

Hydration of Bis(pentamethylphenyl)- and Bismesityl-ketenes leading to Ene-1,1-diols (Enols of Carboxylic Acids)

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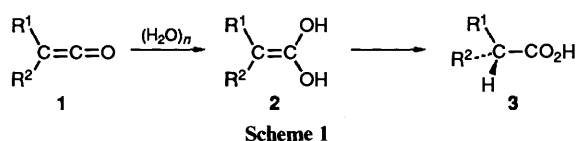
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The reaction of the sterically hindered diarylketenes (Ar = Me₅C₆ or 2,4,6-Me₃C₂H₂) with water is pH independent over the range 1–9 and is not subject to strong buffer catalysis. The primary products formed are the corresponding ene-1,1-diols which result from addition across the C=O (rather than the C=C) of the ketene. These 'enols of carboxylic acids' are relatively long lived owing to slow protonation of the β-carbon (because of steric hindrance caused by the *o*-Me groups) and evidence for their structures in solution is presented. On attempted isolation of the ene-1,1-diols facile oxidation to a stable free radical, as well as ketonisation to the corresponding acids, occurs. Evidence is presented in terms of the large negative entropy of activation (*ca.* 200 J K⁻¹ mol⁻¹), solvent isotope effects and the absence of significant general-base catalysis, that (despite the sterically hindered nature of these ketenes) the characteristics of their hydration are typical of other ketenes and that this most likely involves an initial concerted reaction with a water oligomer. Updated *ab initio* calculations are also presented, which are consistent with this view.

Although not as well studied as cycloadditions, addition of nucleophiles and electrophiles to ketenes has recently been the subject of increasing interest from a mechanistic standpoint.^{1–5} The stimulus for this comes not only from the use of ketenes as reactive synthons but also as a multifunctional substrate it provides several modes of possibly competing reactions. The chemistry of these reactions has been reviewed⁶ but, as was pointed out,^{3,6} the mechanism of even one of the simplest reactions, hydration, remains controversial.

Hydration of ketenes **1** leads ultimately to the corresponding carboxylic acid **3** (Scheme 1). This is a very rapid reaction for most simple aryl and alkyl ketenes (particularly if R¹ or R² = H) and is generally faster than acid- or base-catalysed reactions (up to 0.1 mol dm⁻³ [H⁺] or [HO⁻]). However several questions arise: (a) does addition occur in a concerted fashion and, if so, is this across the C=C or the C=O bond of the ketene; (b) if addition occurs formally across the C=O bond then the ene-1,1-diols **2** are intermediates in the reactions—can these be isolated or observed in solution? These 'enols of carboxylic acids' **2** are inherently interesting since their chemistry has been relatively little studied owing to their high thermodynamic instability relative to the carboxylic acid isomer.

Our approach to this problem was prompted by an *ab initio* study⁷ of the addition of water and water dimer to ketene itself. These studies showed that addition of a single water molecule across the C=C or C=O bond has a prohibitively high barrier but addition of water dimer shows a marked preference for addition across C=O (leading to the diol which has an activation barrier of 13 kcal mol⁻¹)† relative to C=C addition (24 kcal mol⁻¹) leading directly to the carboxylic acid. We now report an extension of these calculations using a higher-level basis set but the conclusion remains the same: a high preference for C=O addition in the concerted hydration.

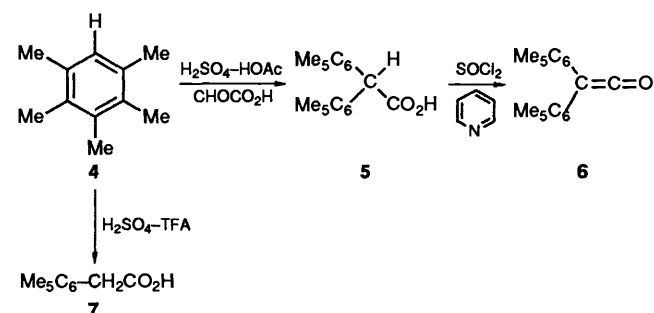


Because of the low thermodynamic stability of these intermediates, our experimental approach has been to incorporate in the ene-1,1-diol (and thus in the starting ketene) structural features which might stabilize it kinetically to acid- and base-catalysed ketonization. We have used a method pioneered by Fuson⁸ and recently used extensively by Rappoport⁹ incorporation of bulky aromatic groups as ketene substituents. In this regard we have found that the pentamethylphenyl (PMP) group is the substituent of choice. Not only is the synthesis of ketenes containing this group (R = R¹ = PMP) straightforward but it is larger in effective size than the 2,4,6-trimethylphenyl [or mesityl (Mes)] group.

This approach complements that recently reported by Kresge¹⁰ and Wirz¹¹ and their co-workers which involves the photochemical generation of highly reactive ketenes which then undergo rapid hydration.

Results and Discussion

Synthesis of Ketenes.—Bis(pentamethylphenyl)ketene **6** was synthesised *via* the corresponding acid by the reaction of pentamethylbenzene **4** with glyoxylic acid in the presence of acid (Scheme 2). Control of the acid concentration was critical



in this reaction since the use of H₂SO₄-TFA (in the place of H₂SO₄-HOAc) resulted in the formation of pentamethylphenylacetic acid **7** as the main product (formed by hydride-ion transfer from pentamethylbenzene). Treatment of **5** with thionyl chloride in the presence of pyridine gave the ketene **6** in good

* 1 cal = 4.184 J.

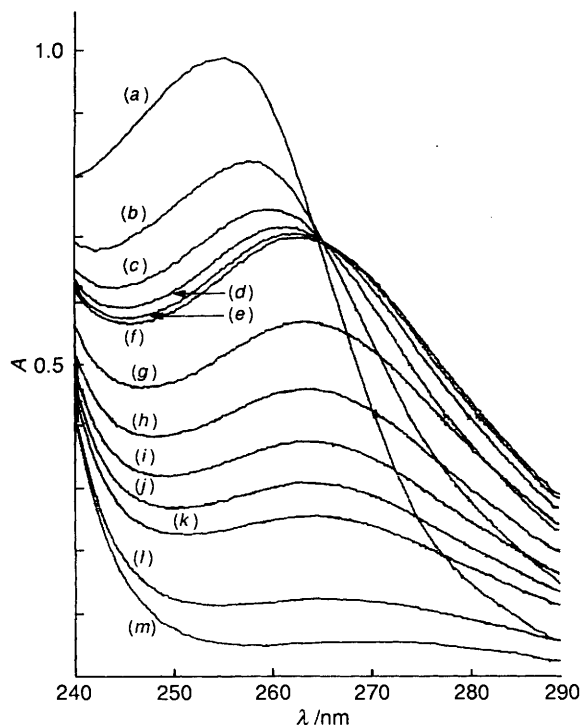


Fig. 1 Repetitive scans of the UV spectrum for the hydration of the bis(pentamethylphenyl)ketene **6** in acetonitrile containing 0.8 mol dm^{-3} water at 25°C . The time interval for scans (a)–(f) is 30 s and between scans (g)–(k) is 40 min.

Table 1 Variation of pseudo-first-order rate constants with pH for the hydration of bis(pentamethylphenyl)ketene **6** and bismesitylketene **12** in 4:1 acetonitrile–water at 25°C ; ionic strength = 0.05 (NaCl).

pH	$k_{\text{obs}}/10^{-2} \text{ s}^{-1}$ 6	$k_{\text{obs}}/10^{-2} \text{ s}^{-1}$ 12
1.34	2.52	6.60
2.34	2.25	7.46
3.43	2.52	7.35
4.56	2.67	6.85
5.37	2.68	6.09
5.96	—	7.16
6.54	—	6.30
7.63	2.98	4.49
8.33	2.33	—
8.48	—	5.52
9.20	—	6.73

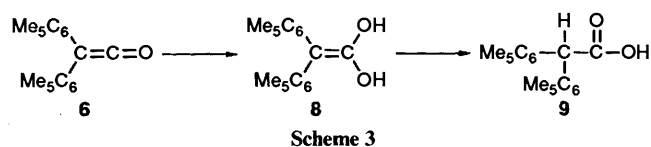
yield. Dimesityl ketene was prepared *via* the corresponding mandelic acid using a longer literature procedure.

Kinetics of Hydration of Ketenes.—Evidence for Ene-1,1-diol Formation (Scheme 3). The kinetics of hydration of the ketenes were studied in mixed acetonitrile–water solution in the range 5–50% water. Below 5% water, the reactions were very slow. Initial repetitive scans of the UV region show the presence of an $A \rightarrow B \rightarrow C$ type reaction with the clear formation of the ene-1,1-diol intermediate. The reaction solutions were deoxygenated to avoid a facile conversion at high pH into a stable free radical (which resulted in the formation of pink solutions). Fig. 1 shows a typical example; the initial six scans, which were characterised by a good isobestic point, were obtained at 30 s intervals. During this time the starting ketene absorption ($\lambda_{\text{max}} = 254 \text{ nm}$) is replaced by that of the ene-1,1-diol ($\lambda_{\text{max}} = 267 \text{ nm}$). The subsequent scans were obtained over a longer time interval (every 30 min for scans f to l) and represent the ketonisation of the ene-1,1-diol to the corresponding

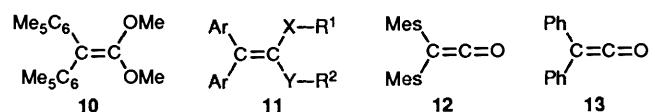
Table 2 Observed rates of hydration of the ketenes **6** and **12** to form the corresponding ene-1,1-diols as a function of water concentration in aqueous acetonitrile at 25°C with ionic strength = 0.05 (NaCl)

$\text{CH}_3\text{CN}:\text{H}_2\text{O}$	$[\text{H}_2\text{O}]/\text{mol dm}^{-3}$	$k_{\text{obs}}/10^{-2} \text{ s}^{-1}$ 6	$k_{\text{obs}}/10^{-2} \text{ s}^{-1}$ 12
9:1	5.56	—	1.94
8:1	6.17	0.507	2.50
7:1	6.95	0.829	2.76
6:1	7.95	0.940	3.39
5:1	9.29	1.20	4.92
4:1	11.1	1.50	5.49
3:1	13.9	2.19	7.94
2:1	18.5	2.78	12.80
1:1	27.8	4.26	16.25

carboxylic acid. It was noted that the final spectrum in Fig. 1 was identical with that of the carboxylic acid **9**.



The following evidence supports the assignment of the ene-1,1-diol structure **8** to the intermediate: (a) the λ_{max} and extinction co-efficient observed are similar to those for the model dimethylketene acetal **10**.



(b) The IR spectrum of **8** (formed *in situ* from the ketene) shows an absorption at 1626 cm^{-1} . This band (at $1625 \pm 1 \text{ cm}^{-1}$) appears to be characteristic of a range of similar enols, acetals and their silicon analogues [**11** (X, Y = O or Si, R, R¹ = alkyl or H)].¹²

(c) When the reaction was run in $\text{H}_2\text{O}-\text{CD}_3\text{C}\equiv\text{N}$, the NMR spectrum showed the absence of any C–H (apart from the CH_3 groups), although the characteristic C–H of the acid did subsequently appear [at the rate which corresponded to the conversion of the intermediate **B** \rightarrow **C** (see Fig. 1)].

(d) Bis(pentamethylphenyl)acetic acid was isolated and characterised as the final product. Similar results were obtained for the hydration of the dimesitylketene **12**.

pH Dependence of Hydration.—The rates of hydration of **6** and **12** were found to be independent of pH in 80:20 acetonitrile–water over the range pH 1–9 (see Table 1). At pHs above 8 or 9, the rate of ketonisation of both ene-1,1-diol intermediates became competitive with the initial hydration of the ketenes so that simple kinetics for the hydration step could not be obtained in this region. Buffer catalysis of hydration was not marked under any of the conditions studied and values quoted for the rate of hydration (Table 1) were obtained either by extrapolation to zero buffer concentration or measured directly in the absence of a buffer using a pH-stat to maintain pH at a constant value.

Rate Dependence on Water Concentration.—The measured rates of hydration of the bis(pentamethylphenyl)- **6** and bismesityl- **12** ketenes at various water concentrations with acetonitrile as the cosolvent are given in Table 2. From the approximately linear plot of k_{obs} vs. $[\text{H}_2\text{O}]$ (Fig. 2) it is seen that the rate dependence is first order in water concentration over the concentration range studied. The non-zero intercept

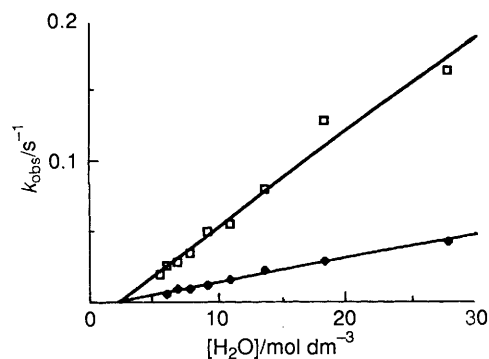


Fig. 2 Observed rates of hydration of the ketenes **6** and **12** as a function of water concentration with acetonitrile as cosolvent: □, ketene **12**; ●, ketene **6**

Table 3 Observed rates of hydration of diphenylketene **13** in aqueous acetonitrile as a function of water concentration

[H ₂ O]/mol dm ⁻³	<i>k</i> _{obs} /10 ⁻² s ⁻¹	[H ₂ O]/mol dm ⁻³	<i>k</i> _{obs} /10 ⁻² s ⁻¹
0.14	0.024	1.750	20.5
0.28	0.069	2.010	31.5
0.56	0.545	2.780	42.0
0.75	1.24	5.550	203.0
0.97	3.00	11.100	417.0
1.39	8.71	15.250	663.0
1.49	13.00	19.400	1095.0
1.62	16.00		

Table 4 Reactivity of various ketenes in water and water-acetonitrile mixtures at 25 °C

Ketene	Solvent	<i>k</i> _{H₂O} /s ⁻¹	Ref.
Mes ₂ C=C=O	H ₂ O	0.36 ^a	<i>c</i>
		1.00 ^b	<i>c</i>
PMP ₂ C=C=O	H ₂ O	0.091 ^a	<i>c</i>
		0.225 ^b	<i>c</i>
Ph ₂ C=C=O	H ₂ O	275	14
		672 ^a	<i>c</i>
		945 ^b	13
CH ₂ C=C=O	H ₂ O	44	23
Bu ¹ (H)C=C=O	H ₂ O	37.9 ^a	34
Et ₂ C=C=O	H ₂ O	8.26 ^a	34
Bu ¹ (Ph)C=C=O	H ₂ O	0.370 ^a	13
Mes ₂ C=C=O	1:1 CH ₃ CN-H ₂ O	0.163	<i>c</i>
Ph ₂ C=C=O	1:1 CH ₃ CN-H ₂ O		<i>c</i>
Bu ¹ (H)C=C=O	1:1 CH ₃ CN-H ₂ O	0.078	34
Et ₂ C=C=O	1:1 CH ₃ CN-H ₂ O	0.319	34
Bu ¹ (Ph)C=C=O	1:1 CH ₃ CN-H ₂ O	0.010	13

^a Extrapolated using *k*_{obs} vs. [H₂O] from the value measured in H₂O-CH₃CN mixtures. ^b Extrapolated using log *k*_{obs} vs. [H₂O]. ^c This work.

indicates that at lower water concentration the rate is higher order in water concentration. Extrapolation of this plot to 100% H₂O (*i.e.* 55.5 mol dm⁻³), gives rate constants of 0.091 s⁻¹ and 0.36 s⁻¹ for **6** and **12**, respectively.

The rates of hydration of the less hindered diphenylketene **13** measured in the same medium (Table 3) also show a first-order dependence on [H₂O] at high water concentrations. However, the hydration could be followed at low [H₂O] and a plot of *k*_{obs}/[H₂O]² versus [H₂O] is linear up to 1.5 mol dm⁻³, indicating a third-order dependence on [H₂O] at these low water concentrations. This is consistent with Satchell's observation⁴ that the hydration of diphenyl- (and dimethyl-) ketene is third order in water concentration when [H₂O] is < 1.5 mol dm⁻³ (using dioxane as a co-solvent) but that the order falls at higher (up to 19 mol dm⁻³) [H₂O].

Interpreting the molecularity of the reaction in the [H₂O]

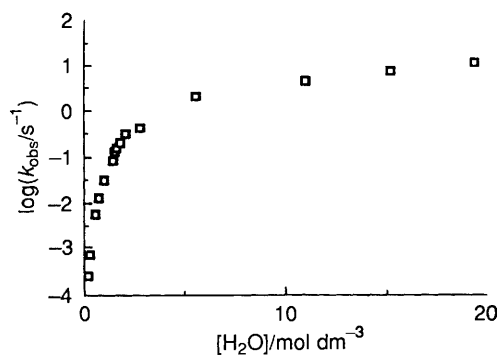


Fig. 3 Plot of log *k*_{obs} versus water concentration for the hydration of diphenylketene at 25 °C using acetonitrile as cosolvent.

from plots of *k*_{obs} versus various powers of water concentration has been used previously but it must be noted that this method neglects the effect of water concentration on the solvent polarity, an effect which could be significant. Plots of log *k*_{obs} versus [H₂O] at high [H₂O] have also been used for extrapolations.¹³ The hydration data for **6**, **12** and **13** yield values of *k*_{H₂O} in 100% water of 0.225, 1.00 and 672 s⁻¹, respectively, using this technique; Kresge¹⁴ has reported a value of 275 s⁻¹ in 100% H₂O for the hydration of diphenylketene.

The bulky pentamethylphenyl group reduces the reactivity of the ketene **6** relative to the bismesitylketene **12** by a factor of 3 to 4 (Table 4). This effect is quite small and suggests only a minor buttressing effect of the *meta*-methyl groups. Buttressing effects are normally invoked whenever the formal introduction of a bulky substituent in a position not directly involved in steric hindrance results in a substantial change in the ground state and/or the transition-state energy of a dynamic process. From the similarity in torsional angles of the aryl rings in the bismesitylketene **12** and (its 3,5-dibromo derivative), Rappoport¹⁵ has also concluded that the buttressing effect of *meta*-substitution in the ketene is not significant.

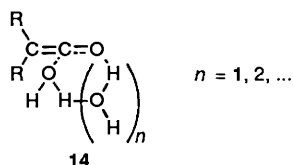
The unsubstituted diphenylketene **13** is more reactive towards H₂O than **6** and **12** by factors of 1222 and 275, respectively (Fig. 3). This may be attributed to the large steric bulk of substituted aromatic rings as seen by the reagent water as it approaches the α-carbon in the plane of the ketene. Comparative rate data for the aliphatic ketenes are shown in Table 4.

Solvent Effect.—To distinguish between a rate dependence on water concentration and on polarity of the solvent media, a series of rates were measured at constant water concentration but with varying cosolvent. Numerous reports on solvent polarity scales have appeared recently^{16–18} and in the past 30 years.^{19–22} These scales are based on some physicochemical property and have been designed using either the single- or multi-parameter approach. While many of the scales have been thoroughly studied for pure liquids, less is known about the polarity of mixtures of liquids. Owing to the nature of ketene reactivity there were several limitations on solvents which can be used—the solvent has to be dipolar, aprotic, water miscible, itself unreactive with ketene, have a UV cut-off absorption < 240 nm and have a known solvent polarity value on a convenient scale. Only three solvents were found to meet these criteria—acetonitrile, *tert*-butyl alcohol and dioxane.

Table 5 shows the observed rates of hydration of the mesitylketene **12** in various solvent-water mixtures. In each case the water concentration was maintained constant (at 20% or 5%) while the cosolvent was varied. In both series log *k*_{obs} does not correlate with *E*_T(30) for that mixture as determined by eqn. (1) using the Langhals²¹ method. This result must however be viewed in the context of the very limited range of solvents used. Several interpretations of this result are possible:

(i) the rate is independent or shows low sensitivity to solvent polarity; (ii) the range of solvent polarity is too small to determine with any accuracy a dependency of rate on polarity; (iii) the Bu'OH disrupts the water structure significantly and the $E_T(30)$ value is not representative of its true polarity.

While it is difficult to draw conclusions from the limited data, the indications are that the solvent effect is small, consistent with a mechanism for the ketene hydration which involves a cyclic transition state **14** involving a water oligomer at low water concentration.



In studies of hydration of ketene, $H_2C=C=O$, in dioxane-water and acetonitrile-water, Bothe and co-workers²³ found that there was no specific solvent effect and suggested that this may also be indicative of a less polar transition state.

Thermodynamic Activation Parameters.—The rates of formation of the bis(pentamethylphenyl) diol **8** and the correspond-

Table 5 Observed rate constants for hydration of bismesitylketene **12** in various solvent-water mixtures

%H ₂ O	[H ₂ O]/ mol dm ⁻³	Co-solvent	$E_T(30)$	$k_{obs}/10^{-2} s^{-1}$
20	11.1	CH ₃ CN	54.94	6.94 ^a
		Bu'OH	50.91	5.33 ^a
		1,4-Dioxane	49.03	3.19 ^a
5	2.775	CH ₃ CN	52.15	0.70 ^b
		Bu'OH	47.63	3.40 ^b
		1,4-Dioxane	43.62	1.10 ^b

^a Calculated using the Guggenheim method. ^b Calculated using intermediate theory (see A. A. Frost and R. G. Pearson, ch. 8, Wiley, New York, 1961).

Table 6 Rate dependence on temperature for the formation of $(Me_5C_6)_2C=C(OH)_2$ and $Mes_2C=C(OH)_2$ from the corresponding ketene in 4:1 acetonitrile-water with ionic strength = 0.05 (NaCl)

$T/^\circ C$	$k_{obs}/10^{-2} s^{-1}$ ^a 6	$k_{obs}/10^{-2} s^{-1}$ ^b 6	$k_{obs}/10^{-2} s^{-1}$ ^b 12	$k_{obs}/10^{-2} s^{-1}$ ^b 12
25.00	1.03	1.07	3.66	3.44
31.04	1.32	1.33	4.41	4.38
39.60	1.74	1.81	5.23	5.82
47.27	2.14	2.48	6.08	6.23
58.06	3.15	3.50	7.57	7.29

^a Solution 1: pH ~ 2. ^b Solution 2: pH ~ 3.

Table 7 Activation parameters for the hydration of various ketenes

Substrate	$E_a/kJ mol^{-1}$	$\Delta H^\ddagger/kJ mol^{-1}$	$-\Delta S^\ddagger/J K^{-1} mol^{-1}$	Reference
$(PMP)_2C=C=O$	29 ± 1	26 ± 1	211 ± 1	<i>a</i>
$Mes_2C=C=O$	18.0 ± 0.3	15.5 ± 0.3	232 ± 1	<i>a</i>
$Me_2C=C=O$	12.7	—	—	35
$Ph_2C=C=O$	—	—	209 to 293	35
$H_2C=C=O$	10.7	—	—	35
				36
$PhEtC=C=O$	—	—	209.3	31
$(ClCH_2)_2C=C=O$	—	—	181.0	37

^a This work.

ing bismesityl diol were determined over a range of 33 °C (Table 6).

The values of ΔH^\ddagger and ΔS^\ddagger obtained (Table 7) are consistent with those for other ketene hydration reactions. The large negative entropy of activation ΔS^\ddagger is characteristic of a bimolecular reaction in which an activated complex is formed from at least three reactant molecules, so three translational and three rotational degrees of freedom (depending on the symmetry of the molecules) are replaced by vibrations of the complex. The modest value of ΔH^\ddagger (ca. 20 kJ mol⁻¹) indicates that the overall energy requirements in the formation of the activated complex is relatively low.

A transition state involving the C=O or C=C of ketene and a water dimer or trimer, such as **14**, is consistent with the thermodynamic activation parameters. Typical values of the activation entropy for water attack on carbonyl groups are close to $-100 J K^{-1} mol^{-1}$ so that the values reported here, well in excess of this, provide strong evidence for reaction *via* a highly ordered transition state. Moreover, since the values obtained for the pentamethyl and mesityl systems are typical of those observed in other ketene hydrations, the reaction at the C=O group is most likely not confined to systems with large aryl groups only.

Solvent Isotope Effects.—The hydration of ketenes **6** and **12** was studied in deuterium oxide over the pH range 1–4 (Table 8). These results lead to solvent isotope effects, k_{H_2O}/k_{D_2O} , of 2.10 and 1.73 for **6** and **12**, respectively.

Isotope effects ranging from 2.2 to 4.0 have been reported for the uncatalysed reaction of H₂O with other C=O groups including ketones, esters and carboxylic acid anhydrides.^{24–26} The values which we report for the hindered ketenes are generally within the range of values obtained for other ketenes and are consistent with a uniformity of mechanism throughout the series (Table 9).

Ab-initio Calculations.—In our previous report^{7a} on the calculated reaction pathways for ketene hydration we have used the Hartree-Fock level with the minimal STO-3G basis set, while all stationary points considered were assumed to be planar. Under these conditions the determination of the nature of stationary points on the potential-energy surface (using the number of negative eigenvalues of the Hessian matrix) cannot be reliable, even though it is expected that deviation from planarity of the hydrogen atoms would only have a small effect on the energy of the most stable structures. A subsequent study^{7b} on the addition of water to ketene ($H_2O + H_2C=C=O$) pointed out that the supermolecules are neither planar nor symmetrical. Surprisingly, a more recent theoretical study²⁷ on the hydration of various substituted ketenes using the water dimer model and larger basis sets (3-21G and 6-31G*) still found planar or symmetrical stationary points. We have

Table 8 Observed first-order rate constants for the hydration of bis(pentamethylphenyl)ketene **6** and bismesitylketene **12** in deuterium oxide-acetonitrile mixtures^a at 25 °C

	$k_{\text{obs}}/10^{-2} \text{ s}^{-1}$		$k_{\text{obs}}/10^{-2} \text{ s}^{-1}$	
	6		12	
pD ^b				
3.97	1.22		4.73	
2.85	1.29		4.28	
0.88	1.18	$k_{\text{D}_2\text{O}}$ 1.23	3.95	$k_{\text{D}_2\text{O}}$ 4.32
pH				
4.50	2.64		7.90	
1 to 5 ^c	2.53	$k_{\text{H}_2\text{O}}$ 2.59	7.07	$k_{\text{H}_2\text{O}}$ 7.48

^a 80% CH₃CN-20% D₂O, ionic strength = 0.05 (NaCl), DCl added to adjust the pH. ^b Determined from the measured pH of the solutions using the relation pD = pH + 0.4. ^c From Table 1.

Table 9 Solvent isotope effect, $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}}$, for several ketenes, ketones and esters

Substrate ^a	$k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}}$	Reference
(PMP) ₂ C=C=O	2.10	<i>b</i>
Mes ₂ C=C=O	1.73	<i>b</i>
Ad(OH)C=C=O	1.30	14
BuCH=C=O	1.45	14
PhHC=C=O	to	
Ph ₂ C=C=O	2.58	
R ₂ C=C=O	1.5 to 1.7	34
Me ₂ C=C=O	1.7 to	35
Ph ₂ C=C=O	2.3	
H ₂ C=C=O	1.9	23
ArHC=C=O	ca. 2	5

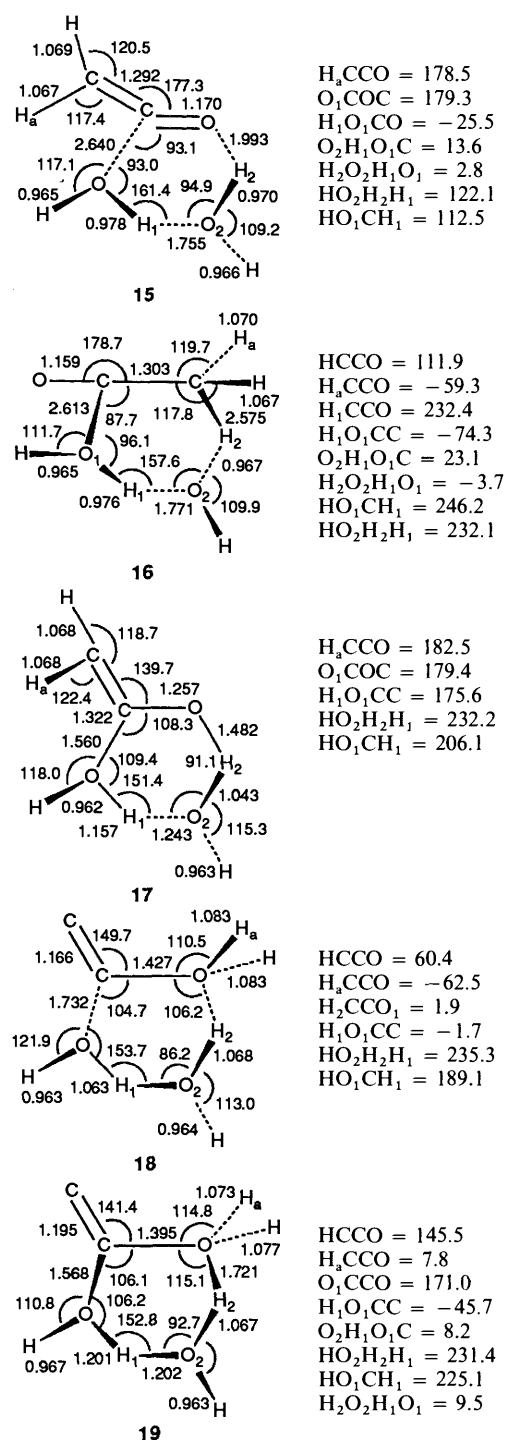
^a PMP = pentamethylphenyl; Mes = mesityl; Ad = adamantyl. ^b This work.

therefore carried out geometry reoptimizations while relaxing all internal parameters for each of the points of interest. These were located at the HF/3-21G basis set making use of the force method with analytical gradient.²⁸ Harmonic vibrational wavenumbers have then been computed for the optimised structures using analytical second derivatives of energy²⁹ in order to characterise stationary points. Relevant calculated results are summarized in Figs. 4 and 5 and Table 10.

As in the case of carbon dioxide,²⁷ complexation involving the C=O bond of ketene and the water dimer occurred giving the cyclic complex **15** (Fig. 4). However the enthalpy of formation of 45.2 kJ mol⁻¹ (at 0 K, Table 10) is about half that observed for CO₂ (H₂O)₂ (at the same level).^{7b} Similarly, the water dimer also forms a cyclic complex with the C=C bond of ketenes; the resulting complex **16** is however much weaker than **15**. The intramolecular distances (C...O₁ and C...H₂) in **16** are in fact longer than the corresponding values in **15** and its enthalpy of formation amounts only to 29 kJ mol⁻¹. Both molecular complexes **15** and **16**, analogous to a 'preassociation mechanism', can be regarded as the starting points for the addition of water dimer across the C=O and C=C bonds of ketene, respectively.

The transition structure **17**, for the C=O addition, having only one imaginary wavenumber 774i cm⁻¹ has been located. Its geometric features are quite similar to those of CO₂ + (H₂O)₂,²⁷ and are not commented on further here.

Of particular interest is the transition structure for the C=C addition. Structure **18** (except for the planarity of the hydrogen atoms) was assumed in refs. 7(a) and 30 to be the transition structure for this reaction. The HF/3-21G level **18** remains

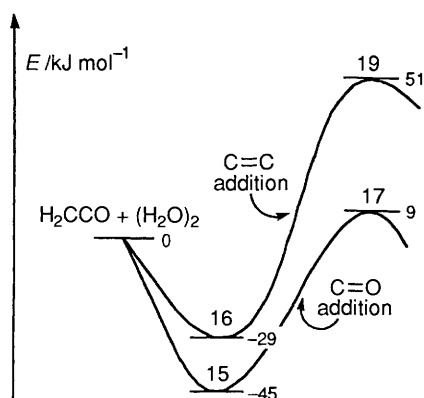
**Fig. 4** HF/3-21G-optimized geometries of stationary points relevant to the addition of water dimer to ketene. Bond lengths are given in ångstroms and bond angles in degrees.

higher in energy (by 90 kJ mol⁻¹, Table 10) than **17**, but a vibrational analysis showed that **18** has in reality *two* imaginary wavenumbers. The larger of these two (689i cm⁻¹) corresponds to the direction of the addition while the smaller (323i cm⁻¹) is mainly associated with the rotation of the CH₂ group of ketene within the supermolecule. Geometry relaxation following the second imaginary vibrational mode of **18** gives rise to **19** which is a true transition structure having only one imaginary wavenumber (1116i cm⁻¹). The gain in energy due to the rotation of the CH₂ group is significant (48.1 kJ mol⁻¹ on going from **18** to **19**). This behaviour can be understood by examining the ketene itself. As previously shown⁷ the ketene molecule

Table 10 Some calculated properties for six stationary points on the $\text{H}_2\text{C}=\text{C}=\text{O} + (\text{H}_2\text{O})_2$ energy surface

Structure ^a	N_1^b	$E_{\text{tot}}/\text{hartree}^c$	$E_{2p}/\text{kJ mol}^{-1d}$	$E_{\text{rel}}/\text{kJ mol}^{-1e}$	$S/\text{J K}^{-1} \text{mol}^{-1f}$
$\text{H}_2\text{CCO} + (\text{H}_2\text{O})_2$	0	-302.065 93	196	0.0	518
Complex 15	0	-302.087 08	207	-45.2	369
Complex 16	0	-302.080 29	205	-28.9	374
TS 17	1	-302.065 94	205	9.2	313
18	2	-302.029 06	199	99.6	310
TS 19	1	-302.049 49	204	51.5	306

^a Using geometries given in Fig. 4; for H_2CCO and $(\text{H}_2\text{O})_2$, see ref. 30. ^b Number of negative vibrational wavenumbers. ^c Total energies at HF/3-21G. ^d Zero-point energies obtained from HF/3-21G wavenumbers and scaled by 0.9 to account for systematic overestimation. ^e Including energy differences at HF/3-21G and E_{2p} . ^f Entropy from HF/3-21G calculations.

**Fig. 5** Schematic energy profile for the addition of water dimer to ketene.

possesses two bending modes having similar energies: the in-plane mode **20** and the *trans* out-of-plane **21** [the HF/3-21G vibrational wavenumbers of 532 and 651 cm^{-1} are associated with the modes **20** (b_2) and **21** (b_1), respectively]. Thus the transition structure for C=O addition **17** involves the normal deformation mode **20** of the ketene. In **18**, the ketene is forced to bend in a disfavoured *cis*-configuration and behaves as a consequence, as a saddle point of second-order. It is worth noting that the transition structure for C=C addition **19** also involves the bending mode **20** with an additional distortion of the CH_2 moiety. It is due to this distortion that **19** lies higher in energy than **17** (42 kJ mol^{-1}). The transition structure **19** apparently corresponds to an addition in two planes: an oxygen atom of water dimer attacks the C_α in the molecular plane of ketene and a hydrogen atom is transferred to the C_β -carbon of ketene in a perpendicular plane (the position of the planes is idealized for the sake of simplicity). We also note that the bending mode **21** is not involved at all in the addition processes.



In summary, the present calculated results confirm that the addition of water dimer across the C=O bond of ketene is favoured over that across the C=C bond (Fig. 5). This is consistent with the previous prediction about the intermediacy of 1,1-diols^{7a} for the least-hindered ketene $\text{CH}_2=\text{C}=\text{O}$, where, unlike the experimental model ketenes **6** and **12**, there is expected to be no large steric barrier to approach of the nucleophile to the C=C bond.

In the transition structure for C=O addition **17**, there is an accumulation of negative charges on both oxygen and C_β of the ketene (-0.8 and -0.6 electron, respectively). In the substituted systems, the build-up of negative charge on the C_β -atom may become even larger (depending on the ability of a

substituent such as Ph to accommodate charge). This is consistent with experimental observations^{5,31} of a Hammett ρ value (for variation of substituent at C_β) of *ca.* +1.2 for water addition.

It is known that for this type of supermolecule, energetic results obtained at the HF-3-21G are quantitatively consistent with those obtained from higher-level calculations such as MP4/6-31G**.²⁹ Therefore, a significant improvement of the geometries of stationary points should be obtained at a level that includes both correlation and polarization effects such as MP2/6-31G**. On the other hand the attack of a water dimer is of particular interest with regard to the two-plane addition across the C=C bond. We are currently planning calculations to consider this possibility.

Table 10 also lists the calculated entropies. These are less sensitive to the levels of theory than the energy differences. Both structures **17** and **19** have similar entropies so that a distinction between C=C and C=O addition cannot be made on the basis of ΔS^\ddagger values. There are two possible ways in which the entropy variations can be estimated depending on the state of the 'reactants'. If we assume a 'preassociation mechanism', considering the complex **15** as the starting point for C=O addition, the calculated ΔS^\ddagger amounts to only -56 $\text{J mol}^{-1} \text{K}^{-1}$. However if, on the other hand, the separated $\text{H}_2\text{C}=\text{C}=\text{O} + (\text{H}_2\text{O})_2$ system is considered as the starting point, ΔS^\ddagger is then calculated to be -205 $\text{J mol}^{-1} \text{K}^{-1}$. The latter value suggests that the initial state measured experimentally is the separated reactants.

In conclusion, we have demonstrated that the sterically hindered ketenes **6** and **12** undergo hydration to give relatively stable ene-1,1-diols, which is in line with the *ab initio* predictions (now updated as part of the present work) that addition across the C=O bond rather than across the C=C bond of the ketene is preferred. While the theoretical work implies that this is a concerted reaction *via* a cyclic transition state and the rapid rate of hydration (compared with the rate of addition of other nucleophiles such as hydroxide ion) and large negative energy entropy of reaction also imply such a special mechanism, it is perhaps too early to make a definitive conclusion on this point. Further theoretical studies involving the addition of trimers of water to ketene are currently under way.

Experimental

Apparatus.—Melting points were determined on a Gallenkamp melting block or a Mettler FP62 automatic melting-point apparatus and are uncorrected. IR spectra were recorded on a Perkin Elmer Infrared Fourier Transform spectrophotometer, model 1710. ¹H NMR spectra were run on either a Jeol 60 MHz or a Perkin Elmer R12. The solvent used was deuteriochloroform with tetramethylsilane as an internal reference. Elemental analyses were carried out by the microanalytical laboratory, University College Dublin.

pH was measured using a Radiometer pH meter 26 and a Metrohm combined pH glass electrode. pH control of unbuffered solutions was achieved using an autoburette, Radiometer ABU12 and a Radiometer Titrator 11 where necessary. UV spectra were obtained from a Cary 210 equipped with a thermostatted cell compartment. Temperature control to $\pm 0.01^\circ$ was achieved using a Techne TE8D Tempette water bath and pump, and a Techne RB12 refrigerated bath *via* a thermostatted cell compartment and cell holders. Stopped-flow experiments were carried out using a Hitech support unit SF-3L connected to a Hitech timer-delay unit TDU-43. A Thorn EMI power supply unit type, PM28B was used with the photomultiplier. Kinetic analysis was carried out by direct link through an ADC to a BBC microcomputer.

Materials.—Inorganic materials used for kinetic measurements were AnalaR grade. The salts employed, *e.g.* sodium acetate and sodium chloride, were finely ground and dried at 120°C for 2 h before use. Water was doubly distilled using an Exelo water still.

Substrates.—*2,4,6-Trimethylphenylglyoxal.* A solution containing 2,4,6-trimethylacetophenone (81 g, 0.5 mol), SeO_2 (55.48 g, 0.5 mol) and water (19.4 cm^3) in 1,4-dioxane (200 cm^3) was heated at reflux for 7 h. During the reaction black selenium precipitated and was broken up to aid stirring. The solvent was decanted from free selenium. Removal of the solvent gave a yellow oil which was distilled at reduced pressure to give 2,4,6-trimethylphenylglyoxal (80.2 g, 91%) b.p. $120^\circ\text{C}/12$ mmHg (lit.,³² $105\text{--}106^\circ\text{C}/4$ mmHg), as a yellow liquid with a pungent odour.

2,4,6-Trimethylphenylglyoxal hydrate. The glyoxal (45 g, 0.26 mol) was added to water (3 dm^3) and heated until the yellow colour disappeared (*ca.* 45 min). White needle-like crystals of 2,4,6-trimethylphenylglyoxal hydrate precipitated from water and were collected by filtration, m.p. $101\text{--}104^\circ\text{C}$ (lit.,³² $100.0\text{--}100.5^\circ\text{C}$) and used directly in the next step.

2,4,6-Trimethylmandelic acid. Crude glyoxal hydrate, (42.1 g, 0.24 mol), was heated with aqueous potassium hydroxide (300 cm^3 ; 1.5 mol dm^{-3}) at 100°C for 1 h and then allowed to cool. The solution was filtered and acidified with conc. HCl to pH 1–3 until precipitation occurred. The solid was collected, washed well with water, air dried and recrystallised from aqueous ethanol to afford white crystalline 2,4,6-trimethylmandelic acid, (26.98 g, 64%), m.p. $150.8\text{--}151.7^\circ\text{C}$ (lit.,³² $152\text{--}153^\circ\text{C}$). $\delta(\text{CDCl}_3)$ 2.25 (s, 3 H), 2.4 (s, 6 H), 5.60 (s, 1 H) and 6.90 (s, 2 H); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3235 (OH) and 1710 (C=O).

Bis-(2,4,6-trimethylphenyl)acetic acid. 2,4,6-Trimethylphenylmandelic acid (8 g, 0.04 mol) and mesitylene (6 cm^3 , 0.04 mol) were dissolved in acetic acid (60 cm^3). The solution was cooled, with stirring, in an ice bath. Sulfuric acid (40 cm^3) was added dropwise at 0°C . The resultant pink suspension was stirred at ambient temperature for 2 days. The grey suspension was added to 800 cm^3 of water and extracted with 800 cm^3 of ether. The organic layer was washed with water and saturated aqueous NaCl and dried over MgSO_4 . Removal of the solvent and recrystallisation from propan-1-ol with charcoal decolourising afforded bis(2,4,6-trimethylphenyl)acetic acid (7.7 g, 64%), m.p. $199\text{--}200^\circ\text{C}$. $\delta(\text{CDCl}_3)$ 2.1 (s, 12 H); 2.3 (s, 6 H), 5.4 (s, 1 H), 6.8 (s, 4 H) and 10.5 (s, 1 H, exchangeable); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3400–2400 (OH) and 1700 (C=O) (Found: C, 81.2; H, 8.25. $\text{C}_{20}\text{H}_{24}\text{O}_2$ requires C, 81.09; H, 8.11%).

Bis(pentamethylphenyl)acetic acid. Glyoxylic acid hydrate, (5.0 g, 0.066 mol) and pentamethylbenzene, (24.5 g, 0.165 mol) were dissolved in glacial acetic acid (70 cm^3). Heat was sometimes necessary to dissolve the glyoxylic acid. The solution was cooled, with stirring in an ice bath and conc. sulfuric acid

(45 cm^3) was added dropwise over 1 h to produce a red suspension. The suspension was then stirred at ambient temperature for 2 days and then added to H_2O (250 cm^3), extracted with ether and the organic layer was processed in the usual manner. Removal of the solvent and recrystallisation from propan-1-ol afforded bis(pentamethylphenyl)acetic acid, (13.8 g, 70.4%), m.p. $254\text{--}256^\circ\text{C}$, $\delta(\text{CDCl}_3)$ 2.10 (s, 12 H), 2.22 (s, 12 H), 2.23 (s, 6 H), 5.67 (s, 1 H) and 10.2 (s, 1 H, exchangeable); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3400–2300 (OH) and 1700 (C=O) (Found: C, 82.1; H, 9.25. $\text{C}_{24}\text{H}_{32}\text{O}_2$ requires C, 81.82, H, 9.09%).

Bis(2,4,6-trimethylphenyl)ketene. Thionyl chloride (0.6 cm^3 , 8 mmol) was added to a cooled suspension of bis(2,4,6-trimethylphenyl)acetic acid, (2.0 g, 11 mmol), in dry toluene (25 cm^3). Pyridine (0.12 cm^3) was added and the bright yellow solution was heated at reflux temperature for 1 h. The hot solution was treated twice with charcoal and filtered. The solvent was removed to leave a yellow solid which was recrystallised from acetonitrile to afford bis(2,4,6-trimethylphenyl)ketene (1.3 g, 69.2%), m.p. $116\text{--}118^\circ\text{C}$, $\delta(\text{CDCl}_3)$ 2.18 (s, 12 H), 2.31 (s, 6 H) and 6.98 (s, 4 H); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 2914 (C–H) and 2094 (C=C=O) (Found: C, 86.1; H, 8.05. $\text{C}_{20}\text{H}_{22}\text{O}$ requires C, 86.33; H, 7.91%).

Bis(pentamethylphenyl)ketene. Thionyl chloride (0.5 cm^3 , 6.8 mmol) was added to a cooled suspension of bis(pentamethylphenyl)acetic acid, (2.0 g, 5.7 mmol) in dry toluene (25 cm^3). Pyridine (0.1 cm^3) was added and the yellow solution was stirred at reflux temperature for 1 h. The reaction was worked up analogously to the preparation of the corresponding bis(2,4,6-trimethylphenyl)ketene. Recrystallisation from acetonitrile afforded bis(pentamethylphenyl)ketene (1.75 g, 92.2%), m.p. 156°C (sharp), $\delta(\text{CDCl}_3)$ 2.18 (s, 12 H), 2.31 (s, 6 H) and 6.98 (s, 4 H); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 2917 (C–H) and 2094 (C=C=O) (Found: C, 86.35; H, 9.45. $\text{C}_{24}\text{H}_{30}\text{O}$ requires: C, 86.23; H, 8.98%).

Diphenylketene was prepared as previously described.³³

Kinetic Method.—The acetonitrile–water solutions used for the kinetic experiments were made up by mixing the appropriate volumes of solvents. Sodium chloride was added as a solution or in solid form, although the former was found to be easier for solubility. Buffers were made up in wholly aqueous media by mixing solutions of the acid and its salt or by addition of sodium hydroxide to the acid solution. The buffer was diluted with the appropriate amount of cosolvent and made up to the standard volume using a mixture of the solvents.

Owing to radical formation solutions were deoxygenated before use. Dissolved CO_2 was removed from water by boiling. Solvents and solutions were deoxygenated by bubbling oxygen-free nitrogen, through them. Nitrogen was passed through a chain of reagents, including Fieser's solution to remove oxygen, saturated lead tetraacetate to remove sulfur dioxide, soda lime to remove CO_2 and calcium chloride and silica gel to remove moisture.

Most of the kinetics were followed spectrophotometrically using a Cary 210 at appropriate wavelengths in the ultraviolet region. In all cases the rates were studied under pseudo-first-order conditions—though this was verified experimentally in each system studied. For a typical experiment, 2 cm^3 of solution were added to a quartz cuvette, with pathlength 1 cm, and the temperature was allowed to equilibrate in the thermostatted cell compartment for about 15 min. The reaction was initiated by adding 20 mm^3 of substrate solution (usually 10^{-2} mol dm^{-3}) from a microsyringe to 2 cm^3 of the solvent in the cuvette.

Pseudo-first-order rate constants were calculated from data covering several half-lives and using experimental infinity values. Plots of $\log(A_t - A_\infty)$ versus t , where A_t is the absorbance

of the solution at any time t , and A_{∞} is the experimental absorbance of the solution under kinetic conditions of $t = \infty$, gave straight lines of slope $k_{\text{obs}}/2.303$. In certain cases, where the infinity value was not well defined, the Guggenheim or Swinburne methods of calculation were used. Rates were reproducible to within 4% of the mean value.

Solutions of 20% water were maintained at an ionic strength of 0.05 mol dm⁻³ using sodium chloride where necessary, which was its maximum solubility in the medium. The absorbance change was monitored at 254 nm.

The deuterium oxide was used as received. For a solution of 20% D₂O in acetonitrile, ionic strength was maintained at 0.05 mol dm⁻³ using anhydrous NaCl. Deuterium chloride (20% in D₂O) was standardised with standard sodium hydroxide. The pH was measured as usual and pD was determined by using the relationship pD = pH + 0.4. As rates of hydrolysis of the ketenes were pH independent in the region pH 2–10, the pH was not critical. Solvent isotope effects were calculated using rate constants in deuterium oxide and in water, which were determined under exactly the same conditions on the same day.

The final product UV spectrum, on completion of a kinetic experiment, was compared with the spectrum of an authentic sample of the product. In most cases the products were also identified by HPLC analysis of the sample from the kinetic run.

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