2'-Hydroxy-1-cyclohexene-1-carboxanilide (12).—To a solution of 1.26 g (10 mmol) of 1-cyclohexenecarboxylic acid in 5 ml of benzene was added dropwise 0.87 ml (12 mmol) of thionyl chloride. The mixture was allowed to stand at room temperature for 1 hr, heated on the steam bath for 30 min, and evaporated. The evaporation was repeated several times with toluene, leaving the 1-cyclohexenecarboxylic acid chloride as an oil. The acid chloride was added dropwise to a stirred, ice-cooled solution of 545 mg (0.5 mmol) of *o*-aminophenol in 2 ml of pyridine. The solution was stirred at room temperature for 2 hr and then poured into 30 ml of ice–water. The resulting oil was rubbed to a solid, which was collected and washed successively with 1 *N* hydrochloric acid, water, and saturated sodium bicarbonate solution to afford 1.05 g of a brown solid. The solid was dissolved in 20 ml of 10% sodium hydroxide solution, treated with activated charcoal, and filtered. The filtrate was acidified with acetic acid to afford 700 mg of white solid, mp 158–160°. A sample of this material, twice recrystallized from acetone–hexane, melted at 163–164°: λ_{max} 215 mμ (ε 20,600), 256 (8250), and 292 (8470); ν 3400, 3030, 2670, 1665, 1630, 1615, 1590, and 1538 cm^{-1}.

Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.86; H, 6.96; N, 6.45. Found: C, 71.82; H, 7.07; N, 6.35.

Registry No.—**2**, 23386-10-9; **4**, 23386-11-0; **5**, 23386-12-1; **6**, 23386-13-2; **7**, 23386-14-3; **11**, 23386-15-4; **12**, 23386-16-5.

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Oxazoline Formation from N-Acylaziridines. Isolation of an Intermediate in an Octahydrophenanthrene System

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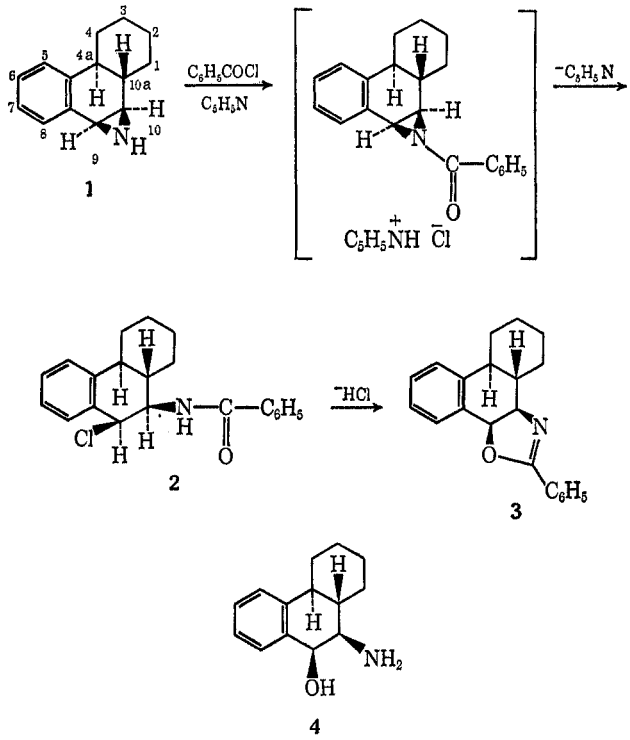
Opening of styrylaziridines and -aziridinium ions has been shown to afford products characteristic of both carbonium ion and displacement mechanisms,[2-4] while the isomerization of N-acylaziridines to oxazolines has been reported to occur under the influences of nucleophilic catalysis or heat.[5] The latter process is thought to involve formation of an intermediate β-halobenzamide in which carbonyl oxygen displacement of the halide occurs.[6] We wish to report a case of opening of an N-acylaziridine capable of forming an intermediate carbonium ion which affords a *cis*-β-halobenzamide stereoselectively, and which is readily converted into the corresponding oxazoline, probably through a solvolytic process.

In a study of amino alcohols in the octahydrophenanthrene system, we attempted the N-benzoylation of *syn*-aziridine 1.[7,8] Aziridine **1** was prepared by the addition of iodoisocyanate (INCO) to 1,2,3,4,4a,10a-(*trans*-4a,10a)-hexahydrophenanthrene, followed by methanolysis, and aqueous potassium hydroxide treatment of the resulting β-iodocarbamate.

Attempted N-benzoylation of **1** with benzoyl chloride in pyridine at 60° afforded only small amounts of the oxazoline **3**. However, when the reaction was performed using a single equivalent of the acyl halide, and of the pyridine in ether, below 10°, an intermediate, 9(*a*)-chloro-10(*e*)-benzamido-1,2,3,4,4a,9,10,10a-(*trans*-4a,10a)-octahydrophenanthrene[9] (**2**), was readily isolated.



1 2 3 4

Structural assignment of **2** is based primarily on infrared and nmr data.[10] The infrared spectrum showed an NH stretching band at 3330 cm^{-1} and amide I and II carbonyl bands at 1630 and 1520 cm^{-1}. The nmr spectrum (60 MHz) showed a broadened NH doublet at δ 6.65 for NH ($J_{10,NH}$ = 9 Hz), a doublet at 5.46 for H_9 ($J_{9,10}$ = 4 Hz) and a sextet at 4.67 for H_{10} ($J_{10,10a}$ = 9 Hz) (Figure 1). The nmr spectrum is consistent with the *cis* disposition of substituents.

When a chloroform solution of **2** was warmed at 75° for 10–20 min, formation of oxazoline **3** hydrochloride was noted by following the course of the reaction by observing the nmr spectrum of the reaction mixture (Figure 1). The nmr spectrum of **3** hydrochloride showed a doublet for H_9 at δ 6.18 ($J_{9,10}$ = 9 Hz) and a triplet for H_{10} at 4.52 ($J_{10,10a} \simeq$ 9 Hz), consistent with *cis*-oxazoline **3**. Cyclization of **2** was more readily accomplished in refluxing acetone in the presence of

(1) Public Health Service Predoctoral Fellowship 1-F1-GM-33,942, 1966–1969.

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(7) We have chosen to designate the epoxides and aziridines in this system as *syn* or *anti* to indicate the relative geometry of the heterocyclic three-membered ring and the hydrogen atom at C-10a.

(8) All materials are racemic, although only a single isomer is drawn.

(9) The central ring is arbitrarily assigned the half-chair conformation where the equatorial (*e*) and axial (*a*) substituents at C-9 are in fact pseudo-equatorial and pseudoaxial, respectively.

(10) Elemental analysis does not distinguish between **2** and the hydrochloride salt of **3**.

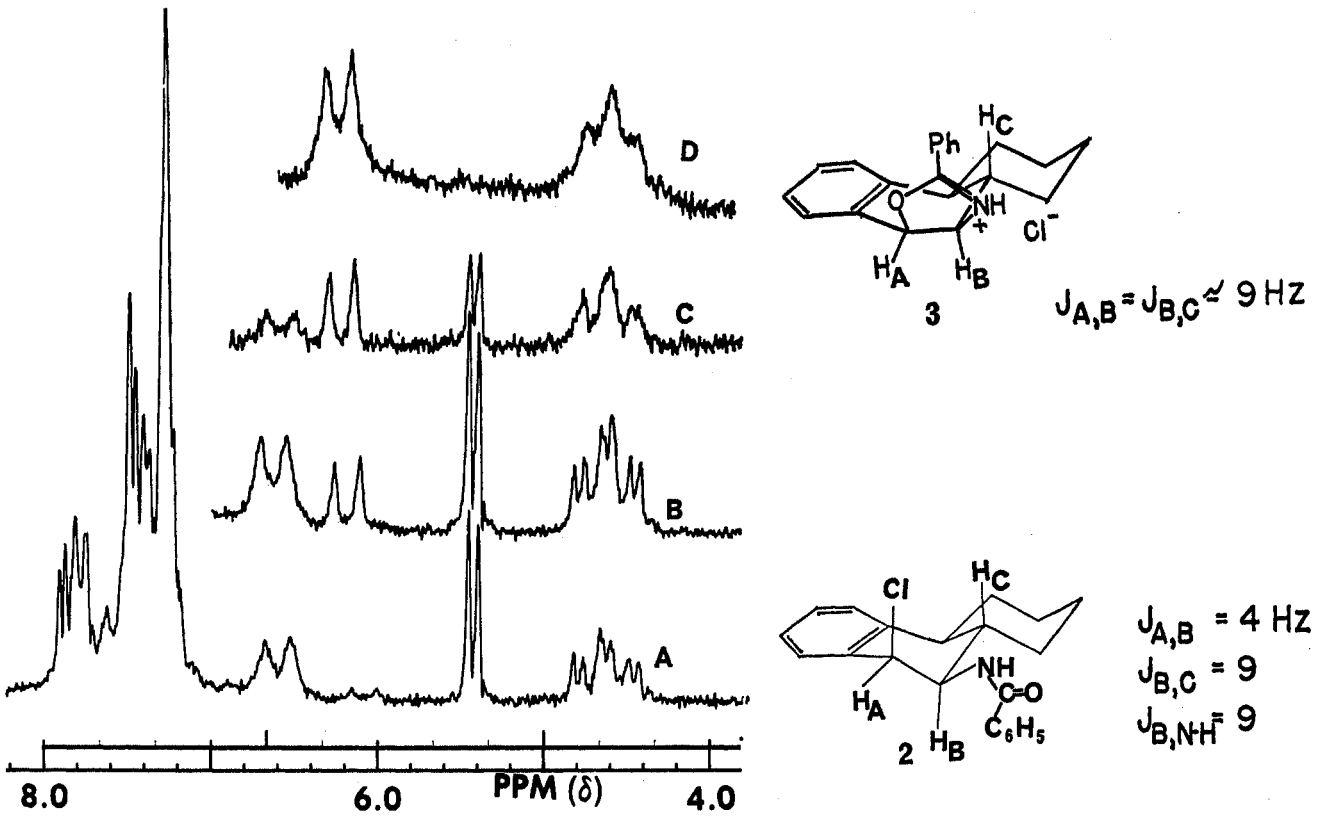

Figure 1.—(A) Nmr spectrum of 2; (B, C) nmr spectra of mixtures of 2 and 3 at 15 and 20 min, respectively; (D) nmr spectrum of oxazoline 3 hydrochloride.

sodium bicarbonate.[11] The nmr spectrum of the free oxazoline showed a doublet for H_9 and a triplet for H_{10} ($J_{9,10} \sim J_{10,10a} \sim 9.5$ Hz) at δ 5.49 and 4.12, respectively.

Amino alcohol 4[13] was converted into the oxazoline 3, utilizing ethyl benzimidate, as further evidence for structure 3. Carefully controlled hydrolysis of 3 also yields 4.

The assignment of *cis* stereochemistry to intermediate 2 is based primarily on the nmr spectral data, comparison of its spectrum with those of other 9(*a*),10(*e*)-disubstituted octahydrophenanthrenes,[14] and similar opening of aziridines and aziridinium ions.[2-4] Opening of other styryl aziridines, which can readily form benzylic carbonium ions, has been shown to occur through mixed SN1 and SN2 processes.[2] Opening of aziridinium ions (ethylene immonium ions) also gives products consistent with both mechanisms.[3,4,15]

In this system, the somewhat unexpected *cis* product probably arises because of some degree of carbonium ion character at the benzylic position in the transition state, which may then be attacked either from above or below the plane of the carbocyclic skeleton. Great differences in the relative degree of steric hindrance to attack are not obvious from Dreiding models. Both the *cis* stereochemistry and the direction of aziridine ring opening are most consistent with a carbonium ion or carbonium ion like intermediate followed by stereoselective addition of chloride. Formation of the oxazoline may similarly be envisioned to occur by solvolytic loss of the halide followed by ring closure.

Although finding products consistent with a double-displacement mechanism for the isomerization would have been academically more satisfactory, the isolation and characterization of an intermediate which readily undergoes the isomerization process lends considerable support to the mechanism of oxazoline formation from the N-acylaziridine which involves the intermediacy of a β-haloamide. The stereochemical configuration of the intermediate isolated in this study is probably a characteristic of this system and therefore not generally applicable to the chemical process of conversion of N-acylaziridines into oxazolines.

(11) Sodium bicarbonate is added to prevent the hydrolysis of the oxazoline hydrochloride to the corresponding β-aminobenzoate.[12]

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(14) D. D. Miller and W. L. Nelson, unpublished results.

(15) Aqueous acid opening of 1 provides a mixture of 9(*e*)- and 9(*a*)-hydroxy-10(*e*)-amino-1,2,3,4,4a,9,10,10a(*trans*-4a,10a)-octahydrophenanthrene (4), with the latter predominating.[14]

Experimental Section

Melting points were determined using a Thomas–Hoover Uni-Melt and are corrected. Microanalyses were conducted by Dr. G. B. Weiler and Dr. F. B. Strauss, Microanalytical Laboratory, Oxford, England. Ultraviolet spectra were recorded on a Cary 14 spectrometer. Infrared spectra were recorded on Beckman IR-5A, IR-8, and IR-20 spectrophotometers. Nmr spectra were obtained on the Varian A-60 and Varian T-60 instruments using tetramethylsilane as internal standard.

9(*a*)-Carbomethoxyamino-10(*a*)-iodo-1,2,3,4,4a,9,10,10a(*trans*-4a,10)-octahydrophenanthrene.—To a cold (−5 to −10°) solution of 3.9 g (0.02 mol) of 1,2,3,4,4a,10a-hexahydrophenanthrene in 200 ml of anhydrous ether was added 4.2 g (0.028 mol) of freshly prepared silver cyanate. To this slurry was added 5.04 g (0.021 mol) of solid iodine in one portion. The slurry was stirred for 2 hr in the cold and then at room temperature for an additional 6 hr. The inorganic salts were removed by filtration, the solution was diluted with 200 ml of anhydrous methanol, and the mixture was refluxed for 2 hr. The light brown precipitate was removed by filtration and washed with ether. The precipi-

tate was then recrystallized from methanol, giving 5.35 g (70%) of white needles: mp 138°; $\lambda_{max}^{95\% EtOH}$ 217 nm (ϵ 7000); ν_{max}^{KBr} 3280 (NH stretching), 3040 (aromatic CH stretching), 2950 and 2870 (aliphatic CH stretching), 1695 (very broad, C=O stretching), 1550, 1490, 1445, 1325, 1265, 1190, 1135, 1120, 1035, 1010, 760, 735, and 705 cm^{-1}; nmr (pyridine) δ 5.59 (quartet, $J_{9,10} = 2$ Hz, $J_{9,NH} = 8$ Hz, benzylic proton H_A), 4.84 (multiplet, $W_{1/2} = 4$ Hz, H_{10} proton), and 2.70–0.7 (multiplet, methylene–methine envelope).

Anal. Calcd for $C_{16}H_{20}INO_2$: C, 49.88; H, 5.23; N, 3.64. Found: C, 49.97; H, 5.32; N, 4.01.

***syn*-9,10-Imino-1,2,3,4,4a,9,10,10a(*trans*-4a,10a)-octahydrophenanthrene (1).**—A mixture of 5.0 g (0.013 mol) of the iodocarbamate and 12.9 g of potassium hydroxide in 130 ml of absolute ethanol was refluxed for 3 hr. The ethanol was then removed *in vacuo* and the remaining solid was dissolved in 500 ml of ether and washed with cold water until the aqueous washings were neutral. The ether layer was dried (Na_2SO_4) and evaporated *in vacuo* to a volume of 50 ml, which was then placed in the refrigerator overnight. A total of 2.49 g (93.5%) of white needles, mp 128–129°, were collected. A small portion of the aziridine was recrystallized from ether for the analytical sample: mp 129–130°; ν_{max}^{KBr} 3200 (NH stretching), 3030 (aromatic CH stretching), and 2870 (aliphatic CH stretching), 1550, 1490, 1450, 1420, 1290, 1050, 910, 870, 850, 815, 794, 770, 745, and 735 cm^{-1}; nmr ($CDCl_3$) δ 7.55–6.90 (multiplet, aromatic protons), 2.79 (doublet, $J_{AB} = 6$ Hz, benzylic H_9 proton), and 2.70–0.70 (multiplet, methylene–methine envelope).

Anal. Calcd for $C_{14}H_{17}N$: C, 84.37; H, 8.60; N, 7.03. Found: C, 84.25; H, 8.56; N, 6.82.

9(*a*)-Chloro-10(*e*)-benzamido-1,2,3,4,4a,9,10,10a(*trans*-4a,10a)-octahydrophenanthrene (2).—Into 250 ml of anhydrous ether was placed 450 mg (2.25 mmol) of the aziridine 1 and 177 mg (2.25 mmol) of pyridine. To this mixture was added 315 mg (2.55 mmol) of benzoyl chloride in 20 ml of anhydrous ether. With an ice bath, the cloudy suspension was maintained below 10° at all times during the addition. The mixture was then allowed to warm to room temperature and stirred for an additional 30 min. The ether mixture was filtered, and the filtrate was evaporated *in vacuo* to a volume of 15 ml, with the water bath kept at room temperature, and placed in the refrigerator. The needlelike crystals that formed were removed by filtration, giving a total of 515 mg (68%) of the benzamide 2, mp 142–143°. The benzamide could not be recrystallized, since upon heating in solution it formed oxazoline hydrochloride 3: ν_{max}^{KBr} 3330 (NH stretching), 2900 and 2180 (aliphatic CH stretching), 1630 (C=O stretching), 1520, 1480, and 690 cm^{-1}; nmr ($CDCl_3$) δ 8.05–7.05 (multiplet, 9 aromatic protons), 6.65 (doublet, amide proton), 5.46 (doublet, $J_{AB} = 4$ Hz, benzylic proton H_9), 4.67 (sextet, $J_{BC} = 9$ Hz, proton H_B), and 3.00–0.90 (multiplet, methylene–methine envelope).

Anal. Calcd for $C_{21}H_{22}ClNO$: C, 74.21; H, 6.53; N, 4.12. Found: C, 74.22; H, 6.13; N, 4.27.

2-Phenyloxazoline of 9(*a*)-Hydroxy-10(*e*)-amino-1,2,3,4,4a,9,10,10a-(*trans*-4a,10a)-octahydrophenanthrene (3). A. Cyclization of 2.—A mixture of 300 mg (0.89 mmol of chlorobenzamide 2, 75 mg (0.90 mmol) of anhydrous sodium bicarbonate, and 200 ml of acetone was refluxed for 5 hr with stirring. The mixture was then evaporated *in vacuo* to dryness and to this was added 100 ml of water. The aqueous mixture was then extracted seversl times with ether. The ether layers were combined, dried (Na_2SO_4), and evaporated *in vacuo* to give 260 mg of solid material. The solid material was passed over a 30-g alumina column (Merck, reagent aluminum oxide) using benzene as an eluent. No material was isolated in the first 160 ml of benzene eluted from the column, but the next 360 ml of benzene solvent eluted afforded 230 mg (86%) of the oxazoline: mp 142–143°; ν_{max}^{KBr} 3050 (aromatic CH stretching), 2910 and 2860 (aliphatic CH stretching), 1640 (C=N stretching), 1575, 1490, 1445, 1080, 1060, 1025, 960, 950, 930, 780, 740, 725, and 685 cm^{-1}; nmr ($CDCl_3$) δ 8.15–7.10 (multiplet, aromatic protons), 5.49 (doublet, $J_{AB} = 9.5$ Hz, benzylic proton H_A), 4.12 (triplet, $J_{BC} = 9.5$ Hz, proton H_B), and 2.80–0.80 (multiplet, methylene–methine envelope).

Anal. Calcd for $C_{21}H_{21}NO$: C, 83.13; H, 6.97; N, 4.61. Found: C, 83.56; H, 6.98; N, 4.82.

B. Oxazoline 3 Synthesis *via* Amino Alcohol 4.—A mixture of 100 mg (0.46 mmol) of amino alcohol 4,[13] 80 mg (0.46 mmol) of ethyl benzimidate prepared by the method of McCasland and Smith,[16] and 100 ml of anhydrous pyridine was refluxed for 5 hr. The pyridine was then removed *in vacuo*, affording 108 mg of an oil which was placed on an alumina column snd eluted with benzene. A total of 94 mg (69%) of the oxazoline (3), mp 141–142°, was isolated. The spectral properties were identical with those of the oxazoline prepared previously.

Acid Hydrolysis of Oxazoline 3.—Oxazoline 3, 300 mg (1.0 mmol), was dissolved in 150 ml of 10% aqueous hydrochloric acid and refluxed for 1 hr. The acidic solution was allowed to cool and extracted with ether to remove benzoic acid. The acidic solution was made alkaline with aqueous 10% NaOH solution and extracted with $CHCl_3$. The $CHCl_3$ was separated, dried (Na_2SO_4), and evaporated *in vacuo*, affording 148 mg (68%) of amino alcohol 4, mp 180°.

Registry No.—1, 23385-94-6; 2, 23385-95-7; 3, 23385-96-8; 3 hydrochloride, 23385-97-9; 9(*a*)-carbomethoxyamino-10(*a*)-iodo-1,2,3,4,4a,9,10,10a(*trans*-4a,10)-octahydrophenanthrene, 23385-98-0.

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The Rearrangement of 1-Acylaziridines to Oxazolinium Cations in Strong Acid Media[1]

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General interest in the ring-opening reactions of aziridine derivatives developed as a result of their biological[2,3] and industrial[3,4] significance. Many biological alkylating agents, such as cancer-inducing mitomycin,[3c] contain aziridine ring functions. The recent preparation[5] of 1-alkylaziridinium ions, 1-acylaziridinium ions, and O-protonated 1-acylaziridines prompts us to report our studies of 1-acylaziridines in strong acid media.

Heine[6] has reviewed the well-known isomerization reactions of 1-acylaziridines. Fanta[7] and Heine[8] have investigated extensively the pyrolytic and catalytic

(1) (a) Acid-Catalyzed Cyclization Reactions. VIII. For other papers in this series, see S. P. McManus, J. T. Carroll, P. M. Grohse, and C. U. Pittman, *Org. Prep. Proc.*, in press. (b) This work was supported in part by the University of Alabama Research Committee and at Huntsville in part by the Petroleum Research Fund (Grant 3501-B) administered by the American Chemical Society and by the National Aeronautics and Space Administration (Grant NGL-01-002-001).

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