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THE IRRELEVANCE OF AN INTRAMOLECULAR SALT BRIDGE FOR SOLVENT-CATALYZED DECARBOXYLATION-- SOLVENT CATALYSIS OF THE DECARBOXYLATION OF 4 AND 6-(2',4',6'-TRIMETHYLPYRIDINIUM)-BENZISOXAZOLE-3-CARBOXYLATES

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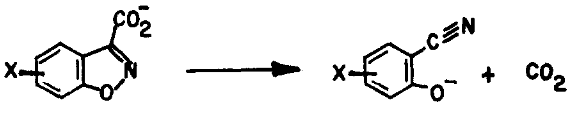
Previously, we have shown that the benzisoxazole-3-carboxylates, **1**, undergo an intermediateless conversion to carbon dioxide and o-cyanophenolate, **2**, that is subject to very large solvent rate accelerations.[2] Recently, Klotz and coworkers have demonstrated a pronounced catalysis by aqueous solutions of polymeric ammonium salts bearing lipophilic regions,[3] and lipophilic polymers bearing crown ether-cation complexes have been shown to be capable of even larger catalytic effects.[4] The decarboxylations of **1** have been used to probe micellar catalysis[5] and have been shown to be suitable models for other decarboxylation reactions.[6] In all these studies, the important role of the cation remains difficult to define. In this paper we examine that role by preparation and study of two zwitterionic derivatives of **1**.



1 **2**

Earlier, we noted that the presence of a 4-hydroxyl group inhibits the decarboxylation of **1**, abolishing the accelerating effects of dipolar aprotic solvents. The strong intramolecular

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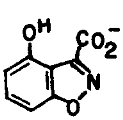

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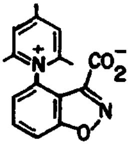

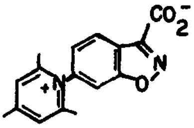

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hydrogen bond of **3** must selectively stabilize the charge of carboxylate inhibiting the reaction. The stability of hydrogen bonds is at least in part attributable to ionic effects,[7] and one is therefore led to predict that a similar inhibition should be observed for a derivative of **1** that carries an internal salt bridge involving the carboxylate. To study this possibility, we prepared the pyridinium zwitterions, **4** and **5**,[8] and studied their rates of decarboxylation,[9] as reported in Table 1.

TABLE 1: RATE CONSTANTS FOR DECOMPOSITION OF **4**, **5**, **1** (X = 6-NO_2); T = 30°

Solvent	Rate Constants (seconds^{-1})		
	4	**5**	**1**(X = 6-NO_2)
H_2O	6.6 x 10^{-6}	1.1 x 10^{-5}	7.3 x 10^{-6}
MeCN	2.3	9.6	2.9
Me_2CO	13	58	24
DMF	27	44	37

From these data, it is clear that both the magnitude and pattern of solvent effects reported earlier for **1** and typified by 1 (X = 6-NO_2) are also observed for **4**. The small increase in reactivity of **5** over **4** that is noted in all solvents is probably the result of a steric effect in **4** that reduces the magnitude of the between-ring conjugation of the pyridinium function.

At least in solvents such as acetonitrile or acetone, **4** is expected to exist as an intimate ion pair, These results demonstrate that a suitable hydrogen bond has a far greater capacity for anionic stabilization than even a neighboring cation. It also carries the important implication that location of cation can be a minor feature in designing catalysts for the decarboxylation of **1**, or by analogy, other decarboxylation-prone carboxylate anions.

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8. Perchlorate salts of **4**, m.p. 133-135° dec, and **5**, m.p. 140° dec, were prepared from the corresponding methyl esters by hydrolysis with 2*N*HCl at 40°, 24 hr, followed by evaporation. The esters were generated from 2,4,6-trimethylpyrylium perchlorate and the corresponding esters of **1**, X = 4 or 6-NH_2.[2] Satisfactory elemental analyses were obtained for the perchlorate salts of **4** and **5** and for their decomposition products, **2**.
9. The rate constants were measured as described previously.[2] Quantitative conversion was observed for both **4** and **5**. Aqueous rates were followed at pH 7 in a phosphate buffer.