Ring-opening Reactions of Some 1-Ethoxycarbonylaziridines with Acetic Acid in Cyclohexane

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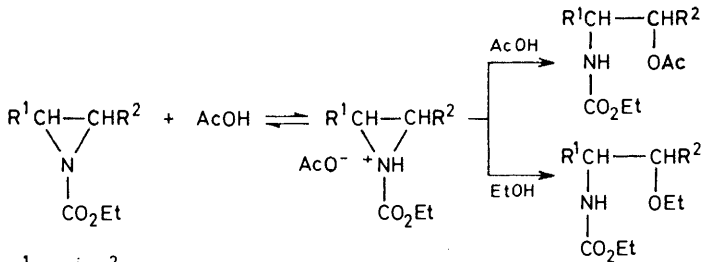
The formation of *N*-(2-acetoxylalkyl)carbamates by acetolysis of 1-ethoxycarbonylaziridines in cyclohexane follows an *A*-2 mechanism where the rate is first order in the aziridine and second order in acetic acid. The regiospecificity of the formation and the reactivity can be interpreted by an *A*-2 mechanism where bond-breaking is more advanced than bond-making, so that these properties are controlled by electronic factors (a so-called borderline *A*-2 mechanism). However, an *A*-2 mechanism largely governed by steric hindrance of initial attack and strain relief on opening, respectively, is proposed for *cis*-aziridines with bulky substituents at 2- and/or 3-positions. *N*-Allylcarbamates formed in some cases appear to result from an *A*-1 mechanism.

AZIRIDINES are of interest as biological alkylating and anti-cancer agents, and their chemistry has been extensively investigated in recent years.[1] Nucleophilic attack on the aziridine ring in non-acidic media generally occurs by an S_N2 mechanism.[2-5] A borderline mechanism which lies between *A*-1 and *A*-2 has been proposed for ring-opening in acidic media.[6-8] The mechanism is mainly based on product criteria, but there is scarcely any detail from the kinetic point of view.[7] In this paper, we examine the direction of ring-opening of representative 1-ethoxycarbonylaziridines by acetic acid in cyclohexane, determine the kinetic form and the reactivity of formation of *N*-(2-acetoxyalkyl)carbamates, and argue for the mechanism on the basis of electronic and steric effects on the directional and kinetic data.



(3) *cis*, $R^1 = Pr^i$, $R^2 = Me$
(4) *trans*, $R^1 = Me$, $R^2 = Pr^i$
(6) $R^1 = H$, $R^2 = Ph$

SCHEME 1

RESULTS AND DISCUSSION

Direction of Ring-opening Reactions of 1-Ethoxycarbonylaziridines with Acetic Acid.—Eight 1-ethoxycarbonylaziridines (1)—(8) were prepared as described in Experimental section. Each of the aziridines (1)—(7) was dissolved in acetic acid at room temperature overnight and the reactions went to completion. The reaction of (8) was carried out under reflux (*ca.* 115°) in acetic acid for 1 h since it did not react under the above conditions. The structures of products (9)—(20) were confirmed by i.r., n.m.r., and mass spectra and elemental analyses. The results obtained are summarized in Table 1. The yields of (9)—(18) were nearly equal to those for reactions with acetic acid in cyclohexane (see later).

Catalytic Action of Acetic Acid and Exclusion of an A-1 *Mechanism.*—The ring-opening reactions of (3), (4), or (6) with ethanol in cyclohexane or in cyclohexane–benzene are very slow, but are greatly accelerated by addition of a small amount of acetic acid to give products of acetolysis and ethanolysis (Scheme 1). First-order rate constants k'_{obs} of the reaction of aziridine (6) were evaluated by using equation (1) where a_t and a_o are the concentrations of aziridine at time t and zero, respectively. The value k'_{obs} in cyclohexane–benzene in the presence of

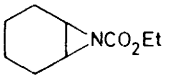
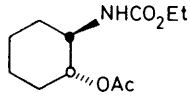
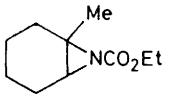
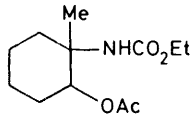
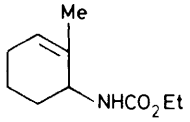
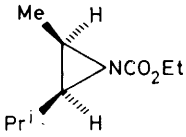
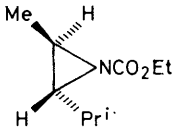
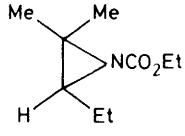
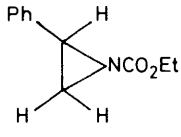
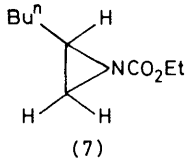
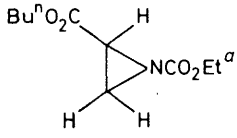
$$\ln a_o/a_t = k'_{obs.}\, t \qquad (1)$$

both ethanol (0.20M) and acetic acid (0.16M) was six times as high as that in the same solvent in the presence of acetic acid (0.16M) only. The results indicate that ring-opening is catalysed by acetic acid, and that nucleophiles such as ethanol and acetic acid attack the protonated intermediate in the rate-determining step. If opening occurred by an *A*-1 mechanism, the rate of loss of aziridine should not be affected by the presence of ethanol. Thus, the reaction does not proceed by an *A*-1 mechanism.

An A-2 *Mechanism for Formation of* N-(2-*Acetoxyalkyl*) *Carbamates.*—In order to determine the reaction order in acetic acid, the acetolysis of aziridines (1)—(7) was carried out in cyclohexane with the condition $[AcOH]_o \gg a_o$, where the concentration of acetic acid could be constant

TABLE 1

Products of ring-opening of 1-ethoxycarbonylaziridines with acetic acid and rate coefficients (Kk/l^2 mol^{-2} s^{-1}) for the formation of *N*-(2-acetoxyalkyl)carbamates at 30° in cyclohexane

 (1)	$(6\cdot6 \pm 0\cdot6) \times 10^{-5}$		 (9) 100%
 (2)	$(1\cdot1 \pm 0\cdot01) \times 10^{-4}$	 (10) 72%	 (11) 28%
 (3)	$(2\cdot1 \pm 0\cdot005) \times 10^{-6}$		$MeCH(OAc)CH(Pr^i)NHCO_2Et$ (12) 100%
 (4)	$(7\cdot9 \pm 0\cdot015) \times 10^{-6}$		$MeCH(NHCO_2Et)CH(Pr^i)OAc$ (13) 100%
 (5)	$(7\cdot7 \pm 0\cdot75) \times 10^{-5}$	$Me_2C(OAc)CH(Et)NHCO_2Et$ (14) 76%	$CH_2{=}C(Me)CH(Et)NHCO_2Et$ (15) 24%
 (6)	$(2\cdot0 \pm 0\cdot1) \times 10^{-3}$		$PhCH(OAc)CH_2NHCO_2Et$ (16) 100%
 (7)	$(9\cdot6 \pm 0\cdot4) \times 10^{-5}$	$Bu^nCH(OAc)CH_2NHCO_2Et$ (17) 66%	$Bu^nCH(NHCO_2Et)CH_2OAc$ (18) 34%
 (8)	~ 0	$Bu^nO_2CCH(NHCO_2Et)CH_2OAc$ (19) 87%	$Bu^nO_2CCH(OAc)NHCO_2Et$ (20) 13%

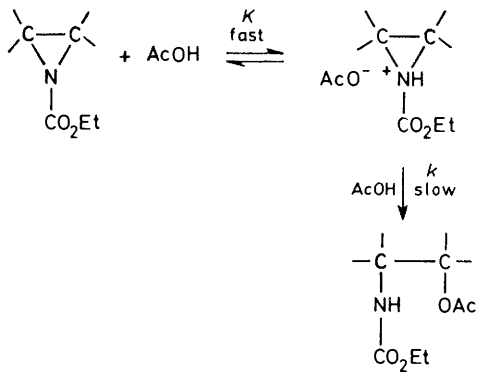
[a] The reaction was carried out under reflux at *ca.* 115° for 1.5 h. No product was formed at room temperature overnight. [b] In the determination of Kk, the concentration of acetic acid was assumed to be that of the monomer.

during the reaction. The first-order rate constants k_{obs} for formation of products were evaluated by using equation (2) where x_t and x_∞ are product concentrations at time t and ∞, respectively. Linear plots of k_{obs} for (1), (3), (4), (6), and (7) *versus* $[AcOH]_0^2$ were obtained, suggesting that the formation obeys *A*-2 kinetics as shown in Scheme 2.

$$\ln x_\infty/(x_\infty - x_t) = k_{obs.}\, t \qquad (2)$$

Equation (3) can be derived for the *A*-2 mechanism.

$$k_{obs} = Kk[AcOH]_0^2 \qquad (3)$$



SCHEME 2

The values of Kk are determined from the slopes of the linear plots, and summarized in Table 1. Figures 1 and 2 present the method for the determination of k_{obs} and Kk for aziridine (1).

Acetolysis of (7) gives two products (17) and (18) and the total rate constant of product formation is indicated as Kk in Table 1. The method above for the determination of k_{obs} and Kk leads to serious errors for aziridines (2) and (5) because of the formation of the *N*-allylcarbamates (11) and (15) along with the *N*-(2-acetoxyalkyl)carbamates. For these aziridines, initial

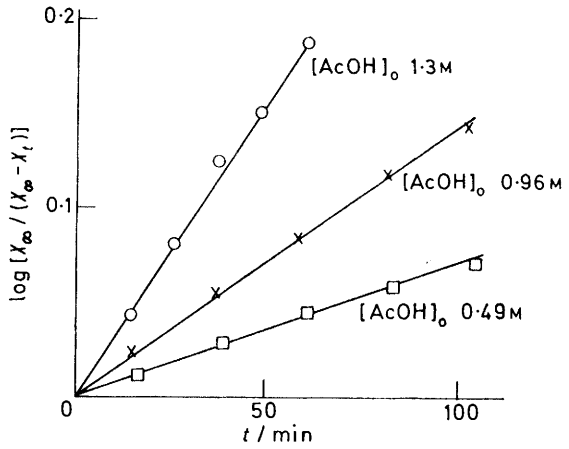


FIGURE 1 Plots of $\log [x_\infty/(x_\infty - x_t)]$ against time for the reaction of 7-ethoxycarbonyl-7-azabicyclo[4.1.0]heptane (1) with acetic acid in cyclohexane

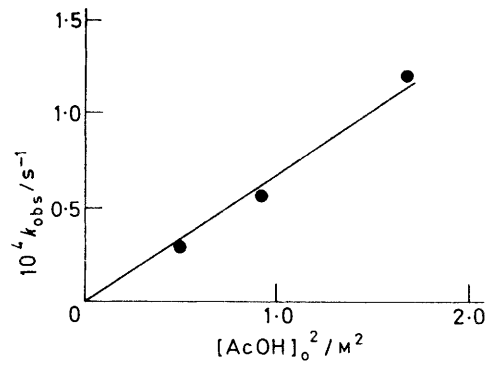


FIGURE 2 Relationship between k_{obs} and $[AcOH]_0^2$ for the reaction of 7-ethoxycarbonyl-7-azabicyclo[4.1.0]heptane (1) with acetic acid in cyclohexane

rates v_0 for the formation of *N*-(2-acetoxyalkyl)carbamates only were evaluated by using equation (4),

$$v_0 = Kka_0[AcOH]_0^2 \qquad (4)$$

expected for *A*-2 kinetics. The data are shown in Table 1. Figures 3 and 4 present the method for the determination of v_0 and Kk for (2).

Mechanism for Ring-opening Reactions.—It was assumed that the basicities (K values) of aziridines (1)—(7) were almost equal to each other for the following

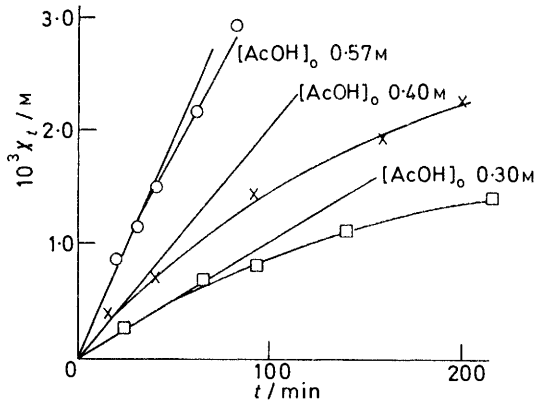


FIGURE 3 Plots of x_t against time for the reaction of 7-ethoxycarbonyl-1-methyl-7-azabicyclo[4.1.0]heptane (2) with acetic acid in cyclohexane. $a_0 = 2.0 \times 10^{-2}$M

reasons. 2-Alkyl- and 2,3-dialkyl-aziridines have nearly the same pK_b values,[9] and 1-acylaziridines are usually protonated not on the carbonyl oxygen but on the nitrogen atom of the three-membered ring.[10] Thus, the magnitude of Kk is proportional to the value k, the rate constant of the rate-determining step.

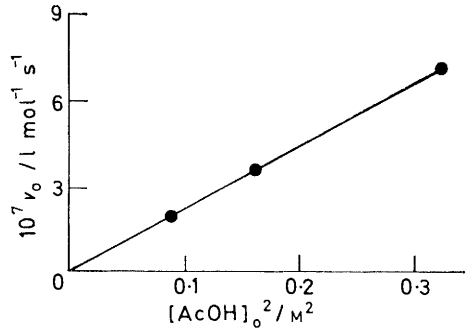
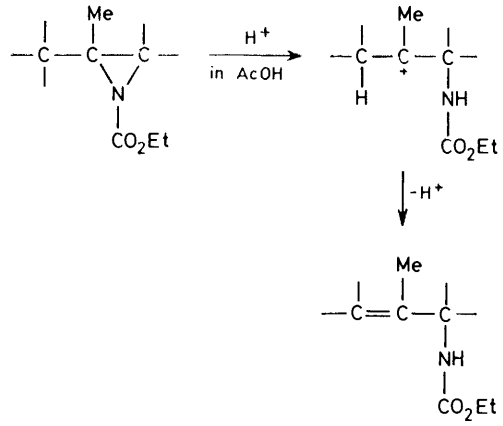


FIGURE 4 Relationship between v_0 and $[AcOH]_0^2$ for the reaction of 7-ethoxycarbonyl-1-methyl-7-azabicyclo[4.1.0]heptane (2) with acetic acid in cyclohexane. a_0 2.0×10^{-2}M

The direction of opening of aziridines (4)—(8) is mainly affected by electronic factors because the acetoxy-group preferentially attacks the carbon atom best able to accommodate some carbocation character. The reactivity order for the formation of *N*-(2-acetoxyalkyl)-carbamates, (6) > (7) > (5) > (4) > (8), except for (7), is compatible with the electronic effect since a substituent stabilizes a positive charge more the higher the reactivity. Bond-breaking in these aziridines is some-

what prior to bond-making, *i.e.* the transition state is in good agreement with that of a borderline *A*-2 mechanism.[6-8] The evidence that the rate of formation of *N*-(2-acetoxyalkyl)carbamates obeys purely *A*-2 kinetics rules out an *A*-1 mechanism for the reaction.

According to the Taft σ* value, the Pr^i group can support a positive charge on a neighbouring carbon atom better than Me. Thus, attack on aziridine (4) takes place on the carbon atom attached to Pr^i to give (13). The partial positive charge at C-2 in (7) is stabilized by the +*I* effect of Bu^n in the transition state leading to the expected product distribution (17) > (18). A similar attack on C-2 in (8) leads to a positive charge highly destabilized by the electron-withdrawing carbonyl group, and the formation of (20) is disfavoured compared with that of (19). This agrees with the marked reduction in rate for (8).



SCHEME 3

The exceptionally high reactivity of (7) perhaps depends upon the relief of the great ring strain due to the bulky Bu^n group upon opening. The direction of opening of (7) is inconsistent with the fact that water attacks mostly the unsubstituted carbon in 2-ethyl- and 2-methyl-aziridine in acidic aqueous solution.[3] The difference in variables may change the direction of ring-opening.

N-Allylcarbamates (11) and (15) may result from an *A*-1 mechanism as shown in Scheme 3. The protonation of (2) or (5) perhaps causes the formation of a tertiary carbocation which yields (11) or (15) after deprotonation.

Aziridine (1) showed a tendency to engage in *trans*-ring-opening as expected.[6] Interestingly, in *cis*-aziridine (3) and *trans*-aziridine (4), ring-opening is highly regiospecific. The formation of (10) from (2) and the cleavage of (3) involve attack on the less hindered carbon atom of the aziridine. The rate of formation of *N*-(2-acetoxyalkyl)carbamates for aziridines (1)—(3) increases with an increase in the strain relief upon ring-opening: (2) > (1) > (3).

It is impossible to explain the results on the grounds of the electronic effects mentioned above. We propose that *N*-(2-acetoxyalkyl)carbamates from *cis*-aziridines (1)—(3) are formed by an *A*-2 mechanism in which the steric hindrance to initial attack controls the direction of ring-opening, and in which the reactivity depends upon the relief of strain upon ring-opening. The proposal is supported by the following considerations. When the acetoxy-group approaches the back-side of the breaking C–N bond, the attacking group and the two substituents in a *cis*-relationship may be susceptible to steric interference. However, this interference is considerably compensated by much greater relief of strain upon ring-opening of *cis*- compared with *trans*-aziridines. Thus, ring-opening involves the scission of the less hindered C–N bond in accord with an *A*-2 mechanism.

The formation of (10) and (11) from (2) does not square with that of (14) and (15) from (5) at first sight since (2) gives no product from attack of the acetoxy-group on C-2 associated with a high degree of positive charge. However, this can be resolved by the explanation that the formation of *N*-(2-acetoxyalkyl)carbamates occurs *via* an aziridinium ion, not a carbocation, *i.e.* the carbocation formed from (2) or (5) much prefers deprotonation giving (11) or (15) to attack of the acetoxy-group. This is supported by the idea that *N*-(2-acetoxyalkyl)carbamates are not produced by an *A*-1 mechanism.

The entropy of activation $\Delta S^{\ddagger}$ may better provide an insight into the transition state of ring-opening. The activation parameters $\Delta S^{\ddagger}$ and $\Delta H^{\ddagger}$ for *cis*- and *trans*-aziridines (3) and (4) were calculated from the *Kk* values at four temperatures by application of transition state theory (Table 2). The values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ of both

TABLE 2

Rate constants and activation parameters for acetolysis of *cis*- and *trans*-aziridines (3) and (4) in cyclohexane

Aziridine	Temperature (°C)	10^6 *Kk*/l^2 mol^{-2} s^{-1}	$\Delta H^{\ddagger}$/kcal mol^{-1}	$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1}
(3)	20.4	1.0 ± 0.03		
	30.4	2.1 ± 0.005		
			10.9 ± 0.1	−48.5 ± 0.5
	39.7	3.85 ± 0.11		
	49.8	7.15 ± 0.32		
(4)	20.4	3.9 ± 0.02		
	30.4	7.85 ± 0.015		
			10.7 ± 0.6	−46.9 ± 1.9
	39.7	13 ± 0.02		
	49.8	24.5 ± 0.03		

aziridines were nearly the same. The magnitude of $\Delta S^{\ddagger}$ for (4) should be considerably greater than that of (3) since bond-breaking in (4) in the transition state proceeds to a greater extent than in (3). However, an increase in freedom ($\Delta S^{\ddagger}$) by the relief of strain upon ring-opening would be greater in the *cis*-aziridine (3) compared with the *trans*-isomer (4). Therefore, the values of $\Delta S^{\ddagger}$ for both aziridines do not differ markedly. This also supports our proposal of an *A*-2 mechanism for *cis*-aziridines. We point out that this relief of strain should be taken into account when discussing the transition state of ring-opening of aziridines in terms of entropy considerations.

Steric and electronic effects on ring-opening of aziridines may be different from those for S_N1 or S_N2 re-

actions for alkyl halides. This probably depends upon the specific character of the aziridines, the great strain energy,[11] and unusual bond angles [12,13] and bond lengths.[13,14]

EXPERIMENTAL

I.r. spectra were obtained on a Hitachi model EPI-G3 spectrometer. ^{1}H N.m.r. spectra were taken with a Varian EM-360 spectrometer with tetramethylsilane as internal standard. ^{13}C N.m.r. spectra were measured with a Nippon Densi JNM-FX 90 Q instrument. Mass spectra were recorded on a Hitachi RMU-6E spectrometer. G.l.c. analyses were carried out with Shimazu GC-6A unit using glass column (1 m × 3 mm) (column A, 10% polyethylene glycol 20 M on 60—80 Uniport KS; column B, 10% silicone SE 30 on 60—80 Uniport KS). Photolyses were performed externally in a quartz tube (25 cm × 1.8 cm) with a 300 W high pressure mercury lamp (Halōs PIH-300).

Acetic acid, cyclohexane, and benzene were purified by standard methods before use. Ethyl azidoformate was obtained by the method described in the literature.[15]

Preparations of Aziridines (1)—(8).—The preparation of *cis*- or *trans*-1-ethoxycarbonyl-2-isopropyl-3-methylaziridine (3) or (4), b.p. 54—55° or 56—60° at 3 mmHg was performed by the literature method.[16] Aziridines (1), (5), and (7) were synthesized by the photolysis of a solution (10—15 ml) of ethyl azidoformate and the corresponding olefins in the molar ratio *ca.* 1 : 2. 7-Ethoxycarbonyl-7-azabicyclo[4.1.0]-heptane (1) had b.p. 125—126° at 20—23 mmHg (lit.,[17] 68° at 1.25 mmHg). 1-*Ethoxycarbonyl*-2-*ethyl*-3,3-*dimethyl*-*aziridine* (5) (47%) had b.p. 53—55° at 4 mmHg, $\nu_{max.}$ (neat) 2 960 (C–H), 1 720 (C=O), 1 460 (C–N), 1 430 (CH_2), 1 370 and 1 330 (CH_3), and 1 260 and 1 100 cm^{-1} (C–O), δ(CCl_4) 3.9 (2 H, q, OCH_2), 1.9 (1 H, t, NCH), and 0.8—1.8 (14 H, m, CH_2 and CH_3), *m/e* 171 (M^+), 142, 98, 84, 70, and 56 (Found: C, 62.85; H, 10.2; N, 8.3. $C_9H_{17}NO_2$ requires C, 63.15; H, 10.0; N, 8.2%). 1-*Ethoxycarbonyl*-2-*n*-*butylaziridine* (7) (18%) had b.p. 107° at 17 mmHg, $\nu_{max.}$ (neat) 2 920 (C–H), 1 725 (C=O), 1 460 (C–N), 1 410 (CH_2), 1 370 (CH_3), and 1 300 and 1 205 cm^{-1} (C–O), δ (CCl_4) 4.1 (2 H, q, OCH_2), 2.0—2.5 (2 H, m, NCH_2), 1.75—2.00 (1 H, m, CH), and 0.7—1.7 (12 H, m, CH_2 and CH_3), *m/e* 171 (M^+), 142, 139, 138, 86, 70, 69, and 56 (Found: C, 62.8; H, 10.35; N, 8.25. $C_9H_{17}NO_2$ requires C, 63.15; H, 10.0; N, 8.25%). A solution (10—15 ml) consisting of ethyl azidoformate and 1-methylcyclohexene, styrene, or n-butyl acrylate in the molar ratio *ca.* 1 : 2 was heated at 120° for 1—3 h. Distillation of the mixture using 1-methylcyclohexene gave 7-*ethoxycarbonyl*-1-*methyl*-7-*azabicyclo*[4.1.0]*heptane* (2) (35%), b.p. 120—122° at 17 mmHg, $\nu_{max.}$ (neat) 2 910 (C–H), 1 710 (C=O), 1 510 (C–N), 1 440 (CH_2), 1 370 (CH_3), and 1 260 and 1 070 cm^{-1} (C–O), δ(CCl_4) 3.9 (2 H, q, OCH_2), 2.2 (1 H, t, NCH), and 0.7—2.0 (14 H, m, CH_2 and CH_3), *m/e* 183 (M^+), 154, 110, and 94 (Found: C, 65.15; H, 9.7; N, 7.65. $C_{10}H_{17}NO_2$ requires C, 65.55; H, 9.35; N, 7.65%). When styrene and n-butyl acrylate are used as olefins, the distillates, b.p. 108—110° at 0.5 mmHg and 115—116° at 1 mmHg, respectively, yielded 1-ethoxycarbonyl-2-phenyl-aziridine (6) (55.5%) and 1-ethoxycarbonyl-2-n-butoxy-carbonylaziridine (8) (60%) according to their ^{1}H n.m.r. data and acetolyses: (6), δ(CCl_4) 7.2 (5 H, s, phenyl), 3.9—4.3 (2 H, q, OCH_2), 3.2—3.5 (1 H, m, 2-CH), 2.15 and 2.6 (2 H, each d, 3-CH_2), and 1.3 (3 H, t, CH_3); (8), δ(CCl_4) 4.0—4.3 (4 H, m, OCH_2), 2.8—3.0 (1 H, m, 2-CH), 2.2—2.5 (2 H, m, 3-CH_2), and 0.7—1.8 (10 H, m, CH_2 and CH_3).

Ring-opening Reactions of 1-*Ethoxycarbonylaziridines* (1)—(8) *with Acetic Acid.*—Each of the aziridines (1)—(8) was dissolved in acetic acid and allowed to stand at room temperature overnight. After the solvent had evaporated, the mixture was distilled under reduced pressure. The following compounds were isolated and identified.

trans-1-*Acetoxy*-2-(*ethoxycarbonylamino*)*cyclohexane* (9).—The structure was confirmed by comparison of the i.r. and n.m.r. spectra with those of an authentic sample.[18]

1-*Acetoxy*-2-(*ethoxycarbonylamino*)-2-*methylcyclohexane* (10).—This had b.p. 121—124° at 1 mmHg, $\nu_{max.}$ (neat) 3 330 (N–H), 2 920 (C–H), 1 730 (C=O), 1 530 (C–N), 1 440 (CH_2), 1 370 (CH_3), and 1 250 cm^{-1} (C–O), δ(CCl_4) 4.6—5.3 (1 H, m, CH). 4.1 (2 H, q, OCH_2), 3.7—4.3 (1 H, NH), 2.0 [3 H, s, C(=O)CH_3], 1.2 (3 H, t, CH_3), and 0.8—2.2 (11 H, CH_2 and 2-CH_3), *m/e* 242 (M^+), 183, 154, and 141 (Found: C, 59.1; H, 8.85; N, 5.9. $C_{12}H_{21}NO_4$ requires C, 59.25; H, 8.7; N, 5.75%).

6-(*Ethoxycarbonylamino*)-1-*methylcyclohexene* (11).—This had m.p. 43—46°, $\nu_{max.}$ (Nujol) 3 300 (NH), 1 720 (C=O), 1 670 (C=C), 1 530 (C–N), and 1 250 cm^{-1} (C–O), δ(CCl_4) 5.2—5.7 (1 H, m, 2-CH), 4.3—4.8 (1 H, m, 6-CH), 4.1 (2 H, q, OCH_2), 3.7—4.2 (1 H, NH), 1.7 (3 H, s, 1-CH_3), 1.3—2.4 (6 H, m, CH_2), and 1.25 (3 H, t, CH_3), *m/e* 183 (M^+), 154, 137, 94, and 79.

Ethyl N-(2-*Acetoxy*-1-*isopropylpropyl*)*carbamate* (12).—This had m.p. 46.5—47°, $\nu_{max.}$ (Nujol) 3 340 (NH), 1 720 (C=O), 1 530 (C–N), and 1 230 and 1 030 cm^{-1} (C–O), δ(CCl_4) 4.8—5.3 (1 H, m, OCH), 4.3—4.8 (1 H, NH), 4.05 (2 H, q, OCH_2), 3.1—3.5 (1 H, m, NCH), 1.5—1.9 (1 H, m, CH), 1.95 [3 H, s, C(=O)CH_3], and 0.7—1.5 (12 H, m, CH_3), *m/e* 231 (M^+), 144, 128, 116, 100, and 72 (Found: C, 56.8; H, 9.45; N, 5.95. $C_{11}H_{21}NO_4$ requires C, 57.1; H, 9.15; N, 6.05%).

Ethyl N-(2-*Acetoxy*-1,3-*dimethylbutyl*)*carbamate* (13).—This had m.p. 46.5—48°, $\nu_{max.}$ (Nujol) 3 300 and 3 065 (NH), 1 730 and 1 690 (C=O), 1 550 (C–N), and 1 240 and 1 060 cm^{-1} (C–O), δ(CCl_4) 4.85 (1 H, t, OCH), 4.3—4.65 (1 H, NH), 4.05 (2 H, q, OCH_2), 3.35—3.8 (1 H, m, NCH), 1.95 [3 H, s, C(=O)CH_3], 1.4—1.8 (1 H, m, CH), and 0.7—1.4 (12 H, m, CH_3), *m/e* 231 (M^+), 144, 128, 116, 100, 72, 55, and 43 (Found: C, 56.75; H, 9.2; N, 6.1. $C_{11}H_{21}NO_4$ requires C, 57.1; H, 9.15; N, 6.05%).

Ethyl N-(2-*Acetoxy*-1-*ethyl*-2-*methylpentyl*)*carbamate* (14).—This had b.p. 91—94° at 1.5 mmHg, $\nu_{max.}$ (neat) 3 310 (NH), 2 970 (C–H), 1 730 (C=O), 1 530 (C–N), 1 460 (CH_2), 1 370 (CH_3), and 1 240, 1 150, and 1 075 cm^{-1} (C–O), δ(CCl_4) 5.0—5.45 (1 H, NH), 4.1 (2 H, q, OCH_2), 3.5 (1 H, t, NCH), 1.95 [3 H, C(=O)CH_3], and 0.7—1.9 (14 H, m, CH_2 and CH_3), *m/e* 231 (M^+), 171, 142, 130, 114, 98, 84, 70, 59, and 43 (Found: C, 57.15; H, 9.35; N, 6.35. $C_{11}H_{21}NO_4$ requires C, 57.1; H, 9.15; N, 6.05%).

Ethyl N-(1-*Ethyl*-2-*methylprop*-2-*enyl*)*carbamate* (15).—The product was isolated by preparative g.l.c. using column A, $\nu_{max.}$ (neat) 3 310 (N–H), 3 050 (C=C–H), 1 705 (C=O), 1 530 (C–N), 1 450 (CH_2), 1 380 (CH_3), and 1 240 and 1 085 cm^{-1} (C–O), δ(CCl_4) 4.85 (2 H, s, $C=CH_2$), 4.3—4.75 (1 H, NH), 4.1 (2 H, q, OCH_2), 3.4—3.8 (1 H, m, NCH), 1.75 (3 H, s, $C=CCH_3$), and 0.7—1.7 (8 H, m, CH_2 and CH_3), *m/e* 171 (M^+), 142, 96, 70, and 56 (Found: C, 62.75; H, 10.2; N, 8.2. $C_9H_{17}NO_2$ requires C, 63.15; H, 10.0; N, 8.15%).

Ethyl N-(2-*Acetoxy*-2-*phenylethyl*)*carbamate* (16).—This had b.p. 155—159° at 0.2 mmHg, $\nu_{max.}$ (neat) 3 325 (N–H), 1 690—1 750 (C=O), 1 525 (C–N), 1 450 (CH_2), 1 370 (CH_3), 1 230, 1 150, and 1 030 (C–O), and 860 and 700 cm^{-1} (Ph),

δ(CCl_4) 7.3 (5 H, s, Ph), 5.8 (1 H, t, OCH), 4.9—5.3 (1 H, NH), 4.05 (2 H, q, OCH_2), 3.45 (2 H, t, NCH_2), 2.05 [3 H, s, C(=O)CH_3], and 1.2 (3 H, t, CH_3), *m/e* 251 (M^+), 205, 163, 162, 149, 118, 107, 102, 91, 79, and 77 (Found: C, 62.55; H, 6.9; N, 5.8. $C_{13}H_{17}NO_4$ requires C, 62.15; H, 6.8; N, 5.55%).

Ethyl N-(2-*Acetoxyhexyl*)*carbamate* (17) *and Ethyl* N-(1-*Acetoxymethylpentyl*)*carbamate* (18).—A mixture of (17) and (18) had b.p. 114.5—115° at 1 mmHg, $\nu_{max.}$ (neat) 3 340 (N–H), 2 960 (C–H), 1 730 (C=O), 1 530 (C–N), 1 470 (CH_2), 1 370 (CH_3), and 1 240 cm^{-1} (C–O), δ_H (CCl_4) 4.6—5.35 (NH and OCH), 4.1 (q, OCH_2), 3.1—3.5 (NCH and NCH_2), 2.0 [s, C(=O)CH_3], and 0.7—1.7 (CH_2 and CH_3), δ_C ($CDCl_3$) 170.9 (s, O–C=O), 170.8 (s, O–C=O), 156.9 (s, C=O), 156.5 (s, C=O), 76.3 (d, OCH), 66.4 (t, AcOCH_2), 60.9 [t, NC(=O)CH_2], 60.8 [t, NC(=O)CH_2], 50.6 (d, NCH), 44.5 (t, NCH_2), 31.7 (t, 3-CH_2), 31.5 (t, 3-CH_2), 28.1 (t, 4-CH_2), 27.5 (t, 4-CH_2), 22.6 (t, 5-CH_2), 21.0 [q, C(=O)CH_3], 20.6 [q, C(=O)CH_3], 14.7 (q, OCH_2CH_3), and 13.9 p.p.m. (q, 6-CH_3), *m/e* 231 (M^+), 158, 143, 129, 112, 97, 86, 83, 82, 69, and 56 (Found: C, 56.7; H, 9.35; N, 6.2. Calc. for $C_{11}H_{21}NO_4$: C, 57.1; H, 9.15; N, 6.05%).

Ethyl N-(2-*Acetoxy*-1-*n*-*butoxycarbonylethyl*)*carbamate* (19).—This had b.p. 143—145° at 0.3 mmHg, $\nu_{max.}$ (neat) 3 340 (N–H), 2 980 (C–H), 1 740 (C=O), 1 525 (C–N), 1 460 (CH_2), 1 370 (CH_3), and 1 225 and 1 065 cm^{-1} (C–O), δ(CCl_4) 5.2—5.7 (1 H, NH), 3.9—4.7 (7 H, m, NCH and OCH_2), 2.0 [3 H, s, C(=O)CH_3], and 0.7—1.9 (10 H, m, CH_2 and CH_3), *m/e* 275 (M^+), 215, 203, 188, 174, 132, 114, 101, 86, 74, 60, and 57 (Found: C, 52.3; H, 7.8; N, 5.45. $C_{12}H_{21}NO_6$ requires C, 52.35; H, 7.7; N, 5.1%).

Ethyl N-(2-*Acetoxy*-2-*n*-*butoxycarbonylethyl*)*carbamate* (20). The compound was isolated by g.l.c. using column A, and identified as follows: $\nu_{max.}$ (neat) 3 330 (N–H), 2 950 (C–H), 1 755 (C=O), 1 530 (C–N), 1 460 (CH_2), 1 370 (CH_3), and 1 225 and 1 095 cm^{-1} (C–O), δ(CCl_4) 4.95 (1 H, t, OCH), 4.6—5.2 (1 H, NH), 3.75—4.6 (4 H, m, OCH_2), 3.55 (2 H, t, NCH_2), 2.0 [3 H, s, C(=O)CH_3], and 0.7—1.8 (10 H, m, CH_2 and CH_3), *m/e* 275 (M^+), 215, 188, 174, 160, 156, 132, 114, 102, 76, 60, 57, and 43 (Found: C, 51.9; H, 7.85; N, 5.0. $C_{12}H_{21}NO_4$ requires C, 52.35; H, 7.7; N, 5.1%).

The yields for products (9)—(20) were determined by n.m.r. and g.l.c. using column A.

Ring-opening Reactions of Aziridines (3), (4), *and* (6) *with Ethanol.*—Aziridine (3) or (4) was dissolved in cyclohexane in the presence of ethanol (6M), and left at room temperature overnight. A product of ethanolysis was detected by g.l.c. analysis.

In ethanol in the presence of acetic acid (0.16M), the reaction of (3) or (4) proceeded regiospecifically to give the ethanolysis products (21) (56%) or (22) (15%), along with the acetolysis products (12) (14%) or (13) (12%). The characterization of the ethanolysis products (21) and (22) is as follows.

Ethyl N-(2-*Ethoxy*-1-*isopropylpropyl*)*carbamate* (21).—This had $\nu_{max.}$ (neat) 3 420 (N–H), 2 920 and 2 870 (C–H), 1 700 (C=O), 1 500 (C–N), 1 370 (CH_3), and 1 210 and 1 070 cm^{-1} (C–O), δ(CCl_4) 4.3—4.8 (1 H, m, OCH), 3.95 [2 H, q, C(=O)OCH_2], 2.9—3.65 (4 H, m, NCH, NH, and OCH_2), 1.3—1.8 (1 H, m, CH), and 0.8—1.4 (15 H, m, CH_3), *m/e* 217 (M^+), 174, 144, 116, 100, 73, 56, and 55 (Found: C, 60.55; H, 10.9; N, 6.45. $C_{11}H_{23}NO_3$ requires C, 60.8; H, 10.65; N, 6.45%).

Ethyl N-(2-*Ethoxy*-1,3-*dimethylbutyl*)*carbamate* (22).—This had $\nu_{max.}$ (neat) 3 300 (N–H), 2 920 (C–H), 1 685 (C=O), 1 520 (C–N), 1 360 (CH_3), and 1 230, 1 150, and 1 090 cm^{-1} (C–O), δ(CCl_4) 4.2—4.7 (1 H, m, OCH), 3.9 [2 H, q, C(=O)OCH_2], 3.0—3.7 (4 H, m, NCH, NH, and OCH_2), 1.5—2.0 (1 H, m, CH), and 0.7—1.4 (15 H, m, CH_3), *m/e* 217 (M^+), 174, 144, 116, 101, 73, and 55 (Found: C, 60.45; H, 10.75; N, 6.6. $C_{11}H_{23}NO_3$ requires C, 60.8; H, 10.65; N, 6.45%).

Ring-opening of (6) was very slow in cyclohexane–benzene in the presence of ethanol (0.2M) at 30°. However, the addition of acetic acid (0.16M) accelerated the reaction to give the ethanolysis product (23) in good yield.

Ethyl N-(2-*Ethoxy*-2-*phenylethyl*)*carbamate* (23).—This had b.p. 133—136° at 2 mmHg, $\nu_{max.}$ (neat) 3 320 (N–H), 2 970 (C–H), 1 710 (C=O), 1 510 (C–N), 1 450 (CH_2), 1 370 (CH_3), 1 240 and 1 100 (C–O), and 760 and 700 cm^{-1} (Ph), δ(CCl_4) 7.5 (5 H, s, Ph), 4.8—5.2 (1 H, NH), 3.9—4.5 [3 H, m, CH and C(=O)CH_2], 3.0—3.8 (4 H, m, OCH_2 and NCH_2), and 1.0—1.3 (6 H, m, CH_3), *m/e* 237 (M^+), 171, 145, 135, 79, 77, and 45 (Found: C, 65.5; H, 8.15; N, 5.95. $C_{13}H_{19}NO_3$ requires C, 65.8; H, 8.05; N, 5.9%).

The yields were determined as described above.

Kinetic Measurements.—A mixture of aziridine and acetic acid in a molar ratio more than 1 : 15 was dissolved in cyclohexane. Mixtures containing three different quantities of acetic acid were made up and analysed at various times for reaction at a given temperature. The yields were estimated by means of g.l.c. using column A, but that of (18) was done using column B.

The rate of ring-opening of (6) in the presence of both acetic acid (0.16M) and ethanol (0.20M) or in the presence of acetic acid (0.16M) was obtained by determination of the amount of (6) as a function of time. In this case, the amount of (6) was measured by g.l.c. using column A.

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