Reversibility of Ketene Hydration[1]

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Ketene chemistry is regarded as being in its "second golden age",[2] and the mechanism of hydration of ketenes to carboxylic acids continues to be a topic of major interest and controversy.[2,3] While attention was paid to the details of the nucleophilic attack step and the further conversion to carboxylic acid, an important mechanistic question, i.e., the reversibility of the hydration, had, to our knowledge, never been directly addressed. The addition of water dimer across the C=C or the C=O bond of ketene was calculated to be exoergic,[4] but the barrier for the reverse reaction was not calculated. Kresge and co-workers, who studied ketene hydration via C=O addition which generates 1,1-enediols, commented that the latter "... have also been called 'ketene hydrates'. Their chemistry, however, is quite different from that of other carbonyls, e.g. aldehyde and ketone hydrates, and more like that of enol isomers of aldehydes and ketones." [5] Since hydration of carbonyl compounds is reversible[6] and, from the calculation in a recent paper,[4c] the thermodynamic barrier for the dissociation of $CH_2{=}C(OH)_2$ to ketene and monomeric water is only 5.4 kcal mol^{-1}, we decided to investigate the reversibility of ketene hydration by using a system substituted by bulky aryl groups.

We have recently prepared ditipylacetic acid (tipyl = 2,4,6-triisopropylphenyl)[7] by a reaction of tipyllithium with excess ethyl formate, followed by reduction of the formed ditipylmethyl formate, conversion of the carbinol to the ether, which was cleaved by K/Na to the ditipylmethyl anion, and carbonation to the acid. Ketene **1** was obtained from the acid and thionyl chloride/pyridine. The ketene is nearly completely hydrated to the enediol **2** in several solvents, e.g., in 42:5:3 (v/v) DMF−THF−H_2O or in 10:1 (v/v) THF−H_2O at 0 °C with little further tautomerization to ditipylacetic acid (**3**) (eq 1).[8] The enediol was identified by its ^1H and ^{13}C NMR spectra including isotopic shifts of partially deuterated **2** and by tautomerization to **3** at room temperature.[1,8] When 2.7×10^{-3} mol of $H_2{}^{18}O$ (95% ^{18}O) (60-fold excess) was added to 4.5×10^{-5} mol of **1** in THF-d_8 at 0 °C, the ^1H NMR spectrum showed after 8 h that the mixture consisted of 3.5% **1**, 93% **2**, and 3.5% **3**.

When this mixture was warmed to 25 °C, the irreversible tautomerization to acid **3** was accompanied by an increase in intensity of the signals of ketene **1** at the expense of those of enediol **2**. The **1** $\rightleftharpoons$ **2** interconversion was reversible, and on cooling, more **1** was converted to **2**.

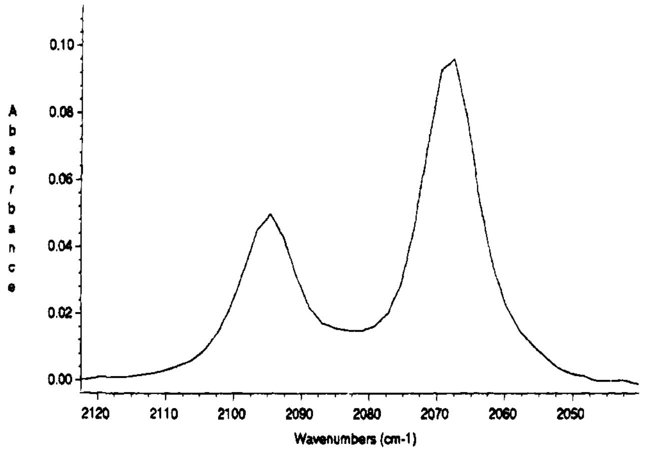
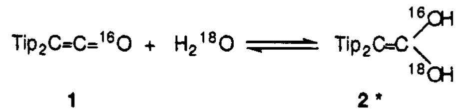


Figure 1. IR spectrum of ketene **1** reisolated on warming of a solution of enediol **2***.

$$\underset{\mathbf{1}}{Tip_2C{=}C{=}O} \xrightarrow{THF-H_2O} \underset{\mathbf{2}}{Tip_2C{=}C(OH)_2} \rightarrow \underset{\mathbf{3}}{Tip_2CHCO_2H} \qquad (1)$$

After 4 h at 25 °C, the same mixture consisted of 8% **1**, 28% **2**, and 64% **3**. When this mixture was rapidly chromatographed on a short silica column using petroleum ether as eluent, 0.5 mg (1.12×10^{-6} mol) of the pure ketene **1** was isolated. Negative ion mass spectrometry gave an *m/z* 448 ($Tip_2C{=}C{=}{}^{18}O$) to 446 ($Tip_2C{=}C{=}{}^{16}O$) ratio of 2:1. Positive ion mass spectrometry showed cluster formation in the *m/z* range of the molecular peak, but the M − Tip fragments at *m/z* 245 ($TipC{=}C{=}{}^{18}O$) and 243 ($TipC{=}C{=}{}^{16}O$) gave again a 2:1 ratio. The IR spectrum of the recovered ketene in a CCl_4 solution showed two signals at 2095 cm^{-1} ($Tip_2C{=}C{=}{}^{16}O$) and at 2068 cm^{-1} (ascribed to $Tip_2C{=}C{=}{}^{18}O$) in a 2:1 intensity ratio (Figure 1).[9] To our knowledge this is only the second observation of an ^{18}O-labeled ketene, and the $\Delta\nu$ value (in cm^{-1}) between the ^{16}O and the ^{18}O species for ketene[10] and benzophenone[11] resemble those for **1**. We conclude that ketene hydration involves formation of a symmetrical intermediate species with respect to the oxygens, which is presumably the labeled enediol **2***, and that the reversibility of ketene hydration leads to extensive exchange in the reisolated ketene **1** (eq 2).



$$Tip_2C{=}C{=}{}^{16}O + H_2{}^{18}O \rightleftharpoons Tip_2C{=}C\begin{matrix}{}^{16}OH\\ {}^{18}OH\end{matrix} \qquad (2)$$

1 2*

The extent of exchange was followed briefly by observing the formation of labeled ketene by IR. Reaction of a 120-fold excess of $H_2{}^{18}O$ (97%) to **1** in THF showed, after 8 and 26 h at 1 °C, 9% and 5% of the ketene which was 40% and 50% labeled, respectively.

The hydration of ketenes and their hydrolysis become slower with the increased bulk of the substituents on the ketene.[2,12] Hence, isolation of more reactive ketenes from the reaction mixture may not be easy. A simpler and more convenient method to obtain evidence for the reversibility of the hydration will be the partial formation of a di-^{18}O-labeled carboxylic acid

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[1] Presented in part at the 12th International Conference of Physical Organic Chemistry, Padova, Italy, August 28−September 2, 1994; abstract, p 35.

[2] Tidwell, T. T. *Acc. Chem. Res.* **1990**, *23*, 273.

[3] (a) Tidwell, T. T. *Ketenes*; Wiley: New York, in press. (b) Blake, P. In *The Chemistry of Ketenes, Allenes and Related Compounds*; Patai, S., Ed.; Wiley: New York, 1980; Chapter 9, p 309. (c) Seikaly, H. R.; Tidwell, T. T. *Tetrahedron* **1986**, *42*, 2587.

[4] (a) Nguyen, M. T.; Hegarty, A. F. *J. Am. Chem. Soc.* **1984**, *106*, 1552. (b) Andraos, J.; Kresge, A. J.; Peterson, M. R.; Csizmadia, I. G. *J. Mol. Struct.* (*THEOCHEM*) **1991**, *232*, 155. (c) Skancke, P. N. *J. Phys. Chem.* **1992**, *96*, 8065.

[5] Andraos, J.; Chiang, Y.; Huang, C.-G.; Kresge, A. J.; Scaiano, J. C. *J. Am. Chem. Soc.* **1993**, *115*, 10605.

[6] For a review, see: Ogata, Y.; Kawasaki, Y. In *The Chemistry of the Carbonyl Group*, Vol. 2; Zabicky, J., Ed.; Wiley-Interscience: New York, 1970; Chapter 1, pp 3−11.

[7] Frey, J.; Rappoport, Z. 57th meeting of the Israel Chemical Society, Haifa, February 12−13, 1992; Abstract L-32.

[8] A brief account of the preparation of **1** and **2** was given in ref 1. A more detailed description will be presented in a forthcoming publication.

[9] The ϵ values of the ^{16}O and the ^{18}O species are not necessarily identical: Pinchas, S.; Samuel, D.; Weiss-Broday, M. *J. Chem. Soc.* **1961**, 2666. Hence, the intensity ratio is only an approximation of the concentration ratio of the labeled and the nonlabeled species.

[10] Hochstrasser, R.; Wirz, J. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 411.

[11] Byrn, M.; Calvin, M. *J. Am. Chem. Soc.* **1966**, *88*, 1916.

[12] Allen, B. M.; Hegarty, A. F.; O'Neil, P.; Nguyen, M. T. *J. Chem. Soc., Perkin Trans. 2* **1992**, 927.

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Table 1. Relative Abundances of Acids Formed on Hydration of Ketenes with 95% $H_2{}^{18}O$ in THF

acid	ketene 1^a	4^a	5^a	6^b
$Ar_2CHC^{16}O_2H$	$(9.3)^c$	$(22.4)^c$	$(16.0)^c$	$(77.8)^c$
$Ar_2CHC^{18}O^{16}OH$	100.0	100.0	100.0	100.0
$Ar_2CHC^{18}O_2H$	60.0	33.5	25.0	21.8

[a] From the $MH^+ - Ar$ signals. [b] From the MH^+ signals. [c] See text.

in the hydration of the labeled ketene with $H_2{}^{18}O$. Consequently, the acid isolated from the experiment above was analyzed by CI mass spectrometry. The most relevant signals appeared as triads of signals at *m/z* 469, 467, and 465 (MH + 4, MH + 2, and MH) and at *m/z* 265, 263, and 261 ($TipCHC^{18}O_2H$, $TipCHC^{18}O^{16}OH$, and $TipCHC^{16}O_2H$). In both cases the ratio of intensities of the $^{18}O_2$ species to the $^{18}O^{16}O$ species was 64:100.[13]

The reversibility of hydration is not restricted to **1**. The hydration of three other ketenes **4**–**6** with 60-fold excess $H_2{}^{18}O$ in THF (conditions: 30 min at −18 °C followed by 24 h at room temperature under argon) was also studied, and the relative abundances of the appropriate signals are given in Table 1.

$Ar_2C=C=O$

4 : Ar= C_6Me_5

5 : Ar= Mes ($2,4,6\text{-}Me_3C_6H_2$)

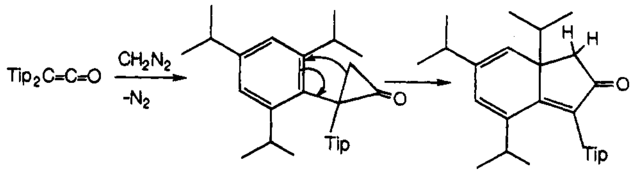
6 : Ar= Ph

Oxygen exchange of carboxylic acids under conditions related to ours is very slow,[14] and likewise **3** and the acids in Table 1 were found (by CI-MS) not to exchange oxygen under the reaction conditions. Hence, the $^{18}O_2$-labeled acids are obtained from the reaction of $H_2{}^{18}O$ with the exchanged ketene **1**-*^{18}O*, formed by the reversible hydration. Since the unlabeled acid arises both from the reaction of unlabeled ketene with $H_2{}^{16}O$ and from traces of the acid in the original ketenes, no significance is ascribed to its relative percentage.

Two interesting results arise from Table 1. First, even the hydration of the more reactive ketene, diphenylketene, whose reactions were extensively investigated, is reversible. Second, the extent of exchange qualitatively increases[13] with increased stability of the intermediate enediol,[1,12,15] which in turn seems to increase with the increased bulk of the ketene substituents.

The observation of exchange is relevant to the argument whether the mechanism of neutral hydrolysis of ketene proceeds via C=C or C=O hydration.[2,3] Whereas formation of **2** and the 1,1-enediols derived from **4** and **5**[12,15] during the hydration suggest that the reaction proceeds via the 1,1-enediol, no 1,1-enediol intermediate was observed with diphenylketene, and the reversibility is the only evidence for its intermediacy.

A relevant observation is the reaction of a >90% enediol **2** solution (prepared by eq 1) with diazomethane at room temperature. Neither $Tip_2C=C(OMe)_2$ nor Tip_2CHCO_2Me was isolated. Instead a nearly quantitative yield of the conjugated bicyclic trienone **7** was obtained.[16] Since independent reaction of **1** with diazomethane also gave **7**, we believe that the reversibly formed ketene from **2** reacts at its double bond to give arylcyclopropanone **8**,[17] which undergoes a vinylcyclopropanone rearrangement involving one of the aromatic double bonds of **8** to give **7** (eq 3).



1 **8** **7**

(3)

The results described above strongly indicate that ketene hydration is reversible. Further studies on the scope of this reaction are in progress.

Acknowledgment. The mass spectral analysis was conducted in the Mass Spectrometry Center at the Technion, Haifa, Israel. We are indebted to Prof. T. T. Tidwell for bringing ref 4c to our attention and to Professors H. H. Wasserman and J. A. Berson for comments regarding the **8** → **7** reaction.

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[13] The M + 1 signals of the three isotopic signals are not always in the expected intensity to the M signal based on the 1.1% ^{13}C isotope. M − 1 peaks may also contribute to these intensities. Hence, we regard our results only as qualitative.

[14] Samuel, D.; Silver, B. L. *Adv. Phys. Org. Chem.* **1965**, *3*, 123.

[15] Frey, J.; Rappoport, Z. Unpublished results.

[16] The structure of **7** was corroborated by X-ray crystallography. We know of no precedent of such a facile rearrangement which is accompanied by a loss of aromaticity.

[17] For reaction of ketene with diazomethane, see: Turro, N. J.; Hammond, W. B. *Tetrahedron* **1968**, *24*, 6017.