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Electronic Effects on Atom Tunneling: Conformational Isomerization of Monomeric *Para*-Substituted Benzoic Acid Derivatives

Shadi Amiri, Hans Peter Reisenauer, and Peter R. Schreiner*

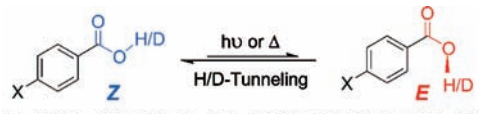
Institute for Organic Chemistry, Justus-Liebig University, Heinrich-Buff-Ring 58, D-35392 Giessen, Germany

Received August 20, 2010; E-mail: prs@org.chemie-uni-giessen.de

Abstract: We present the first generation and spectroscopic identification of the higher-lying *E* conformer of the simplest aromatic carboxylic acid, benzoic acid (**1a**), as its O-deuterated isotopologue (*E*)-d_1-**1a** using matrix-isolation techniques; the parent (*E*)-**1a** could not be observed because of fast H-tunneling to the more stable conformer (*Z*)-**1a**. Even deuterated (*E*)-d_1-**1a** converts quickly back to (*Z*)-d_1-**1a** through D-tunneling with a half-life (τ) of ~12 min in Ar at 11 K. Tunneling computations using an Eckart barrier in conjunction with a CCSD(T)/cc-pVTZ//MP2/cc-pVDZ + ZPVE intrinsic reaction path revealed that τ of (*E*)-**1a** is only $\sim 10^{-5}$ min, in marked contrast to those of simple aliphatic acids, which are in the range of minutes. The electronic substituent effects on D-tunneling in *para*-substituted benzoic acid derivatives (*p*-X-PhCOOD, d_1-**1**) were systematically studied in Ar matrices at 11 K to derive the first Hammett relationships for atom tunneling. σ-Electron donors (X = alkyl) increase the half-life of d_1-**1**, while σ-acceptor/π-donor groups (X = OD, NH_2, halogen) and to an even greater extent a σ-/π-acceptor group (X = NO_2) decrease τ. The latter finding is in line with the smaller *E*-to-*Z* reaction barriers and narrower reaction widths for the isomerization. Tunneling substituent constants (σ^t) for this conformational isomerization were derived experimentally and computationally.

Although double hydrogen transfer in benzoic acid (**1a**) dimers is a fundamental model for studying the molecular dynamics arising from quantum tunneling in complex biological systems,[1,2] there has been no report regarding the conformational isomerizations through tunneling in *monomeric* **1a**; only few simple carboxylic acids have been investigated.[2−4] The lack of systematic studies of electronic substituent effects on tunneling processes motivated us to study the *E*/*Z* isomerizations and the potential H- and D-tunneling in **1** (Scheme 1), especially because the electronic effects in *para*-substituted benzoic acids are one of the pillars upon which our understanding of organic reactivity is built (e.g., through the Hammett equation[5]).

Scheme 1. Conformational Isomerization in **1**



X = H (**1a**), CH_3 (**1b**), *t*-Bu(**1c**), OH/OD (**1d**), Cl (**1e**), NO_2 (**1f**)

The *E*/*Z* conformers of carboxylic acids interconvert through C−O bond rotations (Scheme 1), with the *Z* conformer generally being preferred over a very large temperature range; very few structures, such as glyoxylic acid[6a] and pyruvic[6b] acid, prefer the *E* conformation. While (*E*)-HCOOH [(*E*)-**2**] was first characterized utilizing microwave spectroscopy in the 1970s,[7a] the first IR signatures for (*E*)-HCOOH[7b] and (*E*)-CH_3COOH[8] [(*E*)-**3**] trapped in solid matrices were published only in 1997 and 2003, respectively. In contrast to some of the simple aliphatic acids, the *E* isomers of the aromatic acids have not been studied, although several microwave and IR studies of monomeric (*Z*)-benzoic acid [(*Z*)-**1a**] are available.[9] Noticeably, both trapped (*E*)-**2**[4,10] and (*E*)-**3**[11,12] interconvert to their more stable *Z* isomers through H-tunneling. The lifetime of (*E*)-**2** in solid Ar at 8 K is on the order of minutes; under the same conditions, (*E*)-**3** decays ~10 times faster.[8,12]

The characteristic IR bands for (*Z*)-**1a**, especially the single O−H stretching vibration (3570.5 cm^{-1}, Ar, 11 K) confirmed the presence of only one conformer. We attempted to prepare and identify the higher-lying (*E*)-**1a** either photochemically by irradiation of (*Z*)-**1a** at $\lambda = 254$ nm (**1a** has absorption maxima at $\lambda = 200$, 230, and 280 nm[13]) for 30 min in matrices at 11 K or thermally by flowing (*Z*)-**1a** through an 800 °C quartz glass tube followed by trapping in various matrices at 11 K. Although our CCSD(T)/cc-pVTZ//MP2/cc-pVDZ computations gave an isomerization barrier of 5.0 kcal mol^{-1} (structures optimized using density functional theory at various levels gave similar energy differences; see the Supporting Information), which cannot be overcome thermally at 11 K, we were unable to detect (*E*)-**1a**. The same applies to the *para*-substituted derivatives **1b**−**f**, in stark contrast to the previously observed matrix-isolated (*E*)-**2** and (*E*)-**3**.[7,8]

To examine whether the isomerization through H-tunneling from (*E*)-**1a** to (*Z*)-**1a** is simply too fast on the time scale of our experiments (minutes) or we had not generated the (*E*)-**1a** isomer, we examined d_1-**1a** (OD deuteration) in the same way. Indeed, we were able to record the IR spectrum of (*E*)-d_1-**1a** in Ar at 11 K (Figure 1); its fundamental frequencies ν_{O-D}, $\nu_{C=O}$, and $\delta_{C-H,in\text{-}plane}$ were blue-shifted and the ν_{C-O} and $\delta_{C-H,out\text{-}of\text{-}plane}$ absorptions red-shifted relative to those of (*Z*)-d_1-**1a**.

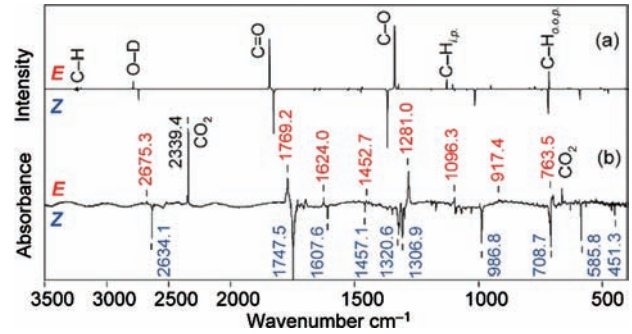


Figure 1. Difference IR spectra of (*E*)-d_1-**1a** (upward-pointing peaks) and (*Z*)-d_1-**1a** (downward-pointing peaks): (a) computed at the MP2/cc-pVDZ level (unscaled); (b) measured in solid Ar at 11 K after 30 min of irradiation at 254 nm. The splitting of the ν_{C-O} band of (*Z*)-d_1-**1a** is due to matrix effects.

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Surprisingly, (*E*)-d_1-**1a** did not persist under these conditions: it converted into (*Z*)-d_1-**1a** with a half-life (τ) of 12 min in Ar (Table 1). The relative temperature independence of the half-lives at 11 and 20 K and the apparently very large primary H/D kinetic isotope effect support the notion of a tunneling mechanism. The D-tunneling of the (*E*)-d_1-**1a** isomer is three orders of magnitude faster than that of (*E*)-d_1-**2**, with a half-life of ~7 days[4] in Ar at 4.3 K. Clearly, the phenyl ring has a decisive electronic effect on the tunneling rate, prompting us to study a selection of *p*ara-substituted, monodeuterated benzoic acids (d_1-**1b**−**f**).

The matrix material influences the tunneling rates significantly (Table 1), a trend also seen in other tunneling processes.[4,14] The rate retardation in N_2 matrices is likely due to formation of a hydrogen-bond complex between the acid function and N_2. Still, the stabilization of the (*E*)-**1a** rotamer in N_2 was not sufficient to allow its spectroscopic observation.

Table 1. Half-Lives τ (min)[a] of (*E*)-d_1-**1a** in Various Matrices

T (K)	Ar	Xe	N_2
11	12 ± 2	22 ± 3	11 ± 1 days
20	12 ± 2	25 ± 3	—[b]

[a] From first-order kinetics measurements based on the slope [k (s^{-1})] of a plot of ln(C=O peak height) vs time. [b] Not determined because of decomposition of the N_2 matrix at this temperature.

The tunneling process was also analyzed through computation of the intrinsic reaction path (IRP) connecting the rotational transition structure (TS-**1a**) with (*E*)-**1a** and (*Z*)-**1a**. A final potential energy curve along the isomerization IRP was then constructed from CCSD(T)/cc-pVTZ energy points and MP2/cc-pVDZ zero-point vibrational energies (ZPVEs). Tunneling probabilities were evaluated using an unscaled asymmetric Eckart potential[15] to the imaginary TS-**1a** barrier frequency $\omega^* = 536i$ cm^{-1} ($394i$ cm^{-1} for TS-d_1-**1a**) as well as the ZPVE-corrected reaction energy of −6.0 kcal mol^{-1} (−6.0 kcal mol^{-1} for d_1-**1a**) and barrier height of +5.0 (+5.3 kcal mol^{-1} for d_1-**1a**). This procedure has been shown to yield tunneling half-lives in good qualitative agreement with experiment for the isotopologues of hydroxycarbene[14] and phenylhydroxycarbene.[16] A vibrational "reaction" mode of (*E*)-**1a** toward TS-**1a** with a frequency of $\omega_0 = 498$ cm^{-1} [358 cm^{-1} for (*E*)-d_1-**1a**] was identified. In good qualitative agreement with the experiment, the computations gave a half-life of 2.8 h (55 min at the MP2/cc-pVDZ level) for (*E*)-d_1-**1a**, while they predicted $\tau \sim 10^{-5}$ min for the H-tunneling in (*E*)-**1a**, which is much too fast to be measured using our present experimental setup. The noted much faster D-tunneling in d_1-**1a** relative to d_1-**2**[4] can be rationalized by the lower reaction barrier [by 2.4 kcal mol^{-1} at the CCSD(T)/cc-pVTZ//MP2/cc-pVDZ level] and especially the much smaller barrier width (Figure 2).

The experimental and computed half-lives for *para*-substituted benzoic acids (Table 2) revealed the preliminary trend that pure σ-electron-donating groups (CH_3, *t*-Bu) increase the tunneling half-life of (*E*)-d_1-**1**, while σ-acceptor/π-donor groups (OD, NH_2, halogen) and to an even greater extent a σ-/π-electron-acceptor group (NO_2) decrease the D-tunneling half-life; the d_1-**1f** analogue had the lowest and narrowest IRP curve among those for d_1-**1** (Figure 2). However, a Hammett plot showed that the substituent constant σ does not correlate well with τ because the tunneling isomerization in **1** apparently is electronically too different from that for simple *para*-substituted benzoic acid ionization (Figure S27). Hence, we specifically derived the tunneling substituent constants σ^t (Table 2) using the relation $\rho\sigma^t = pk_H - pk_X = \log(k_X/k_H)$,[5] with the reaction constant ρ set equal to 1; the excellent fit is depicted in Figure S28 in the Supporting Information. Importantly, the signs of σ and σ^t were the same, even when the absolute values were quite different. Figure 3 underlines these qualitative findings by correlating the computed barrier widths with the experimental half-lives.

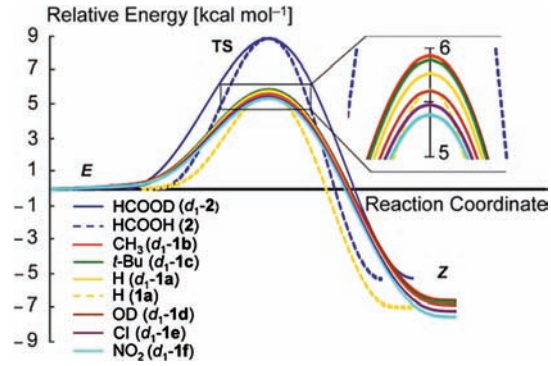

Figure 2. *E*/*Z* isomerization IRPs for **1a**, d_1-**1a**−**f**, **2**, and d_1-**2** computed at the MP2/cc-pVDZ level.

Table 2. Experimental (Ar, 11 K) and Computed (MP2/cc-pVDZ, 11 K; in parentheses) Half-Lives τ of (*E*)-d_1-**1a**−**f** and Derived σ^t Values for the Tunneling *E*/*Z* Isomerizations

	X	τ (min)	σ^t
(*E*)-d_1-**1b**	CH_3	25 ± 2 (188)	−0.38 (−0.53)
(*E*)-d_1-**1c**	*t*-Bu	16 ± 2 (140)	−0.17 (−0.40)
(*E*)-d_1-**1a**	**H**	12 ± 2 (55)	0.00 (0.00)
(*E*)-d_1-**1d**	OD	6 ± 2 (28[a])	+0.26 (+0.30)
(*E*)-d_1-**1e**	Cl	3 ± 1 (8)	+0.60 (+0.85)
(*E*)-d_1-**1f**	NO_2	3 ± 1 (3)	+0.53 (+1.26)

[a] The two C−OD*para* conformers showed slightly different half-lives (for details, see the Supporting Information).

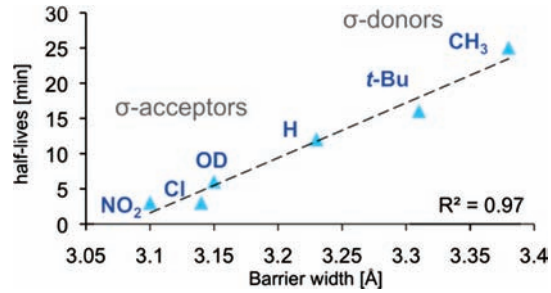

Figure 3. Plot of the barrier widths derived from IRP computations at the MP2/cc-pVDZ vs the experimental half-live of (*E*)-d_1-**1**.

A natural extension of our studies is the examination of conformational tunneling in biologically relevant systems such as amino acids and fatty acids. Comprehensive computational and experimental studies on a generalization of the electronic substituent effects on tunneling processes are in progress.

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Supporting Information Available: Detailed experimental and computational data. This material is available free of charge via the Internet at http://pubs.acs.org.

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