Studies on Decarboxylation Reactions. 3.[1a] Micellar Catalysis in the Decarboxylation of 5-Amino-1,3,4-thiadiazole-2-carboxylic Acid

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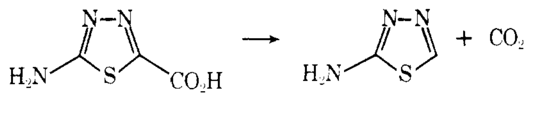
The rate constants of the decarboxylation of 5-amino-1,3,4-thiadiazole-2-carboxylic acid (I) have been measured in the presence of cationic (CTAB), anionic (LSNa), and nonionic (Triton X-100) micelles. The results obtained at constant and/or variable proton activity (an acceleration with cationic and nonionic micelles and almost no effect with anionic micelles), as well as salt addition effects, agree with a decarboxyprotonation mechanism of the zwitterion.

Continuing our researches[1] on the decarboxylation of heterocyclic amino acids we report in this paper data on the behavior of 5-amino-1,3,4-thiadiazole-2-carboxylic acid (I) in water in the presence of cetyltrimethylammonium bromide (CTAB), sodium lauryl sulfate (NaLS), and polyoxyethylenediisobutylphenol(Triton X-100), i.e., surfactants able to give respectively cationic, anionic, and nonionic micelles.



I

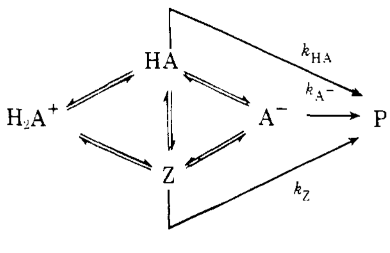
5-Amino-1,3,4-thiadiazole-2-carboxylic acid decarboxylates in water over the pH range 0.25–3.91 and the data obtained agree with two different mechanisms: unimolecular decomposition of the zwitterion (or of the undissociated acid) and/or protiodecarboxylation of the anionic species (Scheme I).

On the basis of chemical considerations[1] we have excluded the mechanism of protiodecarboxylation (carbon–hydrogen bond forming, often rate determining, followed by carbon–carbon bond breaking) and preferred a unimolecular decomposition of the zwitterion (rate-determining carbon–carbon bond breaking followed by carbon–hydrogen bond forming).

Surfactants influence rate and equilibrium constants of many chemical processes.[2] The behavior of micelles is especially interesting in what concerns the simulation of enzyme action.[3] Several studies have been reported on reactions carried out in the presence of micelles, including some unimolecular decarboxylation processes.[4] These have all been concerned with anions which decarboxylate through a transition state where the negative charge is delocalized more than in the initial state and therefore micellar catalysis is expected to be important.

The present study constitutes the first exemplum, in our knowledge, concerning micellar effects on the decarboxylation reaction of zwitterionic species and it seems to us of some interest in that micelles could simulate the enzyme-catalyzed decarboxylation of natural amino acids.

Scheme I



Kinetic Data. The apparent first-order kinetic constants and the thermodynamic parameters measured at variable surfactant concentration in the presence of 0.025 M HCl are collected in Tables I and II. Data at constant surfactant concentration and variable HCl concentration are in Table III. Moreover data related to salt effects are in Table IV.

Kinetic data in Table I (see also Figure 1) clearly indicate a positive catalytic effect by both Triton X-100 and CTAB and a slight effect by NaLS.[5]

One can observe that in spite of high surfactant concentrations (respectively, Triton X-100 0.16 and CTAB 0.17 M) the typical plateau of unimolecular[4a,b,7] reactions is not observed, thus indicating a low incorporation of substrate in micelles. A low binding constant is expected if the species to be decarboxylated is the zwitterion (see below): hence the apparently low k_m/k_w ratios.

Examination of data at constant surfactant concentration and variable proton activity confirms this hypothesis. In fact, we have observed (data in Table III, see also Figure 2) trends of kinetic constants vs. proton activities similar to those observed in the absence of surfactants,[8] thus indicating that the equilibria in Scheme I are only scarcely affected by the present

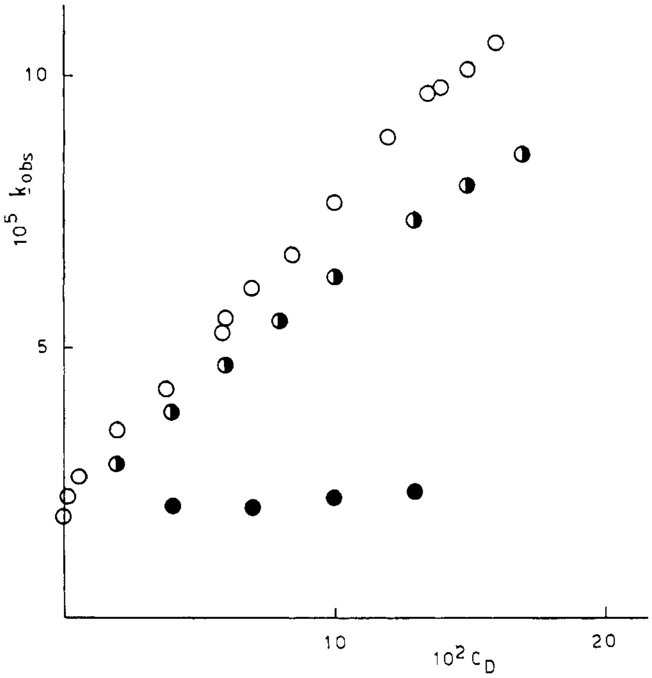


Figure 1. Micellar catalysis by Triton X-100 (○), CTAB (◑), and NaLS (●) for decarboxylation of I in the presence of 0.025 M hydrochloric acid at 40.0 ± 0.1 °C.

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Table I. Apparent Rate Constants for the Decarboxylation of I in the Presence of Surfactants and Hydrochloric Acid (0.025 M) at 40.0 ± 0.1 °C

Triton X-100		CTAB		NaLS	
$C_D \times 10^2$, mol L^{-1}	$k_{obsd} \times 10^5$,[a] s^{-1}	$C_D \times 10^2$ mol L^{-1}	$k_{obsd} \times 10^5$,[a] s^{-1}	$C_D \times 10^2$, mol L^{-1}	$k_{obsd} \times 10^5$,[a] s^{-1}
	1.86		1.86		1.86
	9.60 (50.6 °C)		9.60 (50.6 °C)		9.60 (50.6 °C)
	38.5 (60.3 °C)		38.5 (60.3 °C)		38.5 (60.3 °C)
0.16	2.22	2.0	2.85	4.0	2.08
0.60	2.58	4.0	3.80	7.0	2.07
2.0	3.46	6.0	4.67	10.0	2.22
3.8	4.21	8.0	5.47	13.0	2.35
5.9	5.25	8.0	22.4 (50.6 °C)	13.0	10.9 (50.6 °C)
5.9	22.2 (50.3 °C)	8.0	73.9 (60.2 °C)	13.0	43.8 (60.3 °C)
5.9	76.1 (59.9 °C)	10.0	6.28		
6.0	5.52	13.0	7.32		
7.0	6.08	15.0	7.96		
8.5	6.71	17.0	8.53		
10.0	7.64	17.0	31.9 (50.4 °C)		
12.0	8.84	17.0	106 (60.3 °C)		
13.5	9.65				
14.0	9.76				
15.0	10.1				
16.0	10.6				

[a] The rate constants are accurate to within ±3%.

Table II. Activation Parameters for the Decarboxylation of I in the Presence of Surfactants and Hydrochloric Acid (0.025 M)

surfactant	$C_D \times 10^2$, mol L^{-1}	$\Delta H^{\ddagger}$,[a] kcal mol^{-1}	$\Delta S^{\ddagger}$,[b] cal mol^{-1} K^{-1}
		30.6	17.3
Triton X-100	5.9	27.3	8.8
CTAB	8.0	26.3	5.7
CTAB	17.0	25.3	3.5
NaLS	13.0	29.1	13.2

[a] At 40 °C, the maximum error is 0.6 kcal mol^{-1}. [b] At 40 °C.

surfactants. On the other hand, the close resemblance between the curves in Figure 2 implies that the reaction mechanism in the presence of surfactants is of the same kind as that observed in pure water. Thus, the behavior of I in the presence of micelles can help to elucidate the decarboxylation mechanism.

We have suggested that the decarboxylating species should be the zwitterion. The structure of zwitterion with the positive charge delocalized on exo- and endocyclic nitrogen atoms accounts for the higher catalytic effect of nonionic and cationic micelles compared to anionic micelles, e.g., NaLS, which are likely to cause strong electrostatic repulsive interactions with the negative center of the zwitterion.

On the whole, nonionic and cationic micelles should give weak attractive or feebly repulsive interactions with the reactive species, which turns out destabilized[4b] going from water phase to micelles; of course the situation should be more favorable in the transition states. In fact, because of the higher dispersion of the negative charge, these interact with micelles to a greater extent.

The behavior observed in the decarboxylation of I recalls that observed by Fendler and co-workers[9] in the hydrolysis of potassium 2,4-dinitrophenylsulfate.

The results obtained allows the following conclusions to be drawn: (a) The protiodecarboxylation mechanism can be definitively excluded. In fact, if the species which is decarboxylated were the anion, the trend of apparent first-order kinetic constants vs. surfactant concentration should have been different; i.e., the reaction should have been *inhibited* by cationic micelles. (b) The unimolecular decarboxylation of the undissociated acid is unlikely to occur; in this case there should have been large attractive interactions between

Table III. Apparent Rate Constants for the Decarboxylation of I at Various Hydrochloric Acid Concentrations in the Presence of Surfactants at 40.0 ± 0.1 °C

Triton X-100[a]			CTAB[b]			NaLS[c]		
HCl, mol L^{-1}	pH	$k_{obsd} \times 10^5$,[d] s^{-1}	HCl, mol L^{-1}	pH	$k_{obsd} \times 10^5$,[d] s^{-1}	HCl, mol L^{-1}	pH	$k_{obsd} \times 10^5$,[d] s^{-1}
0.400	0.46	2.57	0.200	0.85	4.89	0.200	0.90	1.37
0.200	0.78	3.58	0.100	1.13	5.77	0.100	1.27	1.65
0.100	1.10	4.54	0.050	1.45	6.20	0.075	1.42	1.77
0.075	1.22	4.83	0.040	1.59	6.18	0.050	1.64	1.96
0.050	1.39	5.42	0.025	1.80	6.28	0.025	2.00	2.07
0.025	1.70	5.52	0.020	1.92	6.27	0.0125	2.46	1.96
0.0125	2.02	5.53	0.0100	2.29	5.51	0.0100	2.64	1.76
0.0100	2.16	5.32	0.0050	2.70	3.84	0.0080	2.75	1.56
0.0075	2.33	4.87						
0.0050	2.60	4.45						
0.0025	3.11	2.62						
0.0010	4.09	0.476						

[a] 6×10^{-2} mol L^{-1}. [b] 10×10^{-2} mol L^{-1}. [c] 7×10^{-2} mol L^{-1}. [d] The rate constants are accurate to within ±3%.

Table IV. Salt Effect on the Decarboxylation of I in the presence of CTAB (0.1 M) and Hydrochloric Acid (0.025 M) at 40.0 ± 0.1 °C

added salt,[a] mol L^{-1}	$k_{obsd} \times 10^5$,[b] s^{-1}
	6.28
A, 0.05	6.51
A, 0.10	6.52
A, 0.20	6.55
A, 0.40	6.52
B, 0.05	6.14
B, 0.10	6.38
B, 0.20	6.53

[a] Added salts: A, KCl; B, KBr. [b] The rate constants are accurate to within ±3%.

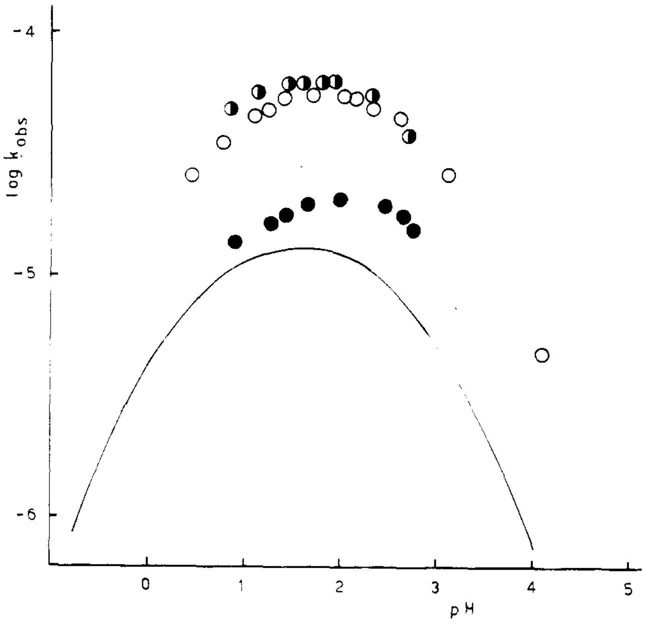

Figure 2. Plot of log k_{obsd} for decarboxylation of I at 40.0 ± 0.1 °C vs. acidity function: ○ Triton X-100 (6×10^{-2} M), ◑ CTAB (10^{-1} M), and ● NaLS (7×10^{-2} M). The curve is that calculated for reactions in the absence of surfactants.

starting material and micelles and low repulsive interactions between transition states (with incipient zwitterionic character) and micelles, especially for nonionic micelles. This prevision disagrees with experimental data. (c) The unimolecular decarboxylation of the zwitterion remains the most probable decarboxylation mechanism of I (see above).

Salt effects on micellar catalysis support the proposed mechanism. In fact, the decarboxylation of I in pure water is retarded by salt addition[10] at variance with what happens in the presence of cationic micelles (see Table IV). This is because salt addition lowers the ionic character of micelles favoring micelle–substrate interactions.

Also the activation parameters agree with the proposed mechanism (see Table II). The activation entropy values are more negative than in pure water, as expected with dependence on the higher order deriving from interactions with micelles; on the other hand the activation enthalpy values are lower than in pure water because interactions with micelles favor the charge dispersion in the transition states.

Experimental Section

Materials. The acid was prepared and purified as described.[11] Commercial CTAB and NaLS (Merck, pro analysis) and Triton X-100 (J. Baker) were used without further purification.

Kinetic Measurements. The kinetics of decarboxylation were followed spectrophotometrically as previously described[1a] by measuring the disappearance of I, respectively, at 290 nm for the runs in the presence of CTAB and NaLS and at 300 nm in the case of Triton X-100.

The pH measurements were made as previously described.[1a]

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References and Notes

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