Kinetics and Mechanisms of Decarboxylation of 4-Phenylallophanate Anions

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The decarboxylation of a series of 4-phenylallophanate anions has been studied as a function of pH and buffer concentration. A changeover in mechanism is revealed from Hammett and Brønsted correlations, entropy values, and solvent isotope effects. A concerted mechanism in acid and neutral media is proposed, whereas in basic media the results may be explained by a spontaneous decomposition or by a cyclic reaction with involvement of a molecule of water.

Owing to its biological interest, the study of CO_2 reactions to and from a nitrogen atom has been the subject of a considerable amount of work on compounds such as carbamic acid anions [1–6] and carboxyimidazolidone, which has a structure similar to that of biotin.[7–9] These compounds have been used as models for the study of the functioning of this coenzyme system. In this work we have paid particular attention to the reactivity of another model, that of the anion of 4-phenylallophanic acid with a substituted or unsubstituted benzene ring.

Allophanic acid, which is unstable,[10] is an intermediate in the enzymatic cleavage of urea;[11–15] it is also an intermediate in the hydrolysis of its esters, the allophanates,[16] some of which are known for their therapeutic and agrochemical properties.[17–24]

The choice of this substrate was prompted by the fact that *N*-carboxybiotin, which is involved in enzymatic carboxylation and transcarboxylation reactions,[25–28] has a structure similar to that of allophanates, and that the nucleophilicity of biotin is of the same order of magnitude as that of the phenylureas, which are the leaving groups of the 4-phenylallophanate anion decarboxylation. Our study concerned a series of 4-phenylallophanate anions: C_6H_4X–NH–CO–NH–CO_2^- variously substituted on the benzene ring (X = 4-OMe, H, 4-Cl, 4-Br, and 3-NO_2).

Results

Two reaction pathways, A and B, may be considered for the hydrolysis of the C_6H_4X–NH–CO–NH–CO_2^- anion according to Scheme 1. In view of the relative stability of the urea

$$C_6H_4X\text{–NH–CO–NH–}CO_2^- \xrightarrow[\text{pathway A}]{k_a} C_6H_4X\text{–NH–CO–}NH_2 + CO_2$$

$$\text{pathway B}\ \downarrow\ k_{b1}$$

$$C_6H_4X\text{–NH–}CO_2^- + NH_2CO_2^- \xrightarrow{k_{b2}} XC_6H_4NH_2 + NH_3 + 2CO_2$$

Scheme 1.

structure, =N–CO–N=, pathway A seems to be the more probable one. This is confirmed by the following results: (*a*) phenylurea was identified by t.l.c. at the end of the hydrolysis reaction; (*b*) for each phenylallophanate anion, the u.v. spectrum at the end of hydrolysis was identical with that of the corresponding phenylurea obtained under the same pH and concentration conditions; (*c*) no variation in the u.v. spectrum was observed at the end of the reaction when the pH varied on either side of the p*K* value of the corresponding aniline.

Influence of pH *on the Rate of Hydrolysis.*—Figure 1 shows the variation, as a function of the pH, of the logarithm of the hydrolysis rate constant for the 4-phenylallophanate anion,

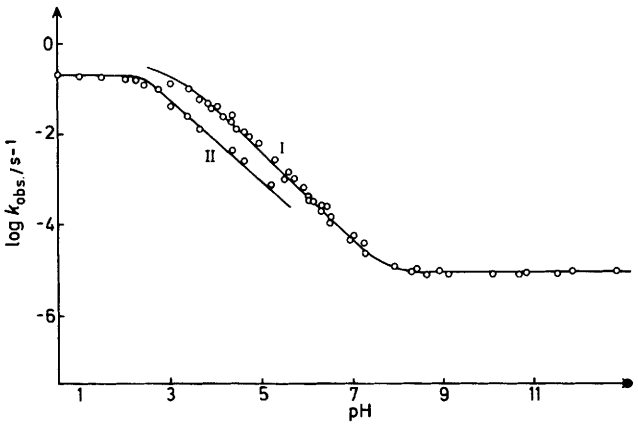


Figure 1. Plots of log $k_{obs.}$ *vs.* pH for the hydrolysis of the phenylallophanate anion at 25 °C (I) and at 10 °C (II), μ = 1 (KCl)

extrapolated to zero buffer concentration. The shape of the plot obtained at 25 °C shows a linear slope of −1.00 (±0.05; r = 0.999), followed by a plateau at the highest pH values and preceded by the beginning of a plateau, which was confirmed at a temperature of 10 °C.

General Acid Catalysis.—The hydrolysis reaction for 4-phenylallophanate anions undergoes general acid catalysis. The results are given in Tables 1 and 2. For certain buffers, such as CH_2ClCO_2H and $CHCl_2CO_2H$, the reaction rate is too high to be measured at pH values close to the p*K* of the acid. The catalytic constant k_{AH} was determined at pH values very much greater than the p*K* value in the presence of other buffers.[6]

From the results given in Tables 1 and 2 a Brønsted correlation between the catalytic constants k_{AH} and the p*K* values of the catalysing acids was obtained:

$$\log k_{AH} = -\alpha pK + G \qquad (1)$$

For the unsubstituted phenyl derivative, by plotting all the acids on the same line, a value of 0.60 was obtained for the coefficient α, with a low correlation coefficient (r = 0.891). But Figure 2 enables three buffer groups located on three segments of line *a*, *u*, and *c*, with an average slope $\alpha = 0.78 \pm 0.02$, to be distinguished. Each line is obtained with a very good correlation coefficient ($r = 0.997 \pm 0.002$). Line *a* is obtained with anionic acids, line *u* with uncharged acids, and line *c* with cationic acids.

The values of constant G in equation (1) are different for each type of buffer and are in the ratio of $G_a:G_u:G_c = 39:11:1$ taking G_c as the reference value. We assumed that for the other allophanate derivatives these relative values could be used to

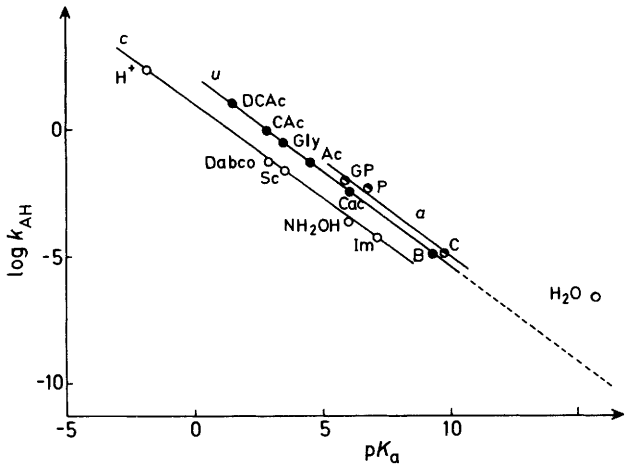


Figure 2. Brønsted dependence of k_{AH} for the hydrolysis of the phenylallophanate anion. Anionic acids (*a*), uncharged acids (*u*), cationic acids (*c*)

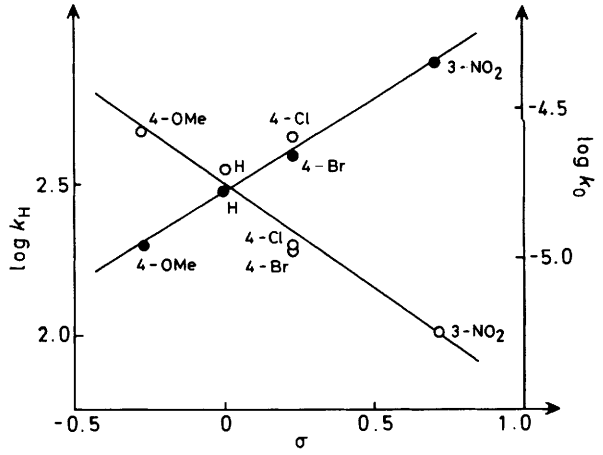


Figure 3. Plots of log k_H (○) and log k_0 (●) *vs.* σ, the Hammett substituent constant

correct the catalytic constants measured in various type of buffers. The corrected values enabled α to be determined for the various substituents: 4-OMe (0.77), 4-Cl (0.74), 4-Br (0.74), and 3-NO_2 (0.72).

Solvent Isotope Effect.—The solvent isotope effect on the reaction rate was investigated for various parts of the curve in Figure 1. The results are summarized in Table 3.

Temperature Effect.—The measurement of the rate constant at several temperatures enabled us to calculate the values of the thermodynamic parameters from the various decarboxylation rate constants of the derivatives examined. The results are summarized in Table 4.

Substituent Effect.—The bimolecular rate constants $k_H = k_{obs.} a_H$ were determined from the descending part of the curve in Figure 1, where the rate constant is proportional to the proton activity a_H. A Brønsted correlation between constants k_H and pK values of the leaving phenylurea group was observed with a coefficient $\beta = 0.84$ ($r = 0.989$). Moreover, a Hammett straight line with a coefficient $\rho = -0.72$ ($r = 0.988$) was obtained (Figure 3).

Brønsted correlations ($\beta = -0.71$, $r = 9.995$) and Hammett correlations ($\rho = 0.61$, $r = 0.996$) were also obtained from pH-independent constants measured in basic media.

Table 5 summarizes all the data used to establish these correlations.

Discussion

The pH–*Rate Profile.*—The plot of the variation of log $k_{obs.}$ with pH, obtained at 25 °C with the 4-phenylallophanate anion (Figure 1), shows a tendency in most acidic media to attain a plateau, which can be interpreted as a protonation of the substrate. The rate constants measured at 10 °C enabled the pK of the protonated substrate to be estimated as 2.5. The phenylallophanate molecule possesses several protonation sites in moderately acidic media: the carboxylate group, the oxygen atom of the ureido group, or possibly the nitrogen atom adjacent to the carboxylate group. Various determinations by u.v., i.r., or n.m.r. spectroscopy showed that ureas are protonated on the oxygen, the *O*-protonated form being stabilized by resonance:[29] The pK of the protonated phenylurea is −1.3.[29] The substitution of the proton of this molecule by a carboxylate group may result in a reduction in the pK, following additional delocalization of the nitrogen lone pair by the carboxylate group. A reduction of 11.0 units in the pK of aliphatic monothiocarbamates, compared with that of the parent amines, has been determined by Jencks and co-workers.[6] Consequently the value of 2.5 for the pK determined in an acidic medium at 10 °C cannot correspond to the protonation of the urea group and must be attributed to that of the carboxylate group. A plateau in acidic media has been found also for the decarboxylation rate of 4-nitrophenylcarbamate by Johnson and Morisson[4] and was also attributed to the protonation of the carboxylate group.

Two kinetically equivalent reaction schemes (Schemes 2 and 3) may account for the plot in Figure 1.

$$\mathrm{PhNHCO{-}NHCO_2^-} + \mathrm{H_3O^+} \overset{1/K_{SH}}{\rightleftharpoons} \mathrm{PhNHCO{-}NHCO_2H} \quad \downarrow k \quad \text{products}$$

Scheme 2.

$$\mathrm{PhNHCO{-}NHCO_2^-} + \mathrm{H_3O^+} \overset{1/K_{SH}}{\rightleftharpoons} \mathrm{PhNHCO{-}NHCO_2H}$$

$$\mathrm{PhNHCO{-}NHCO_2^-} + \mathrm{H_3O^+} \xrightarrow{k'} \text{products}$$

Scheme 3.

The corresponding rate laws are written:

$$k_{obs.2} = \frac{k[\mathrm{H_3O^+}]}{K_{SH} + [\mathrm{H_3O^+}]} \quad (2)$$

$$k_{obs.3} = \frac{k'K_{SH}[\mathrm{H_3O^+}]}{K_{SH} + [\mathrm{H_3O^+}]} \quad (3)$$

These account for the plateau in highly acidic media if $[\mathrm{H_3O^+}] \gg K_{SH}$, and for the line of slope −1 if $K_{SH} \gg [\mathrm{H_3O^+}]$.

Table 1. General acid catalysis of $PhNHCONHCO_2^-$ decarboxylation at 25 °C in water (μ 1.0, KCl)

Buffer or catalyst	pK_a	pH	$[B]_t$/M Range	k_{HA}/M^{-1} s^{-1}
H^+	−1.74[a]			343
Dichloroacetic acid (DCAc)	1.48[b]	6.92	0.02—0.08	9.6
		6.97	0.02—0.10	10.7
Chloroacetic acid (CAc)	2.87[c]	5.73	0.02—0.80	1.21
		7.01	0.02—0.50	0.90
		7.25	0.02—0.50	0.63
Triethylenediamine·2HCl (Dabco)	3.00[d]	3.90	0.07—0.71	6.0×10^{-2}
		4.16	0.08—0.82	6.8×10^{-2}
Glycolic acid (Gly)	3.62[a]	3.98	0.10—1.00	0.212
		4.30	0.10—1.00	0.227
		4.69	0.10—1.00	0.306
Semicarbazide–HCl (Sc)	3.83[e]	3.84	0.05—0.30	2.30×10^{-2}
		4.15	0.05—0.30	2.80×10^{-2}
		4.44	0.05—0.30	2.50×10^{-2}
Acetic acid (Ac)	4.61[a]	4.58	0.10—1.00	4.4×10^{-2}
		4.93	0.10—1.00	4.4×10^{-2}
		5.26	0.10—1.00	4.9×10^{-2}
		5.56	0.10—1.00	4.7×10^{-2}
Acetic acid (in D_2O)		4.67	0.05—0.20	4.5×10^{-2}
		5.10	0.05—0.20	5.1×10^{-2}
		5.45	0.05—0.20	5.8×10^{-2}
		5.81	0.05—0.20	5.0×10^{-2}
β-Glycerophosphate (GP)	6.00[a]	5.49	0.04—0.44	1.20×10^{-2}
		5.98	0.04—0.40	8.9×10^{-2}
		6.29	0.04—0.37	1.00×10^{-2}
Hydroxylamine–HCl	6.09[f]	5.68	0.10—1.00	1.9×10^{-4}
		6.28	0.10—1.00	1.3×10^{-4}
		6.97	0.05—0.50	2.8×10^{-4}
Cacodylic acid (Cac)	6.15[a]	5.81	0.10—1.00	3.48×10^{-3}
		6.19	0.10—1.00	2.92×10^{-3}
		6.42	0.10—1.00	2.65×10^{-3}
Phosphate (P)	6.8[a]	6.00	0.03—0.67	5.52×10^{-3}
		6.53	0.02—0.25	2.74×10^{-3}
		7.22	0.02—0.19	4.24×10^{-3}
Imidazole (Im)	7.21[a]	6.94	0.015—0.30	4.6×10^{-5}
		7.24	0.02—0.40	4.5×10^{-5}
Borate (B)	9.4[a]	8.38	0.02—0.20	1.36×10^{-5}
		8.60	0.01—0.20	0.62×10^{-5}
Carbonate (C)	9.78[a]	8.83	0.08—0.84	1.12×10^{-5}
		9.09	0.07—0.75	1.25×10^{-5}
		10.09	0.02—0.43	1.14×10^{-5}
Water	15.74[g]			1.74×10^{-7}[g]

[a] See ref. 6. [b] Handbook of Chemistry and Physics, 54th edition. [c] See ref. 30. [d] The Merck index, 9th edition. [e] E. H. Cordes and W. P. Jencks, *J. Am. Chem. Soc.*, 1962, **84**, 4319. [f] E. S. Hand and W. P. Jencks, *J. Am. Chem. Soc.*, 1962, **84**, 3503. [g] From experiments in 0.001—1.0M-NaOH, $k_{H_2O} = 0.965 \times 10^{-5}$ s^{-1}/55.5M = 1.74×10^{-7} M^{-1} s^{-1}.

Scheme 2 was considered by Caplow [7] for the decarboxylation catalysed by the proton of a molecule possessing an allophanate function, *N*-carboxy-2-imidazolidone. According to these authors, the unimolecular decomposition of the acid could take place through a cyclic mechanism leading to the formation of an enol. For phenylallophanate, this could be as illustrated in Scheme 4.

This scheme could explain the proton-catalysed reaction, but it corresponds to a specific acid catalysis mechanism and cannot therefore account for the general acid catalysis observed. Moreover, since the proton falls on the Brønsted line obtained for other acids of the same type, this mechanism must be rejected, even for the reaction of the proton. The plot of the variation of log $k_{obs.}$ with the pH may therefore be interpreted by Scheme 3, in which general acid catalysis is involved in the second step.

To account for the pH-independent reaction in basic media, a term k_0 must be added to the term $k'[H_3O^+]$ and the rate law accounting for the plot becomes:

$$k_{obs.} = \frac{K_{SH}(k'[H_3O^+] + k_0)}{K_{SH} + [H_3O^+]k} \quad (4)$$

Mechanism in Acidic and Neutral Media.—The results obtained in this pH range with phenylallophanate anions are very similar to those of Ewing, Lockshon, and Jencks,[6] and Johnson and Morrison[4] for the decarboxylation of *N*-phenylcarbamate anions: (*a*) general acid catalysis with acids of pK between −1.75 and 9.8 for allophanates and between −1.75

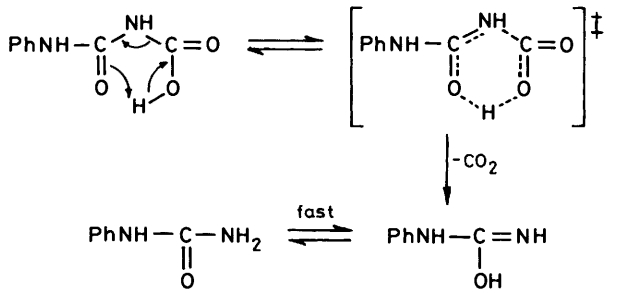
Table 2. General acid catalysis of $XC_6H_4NHCONHCO_2^-$ decarboxylation at 25 °C in water (μ 1.0, KCl)

X	Buffer of catalyst	pK_a[a]	pH Range	k_{HA}/M^{-1} s^{-1}	
3-NO_2	H^+	−1.74		101	
	Acetic acid	4.61	4.17—5.40	0.018	(r = 0.999)
	Phosphate	6.8	5.96—7.28	3.04×10^{-3}	(r = 0.999)
	Water	15.74		4.58×10^{-7}[b]	
4-Cl	H^+	−1.74		190	
	Acetic acid	4.61	4.17—5.40	0.023	(r = 0.994)
	Phosphate	6.8	5.96—7.28	4.67×10^{-3}	(r = 0.999)
	Water	15.74		2.58×10^{-7}[b]	
4-Br	H^+	−1.74		192	
	Acetic acid	4.61	4.17—5.40	0.0245	(r = 0.999)
	Phosphate	6.8	5.96—7.28	4.25×10^{-3}	(r = 0.999)
	Water	15.74		2.27×10^{-7}[b]	
4-OMe	H^+	−1.74		480	
	Acetic acid	4.61	4.17—5.40	0.038	(r = 0.999)
	Phosphate	6.8	5.96—7.28	5.73×10^{-3}	(r = 0.963)
	Water	15.74		1.13×10^{-7}[b]	

[a] See ref. 6. [b] From experiments in 0.001—1.00M-NaOH, $k_{H_2O} = k_0$ s^{-1}/55.5M.

Table 3. Solvent deuterium isotope effects for $PhNHCONHCO_2^-$ decarboxylation in water (μ 1.0, KCl)

pH Profile	Medium	k^{D_2O}	k^{H_2O}	k^{H_2O}/k^{D_2O}
Acidic plateau (at 10 °C)	[HCl] = 0.01	0.081	0.168	2.1
	0.1	0.087	0.202	2.3
	1.0	0.091	0.204	2.2
Slope unity (at 25 °C)	Acetate buffer			
	k_H	328	343	1.05
	k_{HA}	5.33×10^{-2}	4.63×10^{-2}	0.87
Basic plateau (at 50 °C)	[NaOH] = 0.005	2.36×10^{-4}	2.42×10^{-4}	1.02
	0.01	2.33×10^{-4}	2.45×10^{-4}	1.05



Scheme 4.

Table 4. Activation parameters for $XC_6H_4NHCONHCO_2^-$ decarboxylation in water (μ 1.0, KCl)

X	pH Profile	Rate constants/s^{-1}				$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1}	E_a/kcal mol^{-1}
H	Acidic plateau	t/°C	15	10			
		$k_{obs.}$	0.260	0.203		−43	
	Slope unity	t/°C	11	25			
	In acetate buffer	k_H	112	343		−11.9	13.5
		k_{HA}	0.0107	0.0460		−16	19.0
	Basic plateau	t/°C	25	40.3	50.4		
		$10^5 k_0$	0.98	8.10	28.4	−6	24.7
	Basic plateau	t/°C	25	50			
4-OMe		$10^5 k_0$	0.626	21.2		−2.1	
4-Br			1.49	43.3		−4.3	
4-Cl			1.40	34.3		−8.3	
3-NO_2			2.40	52.0		−11.0	

Table 5. Bimolecular rate constants k_H and alkaline rate constants k_0 for the decarboxylation of $XC_6H_4NHCONHCO_2^-$ at 25 °C in water (μ 1.0, KCl)

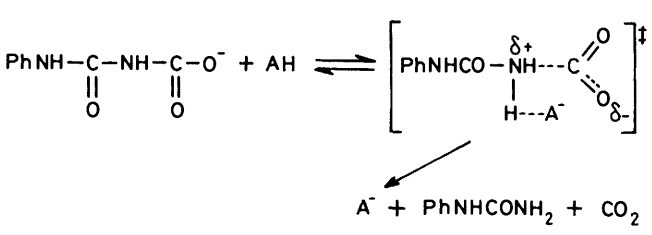
X	pK_a* Urea	σ	k_H/M^{-1} s^{-1}	10^5 k_0/s^{-1}
4-OMe	−0.94	−0.268	480	0.626
H	−1.17	0	343	0.965
4-Br	−1.38	0.227	192	1.26
4-Cl	−1.37	0.232	190	1.43
3-NO_2	−1.78	0.710	101	2.54

* Values computed from pK_a = −1.17 − 0.86 σ, using the data obtained by C. J. Giffney and C. J. O'Connor.[29]

and 15 for carbamates;[4,6] (*b*) a value for the Brønsted α parameter of 0.78 for allophanates and 0.84 for carbamates;[6] (*c*) influence of the pK of the leaving group on the proton catalytic constant k_H:β_{lg} = 0.84 for allophanates and 0.71 for carbamates.[4]

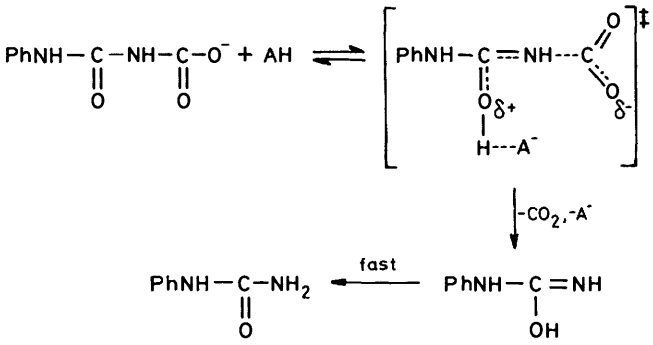
The solvent isotope effects are a little different. In the case of 4-nitrophenylcarbamate, normal isotope effects were observed for catalysis by buffers[6] ($k^{H_2O}_{HCO_3^-}/k^{D_2O}_{DCO_3^-}$ = 1.50) and an inverse isotope effect for catalysis by proton ($K^{H_2O}_H/k^{D_2O}_D$ = 0.67).[6] A normal isotope effect of 1.75 was also determined in the phosphate-buffered catalysis of the decarboxylation of *N*-carboxyimidazoline.[8] In the case of allophanates, the isotope effect $k^{H_2O}_H/k^{D_2O}_D$ = 1.05 for proton catalysis and the isotope effect is inverted for acetic acid catalysis $k^{H_2O}_{CH_3CO_2H}/k^{D_2O}_{CH_3CO_2D}$ = 0.87. On the other hand we determined a normal isotope effect k_{H_2O}/k_{D_2O} = 2.2 on the plateau in acidic media. We supplemented these data, on the one hand, by determining an entropy of activation $\Delta S^{\ddagger}$ = −16 cal mol^{-1} K^{-1} for catalysis by acetic acid, and also by measuring a Hammett parameter ρ of −0.72, which accounts for the effect of the substituents carried by the phenyl group (Figure 3).

A concerted mechanism for the protonation of nitrogen and cleavage of the C–N bond can therefore be proposed for the decarboxylation of 4-phenylallophanates, similar to that adopted by Ewing, Lockshon, and Jencks[6] for phenyl-



Scheme 5.

carbamates and monothiocarbamates. In the transition state, the proton is transferred completely to the nitrogen atom and the leaving base is linked to the protonated substrate by hydrogen bonds. In the case of allophanates however, the oxygen of the ureido group is certainly a more favourable protonation site than nitrogen; the phenylureas, as we have reported, being protonated on the oxygen in acidic media. Under these conditions, the decarboxylation can proceed through a concerted mechanism giving an isourea form:



Scheme 6.

The experimental results do not allow a choice to be made between the two possible protonation sites, though Scheme 6 must be considered more likely.

As in the case of carbamates, the value of α 0.78 is constant over a range of 12 pK units, which excludes a rate-limiting proton transfer with formation of a protonated intermediate. For, if such were the case, the proton transfer would probably be unfavourable for all the acids examined, including H_3O^+ since, as we have shown, the pK of the protonated substrate is probably below −1.75 and α would be 1.

The lines in Figure 2 show that the catalytic constants of the acids fall in parallel straight lines, which depend on the charge carried by the acid. If the catalytic constants of the acids of the same pK are compared with those of cationic acids, the anionic catalytic constants are 39 times greater and uncharged acids 11 times greater. This increase in reactivity may be attributed to a growing stability of the transition state by the hydrogen bonding when passing from an uncharged base to a base carrying one negative charge and then two negative charges. Similar results have been obtained with other compounds[30,31] and in particular with carbamates for which the acids fall into two parallel lines.[6]

The solvent isotope effects values of 1 and 0.87 for proton- and acetic acid-catalysed reactions may be explained, as in the case

of carbamates,[6] by a compensation action between an inverse isotope effect corresponding to an equilibrium proton transfer and the normal isotope effect due to the formation of a hydrogen bond with the leaving base. The isotope effect of 2.2 measured on the plateau in acidic media is composite: in this case, equation (1), in which $K_{SH} \ll |H_3O^+|$, becomes $k_{obs.} =$

$$\frac{k_{obs.}^{H_2O}}{k_{obs.}^{D_2O}} = \frac{k'_{H_2O}}{k'_{D_2O}} \times \frac{K_{HS}^{H_2O}}{K_{DS}^{D_2O}} \quad (5)$$

$k'K_{SH}$ and where k' represents the proton catalytic constant measured in a weakly acidic medium and equation (6) holds. Moreover, deuteriated acids are weaker than protonated acids: $K_{HS}^{H_2O}/K_{DS}^{D_2O} > 1$.

This results in $k_{obs.}^{H_2O}/k_{obs.}^{D_2O} > 1$, which accounts for the observed value of 2.2.

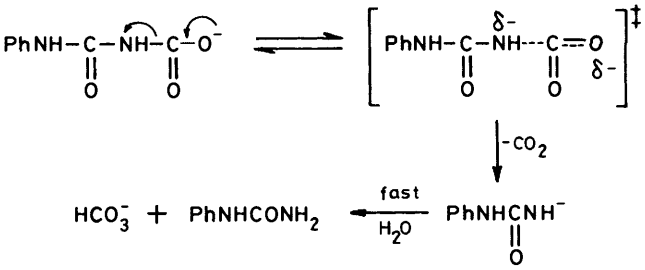
$$\frac{k'_{H_2O}}{k'_{D_2O}} = \frac{k_H^{H_2O}}{k_D^{D_2O}} = 1 \quad (6)$$

The negative value of -16 cal mol^1 K^1 for the entropy of activation for the acetic acid-catalysed reaction may be attributed to the loss of degrees of freedom by the base $CH_3CO_2^-$ linked by hydrogen bonds in the transition state. This effect is partly compensated for by an increase in the number of degrees of freedom of the carboxylate group resulting from the cleavage of the C–N bond, which explains why the value obtained is not highly negative. On the other hand, the charge of the transition state is probably slightly higher than that of the initial state, which gives the entropy a small negative increment, due to a greater reorientation of the molecules of the solvent in the transition state as compared with that in the initial state. The protonation of the oxygen or the nitrogen atom in the transition state is promoted by electron-donor groups carried by the phenyl group; cleavage of the C–N bond is facilitated by attractor groups. If the proton is transferred completely in the transition state and little C–N bond cleavage has occurred, the electron-donor effect predominates, which is consistent with the value of -0.72 obtained for the Hammett parameter ρ.

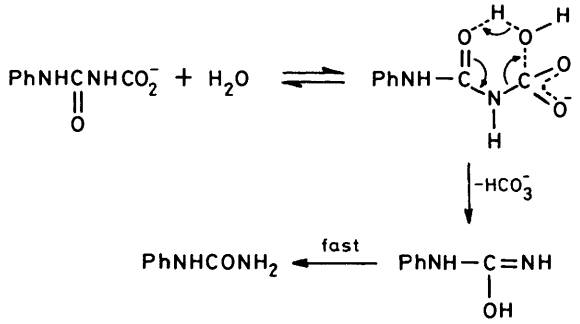
It may be concluded from all these results that acid-catalysed decarboxylation of phenylallophanate anions proceeds through a concerted mechanism similar to that of phenylcarbamates. Such a result is to be expected if a comparison is made of the pK values of the leaving groups for the two types of compounds: phenylureas have a pK at least two units less than that of the corresponding anilines. It follows that the protonated allophanate is still more unstable than a protonated phenylcarbamate and therefore has even less chance of being sufficiently stable to exist as an intermediate in the decarboxylation reaction.

The pH-*Independent Reaction in Basic Media.*—As in the case of carbamate anions, the decarboxylation rate of allophanates is independent of the pH in basic media. For phenylcarbamate, the plateau of the pH curve is followed by a reduction in the rate constant in the most basic media:[4] such a phenomenon was not observed with the allophanates investigated.

We believe that the mechanism of the pH-independent reaction is not general acid catalysis by water for the following reasons: (*a*) if it is assumed that water acts as an acid catalyst, the corresponding catalytic constant is very much above the Brønsted line plotted for other uncharged acids (Figure 2); (*b*) the solvent isotope effect becomes unity in this part of the pH curve, whereas an inverse isotope effect is observed with the acetic acid-catalysed reaction; (*c*) the Hammett parameter ρ (Figure 3) changes from a negative value of -0.72 for the proton-catalysed reaction to a positive value of $+0.61$ on the plateau of the pH curve (Figure 1); (*d*) the entropy of activation of close to zero (-6 cal mol^{-1} K^{-1}) is different from the value (-16 cal mol^{-1} K^{-1}) obtained for catalysis by acetic acid.



Scheme 7.



Scheme 8.

All these results demonstrate a changeover in mechanism in basic media in the absence of a buffer and may be interpreted by two reaction schemes: a spontaneous decomposition, Scheme 7, or a cyclic mechanism involving a molecule of water, Scheme 8.

Scheme 7 accounts for (*a*) the absence of a solvent isotope effect since there is no proton transfer; (*b*) the positive value of ρ, the negative charge which forms on the nitrogen in the transition state being stabilized by the electron-attracting groups; (*c*) the value of $\Delta S^{\ddagger}$ close to zero, since the reaction includes the cleavage of a bond, which increases the number of degrees of freedom of the carboxylate group.

Scheme 8 can account for the solvent isotope effect value of 1 only if the normal effect corresponding to the transfer of a proton to the oxygen is compensated for by the inverse isotope effect that can be expected from the nucleophilic attack of incipient OH^- on the carboxylate group, OD^- being more nucleophilic than OH^-. This seems unlikely since electron-attracting substituents facilitate cleavage of the C–N bond, but inhibit protonation of the oxygen: ρ can be positive if the first predominates over the second effect. The entropy of activation of close to zero is not consistent with the loss of degrees of freedom of the molecule of water in the transition state.

Therefore we can conclude that Scheme 7 is more consistent with the experimental results than Scheme 8. Furthermore, the transition state of Scheme 8 would have to be very late since CO_2^- is not easily attacked by nucleophiles, as a urea C=O group is not a strong enough base to deprotonate water.

In the case of arylcarbamate anions, the pH-independent decarboxylation reaction has been interpreted as a general acid catalysis by water, since the corresponding catalytic constant falls on the Brønsted line of the other acids of the same type. For these compounds, therefore, no spontaneous decarboxylation was considered. The occurrence of such a reaction with allophanates is certainly due to the fact that phenylureas are

very much better leaving groups than anilines, the negative charge of the anion being stabilized by resonance with the carbonyl group of the urea.

Experimental

Preparation of Anions of 4-Phenylallophanic Acids.—The phenyl esters were prepared first by treating phenyl chloroformate with *N*-phenylurea in the presence of pyridine in anhydrous benzene.[32] The anions were obtained by the hydrolysis of the corresponding esters in water–dioxane (1:1) in 1M-NaOH. The mixture was stirred for 30 min at room temperature and the sodium phenolate and the phenylureas formed were extracted with ether–ethyl acetate. This extract contained a small quantity of aniline, which became more significant when a powerful electron-attracting substituent, such as NO_2, was present. This resulted from the high alkalinity of the medium. From the liquid phase, warmed to *ca.* 0 °C, the sodium salt of 4-phenylallophanic acid was extracted as a solid. This was washed several times with anhydrous ether and chloroform. The various salts obtained were stored at low temperature.

Kinetic Determinations.—The course of the 4-allophanate decarboxylation was followed by recording the u.v. absorption at the wavelength of maximum optical variation observed during the reaction. Solutions with a substrate concentration of 10^{-4}—5×10^{-5}M were prepared by introducing with a microsyringe 15—30 μl of an allophanate anion stock solution into the measuring cell containing 3 ml of a solution at a given pH. The stock solution with a substrate concentration of 10^{-2}M was prepared in water–dioxane (60:40), containing 10^{-2}M-NaOH.

The causic soda derived from the stock solution affected the initial pH only to the extent of 0.2 pH units maximum. The ionic strength of the solution was maintained constant at 1.0M by the addition of KCl. Under the experimental conditions, the rate constants measured were of the *pseudo*-first order type. These were obtained graphically from the plot of the variation of log $(A_t - A_\infty) = f(t)$ or by the Guggenheim method.[33] The graphs were always linear up to 3 or 4 times the half-reaction time.

The kinetic measurements were made with a Cary 210 or Pye-Unicam SP 1800 A spectrophotometer fitted with a thermostatted compartment enabling the temperature in the cell to be set to ±0.1 °C. The pH was measured with a PHM 64 Radiometer provided with a Radiometer GK 2301 electrode. To measure the pH values of the solutions in D_2O the values given by the pH-meter were corrected by +0.4.[34] The observed rate constants measured for several buffer dilutions were corrected by the H_3O^+ catalytic constant, using formula (7)[6] every

$$k_{cor.} = k_{obs.} + \Delta(\text{antilog} - \text{pH})k_H \qquad (7)$$

time a deviation of the pH was observed during dilutions.

The inorganic buffers used were reagent grade products. For the preparation of the amino buffers, the amines were recrystallized as hydrochlorides. Fluka dioxane was treated under reflux with HCl under a nitrogen atmosphere for 24 h and then neutralized with KOH before being distilled over sodium. The water of the solutions was treated with $KMnO_4$ in a basic medium and twice-distilled.

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