at the resonance frequency of the 13a protons suggests that **4** does not possess an extended conformation. In fact, since the high field position of H-10 in **4** (5.98 ppm) relative to its position in the 13-cis analogue (7.18 ppm) is probably due to shielding by the 14-carbomethoxy group, the most likely conformation of **4** is one in which the C-12–C-15 moiety is twisted out of the polyene plane. Analogous conformations have been proposed for 11-*cis*-retinal, and since no NOE at H-10 is observed upon irradiation of the 13a protons of 11-*cis*-12-carboxyretinoic acid dimethyl ester (**3**), a similar situation probably obtains.

It has recently been suggested that the extraordinarily high activity of arotinoids in bringing about regression in papillomas may be associated with the s-cis nature of the polyene backbone (see bold lines in structure **5**).[10] To our knowledge, **2** is the only open-chain retinoid with the analogous conformation; whether it has biological activity similar to that of **5** is not known.

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Dimethyl(methylthio)sulfonium Fluoroborate. A Chemoselective Initiator for Thionium Ion Induced Cyclizations

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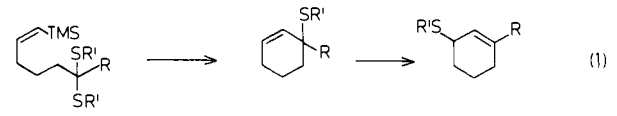
Thionium ions, α-aryl(or alkyl)thio carbocations, offer the possibility of overcoming some of the deficiencies of the carbonyl group in organic synthesis.[1,2] The discovery of a suitable set of conditions to generate such intermediates, which, in part, appear to depend upon the application, becomes critical if such a goal has to be reached. Thioketals represent one of the most useful precursors for thionium ions because (1) thioketals are available by metalation and alkylation of thioacetals[3] and (2) the normally inert thioketal group can be carried through many reactions before chemoselectively unmasking the reactive thionium ion. We wish to report that dimethyl(methylthio)sulfonium fluoroborate (**1**, DMTSF)[4,5] exhibits a remarkable thiophilicity for initiation of cyclization reactions of thioketals and provides an equivalent for a directed intramolecular aldol reaction.[6]

The general utility of allyl sulfides for further structural elaboration[7] led us to examine the cyclization of **2** (reaction 1). Use

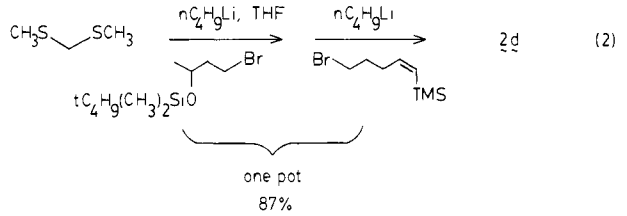


(1)

2 **3** **4**

a, R = H 37%
b, R = CH_3 68%
c, R = C_2H_5 64%
d, R = $CH_3CHCH_2CH_2$ (OSi) 67%

of mercuric chloride, mercuric trifluoroacetate, cupric trifluoromethanesulfonate, stannic chloride, cadmium trifluoroacetate, boron trifluoride, silver fluoroborate, silver trifluoromethanesulfonate, (trimethylsilyl)trifluoromethanesulfonate, among others all failed to effect the desired cyclization. Alternatively, treatment of substrates such as **2** ($R^1 = CH_3$) with salt **1** (1.1 equiv, CH_2Cl_2, room temperature, 20 h) initiated cyclization not to **3** but to **4**[8] in good yields.[9] The rearranged structure **4** was indicated by the NMR spectrum which showed a single vinyl proton, except for **2a** (**b**, δ 5.39; **c**, δ 5.43; **d**, δ 5.58), and a proton on a carbon bearing sulfur (**b**, δ 3.26; **c**, δ 3.31; **d**, δ 3.30). In the case of **2d**, the product **4d** was the free alcohol. The case of **2a** is noteworthy in that a thioacetal in contrast to a thioketal participates in the cyclization—the lower yield in this case attributed to mechanical losses due to volatility of the product during workup. The ready availability of substrates like **2** as shown in reaction 2 for **2d** via



(2)

a lynchpin one-pot sequence from bis(methylthio)methane combined with the flexibility of allyl sulfides gives special merit to this approach. The uniqueness of the cyclization reagent **1** is clearly established. Furthermore, the sulfur byproduct of the cyclization is dimethyl disulfide, which obviously can be recycled to DMTSF.

Extension of this cyclization to substrates such as **5** is particularly intriguing since (1) the high nucleophilicity of the enol silyl ether provides an extreme test of the chemoselectivity of the reagent **1** since it is known to readily add to olefins[10] and (2) cyclizations of diketones normally lead to the 2,3-disubstituted enones rather than the 3-monosubstituted ones.[11] Subjection of **5a** to 1 equiv of **1** (CH_2Cl_2, from −20 to −30 °C, 0.02 M) leads to excellent yields of the desired cyclization products **6**.[8] As the

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(8) This compound has been fully characterized by spectral analysis and for elemental composition by combustion analysis and/or high-resoltuion mass spectroscopy.

(9) The rearrangement of **3** to **4** is presumably initiated by **1**. Reaction of **2b**, $R^1 = C_2H_5$, with **1** leads to **4** where $R^1 = C_2H_5$ and CH_3 in a 1:1 ratio. For reactions of **1** and allyl sulfides, see: Kim, J. K.; Kline, M. L.; Caserio, M. C. *J. Am. Chem. Soc.* **1978**, *100*, 6243.

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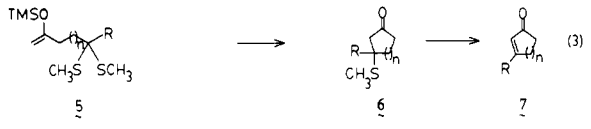
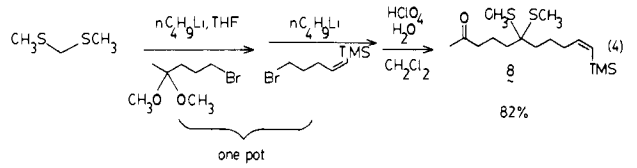


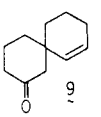
a, R = CH_3	$n = 2$	63–71% (85%)	78%
b, R = C_2H_5	$n = 1$	65%	94%
c, R = CH_3	$n = 3$	62%	90%
d, R = $CH_2CH_2CH_2$–TMS	$n = 2$	86%	94%

examples show, five-, six-, and seven-membered rings form with equal facility in contrast to other cases of thionium ion initiated cyclizations which appear restricted to six-membered ring formation.[1] Substrate **5d** competes the enol silyl ether with a vinyl silane; complete selectivity for cyclization of the enol silyl ether is observed. Most important, only the 3-alkyl-3-(methylthio)-cycloalkanones[8] whose structures are clearly indicated by the NMR spectra are produced. Chemical evidence for these structures derives from the elimination of **6** to the corresponding enones **7**.[8,12] Three methods have been used for this latter transformation: (1) oxidation with MCPBA in CH_2Cl_2 at 0 °C followed by thermolysis in hot xylene (**6a** → **7a**), (2) treatment with HgO or $HgCl_2$ and DBU in CH_2Cl_2 or THF (**6b,c,d** → **7b,c,d**), and (3) further treatment with **1** in CH_2Cl_2 at 0 °C (**6a** → **7a**). In the case of **5a**, a one-pot procedure converted it to **7a** in 52% yield by intially treating with 1 equiv of **1** at −30 °C for 1 h followed by a second equivalent at 0 °C for 16 h.

The utility of this approach is further enhanced by the unique synthetic entry offered by the thioketal. Sequential treatment of bis(methylthio)methane with *n*-butyllithium and the appropriate alkylating agents in one pot produces the unsymmetrical thioketal as illustrated for **8**[8] in excellent yield (reaction 4). Conversion

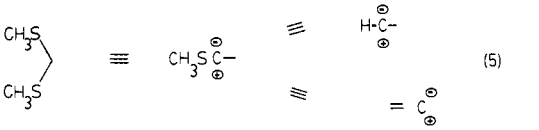


of the methyl ketones to their enol silyl ethers proceeds in standard fashion.[13] Attempts to cyclize the methyl ketones directly failed. In the case of **8**, the spiro compound **9**[8] was obtained. In this case cyclization is initiated by the vinylsilane since neither **6d** nor **7d** produces **9**.



The utility of this approach as a directed aldol cyclization is clearly demonstrated by the case of **5b,c,d**. Direct cyclizations of the simple diketones corresponding to **5b** and **5c** are known to produce 2,3-dimethylcyclopent-2-enone[14] and 1-acetyl-2-methylcyclopentene,[15] respectively, and not **7b** or **c**. Cyclopentenone **7b** is a constituent of tobacco smoke condensates.[16]

Dimethyl(methylthio)sulfonium fluoroborate (DMTSF) greatly expands the range of applications of thionium ion intermediates. The chemoselective ability to activate the thioketal function for C–C bond formation obviates the need for a frequently troublesome hydrolysis and, at the same time, serves as the equivalent of specific activation of one carbonyl group toward addition in a polycarbonyl compound. The sequence outlined further demonstrates the ambident behavior available to thioacetals—initially



as nucleophiles via metalation and subsequently as electrophiles via thionium ions. The ability to replace sulfur with hydrogen or to eliminate it to form an olefin then correspond to the use of the thioacetal as an alkyl or alkylidene 1,1-dipole as represented in (5).

Acknowledgment. We thank the National Science Foundation and the General Medical Sciences Institute of the National Institutes of Health for their generous support of our programs. Work on the use of DMTSF as a catalyst in our laboratories was initiated by Dr. Tohru Shibata whose enthusiasm for its potential spawned this application.

The Automerization of $C_{11}H_{11}$ Chlorides and the Stability of Their Cations

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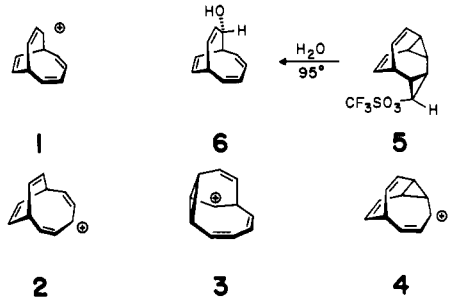
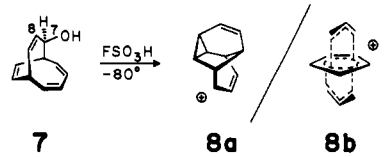
All that is unambiguous about the bicyclo[4.3.2]undecatetraenyl cation (**1**) is a mere prediction of naive π-electron theory: **1** should be stabilized and bicycloaromatic.[2] The available experimental data are much less coherent.



For example,[3] the anti-[4.3.2] alcohol (**6**) was obtained as the exclusive hydrolysis product of the tetracyclic triflate (**5**). α-Deuterated triflate provided this alcohol with its deuterium atom randomly distributed among all 11 carbons. This unprecedented automerization seemed to be more than one could reasonably expect of only the [4.3.2] cation (**1**). At least one of the isomeric cations (**2**, **3**, or **4**) was therefore suggested as a second reactive intermediate, an isomer that was less stable than the [4.3.2] cation (**1**).[3] Nevertheless, **1** can hardly be more stable than the "armilenyl" cation (**8**),[4] the exclusive product of syn-[4.3.2] alcohol (**7**) under strong acid conditions of thermodynamic control.[5a,b,6]



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