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Ring Expansion Reactions *via* Endocyclic Cleavage of Cyclopropylcarbinyl Radicals

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Abstract: Ring expansion reactions *via* endocyclic cleavage of cyclopropylcarbinyl radicals are described.

Keyword; *radical reactions, ring transformation, cyclopropanes*

Radical based ring opening reactions have been successfully exploited in the development of a wide variety of useful synthetic transformations.[1] Especially, recent advances in the ring opening reactions of three-membered rings have led to the steadily increasing utilization of cyclopropyl derivatives as building blocks for organic synthesis.[2] In this respect, ring opening of the cyclopropylcarbinyl radicals and cyclopropyl alkoxy radicals has proved to be a useful strategy for ring expansion because cleavage of the three-membered ring takes place easily and the disfavored entropy effect usually associated with medium and large size ring formation can be avoided.[3] However, the literature on bicyclo[n.1.0] radicals reveals a preference for stereoelectronically controlled exocyclic radical ring opening as opposed to thermodynamically favored endocyclic ring opening.[4] The exocyclic cleavage has usually been achieved under reaction conditions such as electrolysis,[5] samarium iodide,[6] alkali metal[7] and photochemical electron transfer.[8] Ingold has studied the stereoelectronic requirements of the fragmentation of cyclopropylcarbinyl radicals.[9] In addition, Beckwith,[10] Dowd,[11] Baldwin[12] and Crimmins[13] have reported on some unusual radical based ring expansion reactions. Much of the attention in this area has focused on exocyclic cleavage of cycloalkylcarbinyl radicals and endocyclic cleavage of cyclopropyl alkoxy radicals generated *in situ* by the addition of carbon radical centers to a adjacent carbonyl group. Considerably less effort has been expended on the development of ring expansion reactions *via* endocyclic cleavage of cycloalkylcarbinyl radicals. In connection with our reserch interest in the synthetic utility of cyclopropane derivatives, we reported the convenient SmI_2-induced ring opening reactions of alkyl (n+1)-oxobicyclo[n.1.0] alkane-1-carboxylates *via* endocyclic cleavage.[14] We next studied the feasibility of ring expansion reactions *via* endocyclic cleavage of cyclopropylcarbinyl radicals.

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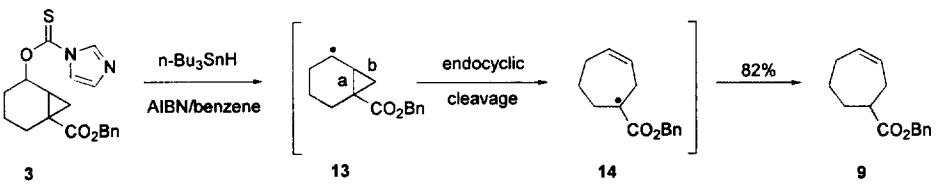
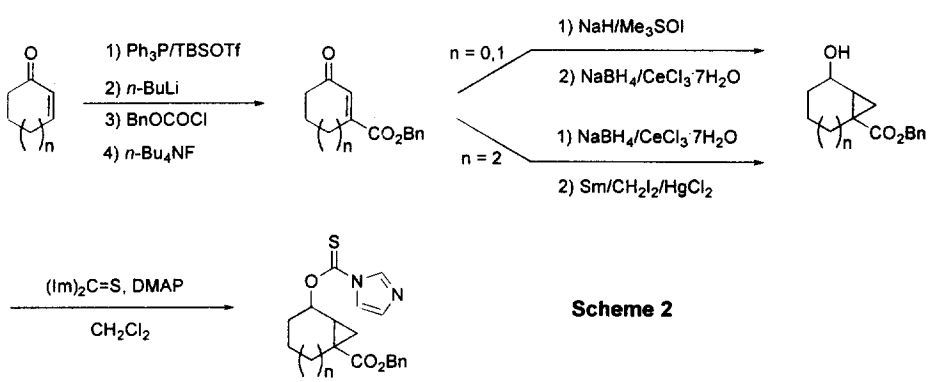


Scheme 1

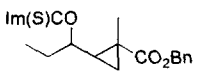
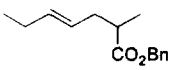
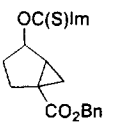
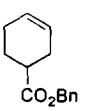
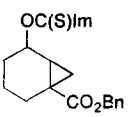
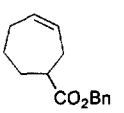
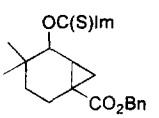
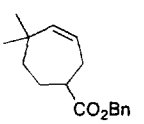
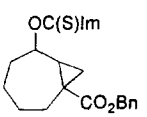
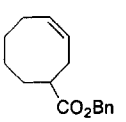
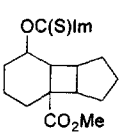
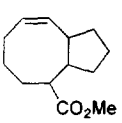
Initial studies were performed with the thiocarbamate **3** (entry 3, Table 1), which could be prepared from phosphoniosilylation,[15] cyclopropanation,[16] reduction[17] followed by acylation[18] of α,β-enones (Scheme 2). Slow addition of a solution of tributyltin hydride and AIBN to thiocarbamate **3** in benzene at 80 °C resulted in reductive cleavage of the cyclopropane to give a 82% yield of benzyl 3-cycloheptenecarboxylate (**9**).[19] The tentative mechanism for this reaction is shown in Scheme 1. The cyclopropylcarbinyl radical **13** fragments to produce the more stable *tertiary* radical **14** which is reduced by tributyltin hydride. Selective cleavage of the cyclopropane bond (**a**), endocyclic to the cyclohexane, results from stabilization of the resultant radical by the carbonyl groups, such as the benzyloxy carbonyl group, which lowers the transition state energy for the final cyclopropane cleavage in the ring expansion. This result is compatible with the fact that thiocarbamate lacking carbonyl group which can stabilize the produced radical undergoes simple exocyclic cleavage to give 3-methylcyclohexene in 82% yield. The generality of this process was evaluated by preparing **2**, **4** and **5** and exposing these to Bu_3SnH in benzene in 80 °C to produce ring expansion compounds in good yields (Table 1). Monocyclic compound **1** (entry 1) reacted readily and gave a good yield of benzyl *trans*-2-methyl-4-heptenoate (**7**). The present method reaches a limit with adduct **6** derived from [2+2]-photoaddition of enone and cyclopentene. In this case, the desired product **12** was obtained in only 30% yield together with the exocyclic ring opening and direct reduction products in 13% and 7% yield, respectively, which is consistent with Ranu's and Beckwith's results on the kinetics of ring opening of radicals containing the cyclobutylcarbinyl system.[20]



Scheme 2

In summary, the free radical ring expansion reactions proceed *via* endocyclic cleavage of the bridged bond of cyclopropylcarbinyl radicals. Because the exocyclic cleavage of cyclopropylcarbinyl radicals was reported mainly in previous work, the present method contrasts with and complements the existing synthetic methods.

Table 1. Ring Expansion Reactions *via* Endocyclic Cleavage of Cycloalkylcarbinyl Radicals

entry	starting material		product		isolated yield/%
1		**1**		**7**	82
2		**2**		**8**	83
3		**3**		**9**	82
4		**4**		**10**	65
5		**5**		**11**	71
6		**6**		**12**	30[a]

[a]The exocyclic cleavage and direct reduction product were produced in 13% and 7% yield, respectively.

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[19] Typical procedure: The thiocarbamate **3** (35 mg, 0.1 mmol) was dissolved in dry, degassed benzene (1 mL, 0.1 M) and heated to reflux. A solution of 1.2 equiv. of tributyltin hydride (34.9 mg, 0.12 mmol) and 0.2 equiv. of AIBN (3 mg, 0.02 mmol) in benzene (0.14 M) was added over 4 h by syringe pump. When the addition was complete, the benzene was removed under reduced pressure and the residue was extracted with ether (3 x 25 mL). The combined organics were washed with saturated potassium fluoride (20 mL) and brine (20 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was then purified by silica gel chromatography to give 18.9 mg (82%) of benzyl 3-cycloheptenecarboxylate.

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