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A CYCLOBUTANONE-BASED TANDEM FREE RADICAL REARRANGEMENT

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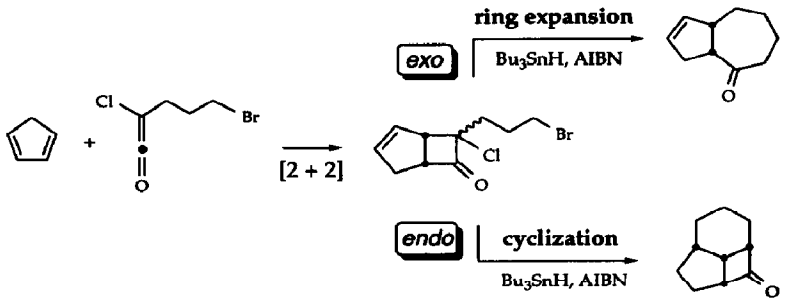
Abstract *Free radical reaction of endo-haloalkylbicyclo[4.2.0]oct-2-en-7-ones* ***1*** *and* ***11*** *leads to sequential rearrangement and formation of the novel, bridged tricyclic ketones* ***2*** *and* ***13****. A mechanism for this unusual transformation is proposed.*

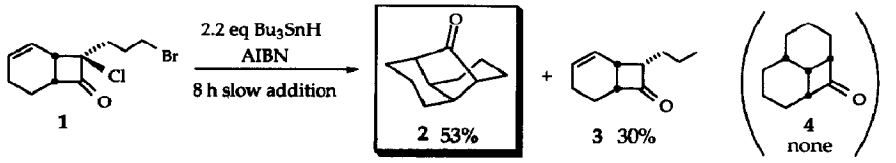
For several years we have been exploring the synthetic potential of cyclobutanone-based free radical ring expansion and annulation reactions.[1,2] To illustrate, entry to the cyclopentenyl-fused cyclobutanone series (Scheme 1) is effected by treatment of cyclopentadiene with an

Scheme 1



ω-bromoalkyl ketene. A mixture of *exo*- and *endo*-haloalkyl fused cyclobutanones is formed (Scheme 1).[2a,b] The *exo*-haloalkyl cyclobutanone undergoes smooth ring expansion in a sequence consisting of addition of the primary radical to the carbonyl group followed by β-scission of the alkoxy radical to afford the *cis*-fused bicyclic product.[2a,b] The *endo*-haloalkyl cyclobutanones produce tricyclic product following cyclization of the alkyl radical to the double bond.[2b,3]

We report here a new tandem free radical reaction of *endo*-halopropylbicyclo[4.2.0]oct-2-en-7-one **1** that leads to deep-seated rearrangement and a novel carbon skeleton. We had anticipated that formation of direct cyclization product **4** would be the main course of the free radical reaction of **1** based on the reaction of *endo*-halopropylbicyclo[3.2.0]hept-2-en-6-one (Scheme 1).

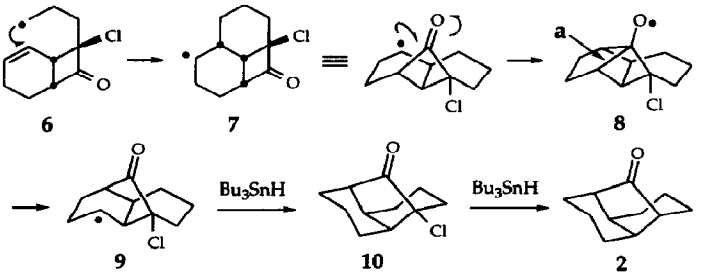


(1)

However, upon treatment of **1** with 2.2 eq of Bu_3SnH and AIBN, it was immediately clear that an unusual rearrangement had taken place. None of the direct cyclization product **4** was observed (eq 1). Thus, the IR spectrum of the major product **2** showed a strong band at 1742 cm^{-1}. Compound **2** clearly contained a cyclopentanone, not a cyclobutanone carbonyl. Likewise the ^{13}C NMR spectrum of **2** showed six lines instead of the seven lines expected of the product **4**. Following these revelations, **2** was demonstrated to be tricyclo[5.4.0.$0^{3,8}$]undecan-2-one.[4,5] To the best of our knowledge, compound **2** has not been synthesized before and this skeletal type is quite rare.

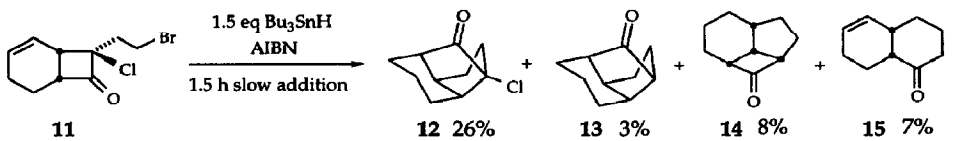
A mechanistic path for the rearrangement of eq 1 might be formulated as follows (Scheme 2). Upon treatment of **1** with Bu_3SnH and AIBN, a primary carbon radical **6** is generated that

Scheme 2



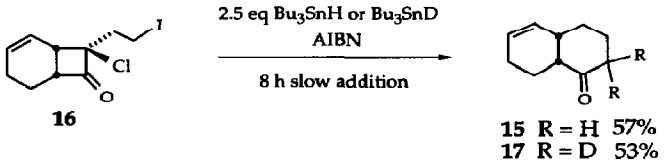
adds to the double bond to form the cyclic radical **7**. The cup-shaped *endo*-tricyclic ring system makes it possible for the cyclohexyl radical **7** to attack the cyclobutanone carbonyl leading to **8**.[6] β-Cleavage of the alkoxy radical **8** at **bond a** provides the greatest relief of four-membered ring strain[7] and leads to the formation of **9**, which is then reduced to **10**.[8] The latter can be isolated or further reduced to **2** depending upon the number of equivalents of Bu_3SnH employed.

This rearrangement was also observed with the cyclohexenyl-fused system **11** which has a bromoethyl side chain (eq 2). Upon tributyltin hydride treatment, a mixture of bridged tricyclic



(2)

ketones (**12** and **13**) was generated, accompanied by a small amount of direct cyclization product **14**[2b] and the *cis*-bicyclo[4.4.0]decenone **15**.[9] When the iodide **16** was used as radical precursor, slow addition of 2.5 eq of Bu_3SnH (or Bu_3SnD) produced bicyclodecenone **15** (or **17**) as the major product (eq 3).



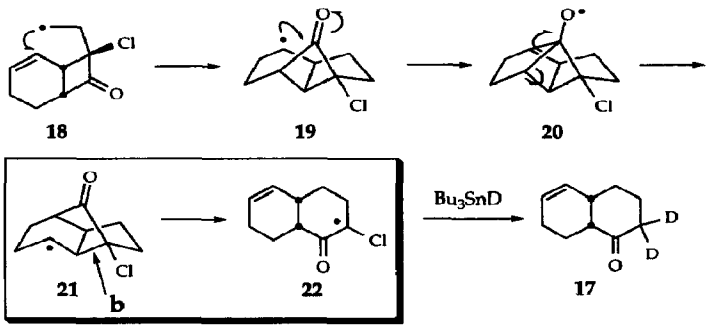
16

15 R = H 57%
17 R = D 53%

(3)

Formation of bicyclodecenone **17** can be envisioned to arise by cleavage of **bond b** of the intermediate radical **21** (Scheme 3). This process is favored by release of ring strain of the bridged

Scheme 3



ring and produces the bicyclo[4.4.0]decenone radical **22**, which is stabilized by both the α-acyl and chlorine groups.

In summary, we have discovered a cyclobutanone-based tandem free radical reaction that leads to the formation of novel bridged tricycloketones and is in itself of substantial mechanistic interest.

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(4) Additional data for compound **2**: 300 MHz ^{1}H NMR ($CDCl_3$) δ 1.27-1.67 (m, 6 H), 1.68 (m, 4 H), 1.93 (m, 2 H), 2.04 (m, 2 H), 2.17 (m, 2 H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 19.0 (t), 30.8 (t), 31.0 (t), 45.4 (d), 51.0 (d), 226.0 (s); MS *m/e* (rel. intensity) 164 (M^+, 98), 146 (37), 136 (27), 121 (40), 104 (49), 94 (60), 79 (100), 67 (64); HRMS calcd for $C_{11}H_{16}O$ 164.1201, found 164.1191.

(5) The structure of **2** was established by direct comparison with an independently synthesized authentic sample.

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(8) Data for compound **10**: 300 MHz ^{1}H NMR ($CDCl_3$) δ 1.25-2.09 (m, 10 H), 2.13 (m, 2 H), 2.19 (br s, 1 H), 2.24 (br s, 1 H), 2.3 (br s, 1 H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 18.6 (t), 21.1 (t), 28.9 (t), 29.6 (t), 31.6 (t), 40.8 (t), 43.9 (d), 49.7 (d), 50.8 (d), 75.0 (s), 216.4 (s); IR (neat) 1759 (s, C=O) cm^{-1}; MS *m/e* (rel. intensity) 198 (M^+, 23), 163 (19), 145 (15), 135 (100), 105 (12), 91 (27), 79 (25), 67 (35); HRMS calcd for $C_{11}H_{15}{}^{35}ClO$ 198.0811, found 198.0818.

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