JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

Protonated Carbonic Acid and Reactive Intermediates in the Acidic Decarboxylation of Indolecarboxylic Acids

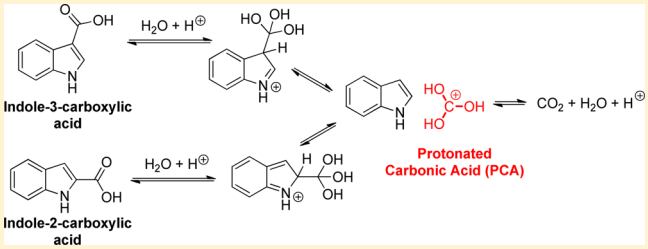
Adelle A. Vandersteen,[†] Scott O.C. Mundle,[‡] and Ronald Kluger*,[†]

[†]Davenport Research Laboratories, Department of Chemistry, University of Toronto, 80 St. George Street, Toronto, Ontario, Canada M5S3H6

[‡]Department of Geology, University of Toronto, 22 Russell Street, Toronto, Ontario, Canada M5S3B1

Supporting Information

ABSTRACT: Elucidation of the mechanism for decarboxylation of indolecarboxylic acids over a wide range of solution acidity reveals the importance of protonated carbonic acid (PCA) as a reaction intermediate. In concentrated acid, the initial addition of water to the carboxyl group of the indolecarboxylic acid leads to a hydrated species that is capable of releasing PCA upon rate-determining carbon−carbon bond cleavage. The overall process is catalytic in water and acid, implicating PCA as a potential carboxylating reagent in the microscopic reverse reaction.



INTRODUCTION

Decarboxylation reactions normally involve the direct formation of CO_2 by a stepwise electrophilic substitution mechanism in which a proton replaces a carboxyl group after formation of CO_2. The accelerated decarboxylation of certain aromatic compounds in concentrated acid solutions has been a puzzling exception to this pattern: the undissociated carboxyl group appears to eliminate CO_2 with the assistance of an additional proton. The very low proton affinity of CO_2 creates an insurmountable energy barrier to the formation of protonated CO_2 (CO_2H^+) as a reaction intermediate.[1,2] However, acid-catalyzed decarboxylation reactions are well-known, and mechanistic proposals have nonetheless assumed the formation of CO_2H^+.[3−8] Our recent kinetic analysis of the decarboxylation of pyrrole-2-carboxylic acid,[9,10] along with theoretical calculations,[11,12] has established a reasonable alternative in which protonated carbonic acid (PCA), first observed by Olah and White in 1968,[13] is the protonated product. Determination of the proton affinity of carbonic acid[14] and the gas-phase structure of PCA[15,16] have been achieved in recent years, further supporting its feasibility as a reaction intermediate. Modification of the acid-catalyzed decarboxylation mechanism to involve a hydrolytic route leads to the conclusion that the reaction proceeds via the formation of a hydrate followed by the release of PCA (rather than CO_2H^+) in the step that cleaves the carbon−carbon bond. In such a reaction, water serves a true catalytic function by altering the path without affecting stoichiometry.

Based on the importance of PCA as a reaction intermediate and the recent applications of this reaction pathway in a variety of areas,[17−20] a complete understanding of the mechanism is of considerable importance. In order to resolve many outstanding questions associated with hydrolytic decarboxylation, we have investigated the decarboxylation reactions of indole-2-carboxylic acid and indole-3-carboxylic acid. These substrates are sufficiently similar to pyrrole-2-carboxylic acid to involve a hydrolytic pathway as a likely mechanism; however, the addition of the fused aromatic ring has a significant effect on their overall reactivity compared to that of pyrrole-2-carboxylic acid.

We have determined the rates of decarboxylation of indole-2-carboxylic acid and indole-3-carboxylic acid over a wide range of solution acidity, including reactions in deuterated media that permit determination of solvent kinetic isotope effects. Previous work by Challis and Rzepa[3] reported the rates of decarboxylation of indole-3-carboxylic acid over a limited range of acidity without consideration of the acid-catalyzed hydrolytic process. The results of the present study provide a complete reaction profile for hydrolytic decarboxylation across both pH and acidity function (H_0) ranges.

RESULTS AND DISCUSSION

Rate constants for the conversion of indole-2-carboxylic acid and indole-3-carboxylic acid to indole and carbon dioxide as a function of Brønsted acidity of the medium (measured as H_0[21] and pH as appropriate) are presented in Figure 1 and Table 1. Indole-3-carboxylic acid undergoes decarboxylation more rapidly than indole-2-carboxylic acid.

In the case of indole-3-carboxylic acid, the data reflect two plateaus and two apparent dissociation constants based on the equation for titration of a dibasic acid. The observations are consistent with both the neutral and protonated forms being converted to products by different mechanisms (Scheme 1).

Received: May 23, 2012
Published: July 17, 2012

dx.doi.org/10.1021/jo301032f | J. Org. Chem. 2012, 77, 6505−6509

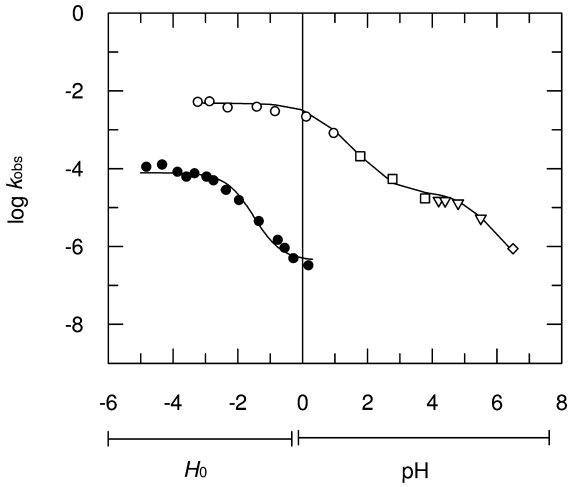


Figure 1. Logarithm of the observed first-order rate coefficients (k_{obs}) for the decarboxylation of indole-2-carboxylic acid (solid) and indole-3-carboxylic acid (open) as a function of solution acidity, measured as H_0[21] or pH at 60 °C. Symbols represent hydrochloric acid solutions (●,○) and 0.1 M buffered solutions of chloroacetic acid (□), acetic acid (▽), and monobasic phosphate (◊) (for all buffered solutions, ionic strength I = 1.0 M with potassium as the counterion). Data are fit to an ionization curve (indole-2-carboxylic acid) and eq 2 (indole-3-carboxylic acid).

The rate equation for Scheme 1 is given below:

$$\frac{d[P]}{dt} = k_1[\mathbf{1H}^+] + k_2[\mathbf{1}] = k_{obs}[S_T] \quad (1)$$

The quantity $[S_T]$ is the total concentration of all protonation states of indole-3-carboxylic acid. A simplified expression for the observed rate coefficient is obtained based on the necessity that $K_2 \ll K_1$:

$$k_{obs} = \frac{K_1k_2 + k_1[H^+]}{(K_1 + [H^+])\left(1 + \frac{K_2}{[H^+]}\right)} \quad (2)$$

Equation 2 was fit to the data for indole-3-carboxylic acid in the H_0/pH rate coefficient profile (Figure 1). The value of the maximum rate coefficient, k_1, was taken as the observed plateau value (k_{obs} = 5.0 × 10^{-3} s^{-1} at H_0 = −3.22) and K_2 as the macroscopic dissociation constant of indole-3-carboxylic acid (pK_2 = 5.0, see K_2 in Scheme 1), which was determined by titration of a solution at 60 °C. Values for k_2 and K_1 were calculated by iterative least-squares analysis of the data using the equation for k_{obs} ($k_2 = 2.5 \times 10^{-5}$; $pK_1 = 0.4$). Indole-2-carboxylic acid is presumably involved in an equilibrium similar to K_1 shown in Scheme 1. Fitting of the data points leads to a value of $pK_{1'} = -1.5$ for indole-2-carboxylic acid.

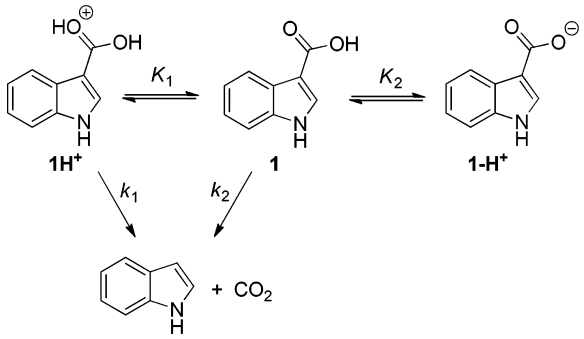
The rate plateau for the decarboxylation reaction of indole-3-carboxylic acid near pH = 4 fits expectations for consequences of the established mechanism of dissociative decarboxylation via the tautomeric zwitterion (**1***, Scheme 2). In that mechanism, the carboxyl group of indole-3-carboxylic acid is predominantly present in its neutral form (**1**), which is converted to (**1***) by steps involving rate-determining transfer of a proton, consistent with the substantial solvent kinetic isotope effect at dilute acid concentrations.[3] Conversion of the carboxylate group of (**1***) to carbon dioxide provides residual electrons required to achieve aromaticity in the indole product. In more dilute acid solutions (pH > 5), the conjugate base of indole-3-carboxylic acid (**1**-H^+) predominates. With the decrease in concentration of proton donors, the rate of decarboxylation decreases. Direct reaction from the conjugate base (**1**-H^+) would require the loss of carbon

Table 1. Observed and Calculated Rate Constants for the Decarboxylation of Indole-2- and Indole-3-carboxylic Acids

indole-2-COOH			
H_0[a]/pH	k_{obs} (s^{-1})	log k_{obs}	log k_{calc}[f]
−4.81	1.1 ± 0.1 × 10^{-4}	−4.0	−4.1
−4.32	1.2 ± 0.1 × 10^{-4}	−3.9	−4.1
−3.84	7.9 ± 0.1 × 10^{-5}	−4.1	−4.1
−3.57	6.0 ± 0.1 × 10^{-5}	−4.2	−4.1
−3.32	7.3 ± 0.1 × 10^{-5}	−4.1	−4.1
−2.95	6.1 ± 0.2 × 10^{-5}	−4.2	−4.2
−2.73	4.8 ± 0.2 × 10^{-5}	−4.3	−4.2
−2.35	2.7 ± 0.1 × 10^{-5}	−4.6	−4.4
−1.94	1.5 ± 0.2 × 10^{-5}	−4.8	−4.8
−1.33	4.4 ± 0.3 × 10^{-6}	−5.4	−5.5
−0.75	1.4 ± 0.2 × 10^{-6}	−5.9	−6.0
−0.54	8.8 ± 0.4 × 10^{-7}	−6.1	−6.1
−0.26	4.8 ± 0.4 × 10^{-7}	−6.3	−6.2
0.20	3.0 ± 1.0 × 10^{-7}[e]	−6.5	−6.4
indole-3-COOH			
H_0[a]/pH	k_{obs} (s^{-1})	log k_{obs}	log k_{calc}[g]
−3.22	5.0 ± 0.2 × 10^{-3}	−2.3	−2.3
−2.86	5.1 ± 0.2 × 10^{-3}	−2.3	−2.3
−2.30	3.6 ± 0.1 × 10^{-3}	−2.4	−2.3
−1.40	3.7 ± 0.1 × 10^{-3}	−2.4	−2.3
−0.83	2.9 ± 0.1 × 10^{-3}	−2.5	−2.4
0.13	2.1 ± 0.1 × 10^{-3}	−2.7	−2.6
0.98	7.9 ± 0.1 × 10^{-4}	−3.1	−3.0
1.8[b]	2.0 ± 0.1 × 10^{-4}	−3.7	−3.7
2.8[b]	5.3 ± 0.1 × 10^{-5}	−4.3	−4.4
3.8[b]	1.7 ± 0.1 × 10^{-5}	−4.8	−4.6
4.2[c]	1.5 ± 0.1 × 10^{-5}	−4.8	−4.7
4.4[c]	1.5 ± 0.1 × 10^{-5}	−4.8	−4.7
4.8[c]	1.3 ± 0.1 × 10^{-5}	−4.9	−4.8
5.5[c]	5.3 ± 0.3 × 10^{-6}	−5.3	−5.2
6.5[d]	8.7 ± 0.4 × 10^{-7}	−6.1	−6.1

[a]Hammett acidity function rates are for HCl solutions.[21] [b−d]Measured pH values of 0.1 M buffered solutions of (b) chloroacetic acid, (c) acetic acid, and (d) monobasic phosphate (all buffered solutions have ionic strength =1.0 M with potassium as the counterion). [e]Larger error is the result of calculating k_{obs} from initial rate kinetics. [f]k_{obs} from fitting of the data to ionization curve. [g]k_{obs} from fitting of the data to eq 2.

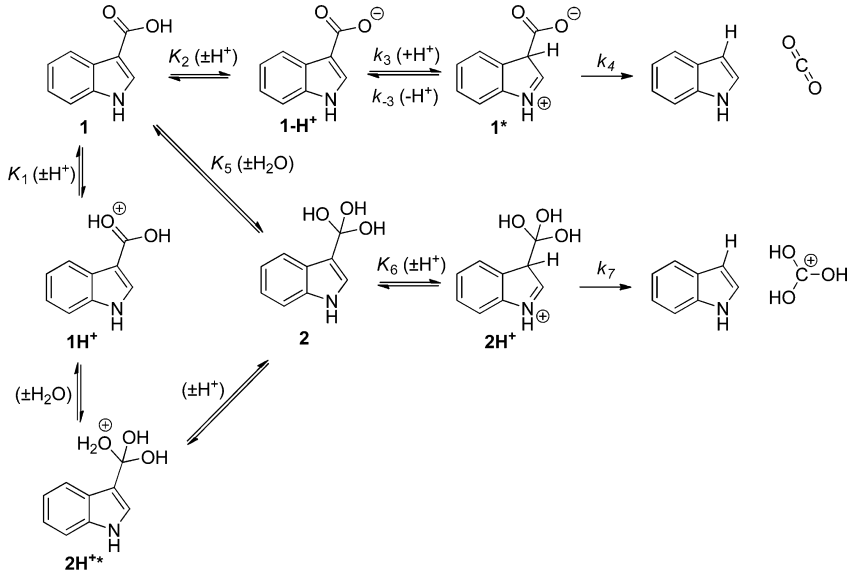
Scheme 1. Decarboxylation of Indole-3-carboxylic Acid Occurs via Two Mechanisms



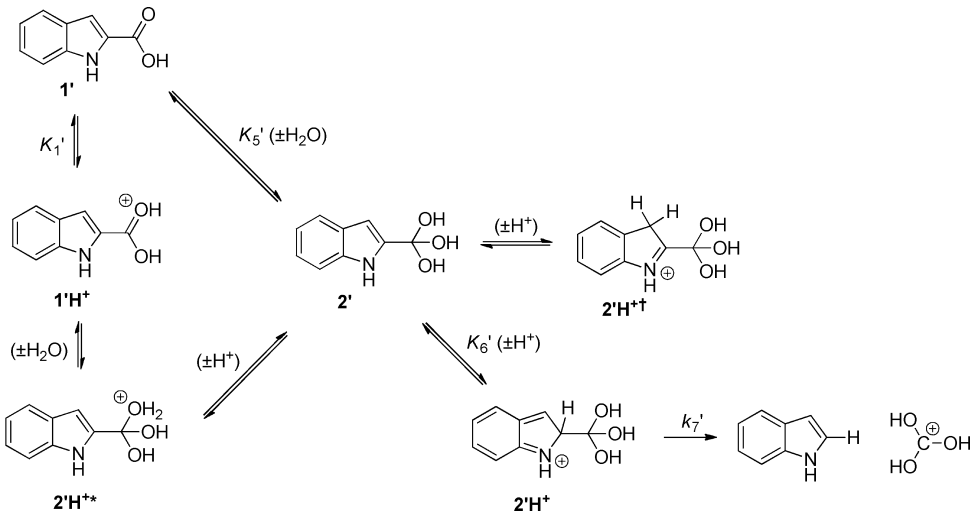
K_1 and K_2 are macroscopic acidity constants; k_1 and k_2 are the apparent rate constants for decarboxylation in the two mechanisms.

dx.doi.org/10.1021/jo301032f | J. Org. Chem. 2012, 77, 6505−6509

Scheme 2. Mechanisms for the Decarboxylation of indole-3-carboxylic Acid



Scheme 3. Hydrolytic Mechanism for the Decarboxylation of Indole-2-carboxylic Acid



dioxide to occur along with formation of a highly energetic residual anion, which creates a very high barrier to this route.

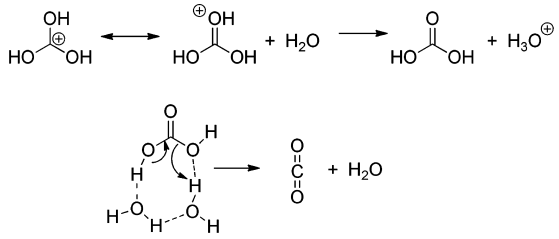
If the dissociative mechanism for decarboxylation were operating in concentrated acid solutions, we would expect that as the acidity of the medium is increased, the observed rate coefficient would decrease (the conjugate acid (**1**) is produced, making the zwitterionic form (**1***) less available). However, the observed first-order rate constant increases with pH < 4 (Figure 1). Interestingly, when the acidity is between pH = 3 and H_0 = 0, the rate is proportional to proton concentration (but not to additional buffer), which is consistent with a mechanism involving specific acid catalysis. As acidity increases beyond this region, the most basic site of indole-3-carboxylic acid, the carboxyl group oxygen, will become protonated (**1H**$^+$).[22] This structure is stabilized by delocalization of the electron pair from nitrogen. The protonated intermediate is subject to rapid addition of water to form the tetrahedral intermediate (**2**) with an expected apparent first-order rate constant of 300 s^{-1} at 25 °C (which is expected to increase to roughly 1 × 10^4 s^{-1} at 60 °C).[23] Upon conversion to the reactive tautomer (**2H**$^+$), carbon−carbon bond cleavage produces PCA and aromaticity is restored to the indole ring system.

The reaction of indole-2-carboxylic acid follows a similar mechanism (Scheme 3) with the additional complication that the reactive tautomer (**2′H**$^+$) is stabilized by delocalization of the lone pair of electrons from nitrogen, leading to a loss of aromaticity. In addition, the preferential protonation at the C-3 position of the indole ring[24] likely results in a higher concentration of the unreactive tautomer (**2′H**$^{+\dagger}$). This is not the case with indole-3-carboxylic acid decarboxylation, as the preferential protonation at the C-3 position produces the reactive predecarboxylation intermediate (**2H**$^+$, Scheme 2). The approximate 50-fold decrease in the observed rate between indole-3- and indole-2-carboxylic acid, shown in the concentrated acid region of Figure 1, is consistent with this consideration.

Following the release of PCA, its in situ decomposition can occur via a series of reasonable steps (loss of a proton, concerted decomposition of carbonic acid[25]) leading to release of carbon dioxide, water, and a proton (Scheme 4). The overall reaction is kinetically equivalent to a process leading to protonated carbon dioxide but avoids that high energy species by producing PCA.

dx.doi.org/10.1021/jo301032f | J. Org. Chem. 2012, 77, 6505−6509

Scheme 4. In Situ Decomposition of Protonated Carbonic Acid



Further insight into the hydrolytic decarboxylation mechanism comes from the solvent kinetic isotope effect (SKIE) $k_H/k_D = 1.7$ at $H_0 = 0.98$ for the decarboxylation of indole-3-carboxylic acid. In concentrated acid solutions, the SKIE decreases to $k_H/k_D = 1$ at $H_0 = -2.30$. This pattern of SKIE values is consistent with the presented mechanisms. In dilute acid solutions, the mechanism of decarboxylation is dissociative, leading to formation of CO_2 from the neutral tautomer of the reactant. In this mechanism, formation of the reactive tautomer (**1***) is rate-determining via proton transfer (where SKIE is significant). In more acidic solutions the hydrolytic mechanism becomes dominant, with rate-limiting carbon−carbon bond-breaking of the protonated hydrate ($\mathbf{2H^+}$) (and therefore a reduced SKIE).

Once in the hydrated form, the electronic effects of the carboxyl group on the protonation of the aromatic ring are eliminated and replaced by that of an ortho acid ($-C(OH)_3$) (**2**). This substituent should have a small effect on the pK_a for C-protonation of the indole ring based on the effects of similar orthoesters ($\sigma_{C(OMe)3,meta} = -0.03$ and $\sigma_{C(OMe)3,para} = -0.04$).[26] This suggests that the pK_a of the reactive intermediate (**2**) at equilibrium would be similar to that of unsubstituted indole ($pK_a = -2.4$).[27] Therefore, the reaction must proceed via initial protonation of the carboxyl group to promote hydration. Once hydrated, protonation of the aromatic ring is dramatically facilitated, unlocking the pathway for the subsequent release of PCA.

A simplified rate expression (eq 3) can be used to represent the overall hydrolytic decarboxylation pathway where the conjugate acid of indole-3-carboxylic ($\mathbf{1H^+}$) acid is the initial substrate. Since the solvent isotope effect indicates that proton transfer steps are not rate-determining, we can estimate the rate constant for cleavage of the carbon−carbon bond (k_7) in concentrated acid solutions for indole-3-carboxylic acid (eq 4).

$$v = k_{obs}[\mathbf{1H^+}] = k_7[\mathbf{2H^+}] \quad (3)$$

$$k_7 = k_{obs}[\mathbf{1H^+}]/[\mathbf{2H^+}] \quad (4)$$

The value of the equilibrium constant for $[\mathbf{1H^+}]/[\mathbf{2H^+}]$ can be estimated from a thermodynamic cycle between ($\mathbf{1H^+}$) and ($\mathbf{2H^+}$) that follows K_1, K_5, and K_6 as shown in Scheme 2. As noted above, the $pK_1 = 0.4$ for O-protonated indole-3-carboxylic acid. An estimate of the extent of hydration of the carboxylic acid is possible by extension of previously calculated values. The equilibrium constant for addition of water to the carboxyl group of methyl glycine (N-protonated) was estimated by Guthrie and Cullimore[28] to be about10^{-6}, which is a good model for indolecarboxylic acids based on the location of the nitrogen substituent. Therefore, the log of the equilibrium constant (K_5) for hydration is ca. −6 while the pK_6 of the C-protonated indole derivative is approximately −2.4. Therefore, the overall equilibrium $[\mathbf{1H^+}]/[\mathbf{2H^+}]$ is approximately equal to 0.4−6−2.4 = −8. This leads to an estimate for the carbon−carbon bond-breaking step of $k_7 \approx k_{obs} \times 10^8 = 10^5\ s^{-1}$ at 60 °C and between 10^3 and $10^4\ s^{-1}$ at 25 °C.

The hydrolytic decarboxylation pathway permits a more rapid reaction in acid solution than does the neutral dissociative reaction mechanism because the latter requires rate-determining formation of the minor tautomer by protonation of the conjugate base on carbon at low acid concentrations. An important consequence is that the microscopic reverse reaction in acidic solution is carboxylation of indole. This should occur via a Friedel−Crafts reaction of PCA, a process in which water and a proton would be catalytic in the overall addition of CO_2.

We propose, by extension, that it is also likely that a Lewis acid could provide the necessary activation to produce a complex of carbonic acid analogous to PCA. Interestingly, Lewis acid promoted carboxylation reactions were demonstrated by Olah and co-workers[29] and recent studies show that regioselective carboxylations of derivatives of both pyrrole and indole are possible.[30] Since protonated CO_2 is too high in energy to exist as a reasonable intermediate in decarboxylation (and hence, in carboxylation), it is possible that similar Lewis acid complexes of CO_2 would be equally high in energy. On the other hand, reactions involving Lewis acid complexes of carbonic acid would be analogous to the more energetically feasible PCA.

CONCLUSION

We have reported kinetic analysis for the decarboxylation of indolecarboxylic acids over a wide range of solution acidities. In dilute acid solutions, the rate-determining step involves formation of the zwitterionic intermediate that is capable of losing CO_2 directly. In concentrated acid solutions, a route for acid catalysis leads to the addition of water to the carboxyl group, resulting in expulsion of the energetically feasible PCA. In this hydrolytic mechanism, the rate-determining step is carbon−carbon bond cleavage. By investigating the hydrolytic decarboxylation pathway for indolecarboxylic acids, we have been able to show that the expulsion of water from the addition intermediate has a lower barrier than that of carbon−carbon bond cleavage to form PCA.

EXPERIMENTAL SECTION

Commercial indole-2-carboxylic acid, indole-3-carboxylic acid, and potassium chloride were used as purchased. Buffers and acid solutions were made from reagent-grade chemicals with distilled water or deuterium oxide.

Kinetics of Decarboxylation. The rates of decarboxylation of indole-2-carboxylic acid and indole-3-carboxylic acid were measured for reactions in hydrochloric acid. The rate of decarboxylation of indole-3-carboxylic acid was also measured in 0.1 M buffers of chloroacetic acid, acetic acid, and monobasic phosphate where the ionic strength (I) of all buffered solutions was maintained at I = 1.0 M by addition of potassium chloride. All measurements were carried out in solutions maintained at 60 °C. The reaction was monitored by the decrease in absorbance at 300 nm (indole-2-carboxylic acid) or 291 nm (indole-3-carboxylic acid) with a UV−vis spectrometer, whose cell compartment was controlled within ±0.1 °C. Data were collected with an interfaced computer, and the observed first-order rate constants (Table 1) were calculated from nonlinear regression fitting to the integrated first-order rate expression. For slow reactions, the method of initial rates was used to calculate rate constants. For determination of solvent kinetic isotope effects, reactions were conducted using comparable concentrations of hydrochloric acid (in water) and deuterium chloride (in deuterium oxide).

dx.doi.org/10.1021/jo301032f | J. Org. Chem. 2012, 77, 6505−6509

■ ASSOCIATED CONTENT

Supporting Information

UV spectra and proton NMR spectra of reactants and UV spectrum of the common product from decarboxylation reactions. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: rkluger@chem.utoronto.ca.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank NSERC Canada for continued support through a Discovery Grant. A.A.V. thanks OGSST for a scholarship.

■ REFERENCES

(1) Guthrie, J. P. *Bioorg. Chem.* **2002**, *30*, 32−52.
(2) Traeger, J. C.; Kompe, B. M. *Org. Mass Spectrom.* **1991**, *26*, 209−214.
(3) Challis, B. C.; Rzepa, H. S. *J. Chem. Soc., Perkin Trans. 2* **1977**, 281−286.
(4) Hay, R. W.; Taylor, M. J. *Chem. Commun.* **1966**, 525.
(5) Johnson, W. S.; Heinz, W. E. *J. Am. Chem. Soc.* **1949**, *71*, 2913−2918.
(6) Longridge, J. L.; Long, F. A. *J. Am. Chem. Soc.* **1968**, *90*, 3092−3098.
(7) Schubert, W. M. *J. Am. Chem. Soc.* **1949**, *71*, 2639−2644.
(8) Dunn, G. E.; Lee, G. K. J. *Can. J. Chem.* **1971**, *49*, 1032−1035.
(9) Mundle, S. O. C.; Kluger, R. *J. Am. Chem. Soc.* **2009**, *131*, 11674−5.
(10) Mundle, S. O. C.; Lacrampe-Couloume, G.; Sherwood Lollar, B.; Kluger, R. *J. Am. Chem. Soc.* **2010**, *132*, 2430−6.
(11) Cheng, X.; Wang, J.; Tang, K.; Liu, Y.; Liu, C. *Chem. Phys. Lett.* **2010**, *496*, 36−41.
(12) Zhang, X. H.; Geng, Z. Y.; Wang, Y. C. *Sci. China Chem.* **2011**, *54*, 762−768.
(13) Olah, G. A.; White, A. M. *J. Am. Chem. Soc.* **1968**, *90*, 1884−1889.
(14) Gerbaux, P.; Turecek, F. *J. Phys. Chem.* **2002**, *106*, 5938−5950.
(15) Andrei, H.-S.; Nizkorodov, S. A.; Dopfer, O. *Angew. Chem., Int. Ed.* **2007**, *46*, 4754−4756.
(16) Chiavarino, B.; Crestoni, M. E.; Fornarini, S.; Lanucara, F.; Lemaire, J.; Maitre, P. *ChemPhysChem* **2009**, *10*, 520−522.
(17) Lu, P.; Sanchez, C.; Cornella, J.; Larrosa, I. *Org. Lett.* **2009**, *11*, 5710−5713.
(18) Rodriguez, N.; Goosen, L. J. *Chem. Soc. Rev.* **2011**, *40*, 5030−5048.
(19) Kim, S. H.; Lim, J. W.; Lim, C. H.; Kim, J. N. *Bull. Korean Chem. Soc.* **2012**, *33*, 620−624.
(20) Zhang, X. H. *J. Mol. Struct.* **2012**, *1015*, 12−19.
(21) Paul, M. A.; Long, F. A. *Chem. Rev.* **1957**, *57*, 1−45.
(22) Andonovski, B. S.; Stojkovic, G. M. *J. Serb. Chem. Soc.* **1999**, *64*, 775−787.
(23) Martin, R. B. *J. Am. Chem. Soc.* **1967**, *89*, 2501−2502.
(24) Hinman, R. L.; Whipple, E. B. *J. Am. Chem. Soc.* **1962**, *84*, 2534−2539.
(25) Guthrie, J. P. *Can. J. Chem.* **1999**, *77*, 934−942.
(26) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165−195.
(27) Andonovski, B. S. *Croat. Chem. Acta* **1999**, *72*, 711−726.
(28) Guthrie, J. P.; Cullimore, P. A. *Can. J. Chem.* **1980**, *58*, 1281−1294.
(29) Olah, G. A.; Torok, B.; Joschek, J. P.; Bucsi, I.; Esteves, P. M.; Rasul, G.; Prakash, G. K. S. *J. Am. Chem. Soc.* **2002**, *124*, 11379−11391.
(30) Nemoto, K.; Onozawa, S.; Egusa, N.; Morohashi, N.; Hattori, T. *Tet. Lett.* **2009**, *50*, 4512−4514.