

**SYNTHETIC APPLICATIONS OF DIMETHYL(METHYLTHIO)SULFONIUM  
FLUOROBORATE: SULFENYLETHERIFICATION AND  
SULFENYLLACTONIZATION**

Gerard J. O'Malley and Michael P. Cava\*<sup>†</sup>

*Department of Chemistry, University of Pennsylvania, Philadelphia, PA 19104*

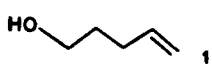
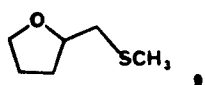
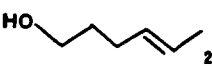
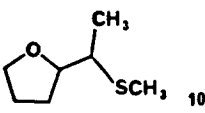
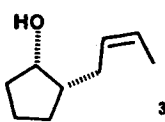
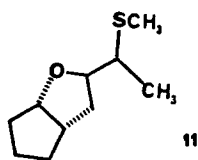
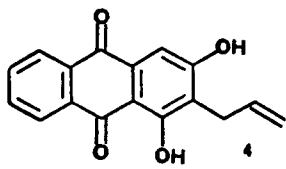
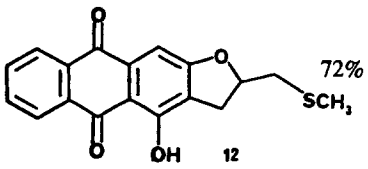
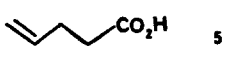
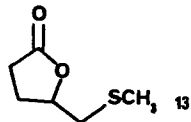
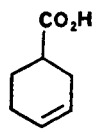
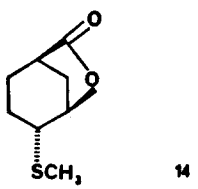
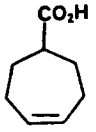
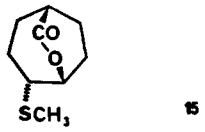
*<sup>†</sup>Department of Chemistry, University of Alabama, University (Tuscaloosa), AL 35486*

**Summary:** A new method for the formation of cyclic ethers and lactones is described. Dimethyl(methylthio)sulfonium fluoroborate (DMTSF) initiates formation of an episulfonium ion, which is followed by internal nucleophilic displacement to give the products in good yields.

The use of dimethyl(methylthio)sulfonium fluoroborate (DMTSF) and related salts as alkylthiolating agents was first observed by Helmkamp<sup>1</sup> and studied extensively by Caserio and co-workers.<sup>2</sup> The synthetic utility of DMTSF was elaborated by Trost and co-workers in the aza-,<sup>3</sup> oxy- and cyanosulfenylation of olefins.<sup>4</sup> Carbon-carbon bond-forming reactions with DMTSF as initiator have also been described including the thionium ion-induced cyclization of silyl enol ethers,<sup>5</sup> alkynylsulfenylations,<sup>6</sup> macrocyclic ring closures<sup>7</sup> and electrophilic aromatic formylation.<sup>8</sup> Recently, while utilizing DMTSF for the cofunctionalization of an olefin, we discovered an intramolecular version of the oxysulfenylation reaction.<sup>9</sup> The results of our initial investigation into the generality of this process is the subject of this communication.

Intramolecular cyclization occurs when  $\gamma$ ,  $\delta$  - unsaturated alcohols and acids are treated with DMTSF in a variety of solvents ( $\text{CH}_3\text{CN}$ ,  $\text{CH}_2\text{Cl}_2$ , acetone) at room temperature, followed by the addition of base ( $i\text{Pr}_2\text{NEt}$ , pyridine,  $\text{K}_2\text{CO}_3$ ), producing cyclic ethers and lactones in good yields (Table I). Although reaction times are somewhat slow (1-3 days) the process is extremely clean with the formation of a single compound. Product formation was observed without the addition of base; however, optimal yields are obtained with the addition of 1.1 equivalents of a non-nucleophilic base. When the base is present prior to the addition of DMTSF no reaction takes place, most likely because of rapid destruction of the reagent.<sup>3b</sup>

TABLE I

Entry	Reactant	Conditions	Product	Yield
1		$iPr_2NEt-CH_3CN$ 48h		76%
2		$iPr_2NEt-CH_3CN$ 48h		80%
3		$iPr_2NEt-CH_3CN$ 40h		95% <sup>14</sup>
4		$iPr_2NEt-CH_3CN$ 36h		72%
5		$iPr_2NEt-CH_3CN$ 72h		96%
6		$iPr_2NEt-CH_3CN$ 24h		70%
7		$iPr_2NEt-CH_3CN$ 24h		60% <sup>15</sup>
8	<b>8</b>	$iPr_2NEt-CH_3CN$ 36h	<b>16</b>	86%

a) All products were fully characterized by  $^1H$  NMR, MS, IR, and HRMS.

b) All reactions were carried out on a 2.5 mmol scale.

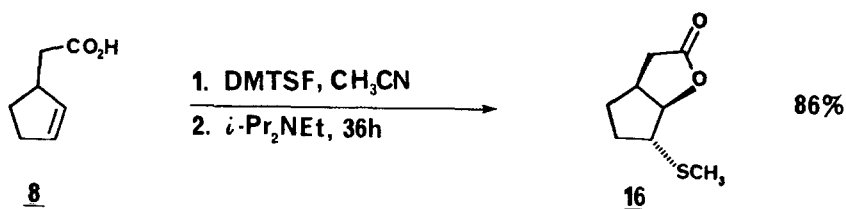
c) The relative stereochemistry of compounds 14, 15 and 16 is indicated.

The presumed mechanism of this process is that which has been invoked by Caserio and Kim<sup>3b</sup> to explain azasulfenylation. An initial adduct between the olefin and DMTSF is formed rapidly followed by the slower formation of an episulfonium ion intermediate, which in turn is displaced by the internal nucleophile. This explanation is also in agreement with the observed trans-stereospecificity of the process which can readily be observed from the 250-MHz <sup>1</sup>H NMR spectral analysis of compounds 14, 15 and 16. For monosubstituted olefins (examples 1,4,5) Markovnikov-type products are produced. There is a clear tendency for cyclization to occur producing five-membered rings, although six-membered rings can also be formed (example 7).

This methodology represents the sulfur analog of the selenium-based etherification and lactonization reactions which have proved to be so useful in synthetic endeavors.<sup>10</sup> The products of these reactions can be further manipulated by oxidative elimination<sup>11</sup> and reductive<sup>12</sup> removal of sulfur. Moreover, DMTSF is easily prepared,<sup>13</sup> relatively inexpensive and stable for long periods. The simplicity of the experimental procedure and the clean product formation makes this current process a viable alternative to the selenium-based methods.

### Typical Experimental Procedure

To a well-stirred solution of 2-cyclopentene-1-acetic acid (315 mg, 2.5 mmol) in dry acetonitrile (7 ml) was added DMTSF (588 mg, 2.5 mmol) in one portion. After stirring under nitrogen for 0.5 h, a solution of *i*-Pr<sub>2</sub>NEt (355 mg, 2.75 mmol) in acetonitrile (3 ml) was added dropwise and the reaction mixture was allowed to stir at room temperature for 36 h. The reaction mixture was diluted with diethyl ether (30 ml) and washed with saturated brine (2 x 10 ml). The organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>), the solvent was removed *in vacuo*, and the crude product was chromatographed (SiO<sub>2</sub>, hexane-EtOAc (3:1)) to give 370 mg (86%) of **16** as a colorless oil.



**Acknowledgement:** This work was supported by a grant from the National Institutes of Health, Grant NIH ES 03959.

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(Received in USA 3 September 1985)