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3. (a) Kitazawa, T.; Nishikiori, S.; Kuroda, R.; Iwamoto, T. *Chem. Lett.* **1988**, 459. (b) Kitazawa, T.; Nishikiori, S.; Iwamoto, T. *J. Chem. Soc., Dalton Trans.* **1994**, 3695.
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5. The crystal data: $Cd_3C_{20}H_{28}N_{10}$, M=735.66, monoclinic, $P2_1/n$, a=8.942(2), b=12.835(5), c=12.222(3) Å, β=92.33(2)°, V=1401.5(7) Å^3, Z=2, D_x=1.74, D_m=1.76(2) gcm^{-3}, 4588 reflections observed, 3151 (>3σ(F_o)) used, 151 parameters to R=0.032 and R_w=0.042. The diffraction data of a crystal were collected on a Rigaku AFC-5S four-circle automated diffractometer with graphite-monochromated Mo-Kα radiation (λ=0.71069 Å) at 296 K. All data were collected with the ω-2θ scan mode in the range of 4°<2θ<60°. Single crystal of this clathrate coated with epoxy resin did never show any decay during the intensity measurement. The crystal structure was solved by heavy-atom method and refined by SHELX 76 and UNICS III programs.
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Sequential Radical Ring Expansion and Allylation Reactions Using 2-Bromo-3-(phenylthio)propene: Their Application to the Synthesis of Bridged Ring Systems

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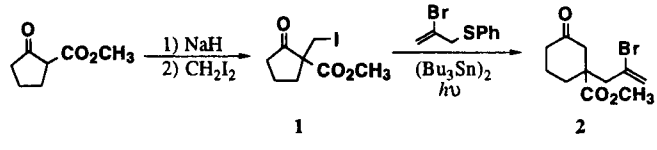
Received May 16, 1997

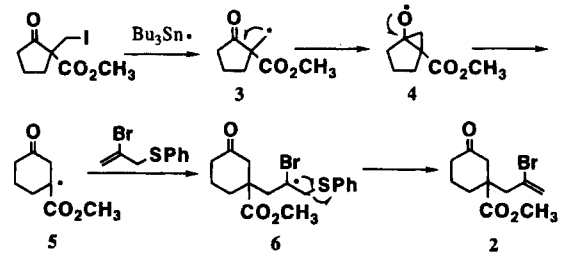
In recent years we have witnessed a remarkable upsurge of the interest among synthetic organic chemists in carbon-centered radical chemistry.[1] Particularly, the development of radical-based synthetic methods for the preparation of bridged systems[2] has been stimulated by the discovery of many biologically active polycyclic natural products that contain a bridged structural unit. For example, the bicyclo[3.2.1]octane ring system has received a relatively large amount of attention due to its frequent presence in various sesqui- and diterpenes.[3]

The ability to sequence radical reactions to accomplish multiple transformations in a single step is an asset of free radical reactions in organic synthesis.[4] Ring expansion *via* an oxy radical is especially interesting because of its potential for the synthesis of medium and large rings. Dowd has shown that sequential radical reactions *via* ring expansions provide a variety of ring compounds.[5] Under these conditions, alkyl radical addition to the ketone can compete favorably with direct hydrogen atom abstraction and the location of the radical-stabilizing ester group controls the direction of fragmentation, which is itself sufficiently rapid so that an intermediate oxy radical can not be intercepted by tin hydride (Scheme 2). It is anticipated that the undesired direct reduction of alkyl radical **3** before expansion can be minimized by using hexabutylditin for initiation instead of tributyltinhydride and trapping the ring-expanded radical **5** with allyl transfer reagent, 2-bromo-3-(phenylthio) propene **6**. The ring-expanded vinyl bromide **2** thus generated is expected to undergo vinyl radical cyclization onto car-



1 2

Scheme 1.



Scheme 2.

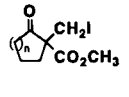
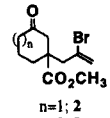
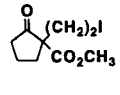
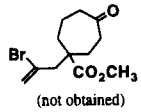
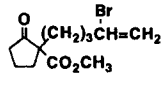
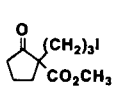
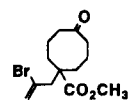
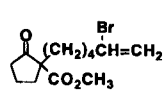
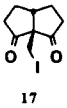
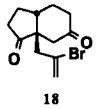
bonyl group. We now wish to report herein that radical ring-expansion and subsequent allylation reaction would provide a new method for bridged ring compounds.

The overall ring expansion and allylation process is summarized in Scheme 1. The structure characterization of **2** was accomplished *via* analysis of IR, ^{1}H NMR, ^{13}C NMR, and mass spectra.[7]

The proposed mechanism for the formation of ring-expanded compound **2** is shown in Scheme 2. The ring expansion reaction occurs by the attack of the first-formed primary radical **3** on the carbonyl carbon. The resulting oxy radical **4** then undergoes ring cleavage to generate the stabilized radical **5** adjacent to the ester group. The addition of the radical **5** to 2-bromo-3-(phenylthio)propene followed by fragmentation of the radical **6** produces the ring-expanded allylation product **2**.

Encouraged by the above successful free radical ring expansion and allylation reaction, the behavior of other β-keto esters and a diketone was next examined. Sunlamp irradiation of a solution of the iodo compound **14** (1.0 equiv) and 2-bromo-3-(phenylthio)propene (2.0 equiv) in the presence of hexabutylditin (1.0 equiv) in benzene gave the ring-expanded product **15** and the non-ring expanded product **16** as a 4/6 mixture in 54% combined yield after purification by silica gel column chromatography (entry 3). In the case of a two-carbon ring expansion and allylation reaction, the only product isolated from the reaction was the directly allylated product **13** without detection of the ring-expanded product **12** (entry 2). Dowd[5] studied a two-carbon ring expansion reaction and concluded that the formation of the four-membered ring oxy radical does not compete favorably with chain transfer reduction of the initial primary radical.

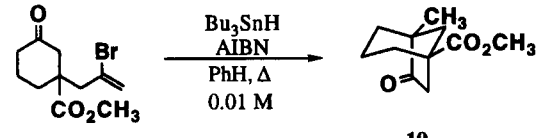
Table 1. Results of Ring Expansion and Allylation Reactions of 2-Bromo-3-(phenylthio)propene with Organic Halides

Entry	Substrate	Product	Isolated yield (%)
1			
	n=1; **1** n=2; **7** n=3; **9**	n=1; **2** n=2; **8** n=3; **10**	49 27 32
2		  (not obtained)	50
	11	**12**	**13**
3		 	54 (40/60)[a]
	14	**15** **16**	
4			43
	17	**18**	

[a] The figure in parenthesis indicates the ratio of isomers. All new compounds exhibited spectroscopic (IR, ^{1}H NMR, ^{13}C NMR) and analytical (HRMS) data in accord with the assigned structure.

Representative results for the ring-expansion-allylation reactions of 2-bromo-3-(phenylthio)propene with alkyl halides are summarized in Table 1.

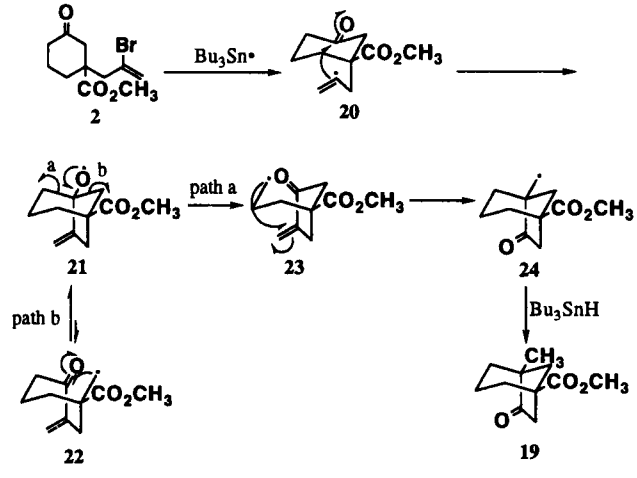
Next we were interested in the addition of vinyl radical to carbon-oxygen double bond. A solution of vinyl bromide **2**, AIBN, and Bu_3SnH in benzene was heated at reflux for 4 h. Use of 0.01 M tin hydride gave only the cyclized product **19**[8] in 49% yield (68% corrected for unreacted vinyl bromide **2**, eq. 1).



2 **19** (1)

A plausible mechanism of consecutive radical reaction process was proposed[4] and is believed to proceed through the addition of vinyl radical **20** to carbonyl group, fragmentation of alkoxy radical **21**, and recyclization of alkyl radical **23**. The fragmentation of alkoxy radical **21** can produce two possible primary radicals **22** and **23**. However, the primary radical **22** can attack the carbonyl group to give the alkoxy radical **21** again. Therefore the primary radical **23** is the most likely intermediate in this sequence. The alkyl radical **23** adds to a double bond to produce another alkyl radical **24**. This alkyl radical abstracts a hydrogen atom from tributyltin hydride to form the cyclized product **19**.

Prompted by the above successful sequential radical reaction, we also explored the cyclization of diketone **18** under the standard reaction condition. The overall process involves three sequential reactions: i) ring expansion, ii) allylation, iii) vinyl radical cyclization. The vinyl radical cyclization reaction was conducted by treatment of diketone **18** with Bu_3SnH (1.2 equiv) in the presence of AIBN (0.1 equiv) in benzene at reflux (eq. 2). Purification by silica gel column chromatography gave only the cyclized product **25** in 46% yield (66% yield based on the recovered starting material). No reduced product was obtained. The ^{1}H NMR, IR, ^{13}C NMR, and mass spectra were consistent with the assigned structure of **25**.[9] The ^{1}H NMR spectrum showed the disappearance of vinyl protons and the appearance of

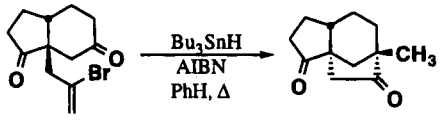


2 **20** **21** **23** **24** **22** **19**

Scheme 3.

methyl group at δ 1.08. The mechanism for the formation of tricyclic compound **25** is the same as that previously described in Scheme 3.

In conclusion, we have demonstrated that consecutive radical ring expansion, allylation, cyclization process provides a facile route to bridged ring sysytems which are frequently present in a variety of biologically active natural products. Further work on the scope and application of this novel process is now being explored.



18 **25** (2)

Acknowledgment. We gratefully acknowledge financial support from the National Institute of Health and partially from Korea University.

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7. Spectroscopic data of **2** is as follows; ^{1}H NMR ($CDCl_3$) δ 5.58 (1H, s), 5.55 (1H, s), 3.70 (3H, s), 3.05 (1H, d, *J*= 14.6 Hz), 2.68 (1H, d, *J*=14.6 Hz), 2.23 (1H, d, *J*=9.1 Hz), 2.26-2.15 (1H, m), 2.45-1.62 (6H, m); ^{13}C NMR ($CDCl_3$) δ 208.2, 175.0, 127.2, 121.5, 52.4, 50.2, 49.5, 47.2, 40.2, 34.0, 21.6; IR (thin film) 2954, 2920, 2872, 1732, 1625, 1450, 1210, 1130, 896 cm^{-1}; MS m/e 245 (M^+-OCH_3), 215, 195, 155, 135, 107, 95, 79, 55; HRMS m/e calculated for $C_{10}H_{12}BrO_2$: 245.0001 (M^+-OCH_3); found: 244.9999.
8. Spectroscopic data of **19** is as follows; ^{1}H NMR ($CDCl_3$) δ 3.71 (3H, s), 2.62 (1H, d, *J*=18.6 Hz), 2.34-2.27 (1H, dd, *J*=18.6 Hz, 3.4 Hz), 2.03 (1H, br), 1.90-1.75 (4H, m), 1.58-1.39 (3H, m), 1.03 (3H, s); ^{13}C NMR ($CDCl_3$) δ 207.9 (s), 176.1 (s), 52.2 (q), 49.3 (s), 46.5 (t), 46.3 (d), 45.5 (s), 37.2 (t), 32.2 (t), 20.1 (q), 19.6 (t); IR (thin film) 2953, 2872, 1734, 1458, 1221, 1167 cm^{-1}; MS m/e 196 (M^+), 168, 154, 137, 109, 94, 79, 69, 55; HRMS m/e calculated for $C_{11}H_{16}O_3$ (M^+): 196.1099; found: 196.1099.
9. Spectroscopic data of **25** is as follows; ^{1}H NMR ($CDCl_3$) δ 2.48-2.28 (6H, m), 1.63-1.25 (7H, m), 1.08 (3H, s); ^{13}C NMR ($CDCl_3$) δ 219.2, 217.1, 52.6, 50.6, 44.9, 44.3, 43.0, 38.1, 37.3, 25.3, 23.5, 19.6; IR (thin film) 2938, 1737, 1460, 1095 cm^{-1}; MS m/e 192 (M^+), 162, 149, 136, 119, 107, 93, 79, 67, 55, 49; HRMS m/e calculated for $C_{12}H_{16}O_2$ (M^+): 192.1150; found: 192.1150.