interest and C.N.R.S. for financial support.

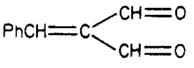
André Lubineau
Institut de Chimie Moléculaire d'Orsay
Laboratoire de Chimie Organique
Multifonctionnelle, Bat. 420
Université Paris-Sud, 91405 Orsay Cedex, France

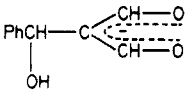
Received November 21, 1985

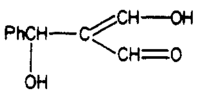
Reaction of Benzylidenemalonaldehyde with Water and Hydroxide Ion[1]

Summary: A stopped-flow kinetic study of the title reaction is reported from which rate and equilibrium constants of various elementary processes are deduced.

Sir: Alkylidene and arylidenemalonaldehydes are not only of interest to the theoretician because of their cross-conjugated π-system but also to the synthetic chemist because of their high bifunctional reactivity. Benzylidenemalonaldehyde (1), a prototype compound and hence of particular interest, has only recently been synthesized,[2] and its chemistry is just beginning to be explored.[3] We report here its kinetic and thermodynamic behavior in aqueous solution which indicates very high reactivity.


1


2


3

Arnold et al.[3a] have already shown that in water, even in the absence of added base, 1 is essentially completely converted to its hydroxide ion adduct 2. In strongly acidic solution UV data suggested that 1 is present in equilibrium with 3, which is the oxygen protonated (enol) form of 2; this suggestion was based on the fact that in acidic aqueous solution the absorbance at 302 nm (λ_{max} of 1) is substantially lower than in acetonitrile.[3a]

Our kinetic results which were obtained in a stopped-flow spectrophotometer confirm these preliminary observations[3a] and put them on a more quantitative basis. In a first set of experiments (pH 4.0 to 13.5) we approached the equilibrium from the reactant side, by adding a dilute buffer or a KOH solution to an acidic solution (0.002 M HCl) of 1 (in equilibrium with 3). The buffers used were acetate, cacodylate and borate, at total buffer concentrations of about 0.05 M or less. In a second set of experiments (pH 1.3 to 4.5), 2 was first generated in a 0.005 M KOH solution which subsequently was mixed with an acidic buffer (acetate and 3-chloropropionate, total buffer concentration $\leq$0.05 M) or an HCl solution in the stopped-flow apparatus. In both types of experiments we measured the rates at 302 nm (λ_{max} of 1) as well as at 270 nm (λ_{max} of 2), with equal results. Since the data obtained at 302 nm had less scatter we used those to construct the pH-rate profile shown in Figure 1. Tests for buffer dependence showed that, at the buffer concentrations used, buffer catalysis is negligible.

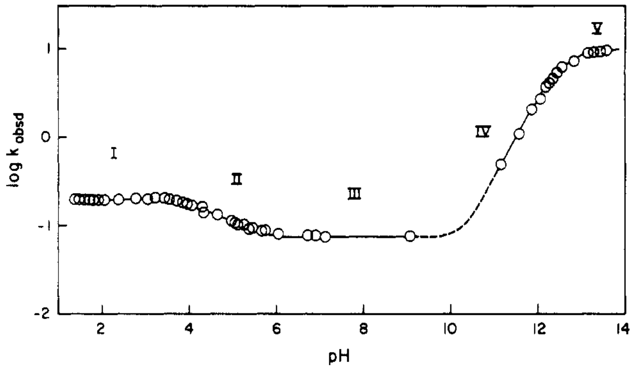


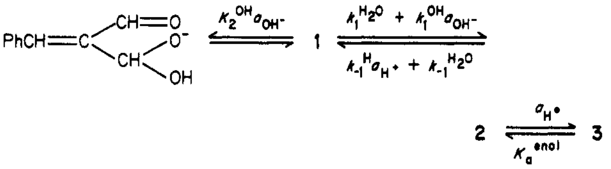
Figure 1. pH-rate profile for the reaction of benzylidenemalonaldehyde with water and OH⁻ at 25 °C, μ = 0.5 M (KCl).

Table I. Rate and Equilibrium Constants for the Reactions of Equation 1 in Water at 25 °C[a]

constant	benzylidene-malonaldehyde	benzylidene Meldrum's acid[b]
$k_1^{H_2O}$, s^{-1}	0.068	0.55
k_{-1}^{H}, M^{-1} s^{-1}	4.20×10^3	1.47×10^5
$K_1^{H_2O}$, M (p$K_1^{H_2O}$)	1.62×10^{-5} (4.79)	3.75×10^{-6} (5.43)
k_1^{OH}, M^{-1} s^{-1}	223	745
$k_{-1}^{H_2O}$, s^{-1}	2.57×10^{-7}	3.73×10^{-6}
$K_1^{OH} = K_1^{H_2O}/K_w{}^c$	8.66×10^8	2.00×10^8
pK_a^{enol}	4.49	
$K_1^{H_2O}/K_a^{enol}$	0.50	
K_2^{OH}, M^{-1}	22	

[a] At μ = 0.5 M (KCl). [b] Reference 4. [c] $K_w = 1.87 \times 10^{-14}$ M^2.

The pH-rate profile is consistent with the following equation:



(1)

Phases III and IV of the profile correspond to water and OH⁻ attack on carbon, respectively, with

$$k_{obsd} = k_1^{H_2O} + k_1^{OH}a_{OH^-} \tag{2}$$

In phase V rapid equilibrium OH⁻ attack on one of the carbonyl carbons (K_2^{OH}) starts to become significant, with k_{obsd} given by

$$k_{obsd} = \frac{k_1^{OH}a_{OH^-}}{1 + K_2^{OH}a_{OH^-}} \tag{3}$$

Phase II is associated with acid-catalyzed loss of OH⁻ from 2 ($k_{-1}^{H}a_{H^+}$) with rapid oxygen protonation of 2 acting as preequilibrium in phase I. Thus for phases I and II k_{obsd} is given by

$$k_{obsd} = k_{-1}a_{H^+}\frac{K_a^{enol}}{K_a^{enol} + a_{H^+}} \tag{4}$$

which becomes

$$k_{obsd} = k_{-1}K_a^{enol} \tag{5}$$

for pH $\ll$ pK_a^{enol}.

The rate and equilibrium constants calculated from our results are summarized in Table I, along with corresponding parameters for benzylidene Meldrum's acid (5),[4]

---

[1] This is part 17 in the series "Nucleophilic Addition of Olefins". Part 16: Bernasconi, C. F.; Renfrow, R. A.; Tia, P. R. *J. Am. Chem. Soc.*, in press.

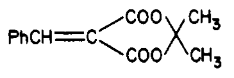
[2] (a) Reichardt, C.; Yun, K.-Y. *Tetrahedron Lett.* **1982**, *31*, 3163. (b) Reidhardt, C.; Yun, K.-Y.; Massa, W.; Schmidt, R. E. *Liebigs Ann. Chem.* **1985**, 1987.

[3] (a) Arnold, Z.; Král, V.; Dvořák, D. *Collect. Czech. Chem. Commun.* **1984**, *49*, 2602. (b) Král, V.; Laatikainen, R.; Arnold, Z. *Tetrahedron* **1985**, *41*, 4919.

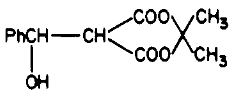
[4] Bernasconi, C. F.; Leonarduzzi, G. D. *J. Am. Chem. Soc.* **1984**, *104*, 5133; **1980**, *102*, 1361.

0022-3263/86/1951-2144$01.50/0

another very reactive electrophile. The following points



5



6

are noteworthy:

(1) The $K_1^{H_2O}$ values indicate that 1 is an even stronger (4.3-fold) Lewis acid than 5, but the *rate* constants for water and OH^- attack on 1 are lower than for attack on 5. This indicates a higher intrinsic barrier[5] toward nucleophilic addition in 1. A likely factor responsible for this difference in intrinsic barriers is that 2 derives its stability mainly from the delocalization of the negative charge into the carbonyl groups while this resonance factor is less important in the corresponding adduct of 5.[6] It is well established that intrinsic barriers in carbanion forming reactions increase with the degree of resonance stabilization of the carbanion.[8]

(2) $K_1^{H_2O}/K_a^{enol} = 0.50$ is the equilibrium constant for the conversion of 1 into 3 upon water addition. If one assumes that the extinction coefficient of 1 is the same in water and in acetonitrile one can calculate a $K_1^{H_2O}/K_a^{enol} = 0.69$ on the basis of the absorbance in aqueous 0.1 M HCl and in acetonitrile reported by Arnold et al.,[3a] in fair agreement with our value. There is no stable form derived from benzylidene Meldrum's acid which corresponds to 3; on the other hand formation of 6 is significant in the benzylidene Meldrum's acid, but no corresponding carbon protonated adduct is formed in the benzylidenemalonaldehyde system. This parallels the fact that the enol form of Meldrum's acid is very unstable[9] but that malonaldehyde exists virtually exclusively in the enol form.[10]

Acknowledgment. This work has been funded by Grant CHE-8315374 from the National Science Foundation.

Registry No. Benzylidenemalonaldehyde, 82700-43-4.

---

(5) Defined as $\Delta G^{\ddagger}$ when $\Delta G^{\circ} = 0$.

(6) A major factor responsible for the high proton acidity of Meldrum's acid and the high Lewis acidity of benzylidene Meldrum's acid is its bislactone structure.[7]

(7) (a) Arnett, E. M.; Maroldo, S. G.; Schilling, S. L.; Harrelson, J. A. *J. Am. Chem. Soc.* **1984**, *106*, 6759. (b) Huisgen, R.; Ott, H. *Tetrahedron* **1959**, *6*, 253.

(8) For recent reviews, see: (a) Bernasconi, C. F. *Pure Appl. Chem.* **1982**, *54*, 2335. (b) Bernasconi, C. F. *Tetrahedron* **1985**, *41*, 3219.

(9) Eigen, M.; Ilgenfritz, G.; Kruse, W. *Chem. Ber.* **1965**, *98*, 1623.

(10) (a) Hüttel, R. *Chem. Ber.* **1941**, *74*, 1825. (b) Bothner-By, A. A.; Harris, R. K. *J. Org. Chem.* **1965**, *30*, 254. (c) Dersch, R.; Reichardt, C. *Synthesis* **1980**, 940.

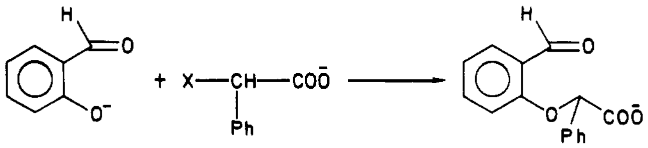
Claude F. Bernasconi,* Michael W. Stronach
Thimann Laboratories of the University of California
Santa Cruz, California 95064

Received October 13, 1985

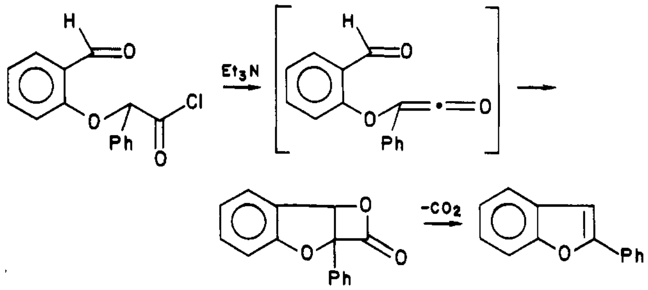
Intramolecular [2 + 2] Cycloaddition Reactions of Ketene and Carbonyl Groups. A New Synthesis of Benzofurans

Summary: (*o*-Carbonylphenoxy)acetyl chlorides are dehydrochlorinated to the corresponding (*o*-carbonylphenoxy)ketenes which undergo a [2 + 2] cycloaddition reaction to yield tricyclic β-lactones which spontaneously decarboxylate to benzofurans.

Scheme I



Scheme II



Sir: Intramolecular [2 + 2] cycloaddition reactions of the ketene function with the carbon–carbon double bond have recently been reported as a powerful synthetic tool for the synthesis of polycyclic compounds. We now report on the intramolecular [2 + 2] cycloaddition reactions of phenoxyketenes to the carbonyl group.[1]

The intermolecular cycloaddition of ketenes to carbonyl compounds is significantly different from the cycloaddition to olefinic compounds. Elevated temperatures, Lewis acid catalysts, or activation of the carbonyl group is usually required for intermolecular ketene carbonyl compound cycloadditions.[2] However, in an appropriate intramolecular cycloaddition of a ketene function with a carbonyl group the proximity of the two functional groups provides a more favorable condition for cycloaddition. We found that the cycloadditions occur readily with both aldehydic and ketone carbonyl groups.

The difunctional compounds used as precursors for the intramolecular cycloadditions were (*o*-carbonylphenoxy)acetic acids. These acids were readily prepared from commercially available *o*-carbonylphenols and α-halocarboxylic acids as illustrated for (*o*-formylphenoxy)phenylacetic acid in Scheme I. Equal molar amounts of salicylaldehyde and α-bromophenylacetic acid in dry THF upon treatment with sodium hydride and refluxing gave a 78% yield of the desired difunctional compound. Yields of 51–78% of the (*o*-carbonylphenoxy)acetic acids were obtained after recrystallization from a mixture of hexane and methylene chloride.

The (*o*-carbonylphenoxy)acetic acids were converted to the corresponding acid chlorides by reaction with 5–8 equiv of oxalyl chloride in benzene at ambient temperature for 4–8 h. The excess oxalyl chloride was removed under vacuum and the crude acid chloride was diluted with dry benzene and very slowly added to a dilute solution of 3 equiv of triethylamine in benzene at reflux. The dehydrochlorination of the acid chloride was evident by the immediate formation of the amine salt. The reaction mixture was refluxed for up to 3–4 h during which time

---

(1) (a) Snider, B. B.; Hui, R. A. H. F.; Kulkami, Y. S. *J. Am. Chem. Soc.* **1985**, *107*, 2194. (b) Marko, I.; Rosmans, B.; Hesbain-Frisque, A.; Dumas, S.; Ghosez, L. *Ibid.* **1985**, *107*, 2192. (c) Snider, B. B.; Hui, R. A. H. F. *J. Org. Chem.* **1985**, *50*, 5167. (d) Brady, W. T.; Giang, Y. F. *Ibid.* **1985**, *50*, 5177.

(2) (a) Staudinger, H. *Chem. Ber.* **1908**, *41*, 1493. (b) Lacey, R. N. In *The Chemistry of Alkenes*; Patai, S., Ed.; Wiley-Interscience: London, 1968. (c) Kung, F. E., U.S. Patent 2 356 459, 1944. (d) Zaugg, H. E. *Org. React.* (*N.Y.*) **1954**, *8*, 314. (e) Borrman, D.; Wegler, R. *Chem. Ber.* **1966**, *99*, 1245. (f) Borrman, D.; Wegler, R. *Ibid.* **1969**, *102*, 64.

0022-3263/86/1951-2145$01.50/0 © 1986 American Chemical Society