ORGANIC LETTERS

2001
Vol. 3, No. 11
1593−1596

Structural, CV and IR Spectroscopic Evidences for Preorientation in PET-Active Phthalimido Carboxylic Acids

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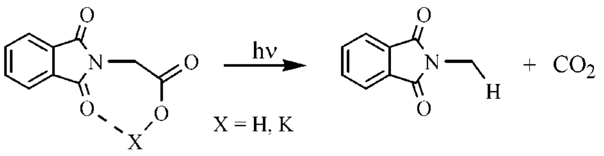
Received January 19, 2001

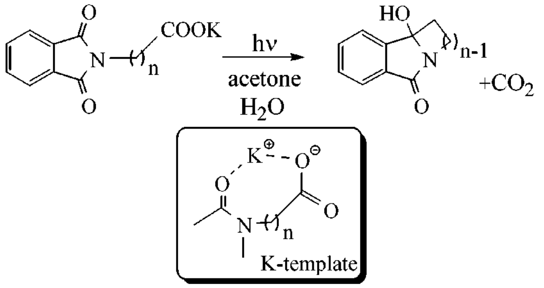
ABSTRACT



Hydrogen bond and potassium cation mediated preorientation were detected for phthalimido acetic acid and the corresponding acetate. Evidence for these phenomena came from X-ray structure analysis as well as cyclic voltammetric and IR spectroscopic measurements. These interactions rationalize the photoinduced electron transfer (PET) reactivity of the substrates in photodecarboxylation reactions.

Hydrogen bonding[1] and template formation with coordinating metals[2] play an important role in reactivity and selectivity control in organic chemistry. Also, photochemical transformations are often influenced by these interactions,[3] which can either activate the desired photochemical reaction or lead to unwanted deactivation or side reactions. During our study on the photophysical[4] and photochemical properties[5] of phthalimides, we developed the photochemical decarboxylation of alkyl carboxylic acids[6] and carboxylates (Scheme 1),[7] respectively. As a simple rationale for the high efficiency and selectivity of the intramolecular version, *preorientation* was postulated in the ground and excited[8] states. The

Scheme 1



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10.1021/ol0155900 CCC: $20.00

templating potassium cation can act as "anchor" and stabilize the donor−acceptor couple in the right geometry for electron transfer and C−C bond formation. Ionic structures have also been assumed to explain solvent and base effects for analogous anilinium carboxylates.[9] Detailed studies by us concerning the structure of the base also supported this assumption: group I and group II metal cations favored the formation of cyclization or decarboxylation products, whereas organic bases did not show sufficient activation.[7] Nevertheless, a convincing proof for the depicted model was missing.

Attempts to detect these *preorientated* conformations by NMR failed in the case of the potassium salts, possibly due to the low population of the templated form in the polar, protic NMR solvents. We therefore focused on simple representative model systems, and following this strategy, we solved the X-ray structure for the potassium salt of phthaloyl glycine[10] **1-K** (Figure 1).[11]

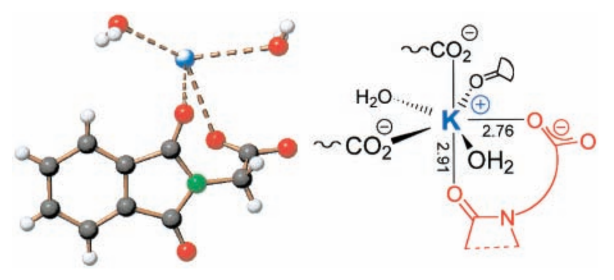
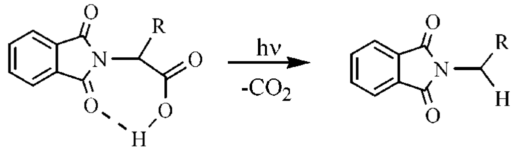


Figure 1. X-ray structure of **1-K** (Schakal plot) and coordination sphere of **K**$^{\oplus}$ (selected bond lengths in Å).

The structure of **1-K** is remarkable, exhibiting both *intra-* (as shown) and *intermolecular* potassium bridges between the carbonyl group of the phthalimide and the terminal carboxylate. Each potassium cation has a (distorted) pentagonal bipyramidal environment and is coordinated with distances in the range of 2.67−3.00 Å to two water molecules, three carboxylic O atoms, and two carbonyl O atoms, respectively. For the free acid **1** or its corresponding silver salt **1-Ag**, only *intermolecular* aggregation exists in the solid state,[12] but similar *intramolecular* interactions were postulated for phthaloyl anthranilic acid and its transition metal complexes.[13]

The efficient α-decarboxylation of phthaloyl amino acids (Scheme 2)[14] is assumed to proceed via excited state proton transfer,[15] facilitated by hydrogen bonding. Consequently, remote carboxylic acid groups were photochemically inert and had to be activated via transformation into the corresponding potassium salts. On the other hand, hydrogen bonding activity of specific linker groups can also deactivate the photochemical decarboxylation.[7]

Scheme 2



Cyclic voltammetry (CV) has recently been used as a powerful tool to observe hydrogen bonding in solution,[16] and we have applied this technique to rationalize the formation of decarboxylative cyclization products during the photolyses of phthalimidoalkylsulfanyl carboxylic acids.[17] This methodology was now applied to phthaloyl glycine **1**, its potassium salt **1-K**, and its methyl ester **2**. At low scan rates (>50 mV s^{-1}), **1** showed a reversible reduction wave (A) at $E_{1/2}$ = −2.01 V (in MeCN) and −2.10 V (in DMF), respectively, leading to its corresponding radical anion. Additionally, anodically shifted *pre*-waves were detected (Figures 2a,b, Table 1), which can be assigned to structures with hydrogen bonds between the carbonyl function of the phthalimide and the carboxylic proton (as shown in the CVs in Figure 2). Because of the partial protonation of the

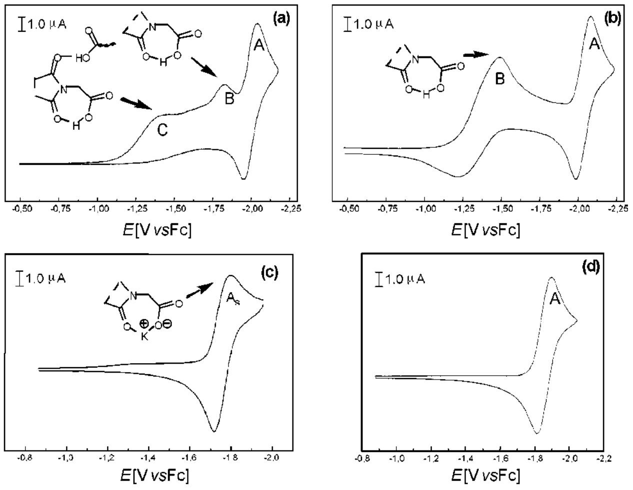


Figure 2. Cyclic voltammograms of (a) **1** in MeCN, (b) **1** in DMF, (c) **1-K** in DMF (s saltbridge), and (d) **2** in MeCN.

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(11) Crystal Data for **1-K** ($C_{10}H_6NO_4K{\cdot}H_2O$, M = 261.27, from water/ethanol): mp >300 °C; monoclinic, space group $P2_1/c$; a = 15.528(1), b = 9.075(1), and c = 8.218(1) Å; β = 94.16(1)°; V = 1155.0(2) Å^3; Z = 4; d_{calc} = 1.503 g/cm^3. Data collection: Enraf-Nonius CAD4-diffractometer, Mo Kα, graphite monochromator, Wyckoff-scan. Theta range (deg): 1.31−27.00. Crystal dimensions (mm): 0.2 × 0.2 × 0.2. Number of reflections measured: 4863. Number of unique reflections: 2518. Number of reflections $F > 2\sigma(F)$: 1854. R, R_w: 0.079, 0.161.

Table 1. Reduction Potentials for **1**, **1-K**, and **2**[a]

compd	solvent	E_{pc}(C)	E_{pc}(B)	$E_{1/2}$(A)
1	MeCN	−1.40 (br)	−1.82	−2.01
1	DMF		−1.52	−2.10
1-K	DMF[b]		−1.76[c]	−2.10[c]
2	MeCN			−1.84

[a] In V vs ferrocene; ca. 4 mM; scan rate $\upsilon = 100$ mV s^{-1}; supporting electrolyte *n*-tetrabutylammonium hexafluorophosphate; br = broad. [b] Insoluble in MeCN. [c] See text.

carbonyl group, its acceptor strength is increased and therefore an anodic shift of the corresponding waves was observed. As described below, the origin of the *pre*-waves can be (B) *intramolecular* or (C) a combination of *intra*- and *intermolecular* bonding mode, the latter accompanying the first type in nonpolar or aprotic solvents and showing an even more pronounced anodic shift.[16d] The assignment of the *pre*-waves was made on the basis of solvent polarity effects, base (DBU) or acid (trifluoromethanesulfonic acid, TFMSA) concentration, scan rate effects, and multisweep experiments.

In acetonitrile, two *pre*-waves were observed for **1** at $E_{pc} = -1.40$ V (C) and −1.82 V (B), respectively, whereas only one strong *pre*-wave was found in DMF at $E_{pc} = -1.52$ V (Figures 2a,b). Obviously, *intermolecular* hydrogen bonding (as shown partialy in structure C) is suppressed in DMF due to interactions with the solvent. The stepwise addition of base to a solution of **1** in MeCN led to a decrease of the wave C, which finally disappeared completely with 1 equiv of DBU (Figure 3). In contrast, even 2 equiv of base did not decrease I_{pc}(B), but a slight cathodic shift was found upon addition of less than 1 equiv of base (ΔE_{pc}(B) = 0.04 V) due to the formation of a weakly hydrogen bonded complex between the base, the electrophore, and the carboxylic proton.[18]

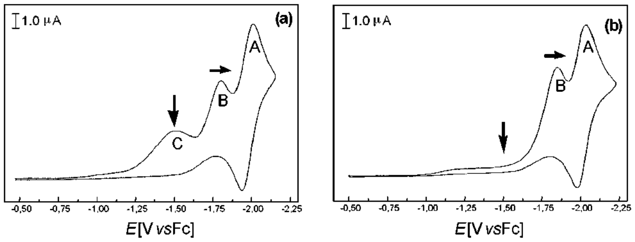

Figure 3. Addition of (a) 0.5 and (b) 1 equiv of DBU to **1** in MeCN.

Stepwise addition of TFMSA to **1** in MeCN led to an increase of current height for E_{pc}(C) due to protonation of the *free* carbonyl functions of the phthalimide (Figure 4a). Additionally, a new *pre*-wave appeared at ca. −0.9 V, which is assigned to an aggregate with one or both carbonyl groups protonated (similar to structure C). Lowering of the concentration slightly decreased the current heights I_{pc} of both *pre*-waves (B and C), but broadening of the signals, however, prevented the observation of the expected, clear cathodic shift for E_{pc}(C).[19] Final evidence came from the multisweep experiments: in both solvents the current heights dropped faster for the *pre*-waves than for the reversible waves, respectively (Figure 4b). This observation can be rationalized by considering a further reaction of the primary phthalimide radical anion as described in the literature for other proton donors.[20] Accordingly, after reduction, the protonation to the 3-hydroxy phthalimidine consumes protons near the electrode. The pH gradient thus generated leads to a rapid disappearance of *pre*-waves C and B.

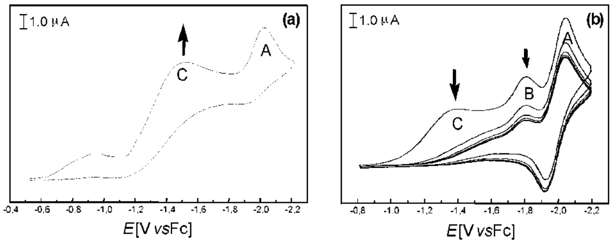

Figure 4. Addition of (a) 0.5 equiv of TFMSA to **1** and (b) multisweep experiment of **1** in MeCN.

The electrochemical behavior of **1-K** in DMF was remarkable. At low scan rates (>20 mV s^{-1}) a reversible wave at $E_{1/2}(A_s) = -1.76$ V (Figure 2c) dominated the CV. Apparently, the potential is anodically shifted with regard to that of the *free* phthalimide ($E_{1/2}$(A) = −2.10 V) because of the intramolecular $C{=}O\cdots K^+\cdots{}^-O_2C$ interaction (as found in the X-ray structure). Additionally, a small reduction wave of the *free* phthalimide was found. Evidence for this assignment came from the addition of acid (upon which the

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potassium salt **1-K** is transferred into its acid form **1**). With ca. 0.5 equiv, the characteristic *intramolecularly* based *pre*-wave of **1** was observed at $E_{pc}(B_a) = -1.55$ V, which disappeared totally in the multisweep experiment (Figure 5).

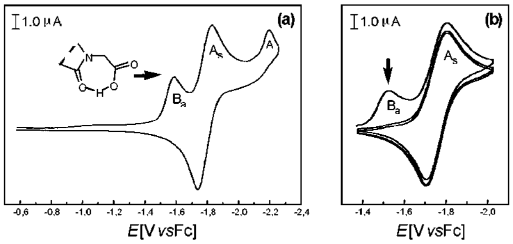

Figure 5. Addition of (a) ca.0.5 equiv of TFMSA to **1-K** in DMF (a acid, s salt) and (b) multisweep experiment with (a).

In agreement with the depicted model, the reduction wave of **1-K** at $E_{1/2}(A_s) = -1.76$ V decreased, whereas the reduction wave of the *free* phthalimide increased significantly. After further addition (ca. 1 equiv), the CV is characterized by a crisp reduction wave for *free* **1** at $E_{1/2} = -2.05$ V, whereas the other waves (i.e., that of **1-K** and the *intramolecular pre*-wave of **1**) were additionally broadened. For the methyl ester **2**, the hydrogen bonding site is blocked and, consequently, solely the reversible reduction wave of the *free* electrophore was found at $E_{1/2} = -1.84$ V (Figure 2d).

The results obtained from the CV measurements were compared to those obtained from IR spectroscopy, which is a well-established technique for the observation of hydrogen bonding.[21] The strong and broad bands attributed to ν C═O of the phthalimide (Figure 6) were found at 1724 cm^{-1} (**1** and **2**) and 1712 cm^{-1} (**1-K**) in the solid state, respectively. **1-K** additionally showed the characteristic ν C═O band of the carboxylate at 1616 cm^{-1}. The slight red shift for the potassium salt **1-K** clearly confirms the participation of the carbonyl group in aggregation processes, whereas compounds **1** and **2** showed similar values as *N*-methyl phthalimide ($\bar{\nu} = 1721$ cm^{-1})[22] indicating the lacking hydrogen bond. For **1**, this observation is in accord with the solid state structure for which only *intramolecular* interactions were reported.[12]

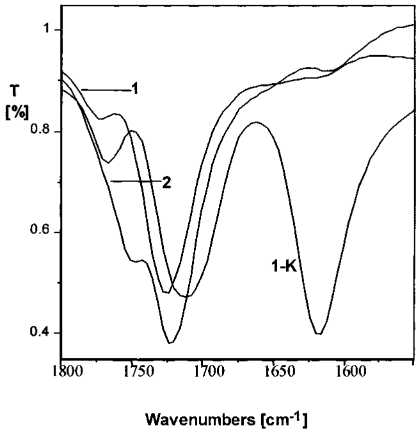

Figure 6. IR spectral data for **1**, **1-K**, and **2** showing the ν C═O region in the solid state (KBr disk).

In summary, we could show that preorientation exists for **1** only in solution via hydrogen bonding and for **1-K** in solution and in the solid state via metal templation. These observations neatly correlate with the reactivity pattern in photodecarboxylation reactions: hydrogen bonding is an activation mode for α-decarboxylation only, whereas metal templation leads to efficient ω-decarboxylation independent of the distance (as seen from the photoreactions). The structural as well as CV and IR spectroscopic information described herein for PET-active phthalimides is also in accord with recent results on acceleration of photoinduced electron transfer reactions by proton as well as Lewis acid catalysis.[23] Detailed studies concerning the correlation of photodecarboxylative ability and the CV and fluorescence behavior of other phthalimido ω-carboxylic acids are currently under investigation.

Acknowledgment. This research project was financially supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, the Volkswagenstiftung, Bayer AG, and Merck KGaA.

Supporting Information Available: IR spectra for **1**, **1-K**, and **2**, additional X-ray data for **1-K**, and cyclic voltammetric details. This material is available free of charge via the Internet at http://pubs.acs.org.

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