Preparation and Reactions of Fatty Acid Azirines[1]

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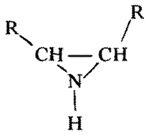
ABSTRACT

The 1-azirine derivatives of *cis*-9-octadecene and methyl oleate have been prepared, and some of their reactions have been studied. The preparation of these novel fatty acid derivatives was accomplished *in* a three-step synthesis with good overall yields. Addition of the electrophile IN_3 to the olefin yielded the β-iodoazide derivatives of octadecane and stearic acid. Treatment of the latter compounds with base resulted in dehydrohalogenation and gave the vinyl azides. Solution photolysis of the vinyl azides yielded the 1-azirine derivatives. Reduction of the 1-azirines with metal hydrides gave the known epimino derivatives of octadecane and octadecanol. Other reducing agents were unsuccessful in preserving the three-membered ring. Reaction with acids caused the dimerization of the 1-azirines with formation of tetrasubstituted pyrazines. The 1-azirines were attacked by acid chlorides and hydrochloric acid to give chlorinated amides as principal products.

INTRODUCTION

In connection with our studies of the preparation and reactions of aziridines (1) derived from fatty acids and related compounds (1), our interest focused upon the unusual monounsaturated analog of aziridine, namely the 1-azirine derivative (2). This novel heterocyclic structure, which incorporates a highly strained carbon nitrogen double bond within a three-membered ring, was first assigned by Neber (2) to an isolated intermediate from his studies of the synthesis of α-aminoketones by the reaction of imine tosylates with base. The correctness of this structural assignment was later confirmed by Cram and Hatch (3).



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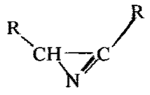

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Although the Neber rearrangement generally does not lend itself to the synthesis of 1-azirines, a few such compounds have been synthesized by modification of this reaction (4). A number of other methods have also been used for the preparation of 1-azirines. Among these procedures are the reaction of nitrile oxides with phosphonium ylides (5), the addition of dimethylsuffonium methylide to nitriles (6), and the photolysis and thermolysis of isoxazoles and mercaptoisoxazoles (7). Smolinsky (8) developed a synthesis based on the pyrolysis of terminal vinyl azides, and this was later extended by Bauer and Hafner (9) and Isomura et al. (10).

All of the above mentioned procedures are severely limited in scope owing to the inaccessability of the requisite starting materials, although the pyrolysis of vinyl azides appears to be the most versatile. With the development of an elegant vinyl azide synthesis by Hassner and Fowler (11), a variety of both internal and terminal vinyl azides have become readily available from olefins. These authors have also demonstrated that the photolysis of vinyl azides generally gives good yields of 1-azirines (12), although their studies were concerned mainly with the preparation of aryl-substituted and fused 1-azirine derivatives.

The purpose of the present investigation was to prepare long chain fatty acid derivatives containing an internal 1-azirine function and to study some of the chemical reactions of such compounds.

EXPERIMENTAL PROCEDURES

Materials and Equipment

Cis-9-octadecene was prepared by the lithium aluminum hydride (LAH) reduction of the tosylate of oleyl alcohol (13). Purity, as determined by gas liquid chromatography (GLC) and thin layer chromatography, (TLC) exceeded 98% (GLC).

Methyl oleate (99%) was purchased from Applied Science Laboratory and was used as received.

All other reagents were used as received from commercial suppliers except for acetonitrile, which was distilled from phosphorus pentoxide prior to use.

The source for UV radiation was the Srinivasan-Griffin Rayonet photochemical reactor equipped with the "black light" phosphor lamp. IR spectra were obtained on a Perkin Elmer Model 237-B spectrophotometer with sodium chloride optics. The spectra were taken as liquid films on sodium chloride discs. NMR spectra were obtained on a Jeolco C-60H spectrometer. Chemical shifts are reported as δ (ppm) relative to tetramethylsilane (TMS). GLC was carried out on a Hewlett-Packard Model 810 gas chromatograph. Silica Gel H (Brinkmann) was used for thin layer analysis. Spots were detected by heat-charring after spraying with 50% sulfuric acid.

Threo-9-azido-10-iodo octadecane (5). Pure *cis*-9-octadecene (3) (20.6 g, 0.082 mole) was converted to the β-iodoazide by reaction with iodine monochloride (15.3 g, 0.090 mole) and sodium azide (15.6 g, 0.24 mole) in acetonitrile (125 ml) by the method of Fowler et al. (14). The product was obtained as a pale yellow oil (97% yield), whose purity was estimated to be > 95% by TLC (benzene-hexane 50:50). The only detectable impurity was starting olefin, which could be easily removed by chromatography on neutral alumina. IR (neat): 2940 (C-H), 2100 (N_3), 1460, 1380, 1260 and 720 cm^{-1}. Analysis calculated for $C_{18}H_{36}IN_3$: C, 51.3; H, 8.61; N, 9.97; I, 30.1. Found: C, 51.6; H, 8.78; N, 10.3; I, 29.6.

Methyl threo-9 (10)-azido-10(9)-iodo octadecanoate (6) was obtained from the reaction of methyl oleate (4) (22.3 g, 0.075 mole) and iodine azide by the procedure of Fowler et al. (14). The iodo-azide, a mixture of positional isomers, was obtained as an amber oil (yield ≈ 100%). Its purity as determined by TLC was > 97% (hexane-benzene 50:50). IR (neat): 2930 (C-H), 2110 (N_3), 1740 (C=O), 1460, 1430, 1250, 1200 and 1160 cm^{-1}. Analysis calculated for $C_{19}H_{36}IN_3O_2$; C, 49.0; H, 7.80; I, 27.3; N, 9.03. Found: C, 49.2, H, 7.86; I, 27.0; N, 9.15.

Trans-9-azido-9-octadecene (7) To a slurry of potassium-*t*-butoxide (3.4 g, 0.030 mole) in anhydrous ether (75 ml) was added a solution of *threo*-9-azido-10-iodooctadecane (10.2 g, 0.025 mole) in ether (25 ml). The reaction mixture was stirred at 0 C for 12 hr. and was poured onto ice (200 g). The ether layer was separated, washed with H_2O (200 ml), dried over anhydrous $MgSO_4$, and the

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solvent was removed in vacuo to give the vinyl azide as a pale yellow oil (93% yield). TLC (benzene-hexane 50:50) and mass spectral analysis of this material indicated a purity of > 95%. IR (neat): 2960 (C-H), 2100 (N_3), 1660 (C=C), 1460, 1380, 1260 and 1100 cm^{-1}. Analysis calculated for $C_{18}H_{35}N_3$: C, 73.7; H, 12.0; N, 14.3. Found: C, 73.5; H, 11.9; N, 14.1.

Methyl trans-9(10)azido-9-octadecenoate (8) was prepared from methyl *threo*-9(10)azido-10(9) iodooctadecanoate (9.3 g, 0.020 mole) in the manner described above for the octadecene derivative. This vinyl azide was obtained as a colorless oil the purity of which was > 95% by TLC (ether-benezene 10:90) and mass spectroscopy. IR (neat): 2930 (C-H), 2150 (N_3), 1750 (C=0), 1660 (C=C) 1460, 1440, 1350, 1260, 1180 and 1160 cm^{-1}. Analysis calculated for $C_{19}H_{35}NO_2$: C, 67.6; H, 10.5; N, 12.5. Found: C, 67.2; H, 10.7; N, 12.3.

2,3-Dioctyl-1-azirine (9). A solution of *trans*-9-azido-9-octadecene (6.6 g, 0.021 mole) in pentane (200 ml) was placed in a quartz vessel and photolyzed. The photolysis was discontinued after 20 hr at which time no vinyl azide remained. The solution was filtered to remove a small amount of polymer, and the solvent was removed in vacuo to give the 1-azirine as a tan oil (92% yield). Distillation gave the pure azirine as a colorless oil, bp 121 C at 0.2 torr (57% yield). GLC and TLC of this material indicated a single component. IR (neat): 2980 (C-H), 1760 (C=N), 1470, 1380 and 980 cm^{-1}. Analysis calculated for $C_{18}H_{35}N$: C, 81.4; H, 13.3; N, 5.28. Found: C, 81.6; H, 13.4; N, 5.16.

2(3)Octyl-3(2)-[7-carbomethoxyheptyl]-1-azirine (10) was obtained from the photolysis of methyl *trans*-9-azido-9-octadecenoate (4.3 g, 0.013 mole) in pentane (100 ml). The crude photolysate was chromatographed on silica gel to yield the pure azirine as a colorless oil (78% yield). GLC and TLC of this material indicated it to be a single component. IR (neat): 2960 (C-H), 1760 (c=N), 1740 (C=0), 1460, 1430, 1380, 1240, 1200, 1180 and 1020 cm^{-1}. NMR ($CHCl_3\delta$): 3.7 (3H,*s*), 2.8 (2H,*t*), 2.4 (2H,*t*) and 1.6 (1H,*t*). Mol wt for $C_{19}H_{35}NO_2$ = 309.498, found (mass spectroscopy): 309.462. Analysis calculated for $C_{19}H_{35}NO_2$: C, 73.7; H, 11.4; N, 4.53. Found: C, 73.6; H, 11.1; N, 4.48.

Cis-9,10-epiminooctadecane (11). To a slurry of lithium aluminum hydride (0.38 g, 0.01 mole) in anhydrous ether (20 ml) was added a solution of 2,3-dioctyl-1-azirine (2.6 g, 0.01 mole) in ether (5 ml). The mixture was stirred for 12 hr at ambient temperature, cooled to 0 C, and 10% sodium hydroxide solution (5 ml) was added over a period of 0.5 hr. The mixture was then filtered. The ether filtrate was dried over anhydrous $MgSO_4$ and the solvent removed in vacuo to leave a solid residue (95% yield). Aziridine analysis (15) indicated a purity of 84%. Crystallization from acetone gave the pure epimino compound with mp 62.5-64.0 C, (lit. mp 63.5-64.0 C [16]).

Cis-9,10-epiminooctadecanol (12) was prepared by the LAH reduction of 2(3)-octyl-3(2)-[7-carbomethoxyheptyl] -1-azirine (3.1 g, 0.01 mole) by the procedure described above. The crude reduction product (82% weight yield, 91% aziridine) was crystallized from acetone to give the pure epimino compound with mp 70-71 C (lit. mp 71.5-72.5 C [16]).

9,9-dimethoxy-10-aminooctadecane (14). A solution of *trans*-9-azido-9-octadecene (2.0 g, 0.007 mole) in methanol (100 ml) containing sodium methoxide (100 mg) was photolyzed for 18 hr. The solvent was removed in vacuo, and the residue was taken up in ether (40 ml) and washed with H_2O (3 x 40 ml). The ether layer was dried over anhydrous $MgSO_4$, and the solvent was removed in vacuo to give the amino ketal as a yellow oil. The pure material was obtained by preparative TLC ($CHCl_3$/MeOH 95:5) on silica gel. IR (neat): 3420 (NH), 2930 (CH), 1460, 1375, 1150, 1100 and 1050 (OCH_3) cm^{-1}. Analysis calculated for $C_{20}H_{43}NO_2$: C, 72.9; H, 13.2; N, 4.25. Found: C, 73.1; H, 13.4; N, 4.10.

Methyl 9,9(10,10)-dimethoxy-10(9)-aminooctadecanoate (15) was obtained from methyl *trans*-9(10)-azido-9-octadecenoate (3.35 g, 0.010 mole) by solution photolysis in methanol (84% yield). The crude product was purified by preparative TLC on silica gel ($CHCl_3$/MeOH 95:5). IR (neat): 3400 (NH), 2940 (CH), 1740 (C=0), 1460, 1430, 1360, 1250, 1150, 1050 and 840 cm^{-1}. Analysis calculated for $C_{21}H_{43}NO_4$: C, 67.5; H, 11.6; N, 3.75. Found: C, 67.7; H, 11.6; N, 3.79.

Tetraoctyl pyrazine (13). To a solution of 2,3-dioctyl-1-azirine (1.6 g, 0.005 mole) in dioxane (15 ml) was added 4 N sulfuric acid (5 ml). The reaction mixture was stirred for 12 hr, poured into 10% NaOH solution (25 ml) and extracted with ether (3 x 20 ml). The ether extracts were washed with H_20 (3 x 20 ml), dried over anhydrous $MgSO_4$, and the solvent was removed in vacuo to give a pale yellow oil. Chromatography on florisil gave the pure pyrazine as a colorless oil (35% yield). IR (neat): 2940 (CH), 1460, 1410, 1375, 1150, 1075, 760 (Aromatic) and 720 cm^{-1}. Analysis calculated for $C_{36}H_{60}N_2$: C, 81.7; H, 13.0; N, 5.30. Found: C, 81.6; H, 12.9; N, 5.38.

Alternatively this material was prepared by the hydrolysis of the dimethylketal amine 14 utilizing the above procedure (yield 70%).

2,5(6)-Dioctyl-3,6(5)di[7-carbomethoxy heptyl]pyrazine (16) was prepared by the acid hydrolysis of the dimethylketal amine 15. The crude product was esterified with BF_3 etherate in methanol and purified by preparative TLC on silica gel ($C_6H_6/Et_20/CH_3OH$ 87:10:3) (yield 68%). IR (neat): 2940 (CH), 1740 (C=0), 1455, 1430, 1410, 1240, 1200, 1160 760 (Aromatic) and 720 cm^{-1}. Analysis calculated for $C_{38}H_{68}N_20_4$: C, 74.0; H, 11.1; N, 4.54. Found: C, 74.2; H, 11.0; N, 4.37.

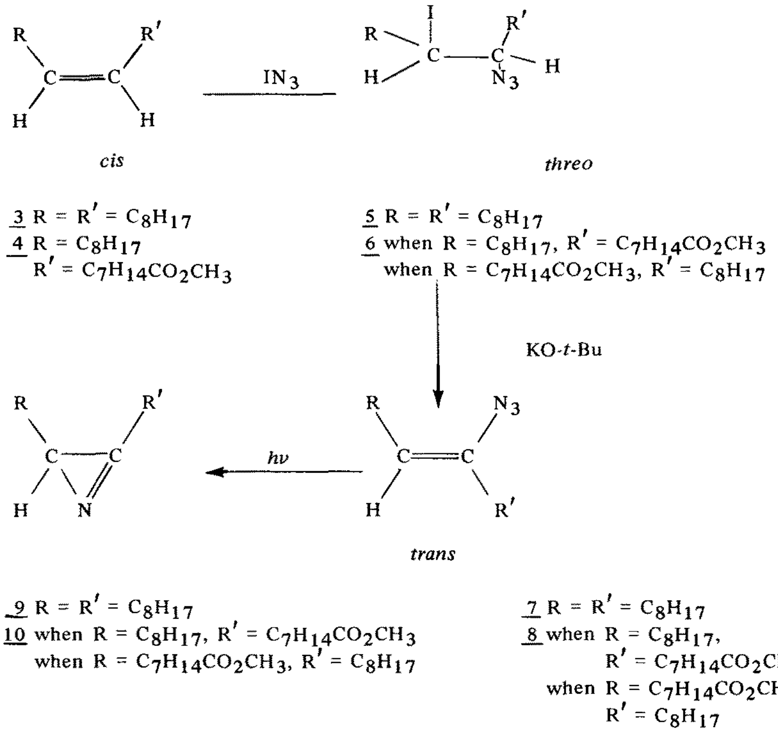
N-Benzoyl-9-chloro-9,10-epiminooctadecane (17). To a solution of azirine 9 (1.0 g, 3.78 mmole) in benzene (10 ml) was added benzoyl chloride (0.54 g, 3.78 mmole). The solution was stored at 5 C for 12 hr, and the solvent was removed in vacuo to leave a viscous oil (yield ≈ 97%). IR (neat): 3100 and 3050 (Aromatic CH), 2940 (CH), 1660 (C=0), 1460, 1320, 1260, 1205, 1175, 875 (C-Cl) and 675 (Aromatic) cm^{-1}.

9-Chloro-10-benzamido-9-octadecene (18). Aziridine 17 on warming to 50 C on a steam bath for 1 hr gave a new compound as determined by TLC (benzene). The pure product was obtained by preparative TLC on silica gel (benzene) (yield 85%). IR (neat): 3300 (NH), 2940 (CH), 1660 (C=0), 1600, 1560, 1525 (Amide II), 1480, 1460, 1300, 1075, 1025, 800 (C-Cl), 720 and 680 cm^{-1}. Analysis calculated for $C_{25}H_{40}Cl$ NO: C, 73.9; H, 9.93; N, 3.45; Cl, 8.73. Found: C, 73.8; H, 9.74; N, 3.40; Cl, 8.89.

9,9-Dichloro-10-benzamidooctadecane (19). To a solution of aziridine 17 (1.0 g, 2.46 mmole) in ether was passed anhydrous HCl for 5 min. The solvent was removed in vacuo to leave a viscous oil. This oil, a mixture of two components, was separated by preparative TLC (benzene) into two bands. The lower band was identified by mass spectrometry as amide 18 (35% yield), while the other was identified as the dichloroamide compound 19 (60% yield). IR (neat): 3420 (NH), 2940 (CH), 1640 (C=0), 1600, 1560, 1520 (Amide II), 1480, 1460, 1375, 1330, 1275, 1150, 1125, 1075, 1025, 800 (C-Cl), 755, 720 and 685 cm^{-1}. Analysis calculated for $C_{25}H_{41}Cl_2NO$: C, 67.9; H, 9.34; N, 3.17; Cl, 16.0. Found: C, 67.7; H, 9.10; N, 3.25; Cl, 16.2.

RESULTS AND DISCUSSION

The model unsaturated compounds selected for this investigation were *cis*-9-octadecene (3) and methyl oleate



Scheme I.

(4). The former compound was chosen as a prototype for long chain internal aliphatic olefins in general, since its symmetry and lack of interfering functional groups were expected to simplify product isolation and identification. The general procedure utilized for the preparation of 1-azirine derivatives was the iodine azide (IN_3) method of Fowler et al. (14) which is illustrated in Scheme I.

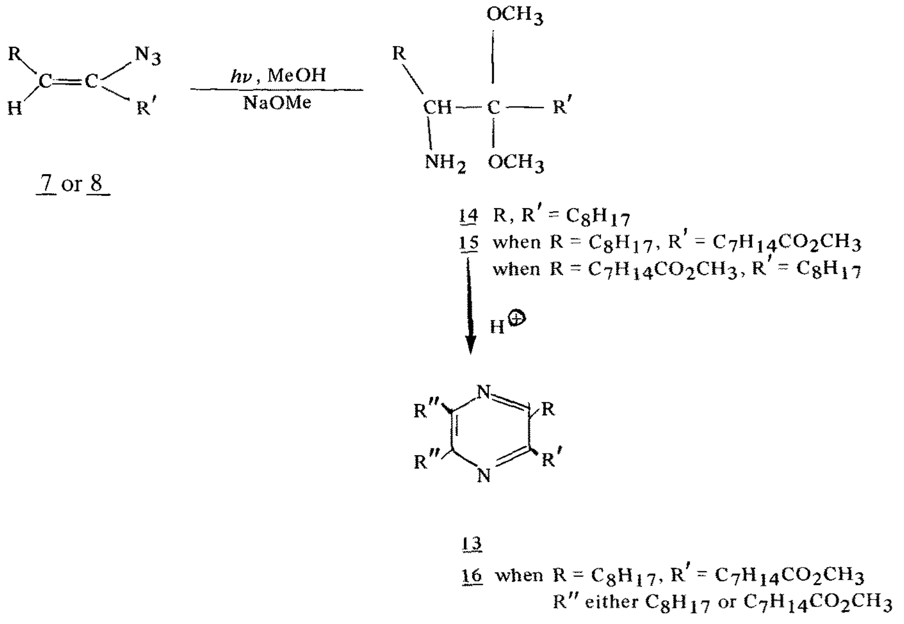
The addition of the electrophilic reagent iodine azide (prepared in situ from sodium azide and iodine monochloride in acetonitrile solution) to olefins has been demonstrated to proceed in a highly stereospecific *trans* manner (17). Accordingly, when a *cis* olefin, such as *cis*-9-octadecene or methyl oleate is used as starting material, one obtains the corresponding *threo*-iodoazide 5 or 6. These addition reactions were found to occur in nearly quantitative yields, and the only detectable contaminant, if any, was the starting olefin. Since both the azido and secondary iodo functions are labile substituents, the adducts were purified, when necessary, by silica gel column chromatography to remove the starting material. Evidence that the addition indeed occurred was obtained from elemental analyses and IR spectroscopy. The spectra of adducts 5 and 6 are characterized by strong absorptions at 2150 cm^{-1} which is ascribed to the asymmetric stretching vibration of the azide functionality (19). Dehydrohalogenation of the iodo azides 5 and 6 with potassium *t*-butoxide in aprotic solvent yielded the corresponding vinyl azides 7 and 8 in excellent yields. The progress of these reactions was readily monitored by IR spectroscopy. The pertinent IR absorptions for the conversion of iodoazide adduct of methyl oleate (6) to the vinyl azide derivative (8) are shown in Figure 1. The spectrum of compound 6 is characterized by strong bands at 2150 and 1740 cm^{-1} assignable to the azido and ester functions, respectively. These bands are still present in the vinyl azide derivative (8). However a new absorption band located at 1660 cm^{-1} appears, which can be assigned to the carbon-carbon double bond stretching vibration which is in conjugation with the azido function (11). The azide band at 2150 cm^{-1} is identical in position and intensity in the iodoazide and the vinyl azide structures. Assignment of the *trans* geometry to the vinyl azide derivatives was made on the basis of the known preference of E_2 elimination reactions to occur with a *trans* antiparallel arrangement of leaving groups (11). Verification of these assignments was made from an inspection of the NMR spectra. Of particular importance is the chemical shift of the vinyl protons which appear in the area of 5.25 τ.

Hassner (17) showed that in simple aliphatic vinyl azides, the vinyl proton absorbtion in the *trans*-isomers is shifted upfield from the corresponding proton in the *cis*-isomers ($\approx 4.75\ \tau$). He also noted that these absorptions fall into a very narrow range of chemical shifts and are reliable criteria for the assignment of the geometry of the double bond of internal vinyl azides.

Solution photolysis of thermolysis, of vinyl azides 7 and 8 resulted in the liberation of nitrogen gas with the concomitant formation of azirines 9 and 10. Photolysis of the vinyl azides in pentane solution is the preferred procedure, since fewer side products are formed. Azirine 9 was obtained as a colorless liquid by distillation, while azirine 10 was purified by column chromatography on silica gel.

Since the vinyl azide 8 is a mixture of 9,10 positional isomers and the unsaturated nitrogen bridge of the azirine structure is asymmetric, azirine 10 was obtained as a mixture of positional isomers with respect to the location of the imine bond within the heterocyclic ring system. That both isomers were indeed formed was evident from the TLC of azirine 10 which showed two closely associated, but inseparable, spots. Aside from elemental analyses and molecular weight determinations by mass spectrometry, proof of structure for these novel heterocyclic derivatives was also obtained from spectroscopic evidence. The IR spectra of the azirines have a characteristic band at 1775 cm^{-1} which has been assigned to the highly strained carbon-nitrogen double bond virbration of the azirine ring (11). The NMR spectrum of azirine 10 showed a triplet centered at 2.8 δ (2H) for the methylene protons adjacent to the imine group of the azirine ring, a broad ill-defined triplet centered at 1.6 δ (1H), assigned to the lone proton on the azirine ring and other absorptions characteristic of the fatty ester structure. These data are consistent with the assigned structure of 10.

Hassner and Fowler (11) have shown that in the



7 or 8

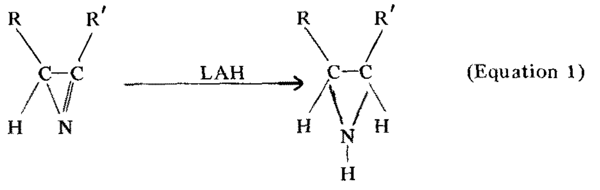
14 R, R' = C_8H_{17}
15 when R = C_8H_{17}, R' = $C_7H_{14}CO_2CH_3$
when R = $C_7H_{14}CO_2CH_3$, R' = C_8H_{17}

13
16 when R = C_8H_{17}, R' = $C_7H_{14}CO_2CH_3$
R'' either C_8H_{17} or $C_7H_{14}CO_2CH_3$

Equation 3.

formation of azirines by the potolysis of vinyl azides, ketenimine formation is the major side reaction. These products, which give intense IR absorptions at 2050 cm^{-1}, were not detected in the present study, and it is doubtful that their formation is important in this series.

Chemical proof of the presence of a three-membered ring for both compounds 9 and 10 was obtained by reduction of the azirine ring to the corresponding epimino derivatives (Equation 1).



(Equation 1)

9

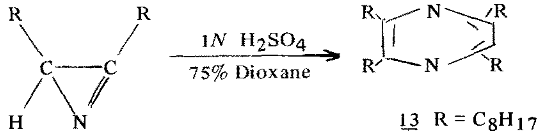
10

cis

11 R,R' = C_8H_{17}
12 R = C_8H_{17}, R' = $C_7H_{14}CH_2OH$

Reduction of 9 with lithium aluminum hydride gave *cis*-9-10-epiminooctadecane (11), while reduction of 10 gave *cis*-9-10-epiminooctadecanol (12), in good yields. The identity of these derivatives was proven by mixed melting point determinations and by a comparison of their IR spectra with those of authentic samples (16). Compound 12 is formed, since reduction of the imine bond is accompanied by reduction of the ester group to the alcohol. According to Hassner et al. (19) the high stereospecificity observed in these reductions can be ascribed to the preferential shielding of the imine bond by the substituent located on the saturated carbon atom of the azirine ring. This allows for the approach of the reducing agent to occur only from the less hindered side of the molecule. Attemps at catalytic reduction with noble metal catalysts were unsuccessful in preserving the three-membered ring and gave amines as principal byproducts.

Having incorporated the 1-azirine ring structure into the fatty acid backbone, we turned our attention to a study of its chemical reactions. Initially we sought to determine whether we could hydrolyze the imine structure, incorporated within the azirine ring, to the α-aminoketone. Reaction of azirine 9 with sulfuric acid in dioxane solution did not yield the α-aminoketone but gave instead a major product readily identifiable by IR and mass spectroscopy as the tetrasubstituted pyrazine 13 (Equation 2).



9

13 R = C_8H_{17}

Equation 2.

The formation of pyrazine 13 most probably arises by the condensation of two α-aminoketone molecules, as they are formed in situ, followed by dehydrogenation to the aromatic ring structure. This view was confirmed by carrying out the hydrolysis in concentrated hydrochloric acid, which gave a product with IR bands at 1710 cm^{-2} (ketone) and 2600-3100 cm^{-1} (amine salt) in agreemen with a hydrochloride salt of an α-aminoketone. Neutralization of this compound with base yielded the same pyrazine derivative that was previously obtained.

Subsequent studies, however, have shown that if the α-aminoketone or pyrazine derivative of the olefin is the desired product, it is best obtained not from the 1-azirine but from the vinyl azide presursor Equation 3. Solution photolysis of the vinyl azides in methanol, containing a catalytic quantity of sodium methoxide, gave the dimethylketal of the α-aminoketones 14 and 15 in nearly quantitative yields. The formation of ketalamines from vinyl azides has been shown to proceed by the addition of two moles of methanol to the 1-azirine as it is formed (12). Reaction of ketals 14 and 15 with acid followed by neutralization with base yielded the previously identified pyrazine 13 and the new pyrazine 16, derived from methyl oleate. The formation of these derivatives via the ketals is preferred over their preparation via the hydrolysis of the azirine, since the overall yields of the former procedure are greater, and fewer steps are required.

The interaction of azirine 9 with benzoyl chloride in benzene solution gave a reaction product which was characterized as the 2-chloro-N-benzoyaziridine 17 (Equation 4). This compound was quite unstable, and evidence for its structure was obtained from IR, which displayed a

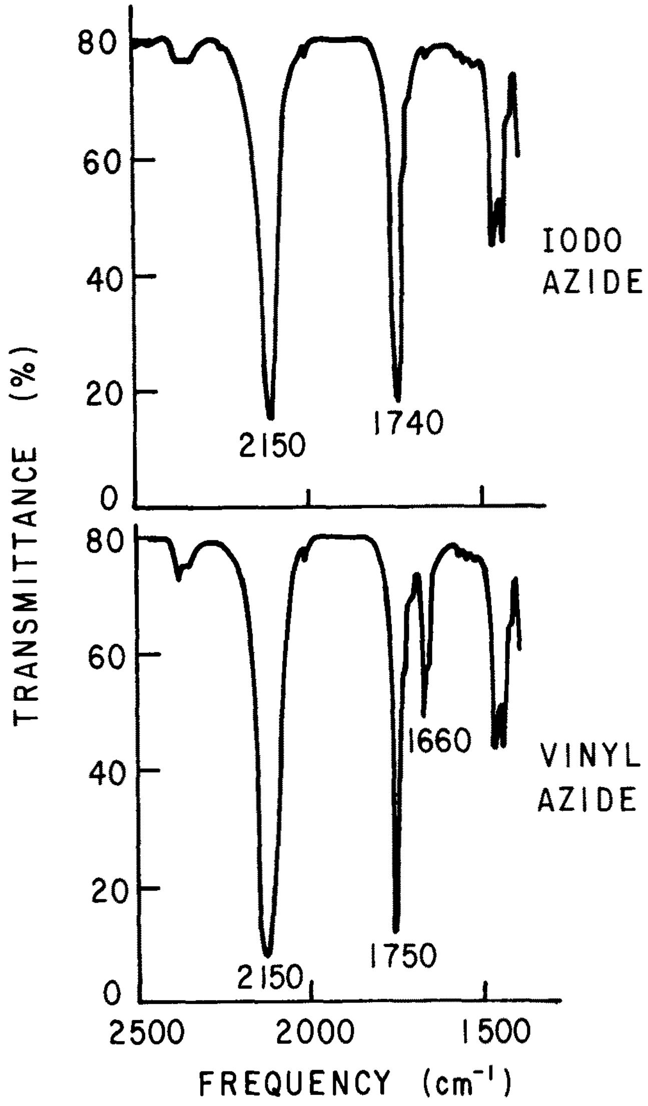
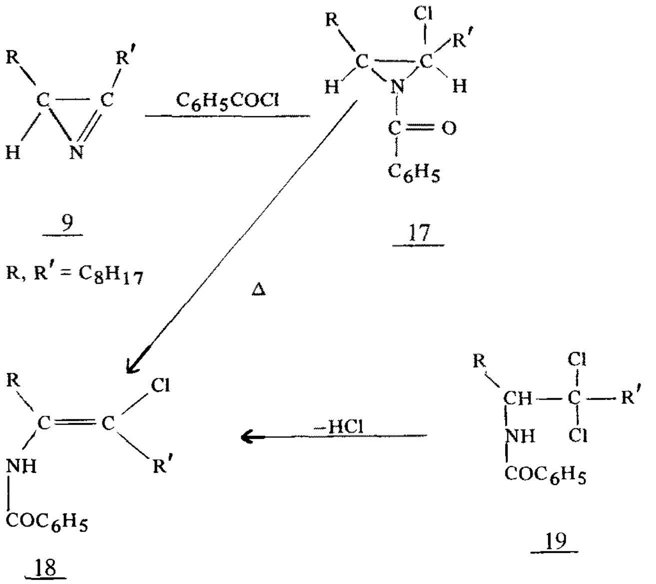


FIG. 1. IR absorptions for the conversion of iodoazide adduct of methyl oleate to the vinyl azide derivative.

strong absorbtion at 1660 cm^{-1}, characteristic of a tertiary amide. Aryl-substituted azirines have previously been shown to react with acid chlorides to yield 2-chloro-N-acylaziridines as the principal products (20).

Upon standing, aziridine 17 underwent a rearrangement to the unsaturated amide 18. Proof of structure for the latter compound was obtained by IR and mass spectrometry. It has been previously reported (21) that the major products from the isomerization of 2-chloro-2-aryl-N-acylaziridines are oxazole derivatives, and that the unsaturated amides are minor byproducts. In the present study, oxazoles were not observed to be formed from aziridine 17 or from other 2-chloro-N-acyl aziridines derived from aliphatic azirines (T.A. Foglia, unpublished results). Reaction of 17 with anhydrous-hydrogen chloride in ether gave two products, identifiable as the dichloroamide 19 and the previously identified unsaturated amide 18. Presumably the chloroamide 19 is formed by the addition of the elements of hydrogen chloride across the aziridine ring with the chlorine substituent exhibiting strong directive effects in the ring opening reaction. Amide 18 could arise via either of two pathways. Its formation could result from the elimination of hydrochloric acid from chloroamide 19 or by the previously mentioned rearrangement of aziridine 17.



Equation 4.

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