J*=159 Hz), 131.1 (s), 131.2 (d, *J*=160 Hz), 137.1 (s), 198.0 (s). IR (neat) 1802 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 240 (11, M^+), 205 (<1), 177 (33), 149 (17), 141 (5), 130 (100), 115 (50), 89 (6).

A mixture of 1.2 g of the dichlorocyclobutanone adduct (5.0 mmol) and 1.3 g of zinc dust (20 mmol) in 15 mL of acetic acid was irradiated in the ultrasonic water bath for 1.2 h at 20-30 °C. Flash chromatography of the crude product on silica gel with 20:1 hexanes:ether afforded765 mg (89%) of **34**. ^{1}H NMR ($CDCl_3$) δ 1.68 (m, 1 H), 2.27 (m, 1 H), 2.69 (m, 2 H), 2.81 (m, 1 H), 3.54-3.85 (3 H), 7.12-7.30 (4 H). ^{13}C NMR ($CDCl_3$) δ 22.2 (t, *J*=131 Hz), 27.2 (d, *J*=142 Hz), 27.7 (t, *J*=127 Hz), 54.5 (t, *J*=135 Hz), 58.8 (d, *J*=138 Hz), 126.1 (d, *J*=158 Hz), 126.5 (d, *J*=154 Hz), 128.7 (d, *J*=161 Hz), 136.8 (s), 138.2 (s), 212.3 (s). IR (neat) 1781 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 172 (<1, M^+), 142 (2), 130 (100), 115 (33), 103 (2), 89 (4), 77 (5), 63 (7). HRMS calcd for $C_{12}H_{12}O$: 172.0888. Found: 172.0900.

Cyclization of *R,R*-37. A solution of 780 mg of ***R,R*-37** (3.0 mmol), 2.2 equiv. of Bu_3SnH (1.8 mL, 6.7 mmol), and 49 mg AIBN (0.3 mmol) in 66 mL of benzene was refluxed for 3.5 h. After DBU workup of the reaction mixture, the crude product was purified by flash chromatography on silica gel, eluting with 10:1 hexanes-ether, to afford 294 mg (51%) of **41** as white crystals: mp 75-77 °C; $[\alpha]^{22}_D$ +142.7° (c 0.011, EtOH). ^{1}H NMR ($CDCl_3$) δ 1.00 (d, *J*=6.6, 3 H), 1.35 (s, 3 H), 2.08 (d, *J*=12.8, 1 H), 2.27 (dt, *J*=12.8, 4.3 Hz, 1 H), 2.38-2.58 (4 H), 2.65 (m, 1 H), 2.82-2.98 (3 H). ^{13}C NMR ($CDCl_3$) δ 12.2 (q, *J*=127 Hz), 20.8 (q, *J*=125 Hz), 37.0 (t, *J*=131 Hz), 38.2 (s), 44.4 (d, *J*=139 Hz), 45.4 (d, *J*=145 Hz), 46.4 (t, *J*=132 Hz), 50.8 (d, *J*=125 Hz), 58.4 (t, *J*=133 Hz), 68.5 (d, *J*=142 Hz), 210.6 (s), 211.1 (s). IR (neat) 1775 (s, C=O), 1709 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 192 (2, M^+), 164 (8), 150 (35), 135 (12), 121 (11), 107 (15), 93 (100), 79 (58), 72 (34), 53 (28). HRMS calcd for $C_{10}H_{14}O$ (M^+-C_2H_2O): 150.1045. Found: 150.1041. X-ray analysis: see supplementary material.[16]

This experiment was repeated by using 1.2 equiv. of Bu_3SnH to give chlorine-bearing product **40** in 71% yield. ^{1}H NMR ($CDCl_3$) δ 1.33 (d, *J*=6.6 Hz, 3 H), 1.34 (s, 3 H), 2.14 (d, *J*=13.3 Hz, 1 H), 2.33 (m, 1 H), 2.45-2.77 (m, 5 H), 2.90 (d, *J*=17.0 Hz, 1 H), 3.05 (d, *J*=1.07 Hz, 1 H). ^{13}C NMR ($CDCl_3$) δ 14.4 (q, *J*=124 Hz), 18.7 (q, *J*=125 Hz), 36.4 (t, *J*=130 Hz), 44.4 (s), 45.4 (t, *J*=126), 45.8 (d, *J*=138 Hz), 47.6 (d, *J*=141 Hz), 53.1 (d, *J*=122 Hz), 57.1 (t, *J*=133 Hz), 68.6 (s), 203.7 (s), 208.6 (s). IR (neat) 1784 (s, C=O), 1707 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 226 (<1, M^+), 184 (100, M^+-C_2H_2O), 149 (71), 128 (67), 107 (31), 91 (74), 77 (48). HRMS calcd for $C_{10}H_{13}{}^{35}ClO$ (M^+-C_2H_2O): 184.0655. Found: 184.0641. X-ray analysis: see supplementary material.[16]

Cyclization of *R,S*-37. A solution of 1.53 g of ***R,S*-37** (5.9 mmol), 2.5 equiv. of Bu_3SnH (4.0 mL, 14.8 mmol), and 97 mg of AIBN (0.6 mmol) in 184 mL of benzene was refluxed for 3.5 h.

After DBU workup of the reaction mixture, the crude product was purified by flash chromatography on silica gel eluting with 3:1 hexanes-ether, to afford 566 mg (50%) of **45** and 181 mg (16%) of **49**.

Data for **45**: ^{1}H NMR ($CDCl_3$) δ 1.12 (d, *J*=7.0 Hz, 3 H), 1.37 (s, 3 H), 2.09 (d, *J*=11.9 Hz, 1 H), 2.20 (m, 1 H), 2.45-2.70 (m, 6 H), 3.02 (dd, *J*=19.1, 3.5 Hz, 1 H), 3.26 (quintet, *J*=3.5 Hz, 1 H). ^{13}C NMR ($CDCl_3$) δ 13.1 (q, *J*=128 Hz), 26.7 (q, *J*=127 Hz), 40.5 (s), 41.9 (t, *J*=128 Hz), 43.8 (d, *J*=139 Hz), 44.5 (d, *J*=135 Hz), 46.4 (t, *J*=132 Hz), 51.1 (d, *J*=122 Hz), 51.3 (t, *J*=126 Hz), 74.0 (d, *J*=38 Hz), 208.6 (s), 210.9 (s). IR (neat) 1771 (s, C=O), 1707 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 192 (2, M^+), 164 (7), 150 (48), 135 (20), 121 (26), 107 (22), 93 (100), 79 (51), 72 (48), 53 (26). HRMS calcd for $C_{12}H_{16}O_2$ (M^+): 192.1150. Found: 192.1143.

Data for **49**: ^{1}H NMR ($CDCl_3$) δ 0.80 (d, *J*=7.0 Hz, 3 H), 1.16 (s, 3 H), 1.36-1.76, (m, 4 H), 1.92 (m, 3 H), 2.08 (m, 2 H), 2.27 (d, *J*=18.7 Hz, 1 H), 2.43 (d, *J*=17.8 Hz, 1 H), 3.80 (br s, 1 H). ^{13}C NMR ($CDCl_3$) δ 13.3 (q, *J*=126 Hz), 29.2 (q, *J*=127 Hz), 36.7 (s), 39.2 (t, *J*=130 Hz), 40.5 (t, *J*=130 Hz), 42.3 (d, *J*=138 Hz), 42.7 (d, *J*=134 Hz), 43.6 (t, *J*=126 Hz), 45.4 (d, *J*=130 Hz), 48.4 (t, *J*=133 Hz), 79.3 (s), 215.9 (s). IR (neat) 3505 (br, OH), 1716 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 194 (20, M^+), 176 (8), 166 (3), 151 (7), 123 (29), 109 (100) 96 (63). HRMS calcd for $C_{12}H_{18}O_2$ 194.1307, found 194.1286

Cyclization of 53. Treatment of 246 mg of the mixture of diastereomers **53** (1.0 mmol) with 2.5 equiv. of Bu_3SnH (672 μL, 2.5 mmol) and 16 mg of AIBN afforded 90.8 mg (51%) of **54** as an 87:13 mixture of two diastereomers together with 37 mg (21%) of direct reduction product. Data for the major diastereomer of **54**. ^{1}H NMR ($CDCl_3$) δ 0.80 (d, *J*=6.6 Hz, 3 H), 0.85-2.10 (9 H), 1.41 (s, 3 H), 2.74-2.91 (m, 3 H). ^{13}C NMR ($CDCl_3$) δ 19.2 (q, *J*=125 Hz), 20.1 (q, *J*=126 Hz), 27.9 (t, *J*=128 Hz), 28.3 (t, *J*=130 Hz), 36.3 (d, *J*=133 Hz), 37.5 (t, *J*=129 Hz), 42.6 (d, *J*=142 Hz), 45.0 (d, *J*=143 Hz), 48.0 (s), 58.4 (t, *J*=130 Hz), 68.0 (d, *J*=141 Hz), 215.0 (s). IR (neat) 1775 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 178 (<1, M^+), 150 (8), 136 (58), 121 (5), 108 (15), 94 (100), 79 (31). HRMS calcd for $C_{10}H_{16}$ (M^+-C_2H_2O): 136.1252. Found: 136.1219.

Free Radical Reaction of 57 and 58. Treatment of 272 mg of dichlorocyclobutanone **57** (1.0 mmol) with 2.5 equiv. of Bu_3SnH (672 μL, 2.5 mmol) and 10 mg of AIBN afforded 190 mg (93%) of **59** as a single product. This reaction was repeated using dibromocyclobutanone **58** and afforded **59** as the only product according to GC analysis.

An authentic sample of **59** was prepared in 94% yield by reduction of dichlorocyclobutanone **57** with zinc in acetic acid. ^{1}H NMR ($CDCl_3$) 1.32-2.60 (m, 14 H), 3.10-3.30 (m, 2 H), 5.08-5.52 (m, 4 H). ^{13}C NMR ($CDCl_3$) δ 23.2, 26.9, 30.7, 30.7, 31.4, 32.3, 32.9, 52.9, 63.7, 129.0, 130.4, 133.2, 133.2, 211.7. IR (neat) 1775 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 204 (<1, M^+), 162 (48), 147 (9), 133 (46), 119 (38), 93 (69), 79 (100).

Free Radical Reaction of 61. Treatment of 32 mg of **61** (0.11 mmol) with 2.2 equiv. of Bu_3SnH (73 μL, 0.24 mmol) and 2 mg of AIBN afforded 22 mg (94%) of **62** as a single product. ^{1}H

NMR ($CDCl_3$) 1.20-1.80 (2 H), 2.30-3.32 (10 H), 4.60 (s, 1 H), 4.68 (s, 1 H). IR (neat) 1786 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 212 (1, M^+), 184 (12), 169 (24), 155 (41), 141 (24), 128 (29), 115 (29), 104 (50), 91 (100).

Ring Opening of Cyclobutanones

Procedure A: TMSI-ZnI_2 Promoted Ring-Opening Followed by Bu_3SnH Reduction. Ring Expansion of 5. Anhydrous ZnI_2 (128 mg, 0.38 mmol) was added to a solution containing 250 mg of **5** (1.6 mmol) and 350 µl of TMSI (2.4 mmol) in 8 mL of CH_2Cl_2. The reaction mixture was stirred at 25°C for 10 min until the starting material was no longer detected by GC. The mixture was worked up by extraction with ether and aqueous 5% Na_2SO_3 to afford 387 mg of **6** (87%) as a 35:65 mixture of two diastereomers. A solution of 200 mg of the iodide **6** (0.70 mmol), Bu_3SnH (300 µL, 1.1 mmol) and AIBN (10 mg) in 8 mL of benzene was heated to reflux for 2 h. DBU workup, followed by flash chromatography on silica gel eluting with 40:1 hexanes-ether provided 103 mg (97%) of **2**. The ^1H and ^{13}C NMR, IR, and MS spectra of **2** agreed well with those reported in the literature.[14]

Procedure B: TMSI-ZnI_2 Promoted Ring-Opening Followed by DBU Treatment. Ring Expansion of 9. Anhydrous ZnI_2 (71 mg, 0.19 mmol) was added to a solution containing 130 mg of the major diastereomer of **9** (0.80 mmol) and 180 µl of TMSI (1.2 mmol) in 8 mL of CH_2Cl_2. The reaction mixture was stirred at 25 °C for 1 h until starting material was no longer detected by GC. After extraction with ether and aqueous 5% Na_2SO_3, the crude product was washed with 10 mL of 10% DBU-ether solution. The reaction mixture was worked up with ether. Flash chromatography of the crude product on silica gel, eluting with 30:1 hexanes-ether, afforded 119 mg (92%) of **11**. ^1H NMR ($CDCl_3$) δ 0.76-0.96 (m, 2 H), 1.17 (br s, 1 H), 1.37 (d, *J*=9.4 Hz, 1 H), 1.49 (d, *J*=8.2 Hz, 1 H), 1.85 (m, 1 H), 2.00 (m, 1 H), 2.22 (br s, 2 H), 2.34 (br s, 1 H), 2.69 (dd, *J*=14.6, 5.2 Hz, 1 H), 2.81 (dd, *J*=14.6, 5.2 Hz, 1 H), 5.77 (d, *J*=12.7 Hz, 1 H), 6.53 (dd, *J*=12.7, 8.2 Hz, 1 H). ^{13}C NMR ($CDCl_3$) δ 34.3 (t, *J*=130 Hz), 36.4 (d, *J*=130 Hz), 36.8 (d, *J*=135 Hz), 40.6 (t, *J*=132 Hz), 41.1 (d, *J*=131 Hz), 42.5 (t, *J*=133 Hz), 44.8 (d, *J*=140 Hz), 47.5 (t, *J*=125 Hz), 129.9 (d, *J*=158 Hz), 148.7 (d, *J*=152 Hz), 203.9 (s). IR (neat) 1698 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 162 (30, M^+), 147 (5), 134 (20), 120 (32), 105 (30), 95 (100), 91 (92), 79 (88), 66 (60). HRMS calcd for $C_{11}H_{12}O$: 162.1045. Found: 162.1062.

Ring Expansion of 14. Following procedure B, treatment of 30 mg of **14** (mixture of two diastereomers, 0.24 mmol) with 53 µL TMSI (0.36 mmol) and 20 mg of ZnI_2 (0.06 mmol) afforded 76 mg (90%) of **15**. The ^1H, ^{13}C NMR IR, and MS of **2** agreed well with those reported in the literature.[15]

Ring Expansion of 18. Following procedure B, treatment of 75 mg of **18** (0.49 mmol) with 111 μL of TMSI (, 0.74 mmol) and 44 mg of ZnI_2 (0.12 mmol) afforded 65 mg (87%) of **20**. ^1H NMR ($CDCl_3$) δ 1.00 (s, 6 H), 1.59 (t, *J*=5.4 Hz, 2 H), 1.94 (s, 3 H), 2.35 (t, *J*=5.5 Hz, 2 H), 2.44 (s, 2 H), 5.86 (s, 1 H). ^{13}C NMR ($CDCl_3$) δ 27.6 (q, *J*=127 Hz), 29.5 (q, *J*=124 Hz), 31.9 (t, *J*=127 Hz), 32.2 (s), 41.5 (t, *J*=127 Hz), 56.3 (t, *J*=127 Hz), 129.8 (d, *J*=158 Hz), 161.7 (s), 202.0 (s). IR (neat) 1700 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 152 (17, M^+), 137 (20), 123 (6), 109 (29), 95 (100), 82 (31), 67 (51). HRMS calcd for $C_{10}H_{16}O$: 152.1201. Found: 152.1191.

Ring Expansion of 19. Following procedure B, treatment of 350 mg of **19** (2.3 mmol) with 510 μL of TMSI (3.5 mmol) and 202 mg of ZnI_2 (0.55 mmol) afforded 140 mg (40%) of cyclooctenone **21** and 168 mg (48%) of alternative ring-opening product **22**.

Data for **21**: ^1H NMR ($CDCl_3$) δ 0.89 (d, *J*=6.3 Hz, 3 H), 1.25-2.52 (7 H), 1.93 (s, 3 H), 2.97 (m, 2 H), 5.99 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 22.6 (q, *J*=124 Hz), 27.9 (q, *J*=124 Hz), 30.0 (t, *J*=127 Hz), 30.8 (t, *J*=126 Hz), 31.9 (t, *J*=124 Hz), 32.5 (d, *J*=126 Hz), 41.4 (t, *J*=127 Hz), 130.0 (d, *J*=156 Hz), 154.2 (s), 204.1 (s). IR (neat) 1701 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 152 (13, M^+), 137 (33), 123 (9), 108 (17), 95 (100), 82 (24), 67 (48).

Data for **22**: ^1H NMR ($CDCl_3$) δ 0.98 (d, *J*=6.4 Hz, 3 H), 1.10-2.20 (6 H), 1.85 (s, 3 H), 2.22 (s, 3 H). ^{13}C NMR ($CDCl_3$) δ 21.4 (q, *J*=127 Hz), 21.7 (q, *J*=125 Hz), 28.5 (d, *J*=127 Hz), 29.7 (q, *J*=127 Hz), 30.4 (t, *J*=127 Hz), 33.4 (t, *J*=129 Hz), 35.3 (t, *J*=129 Hz), 132.7 (s), 141.0 (s), 204.3 (s). IR (neat) 1686 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 152 (69, M^+), 137 (98), 123 (9), 109 (73), 95 (25), 81 (31), 67 (100). HRMS calcd for $C_{10}H_{16}O$: 152.1201. Found: 152.1200.

Ring Expansion of 34. Following procedure B, treatment of 6 mg of **34** (0.03 mmol) with 6.7 μL of TMSI (0.045 mmol) and 3 mg of ZnI_2 (0.01 mmol) afforded 4.3 mg (83%) of **36**. ^1H NMR ($CDCl_3$) δ 2.45 (s, 3 H), 2.59 (t, *J*=7.6 Hz, 2 H), 2.84 (t, *J*=7.6 Hz, 2 H), 7.10-7.42 (5 H). ^{13}C NMR ($CDCl_3$) δ 20.9 (t, *J*=124 Hz), 25.3 (q, *J*=127 Hz), 27.4 (t, *J*=125 Hz), 126.7 (d, *J*=161 Hz), 127.7 (d, *J*=160 Hz), 128.6 (d, *J*=154 Hz), 129.8 (d, *J*=158 Hz), 132.5 (s), 137.2 (d, *J*=159 Hz), 137.4 (s), 138.0 (s), 198.5 (s). IR (neat) 1659 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 172 (70, M^+), 157 (14), 141 (1), 129 (100), 115 (5), 102 (8), 87 (2), 77 (7). HRMS calcd for $C_{12}H_{12}O$: 172.0888. Found: 172.0855.

Procedure C: TMSI-ZnI_2 Promoted Ring-Opening of 41. Anhydrous ZnI_2 (74 mg, 0.20 mmol) was added to a solution containing 207 mg of **41** (1.07 mmol) and 202 μl of TMSI (2.7 mmol) in 2 mL of CH_2Cl_2. The reaction mixture was stirred at 25°C for 20 min or until no starting material was detected by GC. After extraction with ether and 5% aqueous Na_2SO_3, flash-chromatography of the crude product on silica gel, eluting with 10:1 hexanes-ether, gave 151 mg (73%) of **52** as a white solid. mp 128-131 °C. ^1H NMR ($CDCl_3$) δ 0.91 (s, 3 H), 1.07 (s, 3 H), 1.48-1.82 (m, 2 H), 1.93 (d, *J*=18.1 Hz, 1 H), 2.01 (m, 1 H), 2.23 (d, *J*=19.4 Hz, 1 H), 2.30-2.56 (5 H); ^{13}C NMR ($CDCl_3$) δ 8.1 (q, *J*=126 Hz), 19.0 (q, *J*=129 Hz), 34.9 (t, *J*=134 Hz), 35.7 (d, *J*=142 Hz), 43.3 (d, *J*=129 Hz), 43.7 (t, *J*=132 Hz), 44.4 (t, *J*=130 Hz), 48.2 (t, *J*=129 Hz), 49.0 (s), 57.5 (s), 210.0 (s), 218.4 (s). IR (neat) 1740 (s, C=O), 1717 (m, C=O) cm^{-1}. MS *m/e* (rel. intensity) 192 (57), 177 (2), 164 (3), 150 (32), 135 (16), 123 (32), 107 (100), 93 (64), 77 (43), 67 (39). HRMS calcd for $C_{12}H_{16}O_2$: 192.1105. Found: 192.1134.

Ring Expansion of 54. Following procedure B, treatment of 80 mg of the major diastereomer of **54** (0.45 mmol) with 100 µL of TMSI (1.37 mmol) and anhydrous 40 mg of ZnI_2 (0.11 mmol) gave 76 mg (94%) of **55**. ^{1}H NMR ($CDCl_3$) δ 0.93 (d, *J*=7.0 Hz, 3 H), 0.95-2.24 (8 H), 1.91 (s, 3 H), 2.43 (dd, *J*= 15.9, 5.4 Hz, 1 H), 2.54 (br s, 1 H), 2.73 (br d, *J*=15.9 Hz, 1 H), 5.95 (s, 1 H). ^{13}C NMR ($CDCl_3$) δ 19.8 (q, *J*=125 Hz), 26.0 (t, *J*=127 Hz), 27.0 (q, *J*=127 Hz), 29.4 (t, *J*=124 Hz), 34.0 (d, *J*=128 Hz), 34.8 (t, *J*=126 Hz), 35.5 (d, *J*=128 Hz), 40.3 (d, *J*=127 Hz), 45.3 (t, *J*=129 Hz), 130.4 (d, *J*=156 Hz), 158.0 (s), 205.2 (s). IR (neat) 1649 (s, C=O) cm^{-1}. MS *m/e* (rel. intensity) 178 (79, M$^+$), 163 (24), 135 (33), 121 (67), 109 (55), 96 (97), 82 (100), 67 (61). HRMS calcd for $C_{12}H_{18}O$: 178.1358. Found: 178.1333.

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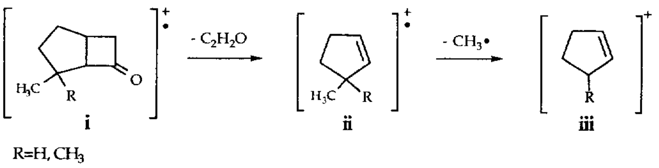
(13) The 3-methylbicyclo[3.2.0]heptan-2-one system exhibits interesting mass spectral behavior. The electron impact mass spectra of **14** and **18** show the apparent loss of a fragment with composition C_3H_5O. This can be understood if the elements of ketene are lost from the cation-radical **i**, followed by cleavage of a methyl fragment from ion **ii** to give the strong mass peak corresponding to the cyclopentenyl cation **iii**.



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