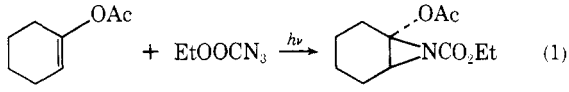
The Addition of Acid Chlorides to Azirines. Functionalized Aziridines and Oxazolines[1a]

Alfred Hassner,*[1b] Susan S. Burke,[1c] and Jesse Cheng-fan I

Contribution from the Department of Chemistry, University of Colorado, Boulder, Colorado 80302. *Received March 25, 1974*

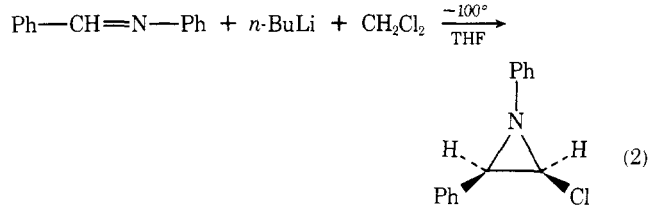
Abstract: Acyl chlorides add readily to 3,3-dimethyl-2-phenylazirine **1**, and the products **3** can be converted to functionalized (azido, acetoxy) *N*-acylaziridines and oxazolines. These conversions are shown to proceed via *N*-acylazirinium ions. Spectral and mechanistic interpretations are presented.

Aziridines have been of interest as biological alkylating and anticancer agents.[2] Although alkyl and aryl substituted aziridines and 2-oxazolines are by now familiar compounds,[2,3,4] relatively few examples of C functionally substituted aziridines have been reported. For instance, ethyl azidoformate has been added to 1-cyclohexenyl acetate[5] (eq 1). In general the reaction of diazomethane with imines af-



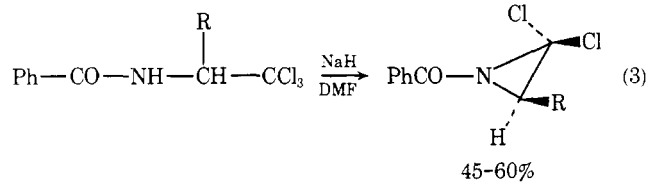
(1)

fords triazolines, but aziridines were obtained from imines with strong electron withdrawing substituents.[6] A number of the relatively unstable 2-halo- and 2,2-dihaloaziridines have been synthesized via carbene addition to benzalaniline derivatives[2,7,8] (eq 2).



(2)

Zaugg and Denet have recently shown that *N*-2-trichloroethylbenzamides can be ring closed with base in polar solvent[9] (eq 3). In addition, substituted aziridines have been



(3)

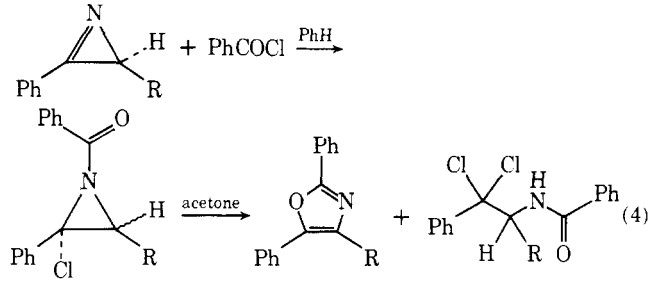
45-60%

proposed[10] and, in some cases, isolated[11] in the reactions of acids with azirines.

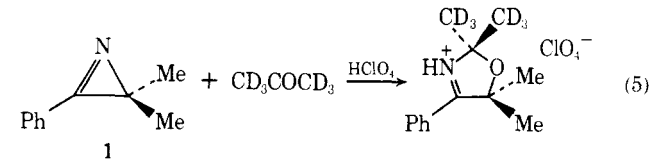
With the exception of perhalogenated compounds,[3] functionalized 2-oxazolines have been reported only recently. A 5-chloro-2-oxazoline was inferred as an intermediate in the cycloaddition of benzoyl chloride to an azomethine ylide.[12] Similarly the reaction of the anion derived from tosyl methyl isocyanide with an acid chloride gave an oxazole.[13]

A cyanoacetoxy oxazoline was characterized in a mixture of products from an electrochemical cyclization,[14] and Padwa et al. reported a stable thiazoline thioether from a photocycloaddition.[15]

A few years ago, it was reported that azirines react with benzoyl chloride to afford addition products which were converted in polar solvent to oxazoles or dichloroamides.[16,17] This reaction was shown to proceed via the 1-benzoyl-2-chloroaziridine intermediate (eq 4).[16] Since the rearrangement to oxazoles (eq 4) proceeded with opposite regiochemistry to that observed in formally similar acid-cata-



(4)



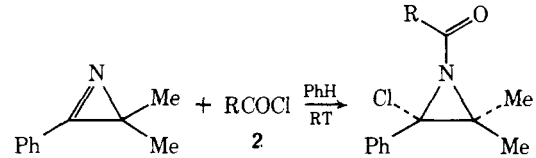
(5)

1

lyzed reactions (eq 5) by Leonard and Zwanenburg,[11] we decided to examine the scope of acyl chloride additions to azirines and the mechanism of ring opening of the adducts. Furthermore, this reaction might be expected to provide a general and convenient route to functionally substituted aziridines and possibly to their isomeric oxazolines.

Results

1. 1-Acyl-2-chloroaziridines. Phenyldimethylazirine (1)[11] was chosen for further study since the addition product could not easily lose HCl (as was the case in eq 4) and instead might lead to the isolation of a 5-chloro-2-oxazoline. The addition of acid chlorides **2** to this azirine proceeded smoothly at room temperature in benzene, affording quantitative yields of aziridines **3** (see Table I). Carbamoyl chloride failed to react with **1**. Only the pivaloyl and benzoyl chloroaziridines **3c** and **3d** were stable crystallizable solids;



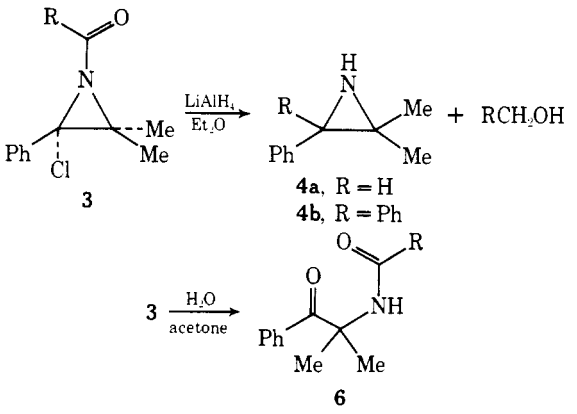
the others could be stored frozen in dry benzene for up to 3–4 months without serious deterioration. However, extensive decomposition ensued within a day if these compounds were left standing at room temperature exposed to air.

Proof of structure for **3** was provided by ir, NMR, and mass spectra (see below), as well as chemically. Thus reduction of **3** with LAH furnished **4a** and the alcohols RCH_2OH. As anticipated, acryloyl aziridine **3e** gave 1-propanol, and ethyl malonyl aziridine **3g** gave propylene glycol. Benzoyl aziridine **3d** was also reacted with phenylmagnesium bromide affording 2,2-diphenyl-3,3-dimethylaziridine (**4b**).[18] The three-membered ring structure of **3** is thus secure.

Table I. Conversion of Azirine 1 into Chloroaziridines 3

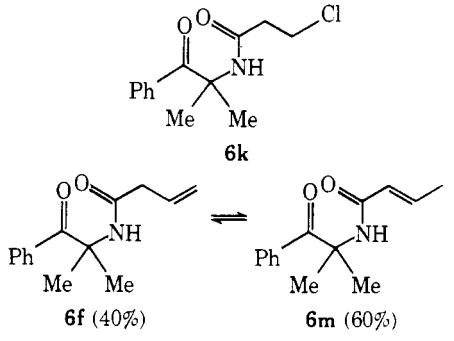
Aziridine 3	R	ν_{max} (CO) cm^{-1} in CCl_4	Time, hr[a]	τ in $CDCl_3$ *cis*-CH_3	*trans*-CH_3	τ in PhD_6 *cis*-CH_3	*trans*-CH_3
a	CH_3–	1700	4.5	8.88	8.30	9.20	8.38
b	$PhCH_2$–	1690	1.5	9.03	8.28	9.23	8.36
c	*t*-Bu–	1685[b]	6	8.93	8.26	9.15	8.36
d	Ph–	1660	15	8.81	8.41	9.09	8.50
e	CH_2=CH–	1680	6.5	8.98	8.34	9.22	8.44
f	CH_2=$CHCH_2$–	1690	1.5	8.95	8.26	9.22	8.42
g	EtO_2CCH_2–	1685	1.5	8.97	8.28	9.25	8.43
h	$ClCH_2$–	1700	0.2	8.94	8.26	9.25	8.51
i	Cl_3C–						
Aziridine 4a				9.07	8.60	9.14	8.88

[a] Time to completion of the reaction as monitored by NMR. [b] In KBr, 1670 cm^{-1}.



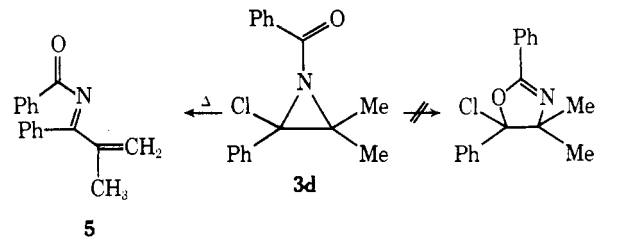
Mild hydrolysis (acetone-water) of most chloroaziridines **3** gave the ketoamides **6** in about 80% yield, within 24 hr. In a few cases (**3e, 3g, 3h**), these mild conditions failed to effect hydrolysis, and it was found necessary to add 1–2 drops of concentrated HCl. The acetamide **6a** possessed spectra identical with those reported, and the remainder of the ketoamides **6** were identified by analogy; all showed carbonyl absorption at 1680 and 1640 cm^{-1} and a singlet for the geminal methyls at τ 8.3. The base peak in the mass spectra of all but two cases is *m/e* 58, corresponding to a dimethyliminium ion, $Me_2C{=}N^+H_2$.

Hydrolysis of the acryloyl homolog **3e** proceeded to **6k**, a product of Michael addition of HCl. Hydrolysis of 3-butenoylchloroaziridine **3f** gave a compound with a sharp melting point, 140–141°, but which after two recrystallizations still showed two amide carbonyls (1640 and 1620 cm^{-1}) and two sets of side-chain signals in the NMR intergrating for a 2:3 mixture of ketoamides **6f** and **6m**. The



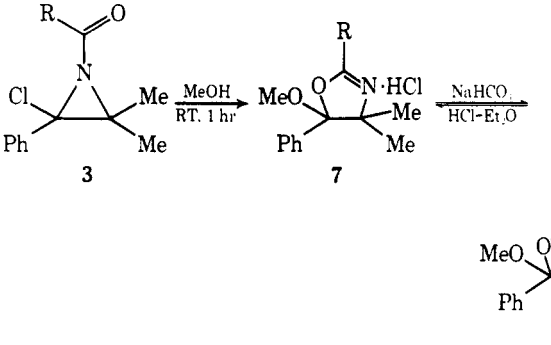
trans stereochemistry about the double bond in **6m** was indicated by the coupling constant (J = 16 Hz).

2. Isomerizations of 3. A number of unsuccessful attempts were made to convert **3d** to the desired 5-chloro-4,4-dimethyl-2,5-diphenyl-2-oxazoline. No products, other than small amounts of **6d**, ring-opened pyrolytic products **5**, and polymeric materials, were observed when **3d** was heated with carefully dried acetone-d_6, deuteriochloroform (100%



polymer), nitromethane, or dimethyl sulfoxide. Not even sodium iodide in acetone effected isomerization. Pyrolysis of **3d** in toluene leads to **5**. Though **3d** is stable for 1 hr in refluxing benzene, heating with silver perchlorate in benzene produced imine **5**. The structure of **5** was evident from its NMR spectrum (=CH_2 at τ 4.37 and 4.74), elemental analysis, and base-catalyzed hydrolysis to benzamide and α-methylpropiophenone.

However, when chloroaziridines **3** were stirred in dry methanol for an hour, and solvent was removed, quantitative yields of methoxyoxazoline hydrochlorides **7** resulted. These were converted to **8** with sodium bicarbonate, and the

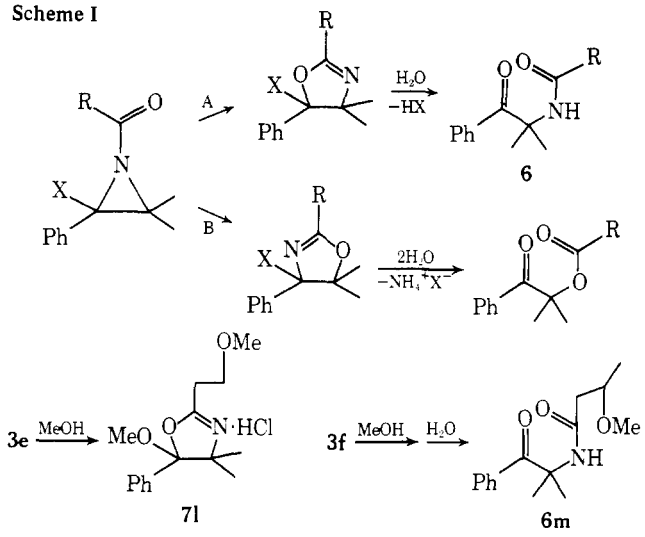


salts were regenerated with ethereal HCl. In several cases, the neutral compound **8** was distilled under vacuum.

Proof of the assigned regiochemistry was obtained by acidic hydrolysis of the oxazoline salts **7a–d.** This hydrolysis, which required considerably more vigorous conditions than that of the chloroaziridines **3,** afforded the same ketoamides **6a–d.** In principle, an X-substituted acyl aziridine can isomerize in two directions giving products of opposite regiochemistry (see Scheme I). A 5-substituted oxazoline will result in ketoamide **6** after hydrolysis, as observed; whereas a 4-substituted oxazoline (Scheme I, path B) would have resulted in the ketoester. Phenyloxazoline **8d** was recovered unchanged after 16 hr of heating in methanolic potassium hydroxide. The presence of additional functional groups in chloroaziridines **3e–h** caused further reactions such as introduction of a methoxy group (see **7l** and **6m**).

The desired neutral oxazolines **8e** and **8f** were obtained by simply stirring bicarbonate with the methanol during the reaction of **3e** and **3f.** Hydrogen chloride in ether converted oxazoline **8e** into polymer; hydrogen chloride in methanol gave salt **7l.** While propenyloxazoline **8m** was stable and

Scheme I



distillable, its 2-propenyl isomer polymerized rapidly on attempted distillation and decomposed on standing overnight.

After an hour in methanol, chloroacetyl aziridine **3h** gave a product which was predominantly oxazoline salt **7h** by NMR but which was apparently contaminated with several other materials. Further stirring in methanol led to complete decomposition. Initial inclusion of bicarbonate gave the chloromethyl oxazoline **8h** cleanly, but 2.5 hr were required to complete the reaction. Ethereal hydrogen chloride, followed by rapid NMR analysis of the products, converted **8h** into a 3:1 mixture of oxazoline salt **7h** and ketoamide **6h.**

The isomerization failed completely for ethyl malonyl aziridine **3g.** After an hour in absolute ethanol, the material was 75% unchanged and 25% tarry materials with no suggestion of oxazoline. Longer time and base merely increased the proportions of tarry materials.

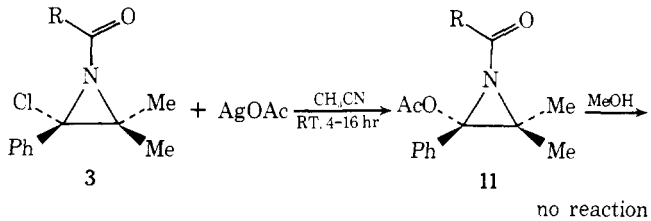
When chloroaziridine **3d** was exposed to $SbCl_5$ in CS_2 and worked up with methanol, α-chloroisobutyrophenone (**20**) was isolated (10%) in addition to methoxyoxazoline **8d** (45%).

3. Azido Acylaziridines and Oxazolines. Since a substitution clearly had taken place at some point in the production of the methoxyoxazolines **8,** we undertook to see if and at what point another nucleophile could be introduced. Treatment of phenyl chloroaziridine **3d** with 2 equiv of sodium azide in dry acetonitrile gave no reaction overnight, but the use of excess sodium azide, or better of the more soluble lithium azide,[19] in methanol overnight led to a 90% yield of azidooxazolines **10d,** uncontaminated with **7d.** Investigation of the reaction after a few minutes demonstrated the existence of an intermediate azidoaziridine **9d** which isomerized to azido oxazoline **10d** in salt free methanol in 10 hr. The *N*-benzoyl and the *N*-*tert*-butyl products **9d** and **9c** were isolated and characterized. In all other cases, the isomerization of **9** to **10** was highly competitive with the substitution reaction (**3** → **9**) and the best attempts to obtain the aziridine, following the reaction at intervals by NMR, gave mixtures of **3, 9,** and **10** (see Table II). Azido oxazolines **10** are stable if kept below 0° and can be distilled under high vacuum.

Azide substitution of chlorine in the side chain of **10h** did take place competitively with the initial azide substitution such that, by the time isomerization was complete, the product contained 20% of the unstable diazidooxazoline **10o.** This product was identified by comparison of its properties with those of **10h** and with those of the similarly unstable **8o,** synthesized by substitution from **8h.**

4. Acetoxy Acylaziridines. The successful introduction of an azide group into aziridines prompted us to attempt substitution of an acetate for chloride in **3.** Different metal acetate–alcohol combinations were tried with benzoyl chloroaziridine **3d** but, presumably because of the low solubility of the acetates, the major product was always methoxyoxazoline **8d** or an analogous alkoxyoxazoline (see Table III).

Silver acetate in nonnucleophilic acetonitrile, however, gave excellent yields of acetoxy acylaziridines **11.** Attempted isomerization of **11** in methanol failed.



5. Reactions of Monomethyl Azirine 12. For comparison with the dimethylazirine **1** and in order to determine the stereochemical consequences of the reactions discussed

Table II. Conversion of Chloroaziridines 3 into Azidoaziridines 9

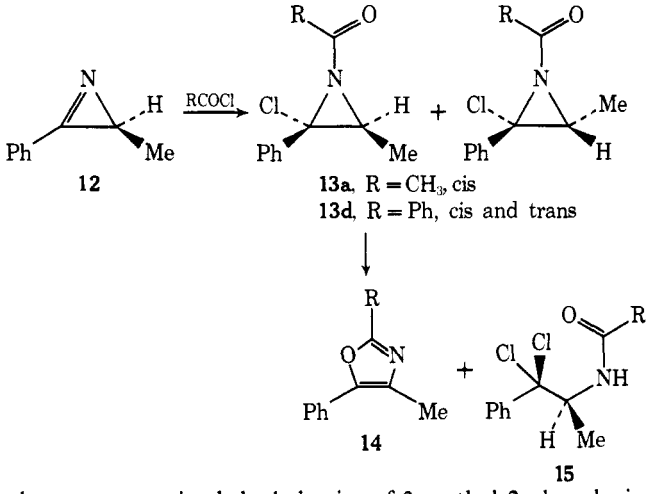
	R	% composition[a] 3	9	10	Time, min[b]	τ ($CDCl_3$) of 9 methyls cis-CH_3	trans-CH_3
a,	CH_3	8	66	26	20	9.01	8.47
b,	$PhCH_2$	0	57	43	15	9.13	8.46
c,	*t*-Bu	0	90	10	20	8.98	8.47
d,	Ph	0	100	0	15	8.82	8.72
e,	CH_2=CH_2	29	53	18	10	9.01	8.55
f,	CH_2=$CHCH_2$	15	68	17	10	9.00	8.47
g,	$EtOCOCH_2$–						
h,	$ClCH_2$–	52	4	44	20	(8.92)	(8.52)

[a] Of the mixture in which the largest concentration of **9** was observed as determined by integration of the NMR spectrum. [b] Length of time the reaction was allowed to proceed before rapid vacuum removal of methanol.

Table III. Product Distributions in the Reaction of 3d with Different Metal Acetate–Alcohol Combinations

3d + MOAc	ROH →	3d	+ 8d[a]	+ 11d	+ 6d
M = Na	R = CH_3		62	26	
M = Na	R = *t*-Bu	100			
M = Li	R = CH_3	10	65	25	
M = Li	R = C_2H_5	7	40	22	17
M = Li	R = C_3H_7	35	35		14

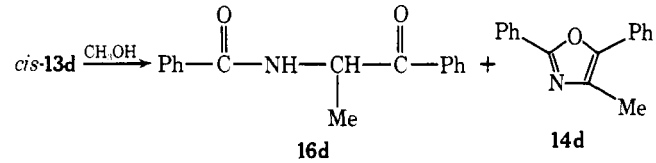
[a] Methoxy oxazoline **8d** or the analogous alkoxy oxazoline when R = Et or *i*-Pr.



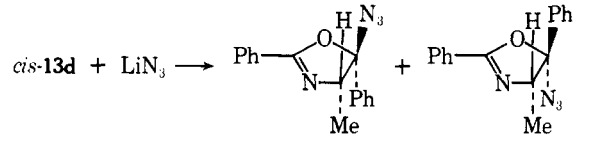
above, we examined the behavior of 3-methyl-2-phenylazirine (**12**). Acetyl chloride addition to **12** afforded adduct **13a**, of greater than 95% cis stereochemistry, and even less stability than the previously reported benzoyl chloride adduct **13d**.[16]

Unlike the *N*-benzoyl derivative **13d**, the *N*-acetylaziridine **13a** had to be prepared in hexane solution since, in benzene, oxazole formation was competitive with the addition reaction. NMR spectra of **13a** in deuteriochloroform could not be obtained since the isomerization to a 75:25 mixture of oxazole **14a** and dichloroamide **15a** occurred instantaneously and completely. When the decomposition was followed by NMR in CCl_4, the liquid phase contained, after 3 hr, 35% chloroaziridine **13a**, 40% oxazole **14a**, and 25% dichloroamide **15a**, and there was a great deal of precipitated oxazole salt. Neat samples of **13a** appeared to be stable for about 5 min at 25° and then rapidly turned black.

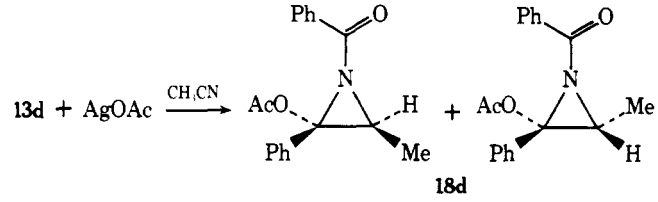
Benzoyl chloride addition to **12** had led to a cis–trans mixture of adducts **13d**.[16] We succeeded in isolating the *cis*-chloroaziridine (*cis*-**13d**) by fractional recrystallization of the mixture. When *cis*-chloroaziridine **13d** was treated with methanol at room temperature overnight, it afforded two products, **16d** (major) and **14d** (minor). No methoxyoxazoline was detected.



Reaction of *cis*-chloroaziridine **13d** with lithium azide in methanol for 16 hr followed by chromatographic work-up, resulted in both *cis*- and *trans*-2,5-diphenyl-4-methyl-5-azido-2-oxazoline **17d** (70%) in a ratio of 3:2 and a small amount of **16d**. No evidence for formation of an azidoaziridine was detected when the reaction was followed by NMR.

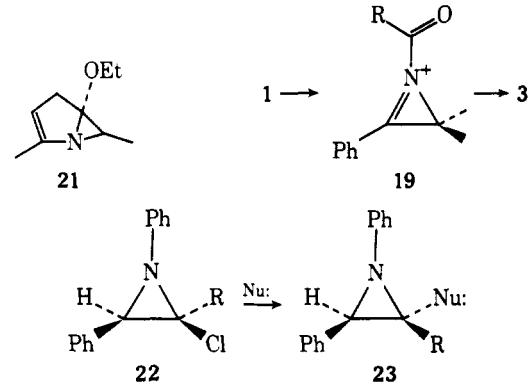


Reaction of *cis*-chloroaziridine **13d** with silver acetate in acetonitrile afforded a mixture of products. The major product purified by crystallization from Skellysolve B or F (50–60% yield) was assigned cis structure **18d** based on NMR data. The NMR spectrum of the crude product (80%) indicated an approximate cis–trans ratio of 7:3. Attempted isomerization of *cis*-**18d** in methanol gave unchanged starting material or decomposition in the presence of acid.



Discussion

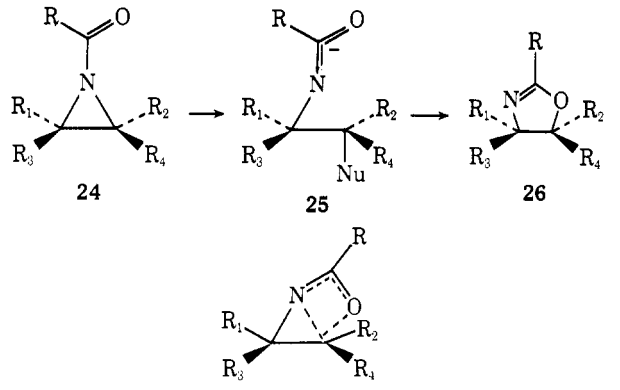
The observed reactivity of azirine **1** toward various acyl halides **2** parallels that expected for addition of a nucleophile to the C=O of the acid chlorides. Electron-withdrawing substituents, as in **2b, 2f, 2g,** and **2h,** increase the rate; electron-donating substituents (**2c**) and conjugation (**2d, 2e**) decrease the rate, consistent with the rate-determining formation of intermediate **19** which then adds chloride ion



to produce **3**. This reaction proceeds quite differently from the acid-catalyzed addition of acetone[11] to **1** where, in the absence of a good nucleophile to add to the activated azirinium 1,2 bond, cleavage of the 1,3 bond took place followed by closure to the five-membered ring. The subsequent reaction of the 2-chloro-*N*-acylaziridines **3** with nucleophiles leading to substituted oxazolines apparently proceeds via the corresponding functionally substituted *N*-acyl aziridines, which are isolable in the case of azide and acetate. The substitution **3** → **9** is best explained as a solvolysis reaction proceeding through the resonance stabilized azirinium ion **19** to which the nucleophile then adds. This interpretation is consistent with the observed instability of dichloroaziridines toward water[20,21] in contrast to the inertness[22] of **21**, as well as with the demonstrated SN1 nature of the conversion **22** → **23**.[7] The stereochemical inversion in **23** is probably due to preferred addition of the nucleophile from the less hindered side of an azirinium ion intermediate.[23] A similar preference (though not as exclusive as in the case of **23**) was found in the formation of cis-substituted chloro- and acetoxy aziridines **13** and **18**.

The facile isomerization of the substituted *N*-acylaziridines to oxazolines requires further comment since the common pathways for *N*-acylaziridine → oxazoline isomerization do not explain all the results. Extensive studies by Heine,[24] Fanta,[25] Iwakura,[26] and others[27] have shown that usually *N*-acylaziridines **24** undergo a modified SN2 opening with sodium iodide or under acid catalysis, followed by ring closure of **25** through O, giving rise to **26** with net retention of configuration. The regiochemistry of the ring opening depends upon a subtle balance of steric and electronic factors.

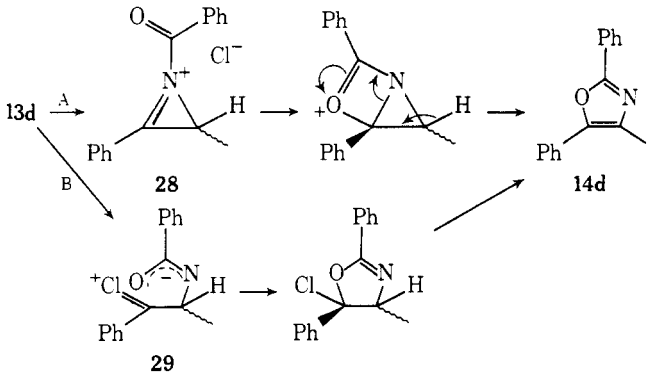
In pyrolysis of *N*-acylaziridines, ring opening generally occurs when a β-H is present to allow a six-membered ring transition state. In the absence of such a proton or during treatment with a Lewis acid, a front side attack by the carbonyl O (see **27**) can lead to retention in the formed oxazoline.



24 25 26 27

To account for the facile transformation in polar solvents of *N*-acyl chloroaziridine **13d** into oxazole **14d,** two possible mechanisms shown in Scheme II were advanced.[16] In the first case (Scheme IIA), solvolysis of chloride ion is followed by isomerization via a four-membered ring transition state (as postulated for pyrolysis). Aside from the fact that this does not explain the formation of the dichloroamide byproduct **15d,** intermediate **28** should, in analogy with the acid-catalyzed opening of **1** by acetone, undergo 1,3-bond cleavage leading to the oxazole of opposite regiochemistry to that observed. The second path (Scheme IIB) involves ionic cleavage of the 1,2 bond followed by ring closure and loss of HCl. The formation of **29** would be favored by the presence of the phenyl and chlorine substituents, as well as by polar solvents (**13d** is stable to refluxing benzene but isomerizes in cold acetone) and also explains the formation of the products **14** and **15.** Scheme IIB also accounts best for the isomerization of **9** to oxazolines and has been incorporated into the generalized Scheme III.

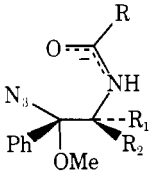
Scheme II



28 14d 29

Ring opening of **30** to **31** occurs only when X is well capable of stabilizing a positive charge (e.g., X = OCH_3, N_3); indeed no isomerization of **3** to a chlorooxazoline was observed even in very polar solvents. The ready conversion of **13d** (R = Ph) to oxazole **14d** is explained as an autocatalytic, acid-catalyzed reaction proceeding via **34** (HCl is produced from **13d** but not from **3**). Indeed **13d** though stable in CCl_4 reacted instantaneously in the presence of catalytic amounts of acid in the same solvent.

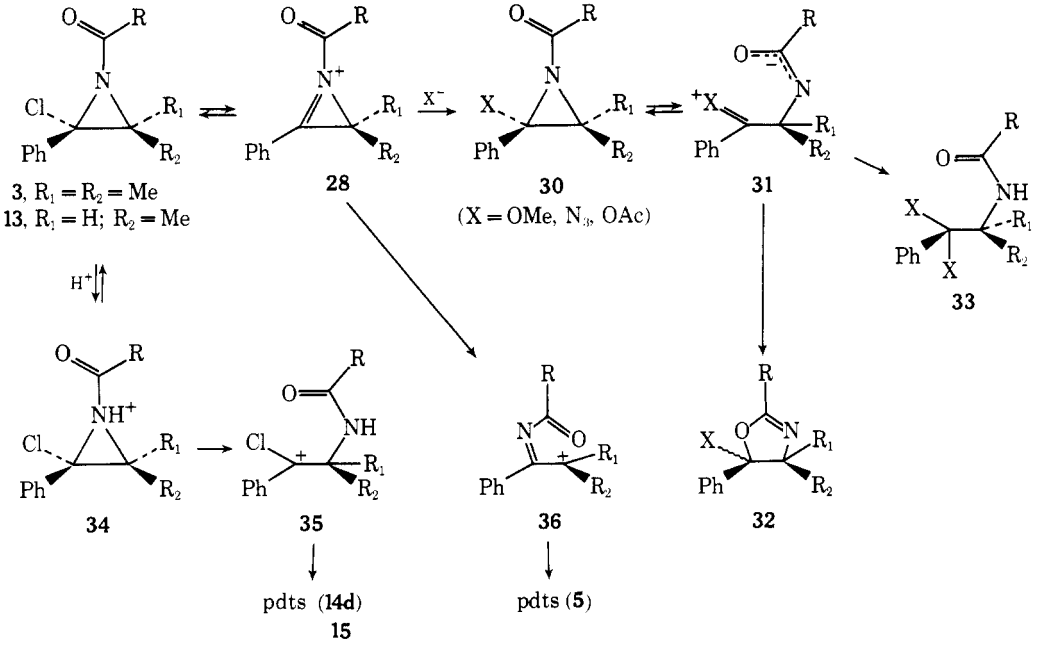
Nucleophilic ring opening of **3, 13,** or **30** leading to an intermediate of type **37** (analogous to **25**) is unlikely on the following grounds. (a) Unlike facile isomerization of **24** by NaI, the chloro compound **3d** remained unchanged on treatment with NaI in acetone or on exposure to Me_2SO. (b) *N*-Pivaloyl azidoaziridine **9c** isomerized to **10c** on heating in toluene or acetonitrile in the absence of nucleophiles. (c) The order of reactivity in the isomerization of **30** to **32** in methanol decreases for X: $OCH_3 > N_3 > Cl > OAc$ (with the latter no isomerization was observed), which is opposite to that expected for an SN2 opening of **30** by nucleophiles, but consonant with the electron-releasing power of these groups. (d) No methoxy incorporation was observed in the isomerization of **30** to **32** (X = N_3) in methanol though an intermediate such as **37** is expected[28] to ring-close at least in part to **32** (X = OCH_3).



37

In agreement with intermediate **31** is also the fact that azidoaziridine **9c,** possessing an electron-donating substituent (**R** = *tert*-butyl), isomerized slowly to **10c,** whereas the chloromethyl analog (R = CH_2Cl), possessing an electron-withdrawing carbonyl substituent, is virtually unisolable

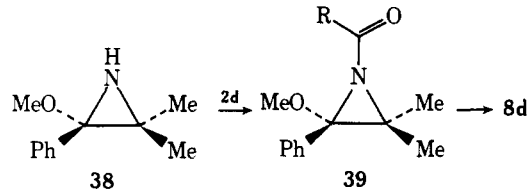
Scheme III



3, $R_1 = R_2 = Me$; 13, $R_1 = H$; $R_2 = Me$ — 28 — 30 (X = OMe, N_3, OAc) — 31 — 33

34 — 35 — pdts (14d) 15 — 36 — pdts (5) — 32

and is immediately transformed to oxazoline **10h.** That methoxyaziridines (**30,** X = OCH_3) were not isolable as intermediates on the way to **32** is not surprising since opening of **30** to **31** is greatly facilitated by the resonance stabilizing effect of OCH_3. Indirect evidence for the intermediacy of **39** during the isomerization of **3d** to **8d** was obtained by the addition of benzoyl chloride (**2d**) to **38** at −5°. Two additional methyl signals at τ 8.75 and 8.96 as expected for **39**



38 **39**

were detected in the NMR, but they disappeared within a few minutes with concurrent enrichment of the signals of oxazoline **8d.** In the presence of the weak electron donors Cl or OAc, no isomerization of **30** to **32** was observed.

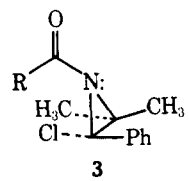
When X was a good leaving group (e.g., Cl), reaction occurred via azirinium ion **28.** This is evident from the reaction of **3d** with methanol (formation of **8d** via **39**), its reaction with $SbCl_5$ followed by methanol (formation of α-chloroisobutyrophenone via **36**), and the silver ion catalyzed or pyrolytic ring opening (heating in toluene) of **3d** to **5** (via **36**). In contrast to the latter ring opening, heating of the azidoaziridine **9c** in toluene caused solely isomerization to **10c,** the azido group facilitating formation of **31.**

With water as the nucleophile, **3** is expected to proceed to an open-chain ketoamide via **28, 30,** and **31** (X = OH). But since HCl is formed in the reaction, acid catalysis will ensue, and 1,2-bond cleavage via **34** and **35** will take over. In fact several of the chloroaziridines **3** required added acid to effect appreciable hydrolysis.

The lack of stereospecificity in the reaction of the *N*-benzoyl-2-chloro-*cis*-2-phenyl-3-methylaziridine **(13d)** with lithium azide, leading to a cis–trans mixture of azidooxazolines **17d,** is also consistent with the intermediacy of **31.** Finally, the ring opening of **32** to **33,** as exemplified by hydrolysis to ketoamides, is much slower than **30** → **33** because of differences in ring strain in the two substrates.

In conclusion, the key intermediate in the reactions discussed appears to be azirinium ion **28,** which can react with nucleophiles X^- to produce aziridine **30** or open to **36** as in pyrolysis or in the case of eq 5 (**28,** with the N substituent being H instead of COR). Facile solvolytic opening of **30** to **31,** leading to substituted oxazolines, occurs only when X is well capable of stabilizing a positive charge (X = OCH_3, N_3). In the presence of HCl, **28** reacts via **34** leading to ring opened products.

Spectra. 1. Acylaziridines. The methyl resonance in the NMR spectra of the **3** shows strong solvent dependence (Table I). In aziridine **4a,**[29] the methyl group trans to phenyl shows a greater benzene-induced shift than the *cis*-methyl group. Since the opposite is true for **3,** and benzene is expected[30] to associate with a positive center (amide-N) in the molecule, one infers that the predominant invertomer of **3** in solution has the acyl function anti to the phenyl



3

group (see below) as expected on the basis of steric considerations. The mass spectra of **3** exhibit characteristic $[M—Cl]\cdot^+$, $[M—RCO]^+$, and $[Ph{\equiv}NH]^+$ peaks. In the azidoaziridines **9,** the *trans*-methyl group is shifted upfield with respect to the CH_3 in **3,** presumably because of shielding by the *cis*-azido function (Table II).

Table IV. Chemical Shifts ($CDCl_3$) of the Geminal Methyl Groups in Phenyldimethylaziridines and Phenyldimethyloxazolines

Compd	Class	*cis*-CH_3, τ	*trans*-CH_3, τ
4a	Aziridine	9.08	8.56
38	Aziridine	9.09	8.51
3	Acylaziridine	8.9	8.3
9	Acylaziridine	9.0	8.5
11	Acylaziridine	8.8	8.5
8	Oxazoline	9.35	8.50
10	Oxazoline	9.3	8.50

2. Oxazolines. In the oxazolines **7** and **8,** the *C*-methyl resonances are at significantly higher field and further split apart than in the three-membered rings of **3** or **4.** The larger chemical shift of the *cis*-methyl group in oxazolines compared with aziridines is due to stronger shielding by the adjacent phenyl group in the former[31] and reflects the greater steric crowding in five-membered rings.[32]

Table IV highlights the differences between the methyl absorptions in three- and five-membered rings.

Experimental[33] Section

General Procedure for Synthesis of Acyl Chloroaziridines (3). To 2.90 g (0.02 mol) of dimethylphenylazirine **1** in 20 ml of dry benzene (decanted from sodium) was added 0.021 mol of the appropriate acid chloride **2.** After stirring 1–6 hr (see Table I) at room temperature, solvent was removed in vacuo to afford aziridine **3** in 88–100% yield. All but **3c** and **3d** were liquids. Decomposition of the liquid products was prevented by storage in the freezer in benzene solution.

***N*-(2,2-Dimethylpropionyl)-2-chloro-2-phenyl-3,3-dimethylaziridine (3c).** From pivaloyl chloride **2c** after 6 hr of stirring, there was obtained 5.27 g of **3c** (99%), mp 92–93°, after recrystallization from hexane: MS *m/e* 267, 265 (M^+), 230 (M^+ − Cl), 210, 208 (M^+ − *t*-Bu), 182, 180 (54%, 19%, M^+ − *t*-BuCO), 145 (19%, M^+ − *t*-BuCOCl), 104 (43%, $PhC{\equiv}N^+H$), 85 (23%, *t*-$BuCO^+$), 57 (100%, *t*-Bu^+). Anal. Calcd for $C_{15}H_{20}ClNO$: C, 67.75; H, 7.60; N, 5.27. Found: C, 67.74; H, 7.66; N, 5.22.

***N*-Benzoyl-2-chloro-2-phenyl-3,3-dimethylaziridine (3d).** From benzoyl chloride **2d** after 15 hr of stirring, there was obtained 4.60 g of solid **3d** (80%), mp 84.5–85.5°: MS *m/e* 250 (M^+ − Cl), 180, 182 ($M^+\cdot$ − PhCO), 145 ($M^+\cdot$ − PhCOCl), 105 ($PhCO^+$, 100%). Anal. Calcd for $C_{17}H_{16}ClNO$: C, 71.45; H, 5.60; N, 4.90. Found: C, 71.65; H, 5.67; N, 4.96.

$LiAlH_4$ Reduction of Acyl Chloroaziridines 3. To a cloudy solution of 0.001 mol of aziridine **3** in 5 ml of dry ether cooled in ice was added 0.1 g (0.0025 mol) of $LiAlH_4$. The mixture was stirred overnight (12–18 hr), and 0.25 ml of 20% NaOH was added with cooling. Half an hour later, the mixture was filtered and extracted with aqueous HCl. Neutralization (20% NaOH, cooling) of the acid layer, extraction, drying, filtration, and solvent removal in vacuo gave 2-phenyl-3,3-dimethylaziridine (**4**)[11] in 60% yield, identified by comparison of ir and NMR spectra with an authentic sample. After drying and filtration, solvent removal from the neutral layer afforded the alcohols, identified by reference to standard spectra. Acryloyl aziridine **3e** gave 1-propanol, and ethyl malonyl aziridine **3g** gave propylene glycol as expected.

Reaction of Acyl Chloroaziridine 3d with Phenylmagnesium Bromide. To 0.96 g (0.04 mol) of magnesium was slowly added 6.28 g (0.04 mol) of bromobenzene in 28 ml of ether. As the reaction stopped, a solution of 2.85 g (0.01 mol) of chloroaziridine **3d** in 5 ml of anhydrous ether was slowly added to the ethereal phenylmagnesium bromide solution. The reaction mixture was refluxed overnight, then poured into saturated aqueous ammonium chloride solution, and extracted with ether. After drying with magnesium sulfate, removal of the solvent under reduced pressure gave a mixture of 2,2-diphenyl-3,3-dimethylaziridine (**4b**)[18] and triphenyl carbinol.

General Procedure for Hydrolysis of Acyl Chloroaziridines. To a solution of 0.001 mol of aziridine **3** in 5 ml of reagent grade ace-

tone was added 2-4 drops of water. After stirring for 14-24 hr, solvent was removed in vacuo. The residue was dissolved in dichloromethane, dried ($MgSO_4$), and filtered before solvent was removed again affording crude **6** as an oily solid, which was recrystallized from benzene or $CHCl_3$-hexane. In certain cases (e.g., **3e, 3g, 3h**), the aziridine proved resistant to these mild conditions and hydrolysis was effected with the addition of 2-3 drops of concentrated HCl, followed by $NaHCO_3$ neutralization before the solvent was removed. Satisfactory elemental analyses were obtained for all amides reported.

2-(Phenylacetamido)-2-methylpropiophenone (6b). The simple procedure for hydrolysis with **3b** afforded 0.216 g of crude **6b** (78%), recrystallized mp 180-181°: NMR ($CDCl_3$) τ 2.08-2.28 (m, 2), 2.45-3.00 (m, 8), 3.72 (s, 1, disappeared in D_2O), 6.58 (s, 2), 8.40 (s, 6); ir (KBr) 3260, 1680, 1640 cm^{-1}; *m/e* 281 (1%, M^+), 190 (1%, $M^+ - PhCH_2$) 176 (32%, $M^+ - PhCO$), 146 (7%, Ph—CO—CMe=Cl_2), 105 (10%, Ph^+CO), 91 (35%, $PhCH_2^+$), 58 (100%, $Me_2C{=}N^+H_2$). Anal. Calcd for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.85; H, 6.92; N, 4.92. **6a:** 84%; mp 119-121° (lit.[11] 120-121°). **6c:** 100%; mp 139-140°. **6d:** 95%; mp 161.5-162°. **6f:** 100%; mp 140-141°; NMR ($CDCl_3$) at τ 4.8, 7.18, and 8.23 indicated a 60:40 mixture of **6m** and **6f. 6h:** 70%; mp 156-157°. **6k:** 78%; mp 134.5-135°. **6l:** 70%; mp 83.5-85°. **6m:** mp 118-121°.

Reaction of 3d with $SbCl_5$. To a solution of 0.7 g (0.0025 mol) of chloroaziridine **3d** in 5 ml of carbon disulfide (CS_2) was added 0.75 g (0.0025 mol) of $SbCl_5$ in 3 ml of CS_2 at 0°. The color of the mixture turned red immediately. Methanol (10 ml) was added, and the color changed from red to yellow. Solvents were removed in vacuo, and the crude product was extracted with two 15-ml portions of Skellysolve B. Solvent was removed in vacuo from the combined extracts to give 0.6 g (85% yield) of a pale-yellow oil. After column chromatography on neutral alumina (Woelm, activity I), two products were separated which consisted of methoxyoxazoline **8d** and α-chloroisobutyrophenone (**20**) in a ratio of 2:1.

Pyrolysis of 3d. (a) A solution of chloroaziridine **3d** (0.57 g, 0.002 mol) in toluene was refluxed for 30 hr and then cooled to room temperature. Toluene was removed in vacuo and the residue extracted with Skellysolve B. The solvent was removed in vacuo to give 0.395 g (90%) of ***N*-benzoyl-α-methylacrylophenone imine (5)** as an oil: NMR ($CDCl_3$) τ 1.99-2.21 (m, 2), 2.42-2.75 (m, 8), 4.37 (m, 1), 4.74 (m, 1), 7.91 (m, 3); ir (film) 1675, 1630 cm^{-1}; *m/e* 249 ($M^{+\cdot}$), 146 ($M^{+\cdot} - PhCN$, 100%), 118 ($M^{+\cdot} - PhC_4H_5$), 105 ($PhCO^{+\cdot}$), 77 ($Ph^{+\cdot}$). Anal. Calcd for $C_{17}H_{15}NO$: C, 81.93; H, 6.02; N, 5.62. Found: C, 82.05; H, 6.03; N, 5.58.

(b) To a suspension of 1 g (0.006 mol) of silver perchlorate in 20 ml of benzene was added slowly a solution of 0.286 g (0.001 mol of chloroaziridine **3d** in 5 ml of benzene. The reaction mixture was refluxed for 1 hr, and benzene was removed in vacuo at room temperature. The oily residue was extracted with Skellysolve B. Removal of Skellysolve B from the extracts afforded 0.20 g (80% yield) of **5.**

Hydrolysis of 5 with Alcoholic Potassium Hydroxide. To a solution of 1 pellet of potassium hydroxide in 9 ml of methanol and 1 ml of water was added 0.249 g (0.001 mol) of acrylophenone imine **5.** The reaction mixture was left at room temperature for 16 hr. After methanol was removed in vacuo, the residue was extracted with ether, and removal of the ether afforded 0.27 g of crude product. Chromatography afforded 0.12 g of benzamide and 0.16 g of α-methylacrylophenone.[34]

General Procedure for the Reaction of Acyl Chloroaziridine 3 with Methanol. A solution of 0.001 mol of aziridine **3** in dry methanol (distilled from CaH_2) was stirred for 1 hr at 25° before solvent was removed in vacuo, affording a quantitative yield of methoxyoxazoline hydrochloride **7** accompanied by a small amount of residual methanol. Oxazoline salt **7** was dissolved in a few milliliters of CH_2Cl_2 and treated with solid $NaHCO_3$ until the bubbling stopped. Drying ($MgSO_4$), filtration, and solvent removal in vacuo left neutral oxazoline **8** in yields greater than 80%. Treatment with hydrogen chloride in ether regenerated the salt **7** in every case. Satisfactory analyses were found for all oxazolines **8.**

5-Methoxy-5-phenyl-2,4,4-trimethyl-2-oxazoline (8a) and Hydrochloride 7a. Aziridine **3a** yielded 0.276 g of crystalline oxazoline salt **7a:** NMR ($CDCl_3$) τ 2.38 (s, 6, decreases to 5 after D_2O), 6.62 (s, 3, OMe), 7.18 (s, 3), 8.21 (s, 3), 8.96 (s, 3) plus a signal for MeOH at 6.51; ir (KBr) 3400, 2600 broad, 2230, 1820, 1665 cm^{-1}; melting point after recrystallization from ether, 141-149° dec. Anal. Calcd for $C_{13}H_{18}ClNO_2$: C, 61.04; H, 7.11; N, 5.78. Found: C, 60.84; H, 7.20; N, 5.62.

Neutralization left oxazoline **8a** (90%): NMR ($CDCl_3$) τ 2.53 (m, 5), 6.86 (s, 3), 7.90 (s, 3), 8.52 (s, 3), 9.36 (s, 3); ir (neat) 1680 cm^{-1}; *m/e* 219 (1%, M^+), 204 (1%, $M^+ - CH_3$), 188 (3%, $M^+ - OMe$), 176 (1%, $M^+ - CH_3CO$), 105 (17%, $PhCO^+$), 100 (32%, $CH_3CONHCMe_2$), 83 (100%, $CH_3C{\equiv}N^{\cdot+}{-}CMe_2$), 77 (24% Ph), 58 (82%, CH_3CONH^+).

7b: mp 155-160° dec. **8b:** 91%. **7c:** mp 133-141°. **8c:** 98%. **7d:** mp 126-130° dec. **8d:** 100%. **8l:** 82%; 52:48 mixture of **8l** and **8e. 8m:** 88%. **8h:** 86%.

5-Methoxy-5-phenyl-4,4-dimethyl-2-vinyl-2-oxazoline 8e. A variation of the usual procedure in which $NaHCO_3$ was added initially with aziridine **3e** gave oxazoline **8e** (72%): NMR ($CDCl_3$) τ 2.58 (s, Ph, 5), 2 H at 3.65 (d, J = 9 Hz) and 3.71 (d, J = 4 Hz), 4.26 (d of d, J = 4, 9 Hz, **1**), 6.85 (s, OMe, 3), 8.51 (s, 3), 9.34 (s, 3); ir (neat) 1670, 1600 cm^{-1}; *m/e* 231 (4%, M^+), 200 (2%, $M^+ - OCH_3$), 185 (1%, $M^+ - OMe$, Me), 176 (<1%, $M^+ - CH_2{=}CHCO$), 105 (14%, $PhCO^+$), 95 (100%, $CH_2{=}CH{-}C{\equiv}N^+{-}CMe_2$), 77 (18%, Ph), 54 (36%, $CH_2{=}CH{-}C{\equiv}NH^+$). Distillation [110-120° (1 mmHg)] gave the analytical sample. Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.71; H, 7.44; N, 5.99. Addition of oxazoline **8e** to HCl in ether gave only polymeric materials; addition to HCl in MeOH gave an oil whose spectra were identical with those of oxazoline salt **7l.**

Procedure for the Hydrolysis of Oxazolines 7. To a solution of 0.001 mol of oxazoline salt **7a** in 5 ml of MeOH was added 10 drops of HCl. After stirring for 16-24 hr at room temperature or 4-12 hr at reflux, the solution was neutralized with solid $NaHCO_3$, dried ($MgSO_4$), and filtered. Solvent was removed from the filtrate, and the product was recrystallized from benzene or $CHCl_3$-hexane. The identity of the hydrolysis products of **7a, 7b, 7c,** and **7d** with ketoamides **6a, 6b, 6c** and **6d** was established by melting point and spectral comparison.

2-(3-Methoxypropionamido)-2-methylpropiophenone (6l). Oxazoline salt **7l** after 5 hr of reflux gave the expected amide **6l:** mp 83.5-85°; NMR ($CDCl_3$) τ 1.85-2.10 (m, 2), 2.40-2.70 (m, 3), 2.92 (bs, 1, NH), 5 H at 6.44 (*t*, J = 6 Hz) and 6.57 (s, OMe), 7.65 (t, J = 6, 2 Hz), 8.30 (s, 6); ir (KBr) 3200, 1675, 1630 cm^{-1}; *m/e* 249 (<1%, M^+), 144 (40%, $M^+ - PhCO$), 105 ($PhCO^+$), 87 ($MeOCH_2CH_2CO$), 58 ($Me_2C{=}NH_2$). Anal. Calcd for $C_{14}H_{19}NO_3$: C, 67.44; H, 7.68; N, 5.62. Found: C, 67.35; H, 7.70; N, 5.60.

General Procedure for Synthesis of Acyl Azidoaziridines 9. Aziridine **3** (0.001 mol) was ground with lithium azide (0.01 mol) and the mixture stirred with 2 ml of dry methanol for 10-20 min before solvent was rapidly removed via the vacuum pump. The residue was stirred with CH_2Cl_2-pentane (1:1) and filtered. Solvent removal in vacuo gave, in 90% yield, a mixture of acyl azidoaziridine **9,** and azidooxazoline **10,** sometimes contaminated with small amounts of starting material **3** (see Table II). Mixtures of azidoaziridine **9** and azidooxazoline **10** were converted quantitatively to the latter on stirring in 5 ml of methanol overnight.

***N*-Benzoyl-2-azido-2-phenyl-3,3-dimethylaziridine (9d).** Aziridine **3d** gave azidoaziridine **9d** (91%): mp 95-97°, after recrystallization from Skelly B; NMR ($CDCl_3$) τ 1.90-2.12 (m, 2 H), 2.25-2.73 (m, 8 H), 8.39 (s, 3 H), 8.82 (s, 3 H); ir (KBr) 2120, 1655 cm^{-1}; *m/e* 292 ($M^{+\cdot}$), 264 ($M^{+\cdot} - N_2$), 250 ($M^{+\cdot} - N_3$), 187 ($M^{+\cdot} - PhCO$), 161 ($PhCONC(CH_3)_2^{+\cdot}$), 145 ($M^{+\cdot} - PhCON_3$), 105 ($PhCO^{+\cdot}$), base peak). Anal. Calcd for $C_{17}H_{16}N_4O$: C, 69.87; H, 5.52; N, 19.18. Found: C, 70.01; H, 5.58; N, 18.95.

General Procedure for Direct Synthesis of Azidooxazolines 10. A solid mixture of 0.001 mol of aziridine **3** and 0.01 mol of lithium azide was stirred in 5 ml of methanol for 4-24 hr before solvent was removed in vacuo. The residue was stirred with 1:1 CH_2Cl_2-pentane and filtered. Solvent removal in vacuo left the crude liquid azidooxazoline **10.** Aliquots were distilled [70-90° (20.0 μm)], affording the analytical samples.

5-Azido-5-phenyl-4,4-dimethyl-2-(1,1-dimethylethyl)-2-oxazoline (10c). Aziridine **3c** with lithium azide gave an 89% yield of azidooxazoline **10c:** NMR ($CDCl_3$) τ 2.48-2.70 (m, Ph, 5), 8.53 (s, 3), 8.64 (s, 9), 9.36 (s, 3); ir (neat) 2120, 1670 cm^{-1}; *m/e* 230 (1%, $M^+ - N_3$), 187 (10%, $M^{+\cdot} - t\text{-}BuCO^+$), 161 (3%, $M^{+\cdot} - RCN_3$), 119 (5%, PhCNO), 105 (19%, $PhCO^+$), 85 (11%, *t*-BuCO), 84

(16%, *i*-PrNCO), 77 (8%, Ph), 69 (10%, *t*-BuC$^+$), 57 (100%, *t*-Bu). Anal. Calcd for $C_{15}H_{20}N_4O$: C, 66.15; H, 7.40; N, 20.57. Found: C, 66.02; H, 7.50; N, 20.65. **10a,** 95%; 1695 cm^{-1}. **10b:** 86%, 1675 cm^{-1}. **10d:** 95%; 1660 cm^{-1}. **10e:** 83%; 1670 cm^{-1}. **10f:** 92%; 1670, 1640 cm^{-1}. **10h:** 90%; 1670 cm^{-1}.

Reaction of 3d with Metal Acetate (Table III). To 8 ml of methanol was added 0.9 g (0.011 mol) of sodium acetate with vigorous stirring to achieve an even suspension. To this suspension was added 0.286 g (0.001 mol) of chloroaziridine **3d.** The suspension was stirred for 2.5 hr before the methanol was removed in vacuo. The solid residue was extracted with dichloromethane and the extract dried. The NMR spectrum of the crude product showed: ring-opened product **5** (12%), methoxyoxazoline **8d** (62%), and acetoxyaziridine **11d** (26%). No reaction occurred in Me_2SO or *tert*-butyl alcohol.

General Procedure for the Synthesis of Acyl Acetoxyaziridines 11. To a solid mixture of 0.001 mol of chloroaziridine **3** and 1.67 g (0.01 mol) of silver acetate was added 10 ml of acetonitrile (dry). The mixture was stirred for 4–16 hr, solvent was removed in vacuo, and the residue extracted with pentane–dichloromethane (1:1). Solvent removal in vacuo gave **11** (100%), purified by trituration with hexane or thick layer chromatography on alumina and recrystallization from hexane. These compounds are extremely susceptible to hydrolysis.

***N*-(2,2-Dimethylpropionyl)-2-acetoxy-2-phenyl-3,3-dimethylaziridine (11c).** Aziridine **3c** with silver acetate gave 0.265 g of crude acetoxyaziridine **11c,** contaminated with a relatively large amount of ketoamide **6c.** Crystallization from hexane gave ketoamide **6c,** crop I, 0.031 g (13%), and pure acetoxyaziridine **11c,** crop II, mp 122–125°: NMR ($CDCl_3$) τ 2.40–2.72 (m, 5), 7.90 (s, 3), 8.48 (s, 3), 12 H at 8.76 (s) and 8.82 (s); ir 1750, 1650 cm^{-1}; *m/e* 247 (<1, M$^+$· − CH_2=C=O), 246 (<1%, M$^+$· − CH_3CO), 232 (1%, M$^+$· *t*-Bu), 204 (20%, M$^+$· − RCO), 162 (83%, PhCNOAc), 145 (23%, dimethylphenylazirinium ion), 142 (26%, *t*-BuCO-NH-CMe_2), 105 (100%, PhCO), 85 (9%, *t*-BuCO), 77 (26%) Ph, 57 (48%, *t*-Bu). Anal. Calcd for $C_{17}H_{23}NO_3$: C, 70.56; H, 8.01; N, 4.84. Found: C, 70.61; H, 8.07; N, 4.85. **11a,** mp 99–101°; **11d,** mp 88–89°.

5-Methoxy-5-phenyl-4,4-dimethyl-2-acetoxymethyl-2-oxazoline (8p). To a solution of 0.254 g (0.001 mol) of chloromethyl oxazoline **8h** in 10 ml of acetonitrile was added 1.67 g (0.01 mol) of silver acetate. After stirring at room temperature for 8 days (shorter times did not suffice), work-up as above for aziridines **11** gave 0.223 g (81%) of acetoxymethyl oxazoline **8p:** NMR ($CDCl_3$) τ 2.58 (s, Ph, 5), 5.15 (s, 2), 6.88 (s, 3), 7.83 (s, 3, OAc), 8.52 (s, 3), 9.35 (s, 3); ir (neat) 1750, 1680 cm^{-1}; *m/e* 246 (1%, M$^+$· − OMe), 141 (8%, M$^+$ − $PhCO_2Me$), 105 ($PhCO^+$, 100%), 82 (61%, M$^+$· − $PhCO_2Me$, OAc). Anal. Calcd for $C_{15}H_{19}NO_4$: C, 64.96; H, 6.91; N, 5.05. Found: C, 64.73; H, 7.00; N, 5.14.

***N*-Acetyl-2-chloro-*cis*-(2-phenyl-3-methyl)aziridine (13a).** The general procedure for acyl chloroaziridine synthesis using phenyl methyl aziridine **12,** acetyl chloride **2a,** and hexane as solvent, after 2 hr of stirring, gave acetyl aziridine **13a** in quantitative yield: NMR (CCl_4) τ 8.35–8.75 (m, 5, Ph), 6.88 (q, J = 6 Hz, **1**), 7.73 (s, 3), 9.02 (d, J = 6, 3 Hz); ir (neat) 1700 cm^{-1}; *m/e* 174 (7%, M$^+$· − Cl), 173 (63%, M$^+$ − HCl), 167, 169 (13, 4%, M$^+$ − CH_2C=O), 166, 168 (19, 8, M$^+$ − CH_3CO), 145 (4%, 173 − CO), 131 (11%, M$^+$ − CH_3COCl), 105 (64%, PhCO), 104 (100%, PhC≡NH). This material decomposed instantaneously in $CHCl_3$ and rapidly in benzene leaving after solvent removal in vacuo an oily solid residue. Trituration with 1:1 pentane–benzene and filtration left 1.80 g of crude oxazole **14a** (10.4%), melting point after recrystallization, 108–110°, picrate 168–170° (lit. 170–171°).[35] The filtrate was concentrated, diluted with ether, and filtered; solvent was removed in vacuo, affording the oily dichloroamide **15a** which crystallized on trituration with hexane: mp 110–111°; NMR ($CDCl_3$) τ 2.12–2.75 (2 m, 5), 4.02 (bd, disappears in D_2O with a trace of acid, 1), 4.98 (d of q, J = 10, 7 Hz, collapse to q with D_2O, 1), 8.05 (s, 3), 8.78 (d, J = 7, 3 Hz); ir (KBr) 3270, 1655 cm^{-1}; *m/e* 210, 212 (3.1%, M$^+$· − Cl), 174 (1%, M$^+$ − HCl_2), 168, 170 (5.2%, **12**·HCl), 132 (9%, **12**·H$^+$), 86 (100%, M$^+$ − $PhCCl_2$). Anal. Calcd for $C_{11}H_{13}NOCl_2$: C, 53.67; H, 5.33; N, 5.69. Found: C, 53.82; H, 5.39; N, 5.72.

2,5-Diphenyl-4-methyl-5-azido-2-oxazoline (17d). The general procedure for the synthesis of azidooxazolines **10** with *cis*-chloroaziridine **13d** gave, in 83% yield, a crude mixture which contained 70% of azidooxazoline **17d** with a cis-trans ratio of approximately 3:2. Chromatographic work-up gave the pure compounds as follows.

2-Phenyl-*cis*-(4-methyl-5-phenyl)-5-azidooxazoline (17d): NMR ($CDCl_3$) τ 1.74–1.94 (m, 2), 2.31–2.71 (m, 8), 5.63 (q, 1, J = 7 Hz), 9.22 (d, 3, J = 7 Hz); ir (film) 3060–2930, 2110, 1650 cm^{-1}; *m/e* 250 (M$^+$· − N_2), 236 (M$^+$· − N_3), 235 (M$^+$· − NH_3), 221 (M$^+$· − Ch_3N_3), 208 ($PhCONCPh^+$·), 166 (Ph_2C^+·), 131 (M$^+$· − $PhCON_3$), 105 ($PhCO^+$·, 100%). Anal. Calcd for $C_{16}H_{14}N_4O$: C, 69.06; H, 5.04; N, 20.14. Found: C, 69.14; H, 5.11; N, 20.02.

2-Phenyl-*trans*-(4-methyl-5-phenyl)-5-azidooxazoline (17d): NMR ($CDCl_3$) τ 1.75–1.98 (m, 2), 2.30–2.75 (m, 8), 5.72 (q, 1, J = 7 Hz), 8.50 (d, 3, J = Hz); ir (film) 2100, 1655 cm^{-1}.

***N*-Benzoyl-2-acetoxy-2-phenyl-3-methylaziridine (18d).** The general procedure for synthesis of acetoxy aziridines with *cis*-chloroaziridine **13d** gave a 92% yield of crude **18d.** The NMR spectrum of the crude mixture showed 70–80% of *cis*- and *trans*-acetoxyaziridines in a 73:27 ratio, 9% oxazole **14d,** and 7% unreacted chloroaziridine. The crude mixture was dissolved in 5 ml of dichloromethane, and 20 ml of Skellysolve B was added. Upon reduction of the volume of the extract with cooling, a crystalline solid formed which was filtered off and dried under reduced pressure to give 0.38 g (60% yield) of *N*-benzoyl-2-acetoxy-*cis*-(2-phenyl-3-methyl)aziridine (**18d**): mp 119–120°; NMR ($CDCl_3$) τ 1.85–2.08 (m, 2), 2.23–2.72 (m, 8), 6.63 (q, 1, J = 6 Hz), 8.09 (s, 3), 8.74 (d, 3, J = 6 Hz); ir (KBr) 1760, 1675 cm^{-1}; *m/e* 295 (M$^+$·), 252 (M$^+$ − CH_3CO), 235 (M$^+$ − CH_3COOH), 208 ($PhCONCPh^+$), 190 (M$^+$ − PhCO), 148 ($PhCONCH_2CH_3^+$), 131 (M$^+$ − PhCO-$COOCH_3$), 105 ($PhCO^+$, 100%). Anal. Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74. Found: C, 73.43; H, 5.59; N, 4.68. The filtrate contained mainly *trans*-acetoxyaziridine **18d** which could not be separated from the by-products with extraction. To obtain the NMR spectrum of the *trans*-acetoxyaziridine **18d,** the spectrum of *cis*-**18d** was subtracted from the NMR spectrum of the crude mixture: NMR ($CDCl_3$) 2.88 (broad s, 5 H), 6.17 (q, 1, J = 5.5 Hz), 8.51 (d, 3, J = 5.5 Hz).

2-Methoxy-2-phenyl-3,3-dimethylaziridine (38). To a solution of 0.54 g (0.01 mol) of sodium methoxide in 10 ml of absolute methanol was added 1.45 g (0.01 mol) of 2-phenyl-3,3-dimethylazirine (**1**). The reaction mixture was stirred at room temperature for 2 hr. Methanol was removed in vacuo and the residue extracted with two 10-ml portions of Skellysolve B. Solvent was removed in vacuo from the combined extract to give 1.65 g (90% yield) of methoxyaziridine **38:** NMR ($CDCl_3$) τ 2.58 (broad s, 6), 6.82 (s, 3), 8.52 (s, 3), 9.09 (s, 3); ir (film) 3300, 2960 cm^{-1}; MS *m/e* 177 (M$^+$·), 162 (M$^+$· − CH_3), 104 ($PhCNH^+$·), 77 (Ph^+·, 100%). Anal. Calcd for $C_{11}H_{15}NO$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.69; H, 8.52; N, 7.97.

Reaction of 38 with Benzoyl Chloride. To a solution of 0.177 g (0.001 mol) of methoxyaziridine **38** in 5 ml of Skellysolve F at −5° were added 0.1 g (0.0001 mol) of triethylamine and 0.14 g (0.001 mol) of benzoyl chloride. After stirring for 5 min, the triethylamine hydrochloride was filtered off, and solvent was rapidly removed in vacuo. The NMR spectrum showed two extra methyl signals at τ 8.75 and 8.96 (assigned to **39**) which disappeared within 2 min. With the disappearance of these two methyl signals, the methyl signals characteristic of methoxyoxazoline **8d** increased correspondingly.

Acknowledgment. Support of this research by PHS Grant CA-4474 from the National Cancer Institute is gratefully acknowledged.

References and Notes

(1) (a) Small Ring Compounds. 21. For previous paper in this series, see S. Hassner, J. O. Currie, A. S. Steinfeld, and R. F. Atkinson, *J. Am. Chem. Soc.*, **95**, 2982 (1973). (b) Address all correspondence to Professor Alfred Hassmer, Department of Chemistry, State University of New York, Binghamton, N.Y. 13901. (c) NDEA Predoctoral Fellow.
(2) O. C. Dermer and G. E. Ham, "Ethylenimine and Other Aziridines", Academic Press, New York, N.Y., 1969, Chapter 1; W. C. J. Ross, "Biological Alkylating Agents", Butterworth, London, 1962.
(3) J. A. Frump, *Chem. Rev.*, **71**, 483–505 (1971), and references contained therein.
(4) R. H. Wiley and L. L. Bennett, *Chem. Rev.*, **44**, 447–476 (1949).
(5) J. F. W. Keana, S. B. Keana, and D. Butham, *J. Org. Chem.*, **32**, 3057 (1967).

(6) A. L. Logothetis, *J. Org. Chem.*, **29**, 3049 (1964).
(7) J. A. Deyrup and R. B. Greenwald, *J. Am. Chem. Soc.*, **87**, 4538 (1965), and references contained therein.
(8) For a variation, see D. Seyferth and W. Tronich, *J. Organomet. Chem.*, **21**, P-3 (1970); D. Seyferth, W. Tronich, and H. Shih, *J. Org. Chem.*, **39**, 158 (1974).
(9) H. E. Zaugg and R. W. Denet, *J. Org. Chem.*, **36**, 1937 (1971).
(10) F. W. Fowler, *Adv. Heterocycl. Chem.*, **13**, 45 (1971).
(11) N. G. Leonard and B. Zwanenburg, *J. Am. Chem. Soc.*, **89**, 4456 (1967).
(12) K. Bunge, R. Huisgen, R. Raab, and H. Stang, *Ber.*, **105**, 1279 (1972).
(13) A. M. von Leusen, B. E. Hoagenboom, and H. Siderius, *Tetrahedron Lett.*, 2369 (1972).
(14) S. H. Pines, *J. Org. Chem.*, **38**, 3854 (1973).
(15) A. Padwa, D. Dean, and J. Smolanoff, *Tetrahedron Lett.*, 4087 (1972).
(16) F. W. Fowler and A. Hassner, *J. Am. Chem. Soc.*, **90**, 2875 (1968).
(17) S. Sato, H. Kato, and M. Ohta, *Bull. Chem. Soc. Jpn.*, **40**, 2938 (1967).
(18) H. M. Kissman, D. S. Tarbell, and J. Williams, *J. Am. Chem. Soc.*, **75**, 2959 (1953).
(19) Solubility in alcohol: sodium azide (0.314 g/100 g); lithium azide (20.26 g/100 g).
(20) R. E. Brooks, J. O. Edwards, G. E. Levey, and F. Smyth, *Tetrahedron*, 1279 (1966).
(21) K. Ichimura and M. Ohta, *Tetrahedron Lett.*, 807 (1966); *Bull. Chem. Soc. Jpn.*, **40**, 1933 (1967).
(22) R. Nicoletti and M. L. Forcellese, *Tetrahedron Lett.*, 153 (1965).
(23) This steric preference has been previously observed in hydride and Grignard additions to azirines: ref 16.
(24) (a) H. W. Heine, *Angew. Chem., Int. Ed., Engl.*, **1**, 528 (1962); (b) *J. Am. Chem. Soc.*, **85**, 2743 (1963); (c) H. W. Heine, D. C. King, and L. A. Portland, *J. Org. Chem.*, **31**, 2662 (1966); (d) H. W. Heine and M. S. Kaplan, *ibid.*, **32**, 3069 (1967).
(25) (a) D. W. Kashelikar and P. E. Fanta, *J. Am. Chem. Soc.*, **82**, 4930 (1960); (b) P. E. Fanta and M. K. Kathan, *J. Heterocycl. Chem.*, **1**, 293 (1964); (c) P. E. Fanta and E. N. Walsh, *J. Org. Chem.*, **30**, 3574 (1965); **31**, 59 (1966); (d) I. J. Burnstein, P. E. Fanta, and B. S. Green, *ibid.*, **35**, 4085 (1970).
(26) (a) Y. Iwakura, A. Nabeya, and T. Nishiguchi, *J. Org. Chem.*, **32**, 2362 (1967); (b) T. Nishiguchi and Y. Iwakura, *ibid.*, **35**, 1591 (1970); (c) T. Nishicuchi, Tochio, A. Nabeya, and Y. Iwakura, *J. Am. Chem. Soc.*, **91**, 5835, 5841 (1969).
(27) (a) P. Scheiner, *J. Org. Chem.*, **32**, 2628 (1967); (b) T. A. Foglia, L. M. Gregory, and G. Maerkel, *ibid.*, **35**, 3779 (1970); (c) W. L. Nelson and B. E. Sherwood, *ibid.*, **39**, 66 (1974); (d) D. Haidukewych and A. I. Meyers, *Tetrahedron Lett.*, 3031 (1972).
(28) A. Hassner and A. B. Levy, *J. Am. Chem. Soc.*, **93**, 5469 (1971).
(29) (a) The assignment is based on the magnetic anisotropic effect of the 2-phenyl group. (b) S. J. Brois, *J. Org. Chem.*, **27**, 3532 (1962). We have observed resonances generally 0.3 ppm to lower field than that reported for compounds in this paper.
(30) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry", Holden-Day, San Francisco, Calif., 1964, Chapter 7.
(31) This is consistent with spectra of the 2-oxazolidones. S. L. Spassov, J. N. Stefanofsky, B. J. Kurtev, and G. Fodor, *Chem. Ber.*, **105**, 2462 (1972).
(32) (a) W. W. Heine, D. C. King, and L. A. Portland, *J. Org. Chem.*, **31**, 2662 (1966); (b) A. Hassner and S. S. Burke, *Tetrahedron*, in press.
(33) All melting points were recorded on a Fisher-Johns melting point block and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 457 infrared spectrometer; mass spectra were recorded on a Varian MAT CH-5 instrument. NMR spectra were obtained using Varian A-60A and EM 360 spectrometers with Me_4Si as internal standard. Microanalysis was performed by Atlantic Microlabs, Atlanta, Ga.
(34) J. H. Burckhalter and R. C. Fuson, *J. Am. Chem. Soc.*, **70**, 4184 (1948).
(35) M. Bachstez, *Chem. Ber.*, **47**, 3163 (1914).

Radical-Induced Decomposition of Peracetic Acid[1,2]

R. A. Kenley and T. G. Traylor*

Contribution from the Department of Chemistry, Revelle College, University of California, San Diego, La Jolla, California 92037. *Received December 17, 1974*

Abstract: The induced decomposition of peracetic acid in acetic acid can be initiated by sources of *tert*-butoxy radicals. This decomposition, studied in the presence of either pure $^{36}O_2$ or pure $^{32}O_2$, is shown to involve the formation of acetyl tetroxide in the same way as does the termination step in acetaldehyde autoxidation. These results confirm the mechanism of interaction of acetylperoxy radicals previously proposed.

The previous papers[3-5] reported studies of the interactions of acylperoxy radicals which are intermediates in aldehyde autoxidation.

$$RC(=O)H \xrightarrow[O_2]{\text{initiator}} RC(=O)OO\cdot \quad (1)$$

$$2RC(=O)OO\cdot \longrightarrow 2CO_2 + 2R\cdot + O_2 \quad (2)$$

To further document reaction 2 and the fate of the resulting alkyl radicals we have sought an alternate source of acylperoxy (in this case acetylperoxy) radicals from induced peracid decomposition.

$$CH_3C(=O)OOH + t\text{-}BuO\cdot \longrightarrow CH_3C(=O)OO\cdot + t\text{-}BuOH \quad (3)$$

The analogous induced decomposition of *tert*-butyl hydroperoxide[6-8] had been used to study the interaction of *tert*-butylperoxy radicals as an alternative to the autoxidation of isobutane.[9] The reaction sequence is, in this case, very simple[6] ($(CH_3)_3COMMOC(CH_3)_3$ is the initiator where MM is $-N_2-$ or $-OC(O)C(O)O-$).

$$(CH_3)_3COMMOC(CH_3)_3 \longrightarrow 2(CH_3)_3CO\cdot + 2M \text{ or } MM \quad (4)$$

$$(CH_3)_3COOH + RO\cdot \longrightarrow ROH + (CH_3)_3COO\cdot \quad (5)$$

$$2(CH_3)_3COO\cdot \rightleftharpoons (CH_3)_3COOOOC(CH_3)_3 \longrightarrow [(CH_3)_3CO\cdot O_2\cdot OC(CH_3)_3]_{cage} \quad (6)$$

$$[(CH_3)_3CO\cdot O_2\cdot OC(CH_3)_3]_{cage} \begin{cases} \xrightarrow[\text{and termination}]{\text{cage collapse}} (CH_3)_3COOC(CH_3)_3 & (7) \\ \xrightarrow[\text{and propagation}]{\text{diffusion}} 2(CH_3)_3CO\cdot + O_2 & (8) \end{cases}$$

This sequence is similar to that found in cumene autoxidation.[10,11]

Because reaction 2 leads to acylperoxy radicals which decarboxylate rapidly, we expect the induced decomposition of peracids to be more complex. But we should find the same oxygen and carbon dioxide evolution as that observed in acetaldehyde autoxidation if the proposed mechanisms are correct. In addition, ^{18}O labeling experiments afford some information not available from autoxidation studies, as we shall see.

But we and others[12] have previously attempted the induced decomposition without success. First, the OH bond is stronger in peracids than in hydroperoxides, and there is strong hydrogen bonding[13] in peracids which would further reduce the reactivity of the O-H bond. Second, there ap-