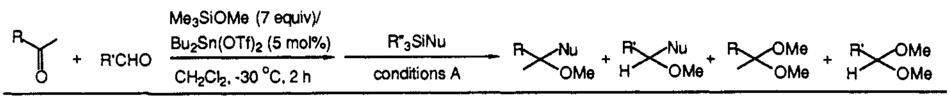
Scheme II



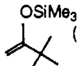
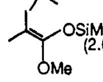
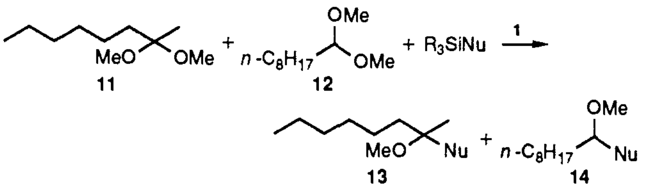
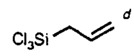
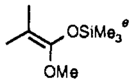
R	R'	R"$_3$SiNu	conditions A					
n-C_4H_9	n-C_7H_{15}	 (1.7 equiv)	-50 °C, 8 h	95%	(94:6)	6%	3%	76%
n-C_6H_{13}	n-C_8H_{17}	 (2.0 equiv)	0 °C, 10 h	89%	(92:8)	8%	11%	71%
		Me_3SiCN (1.1 equiv)	-78 °C, 2 h	90%	(99:1)	1 %	0	72%
		Et_3SiH (2.0 equiv)	-10 °C, 9 h	89%	(92:8)	8%	5%	75%

Table II. Crossover Reaction of Acetals of Ketone and Aldehyde with Various Silyl Nucleophiles[a]



11 12 13 14

R$_3$SiNu	yield,[b] % 13	 14	 (13/14)	13:14
Et_3SiH[c]	87	5		95:5
Me_3SiCN	74	4	(73)	95:5
 [d]	47	1	(44)	98:2
 [e]	63	4	(60)	94:6

[a] Reaction conditions: **11**:**12**:R$_3$SiNu:**1** = 1:1:1:0.05, dichloromethane, −78 °C, 2 h. [b] Determined on the basis of GLC analysis. Isolated yields of the mixtures of **13** and **14** after column chromatography are given in parentheses. [c] Five hours. [d] Temperature −10 °C. [e] Three hours.

$SnCl_2$-TMSCl,[12] and CF_3SO_3H.[13,14] Apparently, **1** can perceive a delicate difference between two kinds of acetals. In this sense, **1** is more selective than the other Lewis acids. Consequently, the reactivities of the ketone and the aldehyde were completely reversed through acetalization.

The synthetic potential of this procedure is demonstrated by the successful employment of other silyl nucleophiles (Table II).

Finally, a novel preferential one-pot transformation of ketones in the presence of aldehydes was achieved. An aldehyde-ketone mixture (each 1 equiv) was converted into the corresponding acetal mixture by treating with trimethylmethoxysilane (7 equiv) using **1** as a catalyst at -30 °C for 2 h in dichloromethane.[15] Then, a silyl nucleophile was added to this solution under the conditions shown in Scheme II. GLC analyses exhibited the selective formation of the ketone adducts. This methodology not only provides a conceptually new mode of carbonyl differentiation but also meets versatile synthetic demands due to recent extensive developments of silicon-based nucleophile reagents.

The success of the present reaction is ascribed to the unique catalytic activity of **1**, which serves for acetalization of carbonyls and the subsequent preferential addition of the silyl nucleophiles to the ketone acetals in a one-pot manner. Probably, the mild reactivity of **1** is primarily responsible for the soft activation of ketone acetals, leaving cationically less reactive aldehyde acetals unchanged.[16] The mildness of **1** as compared with TMSOTf is rather surprising in view of the generally accepted criterion for the Lewis acidity of organotin and -silicon compounds. The difference is attributable to the reduced oxygenophilicity of tin in comparison with silicon.[17]

Acknowledgment. This work was partially supported by a Grant-in-Aid for Scientific Research on Priority Areas, the Ministry of Education, Science, and Culture, Japan. We also thank S. Asada and S. Tokieda for their technical assistance.

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(12) Iwasawa, N.; Mukaiyama, T. *Chem. Lett.* **1987**, 463.

(13) Kawai, M.; Onaka, M.; Izumi, Y. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 1237.

(14) The following Lewis acids resulted in poor yields: Eu(fod)$_3$, $FeCl_3$, $MgBr_2{\cdot}OEt_2$, $ZnBr_2$, ZnI_2, Et_2AlCl, $EtAlCl_2$, BBr_3, BCl_3, $BF_3{\cdot}OEt_2$, and TMSI.

(15) Acetalization with TMSOMe-TMSOTf: Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 1357.

(16) Concerning the possibility of an S_N1 mechanism for some acetal-silyl nucleophile reactions, see ref 2. See also: Denmark, S. E.; Willson, T. M. *J. Am. Chem. Soc.* **1989**, *111*, 3475.

(17) Itoh, K.; Matsuzaki, K.; Ishii, Y. *J. Chem. Soc. C* **1968**, 2709. Itoh, K.; Fukumoto, Y.; Ishii, Y. *Tetrahedron Lett.* **1968**, 3199.

Sequential Radical Cyclization, Alkoxy Radical Fragmentation, and Recyclization Processes: A Novel Method for the Synthesis of Fused Cycloheptanones and Cyclooctenones from Cyclohexanones

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The formation of C-C bonds via radical reactions has witnessed a renaissance recently, particularly in intramolcular cyclization processes leading to the preparation of complex natural products.[1] While C-C multiple bonds have generally served as the radical acceptor in these cyclization approaches, a significant limitation of this methodology is that the cyclization process often results in a decrease in the functional complexity of the substrate. Recently the addition of carbon radicals to carbonyl groups was reported, which should allow for the preparation of cycloalkanols.[2] Another feature of the radical cyclization involving carbonyl groups is that the resulting alkoxy radicals may be useful for

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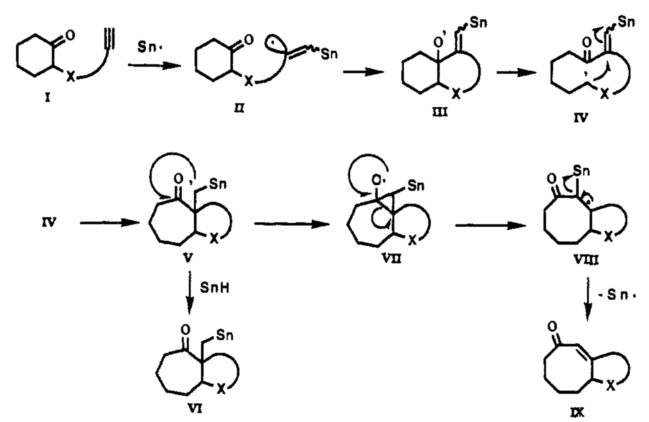
(1) (a) Curran, D. P. *Synthesis* **1988**, 417 and 489. (b) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541. (c) Giese, B. *Radicals in Organic Synthesis; Formation of Carbon-Carbon Bonds*; Pergamon Press: Oxford, 1986.

(2) (a) Fraser-Reid, B.; Vite, G. D.; Yeung, B.-W. A.; Tsang, R. *Tetrahedron Lett.* **1988**, *29*, 1645. (b) Tsang, R.; Dickson, J. K., Jr.; Pak, H.; Walton, R.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1987**, *109*, 3484. (c) Ardisson, J.; Férézou, J. P.; Julia, M.; Pancrazi, A. *Tetrahedron Lett.* **1987**, *28*, 2001. (d) Tsang, R.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1986**, *108*, 2116. (e) Tsang, R.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1986**, *108*, 8102. See also ref 4.

Scheme I[a]



[a] Sn = SnBu$_3$.

Scheme II

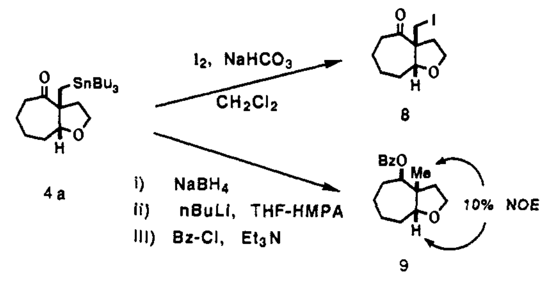
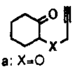
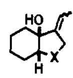
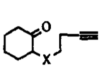
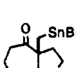
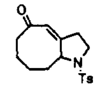
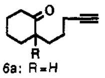
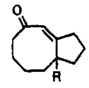


Table I. Radical Cyclization of Keto Acetylenes

Substrate	Conditions[a]	Time (h)	Temp. (°C)	Products and yields[b]
 1a: X=O	A	3.5	-20	 2a: X=O,Y=SnBu$_3$[c,d] 72% 2b: X=O,Y=H 28%
1b: X=NTs	A	1.0	17	2c: X=NTs,Y=SnBu$_3$[c,e] 8% 2d: X=NTs,Y=H 22%
 3a: X=O	A	0.8	20	 4a: X=O 62%
3b: X=NTs	A	1.0	16	4b: X=NTs 38%  5: 19%
	B	4.5	80	4b: X=NTs 12% 5: 29%[f]
 6a: R=H	B	4.0	80	 7a: R=H 18%
6b: R=COOEt	B	4.3	80	7b: R=COOEt 22%[h]
6c: R=OSiEt$_3$	B	6.0	80	7c: R=OSiEt$_3$ 51%[i]

[a] A: Photochemical conditions; a toluene solution of the substrate (20–24 mM), TBTH (1.2–1.4 equiv), and AIBN (1 equiv) was irradiated with a 300-W high-pressure mercury lamp through a Pyrex filter. B: Thermal conditions; a mixture of TBTH (1.2 equiv, 15 mM) and AIBN (1.0 equiv, 15 mM) was added slowly to a benzene solution of the substrate (20 mM) by using a syringe pump at reflux temperature. [b] Isolated yields. [c] Isolated as vinyl iodides after iodolysis (I$_2$, NaHCO$_3$, CH$_2$Cl$_2$). [d] *E*/*Z* = 1.6 by NMR. [e] *E*/*Z* = 7.0 by NMR. [f] **3b** (25%) was recovered. [g] See text. [h] **6b** (52%) was recovered. [i] **6c** (11%) was recovered.

generating new radical centers by a β-cleavage reaction of the C–C bond.[3] We report here in a preliminary form a combination of these features that provides a unique entry for the preparation of complex seven- and eight-membered carbocyclic skeletons.[4]

Beginning with cyclohexanones possessing acetylenic side chains as shown in Scheme I, we anticipated that the triple bond would serve as the precursor to the vinyl radical II after addition of the trialkylstannyl radical, and finally the vinylstannane would also serve as the final radical acceptor IV, which would result from the β-cleavage of the alkoxy radical intermediates III. Reduction of the radical V, would be generated by the intramolecular cyclization of the radical IV, would afford the bicyclic cycloheptanones VI. However, the radical V may afford the bicyclic cyclooctenones IX by the known cyclization–fragmentation reaction.[4] The partitioning of the products between cycloheptanones VI and cyclooctenones IX would be governed by the relative rates for the cyclization (V → VII) and the reduction (V → VI). If the concentration of trialkyltin hydride is sufficiently low, the process for the formation of the cyclooctenones IX will be favored.

Initially we investigated the reaction of **1**, since the radical cyclization of **1a** has been reported to be inefficient.[5] When **1a** was submitted to routine radical conditions [tri-*n*-butyltin hydride (TBTH, 1.4 equiv), azobisisobutyronitrile (AIBN, 0.1 equiv), toluene, 110 °C, 4 h], the cyclized products **2** were isolated in only 30% yield (**2a**/**2b** = 1.1). However, we found that at a higher concentration of AIBN, the reaction was quite facile and the combined yield of **2a** and **2b** was essentially quantitative (Table I),[6,7] although no β-cleavage of the alkoxy radical was observed. On the other hand, **1b** was significantly less reactive and produced **2c** and **2d** in a combined yield of only 30%, but once again no rearrangement was observed.

Reaction of **3a** under photochemical conditions for the generation of the stannyl radical produces the organostannane **4a** in 62% yield.[8] The tin moiety was removed by employing two procedures to simplify the structure elucidation of the cyclized products as shown in Scheme II. The carbocycles **4a**, **8**, and **9** were unequivocally determined as shown by using 2D NMR techniques. The stereochemistry of the ring juncture in **9a** was determined to be cis by NOE experiments. Similar reactions with **3b** under both thermal and photochemical conditions generated the cyclized product **4b** along with the ring-expansion product **5**, albeit in modest yields. Thus, the length of side chains that allowed 5-exo cyclization (IV → V) is essential for secondary reactions.

Because bicyclo[5.3.0]decane and bicyclo[6.3.0]undecane skeletons are frequently present in the structure of many terpenes, we turned our attention to the formation of this system. When **6a** was subjected to the above radical conditions, the desired cyclization product **7a** was isolated in only 18% yield. Considering this unsuccessful result, we anticipated that stabilization of the radical IV by heteroatoms at the α-carbon should facilitate the desired reaction. Therefore two substrates, **6b** and **6c**, which are capable of stabilizing the radical intermediate, were prepared and subjected to the reaction. Although the reaction of **6b** was unexpectedly slow (48% conversion after 4.3 h), the cyclooctenone **7b** was the sole product in 22% isolated yield (46% based on the consumed **6b**). A significantly better result was obtained from the reaction of **6c**, and 5% of **7c** was isolated.[9]

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(3) (a) Beckwith, A. L. J.; Hay, B. P. *J. Am. Chem. Soc.* **1989**, *111*, 230. (b) Beckwith, A. L. J.; Hay, B. P. *J. Am. Chem. Soc.* **1989**, *111*, 2674. (c) Beckwith, A. L. J.; O'Shes, D. M.; Westwood, S. W. *J. Am. Chem. Soc.* **1988**, *110*, 2565. (d) O'Dell, D. E.; Loper, J. T.; Macdonald, T. L. *J. Org. Chem.* **1988**, *53*, 5225. (e) Suginome, H.; Senboku, H.; Yamada, S. *Tetrahedron Lett.* **1988**, *29*, 79. (f) Beckwith, A. L. J.; O'Shes, D. M.; Gerba, S.; Westwood, S. W. *J. Chem. Soc., Chem. Commun.* **1987**, 666. (g) Kobayashi, K.; Itoh, M.; Suginome, H. *Tetrahedron Lett.* **1987**, *28*, 3369. (h) Suginome, H.; Itoh, M.; Kobayashi, K. *Chem. Lett.* **1987**, 1527. (i) Beckwith, A. L. J.; Kazlauskas, R.; Syner-Lyons, M. R. *J. Org. Chem.* **1983**, *48*, 4718. (j) Macdonald, T. L.; O'Dell, D. E. *J. Org. Chem.* **1981**, *46*, 1501. See also ref 1.

(4) Applications of this strategy to the ring expansion of cycloalkanones: (a) Baldwin, J. E.; Adlington, R. M.; Robertson, J. *J. Chem. Soc., Chem. Commun.* **1988**, 1404. (b) Dowd, P.; Choi, S.-C. *J. Am. Chem. Soc.* **1987**, *109*, 3493. (c) Dowd, P.; Choi, S.-C. *J. Am. Chem. Soc.* **1987**, *109*, 6548, and also ref 3c and 3f.

(5) **2a**, 30%; **2b**, 20% (TBTH/AIBN/toluene); see ref 2c.

(6) These high AIBN concentration conditions were employed throughout this work.

(7) The *E*/*Z* ratio of **2a** was variable, depending on the reaction conditions. Details of this reaction will be published elsewhere.

(8) The reaction of **3a** under thermal conditions afforded a complex reaction mixture.

(9) Although a catalytic amount of TBTH should be necessary for this reaction, nearly 1 equiv of TBTH was required to consume most of the starting materials.

In conclusion, a new radical rearrangement, initiated by radical cyclization between ketones and acetylenes followed by β-cleavage of the alkoxy radical and subsequent radical–olefin cyclization, was developed. This reaction realized a single-step conversion from cyclohexanone derivatives to bicyclic cycloheptanones and cyclooctenones. Since the substrates were readily obtainable by using standard methods and the operation is very simple, this reaction allows an easy access to such skeletons. Further investigations to determine the scope and limitations of this reaction and applications to the natural product synthesis are now underway.

Acknowledgment. We thank Professor A. G. M. Barret, Northwestern University, for discussion about the mechanism of this reaction.

Supplementary Material Available: Experimental procedures for preparing **4a** and **7b** as well as full characterization data for **4a**, **5**, **7b**, **8**, and **9** (2 pages). Ordering information is given on any current masthead page.

From the Molecule to an Expanded I-VII Semiconductor Quantum Superlattice: Silver,Sodium Halo-Sodalites

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Received September 26, 1989

Silver bromide exhibiting molecular behavior was produced inside an aluminosilicate matrix by substoichiometric silver ion exchange of sodium bromo-sodalite. At increased Ag$^+$ concentrations up to complete silver exchange, the product is better described as a sodalite lattice containing "expanded silver bromide". Sodalite is unique as a host material, as it consists of bcc packed β-cages that allow trapping of in situ generated molecules and clusters and, therefore, chemical fabrication of monodispersed quantum ultramicrostructures.[1]

Highly crystalline Na,X-sodalites (X = Cl, Br, I) were synthesized hydrothermally as powders or single crystals (1–2 mm).[2] XRD powder patterns showed that the product crystallinity was maintained after the AgNO$_3$/NaNO$_3$ melt exchange at 320 °C. Results obtained from far- and mid-IR spectroscopy and powder XRD indicate that in mixed sodium,silver halo-sodalites the cations are distributed statistically (a solid solution of (Na$^+$)$_n$(Ag$^+$)$_{4-n}$X clusters, n = 0–4).

Rietveld refinements of high-resolution X-ray powder data[3] showed that in fully Ag-exchanged halo-sodalites the Ag–X distances are ca. 8% shorter (2.537 (2) Å, 2.671 (2) Å, 2.779 (2) Å for X = Cl, Br, I, respectively) than in the rock-salt bulk materials. The intracage Ag–Ag separations are ca. 6% longer than in the salts (4.142 (2) Å, 4.361 (2) Å, 4.539 (2) Å for X = Cl, Br, I, respectively) and Ag–Ag distances between cages from 25% to 12% longer (4.920 (2) Å, 4.859 (2) Å, 4.821 (2) Å, respectively). Thus one can consider the Ag$_4$X units as expanded silver halide semiconductors, although electronic band calculations must take into account the effect of the aluminosilicate host matrix.

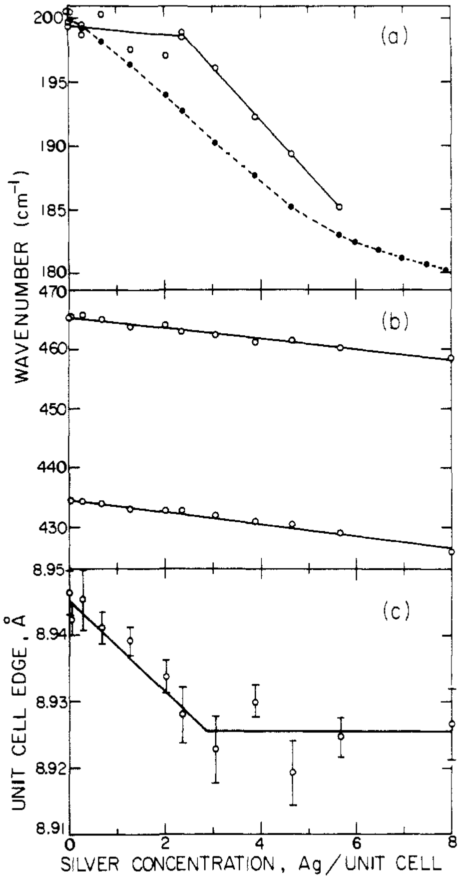

Figure 1. Effect of silver loading on structural and spectroscopic properties of Na,Ag,Br-sodalites. (a) Variations in far-IR Na$^+$ translatory frequencies with Ag$^+$ loading (—, untreated samples; ---, simulated peak positions assuming a binomial distribution of Na$_n$Ag$_{4-n}$Br moieties with absorption frequencies centered around equally spaced positions between the n = 0–4 extrema). (b) Variations in the mid-IR framework vibrations. (c) Variations in the unit-cell edge.

The Rietveld refinement of Na,Ag,Br-sodalite containing 0.3 Ag$^+$/unit cell (uc) yielded an Ag–Br bond length of 2.21 Å. A relatively large isothermal temperature factor for the bromide ion of $\langle U\rangle^2$ = 0.052 Å^2 indicates that the anion may be slightly displaced from the center of the cage. After correction for the thermal ion motion,[4] the mean separation of Ag and Br falls in the range 2.21–2.24 Å. A more extreme view based on three standard deviations yields a range from 2.0 to 2.4 Å. This distance compares with the internuclear separation of gaseous Ag–Br (2.39 Å).[5] The Na–Br distance in this sodalite is 2.94 Å, i.e., only 2% shorter than in the salt. Due to the more extensive covalent bonding of AgBr compared to NaBr, the Na$_3$AgBr aggregate behaves like a slightly perturbed AgBr molecule. On the basis of a binomial distribution of Na$_n$Ag$_{4-n}$Br moieties, at the silver loading level of this sample one in every eight cages is occupied with an AgBr molecule. The connectivity of AgBr molecules between cages is therefore small, and the AgBr molecules can be considered isolated.

Figure 1 shows that the mid-IR frequency of the aluminosilicate framework vibrations varies linearly with the silver concentration. However, both the far-IR absorptions associated with a translatory mode of Na$^+$ near the sodalite six-ring site,[6] and the cell edge of the cubic sodalite cage, exhibit abrupt breaks at loading levels near 2.5–3 Ag$^+$/uc. Both effects may be related to a percolation threshold for connectivity between AgBr units. The unit-cell size decreases slightly as the silver concentration is increased, forming a tighter, more covalent bond between the guest cation and the

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[†] University of Toronto.

[‡] University of California.

(1) Ozin, G. A.; Kuperman, A.; Stein, A. *Angew. Chem.* **1989**, *101*, 373–390.

(2) Ozin, G. A.; Stein, A.; Stucky, G. D.; Godber, J. P. *J. Inclusion Phenom.*, in press. Barrer, R. M. *Hydrothermal Chemistry of Zeolites*; Academic Press: London, 1982.

(3) Rietveld refinement, using the Generalized Structure Analysis System, provided by Larson and Von Dreele: Larson, A. C.; Von Dreele, R. B.; LANSCE, Los Alamos National Laboratory.

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(6) Ozin, G. A.; Godber, J. *J. Phys. Chem.* **1988**, *92*, 2841–2849, 4980–4987.