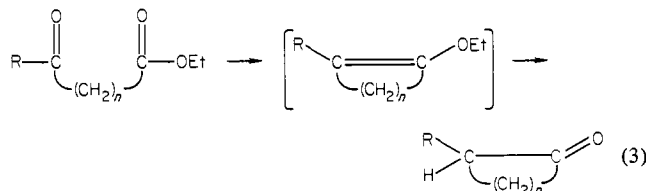


Table I. Synthesis of Cycloalkanones by Titanium-Induced Cyclization of Keto Esters

entry	keto ester	cycloalkanone	ring size	isolated yield, %
1	R = <i>tert</i> -butyl; n = 1		4	57
2	R = H; n = 2		5	75
3	R = H; n = 3		6	80
4	R = H; n = 4		7	82
5	R = H; n = 5		8	52
6	R = H; n = 6		9	50
7	R = H; n = 11		14	54
8	R = CH <sub>3</sub> ; n = 8		10	50
9	R = CH <sub>3</sub> CH <sub>2</sub> ; n = 9		11	45
10	R = CH <sub>3</sub> CH <sub>2</sub> ; n = 10		12	63
11	R = CH <sub>3</sub> ; n = 11		13	60

The mechanism of this titanium-induced keto ester cyclization appears to be an exact analogue of the diketone coupling.<sup>2</sup> Thus, an initial pinacol-type coupling reaction forms the carbon-carbon bond,<sup>5</sup> followed by deoxygenation to yield an enol ether, and acidic hydrolysis to yield the final ketone product (eq 3). Evidence for



this proposed mechanism comes from the fact that the enol ether can indeed be isolated if the acidic step is eliminated from the workup.

The finding that enol ethers are initial reaction products opens up a host of possibilities for further exploration; for example, does the coupling reaction occur with keto trialkylsilyl esters to yield enol silyl ethers? We are actively pursuing this and other possibilities.

**Acknowledgment.** We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for their support of this research.

**Registry No.** TiCl<sub>3</sub>, 7705-07-9; LiAlH<sub>4</sub>, 16853-85-3; ethyl 5-*tert*-butyl-2-oxocyclohexaneacetate, 4857-18-5; ethyl 2-oxocyclohexanepropanoate, 4095-02-7; ethyl 2-oxocyclohexanobutanoate, 84751-60-0; ethyl 2-oxocyclohexanepentanoate, 84751-61-1; ethyl 2-oxocyclohexanohexanoate, 84751-62-2; ethyl 2-oxocyclohexanheptanoate, 41301-64-8; ethyl 2-oxocyclohexanododecanoate, 84751-63-3; methyl 10-oxoundecanoate, 18993-09-4; methyl 11-oxotridecanoate, 84751-64-4; methyl 12-oxotetradecanoate, 74515-89-2; methyl 13-oxotetradecanoate, 18993-10-7; 2-*tert*-butylbicyclo[4.2.0]octan-7-one, 84751-65-5; octahydro-1*H*-inden-1-one, 29927-85-3; octahydro-1(2*H*)-naphthalenone, 4832-16-0; decahydro-5*H*-benzocyclohepten-5-one, 84751-66-6; decahydrobenzocycloocten-5(6*H*)-one, 84751-67-7; dodecahydro-5*H*-benzocyclononen-5-one, 84751-68-8; hexadecahydrobenzocyclotetradecen-5(6*H*)-one, 84751-69-9; 2-methylcyclodecanone, 73674-38-1; 2-ethylcycloundecanone, 26644-85-9; 2-ethylcyclododecanone, 1138-00-7; 2-methylcyclotridecanone, 63662-71-5.

**Supplementary Material Available:** Analytical data and structures for entries in Table I (4 pages). Ordering information is given on any current masthead page.

(5) Intramolecular pinacol-type couplings of keto esters have been observed previously by using sodium in ammonia as the reducing agent, but the products of such couplings are mixtures of ketones and  $\alpha$ -hydroxy ketones, yields are not good, and the reactions are limited to the formation of five- through seven-membered rings. See: Gutsche, C. D.; Tao, I. Y. C.; Kozma, J. J. *Org. Chem.* **1967**, *32*, 1782.

## Rotational Excitation in the Carbon Monoxide Product of Ketene Photodissociation

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The consequences of photodissociation reactions, vis-à-vis the distribution of available energy among products' degrees of freedom, has been the subject of much recent study.<sup>1</sup> Infrared fluorescence<sup>2,3</sup> and laser absorption<sup>4,5</sup> methods have been employed in characterizing vibrational energy disposal, while in the case of rotational energy disposal, laser-induced fluorescence has proved useful in some cases.<sup>6,7</sup>

We report here the application of an infrared fluorescence method in probing rovibrational energy release to carbon monoxide, formed upon the photodissociation of ketene. Our data are in qualitative accord with published data on the CO vibrational energy distribution for this chemistry<sup>8</sup> but additionally demonstrate that rotational energy release is a dominant feature of the reaction dynamics. This result has important bearing on the problem of elucidating the nature of the potential surface for ketene photofragmentation.

The spectroscopy and photofragmentation of ketene have been extensively studied. Lee and co-workers<sup>9</sup> have found that photodissociation at 308 nm yields only CH<sub>2</sub>(<sup>1</sup>A<sub>1</sub>). Lin and co-workers<sup>8</sup> have determined a vibrational temperature for CO formed upon ketene photodissociation at 193 nm where again the CH<sub>2</sub> product is formed in the <sup>1</sup>A<sub>1</sub> state. Little information is available on the rotational energy disposal associated with this chemistry. Although <sup>14</sup>C-labeling experiments have provided evidence of isomerization channels available to photoactivated ketene,<sup>10</sup> these are apparently not coupled to the fragmentation channel.<sup>10,11</sup> Detailed ab initio studies of the ketene photodissociation problem have been reported,<sup>12,13</sup> but the nature of the relevant potential surface has not been conclusively established.

In our experiments, ketene flowed through an aluminum fluorescence cell equipped with quartz windows through which an ArF\* (193 nm) laser beam is propagated. The cell has a CaF<sub>2</sub> window for viewing IR radiation at 90° relative to the direction of propagation of the UV laser. A cold gas filter (CGF) cell, a 4.7- $\mu$ m band-pass filter and a 1- $\mu$ m long-pass filter are interposed between the cell and an IR detector. An InSb detector with a 7- $\mu$ m cutoff is employed. Its output is processed by using a boxcar averager. The detection system risetime is  $\leq 1$   $\mu$ s, and the laser pulse width is ca. 15 ns.

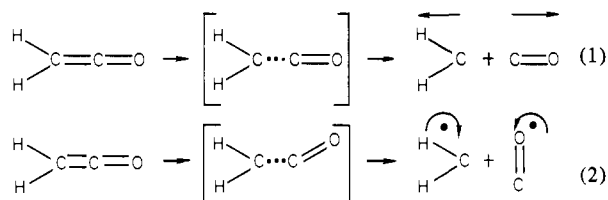
Irradiation of ketene at 193 nm (ca. 4 mJ/cm<sup>2</sup>) yields intense IR fluorescence<sup>14</sup> at 4.7  $\mu$ m due to CO. Fluorescence decay curves were recorded at several pressures of pure ketene between 0.04 and 4.5 torr and for dilute mixtures of ketene in argon. In every case, decay curves were obtained with the CGF cell both evacuated

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- (14) Under our experimental conditions, IR fluorescence intensity is found to vary linearly with laser intensity.

and filled with CO ( $p_{\text{CGF}} \geq 15$  torr).

Under conditions where rotational relaxation is complete, measurements of the CO fluorescence intensity transmitted through an evacuated ( $I_0$ ) and filled ( $I_{\text{CGF}}$ ) CGF cell allow the extent of vibrational excitation in the photofragment to be characterized in terms of a vibrational temperature,<sup>15</sup>  $T_v$ . Thus, at total pressures greater than 10 torr (4% ketene in argon), we find  $T_v \sim 2200$  K ( $I_{\text{CGF}}/I_0 \sim 0.4$ ). This is in qualitative accord with the CO laser absorption results on this system reported by Lin and co-workers<sup>8,16</sup> and suggests that the  $T_v$  observed here corresponds to a nearly unrelaxed vibrational distribution. At ketene pressures of 0.04 torr, in the absence of argon, significantly less attenuation is observed with a CGF containing up to 500 torr of CO:  $I_{\text{CGF}}/I_0 \geq 0.6$ . Since this fluorescence is viewed through a band-pass filter centered at 4.7  $\mu\text{m}$ , it is not likely due to species other than CO. A CGF functions by selectively quenching emission from transitions that terminate on rovibrational states that are thermally populated. Thus, we conclude that at low pressures, a significant component of the CO fluorescence originates from high rotational states, i.e., rotational states not appreciably populated at 300 K. The extent to which CO emission associated with a specified rovibrational distribution would be attenuated by a CO CGF can be numerically simulated.<sup>17</sup> Thus, a CO rotational temperature,  $T_r$ , can be qualitatively estimated from our experimental  $I_{\text{CGF}}/I_0$  at low pressures by assuming a Boltzmann distribution of rotational states. We find  $T_r \sim 7000$  K, which is a lower limit since the nascent rotational distribution may relax to some extent during the rise time of our detection system. A non-Boltzmann rotational distribution could, however, give rise to the observed CGF behavior, and the average rotational energy might then be lower than that suggested by our  $T_r$  value.

Our data provide compelling evidence for the importance of rotational energy release in the photofragmentation of ketene at 193 nm. This has some relevance in the analysis of models for the potential surface associated with this reaction. Fluorescence has never been observed from excited ketene. Constraints imposed by electronic symmetry conservation indicate that only the ground state of ketene correlates with  $\text{CH}_2(^1A_1)$  product. These points suggest that regardless of the reactant state populated at 193 nm, internal conversion to the ground state occurs prior to fragmentation. Ab initio surfaces for the dissociation of ketene suggest that both linear (eq 1) and/or nonlinear (eq 2) fragmentation



channels may be feasible.<sup>12,13</sup> These paths should be differentiable since, in (1), motion along the "reaction coordinate" correlates with product relative translation while in (2), this motion correlates with rotational excitation in the products. Thus (2) provides a means for efficiently coupling available energy into CO rotational degrees of freedom that is not available in the case of a linear decay mechanism, (1).

In conclusion, infrared fluorescence methods can provide useful information on rovibrational energy disposal in photofragmentation reactions. The photodissociation of ketene at 193 nm yields CO with a vibrational temperature of ca. 2200 K and a rotational temperature of  $\geq 7000$  K. This result indicates that fragmentation occurs predominantly via a nonlinear channel (2).

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(17) Essentially, we calculate the emission spectrum of CO for a specified  $T_v$  and  $T_r$  and then the extent to which this emission is attenuated by a CGF containing CO at  $T_v = T_r = 300$  K. Rosenfeld, R. N.; Sonobe, B. I., to be submitted for publication.

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**Registry No.** Ketene, 463-51-4; carbon monoxide, 630-08-0.

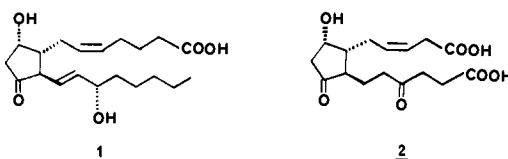
## Total Synthesis of the Major Human Urinary Metabolite of Prostaglandin D<sub>2</sub>, a Key Diagnostic Indicator

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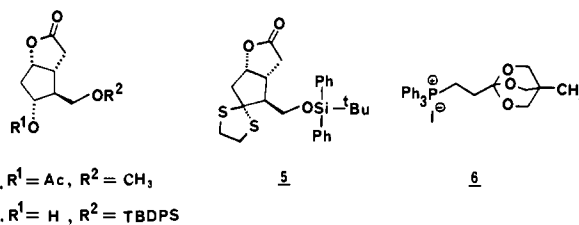
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Systemic mastocytosis is a potentially fatal disease in which tissue mast cells proliferate excessively and produce abnormally large amounts of histamine and/or prostaglandin D<sub>2</sub> (1).<sup>1</sup> Di-



agnosis and proper treatment of this and other human illnesses in which PGD<sub>2</sub> is overproduced could in principle be facilitated by a urinary immunoassay for the major metabolite of PGD<sub>2</sub>, the diketo acid 2.<sup>2</sup> Surprisingly this key substance, which is not available in significant amount from any natural source, has not previously been synthesized. We report herein a practical synthetic route to 2 that also introduces several new and potentially valuable methods.

The readily available methoxy acetate 3<sup>3</sup> was converted to the



silyloxy alcohol 4 in 95% overall yield by the following sequence: (1) demethylation by exposure to 2 equiv of trimethylchlorosilane and 2 equiv of sodium iodide in dry acetonitrile at 50 °C for 4 h and subsequent extractive isolation;<sup>4,5</sup> (2) silylation by reaction with 1.5 equiv of *tert*-butyldiphenylsilyl (TB DPS) chloride and 2 equiv of 4-(dimethylamino)pyridine in methylene chloride at 0 °C for 30 min; (3) deacetylation with 1 equiv of potassium carbonate in dry methanol at 23 °C for 1.5 h followed by extractive isolation and stirring of the product with a catalytic amount of tosic acid in methylene chloride to cyclize a small amount of byproduct formed by lactone saponification. Oxidation of the

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(4) Reactions involving air-sensitive reagents or substances were conducted under an inert atmosphere. Satisfactory spectroscopic data (infrared, proton magnetic resonance, and mass spectral) were obtained for each synthetic intermediate by using chromatographically purified and homogeneous samples.

(5) This procedure represents a major improvement over existing processes,<sup>3</sup> which is especially welcome because of its value in industrial PG synthesis.