

REARRANGEMENTS INITIATED BY TRIMETHYLSILYL IODIDE: THE FACILE RING  
OPENING OF SOME CYCLOBUTANONE DERIVATIVES

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
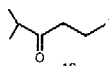
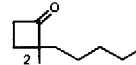
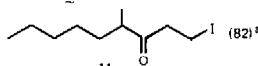

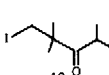
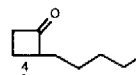
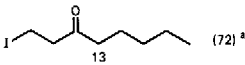
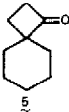
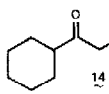
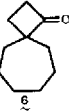
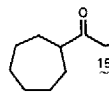

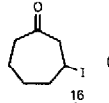
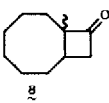
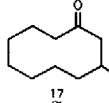
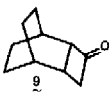
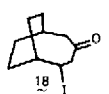
ABSTRACT: The powerful electrophile trimethylsilyl iodide in the presence of certain catalysts rapidly and cleanly initiates the ring opening of a variety of cyclobutanone derivatives in a highly regioselective fashion yielding ultimately  $\beta$ -iodoketones.

The synthetic accessibility and high reactivity of cyclobutanone derivatives has marked them as valuable synthetic reagents.<sup>1</sup> While most useful transformations are initiated by nucleophilic addition to the strained carbonyl and subsequent ring expansion, contraction or opening,<sup>2</sup> a limited number of electrophilically initiated rearrangements have been reported.<sup>3</sup> While the synthetic utility of these electrophilic processes has been limited by structural requirements and the strongly acidic conditions required, we have recently described a useful and regioselective ring opening reaction of cyclobutanone derivatives initiated by hydrogen chloride-thiophenol which shows some generality.<sup>4</sup> In this study it was demonstrated that a strong electrophile-nucleophile combination was an essential ingredient.

In a continuing study of this phenomenon, we now report that the potent electrophile trimethylsilyl iodide<sup>5</sup> in the presence of certain catalysts initiates the ring opening of a wide variety of cyclobutanone derivatives (see Table 1). The products of this rearrangement are  $\beta$ -iodoketones which are themselves useful reagents for subsequent synthetic transformations.<sup>6,7</sup>

While trimethylsilyl iodide alone initiated rearrangement of a number of the more reactive cyclobutanone derivatives, (e.g., **1**), the results were somewhat erratic and the  $\beta$ -iodoketones were often isolated in low yield. This difficulty was circumvented by the use of certain catalysts, which not only increased the reaction rate but led to much improved yields of the  $\beta$ -iodoketones. Of the two catalyst systems described here, (i.e., Hg-H<sub>2</sub>O and ZnI<sub>2</sub>), the latter

Table I

Ketone	Method	Conditions	Product
	A	24°, 6h	 (83) <sup>a</sup>
	A	24°, 16h	 (82) <sup>a</sup>
	B	24°, 4d	 (75) <sup>a</sup>
	B	24°, 7h	 (72) <sup>a</sup>
	B	24°, 16h	 (78) <sup>a</sup>
	A	24°, 9h	 (88) <sup>a</sup>
	A	24°, 5h	 (85) <sup>a</sup>
	A	24°, 18h	 (95) <sup>a</sup>
	B	24°, 21h	 (81) <sup>a</sup>

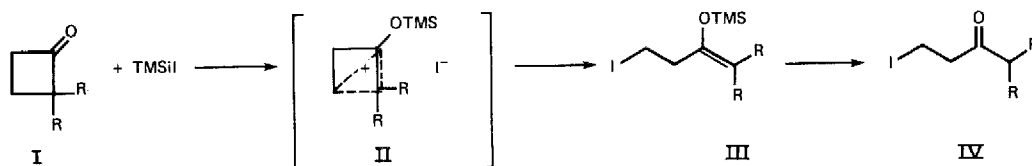
<sup>a</sup> isolated yields

appeared to be the more reactive. In this respect, it should be noted that zinc iodide in the absence of trimethylsilyl iodide produced no significant rearrangement even in the more reactive cases. Although the actual catalytic species generated upon mixing mercury, TMS.I and water in a chlorinated solvent is unknown, the desired rearrangement is catalyzed either by the addition of solid mercuric iodide or by its generation in situ by the reaction of mercury and iodide. In addition, the presence of a small quantity of unreacted mercury seemed to stabilize the resulting  $\beta$ -iodoketones in the reaction media.

The results in Table I show the  $\alpha,\alpha$ -disubstitution is not essential for a successful rearrangement since monosubstituted derivatives, (e.g., 4), as well as the fused ring compounds 7-9 also open regioselectively and in good yield. The success of the technique when applied

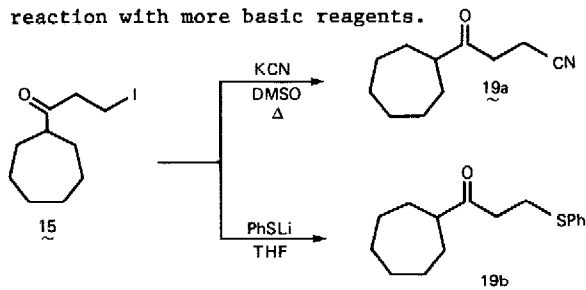
to fused ring derivatives is particularly significant since it represents a simple two carbon cyclohomologation of a cyclic olefin to a  $\beta$ -functionalized cyclic ketone via the olefin-ketene or dichloroketene cycloadduct.<sup>8</sup>

While additional studies are needed, the mechanistic hypothesis shown below rationalizes the observed regioselectivity of the rearrangement in terms of formation of the more highly substituted enol (or the corresponding trimethylsilylenol ether). Similar suggestions have been made regarding the rearrangement of highly substituted cyclobutanone derivatives in strongly acid media.<sup>3</sup>



In this respect, we have been unable spectroscopically (ir and nmr) to unambiguously detect intermediates such as III in the reaction media. Infrared monitoring has shown the product  $\beta$ -iodoketones to be present early in the reaction progress. The addition of unreactive bases such as hexamethyldisilazane (HMDS) to the media in an effort to stabilize the iodotrimethylsilyl ethers usually resulted in rapid deprotonation and formation of the corresponding trimethylsilyloxycyclobutene derivatives.<sup>9</sup> In the case of 3, which has no alpha hydrogens for deprotonation, the addition of HMDS resulted in an intolerably slow rate of rearrangement.<sup>10</sup>

The halogen is easily removed from the  $\beta$ -iodoketones with tri-*n*-butyl tin hydride or displaced by powerful nucleophiles without prior protection of the carbonyl group as shown below for 15. Preliminary studies have also demonstrated that, when necessary, the carbonyl group of the corresponding iodoketones could be protected as the 1,3-dioxolane derivative using standard techniques prior to reaction with more basic reagents.



#### Procedure A: Mercury-H<sub>2</sub>O Catalysis

A solution of 1 mmole of ketone, 150 mg (0.38 mmole) of mercury in 2 ml of carbon tetrachloride was treated with 0.35 ml (2.5 mmole) of distilled TMS:I. After 10 minutes at 25°, 4.5 ul (0.25 mmole) of distilled water was added with vigorous stirring. The progress of the reaction was monitored by the disappearance of the starting material carbonyl absorption at 1775 cm<sup>-1</sup>. The consumption of the trimethylsilyl iodide could be monitored by nmr. When the starting material was gone, the reaction mixture was poured into a two phase mixture composed of 20 ml of 5% Na<sub>2</sub>SO<sub>3</sub> and 60 ml of ether. The ether phase was washed with 10% sodium bicarbonate solution and dried over MgSO<sub>4</sub>. A few chips of copper was employed to stabilize the iodoketones and the solutions were protected from light. Removal of the solvent yielded material which was pure enough for most purposes.

#### Procedure B: Zinc Iodide Catalysis

To a solution containing 1 mmole of ketone and 0.22 ml (1.5 mmole) TMSiI, in 2 ml of methylene chloride was added 80 mg (0.24 mmole) of anhydrous zinc iodide. The reaction was stirred at 25° and the progress monitored by ir. When the starting material was consumed, the mixture was worked up as in A.

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- The β-iodoketones were completely characterized by their spectral data. Subsequently most were transformed to the corresponding γ-ketosulfides with lithium thiophenoxide and compared with authentic samples. Elemental analysis and/or high resolution mass spectroscopic data were obtained on the resulting γ-ketosulfides.
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- In the case of 3 it is difficult to quantitatively assess the effect of the added HMDS on the rate of the rearrangement which is particularly slow even in the absence of base presumably due to steric effects.

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