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The Unusual Hydration Reactivity of Acylketenes: Theoretical and Experimental Studies

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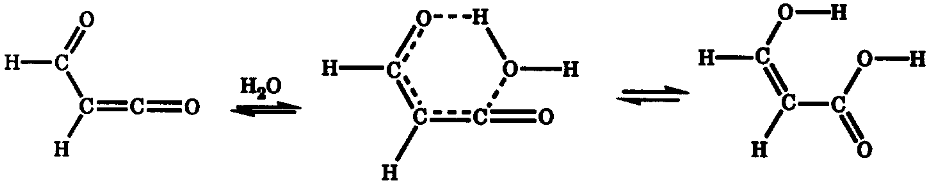
Abstract: Ab initio MO calculations indicate that the hydration of acylketenes may be assisted by complexation of the nucleophilic H_2O molecule to the oxygen of the acyl substituent. Experimental studies for hydration of $EtO_2CC(Bu\text{-}t)=C=O$ (**4**) support this pathway.

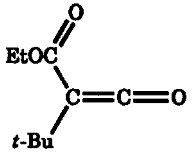
Acylketenes are the object of major current interest in mechanistic and synthetic studies,[1] but despite this attention their reactivity is not well understood. Thus it has been reported[1a] "α-oxyketenes are particularly reactive and cannot normally be isolated under usual reaction conditions." However acylketenes with bulky substituents are long lived species,[1a,f;2a,b] and $PhC(COCl)=C=O$ is an isolable intermediate that is widely used.[2c] There are also reports that acylketenes react with hydroxylic reagents by unique 6-membered transition states in reversible processes,[1b,d,g,j] as shown in equation 1 for the parent **1**.



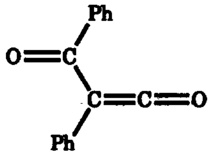
(1)

syn-**1** **2** **3**

In previous[3b-d] kinetic studies of ketene hydration we have studied **4**[3b] and **5**,[3d] in 100% H_2O, and find k_{H_2O} of 0.124 s^{-1} and 6.29×10^3 s^{-1} at 25 °C, respectively. The crowded ketene **6** has however been reported to be almost inert to H_2O.[1e] Ab initio molecular orbital calculations indicate that **1** is stabilized relative to $CH_3CH=C=O$ by 3.6 kcal/mol by the isodesmic reaction of eq. 2.[3a] We now report theoretical and experimental tests of the mechanism of eq. 1.



4



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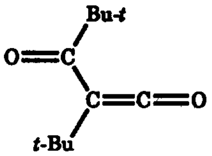


6

$$O{=}CHCH{=}C{=}O + CH_3CH{=}CH_2 \rightarrow CH_3CH{=}C{=}O + O{=}CHCH{=}CH_2 \qquad (2)$$

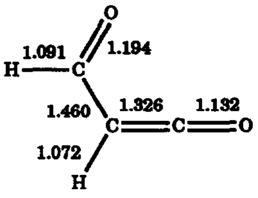
Energies and geometries calculated[4] at the 6-31G*//6-31G* level for the planar species involved in the conversion of **1** to **3** are given in Table 1. Interaction of *syn*-**1**, which is 0.9 kcal/mol more stable than *anti*-**1**, with H_2O gives the complex **7** (Table 1) as an intermediate 4.8 kcal/mol more stable than the reactants. This complex passes through what is evidently a low barrier of less than 3 kcal/mol to give structure **3**, which is 31.7 kcal/mol more stable than the reactants. At the 3-21G//3-21G level there is no barrier at all for conversion of **7** to **3**. By contrast the calculated barrier to hydration of $CH_2{=}C{=}O$ by water dimer is 33.4 kcal/mol,[3e] showing a major kinetic enhancement due in **4** to the conjugative and coordinating ability of the acyl substituent.

Experimentally the rates of the neutral hydrolysis of the persistent acyl ketenes **4** and **6** in H_2O/CH_3CN were examined as we have done previously,[3b,c] and the data are reported in Table 2. The reactivity of **6** is very low but resembles that found for the very crowded $t\text{-}Bu_2C{=}C{=}O$,[3c] especially in the linear dependence of log k_{obs} on $[H_2O]$, the solvent isotope effect k_{H_2O}/k_{D_2O} of 1.37, and $k_{rel} = 1.5$ in pure H_2O. Accordingly the reaction of **6** is interpreted to occur similarly to that of $t\text{-}Bu_2C{=}C{=}O$, namely by in plane attack on the ketene carbonyl group to give an intermediate resembling $t\text{-}BuCOC(Bu\text{-}t){=}C(OH_2^+)O^-$, with solvation by H_2O. For steric reasons **6** is constrained[1h] to react in the *anti* conformation shown. The reactivity of **6** is much lower than that reported[3d] for **5** due to the greater crowding in **6** , and the phenyl at C_β in 5 which stabilizes the polar transition state.

The hydration reactivity of **4** is 530 to 12,000 times greater than for **6** and is unique among ketenes we have examined,[3b,c] in that the rate in H_2O/CH_3CN is almost unchanged between 2 and 100% H_2O, with a shallow maximum in the rate between 50 and 100% H_2O.

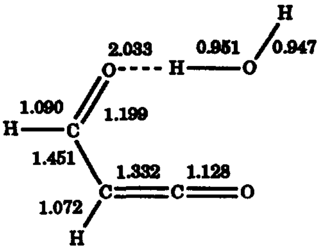
Table 1. 6-31G*//6-31G* Bond distances (Å), bond angles (deg), and energies (Hartrees) for hydration of formylketene

syn–1



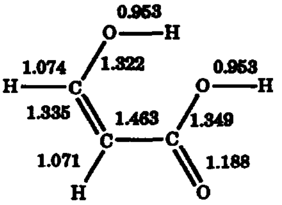
E = –264.4573

7

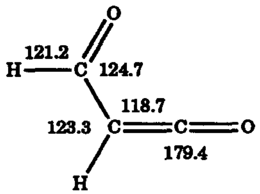


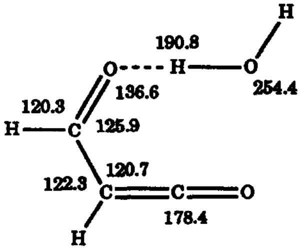
E = –340.4756

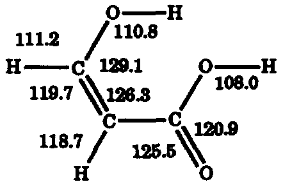
3

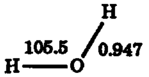


E = –340.5187









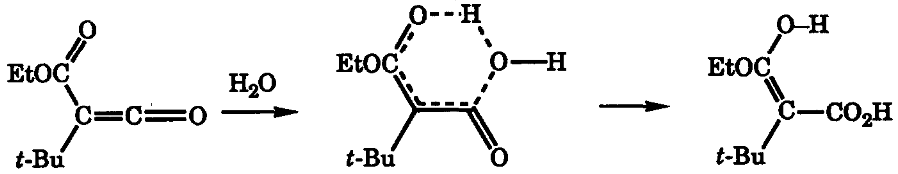
E = –76.0107

Table 2. Reactivity of ketenes t-BuC(COR)=C=O in H_2O/CH_3CN, 25 °C

$[H_2O]$ M	$k_{obs}(s^{-1})$:	R = OEt (4)[a]	R = t-Bu (6)[a,b]	$[H_2O]$M	R = OEt
55.5		0.124	2.35×10^{-4}	22.2	0.202
55.5 (D_2O)		0.0843[c]	1.72×10^{-4}[d]	16.7	0.203
50.0		0.136	1.58×10^{-4}	11.1	0.190
44.4		0.160	9.91×10^{-5}	5.56	0.151
38.9		0.175	5.33×10^{-5}	1.11	0.0515
33.3		0.195	3.02×10^{-5}		
27.8		0.212	1.81×10^{-5}		

[a] Measured by the decrease in absorbance at 228 nm (R = OEt) and 221 nm (R = t-Bu). [b] $\log k_{obs} = 0.0410[H_2O] - 5.87$, r = 0.998. [c] $k_{H_2O}/k_{D_2O} = 1.48$. [d] $k_{H_2O}/k_{D_2O} = 1.37$.

This suggests that a non-polar transition state is involved, and a carbonyl assisted pathway leading eventually to t-BuCH(CO_2Et)CO_2H appears to be consistent with this result.



syn-4

In summary the unique acyl assisted pathway shown in equation 1 for hydration of acylketenes is supported by both theoretical and experimental studies.

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(4) (a) Calculations were carried out using the Monstergauss[4b] program incorporating the GAUSSIAN 88 package with Apollo DN100000 and IBM 6000 minicomputers. Geometry optimization was effected by gradient techniques using the optically conditioned method.[4c] All stationary points were optimized at the Hartree-Fock (HF) level using the split-valence 6-31G* basis set.[4c] (b) Peterson, M.R.; Poirier, R.A. Department of Chemistry, Univ. of Toronto. (c) Hehre, W.J.; Radom, L.; Schleyer, P.v.R.; Pople, J.A. *Ab Initio Molecular Orbital Theory*; Wiley-Interscience: New York, 1986.

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