Bimanes. 15. Kinetics and Mechanism of the Hydroxide Ion Reaction with 1,5-Diazabicyclo[3.3.0]octadienediones (9,10-Dioxabimanes)

Hannah Kanety[1a] and Edward M. Kosower*[1a,b]

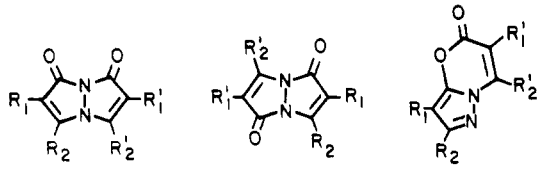
Department of Chemistry, Tel-Aviv University, Ramat-Aviv, Tel-Aviv, Israel 69978, and Department of Chemistry, State University of New York, Stony Brook, New York 11794

Received February 9, 1982

The rate constants for the reaction of hydroxide ion with *syn*- and *anti*-9,10-dioxabimanes (1,5-diazabicyclo[3.3.0]octadienediones) correlate with the function [σ (R_1) + 0.5σ (R_1')], ρ value of 3.0 (R_2 = CH_3 or H), and with [σ (R_2) + 0.5σ (R_2')], ρ value of ca. 4 (R_1 = Cl or H). The ρ value for hydrolysis of lactones produced by photoisomerization of *anti*-bimanes is 3.7. Structures of the ring-opened hydrolysis products as 1(2)-pyrazolinonylacrylic acids have been confirmed for both *syn*- (2-acid) and *anti*-bimanes (1-acid). The *E* configuration is established by ^{1}H NMR for the side chain of the hydrolysis product of *syn*-(H,H)B. Identical ring-opened acids are obtained from *anti*-bimanes and the lactones. The ring-opened acids are cyclized readily to the *anti*-bimanes and/or lactones; some data on the facility of the conversion are presented. The present study provides information valuable for improving the yields of bimanes and the design of biological labeling experiments.

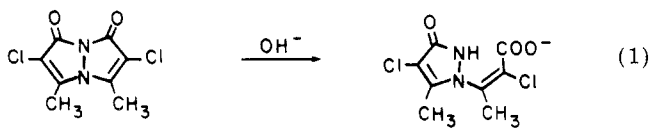
Introduction

In the course of studies on the syntheses and reactions of the *syn*- and *anti*-9,10-dioxabimanes (**1** and **2**), the



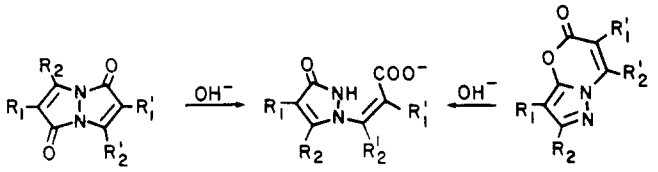
1 2 3

sensitivity of the bimane system toward base was noted.[2,3] The product of the reaction of hydroxide ion with a typical *syn*-bimane was shown to be the 2-pyrazolinonylacrylic acid (eq 1). The reaction of hydroxide ion with *anti*-bi-



(1)

manes led to the same product as that formed by hydrolysis of the lactone (**3**) generated by photoisomerization of *anti*-bimane (eq 2).[4]



(2)

Since most bimane syntheses are carried out under basic conditions, greater understanding of the ring-opening reaction was needed to avoid unnecessary loss of bimane product. Some of the biological applications[5-11] involve exposure of the bimane to mildly basic conditions. In addition, the bimane system is also an interesting candidate for mechanistic studies, a variety of substituted bimanes and lactones produced by photoisomerization being available.[4,12,13] ["Short-form" names for the bimanes are *syn*- or *anti*-(R_2,R_1)B.][3]

Results

The rates of the hydroxide ion reaction with *syn*-bimanes, *anti*-bimanes, and lactones (eq 1 and 2) are readily followed spectrophotometrically. The absorption maximum of *syn*-bimanes (370–400 nm in water) is replaced by that of the hydrolysis product (290–320 nm) during the reaction. The reaction may also be followed by the loss of fluorescence of the *syn*-bimane, an approach useful for very dilute solutions. The spectroscopic absorption and fluorescence changes for the hydrolysis of *syn*-(CH_3,Cl)B at pH 10.8 and 20 °C are shown in Figure 1. Easily measurable changes in the absorption spectrum also occur on hydrolysis of *anti*-bimanes (320 nm → 250 nm) and lactones (290 nm → 250 nm). Neither *anti*-bimanes nor lactones are fluorescent.[2,14]

Product Identification. Hydrolysis of *syn*-(CH_3,Cl)B yields the 2-pyrazolinonylacrylic acid.[2] Reaction of hydroxide ion with *syn*-(H,Cl)B (**1**, R_2, R_2' = H; R_1, R_1' = Cl) (^{1}H NMR, single peak at 7.95 ppm)[15,16a] yields, after acidification, the 2-pyrazolinonylacrylic acid **4**, which has two different vinyl hydrogens (^{1}H NMR, 8.17 and 7.50 ppm).

4 5

(1) (a) Tel-Aviv University. (b) State University of New York, Stony Brook.
(2) Part 5: Kosower, E. M.; Pazhenchevsky, B. *J. Am. Chem. Soc.* **1980**, *102*, 4983-4993.
(3) The nomenclature for 9,10-dioxabimanes is explained in ref 2.
(4) Part 10: Kanety, H.; Dodiuk, H.; Kosower, E. M. *J. Org. Chem.* **1982**, *47*, 207-213.
(5) Part 4: Kosower, N. S.; Kosower, E. M.; Newton, G. L.; Ranney, H. M. *Proc. Natl. Acad. Sci. U.S.A.* **1979**, *76*, 3382-3386.
(6) Kosower, N. S.; Newton, G. L.; Kosower, E. M.; Ranney, H. M. *Biochim. Biophys. Acta* **1980**, *622*, 201-209.
(7) Fahey, R. C.; Newton, G. L.; Dorian, R.; Kosower, E. M. *Anal. Biochem.* **1980**, *107*, 1-10.
(8) Kosower, N. S.; Kosower, E. M.; Zipser, J.; Faltin, Z.; Shomrat, R. *Biochim. Biophys. Acta* **1981**, *640*, 748-759.
(9) Gainer, H.; Kosower, N. S. *Histochemistry* **1980**, *68*, 309-315.
(10) Fahey, R. C.; Newton, G. L.; Dorian, R.; Kosower, E. M. *Anal. Biochem.* **1981**, *111*, 357-365.
(11) Newton, G. L.; Dorian, R.; Fahey, R. C. *Anal. Biochem.* **1981**, *114*, 383-387.
(12) Part 6: Kosower, E. M.; Pazhenchevsky, B.; Dodiuk, H.; Kanety, H.; Faust, D. *J. Org. Chem.* **1981**, *46*, 1666-1673.
(13) Part 7: Kosower, E. M.; Pazhenchevsky, B.; Dodiuk, H.; Ben-Shoshan, M.; Kanety, H. *J. Org. Chem.* **1981**, *46*, 1673-1679.
(14) Part 8: Kosower, E. M.; Kanety, H.; Dodiuk, H., *J. Photochem.* **1982**, in press.
(15) Part 14: Kosower, E. M.; Ben-Shoshan, M.; Faust, D.; Goldberg, I. *J. Org. Chem.* **1982**, *47*, 213-221.
(16) Part 13: (a) Goldberg, I.; Kosower, E. M. *J. Phys. Chem.* **1982**, *86*, 332-335. (b) Brügel, W. "Nuclear Magnetic Resonance Spectra and Chemical Structure"; Academic Press: New York, 1967; p 97.

0022-3263/82/1947-4222$01.25/0 © 1982 American Chemical Society

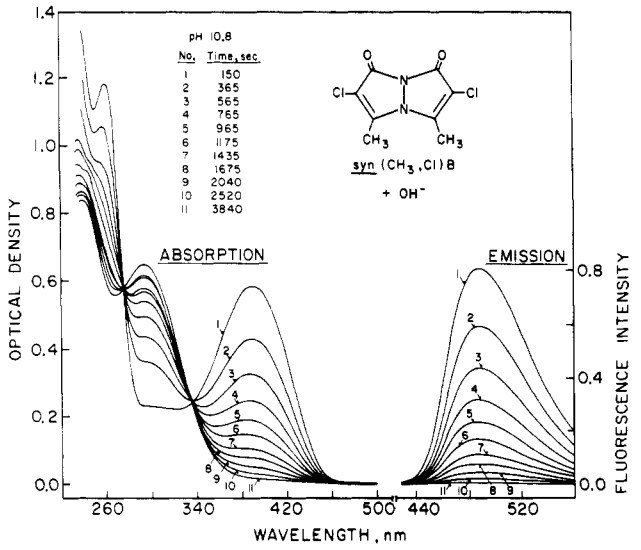


Figure 1. Absorption and emission curves for a solution of *syn*-(CH_3,Cl)B in 0.1 M sodium carbonate buffer, pH 10.8, at 20 °C over a period of 4000 s. The absorption maximum for the bimane at 386 nm decreases smoothly and is replaced by the absorption of the ring-opened product, a pyrazolinonylacrylic acid anion, at 295 nm. An isosbestic point at 340 nm shows that the conversion is quantitative and that no appreciable concentrations of intermediates are accumulated.

Table I. Ring Closure Products (*anti*-Bimane and Lactone) Produced by Electrophilic Agents

1-pyrazolinonylacrylic acid			*anti*-bimane,[a] %	lactone,[a] %
R_2	R_1	reagent		
CH_3	Cl	HCl (pH 1)	90	10
CH_3	Cl	acetic anhydride	30	70
CH_3	CH_3	HCl (pH 1)	88	12
CH_3CH_2	CH_3	HCl (pH 1)	80	20
benzo[b]		acetic anhydride	50	50
benzo[b]		heat	100	

[a] Ratio of products determined by NMR; total yields not determined in all cases. [b] Data from Gibson, G. K. J.; Lindsey, A. S.; Paisley, H. M. *J. Chem. Soc. C* **1967**, 1792-1795.

Hydrolysis of *syn*-(H,H)B yields an acid (**4a**, H in place of Cl) that exhibits an ^1H NMR spectrum showing four different types of hydrogen, the pair on the ring with J = 3 Hz and the pair on the side chain with J = 11.1 Hz. Thus, the acid has *E* stereochemistry on the side chain on the basis of the H,H coupling constants (cis-H,H: 6–12 Hz; trans-H,H: 14–16 Hz).[16b] It is reasonable to presume that all of the acids formed through hydrolysis preserve the *E* stereochemistry of the ring.

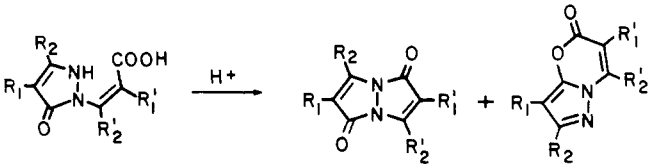
Both *anti*-(CH_3,Cl)B and the lactone formed by photoisomerization[4] yield the same 1-pyrazolinonylacrylic acid, **5**, as shown by NMR, UV, IR, mass spectra, and mp for the isolated acid.

Strong support for the assigned structures is found in the electrophile-induced conversion to the bimanes from which the acids were produced by hydrolysis (next section).

Ring Closure of Pyrazolinonylacrylic Acids. Treatment of the 1(2)-pyrazolinonylacrylic acids with electrophilic agents (aqueous acid, acetic anhydride, thionyl chloride) leads to *syn*-bimanes (from the "2-acid") or to mixtures of *anti*-bimanes and lactones (from the "1-acid"). Ring closure of both the 2-pyrazolinonylacrylic acid and its methyl ester to *syn*-(CH_3,Cl)B had been demonstrated previously.[2]

The ease with which conversion to the bimanes takes place varies greatly with the substituents on the bimane system. *syn*-(CH_3,Cl)B is formed from the acid in aqueous HCl, pH 2, fairly rapidly and in high yield (>90% by spectroscopic measurement). The corresponding methyl ester produces *syn*-(CH_3,Cl)B in 78% yield (isolated) on treatment with pH 6.7 phosphate buffer for 14 h.[2] In contrast, *syn*-(H,Cl)B is found only in trace amounts in a solution of the acid, pH 1, after 50 h. However, reaction of the acid with thionyl chloride leads to *syn*-(H,Cl)B in at least 75% yield.

The 1-pyrazolinonylacrylic acids yield both *anti*-bimane and lactone, with the bimane predominant in most cases. Results are given in Table I for the conversion described in eq 3.

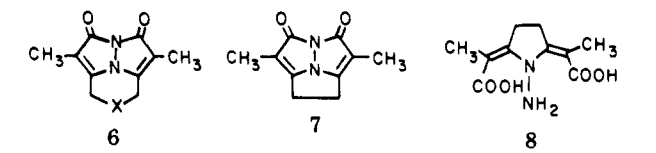


(3)

Kinetics of Hydrolysis. The rate of decrease of the UV absorption spectra of both *syn*- and *anti*-bimanes is convenient to follow at pH 9.80 and 50 °C (see Figure 1). More reactive bimanes [e.g., *syn*-(H,Cl)B] are studied at pH 8.83 and 50 °C, whereas the kinetics of the lactones are measured in solutions of pH 9.0 at 25 °C. Plots of log ($OD_t - OD_{inf}$) against time give straight lines. The second-order rate constants for the reactions are derived from the slope of the plots divided by [OH^-].

Rate constants for the hydrolysis of *syn*-(CH_3,Cl)B increase with pH as follows: (pH, 10_4k, s^{-1}) 6.97, 0.17; 7.94, 1.54; 8.83, 11.7; 9.80, 98.8. A plot of log k against pH yields a line with a slope of 0.99 ± 0.02, showing that the reaction is first order in hydroxide ion.

The rate constants for the hydrolysis of *syn*-bimanes, *μ-syn*-bimanes (bridged) (**6**),[13] and *anti*-bimanes are summarized in Table II. The hydrolysis products from two of the bridged bimanes [**6**, X = NCH_3, $C(CN)_2$] have the usual λ_{max} at 290 nm. The hydrolysis product from the "zero-bridged" bimane **7** (λ_{max} 315 nm) has λ_{max} 305 nm and yields by further hydrolysis a compound, probably **8**, that absorbs at wavelengths below 240 nm. Due to the overlap of bimane and initial product absorption bands, the hydrolysis rate data were obtained for **7** with the loss of fluorescence. The rate constants for the hydrolysis of lactones are listed in Table III. To facilitate comparison between the reactivities of the bimanes and the lactones, we determined the activation energies for the hydrolysis of *syn*-(CH_3,Cl)B, *anti*-(CH_3,Cl)B, and (CH_3,Cl)-(CH_3,Cl)lactone and obtained values of 24 ± 1, 24 ± 1, and 21 ± 1 kcal/mol, respectively. The rate constants used for the plot of log k against $1/T$ are listed in Table IV.



6 7 8

Discussion

The present study provides (a) quantitation of the hydroxide ion reactivity of *syn*- and *anti*-bimanes, (b) verification of the course of the ring-opening reaction, (c) data on the facility with which the hydrolysis products may be reconverted to bimanes (or lactones) with electrophilic reagents, and (d) information valuable for improving the

Table II. Second-Order Rate Constants for the Reaction of Hydroxide Ion with *syn*-Bimanes, *μ*-*syn*-Bimanes, and *anti*-Bimanes at pH 9.80 and 50 °C[a]

$R_2 = R_2'$	R_1	R_1'	X	k_2, M^{-1} s^{-1}
		syn-Bimane		
CH_3	Cl	Cl		157
CH_3	Br	Br		114
CH_3	I	I		52
CH_3	H	H		1.9
CH_3	CH_3	CH_3		1.0
CH_3	CH_3	Cl		15
CH_3	H	Cl		24
CH_3	$(CH_3)_3C$	$(CH_3)_3C$		0.032
H	Cl	Cl		1470[b]
H	H	H		21
H	CH_3	CH_3		9.7
H	H	Cl		254
$COOC_2H_5$	Cl	Cl		>5000[c]
		μ(X)-*syn*-Bimane		
CH_2	CH_3	CH_3	$C(CN)_2$	29[d]
CH_2	CH_3	CH_3	NCH_3	15[d]
CH_2	CH_3	CH_3	(zero bridge)	60, 1.4[d,e]
		anti-Bimane		
CH_3	Cl	Cl		230
CH_3	Br	Br		155
CH_3	CH_3	CH_3		1.9
CH_3	H	H		3.6

[a] 0.1 M sodium carbonate buffer was used; the rate constants are ±10%. [b] 0.1 M sodium carbonate buffer, pH 8.83, was used in this experiment. [c] Estimated from rapid decrease in absorption at pH 9.0 and 25 °C. [d] 0.1 M sodium carbonate buffer, pH 10.0, was used at 25 °C. The rate constant listed was estimated for 50 °C with an E_a of 24 kcal/mol. [e] The "zero-bridged" bimane (λ_{max} 315 nm) in an initial fast reaction yields an acid (λ_{max} 305 nm) that disappears at the lower rate listed in the table. The amounts of material available have been too small to allow structural studies of the final product.

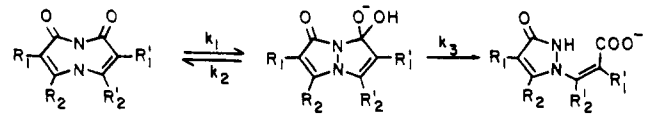
Table III. Rate Constants for the Reaction of Hydroxide Ion with Lactones at pH 9.0 and 25 °C[a]

$R_2 = R_2' = CH_3$		
R_1[c]	R_1'	k_2,[b] M^{-1} s^{-1}
H	H	4.0
H	Cl	13
CH_3	CH_3	3.0
Br	CH_3	100[d]
CH_3	Br	9.8[d]
Cl	CH_3	180[e]
CH_3	Cl	15[e]
Cl	Cl	640

[a] 0.1 M sodium carbonate buffer. [b] ±10%. [c] Photoisomerization of an unsymmetrically substituted *anti*-bimane produces a mixture of two isomeric lactones. R_1 represents the substituent on the lactone ring opened by the hydrolysis (cf. ref 4). [d] Measured with the mixture of two lactones derived from photoisomerization of *anti*-(CH_3, Br)(CH_3,CH_3)B (cf. ref 4). [e] Measured with the mixture of two lactones derived from photoisomerization of *anti*-(CH_3,Cl)(CH_3,CH_3)B (cf. ref 4).

yields of bimanes and the design of biological labeling experiments.

The overall mechanism for the hydrolysis of *syn*- and *anti*-bimanes is no doubt similar to that for other carboxylic acid derivatives (eq 4).[17] No intermediate was



(4)

Table IV. Rate Constants for the Hydrolysis of *syn*-(CH_3,Cl)B, *anti*-(CH_3,Cl)B, and (CH_3,Cl)(CH_3,Cl)lactone at Different Temperatures

	k_2,[b] M^{-1} s^{-1}		
T,[a] K	*syn*-(CH_3,Cl)B	*anti*-(CH_3,Cl)B	lactone
288.7			200
293.9			364
298.2	6.5	10	640
303.4			985
308.2	24.6	43.1	
313.3	50.0	76.9	3600
318.1	96.8	138	
323.0	157	230	

[a] ±0.1. [b] ±10%.

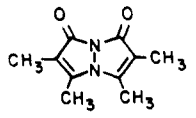
detected, as in the case of *N*,*N*-dimethyltrifluoroacetamide and potassium *tert*-amyl oxide in isooctane[18] or sodium methoxide and ethyl trifluoroacetate.[19] The overall rate constant for hydrolysis may be written (eq 5) in terms of rate constants for the steps shown in eq 4.

$$k_{hydrol} = k_1[k_3/(k_2 + k_3)] = k_1[1/(k_2/k_3 + 1)] \quad (5)$$

Oxygen exchange experiments suggest that $k_3 \gg k_2$ if a good leaving group is present in the tetrahedral intermediate (as in the case of esters), but that $k_3 \ll k_2$ for poor leaving groups (like amides). Since the pK_a of the leaving group in the case of the bimanes is probably 12 or less[20] (there is remarkably little difference between *syn*- and *anti*-bimanes with respect to hydrolysis rate), k_3 is expected to be greater than k_2, and the rate-limiting step in hydrolysis is that of addition to the carbonyl group.

The rate constants at 25 °C for the hydrolysis of bimanes [k_2 0.86 M^{-1} s^{-1} for *syn*-(H,H)B] are much higher than those for *N*,*N*-dimethylformamide (ca. 2×10^{-4} M^{-1} s^{-1})[21] or benzamide (2×10^{-5} M^{-1} s^{-1}).[22]

The carbonyl group in bimanes is only weakly conjugated to the adjacent atoms, as shown by the C=O bond lengths (1.21–1.22 Å) in all bimanes thus far examined.[23-28] High rates of hydroxide ion addition to bimane carbonyl groups may thus be expected. The relatively small increase in hydrolysis rate constant (factor of 60) observed for the strained "zero-bridged" *syn*-bimane (7)[29] over that for **9** indicates that relief of strain contributes only modestly to the hydrolysis rate.



9

(17) Jencks, W. P. *Progr. Phys. Org. Chem.* **1964**, *2*, 63.
(18) Fraenkel, G.; Watson, D. *J. Am. Chem. Soc.* **1975**, *77*, 231–232.
(19) Bender, M. L. *J. Am. Chem. Soc.* **1953**, *75*, 5986.
(20) Veibel, S.; Lillelund, H. *Tetrahedron* **1957**, *1*, 201–213.
(21) Guthrie, J. P. *J. Am. Chem. Soc.* **1974**, *96*, 3608–3615.
(22) Bender, M. L.; Ginger, R. D. *J. Am. Chem. Soc.* **1955**, *77*, 348.
(23) Kosower, E. M.; Bernstein, J.; Goldberg, I.; Pazhenchevsky, B.; Goldstein, E. *J. Am. Chem. Soc.* **1979**, *101*, 1620–1621.
(24) Bernstein, J.; Goldstein, E.; Goldberg, I. *Cryst. Struct. Commun.* **1980**, *9*, 295.
(25) Bernstein, J.; Goldstein, E.; Goldberg, I. *Cryst. Struct. Commun.* **1980**, *9*, 301.
(26) Goldberg, I. *Cryst. Struct. Commun.* **1980**, *9*, 329.
(27) Goldberg, I.; Bernstein, J.; Kosower, E. M.; Goldstein, E.; Pazhenchevsky, B., to be submitted.
(28) Goldberg, I.; Bernstein, J.; Kosower, E. M. *Acta Crystallogr.*, in press.
(29) Kosower, E. M.; Hermolin, J.; Pazhenchevsky, B.; Goldberg, I., work in progress.

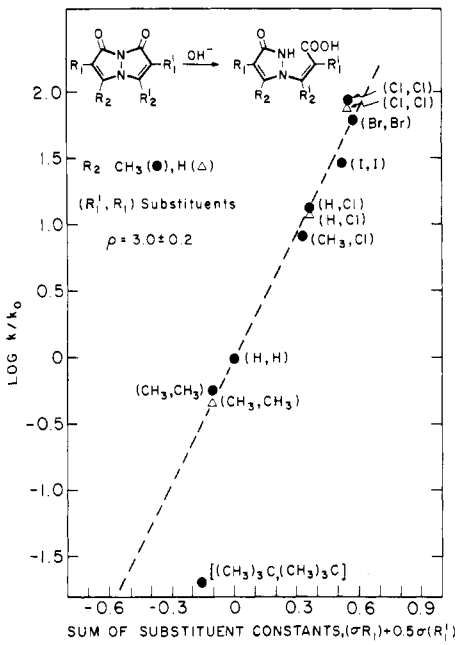


Figure 2. A plot of log k/k_0 vs. the function, σ (R_1) + 0.5σ (R_1') in which k represents the rate constants for the hydrolysis of the *syn*-bimanes shown on the figure (k_0 is the corresponding rate constant for the H,H derivatives). Rate constants for two series of compounds are included in the plot, one group with R_2 = CH_3, and a second group for compounds in which R_2 = H. The rate constant for the di-*tert*-butyl derivative deviates substantially from the linear correlation shown in the plot (see text).

Both R_1 substituents influence the rate of hydrolysis, electron-withdrawing groups increasing the rate. The best correlation [ρ = 3.0 (syn), 3.2 (anti)] of the hydrolysis rate constants with Hammett σ constants was obtained with the function σ (R_1) + 0.5σ (R_1') (Figure 2).[30] The effect of substituents on the rate of hydrolysis of lactones is somewhat greater than that on the hydrolysis of bimanes, with a ρ of 3.7. From the arguments given above, it is likely that the major effect of the substituents is on the rate of addition to the carbonyl group. *tert*-Butyl groups at R_1 impede the attack of OH^- on *syn*-bimanes, probably by a steric effect.

R_2 substituents affect the hydrolysis rate somewhat more than R_1 substituents, but data are insufficient to define the relative effects of R_2 and R_2'. We have estimated the ρ values as 4 with the same function as that used to correlate the rate constants in which R_1 is varied.

Reversal of the ring-opening process should proceed through attack of the pyrazolinone anion on a neutral carboxylic acid derivative. Indeed, ring closure of a 2-pyrazolinonylacrylic acid methyl ester in pH 6.7 buffer has been reported.[2] The consequence of the requirement for a pyrazolinone anion and a neutral carboxylic acid species would be a peculiar pH dependence, complicated by the possibility that NH can attack a carboxylic acid derivative with a sufficiently good leaving group, as in ring closure promoted by thionyl chloride. It is worth noting that the strongest peak in the mass spectrum of most of the pyrazolinonylacrylic acids corresponds to the mass of the bimane (molecular weight of the acid − 18).

Implications. A more systematic approach to maximizing the yield of bimanes is made possible by our results. A search for the pyrazolinonylacrylic acid or treatments of the residues from bimane syntheses with a series of electrophilic agents should improve the yields in a number of critical cases. The choice of base for the bimane syntheses may now be made with greater precision so as to avoid unnecessary loss of product through the ring-opening reaction.

The bimane-labeled proteins and cells may be stored for long periods of time. However, it is clear that alkaline treatment at any stage of a procedure involving electronegatively substituted bimanes should be as brief as possible to avoid loss of label. The hydrolysis rate constants are straightforward enough to measure and should be considered as necessary background in any extensive use of bimanes for particular problems.

(30) Plots of log k/k_0 vs. [σ (R_1 + $X\sigma$ (R_1')], in which X was set equal to 0, 0.25, 0.75, or 1, were definitely less well correlated by a straight line. Many additional studies would be needed to establish the accuracy of the correlation using X = 0.5; for the present, it seems to be a useful guide for the evaluation of reactivity in bimane systems.

Experimental Section

Materials. The synthesis and proof of structure of all bimanes and lactones used for the hydrolysis studies have been reported elsewhere.[2,4,13,15]

***syn*-(H,Cl)B Reaction with Hydroxide Ion.** *syn*-(H,Cl)B (10 mg, 0.05 mmol) in sodium hydroxide solution (10 mL, 0.1 M, 1 mmol) was stirred at 23 °C until the fluorescence had disappeared (2 h) and then brought to pH 2 with 1 N HCl. After the solution was stirred for 24 h, no fluorescence was noted, and the pH was brought to pH 1 with 1 N HCl. After 0.5 h, the 2-pyrazolinonylacrylic acid [2-(2-chloro-2-carboxyvinyl)-4-chloro-3-pyrazolin-5-one, **4**] was filtered off as a white solid: yield 9 mg (ca. 90%); mp 214 °C. A second experiment with *syn*-(H,Cl)B (80 mg, 0.4 mmol) gave 87 mg (96%) of acid: ^{1}H NMR (Me_2SO) 7.50 (s), 8.17 (s) ppm; UV (CH_3CN) λ_{max} 308 (ϵ 6000); mass spectrum, m/e 222, 224, 226 (M^+).

Regeneration of *syn*-(H,Cl)B from the Acid 4. A mixture of thionyl chloride (0.5 mL) and the acid **4** (80 mg) was stirred for 24 h, the thionyl chloride was removed under vacuum, and the residue was crystallized from CH_3CN. Unreacted acid (15 mg, 20%) was recovered by filtering the hot CH_3CN, which yielded 45 mg (63%) of pure *syn*-(H,Cl)B on cooling. Absorption (389 nm) and emission maxima (443 nm) and chromatographic behavior were identical with those of authentic *syn*-(H,Cl)B.

***syn*-(H,H)B Reaction with Hydroxide Ion.** *syn*-(H,H)B (6 mg, 0.045 mmol) in sodium hydroxide solution (2 mL, 1 M, 2 mmol) was heated at 50 °C until the fluorescence had disappeared (ca. 1 h) and then the solution was cooled to ca. 0 °C and brought to pH 1 with 6 N HCl. The precipitated acid, 2-pyrazolinonylacrylic acid [2-(2-carboxyvinyl)-3-pyrazolin-5-one, **4a**] was filtered off as a white solid: mp 187 °C (dec with bubbling); ^{1}H NMR (Me_2SO) 8.31 (d, J = 3 Hz), 7.15 (d, J = 11.1 Hz), 5.93 (d, J = 3 Hz), 5.18 (d, J = 11.1 Hz) ppm.

***anti*-(CH_3,Cl)B Reaction with Hydroxide Ion.** *anti*-(CH_3,Cl)B (54 mg, 0.2 mmol) in sodium hydroxide solution (5 mL, 0.1 M, 0.5 mmol) was heated at 70 °C until the starting material had disappeared (2 h), cooled, and then brought to pH 1 with 1 N HCl. The acid **5** [1-(1-methyl-2-chloro-2-carboxyvinyl)-3-methyl-4-chloro-3-pyrazolin-5-one] was filtered off as a white solid: yield 30 mg (53%): mp 170 °C; IR (KBr) 3400–2500, 1720, 1620, 1570, 1560, 1420, 1250, 1220, 1140, 1085, 1060, 1010, 960, 890, 790, 770, 750 cm^{-1}; ^{1}H NMR (D_2O) 2.19 (s), 2.23 (s) ppm. UV (CH_3CN) λ_{max} 257 nm (ϵ 10 200); mass spectrum, m/e 232, 234, 236 (M^+ − 18).

The (CH_3,Cl)(CH_3,Cl)lactone (32 mg, 0.14 mmol) was stirred with sodium hydroxide solution (5 mL, 0.1 M, 0.5 mmol) for 1 h at 25 °C and brought to pH 1 with 1 N HCl, and the acid **5**, 20 mg (60%), was filtered off.

Regeneration of *anti*-(CH_3,Cl)B and (CH_3,Cl)(CH_3,Cl)-lactone. A solution of the acid **5** in 1 N HCl was stirred for 48 h, the solvent was removed, and the residue was extracted with CH_2Cl_2 to yield 20 mg of *anti*-(CH_3,Cl)B (90%) and (CH_3,Cl)-(CH_3,Cl)lactone (10%) as determined by NMR.

The acid **5** (10 mg, 0.04 mmol) was stirred with acetic anhydride (2 mL) for 15 h. The solvent was evaporated from the clear solution, water was added, the acid was neutralized carefully with sodium carbonate, and the mixture was extracted with CH_2Cl_2.

Removal of the solvent left 8 mg (90%) of a mixture of *anti*-(CH_3,Cl)B (27%) and (CH_3,Cl)(CH_3,Cl)lactone (73%) as determined by NMR.

Conversion of (CH_3,CH_3)(CH_3,CH_3)lactone to *anti*-(CH_3,CH_3)B. The lactone (28 mg, 0.15 mmol), initially a suspension, was stirred in sodium hydroxide (15 mL, 0.1 M, 1.5 mmol) for 2 h, the light yellow solution was acidified (ca. pH 2.5), the solution was stirred for a few hours and then extracted with $CHCl_3$, the extract was dried ($MgSO_4$), and the solvent was removed to yield 26 mg (93%) of *anti*-(CH_3,CH_3)B (90%) and lactone (10%) as shown by NMR.

A similar experiment with (CH_3CH_2,CH_3)(CH_3CH_2,CH_3)lactone yielded *anti*-(CH_3CH_2,CH_3)B (79%) and lactone (21%).

Rate Measurements. Low Rates. Bimane in CH_3CN (0.1 mL) was added to temperature-equilibrated buffer (3 mL) contained in a quartz cell. The absorption spectrum was measured with a Cary Model 17 spectrophotometer. For several *syn*-bimanes, fluorescence spectra were recorded with a Hitachi-Perkin-Elmer MPF 4.

High Rates. The bimane solution was added to the buffer being stirred by a small Teflon-coated bar moved by a small motor mounted below the cell holder with the chart paper running and the wavelength fixed at the absorption maximum. Smooth curves were usually observed after 1–2 s (mixing time). Sodium phosphate (pH 7–8) and sodium carbonate (pH 9–10) buffers were used. The pH values were measured at 25 °C and corrected to 50 °C with temperature factors recorded in the literature.[31]

Registry No. 4, 82666-04-4; 4a, 82666-05-5; 5, 82665-99-4; 6 (X = CH_2), 70090-46-9; 6 (X = NMe), 76421-32-4; 7, 82666-03-3; *anti*-(CH_3CH_2,CH_3)(CH_3CH_2,CH_3) B, 79746-62-6; *anti*-(benzo)(benzo)B, 18428-89-2; (CH_3CH_2)CH_3)(CH_3CH_2,CH_3)lactone, 79746-57-9; (benzo)(benzo)lactone, 3848-48-4; *syn*-(CH_3,Cl)(CH_3,Cl) B, 68654-19-3; *syn*-(CH_3,Br)(CH_3,Br) B, 74235-58-8; *syn*-(CH_3,I)(CH_3,I) B, 74235-76-0; *syn*-(CH_3,H)(CH_3,H) B, 74235-71-5; *syn*-(CH_3,CH_3)-(CH_3,CH_3)B, 68654-22-8; *syn*-(CH_3,CH_3)(CH_3,Cl)B, 68654-21-7; *syn*-(CH_3,H)(CH_3,Cl)B, 68654-24-0; *syn*-(CH_3,(CH_3)$_3$C)-(CH_3,CH_3)$_3$C)B, 82666-02-2; *syn*-(H,Cl)(H,Cl)B, 78763-68-5; *syn*-(H,H)(H,H)B, 79769-56-5; *syn*-(H,CH_3)(H,CH_3)B, 79746-89-7; *syn*-(H,H)(H,Cl)B, 79746-92-2; *syn*-($COOC_2H_5$,Cl)($COOC_2H_5$,Cl)B, 79746-74-0; *anti*-(CH_3,Cl)(CH_3,Cl)B, 68654-20-6; *anti*-(CH_3,Br)-(CH_3,Br) B, 74235-59-9; *anti*-(CH_3,CH_3)(CH_3,CH_3) B, 68654-23-9; *anti*-(CH_3,H)(CH_3,H)B, 74235-72-6; (CH_3,H)(CH_3,Cl)lactone, 82665-98-3; (CH_3,CH_3)(CH_3,CH_3)lactone, 79746-44-4; (CH_3,Br)-(CH_3,CH_3)lactone, 79746-50-2; (CH_3,CH_3)(CH_3,Br)lactone, 79746-49-9; (CH_3,Cl)(CH_3,CH_3)lactone, 79746-48-8; (CH_3,CH_3)(CH_3,Cl)-lactone, 79746-47-7; (CH_3,Cl)(CH_3,Cl)lactone, 79746-46-6; (CH_3,H)(CH_3,H)lactone, 74235-88-4; 2-(2-carboxyphenyl)benzopyrazoline-3-one, 18428-91-6; 2-(1,2-dimethyl-2-carboxyvinyl)-3,4-dimethyl-3-pyrazolin-5-one, 82666-00-0; 2-(1-ethyl-2-methyl-2-carboxyvinyl)-4-ethyl-3-methyl-3-pyrazolin-5-one, 82666-01-1; oxygen, 7782-44-7.

(31) (a) "Data for Biochemical Research"; Oxford University Press: Oxford, 1959; p 193. (b) "Handbook of Biochemistry and Molecular Biology"; 2nd ed.; CRC Press: Cleveland, 1970; pp 227–228.

Chemistry of Diazoacenaphthenones and Diazoacenaphthenes

S.-J. Chang, B. K. Ravi Shankar, and H. Shechter*

Department of Chemistry, The Ohio State University, Columbus Ohio 43210

Received December 29, 1981

Wolff rearrangements do not occur in photolyses or thermolyses of diazoacenaphthenone (**1**), 2-diazo-5-nitroacenaphthenone (**2**), and 2-diazoaceanthrenone (**3**) in various environments. Thermal and photochemical decompositions of **1** in cyclooctane result in loss of nitrogen and formation of 2-cyclooctylacenaphthenone (**29**). In 2-propanol containing oxygen, **1** converts photolytically to acenaphthenone (**22**), acetone (**23**), and 1,8-naphthalic anhydride (**25**). Irradiation of **1** in *tert*-butyl alcohol/oxygen yields 2-*tert*-butoxyacenaphthenone (**28**) by solvent capture along with **25**. Diazo ketones **1–3** do not effect photochemical cyclopropanation of simple olefins; electronegatively substituted olefins such as acrylonitrile and methyl acrylate do give spirocyclopropanes however. Oxazoles are formed by 1,3-dipolar reactions of **1–3** with nitriles with loss of nitrogen. Acetylenes also react photolytically with **1–3** with nitrogen expulsion to yield furans regiospecifically. Thermolyses of **1–3** in acetylenes, however, result in initial 1,3-dipolar addition reactions to give spiropyrazoles which undergo spontaneous [1,5] sigmatropic migrations of their carbonyl groups to nitrogen to form isoquinolines. Diazoacenaphthene (**13**) decomposes carbenically to acenaphthylene (**66**). Similarly, 2-diazo-1,1-dimethylacenaphthene (**14**) converts to 8-methylcycloprop[*a*]acenaphthylene (**66**) which then isomerizes thermally to methylphenalenes (**70a–d**). Further, 2-diazoacenaphthenone ethylene acetal (**17**) thermolyzes and photolyzes with migration of one of its acetal oxygen moieties to yield 8,9-dihydroacenaphtho[1,2-*b*]-*p*-dioxin (**73**). Ring contraction does not occur in carbenic decompositions of **13**, **14**, and **17**.

A study is now summarized of various thermal, photolytic, metal ion catalyzed, and 1,3-dipolar reactions of diazoacenaphthenone (**1**), 2-diazo-5-nitroacenaphthenone (**2**), and 2-diazoaceanthrenone (**3**)[1] (Chart I). Thermolysis of **1** has been reported to yield biacenedione (**7**) and acenaphthenequinone monoazine[2] (minor). Of major interest to the present effort is that previous attempts to prepare (1*H*-cyclobuta[*de*]naphthalen-1-ylidene)methanone (**8**) from 2-oxoacenaphthenylidene (**10**) as generated thermally from **1** failed.[3,4] While the present investigation was in progress, photolysis of **1** in an argon matrix at 8 K was found to give **8**, as assigned by IR methods.[5] Because of

(1) Summarized in part from the Ph.D. Dissertations of (a) S.-J.C. (1979) and (b) B.K.R.S. (1981) at The Ohio State University.

(2) Tsuge, O.; Shinkai, I.; Koga, M. *J. Org. Chem.* **1971**, *36*, 745.

(3) (a) Cava, M. P.; Litle, R. L.; Napier, D. R. *J. Am. Chem. Soc.* **1958**, *80*, 2257. (b) Reid, W.; Lowasser, H. *Justus Liebigs Ann. Chem.* **1965**, *683*, 118. (c) DeJongh, D. C.; Van Fossen, R. Y. *Tetrahedron* **1972**, *28*, 3603.

(4) For reviews of the Wolff rearrangement see: (a) Meier, G. G.; Zeller, K. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 32. (b) Kirmse, W. "Carbene Chemistry", 2nd ed.; Academic Press: New York, 1971; pp 475–493. (c) Weygand, F.; Bestmann, H. J. *Angew. Chem.* **1960**, *72*, 535. (d) Rodina, L. L.; Korobitsyna, I. K., *Russ. Chem. Rev. (Engl. Transl.)* **1967**, *36*, 260. (e) Smith, P. A. S. In Mayo, P. "Molecular Rearrangements"; Interscience: New York, 1963, pp 528–550, 558–564.

0022-3263/82/1947-4226$01.25/0 © 1982 American Chemical Society