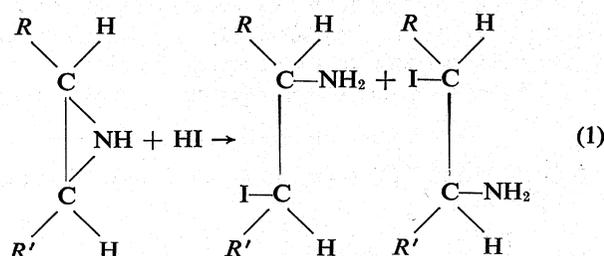


Determination of 2,3-Dialkylaziridines by Direct Titration with Hydrogen Iodide

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THE CHEMISTRY of 2,3-dialkylaziridines unsubstituted on nitrogen, has recently aroused considerable interest and is being studied in this laboratory. No suitable direct titrimetric method has been reported for the determination of aziridines of this type, most of which are insoluble in aqueous media. Jay (1) described the direct titration of epoxides and aziridines with perchloric acid in the presence of quaternary ammonium halides. In this procedure the active agent is the hydrogen halide generated *in situ* (HBr for epoxides, HI for aziridines). This method, developed for application to aziridines bearing electron-withdrawing substituents on nitrogen, is unsatisfactory for compounds of type I, because the iodoamines formed (Equation 1) interfere with the determination of the end point.



The following procedure, a modification of the Jay method, permits the direct titration of 2,3-dialkylaziridines unsubstituted on nitrogen. Prior to titration the sample is treated with acetic anhydride to form the *N*-acyl derivative which is not isolated. The anhydride is usually used as the solvent in which the titration is carried out, but may be used as reagent in conjunction with another, inert, solvent.

(1) R. R. Jay, *ANAL. CHEM.*, **36**, 667 (1964).

EXPERIMENTAL

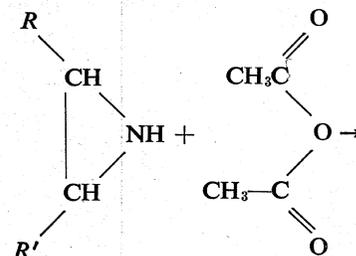
Reagents. Standard 0.02*N* HClO₄ in glacial acetic acid. Add 1.7 ml of 72% HClO₄ and 4 ml of acetic anhydride to 300 ml of glacial acetic acid. Dilute to 1 liter with glacial acetic acid and allow to stand overnight. Standardize against potassium acid phthalate dissolved in 10 ml of glacial acetic acid using crystal violet indicator (1% solution in glacial acetic acid).

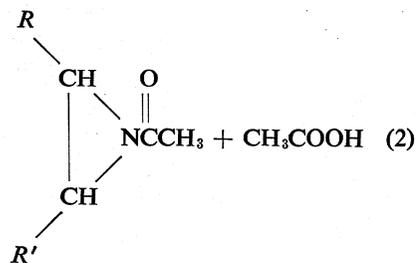
Tetra-*n*-butylammonium iodide reagent, 10% in chloroform. Prepared by the method of Jay (1). The reagent should be prepared fresh daily.

Procedure. A sample containing 0.2 to 0.4 meq of titratable function is weighed into a 50-ml Erlenmeyer flask, dissolved in 10 ml of acetic anhydride, and allowed to stand in the stoppered flask for 15 min. Solution may be aided by slight warming, but the solution must be returned to room temperature before proceeding further. Five milliliters of tetra-*n*-butylammonium iodide solution and one drop of crystal violet indicator solution are added, and the magnetically stirred mixture is titrated rapidly with standard HClO₄ from a 25-ml buret to the first true blue end point. The reagent blank should not be in excess of 0.2 to 0.4 ml.

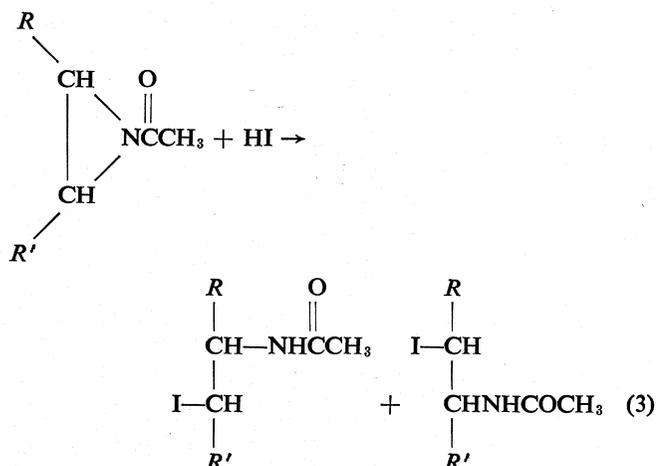
DISCUSSION AND RESULTS

Aziridines which are unsubstituted on nitrogen react with acetic anhydride according to Equation 2. The acylated





aziridine slowly reacts with the acetic acid formed as byproduct, and care should be taken to avoid letting the acylating solution stand for much longer than 15 min. Reaction of the acylated aziridine with hydrogen iodide formed *in situ* leads to the iodoamide (Equation 3) which is not basic and therefore does not react further with HI or with HClO₄. The rate of reaction of the hydrogen halide with *N*-acylaziridines



depends on the nucleophilicity of the anion, and HBr and HCl react too slowly for satisfactory titration.

Basic functional groups, such as primary and secondary amines, if present as impurities, do not interfere in this procedure because they are also acylated by acetic anhydride, and the amides formed do not react with HI or HClO₄. Tertiary amines, however, do interfere and must be absent. Other functional groups which react with HI—*e.g.*, epoxides and α,β -unsaturated ketones, interfere, as do groups which exchange iodide for less nucleophilic anions.

The use of HBr in acetic acid for the determination of alkali metal salts of carboxylic acids was described in an earlier report (2). Salts of carboxylic acids are also basic toward HI, and if they are present as impurities they will interfere with the determination.

(2) E. T. Haeberer and G. Maerker, *J. Amer. Oil Chem. Soc.*, **40**, 274 (1963).

Table I. Determination of 2,3-Dialkylaziridines

Compound	Purity by acylation-titration (%)	Estimated purity (%)
<i>cis</i> -9,10-Epiminooctadecane	98.0, 97.7	98.0 ^a
<i>trans</i> -9,10-Epiminooctadecane	99.2, 100.3	>99.0 ^a
Methyl <i>cis</i> -9,10-epimino-octadecanoate	99.3, 99.2	99.0 ^b
Methyl <i>trans</i> -9,10-epimino-octadecanoate	99.5, 99.1	99.1 ^b
<i>cis</i> -9,10-Epimino-1-octadecanol	99.4, 99.4	>99.0 ^a
<i>cis</i> -2,3-Epiminohexane	95.0, 94.4	92.8 ^b
<i>trans</i> -2,3-Epiminohexane	93.3, 93.5	94.3 ^b

^a Estimated by thin-layer chromatography.

^b Estimated by gas-liquid chromatography.

Table II. Analysis of Alkylaziridines Substituted on Nitrogen

Compound	Acylation-titration % purity	Estimated % purity
<i>cis</i> -3,4-(<i>N</i> -Benzenesulfonyl epimino)hexane	98.7, 98.2	>99 ^a
<i>trans</i> -3,4-(<i>N</i> -Benzenesulfonyl-epimino)hexane	101.0, 100.7	>99 ^a
Methyl <i>cis</i> -9,10-(<i>N</i> -benzenesulfonylepimino) octadecanoate	99.2, 98.7	>99 ^a
1,2-(<i>N</i> -Acetylepimino)octadecane	97.4, 97.9	>99 ^a

^a Homogeneous to thin-layer chromatography.

The assay of a series of internal aliphatic aziridines is shown in Table I. The synthesis of these compounds was carried out by the iodine isocyanate route (3) and will be reported elsewhere. The purity values obtained by titration compare well with independent estimates of purity obtained by thin-layer or gas-liquid chromatography. Also analyzing correctly, but not listed in Table I was a sample of *cis*-2,3-diphenylaziridine obtained from D. Swern (Chemistry Department, Temple University, Philadelphia, Pa.). The procedure failed to give satisfactory results with four terminal aziridines (2-hexyl-, 2-octyl-, 2-decyl-, and 2-hexadecylaziridine) all of which gave titration purities which were about 15% lower than expected from independent purity determinations. It is believed that the failure of the terminal aziridines to give correct analyses stems from the interference by a side reaction, perhaps ring-opening by acetate anion, during the acylation step. Support for this view is found in the fact the 1-acetyl-

(3) C. A. Gebelein, G. Swift, and D. Swern, *J. Org. Chem.*, **32**, 3314 (1967).

Table III. Determination Carboxylic Acid Salts

Compound	Acylation-titration		Elemental anal.	
	% Purity	Color of endpoint	% Metal by ash	% N
Potassium palmitate	100.5, 100.7, 100.0	blue	101.1	...
Sodium stearate	99.1, 98.8	blue-green	99.6	...
Potassium 9,10-epiminooctadecanoate	99.2, 99.6	blue	102.3	96.9
Sodium 9,10-epiminooctadecanoate	98.2, 98.2	blue-green	98.1	98.9
Lithium 9,10-epiminooctadecanoate	96.8, 96.9	blue	101.3	99.8
Barium 9,10-epiminooctadecanoate	94.4, 94.5	blue	99.5	101.8

2-hexadecylaziridine, the purified acetylation product of 2-hexadecylaziridine, gave correct results (see Table II).

Alkylaziridines bearing electron withdrawing substituents on nitrogen are expected to be assayed satisfactorily by the present method as well as by the method of Jay. Because these compounds contain no replaceable hydrogen on nitrogen, they should not, and in fact do not, react with acetic anhydride. Table II shows that such types of aziridines can be determined by the present method.

Carboxylic acids react readily with 2,3-dialkylaziridines, causing the heterocyclic ring to open. For this reason aliphatic carboxylic acids containing aziridine rings have not yet been isolated as pure compounds. Salts of such acids, however, are synthesized fairly readily and a number of such salts

have been prepared in this laboratory. The analysis of these salts, shown in Table III, presents a special analytical problem, because these compounds contain two different titratable groups. Three of the four different metal salts tested are assayed correctly using the blue end point of crystal violet. The sodium salt, however, requires the blue-green end point of this indicator as determined by potentiometric titration of sodium 9,10-epiminooctadecanoate and by titration of a sample of sodium stearate of known purity. Lithium 9,10-epiminooctadecanoate is poorly soluble in acetic anhydride but goes into solution during titration.