Aziridines. XIX. Substituent Effects in the Pyrolytic Isomerization of 1-Aroyl-2,2-dimethylaziridines[1]

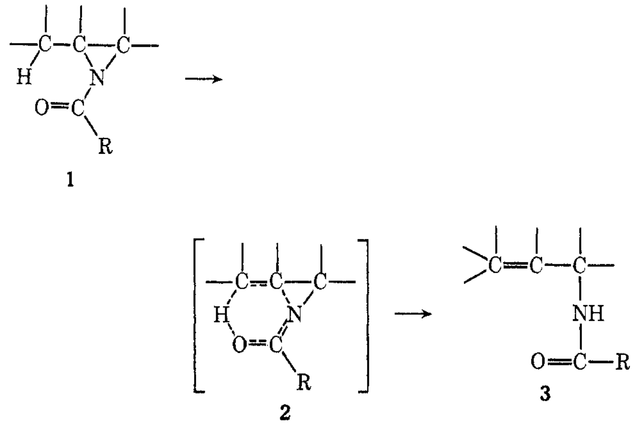
CHENG HSIUNG CHANG AND PAUL E. FANTA*

Department of Chemistry, Illinois Institute of Technology, Chicago, Illinois 60616

Received June 14, 1971

In a kinetic study of the pyrolytic rearrangement of seven substituted 1-benzoyl-2,2-dimethylaziridines at 79.2°, it was found that the isomeric *N*-(β-methallyl)benzamides are formed in a first-order reaction. The Hammett plot of the rate constants is linear with $\rho = +1.19$. These results provide further support for the conclusion that the rearrangement occurs *via* a transition state with charge separation in the rate-determining step.

The thermal isomerization of *N*-acyl- or aroylaziridines **1** to the isomeric *N*-allylcarboxamides **3** was first reported from our laboratory in 1956 and has been the subject of extensive investigation since that time.[2] These studies have provided support for the view that the reaction is a stereospecific cis elimination involving the transition state **2**. This paper is concerned with a study of the substituent effect in the aroyl group R, which further clarifies the nature of this transition state.

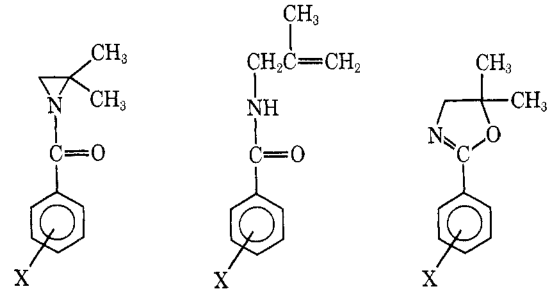


1

2

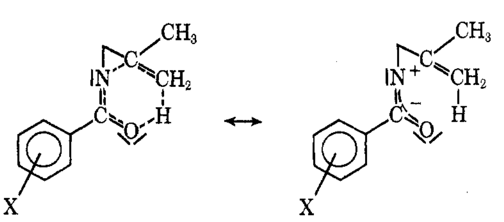
3

In an earlier publication,[3] it was reported that the thermal isomerization of 1-(*p*-nitrobenzoyl)-2,2-dimethylaziridine (**4a**) to *N*-(β-methallyl)-*p*-nitrobenzamide (**5a**) in diglyme is a first-order reaction with a large negative entropy of activation, which is also in agreement with the proposed mechanism. We have now extended the kinetic study to the six additional benzoyl derivatives **4b**–**g**. In diglyme at 79.2°, each of these *N*-acylaziridines formed the isomeric amide **5a**–**g** according to first-order kinetics, with rate constants summarized in Table I. The Hammett plot[4] for these data was found to be linear with no deviations and $\rho = +1.19$ as shown in Figure 1.

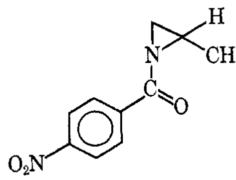


Substituent X			
p-NO_2	4a	5a	6a
m-NO_2	b	b	
p-CN	c	c	
m-Br	d	d	
p-Br	e	e	
H	f	f	
p-CH_3	g	g	g

The sign and magnitude of the ρ value indicates that the rate-determining step in the unimolecular reaction is the formation of a polarized transition state in which the negative charge is stabilized by the electron-attracting substituents in the phenyl ring. In terms of conventional resonance theory, **8** may be regarded as an important contributing form to the resonance hybrid **7**.



7 **8**



9

We also observed that, whereas 1-(*p*-nitrobenzoyl)-2,2-dimethylaziridine (**4a**) underwent isomerization in nitrobenzene with a half-life of about 5 hr at 82°, the homologous monomethyl compound **9** did not rearrange under the same conditions even after 140 hr. This provides further evidence for the participation of contributing structure **8**, in which the positive charge is on a tertiary carbon atom, rather than on a secondary carbon atom as it would be in the analogous transition state from compound **9**.

It is well known that the rate of a reaction increases with the dielectric constant of the medium if the transition state is more polar than the reactants or if the products are ions. Therefore we measured the rate of the isomerization of 1-(*p*-nitrobenzoyl)-2,2-dimethyl-

---

[1] Abstracted from the Ph.D. Thesis of C. H. Chang, submitted to Illinois Institute of Technology in 1969.

[2] I. J. Burnstein, P. E. Fanta, and B. S. Green, *J. Org. Chem.*, **35**, 4084 (1970), and earlier papers summarized in O. C. Dermer and G. E. Ham, "Ethylenimine and Other Aziridines," Academic Press, New York, N. Y., 1969, p 280.

[3] P. E. Fanta and M. K. Kathan, *J. Heterocycl. Chem.*, **1**, 293 (1964).

[4] E. S. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Rinehart and Winston, New York, N. Y., 1959, p 220.

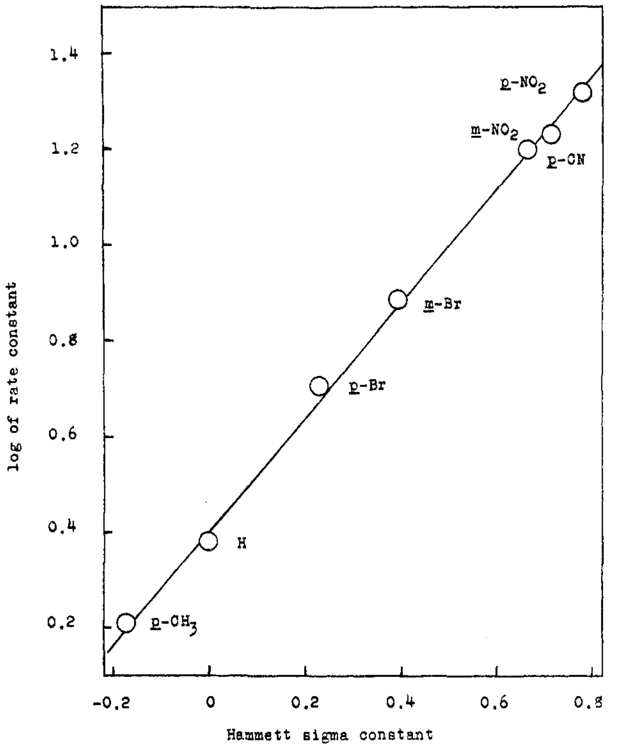


Figure 1.—Hammett plot for the formation of substituted *N*-(β-methallyl)benzamides in diglyme at 79.2°.

TABLE I

RATE CONSTANTS FOR THE FORMATION OF SUBSTITUTED *N*-(β-METHALLYL)BENZAMIDES IN DIGLYME AT 79.2°

Substituent	10^6k, sec^{-1}	Av 10^6k, sec^{-1}
p-NO$_2$	21.7 ± 0.5	21.3 ± 0.5
	21.6 ± 0.4	
	20.7 ± 0.6	
m-NO$_2$	18.4 ± 0.4	17.8 ± 0.3
	17.8 ± 0.1	
	17.3 ± 0.3	
p-CN	15.9 ± 0.2	16.1 ± 0.2
	16.1 ± 0.2	
	16.4 ± 0.2	
m-Br	7.52 ± 0.08	7.57 ± 0.10
	7.45 ± 0.15	
	7.75 ± 0.08	
p-Br	5.15 ± 0.13	5.17 ± 0.13
	5.18 ± 0.10	
	5.19 ± 0.16	
H	2.47 ± 0.05	2.43 ± 0.04
	2.28 ± 0.03	
	2.53 ± 0.03	
p-CH$_3$	1.61 ± 0.02	1.63 ± 0.03
	1.63 ± 0.03	
	1.64 ± 0.02	

aziridine (**4a**) in various solvents of different dielectric constant as summarized in Table II. The small difference in reaction rates suggests that the transition state **7** is not much more polarized than the ground state or that it is poorly solvated.

The effect of variation of temperature on the rate of isomerization of 1-(*p*-nitrobenzoyl)-2,2-dimethylaziridine in both nitrobenzene and chlorobenzene was measured as shown in Table III. These data gave a linear Arrhenius plot and were used for the calculation of the activation parameters, $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, which are included in Table III. The large negative value for the entropy of activation, $\Delta S^{\ddagger}$, is consistent with the formation of a cyclic transition state **2**.

TABLE II

RATE CONSTANTS FOR THE DISAPPEARANCE OF 1-(*p*-NITROBENZOYL)-2,2-DIMETHYLAZIRIDINE IN VARIOUS SOLVENTS AT 145°

Solvent	Dielectric constant (25°)	10^3k, sec^{-1}
Nitrobenzene	34.82	6.65 ± 0.16
o-Dichlorobenzene	9.93	5.80 ± 0.21
Chlorobenzene	5.62	5.10 ± 0.04
Bromobenzene	5.40	5.09 ± 0.04

TABLE III

RATE CONSTANTS AND REACTION PARAMETERS FOR THE DISAPPEARANCE OF 1-(*p*-NITROBENZOYL)-2,2-DIMETHYLAZIRIDINE IN NITROBENZENE AND CHLOROBENZENE

Temp, °C	10^5k, sec^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$-\Delta S^{\ddagger}$, eu
	In Nitrobenzene		
82.0	3.97 ± 0.04	23.3	14
110.4	50.6 ± 0.4		
132.0	268 ± 4		
145.0	665 ± 16		
	In Chlorobenzene		
82.0	3.37 ± 0.04	22.9	15
110.4	39.4 ± 0.6		
132.0	217 ± 2		
145.0	510 ± 4		

By careful examination of the nmr spectrum of the reaction mixture from the pyrolysis of 1-(*p*-nitrobenzoyl)-2,2-dimethylaziridine in nitrobenzene, it was found that the formation of unsaturated amide is accompanied by a small amount of the isomeric oxazoline (**6a**), representing about 3% of the product at 82° and 2% at 145°. This relatively small side reaction is not sufficient to affect the conclusions we have thus far drawn about the mechanism of isomerization.

On the other hand, we found that the isomerization product from the pyrolysis of the *p*-toluyl derivative **4g** in nitrobenzene contained a significantly larger fraction of oxazoline: about 12.8% at 145° and 32.8% at 82°. At 82° in nitrobenzene, 1-(*p*-toluyl)-2,2-dimethylaziridine isomerizes by parallel first-order reactions to give a ratio of unsaturated amide **5g** and oxazoline **6g** which is time independent, as shown by the data in Table IV.

Latvian workers had previously observed an analogous qualitative substituent effect in the isomerization of an aroylaziridine to an oxazoline. On heating at 110° for 2 hr, 1-furoylaziridine gave a 33% yield of the oxazoline, while the 5-nitrofuroyl derivative gave no reaction.[5] This observation, as well as our data, shows that in contrast to the substituent effect found for the isomerization of the acylaziridine to the unsaturated amide, the isomerization to oxazoline is *hindered* by an electron-attracting group in the aroyl moiety.

Such a result can be rationalized by a mechanism in which the rate-determining step is the formation of a transition state represented by the hybrid **10**, with contributing forms **11**, **12**, and **13**. Obviously, contributing form **11** will be destabilized when X is an electron-

---

(5) M. Lidaks and S. Hillers, *Latv. PSR Zinat. Akad. Vestis, Kim. Ser.*, **2**, 211 (1961); *Chem. Abstr.*, **58**, 4530 (1963), and private conversation.

TABLE IV

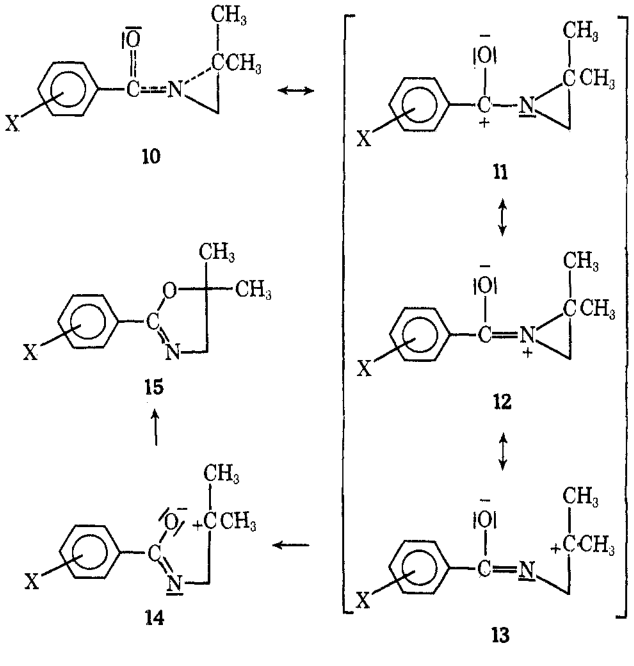
DATA FOR THE PYROLYTIC ISOMERIZATION OF 1-(p-TOLUYL)-2,2-DIMETHYLAZIRIDINE IN NITROBENZENE AT 82°

Time, hr	A_t,[a] %	B_t,[b] %	C_t,[c] %	B_t/C_t (= k_1/k_2)[d]
0	100	0	0	
12	85.52	9.80	4.68	2.09
24	73.17	17.68	9.15	1.93
40	56.84	28.40	14.76	1.92
54	45.15	37.00	17.85	2.07
82	28.66	47.10	23.83	1.98
117.5	16.12	56.15	27.24	2.06
135	11.89	58.62	29.01	2.02
∞	0	67.19	32.81	2.05

[a] The percentage of 1-(p-toluyl)-2,2-dimethylaziridine in the reaction mixture at time t. [b] The percentage of N-(β-methallyl)-p-toluamide in the reaction mixture at time t. [c] The percentage of 2-(p-toluyl)-5,5-dimethyl-2-oxazoline in the reaction mixture at time t. [d] The ratio of the rate constants for the formation of amide and oxazoline.

attracting substituent, and **13** will be destabilized in the homologous monomethylaziridine. In this mechanism, oxazoline formation is completed by the "unfolding" of **10** to the zwitterion **14**, which then cyclizes to the oxazoline **15** in a fast step.

Interestingly, the nmr chemical shifts of both the methyl and the methylene protons of the aroylaziridines **4a–g** were found to have a linear variation with the Hammett substituent constant σ, as summarized in Figure 2.



Experimental Section

Diglyme was refluxed over calcium hydride and then distilled in the presence of lithium aluminum hydride *in vacuo* prior to use. p-Nitrobenzoyl chloride was recrystallized from low-boiling petroleum ether. Microanalyses were carried out by Micro-Tech Laboratories, Inc., Skokie, Ill., and M-H-W Laboratories, Garden City, Mich.

General Procedure for the Preparation of 1-Aroyl-2,2-dimethylaziridines 4a–g.—To a solution of 7.1 g (0.10 mol) of 2,2-dimethylaziridine and 12.1 g (0.12 mol) of triethylamine in 200 ml of dry benzene was added dropwise with stirring a solution of 0.10 mol of substituted benzoyl chloride in 200 ml of dry benzene over a period of 1 hr at *ca.* 5°. The mixture was stirred at *ca.* 5° for an additional 4 hr and then allowed to warm to room temperature. The triethylamine hydrochloride was removed by filtration and solvent was evaporated *in vacuo* with a rotary evaporator leaving a crude product in 96–98% yield, which was chromatographed on a column containing 15 g of Woelm neutral alumina (grade I). Rapid elution with hexane gave, after evaporation of the solvent, 1-aroyl-2,2-dimethylaziridine. Solid products were recrystallized quickly from low-boiling petroleum ether. Liquid products were chromatographed again on another 10 g of Woelm neutral alumina; the middle fraction from elution with low-boiling petroleum ether was used. Yields of pure products were *ca.* 80%. Physical and analytical data are summarized in Table V.

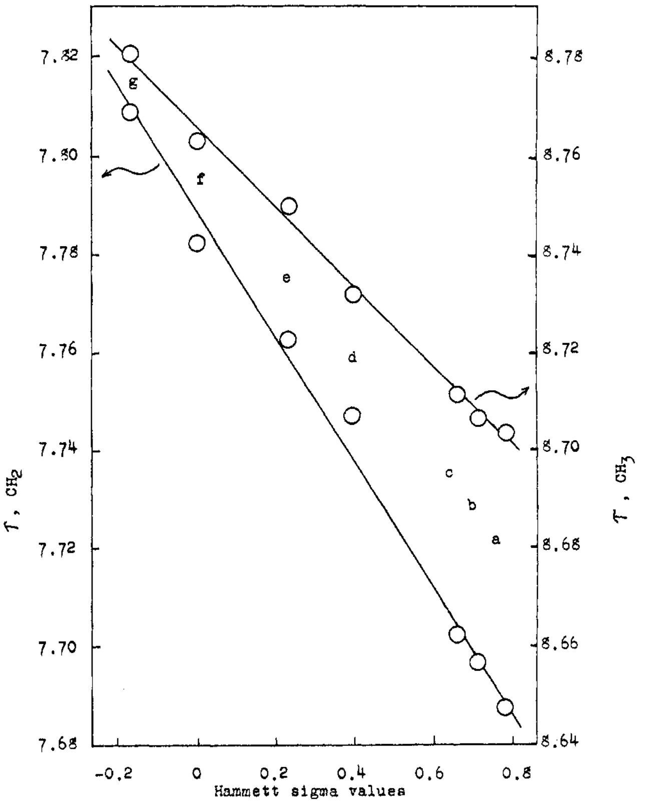


Figure 2.—Correlation of chemical shifts with the substituent constants for substituted 1-benzoyl-2,2-dimethylaziridines **4a–g** (CCl_4, 15% w/v).

TABLE V

DATA FOR 1-AROYL-2,2-DIMETHYLAZIRIDINES **4a–g**[a]

Substituent	$n^{25}D$ or mp, °C
p-NO_2	69–70[b]
m-NO_2	58.5–59.5
p-CN	63–64
m-Br	1.5514
p-Br	36.5–37.5
H	1.5328
p-CH_3	40.5–41.5

[a] Satisfactory analytical values (±0.3% for C and H) were reported for all new compounds: Ed. [b] Lit.[6] 78°.

Isolation of Substituted N-(2-Hydroxy-2-methylpropyl)benzamides.—Further elution with 4:1 benzene–methanol of each chromatographic column used for the purification of a substituted 1-benzoyl-2,2-dimethylaziridine gave a small yield of the corresponding hydrolysis product, a substituted N-(2-hydroxy-2-methylpropyl)benzamide, which was purified by recrystallization from benzene. Data for these derivatives are summarized in Table VI.

2-(p-Nitrophenyl)-5,5-dimethyl-2-oxazoline.—An authentic sample was prepared as previously described, mp 144–146° (lit.[6] 146–147.5°).

---

[6] H. W. Heine, M. E. Fetter, and E. M. Nicholson, *J. Amer. Chem. Soc.*, **81**, 2202 (1959).

TABLE VI

DATA FOR SUBSTITUTED *N*-(2-HYDROXY-2-METHYLPROPYL)BENZAMIDES[a]

Substituent	Registry no.	Mp, °C	Infrared bands (KBr), cm^{-1} ν_{OH}	ν_{NH}	ν_{CO}
p-NO_2	32158-96-6	139–140	3311	3222	1672
m-NO_2	6332-97-4	129.5–130.5	3312	3233	1672
p-CN	32158-98-8	116–117	3315	3242	1671
m-Br	32158-99-9	96.5–97	3320	3240	1672
p-Br	32159-00-5	139–140	3364	3250	1671
H		105–106	3378	3255	1672
p-CH_3	32159-01-6	133.5–134.5	3398	3264	1674

[a] Satisfactory analytical values (±0.3% for C and H) were reported for all new compounds: Ed.

TABLE VII

DATA FOR SUBSTITUTED *N*-(β-METHALLYL)BENZAMIDES

Substituent	Molecular formula	Mp, °C	Calcd, % C	Calcd, % H	Found, % C	Found, % H
p-NO_2	$C_{11}H_{12}N_2O_3$	127–128[a]				
m-NO_2	$C_{11}H_{12}N_2O_3$	94.0–95.5	59.99	5.49	59.84	5.50
p-CN	$C_{12}H_{12}N_2O$	119–120	72.00	6.05	72.52	6.11
m-Br	$C_{11}H_{12}BrNO$	93–94	51.99	4.76	52.09	4.55
p-Br	$C_{11}H_{12}BrNO$	97–98	51.99	4.76	52.14	4.61
H	$C_{11}H_{13}NO$	69–70[b]				
p-CH_3	$C_{12}H_{15}NO$	77–77.5	76.11	8.07	76.25	8.28

[a] Lit.[6] mp 126–127.5°. [b] Mp 69.5–70.5°: J. C. Sheehan and G. D. Laubach, *J. Amer. Chem. Soc.*, **73**, 4376 (1951).

2-(*p*-Toluyl)-5,5-dimethyl-2-oxazoline.—An authentic sample was prepared in 81% yield by treatment of 1-(*p*-toluyl)-2,2-dimethylaziridine with anhydrous aluminum chloride in refluxing hexane, mp 47–48° after sublimation.

Anal. Calcd for $C_{12}H_{15}NO$: C, 76.11; H, 8.07. Found: C, 76.32; H, 8.25.

1-(*p*-Nitrobenzoyl)-2-methylaziridine was prepared by treatment of 2-methylaziridine and triethylamine in benzene with *p*-nitrobenzoyl chloride. A sample purified by sublimation had mp 78.5–79.5°. The nmr spectrum (in $CDCl_3$) showed multiplets in the following regions: τ 8.62–8.53 (3 H, CH_3), 8.80–8.74 (1 H, CH), 7.46–7.28 (2 H, CH_2), and 1.98–1.58 (4 H, aromatic protons).

Anal. Calcd for $C_{10}H_{10}N_2O_3$: C, 58.25; H, 4.89. Found: C, 58.52; H, 4.90.

Preparation of Substituted *N*-(β-Methallyl)benzamides 5a–g.—A solution of 3.0 g of the substituted 1-benzoyl-2,2-dimethylaziridine in 50 ml of dry xylene was refluxed for 3 hr. After removal of the solvent, the solid residue was recrystallized twice from benzene–hexane. Each compound discharged the purple color of a solution of potassium permanganate in aqueous methanol and had the expected spectral characteristics: an NH band in the infrared at 3235–3280 cm^{-1} and nmr bands ($CDCl_3$) at τ 8.21–8.26 (m, 3 H), 5.96–6.06 (d, J = 6 Hz, 2 H), and 5.10–5.17 (m, 2 H). The nmr NH band was broad and its location was concentration dependent. Other data are summarized in Table VII.

Kinetic Measurements. Infrared Method.—The kinetic values for the formation of the *N*-(β-methallyl)benzamides (data in Table I) were obtained by measuring the change in the NH band in the infrared spectrum near 3347 cm^{-1}, as described in a previous publication.[3] To prevent absorption of atmospheric moisture, the samples in diglyme were prepared and the ampoules were filled in a dry nitrogen atmosphere in a glove box. An initial concentration of 0.200 *M* aroylaziridine was used, and spectra were measured on the Perkin-Elmer Model 257 spectrophotometer, using 0.2-mm NaCl cells.

Nmr Method.—The data shown in Tables II–IV were obtained from integration curves of nmr spectra obtained on the Varian A-60 spectrometer. Solutions with a concentration of 10% w/v of aroylaziridine were prepared and handled in a dry nitrogen atmosphere. Only one sealed nmr tube was prepared for each kinetic run. The tube was placed in a thermostated bath and removed at intervals and quenched in an ice bath for determination of the spectrum. It was then returned to the bath for further suitable intervals, until the infinity point at 10 half-lives was reached.

The kinetics of the isomerization of 1-(*p*-nitrobenzoyl)-2,2-dimethylaziridine was followed by measuring the disappearance of the methylene proton band in **4a** and the appearance of the methyl proton bands of **5a** and **6a**. Each integration was run three to five times, and a mean value was calculated. The integration value of the methylene peak of **4a** was tripled and the methyl peak of **5a** was doubled to convert all values to the same scale.

Similarly, the kinetics of the rearrangement of 1-(*p*-toluyl)-2,2-dimethylaziridine in nitrobenzene were followed by measuring the disappearance of the methyl peak in the aroylaziridine (τ 8.75), the appearance of the methyl peak in the unsaturated amide (τ 8.19), and the appearance of the methyl peak in the oxazoline (τ 8.53).

Registry No.—**4a**, 781-86-2; **4b**, 32044-15-8; **4c**, 32044-16-9; **4d**, 32158-84-2; **4e**, 32158-85-3; **4f**, 21384-58-7; **4g**, 32158-87-5; **5a**, 782-83-2; **5b**, 32158-89-7; **5c**, 32158-90-0; **5d**, 32158-91-1; **5e**, 32158-92-2; **5f**, 709-25-1; **5g**, 32158-94-4; **6g**, 32136-34-8; **9**, 21384-47-4.