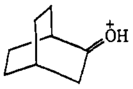
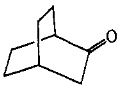
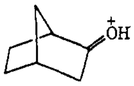
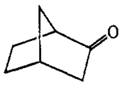
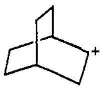
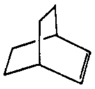
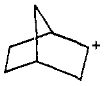
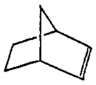
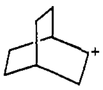
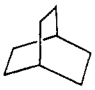
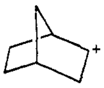
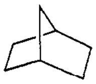
Table I. Heats of Formation of Bicyclic Species

Line	Species A	Species B	$\Delta H_f(A - B)$,[a,b] kcal/mol
1			159
2			161
3			171.5 ± 1.5
4			160 ± 1
5			199.5 ± 1.5[c]
6			193 ± 1[c]

[a] The following scales of relative ΔH_f's were used to place limits on $\Delta H_f(A - B)$: $\Delta H_f[(CH_3)(C_2H_5)OH^+ - (CH_3)(C_2H_5)O] > \Delta H_f$[bicyclo[2.2.2]octyl cation − bicyclo[2.2.2]octene] $> \Delta H_f[(CH_3)(C_2H_5)COH^+ - (CH_3)(C_2H_5)CO]$; ΔH_f[cyclohexanone-H$^+$ − cyclohexanone] $\cong \Delta H_f$[2-bicyclo[2.2.1]heptanone-H$^+$ − 2-bicyclo[2.2.1]heptanone] $> \Delta H_f$[bicyclo[2.2.1]heptene-H$^+$ − bicyclo[2.2.1]heptene] $> \Delta H_f$[2-bicyclo[2.2.2]octanone-H$^+$ − 2-bicyclo[2.2.2]octanone] $\cong \Delta H_f[((CH_3)_2CH)_2OH^+ - ((CH_3)_2CH)_2O]$. Heats of formation not listed in the table were taken from J. Beauchamp, Ph.D. Thesis, Harvard University, 1968. [b] The listed errors represent differences between bracketing reagents. [c] Value obtained using the heat of hydrogenation of the olefin: R. B. Turner, W. Meador, and R. Winkler, *J. Am. Chem. Soc.*, **79**, 4116 (1957).

the classical bicyclo[2.2.2]octyl cation compared to its hydrocarbon than for the corresponding species in the bicyclo[2.2.1]heptyl system. The experimental results are in direct opposition to this. The 6-kcal/mol energy difference is explicable in terms of σ delocalization, a method for dispersing charge, which would be expected to be of considerable importance in the absence of any compensating solvation phenomena. The experimental results do not negate σ participation in the bicyclo[2.2.2]octyl cation but indicate that it is at least 6 kcal/mol greater in the bicyclo[2.2.1]heptyl cation where the geometry is more favorable.[9]

Any unforseen effects in the bicyclo[2.2.1]heptyl or bicyclo[2.2.2]octyl system can be evaluated by examining 2-keto compounds. The results are summarized in lines 1 and 2 of Table I. The difference in heat of formation of protonated 2-bicyclo[2.2.2]octanone and its ketone is 2 kcal/mol less than the difference in heat of formation of protonated 2-bicyclo[2.2.1]heptanone and its ketone. This corresponds to the same difference observed for protonated cyclohexanone and cyclohexanone when compared to protonated cyclopentanone and cyclopentanone.[10] Thus the bicyclo[2.2.1]heptyl and bicyclo[2.2.2]octyl systems appear to exhibit no unique stabilization of protonated carbonyls.[11] The localization of charge on the oxygen at the 2 position in the bicyclic systems is competitive with and more favorable than σ participation.

Finally, using −17[12] and −14[13] kcal/mol as the heats of formation of bicyclo[2.2.2]octane and bicylo[2.2.1]heptane, respectively, one may calculate a ΔH_f value of 182 kcal/mol for the bicyclo[2.2.2]octyl cation and 179 kcal/mol for the bicyclo[2.2.1]heptyl cation. The latter value is approximately 20 kcal/mol lower than one obtained by a quantum mechanical approach.[14]

Acknowledgment. The partial support of the National Science Foundation (GP 4924X), NASA (NGL 05-020-250-S1), and the Center of Material Research at Stanford University is gratefully acknowledged. The authors wish to thank J. Baldeschwieler and his group for many helpful discussions.

[9] A choice of an appropriate model, in which σ participation does not occur, will be the subject of a forthcoming publication.

[10] J. Beauchamp, Ph.D. Thesis, Harvard University, 1968.

[11] The use of protonated bicyclic ketones as models is discussed in D. Farnum and G. Mehta, *J. Am. Chem. Soc.*, **91**, 3256 (1969).

[12] N. Allinger, J. Hirsch, M. Miller, I. Tyminski, and F. Van-Catledge, *ibid.*, **90**, 1199 (1968).

[13] A. Bedford, A. Beezer, C. Mortimer, and D. Springall, *J. Chem. Soc.*, 3823 (1963). The heats of fusion and vaporization were assumed to be 8.0 kcal/mol.

[14] G. Klopman, *J. Am. Chem. Soc.*, **91**, 89 (1969).

[15] Public Health Service Special Fellow on sabbatical leave at Stanford University, 1967–1968.

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Thermal and Photodecarboxylation of Pyridylacetic Acids and Photocleavage of Some 2-Substituted Pyridines[1]

Sir:

Our discovery[1,2] of a facile photocleavage of 2-substituted quinolines led us to consider establishing the generality of the reaction. Some substituted pyridines similar to the quinolines were available as well as the 2-, 3-, and 4-pyridylacetic acids. The thermal decarboxylation of 2-pyridylacetic acid has been studied[3] and a mechanism similar to our proposal for the quinoline cleavage was considered. Photodecarboxylation of 2-, 3-, and 4-nitrophenylacetate ions was recently thoroughly studied[4] and it was of interest to learn if the similarities observed between pyridyl and nitrophenyl reactivities in some chemical reactions could be extended to a photoreaction.

Irradiation[5] of the 2-, 3-, and 4-pyridylacetic acids in aqueous solutions did indeed yield the corresponding 2-, 3-, and 4-methylpyridines and CO_2. The initial rate of decarboxylation of each acid was a maximum at or near the isoelectric point (pH 4.0–4.2) and at this point the following quantum yields for conversion of the acid to the methylpyridine were found: 2-pyridyl, 0.49; 3-pyridyl, 0.46; 4-pyridyl, 0.20. At pH values higher

[1] Photochemistry of N-Heterocycles. VI. Previous paper: F. R. Stermitz, C. C. Wei, and C. M. O'Donnell, *J. Amer. Chem. Soc.*, in press. This work was supported in part by Grant No. GM-15425 from the National Institute of General Medical Sciences, U. S. Public Health Service.

[2] F. R. Stermitz and C. C. Wei, *ibid.*, **91**, 3103 (1969).

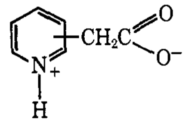
[3] W. von E. Doering and V. Z. Pasternak, *ibid.*, **72**, 143 (1950).

[4] J. D. Margerum and C. T. Petrusis, *ibid.*, **91**, 2467 (1969).

[5] Irradiations were carried out on 0.01 *M* solutions in a Rayonet reactor employing 2537-Å lamps. They were accomplished under N_2 although the presence of air did not appear to affect the reaction. Quantum yields were determined by nmr analysis at about 9% reaction on degassed samples using a "merry-go-round" apparatus and ferrioxalate actinometry.

or lower than the isoelectric points each photoreaction slowed considerably and eventually a reaction involving the pyridine ring, presumably hydration and cleavage, became faster than decarboxylation.

A maximum rate at the isoelectric point suggests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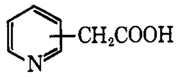
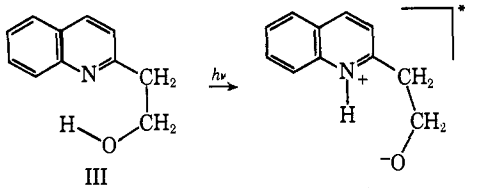
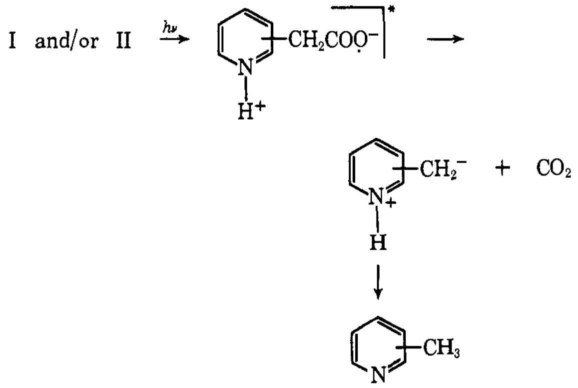

II

either I or II as the ground-state species involved in the photoreaction and spectral data suggest that both could be present. However, it has been shown[6] that photocleavage of III involves proton transfer to give IV in the excited state (and subsequent cleavage from IV) and

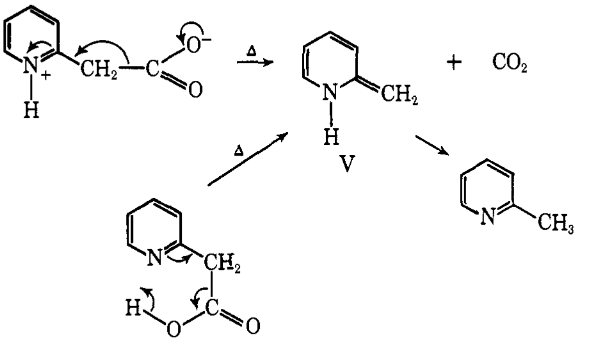

III

IV


(1)

hence it seems likely that eq 1 represents the basic mechanism for the pyridylacetic acid decarboxylations.[7] Although Margerum observed photodecarboxylation of all three nitrophenylacetates, he found an abnormally low quantum yield for 2-nitrophenylacetate and that the major product from 4-nitrophenylacetate was 4,4′-dinitrobibenzyl instead of 4-nitrotoluene.

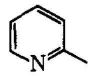
Thermal decarboxylation of the pyridylacetic acids has apparently not been quantitatively studied. Stereochemical studies led Doering and Pasternak[3] to postulate eq 2 for the thermal decarboxylation of 2-pyridylacetic acid, but they pointed out that eq 3 could not be ruled out. No work on 4-pyridylacetic acid was reported.[3] However, Jurch and Ramey[8] interpreted early literature work to mean that 4-pyridylacetic acid was much more difficult to decarboxylate thermally than was the 2 derivative and reported[8] that no decarboxylation of 4-pyridylacetic acid occurred in D_2O after 24 hr at 90°, although a facile decarboxylation took place in DMSO. A large rate difference between the 2- and 4-pyridylacetic acids might indeed point to the importance of eq 3 which might be expected to be rapid only for the 2 derivative. We have found, however, that both derivatives actually decarboxylate thermally with equal ease (0.02 M in H_2O at 90°): 2-pyridylacetic acid (pH 2.3, $0.71 \times 10^{-4}\ \mathrm{sec}^{-1}$; pH 4.3, $1.4 \times 10^{-4}\ \mathrm{sec}^{-1}$; pH 6.5, $0.15 \times 10^{-4}\ \mathrm{sec}^{-1}$) and 4-pyridylacetic acid (pH 2.3, $0.63 \times 10^{-4}\ \mathrm{sec}^{-1}$; pH 4.0, $1.0 \times 10^{-4}\ \mathrm{sec}^{-1}$; pH 6.1, $0.19 \times 10^{-4}\ \mathrm{sec}^{-1}$). At 90°, no decarboxylation of 3-pyridylacetic acid was observed.[9] The lack of reactivity of the 3 isomer and near equivalence of decarboxylation rates for the other two isomers both point to eq 2 as the proper one for the thermal reaction.


(2)

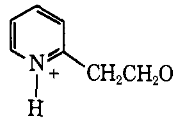
(3)

Although a process similar to eq 2 can also be written for the photochemical reaction of the 2 and 4 derivatives, it is not possible for 3-pyridylacetic acid and yet the decarboxylation is equally facile for all isomers. Hence, we have described the photoreaction only in terms of eq 1 in order to indicate that the pyridinium substituent is evidently sufficient to promote reaction regardless of the availability of a noncharged canonical form such as V. Although a contribution from forms such as V is important in the thermal reaction, it is unimportant in the photochemical reaction.

Finally, we were able to extend the photocleavage reaction to 2-(2-pyridyl)-1-ethanol (VIa), 3-(2-pyridyl)-1-propanol (VIb), and 1-(2-pyridyl)-propane (VIc). Upon irradiation in tetrahydrofuran, all yielded 2-methylpyridine, while similar 3- and 4-pyridyl derivatives remained unchanged.[10] Although absolute results are not yet available, relative quantum yields of photocleavage were VIa > VIb > VIc, an order similar to that found for the quinolines.[1] Compound VIa also showed the interesting decrease in cleavage quantum yield with increasing solvent polarity, as was observed for the corresponding quinoline, and probably photocleaves through



VIa, R = CH_2CH_2OH
VIb, R = $CH_2CH_2CH_2OH$
VIc, R = $CH_2CH_2CH_3$


VII

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(6) C. M. O'Donnell, T. Spencer, G. Knesel, and F. R. Stermitz, unpublished results.

(7) Preliminary results on 3-pyridylacetic acid show the decarboxylation to be unaffected by oxygen and not quenched by biacetyl. The absorption spectra of the 2- and 3-pyridylacetic acids at pH 4 are very similar (λ_{max} 267 nm (ϵ 7600) and λ_{max} 265 nm (ϵ 5500), respectively), while that of 4-pyridylacetic acid is considerably different (λ_{max} 255 nm (ϵ 6700)).

(8) G. R. Jurch and K. C. Ramey, *Chem. Commun.*, 1211 (1968).

(9) W. N. White and D. Lazdins (*J. Org. Chem.*, 34, 2756 (1969)) reported the qualitative observation that the 2- and 4-pyridylacetic acids decarboxylated readily at 100° in H_2O, but that a temperature of 215° was necessary in the case of the 3 isomer.

(10) I. M. Goldman (*ibid.*, 28, 1921 (1963)) reported the pyrolytic cleavage of VIa and the corresponding pyrazine to the 2-methyl compounds and suggested a concerted H transfer and elimination mechanism for these thermal reactions.

VII. It is presumed that VIb and VIc react *via* the proposed[1] type-II-like cleavage and hence this reaction should prove to be general for properly substituted aromatic N-heterocycles.

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Base-Catalyzed Deuterium Exchange of Bicyclo[2.2.1]heptanones[1]

Sir:

There has recently been considerable interest in the investigation of rates of base-catalyzed deuterium exchange of ketones,[2] the stereochemistry of protonation of enolates and other anions,[3] and the selectivity of deuterium exchange in bicyclic ketones.[4] This communication reports measurements of the rates and stereochemistry of base-catalyzed deuterium exchange in representative bicyclo[2.2.1]heptan-2-ones and application of these studies to the preparation of selectively deuterated compounds in this series.

The rates of deuterium uptake of the ketones in 2:1 dioxane–D_2O containing NaOD at 25.0° were monitored by mass spectrometry; in all cases there was a relatively rapid uptake of a first deuterium, followed by the slower incorporation of a second deuterium. No trideuteration was observed. The stereochemistry of the first deuterium was found to be *exo* in all cases by isolating monodeuterated ketone, reducing with $LiAlH_4$, isolating the predominant epimeric alcohol, and examining the characteristic nmr spectrum.[4a,c] The ketones examined were norcamphor (**1**), camphor (**2**), dehydronorcamphor (**3**), and benzodehydronorcamphor (**4**). The relative rates of deuterium uptake at various positions (all relative to the *endo*-3 position of **1**) are summarized in Chart I and the measured rate constants and *exo*:*endo* rate ratios are given in Table I. The kinetic procedure involved removing samples at intervals and quenching the base with dilute nitric acid. The ketones were extracted into pentane and each sample was purified by gas chromatography. Rates of deuterium uptake were calculated by the variation in the mass distribution of the molecular ion peaks of the ketones in their mass spectra. In several cases the two ketones were deuterated competitively in the same reaction solution and separated into the individual components by vpc for mass analysis.

The detailed steps of the exchange are not established and no attempt is made herein to interpret the observed rates of exchange in terms of specific processes at the molecular level.[5] As examples of the complexities involved there are dissenting views as to whether proton abstraction from ketones by bases such as deuteroxide[2e] and methoxide[6] leads to transition states and/or intermediates with the character of enols[2e] or enolates,[6] and it has been further suggested that ketonization of the enolate of 4-*t*-butylcyclohexanone with deuterioacetic acid–D_2O occurs with initial attack both on carbon and oxygen and that the final stereochemistry of the ketone is different for the two pathways.[7] Further work is in progress to clarify the mechanism of the exchange.

Chart I. Relative Rates of NaOD-Catalyzed Deuterium Exchange of Ketones at 25.0° in 2:1 Dioxane–D_2O

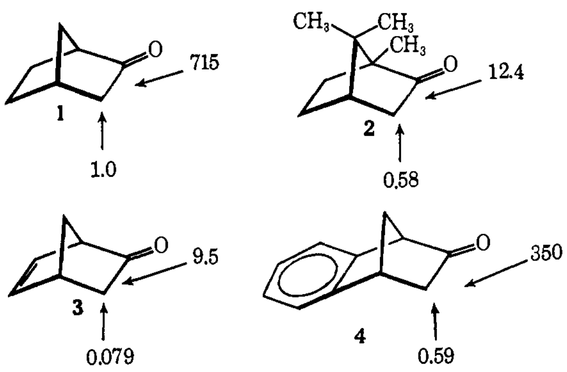

Table I. Second-Order Rate Constants of NaOD-Catalyzed Deuterium Exchange of Ketones at 25.0° in 2:1 Dioxane–D_2O

Ketone		k_2 (l. M^{-1} sec^{-1})[a,b]	*exo*:*endo*
1	*exo*	5.48×10^{-2}	715
	endo	7.67×10^{-5}	
2	*exo*	9.50×10^{-4}	21
	endo	4.46×10^{-5}	
3	*exo*	7.30×10^{-4}	120
	endo	6.06×10^{-6}	
4	*exo*	2.68×10^{-2}	595
	endo	4.50×10^{-5}	

[a] Second-order rate constants were obtained by dividing the measured pseudo-first-order rate constants by the base concentration, and were invariant with concentration in the range 0.08–0.004 *M* used. [b] Rates were reproducible with maximum deviations of ±10%. Competition experiments verified the relative orders of reactivity between **1** and **4** *exo*, **1** and **4** *endo*, and **1** and **2** *endo*.

With this caveat in mind the relative reactivities and *exo*:*endo* rate ratios of **1–4** would appear to be of significance to the relationship between structure and reactivity in these compounds and may be profitably examined in more detail.

A preference for *exo* exchange in **1** would have been predicted on steric grounds but the magnitude of the selectivity is perhaps surprisingly large. For comparison the *exo*:*endo* ionization rate ratio for norbornyl brosylate is 1600,[8a] and there is a >5000:1 preference for *exo* hydration of the norbornyl cation.[8a] Free radical chlorination of norbornane with sulfuryl chlo-

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[1] Presented at the 157th National Meeting of the American Chemical Society, Minneapolis, Minn., April 1969, Abstracts, ORGN 42.

[2] (a) C. Rappe and W. H. Sachs, *Tetrahedron*, **24**, 6287 (1968); (b) W. Th. van Wijnen, H. Steinberg, and Th. J. de Boer, *Rec. Trav. Chim. Pays-Bas*, **87**, 844 (1968); (c) A. A. Bothner-By and C. Sun, *J. Org. Chem.*, **32**, 492 (1967); (d) E. N. Marvell, G. J. Gleicher, D. Sturmer, and K. Salisbury, *ibid.*, **33**, 3393 (1968); (e) J. Warkentin and C. Barnett, *J. Amer. Chem. Soc.*, **90**, 4629 (1968); (f) H. W. Amburn, K. C. Kauffman, and H. Schechter, *ibid.*, **91**, 530 (1969); (g) F. G. Bordwell and R. G. Scamehorn, *ibid.*, **90**, 6749 (1968); (h) J. Hine, K. G. Hampton, and B. C. Menon, *ibid.*, **89**, 2664 (1967).

[3] F. Johnson, *Chem. Rev.*, **68**, 375 (1968); (b) H. E. Zimmerman and P. S. Mariano, *J. Amer. Chem. Soc.*, **90**, 6091 (1968); (c) R. A. Abramovitch, M. M. Rogić, S. S. Singer, and N. Venkateswaran, *ibid.*, **91**, 1571 (1969).

[4] A. F. Thomas and B. Willhalm, *Tetrahedron Lett.*, 1309 (1965); (b) J. M. Jerkunica, S. Borčić, and D. E. Sunko, *ibid.*, 4465 (1965); (c) A. F. Thomas, R. A. Schneider, and J. Meinwald, *J. Amer. Chem. Soc.*, **89**, 68 (1967).

[5] Professor L. K. Montgomery (private communication) has independently made considerable progress in dissecting the various steps involved in these exchange reactions.

[6] J. F. Bunnett and L. A. Retallick, *J. Amer. Chem. Soc.*, **89**, 423 (1967).

[7] H. O. House, B. A. Terfertiller, and H. D. Olmstead, *J. Org. Chem.*, **33**, 935 (1968).

[8] (a) S. Winstein, E. Clippinger, R. Howe, and E. Vogelfanger, *J. Amer. Chem. Soc.*, **87**, 376 (1965); (b) E. C. Kooyman and G. C. Vegter, *Tetrahedron*, **4**, 382 (1958).