Free Radical Fragmentation of [2 + 2] Photoadduct Derivatives. Formal Synthesis of Pentalenene

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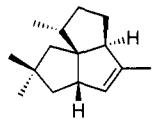
A series of [2 + 2] photoadducts **3a–d** are converted to cyclobutylcarbinyl iodides **6a–d**. Free radical fragmentation of the iodides yields bicyclo[*x*.*y*.0] carbon skeletons **7a–d** which are present in a variety of natural products. Application of this methodology to terpenoid synthesis is illustrated by the preparation of unsaturated ketone **19** in only six steps (33% overall yield). As **19** has been converted to pentalenene (**1**) this constitutes a formal synthesis of the angular triquinane sesquiterpenoid.

Free radical *cyclizations* have been extensively investigated over the last decade and are now important reactions in synthetic organic methodology.[1] Free radical *fragmentations* have received less attention, and much of the research has had a mechanistic rather than a synthetic emphasis.[2] We wish to report on fragmentations of a series of cyclobutylcarbinyl systems derived from [2 + 2] photoadducts which lead to bicyclo[*x*.*y*.0] carbon skeletons present in a variety of terpenoid natural products.[3] We will then discuss the formal synthesis of the angular triquinane pentalenene (**1**) to illustrate the application of this fragmentation methodology in natural product synthesis.



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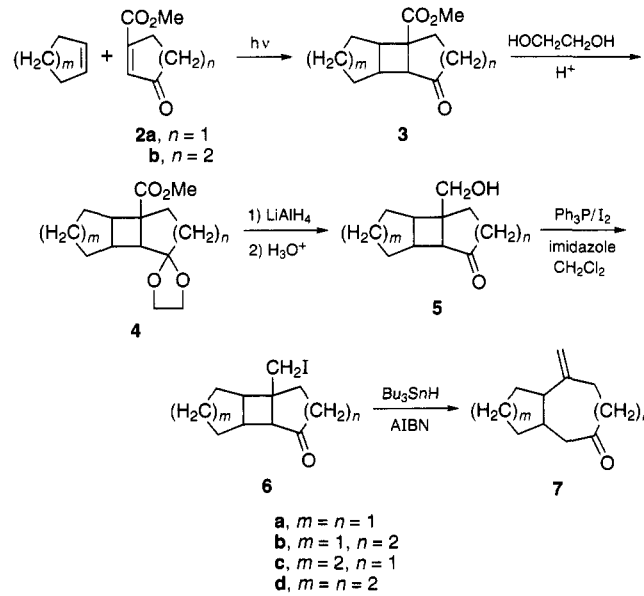
Results and Discussion

Preparation of Substrates. Our objective was to prepare a series of cyclobutylcarbinyl iodides derived from [2 + 2] photoadducts and to examine the fragmentation of these substrates under free radical conditions. The required photoadducts **3a–d** (Scheme 1) were obtained by irradiation of **2a**[4] or **2b**[5] with excess cyclopentene or cyclohexene in dichloromethane. Adduct **3a** was reported previously and was prepared in 78% yield as a 9:1 ratio of *cis-anti-cis* and *cis-syn-cis* isomers, respectively.[4] The *anti/syn* ratio of these adducts is of no consequence in the overall sequence as this stereochemistry is lost in the fragmentation step. Adduct **3b** was prepared previously in 91% yield as a 87:13 *anti/syn* mixture.[4] The structure of the major *anti* isomer of **3b** was established by single-crystal X-ray analysis.[6] Adduct **3c** was not reported previously and was obtained in 76% yield as a 1:1 mixture of *anti* and *syn* isomers while **3d**, also a new adduct, was obtained in 63% yield as a 3:2 mixture of *anti* and *syn* isomers, respectively.

Scheme 1



We wished to convert the ester group in adducts **3a–d** to an iodomethyl group for the free radical studies, but first it was necessary to protect the ketone function in each. Ketals **4a** and **4b** have been prepared previously in high yields,[4] so ketals **4c** and **4d** were prepared using a similar procedure. Reduction of ketal esters **4** with $LiAlH_4$, followed by acidic workup to hydrolyze the ketal function, gave hydroxy ketones **5a–d** in excellent yields. The neopentyl alcohols **5** were converted to the iodides **6** using an I_2/Ph_3P/imidazole protocol described by us.[7] Iodide **6a** has been prepared previously in lower yield using a different procedure.[4] We now had in hand the four cyclobutylcarbinyl iodides **6a–d** required for the free radical fragmentation study.

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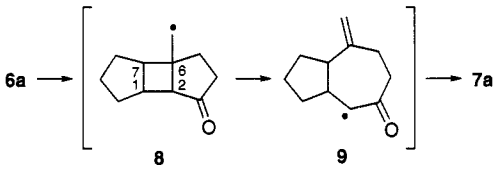
Free Radical Fragmentations. The free radical study was conducted using standard conditions of tri-n-butyltin hydride (TBTH) with a catalytic amount of AIBN in benzene and heating to reflux for 1.5–3.0 h. Very slow vs rapid addition of TBTH/AIBN to the heated iodide resulted in no difference in the yield or product distribution of these reactions. Fragmentation of the most strained iodide **6a** gave in excellent yield (90%) the 5-7 or bicyclo[5.3.0]decane ring system **7a**. In this reaction, abstraction of the iodide atom from **6a** gives the highly labile cyclobutylcarbinyl radical **8**. Even in the presence of a large excess of TBTH (e.g. addition of the iodide to excess TBTH) we were unable to trap **8** as the reduced product. Fragmentation of an internal cyclobutane bond in **8** gives **9** with the formation of a seven-membered ring containing a methylene group and a radical stabilized by an α-oxo group. If the carbonyl function in **6a** is replaced by a ketal, the fragmentation still proceeds readily so the stabilization by the α-oxo group is not critical to the overall process. Radical **9** then abstracts a hydrogen atom from TBTH to complete the cycle and give **7a**. The 5-7 ring system of **7a** is found in the guaiane and pseudoguaiane sesquiterpenoids, and many of these natural products also have a methylene group at the same position as in **7a**.[8] The twelve-carbon clavukerins,[9] the isodaucane[10] and tremulane sesquiterpenoids,[11] and the phorbols[12] also possess this 5-7 carbon skeleton.



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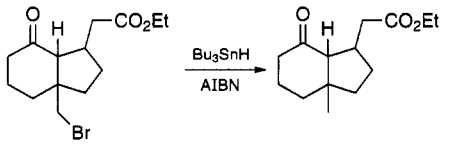
Fragmentation of iodide **6b** using the standard free radical conditions gave the 5-8 or bicyclo[6.3.0]undecane ring system **7b** in moderate yield (60%). **6b** is less strained than **6a** but there is still sufficient driving force to effect the desired fragmentation. In another study involving reaction of neopentyl bromide **10** with TBTH no fragmentation occurred and only reduced product **11** was isolated in high yield.[13] Obviously, the driving force for our fragmentation reactions is the release of strain upon breaking a cyclobutane bond. The 5-8 ring system of **7b** is present in several classes of natural products including the asteriscane sesquiterpenoids,[14] the basmane[15] and fusicoccin diterpenoids[16] and the ophiobolane sesterterpenoids.[17]



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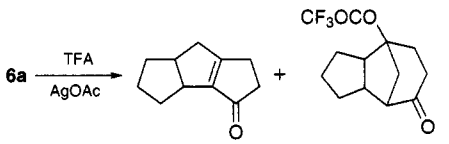
Fragmentation of iodide **6c** gave the 6-7 or bicyclo-[5.4.0]undecane system **7c** in 51% yield. This ring system is present in the himachalene sesquiterpenoids[8] and in α-himachalene the methylene group is at the same position as in **7c**.[18] The last model compound and the least strained of the four substrates, **6d**, gave upon fragmentation the 6-8 ring system **7d** in 60% yield. Thus, in all four substrates (**6a–d**) examined, the *internal* (e.g. C2–C6 in **8**) rather than the external cyclobutane bond (C6–C7 in **8**) fragmented. Possibly these regioselective fragmentations arise from a conformation of **8** in which there is more effective alignment of the p-orbital of the neopentyl radical with the internal cyclobutane bond.

The iodides discussed in this report not only undergo free radical reactions but also participate in rearrangements under ionic conditions. We reported previously that solvolysis of **6a** gave the linear triquinane **12** and the bridged product **13**.[4] The iodide **6a** derived from the *anti* adduct gave predominantly **13** while that from the *syn* adduct gave **12** as the major product.[4]



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We wished to apply the free radical methodology developed in this study to the synthesis of a natural product. In the following section we describe the formal synthesis of pentalenene **1** using this fragmentation reaction as a key step.

Formal Synthesis of Pentalenene. Pentalenene (**1**) is an angular triquinane sesquiterpenoid first isolated from the mycelia of *Streptomyces griseochromogenes*.[19] It is the parent hydrocarbon of the pentalenolactones, which are antimicrobial agents that function specifically against both Gram positive and negative bacteria and fungi.[20] This activity coupled with the antitumor activity of a pentalenene derivative[21] has made **1** an attractive synthetic target. Of the several reported approaches to the synthesis of **1**[22] two of them employed the bicyclic ketone **19** as a relay compound.[23,24] Pattenden has reported the

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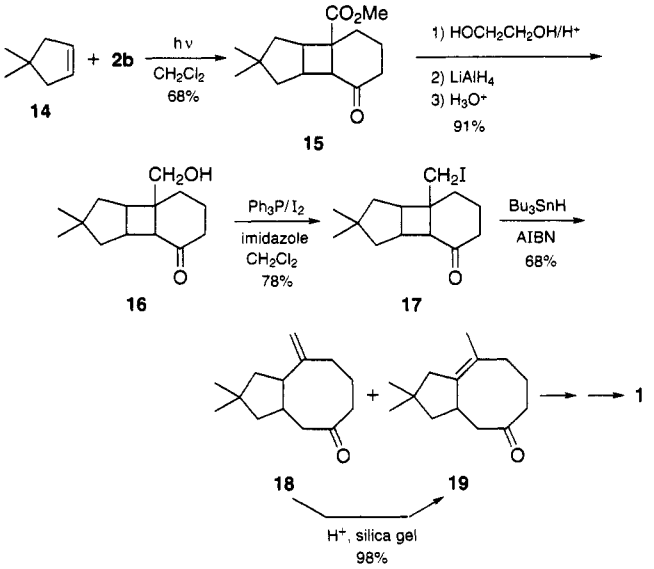
Scheme 2



three-step conversion of **19** to pentalenene.[23] Thus our formal synthesis of **1** involves an improved preparation of **19**.

In the first step of our synthesis, [2 + 2] photoaddition of excess 4,4-dimethylcyclopentene (**14**) to enone ester **2b** gave adduct **15** as one isomer in 68% yield (Scheme 2). Enone **2b**[5] was used in our model study described above and alkene **14** was prepared from 4,4-dimethylcyclopentane-1,2-diol.[25] Treatment of this diol with the I_2/Ph_3P/imidazole protocol[26] using our modified conditions[7] gave alkene **14** (see Experimental Section). *Cis-anti-cis* stereochemistry was assigned to **15** on the basis of the typically small H6–H7 *trans* coupling constant of 5.5 Hz found in such adducts.[4] Surprisingly, ^1H and ^{13}C NMR spectra showed no evidence of the *syn* isomer. Following the photoaddition step, the ketone function in **15** was protected as the ketal, the ester group was reduced with $LiAlH_4$, and the ketal was hydrolyzed to give hydroxy ketone **16** using procedures similar to those employed in our model study. Neopentyl alcohol **16** was converted to iodide **17** using I_2/Ph_3P/imidazole.[7] In the critical step of the synthesis, reaction of **17** with TBTH/AIBN in benzene gave, after purification on silica gel, a mixture of fragmentation products **18** and **19** in a combined yield of 68% (higher than the 60% obtained in the model study to give the 5-8 ring system **7b**). ^1H NMR spectral analysis of the *crude* reaction mixture obtained from **17** indicated the presence of unsaturated ketone **18** but not isomer **19**. We concluded that isomerization of **18** to **19** had taken place on the slightly acidic silica gel during purification ("recycled" silica gel had been used for the purification). Thus treatment of a hexane solution of the crude product from fragmentation of **17** with acidic silica gel gave only the desired isomer **19** as a crystalline product. The mp and spectral properties of this product are in good agreement with those reported for relay compound **19**.[23]

This preparation of **19** in only six steps (33% overall yield) constitutes a formal synthesis of pentalenene as **19** has already been converted to **1**.[23] The approach offers considerable improvement over previous preparations of **19** which required either nine[24] or fourteen steps.[23] The synthesis also illustrates the potential of the free radical fragmentation sequence in the preparation of natural products. The application of this methodology to the synthesis of other terpenoids is currently under investigation.

Experimental Section

General. ^1H and ^{13}C NMR spectra were obtained on a 200 MHz or a 400 MHz spectrometer in $CDCl_3$. The multiplicities of the ^{13}C spectra were determined by the attached proton test (200 MHz) or the distortionless enhancement by polarization transfer (DEPT) experiment (400 MHz). Infrared spectra were obtained on a FTIR spectrophotometer using NaCl liquid cells and the solvent used is indicated in the procedure. TLC analyses were performed on silica gel GF 254 plates of 0.25 mm thickness, and flash chromatography (FC)[27] purifications were done with 230–400 mesh silica gel. The irradiations were performed using a Rayonet RPR 208 preparative reactor with 350-nm lamps or a Hanovia 450 W light source with a Pyrex filter.

The preparations of **2b**,[5] **2a**, **3a**, **3b**, **4a**, **4b**, **5a**, and **5b** have been reported previously in the literature.[4] The preparation of compound **6a** has been reported previously[4] and is included here using an improved procedure.

General Irradiation Procedure. The appropriate amounts of the enone and cycloalkene were placed in oven-dried Pyrex irradiation tubes (15 × 0.8 cm) and dissolved in CH_2Cl_2 to give an enone concentration of 0.7–0.8 M. The solutions were deoxygenated with argon (1 min) and the tubes sealed with rubber septa. The irradiation tubes were placed in a water-cooled quartz immersion well centered in the Rayonet reactor. The reactions were followed by TLC and typically took 72 h. At the end of the irradiations the solvent was removed and the crude mixture separated by flash chromatography.

Methyl 5-Oxotricyclo[5.4.0.0^{2,6}]undecane-2-carboxylate (3c). Using the general conditions, enone **2a** (400 mg, 2.86 mmol) and cyclohexene (2.58 g, 31.4 mmol, 10 equiv) were dissolved in CH_2Cl_2 (4.0 mL) and irradiated for 72 h. Separation of the reaction mixture by FC (25% EtOAc/hexanes) gave **3c** (480 mg, 76%) as a yellow oil in a 1:1 ratio of *syn* and *anti* isomers: IR (CCl_4) 1736, 1729 cm^{-1}; ^1H NMR δ 3.73 (s, 3H), 3.10 (d, J = 8.5, 1H), 3.00 (d, J = 6.7, 1H), 2.90 (d, J = 8.6, 1H), 2.60 (m, 2H), 2.48 (dt, J = 9.4, 3.4, 1H), 1.20–1.50 (m, 3H); ^{13}C NMR *anti* isomer δ 219.8, 59.8, 53.5, 49.4, 42.4, 41.1, 34.0, 32.8, 29.7, 28.0, 26.9, 23.5, 23.1; ^{13}C NMR *syn* isomer δ 220.0, 56.0, 53.6, 52.3, 44.9, 42.6, 40.8, 32.5, 30.7, 28.6, 27.8, 24.4, 24.1; HRMS calcd for $C_{13}H_{18}O_3$ 222.1256, found 222.1265.

Methyl 9-Oxotricyclo[6.4.0.0^{2,7}]dodecane-1-carboxylate (3d). Using the general conditions, enone **2b** (500 mg, 3.24 mmol) and cyclohexene (2.93 g, 35.7 mmol, 10 equiv) were dissolved in CH_2Cl_2 (4.0 mL) and irradiated for 72 h. Separation of the reaction mixture by FC (20% EtOAc/hexanes) gave **3d** (480 mg, 63%) as a yellow oil in a 3:2 ratio of *anti* and *syn* isomers: IR (CCl_4) 1724, 1703, 1442, 1308, 1153 cm^{-1}; ^1H NMR δ 3.69 (s, 3H), 2.95 (d, J = 9.7, 1H), 2.65 (m, 1H), 2.40 (m, 2H), 2.20 (m, 1H), 1.90–2.05 (m, 4H), 1.80 (m, 3H), 1.25–1.45 (m, 4H), 1.10 (dt, J = 13.4, 2.9, 1H); ^{13}C NMR *anti* isomer δ 211.6, 53.6, 51.9, 48.7, 47.0, 43.5, 40.0, 38.2, 32.9, 30.7, 25.9, 25.1, 22.3, 21.1; ^{13}C NMR *syn* isomer δ 212.1, 51.8, 51.5, 49.6, 46.8, 42.4, 39.9, 38.5, 32.9, 26.3, 25.9, 23.5, 21.4, 21.1; HRMS calcd for $C_{14}H_{20}O_3$ 236.1412, found 236.1418.

General Procedure for the Preparation of the Ketal of 3. A solution of adduct **3**, ethylene glycol, toluene, and *p*-toluenesulfonic acid was refluxed for 4 h using a Dean–Stark trap to effect removal of the water. The solution was cooled and diluted with a saturated $NaHCO_3$ solution in water, and the aqueous phase was extracted three times with ether. The combined organic phases were washed with brine and dried ($MgSO_4$) and the solvent was removed.

Ketal of Methyl 5-Oxotricyclo[5.4.0.0^{2,6}]undecane-2-carboxylate (4c). Adduct **3c** (400 mg, 1.80 mmol), ethylene glycol (10 mL), toluene (18 mL), and *p*-toluenesulfonic acid (16

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mg) were refluxed to give **4c**. The ketal was not purified: IR (CCl_4) 1717, 1266, 1160, 1034 cm^{-1}.

Ketal of Methyl 9-Oxotricyclo[6.4.0.0^{2,7}]dodecane-1-carboxylate (4d). Adduct **4c** (480 mg, 2.03 mmol), ethylene glycol (5.0 mL), toluene (18 mL), and *p*-toluenesulfonic acid (25 mg) were refluxed to give **4d**. The ketal was not purified: IR (CCl_4) 1729, 1150 cm^{-1}.

General Procedure for the Preparation of the Hydroxy Ketone 5. To a solution of ketal **4** in anhydrous diethyl ether was added $LiAlH_4$, and the suspension was refluxed for 2.5 h. Excess $LiAlH_4$ was destroyed by the dropwise addition of H_2O. A 1 M solution of H_2SO_4 in H_2O was added and stirring was continued for 2 h. The aqueous phase was extracted with diethyl ether, the combined organic phases were washed with a saturated solution of $NaHCO_3$ in water and brine and dried ($MgSO_4$), and the solvent was removed.

2-(Hydroxymethyl)tricyclo[5.4.0.0^{2,6}]-5-undecanone (5c). Ketal **4c** (400 mg, 1.5 mmol), anhydrous diethyl ether (8.0 mL), and $LiAlH_4$ (86 mg, 2.3 mmol) were refluxed for 2.5 h. 1 M H_2SO_4 in water (18.0 mL) was added, and the mixture was stirred for 2 h. Separation of the reaction mixture by FC (60% EtOAc/hexanes) gave **5c** (260 mg, 90%) as a yellow oil: IR (CCl_4) 3427, 1730, 1260, 1173 cm^{-1}; ^1H NMR δ 3.82 (d, J = 10.9, 1H), 3.65 (d, J = 11.0, 1H), 3.58 (s, 1H), 2.40–2.70 (m, 5H), 2.25 (m, 1H), 1.50–2.00 (m, 6H), 1.30–1.50 (m, 3H); ^{13}C NMR δ 221.2, 65.3, 56.2, 52.2, 47.5, 42.0, 39.2, 32.5, 31.2, 26.3, 22.7, 21.8; HRMS calcd for $C_{12}H_{18}O_2$ 194.1307, found 194.1304.

7-(Hydroxymethyl)tricyclo[6.4.0.0^{2,7}]-3-dodecanone (5d). Ketal **4d** (500 mg, 1.78 mmol), anhydrous diethyl ether (8.0 mL), and $LiAlH_4$ (102 mg, 2.68 mmol) were refluxed for 2.5 h. 1 M H_2SO_4 in water (18.0 mL) was added, and the mixture was stirred for 2 h. Separation of the reaction mixture by FC (60% EtOAc/hexanes) gave **5d** (330 mg, 90%) as a yellow oil: IR (CCl_4) 3450, 1696, 1458, 1049 cm^{-1}; ^1H NMR δ 3.51 (d, J = 11.1, 1H), 3.47 (d, J = 11.1, 1H), 2.69 (m, 1H), 2.45 (m, 2H), 2.30 (m, 1H), 1.96 (m, 3H), 1.77 (dt, J = 113.4, 2.9, 3H), 1.50–1.77 (m, 5H), 1.36 (m, 3H); ^{13}C NMR δ 213.3, 68.9, 53.8, 49.3, 47.1, 43.9, 39.1, 38.7, 31.0, 26.9, 26.4, 23.5, 22.6; HRMS calcd for $C_{13}H_{20}O_2$ 208.1463, found 208.1463.

General Procedure for the Preparation of Iodide 6. To a solution of **5** in CH_2Cl_2 was added in order Ph_3P, imidazole and iodine. The mixture was stirred at room temperature for 1.5–3 h. The solvent was removed, and the residue was purified using FC.

6-(Iodomethyl)tricyclo[5.3.0.0^{2,6}]-3-decanone (6a). To a solution of alcohol **5a** (120 mg, 0.67 mmol) in CH_2Cl_2 (5.0 mL) were added Ph_3P (262 mg, 1.00 mmol), imidazole (68.1 mg, 1.00 mmol), and iodine (254 mg, 1.00 mmol) and the mixture was stirred for 1.5 h. Purification (10% EtOAc/hexanes) gave **6a** (150 mg, 77%) as a yellow oil. Spectral data were consistent with those reported previously for this compound.[4]

1-(Iodomethyl)tricyclo[5.4.0.0^{2,6}]-8-undecanone (6b). To a solution of alcohol **5b** (130 mg, 0.67 mmol) in CH_2Cl_2 (5.0 mL) were added Ph_3P (210 mg, 0.80 mmol), imidazole (55 mg, 0.80 mmol), and iodine (200 mg, 0.80 mmol), and the mixture was stirred for 2 h. Purification (15% EtOAc/hexanes) gave **6b** (170 mg, 81%) as white crystals: mp 90–92 °C; IR(CCl_4) 1699, 1180, 1139 cm^{-1}; ^1H NMR δ 3.20 (dd, J = 9.8, 9.7, 2H), 2.60 (q, J = 6.9, 2H), 2.53 (d, J = 4.1, 1H), 2.44 (t, J = 8.1, 2H), 2.18 (m, 4H), 1.93 (m, 1H), 1.77 (m, 1H), 1.50 (m, 4H); ^{13}C NMR δ 212.3, 54.2, 4.3, 40.0, 37.7, 35.6, 31.4, 27.0, 26.1, 23.9, 18.7, 16.5; HRMS calcd for $C_{12}H_{17}IO$ 304.0326, found 304.0312. Anal. Calcd for $C_{12}H_{17}IO$: C, 47.36; H, 5.64. Found: C, 47.26; H, 5.50.

2-(Iodomethyl)tricyclo[5.4.0.0^{2,6}]-5-undecanone (6c). To a solution of alcohol **5c** (290 mg, 1.50 mmol) in CH_2Cl_2 (5.0 mL) were added Ph_3P (590 mg, 2.25 mmol), imidazole (153 mg, 2.25 mmol), and iodine (571 mg, 2.25 mmol), and the mixture was stirred for 1.5 h. Purification (35% EtOAc/hexanes) gave **6c** (390 mg, 86%) as a yellow oil: IR (CCl_4) 1738, 1181, 1142 cm^{-1}; ^1H NMR δ 3.32 (dd, J = 10.4, 10.4, 2H), 2.55 (m, 3H), 2.48 (m, 3H), 2.21 (m, 4H), 1.89 (m, 3H), 1.61 (m, 1H), 1.40 (td, J = 9.1, 3.4, 1H); ^{13}C NMR δ 219.7, 62.7, 57.4, 49.4, 41.0, 36.7, 29.9, 27.7, 24.5, 23.4, 16.6, 14.7; HRMS calcd for $C_{12}H_{17}IO$ 304.0326, found 304.0312.

7-(Iodomethyl)tricyclo[6.4.0.0^{2,7}]-3-dodecanone (6d). To a solution of alcohol **5d** (300 mg, 1.4 mmol) in CH_2Cl_2 (5.0 mL) were added Ph_3P (570 mg, 2.2 mmol), imidazole (150 mg, 2.2 mmol), and iodine (550 mg, 2.2 mmol), and the mixture was stirred for 2 h. Purification (15% EtOAc/hexanes) gave **6d** (420 mg, 92%) as white crystals: mp 125–127 °C; IR (CCl_4) 1702, 1456, 1188; ^1H NMR δ 3.20 (dd, J = 9.8, 9.8, 2H), 2.64 (m, 1H), 2.42 (m, 1H), 2.39 (m, 1H), 2.35 (m, 1H), 2.00 (m, 4H), 1.92 (m, 3H), 1.78 (m, 3H), 1.65 (td, J = 13.0, 1.4, 1H), 1.59 (m, 2H); ^{13}C NMR δ 212.5, 58.5, 52.6, 42.1, 38.8, 32.7, 30.7, 27.0, 26.5, 25.4, 21.9, 19.3, 14.2. Anal. Calcd for $C_{13}H_{19}IO$: C, 49.05; H, 6.02. Found: C, 49.22; H, 6.12.

General Procedure for the Radical Fragmentation. To a refluxing solution of the iodide **6** in benzene was added dropwise over 2–3 h a solution of Bu_3SnH and AIBN (catalytic) in benzene. After the addition was complete the solution was refluxed for an additional 1.5 h. The solvent was removed and the reaction mixture separated by FC.

6-Methylenebicyclo[5.3.0]-3-decanone (7a). To a solution of **6a** (59 mg, 0.20 mmol) in benzene (2.0 mL) were added Bu_3SnH (72 mg, 0.25 mmol) and AIBN (3 mg) in benzene (0.6 mL). Purification (10% EtOAc/hexanes) gave **7a** (30 mg, 90%) as a yellow oil: IR (CCl_4) 1699, 894 cm^{-1}; ^1H NMR δ 4.91 (d, J = 5.4, 2H), 2.74 (q, J = 8.3, 1H), 2.38–2.57 (m, 3H), 2.28–2.36 (m, 2H), 2.28 (dd, J = 18.0, 5.4, 1H), 1.89–1.98 (m, 1H), 1.68–1.85 (m, 3H), 1.52 (td, J = 8.0, 3.5, 1H), 1.25–1.32 (m, 2H); ^{13}C NMR δ 214.5, 148.9, 112.5, 49.0, 46.4, 44.1, 38.8, 33.7, 30.5, 29.7, 24.3; HRMS calcd for $C_{11}H_{16}O$ 164.1201, found 164.1208.

7-Methylenebicyclo[6.3.0]-3-undecanone (7b). To a solution of **6b** (170 mg, 0.54 mmol) in benzene (3.5 mL) were added Bu_3SnH (240 mg, 0.81 mmol) and AIBN (3 mg) in benzene (0.9 mL). Purification (25% EtOAc/hexanes) gave **7b** (58 mg, 60%) as a yellow oil: IR (CCl_4) 1703, 1640, 906 cm^{-1}; ^1H NMR δ 4.90 (dd, J = 13.1, 1.1, 2H), 2.83 (m, 1H), 2.66 (td, J = 11.9, 3.4, 1H), 2.52 (m, 2H), 2.34 (q, J = 15.6, 1H), 2.25 (m, 1H), 2.10 (dd, J = 15.6, 3.8, 1H), 1.85–2.09 (m, 4H), 1.60–1.85 (m, 4H), 1.40–1.50 (m, 1H); ^{13}C NMR δ 214.6, 148.5, 114.2, 50.5, 47.0, 40.7, 37.0, 36.1, 32.1, 28.9, 26.5, 22.0; HRMS calcd for $C_{12}H_{18}O$ 178.1358, found 178.1359.

6-Methylenebicyclo[5.4.0]-3-undecanone (7c). To a solution of **6c** (290 mg, 0.96 mmol) in benzene (4.0 mL) were added Bu_3SnH (335 mg, 1.15 mmol) and AIBN (3 mg) in benzene (0.9 mL). Purification (30% EtOAc/hexanes) gave **7c** (87 mg, 51%) as a yellow oil: IR (CCl_4) 1706, 1639, 1147, 900 cm^{-1}; ^1H NMR δ 4.84 (d, J = 5.8, 2H), 3.11 (t, J = 12.4, 1H), 2.66 (t, J = 12.4, 1H), 2.47–2.52 (m, 2H), 2.27–2.39 (m, 2H), 2.25 (dd, J = 12.5, 5.8, 1H), 1.70–1.82 (m, 3H), 1.42–1.65 (m, 2H), 1.25–1.40 (m, 3H), 1.19 (td, J = 11.7, 4.1, 1H); ^{13}C NMR δ 212.6, 152.3, 111.5, 50.6, 45.0, 41.6, 35.5, 31.8, 31.1, 26.3, 25.6, 21.0; HRMS calcd for $C_{12}H_{18}O$ 178.1358, found 178.1351.

7-Methylenebicyclo[6.4.0]-3-dodecanone (7d). To a solution of **6d** (360 mg, 1.1 mmol) in benzene (4.0 mL) were added Bu_3SnH (390 mg, 1.4 mmol) and AIBN (3 mg) in benzene (0.9 mL). Purification (30% EtOAc/hexanes) gave **7d** (130 mg, 60%) as a yellow oil: IR (CCl_4) 1700, 1637, 1136, 905 cm^{-1}; ^1H NMR δ 4.85 (d, J = 9.1, 2H), 2.46 (m, 1H), 2.32 (m, 3H), 2.16 (dd, J = 13.5, 3.1, 1H), 1.50–2.10 (m, 9H), 1.16–1.40 (m, 3H), 1.05–1.18 (m, 1H); ^{13}C NMR δ 214.7, 151.3, 115.6, 50.5, 45.2, 40.4, 34.3, 33.3, 21.9, 29.8, 26.1, 23.8, 21.0; HRMS calcd for $C_{13}H_{20}O$ 192.1514, found 192.1521.

4,4-Dimethylcyclopentene (14). To a solution of 4,4 dimethylcyclopentane-1,2-diol[25] (0.130 g, 1.00 mmol) in CH_2Cl_2 (5.0 mL) were added Ph_3P (1.05 g, 4.00 mmol) and imidazole (0.272 g, 4.00 mmol) at room temperature. Iodine (0.761 g, 3.00 mmol) was added slowly and the mixture was stirred at room temperature for 1 h and then refluxed for 1 h. Alkene **14** in CH_2Cl_2 was obtained by distillation at 78 °C and the spectra compared to literature data.[25] This solution was used directly in the next step because of the volatility of **14**.

Methyl 4,4-Dimethyl-8-oxotricyclo[5.4.0.0^{2,6}]undecane-1-carboxylate (15). A solution of **14** (0.385 g, 4.00 mmol) and **2b** (0.308 g, 2.00 mmol) in CH_2Cl_2 (3.0 mL) was placed in a Pyrex irradiation tube and degassed with argon. The tube was sealed with a serum cap and irradiated at 10 °C for 4 h using a Hanovia 450 W light source. The solvent was removed

and the adduct purified by FC (18% EtOAc/hexanes) to give **15** (0.340 g, 68.0%) as a yellow oil: IR (CCl_4) 1735, 1703, 1462, 1237, 1202 cm^{-1}; ^1H NMR δ 3.64 (s, 3H), 3.04 (d, J = 5.5 Hz, 1H), 2.65 (m, 2H), 2.32 (m, 2H), 1.50–2.20 (m, 6H), 1.43 (dd, J = 3.7 Hz, 1H), 1.10 (m, 1H), 1.03 (s, 3H), 0.73 (s, 3H); ^{13}C NMR δ 212.3 (+), 176 (+), 54.0 (+), 52.2 (+), 48.9 (−), 48.4 (−), 47.8 (+), 44.3 (−), 39.3 (+), 38.7 (−), 32.7 (−), 28.8 (+), 28.6 (+), 28.2 (+), 20.9 (+); HRMS calcd for $C_{15}H_{22}O_3$ 250.1569, found 250.1571. Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.66; H, 8.90.

Ethylene Ketal of Methyl 4,4-Dimethyl-8-oxotricyclo-[5.4.0.0^{2,6}]undecane-1-carboxylate. A mixture of ethylene glycol (10.0 g, 9.00 mL, 161 mmol), toluene (18.0 mL) and *p*-toluenesulfonic acid (0.02 g, catalytic) was refluxed to remove water (Dean–Stark trap). A solution of **15** (1.00 g, 3.99 mmol) in toluene (5.0 mL) was added and refluxing was continued for 4.5 h. The cooled solution was poured into a saturated, cold $NaHCO_3$ solution (25 mL). The aqueous layer was separated and extracted with ether (3 × 20 mL). The organic layers were combined, washed with brine, dried over $MgSO_4$, and concentrated. The ketal was used directly in the next step: IR ($CHCl_3$) 1728 cm^{-1}; ^1H NMR δ 3.76–3.96 (m, 4H), 3.59 (s, 3H), 2.53 (m, 2H), 1.28–1.70 (m, 10H), 1.20 (dd, J = 2.7 Hz, 1H), 1.01 (s, 3H), 0.73 (s, 1H).

4,4-Dimethyl-1-(hydroxymethyl)tricyclo[5.4.0.0^{2,6}]undecan-8-one (16). To a solution of the ketal of **15** (1.29 g, 4.39 mmol) in anhydrous diethyl ether (20.0 mL) was added $LiAlH_4$ (0.200 g, 5.27 mmol). The suspension was stirred for 2.5 h at room temperature under an argon atmosphere. The excess $LiAlH_4$ was quenched by the dropwise addition of water. 1 M H_2SO_4 (18.0 mL) was added and vigorous stirring continued for 2 h. The aqueous layer was extracted with ether (3 × 15 mL). The organic layers were combined, washed with a saturated $NaHCO_3$ solution (10 mL) and brine (10 mL), dried over $MgSO_4$, and concentrated. The alcohol was purified by FC (30% EtOAc/ hexanes) to give **16** (0.889 g, 91.1%) as a yellow oil: IR ($CHCl_3$) 3622, 3467, 1689, 1036 cm^{-1}; ^1H NMR δ 3.53 (abq, J = 11.1 Hz, 2H), 2.61 (m, 1H), 2.23 (m, 2H), 1.60–2.10 (m, 5H), 1.57 (d, J = 8.7 Hz, 2H), 1.33 (dd, J = 5.7 Hz, 1H), 1.23 (t, J = 7.1 Hz, 1H), 1.10 (s, 3H), 0.79 (s, 3H); ^{13}C NMR δ 214.3 (+), 67.0 (+), 55.3 (−), 48.8 (+), 45.2 (−), 44.6 (+), 42.4 (+), 41.4 (−), 39.4 (+), 32.2 (+), 29.0 (+), 28.3 (−), 28.2(−), 20.6 (+); HRMS calcd for $C_{14}H_{22}O_2$ 222.1620, found 222.1625.

4,4-Dimethyl-1-(iodomethyl)tricyclo[5.4.0.0^{2,6}]undecan-8-one (17). To a solution of **16** (0.200 g, 0.900 mmol) in CH_2Cl_2 (5.0 mL) were added Ph_3P (0.354 g, 1.35 mmol), imidazole (0.092 g, 1.4 mmol), and iodine (0.343 g, 1.35 mmol). The solution was stirred at room temperature under an argon atmosphere for 4 h. A 1 M sodium bisulfite solution (5 mL) was added, and the aqueous phase was extracted with CH_2Cl_2 (3 × 5 mL). The organic layer was dried ($MgSO_4$) and concentrated. The iodide **17** was purified by FC (10% EtOAc/ hexanes) to give **17** (0.234 g, 78.2%) as a white solid: mp 108–111°C; IR(CCl_4) 1700, 1462, 1183 cm^{-1}; ^1H NMR δ 3.24 (abq, J = 9.9 Hz, 2H), 2.61 (m, 1H), 2.40 (t, J = 8.6 Hz, 2H), 2.26 (m, 1H), 2.05 (m, 1H), 1.60–1.90 (m, 5H), 1.38 (m, 3H), 1.11 (s, 3H), 0.808 (s, 3H); ^{13}C NMR δ 212.6 (+), 58.8 (−), 48.3 (+), 46.9 (−), 44.0 (+), 41.8 (+), 41.6 (+), 38.8 (+), 37.6 (−), 35.6 (+), 29.0 (−), 28.4 (−), 20.5 (+), 17.7 (+); HRMS calcd for $C_{14}H_{21}IO$ + H^+ 333.0709, found, using chemical ionization (CH_4), M + 1 333.0700. Anal. Calcd for $C_{14}H_{21}IO$: C, 50.61; H, 6.37. Found: C, 50.51; H, 6.41.

Reaction of 17 with Tributyltin Hydride. To a refluxing solution of the iodide **17** (0.100 g, 0.300 mmol) in benzene (5.0 mL) was added a solution of Bu_3SnH (0.131 g, 0.451 mmol) and AIBN (0.005 g, 0.1 equiv.) in benzene (0.5 mL) via syringe pump over 2.5 h. Refluxing was continued for 1 h. The solution was cooled and stirred overnight with an aqueous solution of KF (10%). Drying agent ($MgSO_4$) was added and removed by filtration. The benzene was removed *in vacuo* and the product purified by FC (10% EtOAc/hexanes) to give 10,10-dimethyl-7-methylenebicyclo[6.3.0]undecan-3-one (**18**) (0.012 g, 20%), as a yellow oil, and 7,10,10-trimethylbicyclo[6.3.0]-undec-7-en-3-one (**19**) (0.029 g, 48%), as white crystals. The combined yield of products was 68%. **10,10-Dimethyl-7-methylenebicyclo[6.3.0]undecan-3-one (18)**: IR (CCl_4) 1700, 902 cm^{-1}; ^1H NMR δ 4.89 (s, 1H), 4.86 (s, 1H), 2.90 (m, 1H), 2.75 (m, 1H), 2.60 (m, 1H), 2.47 (m, 2H), 2.34 (m, 1H), 2.23 (m, 1H), 2.05 (dd, J = 3.7, 3.7 Hz, 1H), 1.55–1.95 (m, 3H), 1.44 (dd, J = 6.2, 5.9 Hz, 1H), 1.25 (dd, J = 2.8 Hz, 2H), 1.10 (s, 3H), 1.01 (s, 3H); ^{13}C NMR($CDCl_3$): δ 215.5 (+), 148.8 (+), 114.6 (+), 49.2 (−), 48.3 (−), 47.9 (+), 45.9 (+), 42.5 (+), 40.4 (+), 37.3 (+), 36.1 (+), 31.7 (+), 31.3 (−), 29.0 (−); HRMS calcd for $C_{14}H_{22}O$ 206.1671, found 206.1679.

7,10,10-Trimethylbicyclo[6.3.0]undec-7-en-3-one (19). A slurry of 10,10-dimethyl-7-methylenebicyclo[6.3.0]undecan-3-one (**18**) (0.050 g, 0.24 mmol), silica gel (0.50 g, 0.040–0.063 mesh), and 1% aqueous H_2SO_4 (0.50 mL) in hexanes (5.0 mL) was stirred at room temperature overnight. The water was removed by the addition of anhydrous $MgSO_4$ which was removed by filtration along with the silica gel. The solvent was removed *in vacuo* to give **19** (0.049 g, 98%) as white crystals. The spectral data for **19** were compared to the literature data:[23] mp 37–39 °C (lit. mp 40–41 °C); IR (CCl_4) 1695 cm^{-1} (lit. IR ($CHCl_3$) 1700 cm^{-1}); ^1H NMR δ 2.55 (m, 1H), 2.36 (m, 3H), 2.28 (m, 1H), 1.95 (m, 1H), 1.50–1.87 (m, 4H), 1.53 (s, 3H), 1.20–1.50 (m, 3H), 0.952 (s, 3H), 0.822 (s, 3H) (lit. ^1H NMR δ 3.0–1.0 (m, 13H), 1.70 (Me), 1.12 (Me), 0.86 (Me)); ^{13}C NMR δ 214.8, 138.2, 126.9, 57.4, 55.1, 48.6, 44.8, 40.2, 37.0, 31.8, 28.3, 27.1, 20.9, 19.2 (lit. ^{13}C NMR δ 214.3, 139.5, 126.1, 57.4, 55.6, 48.8, 45.1, 39.4, 37.6, 32.6, 29.1, 27.7, 21.3, 19.4).

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Supplementary Material Available: ^1H NMR spectra of **6c**, **7a**, and **18** and ^{13}C NMR spectra of **3c**, **3d**, **5c**, **7b**, **7d**, and **16** (11 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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