A Kinetic Study of the Thermal Decarboxylation of α,α-Difluoro β-Lactones

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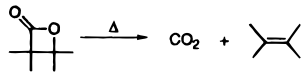
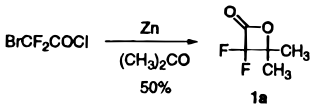
The rates of thermolysis of α,α-difluoro β-lactones **1**, leading to CO_2 and 1,1-difluoro olefins, have been obtained in the gas phase and in solution, and the activation parameters are reported. *Ab initio* calculations on the fluoro and nonfluorinated β-lactone systems are also reported. The gas-phase kinetic and theoretical results are discussed in terms of a probable concerted, asynchronous, nonpolar mechanism, whereas the solution kinetics, which include extensive solvent effect studies, are discussed in terms of a polar mechanism which probably involves formation of a zwitterionic intermediate.

The thermal decarboxylation of a β-lactone was postulated for the first time by Erlenmeyer in 1880 to account for the formation of styrene from an alkaline solution of β-bromo-β-phenylpropionic acid.[1] Since then, the decarboxylation of β-lactones, which depending upon substitution usually takes place between 80 and 160 °C, has been widely studied.[2]

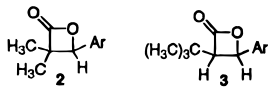


Although β-lactones have thus been known and studied for more than 100 years, α,α-difluoro β-lactones have received little attention. To our knowledge, there have been only two reports of β-lactones bearing fluorine as a substituent on the ring. In 1968, England and Krespan, claiming evidence for the formation of difluoroketene, reported the synthesis of the α,α-difluoro-β-lactone, **1a**



(3,3-difluoro-4,4-dimethyloxetan-2-one), as the product of a [2 + 2] reaction of the solvent with difluoroketene which was generated *in situ* in acetone.[3] Then, recently we reported[4] a general method for the synthesis of α,α-difluoro-β,β-dialkyl β-lactones *via* a modification of Adam's well-established procedure for the synthesis of β-lactones.[5]

The mechanism for decarboxylation of β-lactones remains somewhat controversial. Largely because of the necessary but not sufficient criterion of stereospecificity in the reaction, there has from the beginning been a strong bias among most workers in the field in favor of a concerted mechanism for this retro [2 + 2] decarboxylation process.[6] Interestingly, Imai and Nishida's observation of a relatively large ρ-value (−1.52), accompanied by a good correlation of rates with σ^+ in their kinetic study of 4-aryl-3,3-dimethyloxetan-2-ones, **2**, did not sway



them from considering the reaction to be most likely concerted.[7] On the other hand, armed with similar Hammett results along with their observation of a substantial effect of solvent polarity on rate, Mulzer and Zippel, in spite of the observation of consistent stereospecificity in their kinetic study of the decarboxylation of 4-aryl-3-*tert*-butyloxetan-2-ones, **3**, concluded that their data provided strong evidence for the intermediacy of a zwitterionic intermediate.[8]

In the most substantial attempt to examine the reaction theoretically, Moyano and co-workers concluded in a semiempirical AM1 study that the decarboxylation proceeds in a concerted but highly asynchronous manner, proceeding *via* a transition state which has "high zwitterionic character".[9] In their study, Moyano *et al.* were also able to do a reasonable job of reproducing experimentally observed substituent effects in the reaction.

Consistent with our abiding interest in the kinetic influence of fluorine substituents upon the rates of thermal homolytic and pericyclic reactions, we have carried out a systematic study of the impact of geminal α-fluorine substituents upon the rate of decarboxylation of β-lactones. Specifically, we report results from a kinetic study of the decarboxylation of prototypical α,α-difluoro β-lactones, in particular of 3,3-difluoro-4,4-dialkyloxetan-2-ones, **1**. Like their non-fluorine-containing

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(7) (a) Imai, T.; Nishida, S. *J. Org. Chem.* **1979**, *44*, 3574. (b) Imai, T.; Nishida, S. *J. Org. Chem.* **1980**, *45*, 2354.
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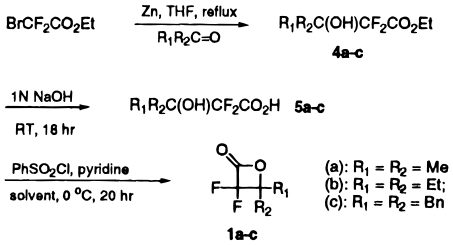
Table 1. Decarboxylation of α,α-Difluoro β-Lactones: Activation Parameters

compd	medium	log A	E_a (kcal/mol)	$\Delta H^{\ddagger}$ (kcal/mol)	$\Delta S^{\ddagger}$ (cal/deg)	$\Delta G^{\ddagger}$ (kcal/mol)	k_{rel} (168.1°)
1a	gas phase	16.2 ± 0.1	45.2 ± 0.1	44.2 ± 1.3	12.7 ± 2.7	38.1 ± 2.6	1
1a	mesitylene	11.9 ± 0.8	32.9 ± 1.6	32.0 ± 1.6	−6.7 ± 3.6	35.0 ± 3.2	62
1a	acetonitrile	11.0 ± 0.4	27.5 ± 0.6	26.7 ± 0.6	−10.8 ± 1.5	31.1 ± 1.3	3600
1a	mesitylene	11.4 ± 0.3	31.4 ± 0.5	30.5 ± 0.5	−8.2 ± 1.1	34.1 ± 1.0	110
6	gas phase[a]	15.0 ± 0.4	37.0 ± 0.8	36.1 ± 0.8	7.3 ± 1.7	32.9 ± 1.5	725

[a] Reference 10.

Scheme 1. Synthesis of β-Lactones



counterparts, α,α-difluoro β-lactones undergo smooth thermal decarboxylation to form alkenes, *via* well-behaved unimolecular processes. Our investigation comprises what is probably the most comprehensive kinetic study of β-lactone decarboxylations to date, with the work encompassing gas-phase and liquid-phase studies and including a detailed examination of the impact of solvent polarity upon activation parameters. We have also reexamined the reaction computationally, carrying out the first *ab initio* calculations which evaluate the structure of the transition state for both fluorinated and nonfluorinated β-lactone decarboxylations. We believe that our analysis of these experimental and computational results provides new insight into this interesting mechanistic problem.

Results

Syntheses. The 3,3-difluoro-4,4-dialkyloxetan-2-ones **1a**−**c** were prepared from their respective β-hydroxy acid precursors **5a**−**c** by the lactonization procedure shown in Scheme 1, which has been described earlier.[4] They were characterized by their ^{19}F NMR signals in the δ −118 to −122 ppm range and their IR carbonyl absorptions at 1858 cm^{-1}.

Kinetic Studies. Arrhenius Parameters. The thermal decarboxylations of oxetan-2-ones **1a**−**c** were well-behaved first-order processes, both in the gas phase and in solution. Rates for the decarboxylation of the 4,4-dimethyl derivative **1a** were determined at five temperatures each in the gas phase, in mesitylene, and in acetonitrile.

Likewise, rates for the decarboxylation of the 4,4-dibenzyl derivative **1c** were obtained at five temperatures in mesitylene. Arrhenius plots of these rate data led to the activation parameters which are given in Table 1, along with those for hydrocarbon analog, 4,4-dimethyloxetan-2-one, **6**.[10]

Kinetic Studies. Solvent Effects. A study of the solvent−polarity dependency of such decarboxylation reactions was carried out using 3,3-difluoro-4,4-diethyloxetan-2-one, **1b**, as the substrate. The data in Table 2 confirms the significant dependency of the rates on solvent polarity.

Table 2. Rates of Decarboxylation of 3,3-Difluoro-4,4-diethyloxetan-2-one, 1b, in Various Solvents at 168.1 °C

solvent	$E_T(30)$ value[a]	SPP value[b]	10^5k, s^{-1}	k_{rel}
cyclohexane	30.9	0.557	2.2 ± 0.1	1
mesitylene	32.9	0.581	10.8 ± 0.4	4.9
benzene	34.3	0.667	15.3 ± 0.2	7.0
cyclohexanone	39.8	0.874	143 ± 4	65
acetonitrile	45.6	0.895	312 ± 15	142
DMF	43.8	0.952	1070 ± 40	486

[a] Reference 11. [b] Reference 12.

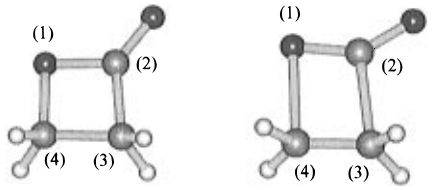
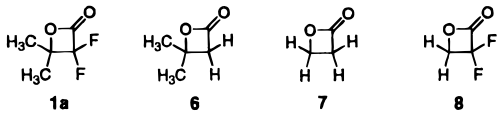


Figure 1. Ground-state structure of oxetan-2-one, **7**, and its corresponding decarboxylation transition-state structure, with numbering scheme of relevant atoms shown. Interatomic distances of structures **1a** and **6**−**8** are found in Tables 3 and 4.

Computational Results. In order to gain additional insight into the nature of the transition state for the decarboxylation of β-lactones, and more specifically how fluorine substituents at the 3-position affect that transition state, molecular orbital calculations were performed.

Geometries of oxetan-2-one, **7**, 3,3-difluorooxetan-2-one, **8**, 4,4-dimethyloxetan-2-one, **6**, 3,3-difluoro- 4,4-dimethyloxetan-2-one, **1a**, and their corresponding decarboxylation transition structures were investigated with semiempirical (AM1) and *ab initio* molecular orbital calculations ranging from RHF/4-31G to MP2/6-311++G** (Figure 1). Our AM1 calculations gave results which were virtually identical to those of Moyano *et al*.[9]



Ground and Transition Structure Geometries. Interatomic distances for the ring atoms of **1a** and **6**−**8** are found in Table 3. Corresponding distances in the decarboxylation transition structures (and changes therein relative to the ground state) are found in Table 4.

Focusing attention on the differences between ground- and transition-state geometries for the four β-lactones,[13] it is seen that bond breaking of the O1−C4 and C2−C3 bonds in transition states for the parent system **7** appears

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(13) Moyano *et al.* (ref 9) have elaborated on the merits of a bond index approach to the examination reaction coordinates for the decarboxylation of β-lactones. In our case we believe that an analysis of changes in geometry in going from ground state to transition state is a more convenient approach to understanding the mechanism.

Table 3. Optimized Interatomic Distances (in Angstroms) for Ground-State Geometries of 1a and 6−8 at Various Levels of Theory

	7	6	8	1a
O1−C2	1.403[a]	1.398[a]	1.396[a]	1.389[a]
	1.377[b]	1.370[b]	1.374[b]	1.364[b]
	1.343[c]	1.339[c]	1.342[c]	1.336[c]
	1.379[d]		1.377[d]	
C2−C3	1.522[a]	1.519[a]	1.578[a]	1.573[a]
	1.522[b]	1.516[b]	1.537[b]	1.531[b]
	1.519[c]	1.515[c]	1.537[c]	1.532[c]
	1.528[d]		1.549[d]	
C3−C4	1.551[a]	1.564[a]	1.588[a]	1.610[a]
	1.541[b]	1.550[b]	1.524[b]	1.542[b]
	1.533[c]	1.542[c]	1.525[c]	1.540[c]
	1.532[d]		1.526[d]	
C4−O1	1.471[a]	1.491[a]	1.457[a]	1.476[a]
	1.483[b]	1.506[b]	1.482[b]	1.508[b]
	1.438[c]	1.457[c]	1.438[c]	1.459[c]
	1.468[d]		1.469[d]	

[a] AM1. [b] RHF/4-31G. [c] RHF/6-31G**. [d] MP2/6-311++G**.

much more synchronous when examined by *ab initio* than by AM1. AM1 results for difluoro analog **8**, moreover, are anomalously inconsistent with the *ab initio* calculations and thus would appear to be in this case untrustworthy. The *ab initio* results for **8**, like those for **7**, indicate a high degree of synchronous bond breaking.

In contrast to the results obtained for the parent systems **7** and **8**, their 4,4-dimethyl-substituted analogs **6** and **1a** exhibit highly asynchronous bond breaking in their transition states (with O1−C4 bond breaking far ahead of that of C2−C3), regardless of the level of computation. Also, the transition state for fluorinated **1a** is observed to be more advanced along the reaction coordinate than that of nonfluorinated analog **6**.

Decomposition of the transition state for decarboxylation of **1a** along the intrinsic reaction coordinate was observed to lead to carbon dioxide and $(CH_3)_2C{=}CF_2$, with no evidence of an intermediate. Thus, on the RHF/6-31G** energy surface the reaction appears to be concerted, a conclusion which is consistent with the AM1 results of Moyano.[9]

Activation Barriers. Activation barriers computed at various levels of theory are found in Table 5. It is observed that the inclusion of a modest amount of electron correlation and a larger basis set (whether in the form of MP2/6-311++G** single-point energies on the RHF/6-31G** geometries or full MP2/6-311++G** optimizations) leads to excellent agreement with experiment in the three cases for which values are known. RHF/4-31G, most likely fortuitously, does not fare too badly, whereas inclusion of polarization functions at the RHF level leads, not unexpectedly, to activation barriers which are too high. AM1 performs well with **6** and **8** (the latter yielding good agreement with the MP2 values, though no experimental value is known), but not quite so well in the cases of **1a** and **7**.

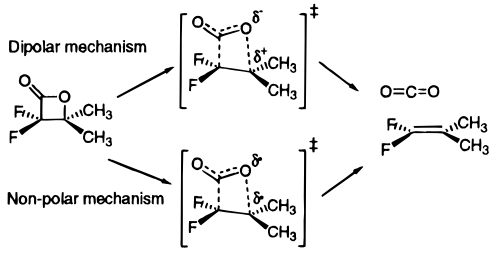
Mulliken Analysis of Partial Charges. Partial charges based on Mulliken populations at the AM1, RHF/4-31G, and RHF/6-31G** levels are found in Table 6. Corresponding values for the transition structures and differences are located in Table 7. Although values obtained by Mulliken analyses are prone to be dependent on the selection of the basis set, the observed RHF/4-31G and RHF/6-31G** values presented here are reasonably consistent.

Again focusing attention on the *differences* between the ground-state oxetanones and their respective decarboxylation transition-state structures, one can see that AM1 estimates of charge separation are inconsistent with those derived from *ab initio* calculations, which predict that in spite of a considerable degree of O1−C4 bond cleavage in the decarboxylation transition state, there is apparently *little charge separation*. This analysis, which indicates little change in partial charges in going to the decarboxylation transition state, constitutes the most significant new insight that our *ab initio* calculations have provided.

Discussion

Gas-Phase Data. A comparison of the Arrhenius data for the gas-phase decarboxylation of **1a** with the analogous data for its nonfluorinated analog **6**[10] clearly reveals the significant kinetic impact of the geminal fluorine substituents of **1a**−**c**. Its rate of decarboxylation at 168.1 °C is a factor of *725 times slower* than that of **6**. The data reveals an increase in activation enthalpy of ∼8 kcal/mol, which is partially compensated by a more positive entropy of activation (∼5 cal/deg), with a net 5 kcal/mol difference in their free energies of activation. The *ab initio* calculations (MP2/6-311++G**//RHF/6-31G** + ΔZPE) predict the gas phase E_a's for both **6** and **1a** quite accurately (each within ±1 kcal/mol of the experimental values), and they predict a more advanced transition state for the decarboxylation of the fluorinated **1a**.

It is possible for the observed inhibition of β-lactone decarboxylation by geminal fluorine substitution at the 3-position to be rationalized as deriving either from an increase in the C−O bond dissociation energy which would increase the nonfluorinated of a homolytic, nonpolar pathway or by the deleterious effect of the β-fluorines on a heterolytic, dipolar transition state. Indeed, fluorine substituents are known to give rise to an increase



of BDE for C−C bonds which are α and C−X bonds which are β to the fluorinated carbon.[16] Hence the homolytic mechanism should be inhibited by the fluorine substituents in **1a**−**c**. Fluorine substituents are also known to severely inhibit the formation of a β-cationic site.[16] Thus the heterolytic mechanism would also be disfavored for **1a**−**c**, relative to **6**.

However, the lack of apparent charge separation in the transition state and the absence of a discernible intermediate, as indicated by *ab initio* calculation, leads us to conclude that the gas-phase reaction takes place *via* a highly asynchronous concerted process which proceeds *via* a planar, homolytic, *nonpolar* transition state. Although a concerted and completely synchronous [$2\pi_s$ +

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Table 4. Optimized Interatomic Distances and Differences between Ground-State Geometries (in Angstroms) for Decarboxylation Transition Structures of 1a and 6−8 at Various Levels of Theory

	7	6	8	1a
O1−C2	1.271 (−0.132)[a]	1.281 (−0.117)[a]	1.263 (−0.133)[a]	1.261 (−0.128)[a]
	1.258 (−0.119)[b]	1.252 (−0.118)[b]	1.250 (−0.124)[b]	1.240 (−0.124)[b]
	1.231 (−0.112)[c]	1.229 (−0.110)[c]	1.226 (−0.116)[c]	1.216 (−0.120)[c]
	1.258 (−0.121)[d]		1.261 (−0.116)[d]	
C2−C3	1.722 (+0.200)[a]	1.592 (+0.073)[a]	2.206 (+0.628)[a]	1.696 (+0.123)[a]
	1.808 (+0.286)[b]	1.712 (+0.196)[b]	1.874 (+0.337)[b]	1.710 (+0.179)[b]
	1.812 (+0.293)[c]	1.726 (+0.211)[c]	1.807 (+0.270)[c]	1.753 (+0.221)[c]
	1.889 (+0.361)[d]		1.863 (+0.314)[d]	
C3−C4	1.422 (−0.129)[a]	1.470 (−0.094)[a]	1.454 (−0.134)[a]	1.527 (−0.083)[a]
	1.404 (−0.137)[b]	1.427 (−0.123)[b]	1.403 (−0.121)[b]	1.452 (−0.090)[b]
	1.399 (−0.134)[c]	1.422 (−0.120)[c]	1.402 (−0.121)[c]	1.431 (−0.109)[c]
	1.399 (−0.133)[d]		1.392 (−0.134)[d]	
C4−O1	2.091 (+0.620)[a]	2.216 (+0.725)[a]	1.730 (+0.273)[a]	2.239 (+0.763)[a]
	2.121 (+0.638)[b]	2.294 (+0.788)[b]	2.113 (+0.631)[b]	2.509 (+1.001)[b]
	2.061 (+0.623)[c]	2.243 (+0.786)[c]	2.114 (+0.676)[c]	2.370 (+0.911)[c]
	1.969 (+0.501)[d]		1.993 (+0.524)[d]	

[a] AM1. [b] RHF/4-31G. [c] RHF/6-31G**. [d] MP2/6-311++G**.

Table 5. Activation Barriers for the Decarboxylation Reactions of 1a and 6−8 (kcal/mol)

β-lactone	7	6	8	1a
E_a (calcd)	50.6[a]	36.2[a]	47.8[a]	39.1[a]
E_a (calcd)	44.3[b]	33.9[b]	54.4[b]	40.9[b]
E_a (calcd)	50.8[c]	40.5[c]	62.4[c]	48.9[c]
E_a (calcd)	41.6[d]	37.7[d]	50.7[d]	44.6[d]
E_a (calcd)	40.9[e] (41.4)[f]		49.9[e]	
experiment	43.1,[14] 45.8[15]	36.8[10]		45.2

[a] AM1, $\Delta H_{act}/\Delta H_{rxn}$. [b] RHF/4-31G + ΔZPE. [c] RHF/6-31G** + ΔZPE. [d] MP2/6-311++G**//RHF/6-31G** + ΔZPE. [e] MP2/6-311++G**//MP2/6-311++G** + ΔZPE (RHF). [f] MP2/6-311++G**//MP2/6-311++G** + ZPE (MP2).

Table 6. Charges for relevant atoms in oxetanones 1a, & 6−8

	7	6	8	1a
q_1	−0.265[a]	−0.264[a]	−0.233[a]	−0.234[a]
	−0.669[b]	−0.654[b]	−0.667[b]	−0.651[b]
	−0.600[c]	−0.612[c]	−0.608[c]	−0.622[c]
q_2	+0.300[a]	+0.331[a]	+0.266[a]	+0.267[a]
	+0.812[b]	+0.816[b]	+0.846[b]	+0.850[b]
	+0.794[c]	+0.797[c]	+0.767[c]	+0.773[c]
q_3	−0.224[a]	−0.220[a]	+0.225[a]	+0.219[a]
	−0.472[b]	−0.431[b]	+0.610[b]	+0.674[b]
	−0.424[c]	−0.402[c]	+0.633[c]	+0.679[c]
q_4	−0.041[a]	+0.067[a]	−0.074[a]	+0.046[a]
	+0.005[b]	+0.161[b]	+0.010[b]	+0.105[b]
	+0.106[c]	+0.263[c]	+0.064[c]	+0.171[c]

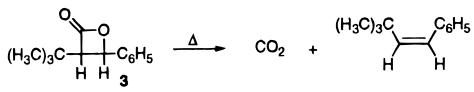
[a] AM1. [b] RHF/4-31G. [c] RHF/6-31G**.

$2\pi_s$] cycloreversion should be forbidden in the Woodward−Hoffmann sense,[17] it appears that asynchronicity can be the means by which such a thermal reversion can avoid the forbidden character of the hypothetical synchronous process. Neither our calculations nor those of Moyano provide any credibility for the twisted transition state which would be characteristic of a concerted [$2\pi_s$ + $2\pi_a$] process, such as that suggested for ketene cycloadditions.

Solvent Effects. A comparison of activation parameters indicates that the nature of the mechanism in solution is quite different from that in the gas phase. Decarboxylation of **1a** in solution (mesitylene versus acetonitrile) reveals a significant dependence of the rate upon solvent polarity ($k_{rel} = 58$), which indicates that, at least in solution, there must be *substantial charge development in the transition state* for the decarboxylative process.

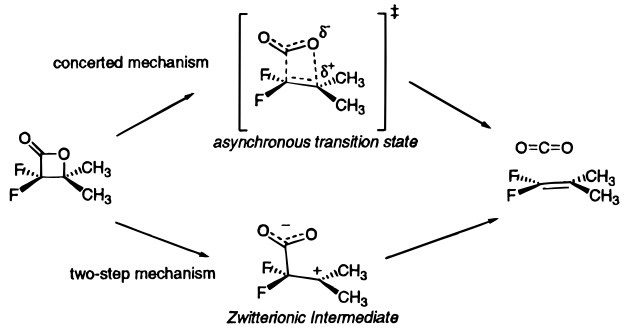
Moreover, in the broader study of solvent effects, using diethyl derivative **1b** we have observed good correlations of the rates of decarboxylation with the oft cited E_T values of the solvents[11] as well as with the recently introduced SPP scale of solvent dipolarity−polarizability[12] (Figure 2).

These correlations, which have slopes of 0.158 (r = 0.952) and 5.7 (r = 0.974), respectively, can be compared with those derived from what is perhaps the most comprehensive study of solvent effects for the decarboxylation of a non-fluorine-containing β-lactone. In their study of the decarboxylation of 3-*tert*-butyl-4-phenyloxetan-2-one, **3**, in a variety of solvents, Mulzer and Zippel



reported a good correlation of the rates with the E_T values of the solvents (slope = 0.128, r = 0.981).[8a] Interestingly their data does not correlate nearly as well with solvent SPP values (slope = 3.4, r = 0.817). Such comparisons indicate that the decarboxylations of the fluorinated β-lactone **1b** exhibit a greater dependence upon solvent polarity than do those of Mulzer and Zippel's system,[8a] a result which is consistent with the later transition state for the decarboxylation of **1b**.

An issue which is more difficult to address definitively is whether the solvent effect data and the overall kinetic data are more consistent with a two-step mechanism involving formation of a zwitterion intermediate or with an asynchronous but concerted mechanism involving a dipolar transition state.



(17) Woodward, R. B.; Hoffmann, R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 781.

Table 7. Charges and Differences for Relevant Atoms in Decarboxylation Transition Structures for 1a and 6−8

	7	6	8	1a
q_1	−0.498 (−0.233)[a] −0.688 (−0.019)[b] −0.652 (−0.052)[c]	−0.567 (−0.303)[a] −0.724 (−0.070)[b] −0.681 (−0.069)[c]	−0.323 (−0.090)[a] −0.667 (+0.000)[b] −0.647 (−0.039)[c]	−0.521 (−0.287)[a] −0.727 (−0.076)[b] −0.668 (−0.046)[c]
q_2	+0.450 (+0.150)[a] +0.872 (+0.060)[b] +0.835 (+0.041)[c]	+0.385 (+0.054)[a] +0.856 (+0.040)[b] +0.818 (+0.021)[c]	+0.524 (+0.258)[a] +0.880 (+0.034)[b] +0.811 (+0.044)[c]	+0.401 (+0.134)[a] +0.850 (+0.000)[b] +0.796 (+0.023)[c]
q_3	−0.459 (−0.235)[a] −0.604 (−0.132)[b] −0.520 (−0.096)[c]	−0.367 (−0.147)[a] −0.576 (−0.145)[b] −0.489 (−0.087)[c]	−0.180 (−0.405)[a] +0.534 (−0.076)[b] +0.561 (−0.072)[c]	+0.054 (−0.165)[a] +0.578 (−0.096)[b] +0.601 (−0.078)[c]
q_4	+0.241 (+0.282)[a] +0.000 (−0.005)[b] +0.057 (−0.049)[c]	+0.363 (+0.296)[a] +0.294 (+0.133)[b] +0.280 (+0.017)[c]	+0.100 (+0.174)[a] −0.028 (−0.038)[b] −0.023 (−0.087)[c]	+0.299 (+0.253)[a] +0.250 (+0.145)[b] +0.175 (+0.004)[c]

[a] AM1. [b] RHF/4-31G. [c] RHF/6-31G**.

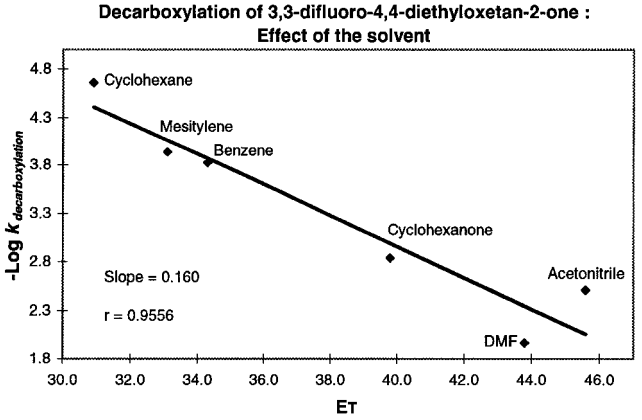
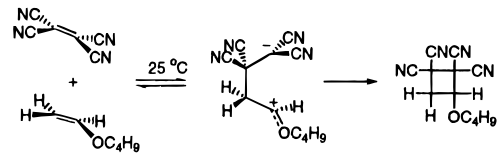


Figure 2.

A comment needs to be made that just because calculations indicate a nonpolar, concerted, asynchronous mechanism for the gas-phase reaction, this need not mean that the reaction in solution, particularly in a polar solvent, also need be concerted. In Huisgen's excellent analysis of the nature of tetramethylene species,[18] he concluded that, although the parent tetramethylene diradical does not appear to exist in an energy trough, such energy troughs should indeed arise when the terminal atoms (or substituents) and polar solvent conditions can stabilize a zwitterionic intermediate.

There are a number of solvent effect studies in the literature, most of them by Huisgen,[19] which are good systems for comparison with our study of what is formally a retro [2 + 2] cycloaddition. In the two-step [2 + 2] cycloaddition reaction of *n*-butyl vinyl ether with TCNE,



a reaction which is acknowledged to involve a zwitterion intermediate, Huisgen observed a 2600-fold rate enhancement in changing solvent from cyclohexane to acetonitrile.[20]

In contrast, in a study of the [2 + 2] cycloaddition of diphenyl ketene with *n*-butyl vinyl ether, a reaction which is considered to proceed *via* a concerted, asynchronous mechanism, the comparable observed rate enhancement was only 163,[21] both studies being carried out at room temperature. Such rate enhancements correspond to $\Delta\Delta G^{\ddagger}$'s of 4.7 and 3.0 kcal/mol, deriving from the increase in solvation in the respective transition states.

Likewise, Huisgen observed competing two-step and concerted [2 + 2] cycloaddition pathways in the reaction of dimethylketene with the enamine *N*-isobutenylpyrrolidine, with the rate of the zwitterionic pathway exhibiting a 560-fold rate enhancement ($\Delta\Delta G^{\ddagger} = 3.7$ kcal/mol) while the rate of the concerted pathway was only increased by a factor of 36 ($\Delta\Delta G^{\ddagger} = 2.1$ kcal/mol).[22]

In comparison to these observed solvent effects for clear concerted and two-step asynchronous [2 + 2] cycloaddition processes, our observed 142-fold rate enhancement for the retro [2 + 2] decarboxylation of **1b** at 168.1 °C corresponds to a $\Delta\Delta G^{\ddagger}$ of 4.3 kcal/mol, a value which would appear to be most consistent with a two-step mechanism involving a zwitterionic intermediate.

Another factor which points strongly toward the two-step mechanism is the dramatic trend in $\Delta S^{\ddagger}$ as one modifies conditions from gas phase (+12.7 cal/deg) to nonpolar solvent (−6.7 cal/deg) to polar solvent (−10.8 cal/deg). Although the gas-phase activation parameters are fully consistent with a simple homolytic dissociative process being involved, the activation parameters for the decarboxylation in solution provide clear evidence for increased electrostriction and/or organization of the solvent as one proceeds to increasingly polar solvents, with the increasingly negative $\Delta S^{\ddagger}$ partially counteracting the increasingly lower enthalpy of activation. Such a result is that which one would expect for a mechanism involving the tighter and more organized solvation shell which is characteristic of an ionization process.

Gas-Phase Nonpolar versus Solution-Phase Dipolar Transition States. Both computational and experimental kinetic data point toward a concerted, nonpolar (homolytic) process being involved in the gas-phase decarboxylation of **1a**−**c**, whereas the solvent effect data clearly indicate a dipolar transition state (probably leading to a zwitterionic intermediate) for their decarboxylations in solution. Can mechanisms vary in such a manner as one changes medium? Huisgen once asked rhetorically whether a 1,4-diradical and a 1,4-zwitterion were fundamentally different.[18] His answer was an emphatic "no", and he referred to work by Hoffmann[22] and Salem and Rowland[23] which indicated that the

(18) Huisgen, R. *Acc. Chem. Res.* **1977**, *10*, 199.
(19) Huisgen, R. *Acc. Chem. Res.* **1977**, *10*, 117.
(20) Huisgen, R.; Steiner, G. *J. Am. Chem. Soc.* **1973**, *95*, 5056.
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(22) Hoffmann, R.; Swanminathan, S.; Odell, B. G.; Gleiter, R. *J. Am. Chem. Soc.* **1970**, *92*, 7091.
(23) Salem, L.; Rowland, C. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 92.

diradical and the zwitterion could essentially be "regarded as resonance forms, the relative importance of which would be determined by the substituents at the terminal centers". We would add to this the proposition that the relative importance of homolytic and dipolar transition states, indeed whether a given reaction should be concerted or proceed *via* a diradical or zwitterionic intermediate, should also be strongly dependent upon the *polarity of the medium*, which, along with the important effect of substituents, would determine where a given cycloreversion (-addition) mechanism should be located within a continuous spectrum of possible concerted and nonconcerted, polar and nonpolar mechanisms.

Experimental Section

General. All NMR spectra were run in $CDCl_3$ on a Varian VXR-300 spectrometer, with ^1H at 299.949 MHz using TMS as reference; ^{19}F at 282.202 MHz using $CFCl_3$ as reference; ^{13}C at 75.430 MHz using $CDCl_3$ as reference at 77.0 ppm.

Synthesis of Substrates 1. α,α-Difluoro *β*-lactones **1** were prepared as previously reported.[4] One equiv of the starting α,α-difluoro-*β*-hydroxy acid was dissolved in the anhydrous solvent, and 2.0 equivs of anhydrous pyridine were added dropwise. Then, while cooling at 0−5 °C, 1.0 equiv of benzenesulfonyl chloride was added very slowly and the mixture was vigorously shaken. After 18 h **1** was isolated as specifically indicated below.

Synthesis of 3,3-Difluoro-4,4-dimethyloxetan-2-one (1a). Starting from 2,2-difluoro-3-hydroxy-3-methylbutanoic acid dissolved in tetraglyme and after 18 h of reaction, **1a** was vacuum transferred out of the reactant mixture at 0.05 mmHg, in 60% yield, and the product exhibited the same spectroscopic properties as those reported.[4]

^1H NMR: δ 1.6 ppm (t, $J_{H-F} = 1.5$ Hz). ^{19}F NMR: δ −121.2 ppm (p, $J_{H-F} = 1.5$ Hz). ^{13}C NMR: δ 20.1 (t-like), 89.0 (t, $J_{C-F} = 22.4$ Hz), 119.4 (t, $J_{C-F} = 291.1$ Hz, CF_2), 161.6 ppm (t, $J_{C-F} = 32.2$ Hz, C=O).

Synthesis of 4,4-Diethyl-3,3-difluorooxetan-2-one (1b). Starting from 2,2-difluoro-3-hydroxy-3-ethylpentanoic acid dissolved in tetraglyme, **1b** was vacuum transferred out of the reactant mixture at 0.05 mmHg, in 95% yield.

^1H NMR: δ 1.0 (t, 6H, $J_{H-H} = 7.6$ Hz), 2.0 (q, 2H, $J_{H-H} = 7.6$ Hz), 2.0 ppm (q of t, 2H, $J_{H-H} = 7.6$ Hz, $J_{H-F} = 1.5$ Hz). ^{19}F NMR: δ −122.1 ppm, (s). ^{13}C NMR: 7.2 (s), 23.1 (t-like), 94.1 (t, $J_{C-F} = 20.4$ Hz), 119.9 (t, $J_{C-F} = 291.3$ Hz, CF_2), 161.9 ppm (t, $J_{C-F} = 32.2$ Hz, C=O); IR (neat): 2987, 2943, 2886, 1858, 1460, 1370, 1312, 1206, 1172, 1142 cm^{-1}.

Synthesis of 4,4-Dibenzyl-3,3-difluorooxetan-2-one (1c). Starting from 3-benzyl-2,2-difluoro-3-hydroxy-4-phenylbutanoic acid (**5c**) dissolved in chloroform and after 18 h of reaction, the solvent was evaporated, and the remaining white solid was treated with dried hexanes. Evaporation of the hexane extract gave rise to **1c**, which was then recrystallized from hexanes in 85% yield; mp 51−52 °C.

^1H NMR (AB system): δ 3.15 (d, $J_{H-F} = 15.3$ Hz), 3.23 (d, 4H, $J_{H-F} = 15.3$ Hz), 7.06−7.10 (m, 4H), 7.30−7.33 ppm (m, 6H). ^{19}F NMR: δ −118.4 ppm (s). ^{13}C NMR: δ 36.9 (bs), 92.5 (t, $J_{C-F} = 20.6$ Hz), 120.2 (t, $J_{C-F} = 293.0$ Hz, CF_2), 127.5, 128.6, 130.3 and 132.8 (aromatic carbons), 161.0 ppm (t, $J_{C-F} = 32.4$ Hz, C=O). IR ($CHCl_3$): 1858 cm^{-1}. MS (EI) *m/e*: 288.0971 (36.7) [$M^{\bullet+} = C_{17}H_{14}F_2O_2$], 193.1079 (11.4) [$C_9H_5F_2O_2$], 166.0655 (12.1) [$C_{10}H_8F_2$], 115.062 (13.2) [$C_6H_8OF$], 91.0563 (100) [$C_4H_8FO$], 65.0428 (23.2) [$C_2H_6OF$]. Anal. Calcd for $C_{17}H_{14}F_2O_2$: C, 70.83; H, 4.89; F, 13.18. Found: C, 70.56; H, 5.06.

Kinetic Measurements. Kinetics of the Gas-Phase Decarboxylation of 1a. The pyrolysis was carried out in a Pyrex vessel immersed in a thermostated molten salt bath and connected to a vacuum line. **1a** was vacuum transferred into the pyrolysis vessel which was maintained at the desired temperature, and aliquots were removed by vacuum transfer at appropriate intervals of time into 25 mL sample tubes and analyzed by GC on a OV-17 column using a gas-sampling valve. The analysis by both ^{19}F NMR and GC of standard solutions of **1a** and 1,1-difluoro-2-methylpropene in toluene demonstrated that, within experimental error, they have the same detector response factor. The values of *k* of decarboxylation were estimated by linear regression from the slope of the plot of the natural logarithm of the fraction of area of **1a** versus time.

Rates of Gas-Phase Decarboxylation of 1a: $2.8 \pm 0.1 \times 10^{-5}$ s^{-1} at 202.4 °C, $4.6 \pm 0.2 \times 10^{-5}$ s^{-1} at 207.7 °C, $6.9 \pm 0.2 \times 10^{-5}$ s^{-1} at 211.2 °C, $9.7 \pm 0.1 \times 10^{-5}$ s^{-1} at 215.5 °C, $15.9 \pm 0.2 \times 10^{-5}$ s^{-1} at 220.4 °C.

Kinetics of the Decarboxylation of 1 in Solution. A stock 0.04 M solution of **1** was prepared in the anhydrous solvent containing α,α,α-trifluorotoluene of known concentration as internal standard. The decarboxylation was carried out in sealed NMR tubes immersed in a thermostated silicon oil bath set at the desired temperature, and the kinetics were monitored by ^{19}F-NMR analysis of samples quenched in an 2-propanol−dry ice bath at appropriate intervals of time. For each experiment, the respective value of *k* of decarboxylation was estimated by linear regression from the slope of the plot of the natural logarithm of the fraction of area of **1** versus time.

Rates of Decarboxylation of 1a in Acetonitrile: $5.4 \pm 0.1 \times 10^{-5}$ s^{-1} at 119.6 °C, $8.1 \pm 0.1 \times 10^{-5}$ s^{-1} at 125.8 °C, $1.3 \pm 0.1 \times 10^{-4}$ s^{-1} at 130.2 °C, $2.0 \pm 0.1 \times 10^{-4}$ s^{-1} at 135.3 °C, $3.1 \pm 0.1 \times 10^{-4}$ s^{-1} at 140.2 °C.

Rates of Decarboxylation of 1a in Mesitylene: $4.1 \pm 0.2 \times 10^{-5}$ s^{-1} at 168.1 °C, $6.3 \pm 0.1 \times 10^{-5}$ s^{-1} at 171.9 °C, $8.3 \pm 0.4 \times 10^{-5}$ s^{-1} at 176.6 °C, $13.4 \pm 0.3 \times 10^{-5}$ s^{-1} at 181.5 °C, $19.8 \pm 0.6 \times 10^{-5}$ s^{-1} at 187.2 °C.

Rate of Decarboxylation of 1a in Toluene at 171.8 °C: $6.7 \pm 0.3 \times 10^{-5}$ s^{-1}.

Rates of Decarboxylation of 1b in Solution at 168.1 °C: In *N,N*-dimethylformamide (DMF) $1.07 \pm 0.04 \times 10^{-2}$ s^{-1}, in acetonitrile $3.1 \pm 0.2 \times 10^{-3}$ s^{-1}, in cyclohexanone $1.4 \pm 0.1 \times 10^{-3}$ s^{-1}, in benzene $1.5 \pm 0.1 \times 10^{-4}$ s^{-1}, in mesitylene $1.1 \pm 0.1 \times 10^{-4}$ s^{-1}, in cyclohexane $2.2 \pm 0.1 \times 10^{-5}$ s^{-1}.

Rates of Decarboxylation of 1c in Mesitylene: $2.3 \pm 0.2 \times 10^{-5}$ s^{-1} at 148.9 °C, $4.2 \pm 0.1 \times 10^{-5}$ s^{-1} at 156.5 °C, $1.2 \pm 0.1 \times 10^{-4}$ s^{-1} at 169.2 °C, $1.5 \pm 0.1 \times 10^{-4}$ s^{-1} at 171.1 °C, $2.0 \pm 0.1 \times 10^{-4}$ s^{-1} at 175.0 °C.

Computational Methodology. All *ab initio* calculations were performed with the Gaussian92 program system.[24] Semiempirical results were obtained using the AM1 parameter set[25] as implemented in MOPAC93. Transition structures computed at the AM1 and RHF levels (and in the case of **7**, at the MP2 level) were characterized by harmonic frequency analysis and verified by a single imaginary (negative) vibrational frequency, analysis of which indicated motion along the expected reaction coordinate. Hartree−Fock vibrational frequencies and zero-point energy corrections were scaled by 0.89. MP2 frequencies and zero-point energy corrections of **7** were scaled by 0.94. AM1 geometries and energies of ground and transition structures of **7** and **6** and the RHF/6-31G** ground-state geometry of **7** were essentially identical to those of previous studies by Moyano[9] and Stephens,[26] respectively. MP2 geometry optimizations and single-point energies utilized the frozen-core approach.

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