

COMPETITION BETWEEN DECARBOXYLATION AND ISOMERIZATION IN THE $C_3H_5O_2^+$ ENERGY SURFACE. JUSTIFICATION OF THE EXPERIMENTAL RESULTS BY MOLECULAR ORBITAL CALCULATIONS ON THE SOLVATED IONS

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In contrast with recent molecular orbital calculations on the decarboxylation of *O*-protonated 2-oxetanone, this experimental work indicates that no decarboxylation of this cation occurs in sulphuric acid solution up to 150 °C, but instead a clean isomerization to protonated acrylic acid takes place. Parallel theoretical work shows that the gas-phase model is too crude to account successfully for the experimental facts obtained in acidic media. However, the latter are well reproduced when the effect of the solvent is taken into account. The present findings do not necessarily invalidate the reaction mechanism currently accepted to explain the rate enhancement and change of stereochemistry accompanying the decarboxylation of 3,4-disubstituted 2-oxetanones under acid catalysis.

INTRODUCTION

In spite of the fact that the thermal decarboxylation of 2-oxetanones is already a classical well established method for the stereospecific synthesis of substituted olefins,¹ there being several kinetic studies on this type of process,² the first theoretical investigation on the reaction mechanism appeared only relatively recently.³ This was based on the study of the potential energy hypersurface of 26 different substituted 2-oxetanones

yielding carbon dioxide and the corresponding olefins. In all the cases studied, thermal decarboxylation is predicted to be a concerted process going through a planar zwitterionic transition state. Thus, the involvement of radicals is ruled out and the stereospecific character of the synthesis is explained through 1,4-interactions.

A very interesting experimental fact in the framework of these reactions is the role of acidic catalysts. It has been reported that when the latter are present in the medium the stereochemistry of decarboxylation in the case of *cis*-4-aryl-3-*tert*-butyl-2-oxetanones involves total inversion of configuration, instead of stereoretention as in non-catalytic media.⁴ Further, it has been

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shown that the reaction rate is markedly enhanced in a simultaneous way.⁴ In the above theoretical work³ the decarboxylation of 2-oxetanone protonated at the carbonyl oxygen (**1**) was also studied as a model for the acid-catalysed reaction (see Figure 1 for structures **1**–**8**). According to this approach, the mechanism changes dramatically in the presence of acids, taking place through two well defined intermediates, **3** and **4**, instead of being a concerted process. The almost free rotation around the C-3–C-4 bond of the first intermediate **3** explains the stereochemical outcome of the process in the presence of acidic catalysts. On the other hand, the observed increase in the reaction rate under these conditions is explained as a result of the lower energy barrier associate with the new reaction path.

In this paper, we present experimental evidence showing that, against expectations, 2-oxetanone is not converted into ethylene and protonated carbon dioxide under strongly acidic conditions (96% sulphuric acid) in the temperature range 30–150 °C.⁵ Instead, an equilibrium is reached between *O*-protonated 2-oxetanone (**1**) and *O*-protonated acrylic acid (**8**). However, cleavage of **1** giving protonated carbon dioxide was observed by chemical ionization mass spectrometry (CIMS), indicating that this process takes place in the gas phase and requires much more energy than that provided by simple heating of the substrate in strongly acidic solution. This prompted us to perform more refined theoretical calculations, trying to overcome the apparent contradiction between facts and theory. We show that, using the same kind of methodology as described in a previous report,³ inclusion of the solvent effect in the model allows a satisfactory qualitative explanation of all the experimental results obtained in solution.

EXPERIMENTAL

Proton spectra were recorded at 60 MHz with a Hitachi Perkin-Elmer Model R-24 B NMR spectrometer. ¹³C NMR spectra were recorded with a Bruker WP 80 SY NMR spectrometer using dioxane as external standard (capilar). ¹H and ¹³C chemical shifts (δ) are reported in ppm relative to TMS. CIMS was carried out with a Hewlett-Packard Model 5930 A mass spectrometer, using methane as reactant gas; *m/z* values and relative intensities (%) of the peaks are presented.

Neutral substrates were purchased from Aldrich and used without further purification. Ions were prepared by slow addition, with efficient stirring, of the cooled substrate to the mineral acid in an ice–water bath to give *ca* 1 M solutions. These solutions were heated in tightly closed NMR sample tubes by using a thermostated bath at the temperatures indicated.

Spectral data found for ion **8** were in agreement with those reported previously.⁶ Ion **1** exhibited the following ¹³C NMR parameters: δ (96% H₂SO₄, 20

MHz) = 187.5 (s), 67.3 (t), 34.1 (t). The ¹H NMR spectrum of **1** was in agreement with literature data.⁷ CIMS of 2-oxetanone gave the following peaks: *m/z*(%) = 73(100), 55(5), 45(5), 43(21).

CALCULATIONS AND MODELS

Semi-empirical PM3⁸ and AM1⁹ molecular orbital calculations were carried out with the MOPAC package of programs.¹⁰ We used the AM1 hamiltonian comparison with previous theoretical results.³ Further, the PM3 hamiltonian was used because it is more suitable for describing hypervalent interactions⁸ which are present in our model of solvated molecules. In general, both methods give similar results and appear to be the best available semi-empirical approaches to the study of chemical reactions. The type of strategies used here (location and characterization of the stationary points, building up of the minimum reaction path, etc.) are analogous to those used previously³ and therefore no detailed description is provided here.

We studied decarboxylation versus isomerization of *O*-protonated 2-oxetanone (**1**) in both the gas phase and in solution. The gas-phase study included construction of the minimum energy reaction paths corresponding to the two alternative processes, location and characterization of the stationary points and all the pertinent analyses. Our model of solvated reaction consists in adding water molecules to the structures of the above critical points according to the following procedure: we add the first water molecule in several possible sites and allow the system to relax until it reaches the most stable arrangement. Among the different monohydrated structures, the most favourable in terms of energy content is chosen. Then its geometry is starred and a second water molecule is added. Again, different sites are considered and the system is allowed to relax until stable geometries are reached. The two water molecules are allowed to relax once more and the most stable among the different final structures is chosen.

It should be stressed that when two water molecules are present it may happen that some of the dihydrated structures show inter-water hydrogen bonds. Obviously, the extra stability provided by these bonds concerns the quasi-crystalline structure of liquid water but not the solvent–solute interaction. Hence these structures were not taken into account and the most stable among the remaining optimized structures have been chosen.

We proceeded in the same way, adding up to four water molecules, realizing that this involves starting building the quasi-crystalline liquid water structure in such a way that the situation of the different critical points of the energy hypersurface becomes not completely comparable. Further, since the model behaves consistently when the number of water molecules is increased from one to four (if one excludes the struc-

tures containing inter-water hydrogen bonds), all the meaningful chemical conclusions can be drawn at this model level.

RESULTS AND DISCUSSION

Experimental observations on ion 1 in solution and in the gas phase

O-Protonated 2-oxetanone (**1**) was obtained as a stable ion when its neutral precursor was dissolved in concentrated sulphuric acid, at room temperature. This species was studied over the temperature range 30–150 °C, using ¹H NMR spectrometry to monitor the progress of the reaction at regular time intervals for up to several hours. It was expected that, according to previous predictions,³ ion **1** would undergo fragmentation to give ethylene and protonated carbon dioxide. In concentrated sulphuric acid, ethylene would have been quantitatively trapped as ethyl sulphate or, after prolonged heating, as isethionic acid.¹¹ Surprisingly, formation of ethylene could not be detected under the experimental conditions used. Instead, *O*-protonated 2-oxetanone (**1**) was progressively transformed into *O*-protonated acrylic acid (**8**),⁶ which was identified by comparison of its ¹H and ¹³C NMR spectral data with those of authentic **8** generated directly by protonation of a commercial sample of acrylic acid in concentrated sulphuric acid. The conversion of **1** into **8** was clean and, in spite of the drastic conditions of the treatment (heating for several hours up to 150 °C), no polymers were formed. This was assessed by adding a known amount of methanesulphonic acid as an internal standard to determine the composition of the reaction mixtures by ¹H NMR integration.

Since the available theoretical calculations had been performed for the species **1** in the gas phase, we decided to record the mass spectrum of 2-oxetanone under conditions of chemical ionization (CIMS), using methane as reactant gas. It is known that this technique is useful for generating protonated molecules, whose fragmentation patterns are highly relevant in terms of gas-phase ion chemistry.¹² In the CI mass spectrum of 2-oxetanone, the (*M* + 1) peak with *m/z* 73 was the most intense. Since *O*-protonated 2-oxetanone (**1**) and *O*-protonated acrylic acid (**8**) are isomeric ions, it is difficult to determine whether the peaks at *m/z* 73 is due to a single ion or to the contributions of **1** and **8**. However, the fact that a fragment of *m/z* 55 was clearly observable in the CI mass spectrum of 2-oxetanone (relative intensity 5%) suggests that isomerization of **1** actually takes place in the gas phase, to give **8**. Dehydration of the latter to the corresponding acyl cation would account for the peak with *m/z* 55.

Concerning the feasibility of the predicted fragmentation of *O*-protonated 2-oxetanone (**1**) into ethylene

and protonated carbon dioxide (**5** and **6**), it is interesting that in the CI mass spectrum of 2-oxetanone a small peak at *m/z* 45 (5%), assignable to protonated carbon dioxide, was clearly distinguished, indicating that such a transformation can indeed take place under the highly energetic conditions associated with mass spectrometry. However, this still continues to be a minor reaction pathway, as evidenced by the presence of a significant peak at *m/z* 43 (21%), probably arising from the alternative (formal) [2 + 2] cycloreversion of **1** to formaldehyde and protonated ketene. This fragmentation was detected in solution through the formation of trace amounts of acetic acid, the trapping product of protonated ketene (or its tautomer, the acetyl cation) by water.

Theoretical calculations on the gas-phase reactivity

The located stationary points and the calculated PM3 energy profiles for the decarboxylation of *O*-protonated 2-oxetanone (**1**) and for its isomerization to *O*-protonated acrylic acid (**8**) are presented in Figure 1. When the AM1 hamiltonian is used instead of the PM3 hamiltonian and the profiles in Figure 1 are rebuilt, the same trends are observed. Both alternative processes have in common the first step: ring opening of **1** to the intermediate **3**. Hence, we shall consider hereafter intermediate **3** as the starting point for our study and focus our attention on the further steps. It is worth mentioning that the minimum energy reaction path for decarboxylation reaches the dissociation products (ethylene and protonated carbon dioxide, **5** and **6**) after an almost continuous energy rise, although the path crosses a flat shoulder where a stationary π -complex has been located. Structure **4** in Figure 1 corresponds to the PM3 transition state found in this flat area.

Table 1 shows the most important geometric parameters, bond indexes and enthalpies of formation for the stationary points in the studied reaction paths. As we have just mentioned, the same main trends are observed and similar conclusions can be reached regardless of the hamiltonian employed (PM3 or AM1). The main difference is that the PM3 energy hypersurface is more 'flat', which means that the PM3 energy barriers are predicted to be lower.

A key point is that, without overemphasizing the validity of quantitative estimations of enthalpy values, Table 1 show that decarboxylation is a clearly endothermic process, while isomerization is very exothermic. In addition, the enthalpy of formation of the transition state **7** corresponding to the isomerization pathway is of the same order as the added enthalpies of formation of the decarboxylation products (see Figure 1). Hence both processes can be reached in parallel, their relative importances depending on the reaction conditions. This could be in agreement with the experimental data on gas-phase chemistry (CI mass spec-

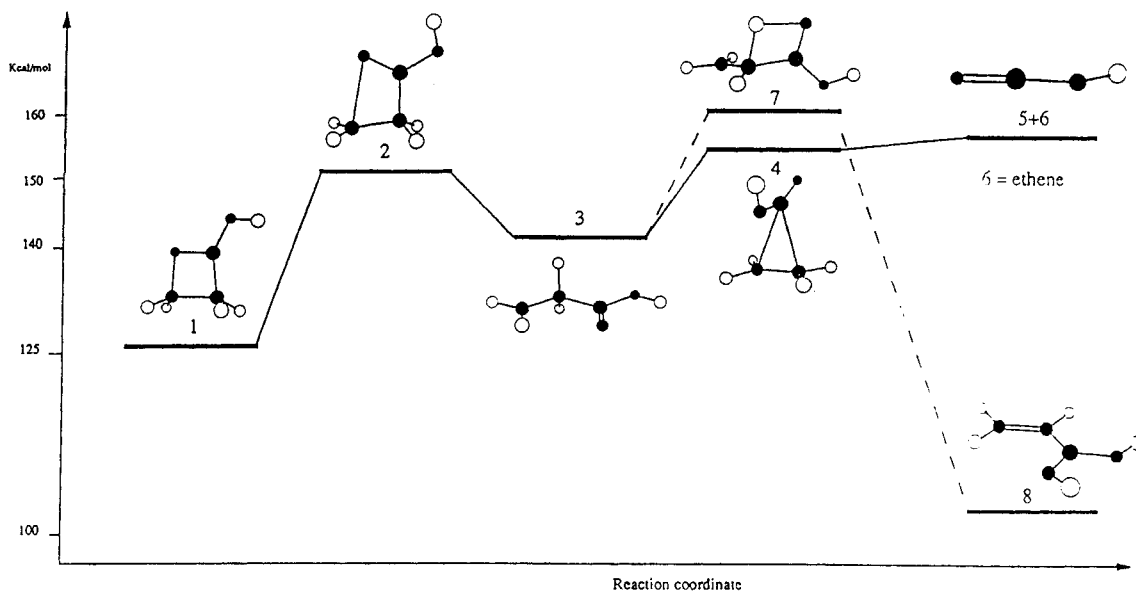
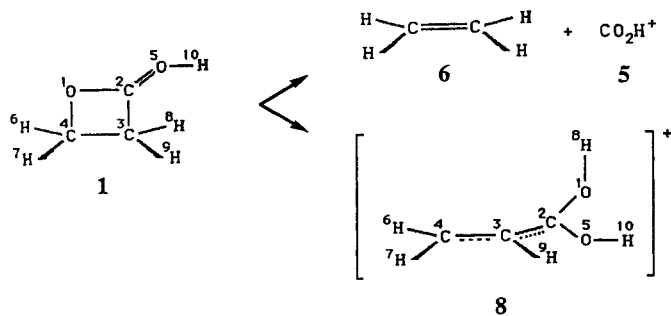


Figure 1. Calculated PM3 energy profiles for the thermal decarboxylation of *O*-protonated 2-oxetanone and for its isomerization yielding *O*-protonated acrylic acid

Table 1. Relevant parameters of the reaction paths for decarboxylation and isomerization of ion **1**^a

Structure	Hamiltonian	r_{1-2}	r_{2-3}	r_{3-4}	r_{1-8}	r_{3-8}	$\phi_{6-4-3-2}$	$\phi_{8-3-2-5}$	B_{1-2}	B_{2-3}	B_{3-4}	B_{1-8}	B_{3-8}	ΔH_f
3	PM ₃	1.21	1.52	1.42	3.20	1.13	0.00	55.40	1.84	0.90	1.24	0.01	0.85	140.8
	AM ₁	1.23	1.51	1.42	3.20	1.15	0.00	54.50	1.82	0.90	1.24	0.01	0.82	133.9
4	PM ₃	1.17	2.17	1.36	2.90	1.09	93.03	-146.9	2.14	0.24	1.58	0.00	0.96	154.5
	AM ₁	1.18	2.17	1.36	2.82	1.10	90.90	-150.7	2.11	0.25	1.59	0.00	0.94	155.4
7	PM ₃	1.26	1.50	1.36	1.56	1.48	2.93	-178.1	1.59	0.94	1.60	0.35	0.35	159.7
	AM ₁	1.27	1.48	1.36	1.59	1.50	1.70	-178.9	1.59	0.93	1.59	0.29	0.35	164.5
8	PM ₃	1.31	1.44	1.35	0.95	2.61	0.00	180.0	1.26	1.09	1.78	0.89	0.00	101.4
	AM ₁	1.33	1.43	1.35	0.98	2.60	0.00	180.0	1.26	1.07	1.76	0.87	0.00	95.9

^a The atom numbering is defined in Scheme 1; r are in Å and ϕ in degrees; B are bond indexes and ΔH_f are enthalpies of formation (kcal mol⁻¹) at 298 K.



Scheme 1

Table 2. Relevant net atomic charges for structures 4, 5 and 7

Structure	O-1	C-2	C-3	C-4	O-5	H-6	H-7	H-8	H-9	H-10
4	-0.082	0.489	-0.020	-0.016	-0.016	0.125	0.125	0.125	0.126	0.293
5	0.114	0.591			-0.030					0.326
7	-0.311	0.437	-0.370	0.292	-0.164	0.108	0.112	0.408	0.206	0.279

trum), although it fails to explain the behaviour of 2-oxetanone in sulphuric acid solutions.

The most significant net atomic charges of the stationary points 4, 5 and 7 are collected in Table 2. It is very interesting that the transition state 7 for isomerization (H-8 jump from C-3 to O-1) contains a hydrogen atom (H-8) with a highly positive net charge (0.41 e). Even the hydrogen of protonated carbon dioxide has a much lower net charge (0.33 e). Table 2 shows that some carbon or oxygen atoms possess charges of the same order, but we focused on the hydrogen atoms because their charge density is much higher. Hence, interaction of the 'more spread' charge of heavier atoms with a nucleophilic solvent is expected to be less important than interaction between the 'more concentrated' charge of hydrogen and the solvent.

The above reasoning might be the key to explain the reactivity of protonated 2-oxetanone (1) in acidic solution. In the next section we check this hypothesis on the influence of the solvent, as suggested by the atomic net charge analysis.

Theoretical calculations on the reactivity in acid solution

The simplest model of a solvated reaction is a single water molecule interacting with the reactive solute. We have taken this model (i.e. water interaction with the different ionic structures corresponding to stationary points in the energy hypersurface) as the first step in our study on the reactivity of 2-oxetanone in acidic solutions.

As indicated in the sections Calculations and Models, several monohydrated structures were found for each stationary point of the gas phase profiles. The most stable among them was always taken as a model.

The enthalpies of formation for the different monohydrated complexes relative to that of the monohydrated ionic intermediate 3 are given in Table 3. According to these data, the highest stabilizations correspond to structures 5 and 7, which is consistent with the net atomic charge analysis performed in the previous section. The hydration site in both cases is the highly positive hydrogen atom of the structures. Hydration produces a differential stabilization of the different ions, with an inversion of the relative stabilities of 4 and 7. Since these are the transition states for decarboxylation and isomerization, respectively, an

Table 3. Enthalpies of formation of the monohydrated complexes for decarboxylation and isomerization of ion 1^a

Hamiltonian	4·H ₂ O	(5+6)·H ₂ O	7·H ₂ O	8·H ₂ O
AM ₁	14.41	17.30	9.05	-40.12
PM ₃	6.70	3.24	4.16	-44.23

^a Values are in kcal mol⁻¹ relative to monohydrated 3.

important conclusion is that the solvent is expected to produce a significant increase in the isomerization-to-decarboxylation ratio.

In order to confirm the reliability of this simple model and the conclusions derived therefrom, we proceeded to a better simulation of the solvent by increasing the number of water molecules as detailed in the section Calculations and Models.

Table 4 summarizes the PM3 'corrected' enthalpies of formation of the different *n*-hydrated ions which are stationary points of the energy profiles for isomerization and decarboxylation. Here, 'corrected' means that we have subtracted *n* times the enthalpy of formation

Table 4. Enthalpies for formation of the *n*-hydrated complexes for decarboxylation and isomerization for ion 1^a

<i>n</i>	$\Delta H_f^{\text{rel}}(4)$ $\Delta H_f^{\text{diff}}(4)$	$\Delta H_f^{\text{rel}}(5+6)$ $\Delta H_f^{\text{diff}}(5+6)$	$\Delta H_f^{\text{rel}}(7)$ $\Delta H_f^{\text{diff}}(7)$	$\Delta H_f^{\text{rel}}(8)$ $\Delta H_f^{\text{diff}}(8)$	Δ
0	13.67 —	15.23 —	18.87 —	-39.45 —	5.20
1	6.70 -15.74	3.24 -20.76	4.16 -23.48	-44.23 -13.87	-2.54
2	12.17 -8.79	5.21 -12.29	7.55 -10.87	-43.84 -13.55	-4.62
3	18.25 -7.08	9.10 -9.27	10.65 -10.06	-36.68 -12.00	-7.60
4	22.25 -6.32	12.74 -6.69	14.47 -6.51	-30.94 -4.59	-7.78

^a In kcal mol⁻¹ at 298 K. ΔH_f^{rel} are values relative to 3·*n*H₂O. ΔH_f^{diff} are differences between the values for *n* and *n*-1 water molecules. Δ are differences between 7·*n*H₂O and 4·*n*H₂O.

calculated for the water molecule:

$$\Delta H_{\text{f}}^{\text{corr}} = \Delta H_{\text{f}}^{\circ} - n \Delta H_{\text{f}}^{\circ}(\text{H}_2\text{O})$$

Table 4 also shows the 'corrected' enthalpies of formation of the different n -hydrates relative to the n -hydrated intermediate **3**. The last column in the table shows the relative stabilities of the transition states for isomerization and decarboxylation.

The results obtained with AM1 are not very different (energetically) from those obtained with PM3 and displayed in Table 4. They show the same main trends, although the distribution of the water molecules in the complexes is not always completely free from inter-water interactions. This constitutes a difficulty in making a reliable comparison of the amount of stabilization due to solvent-solute interaction. The higher performance of PM3 was not unexpected, since it is known that this hamiltonian is better suitable than the AM1 (and, of course, than MNDO, MINDO/3, etc.) for description of hypervalent compounds.

Without overemphasizing the validity of quantitative estimations of numerical values, several conclusions can be drawn from Table 4: (a) the hydration model employed behaves well with an increasing number of water molecules, (b) the most important interactions, and the qualitative changes of the energy profiles, occur after addition of the first water molecule, (c) additional water molecules enhance the effects already produced by the first water molecule, (d) structure **4** becomes less stable than the decarboxylation products on interaction with water molecules and (e) isomerization of *O*-protonated 2-oxetanone in solution is definitely a much easier process than decarboxylation.

The above points, especially the last one, are in good agreement with the experimental facts on the reactivity of 2-oxetanone in acidic solution. Nevertheless, none of these results invalidate the overall description of the less favourable (in this case) decarboxylation process. Hence, the use of *O*-protonated 2-oxetanone (**1**) as a model for the decarboxylation of substituted β -lactones might be valid, in spite of the fact that, in the case of the parent molecule, an alternative reaction (isomerization) is more favourable than decarboxylation, especially in acidic media.

CONCLUSIONS

We have shown that the only significant process undergone by *O*-protonated 2-oxetanone (**1**) in concentrated sulphuric acid solution is isomerization to *O*-protonated acrylic acid (**8**). Under these conditions, fragmentation of **1** to give ethylene and protonated carbon dioxide is not observed. The latter process constitutes a minor reaction pathway in the gas phase (CIMS).

Our theoretical study shows that the transition state for isomerization contains a highly positive hydrogen

atom. Such a charged hydrogen atom is not present in the transition state for decarboxylation. The decarboxylation rate is determined in the gas phase by the stability of the products, whereas in solution it depends on the stability of the transition state **4**. The transition state for isomerization (**7**) is highly stabilized in solution, through interaction with a water molecule. This explains the fact that isomerization is the only process experimentally observed in acidic solutions.

ACKNOWLEDGEMENT

This research was supported in part by the DGICYT, Spain, Grants PB 90-0412 and OP 90-0042. We also thank the Centro de Informática de la Universitat de València for providing facilities.

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