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AZIRIDINE FORMATION BY LITHIUM ALUMINUM HYDRIDE REDUCTION OF DIBENZO[a.c]CYCLOHEPTADIEN-6-ONE OXIME[1]

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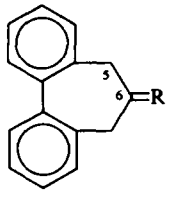
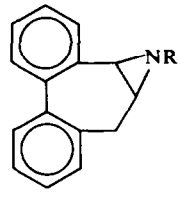
Abstract—LAH reduction of dibenzo[a.c]cycloheptadien-6-one oxime (Ib) in refluxing THF gives an aziridine,5,6-imino-dbenzo[a.c]cycloheptadiene (IIa), in good yield together with a small amount of the expected primary amine, 6-amino-dibenzo[a.c]cycloheptadiene (IIIa). The structure of the aziridine has been established by a reliable synthesis through an addition of iodine isocyanate to dibenzo[a.c]cycloheptatriene (V). Ring-opening reactions of the aziridine with acids have been carried out. The yields of the aziridine depend upon the solvent and temperature used in the reaction.

WHILE trying to synthesize some biologically active N-substituted derivatives of 6-amino-dibenzo[a.c]cycloheptadiene,[2] dibenzo[a.c]cycloheptadiene-6-one oxime (Ib) was treated with LAH. The reaction however yielded only a small quantity of the expected 6-amino-dibenzo[a.c]cycloheptadiene (IIIa) and the major product was a new basic compound, which was found to be an aziridine, 5,6-imino-dibenzo-[a.c]cycloheptadiene (IIa). This paper is concerned with the new reaction of aziridine formation by LAH reduction of the oxime Ib.*

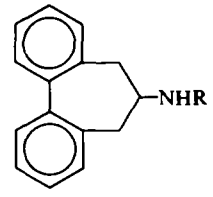
The starting material, dibenzo[a.c]cycloheptadien-6-one (Ia) was synthesized from diphenic acid.[4a]



Ia, R = O
b, R = NOH



IIa, R = H
b, R = —$CONHC_6H_5$
c, R = —$COC_6H_5NO_2$ (p)



IIIa, R = H
b, R = CHO

Chart 1

Dibenzo[a.c]cycloheptadien-6-one oxime (Ib) was reduced with LAH in THF, affording two basic products, which were realized as two spots of R_f-values 0·68 and 0·23 on TLC using silica gel and the solvent system of chloroform:methanol (25:1, v/v). The reduction products were easily separated into the respective fractions in a ratio of 7:1. The minor product was characterized as the hydrochloride, m.p.

* Kitahonoki *et al.* have found similar reactions in LAH reductions of some ketoximes of bridged systems[1] and details will be reported in the near future.

261–262° (dec), and identified with the primary amine IIIa, which was prepared by the following reaction sequence. The Leuckart reaction of the ketone Ia with urea and formic acid gave a formylamino derivative IIIb, m.p. 135–136°, which was hydrolyzed with 10% hydrochloric acid to give the primary amine.[3b,4] The major oily product exhibited an IR band at 3270 cm^{-1} due to a secondary amine and a UV max at 250 mμ (ε 65,500), and its trituration with ethylene glycol followed by recrystallization from ether gave needles containing ethylene glycol, m.p. 95–97°. Treatment with phenylisocyanate gave a phenylcarbamoyl derivative IIb, m.p. 152–153°, showing the IR bands at 3300 (>NH) and 1668 cm^{-1} (>C=O), characteristic of a carbamoyl group. Reaction with *p*-nitrobenzoyl chloride and pyridine afforded the corresponding *p*-nitrophenyl derivative IIc, m.p. 193–194°, which showed in the IR spectrum no NH absorption band but an absorption at 1680 cm^{-1} reasonable for benzoyl derivatives of aziridines.[5]

Catalytic hydrogenation of the new base with platinum oxide in acetic acid afforded the primary amine IIIa and the LAH reduction in refluxing dioxan also gave the same primary amine. From these results, the structure of the new base was presumed to be an aziridine, 5,6-imino-dibenzo[a.c]cycloheptadiene (IIa). In order to confirm the assigned structure, synthesis of IIa by the known method was carried out starting from dibenzo[a.c]cycloheptadien-6-one (Ia).

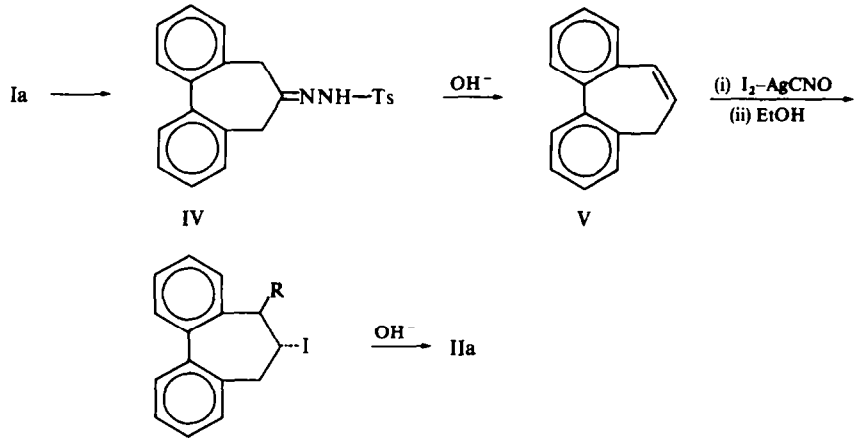


Chart 2

Dibenzo[a.c]cycloheptadien-6-one tosylhydrazone (IV) derived from Ia, was subjected to the Stevens–Bamford reaction giving dibenzo[a.c]cycloheptatriene (V)[3] as an oil, which was characterized as its dibromide, m.p. 91–93°. The triene was treated with the iodine-silver cyanate reagent[6,7] to give an iodoisocyanate derivative VIa (80% yield), m.p. 121–122°, showing an IR absorption band at 2275 cm^{-1} due to an NCO group. Refluxing of VIa in ethanol gave, in 75% yield, an iodourethane derivative VIb, m.p. 163–164° (dec), which was transformed to the aziridine IIa by treatment with ethanolic potassium hydroxide. The synthetic IIa was identical in all respects with the major product obtained from the LAH reduction of Ib.

Before the independent synthesis, the ring-opening reaction by acids was investigated to prove the structure of the new base. Treatment of the aziridine with 10%

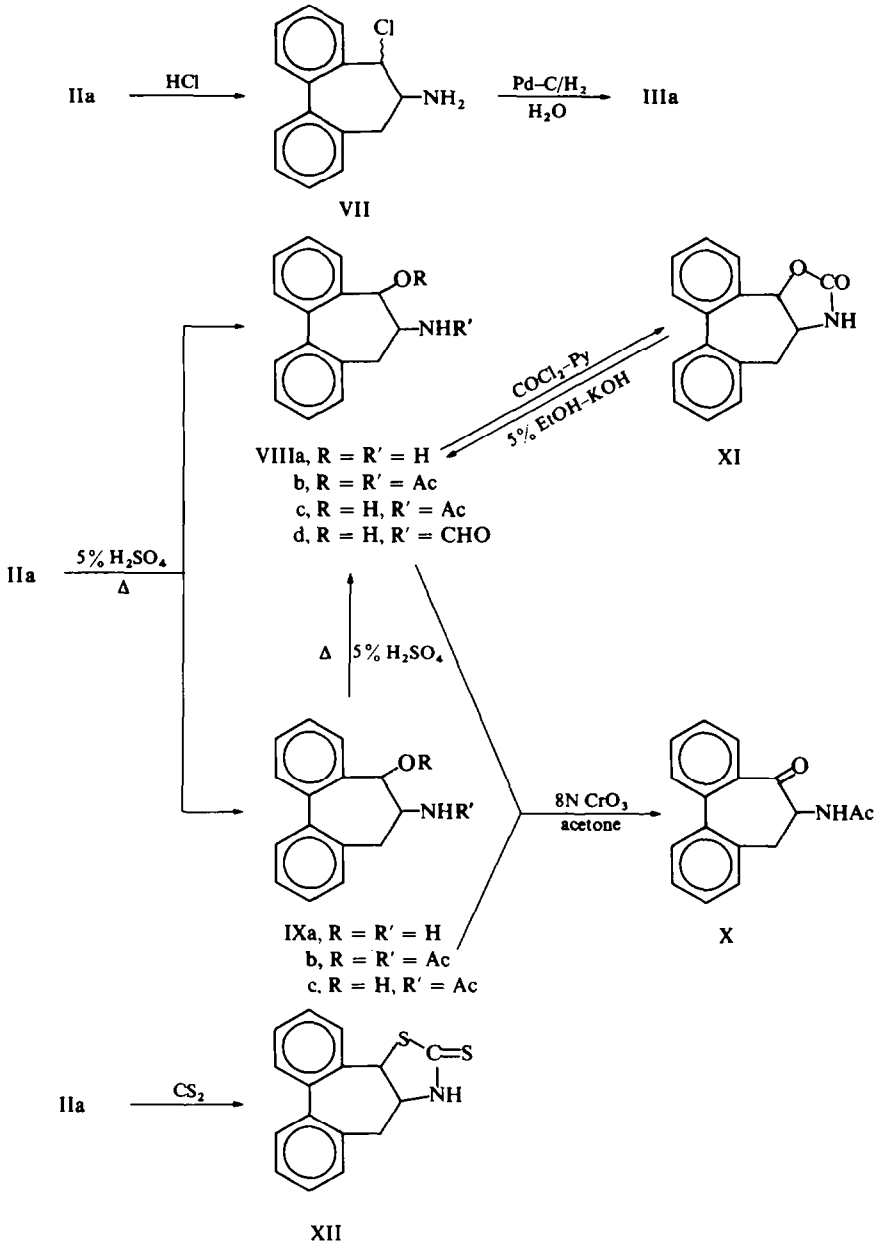


Chart 3

hydrochloric acid at room temperature yielded a chlorine-containing base, which was characterized as the hydrochloride, $C_{15}H_{14}NCl \cdot HCl$, m.p. 242–243° (dec) and the picrate, $C_{15}H_{14}NCl \cdot C_6H_3N_3O_7$, m.p. 189–190° (dec). The hydrochloride was very readily reduced with 10% Pd-carbon catalyst to give the primary amine IIIa. Such easy reductive elimination of the chlorine atom suggested that the chlorine was attached to the benzylic carbon and the structure of the base was depicted as

VII. Refluxing of the aziridine with 5% sulfuric acid for 1 hr gave two basic products, m.p. 158–159° and m.p. 217–218° in a ratio of 3:1, which were separable by column chromatography on alumina. Since two products corresponded to the same molecular formula $C_{15}H_{15}ON$ and their IR spectra were similar to each other, these were presumably stereoisomers of vicinal alkanolamines. On acetylation and subsequent partial hydrolysis with potassium carbonate, these were converted into N-monoacetates m.p. 223–224° and m.p. 210–211° *via* the respective O,N-diacetates, m.p. 205–206° and m.p. 230–231°, respectively. Both the N-monoacetates on oxidation with 8N chromic acid in acetone gave an identical ketone, m.p. 171–172°. Its IR absorption at 1693 cm^{-1} and the UV maxima at 237 mμ (ε 24,400) and 300 mμ (ε 1920) indicated that the ketonic function is located at the benzylic position as shown in formula X. The two alkanolamines were proved as expected to be epimers of the hydroxyl group. Treatment of the epimer, m.p. 158–159° with phosgen in pyridine gave the corresponding oxazolidone, m.p. 196–197°, which was reversely transformed to the starting epimer with 5% ethanolic potassium hydroxide. On the other hand, the epimer, m.p. 217–218° under similar conditions gave a complicated mixture and no oxazolidone derivative was obtained. In addition, this epimer on treatment with 5% sulfuric acid under reflux for 3 hr was partly isomerized to the former epimer as examined on TLC, but the reverse isomerization did not occur.[8] From these results, it was concluded that the epimer, m.p. 158–159° is *cis* as shown in VIIIa and the epimer, m.p. 217–218° is *trans* as IXa and the structures of the respective O,N-diacetates, N-monoacetates and the oxazolidone derivative were assigned as shown in the formulae, VIIIb and IXb, VIIIc and IXc, and XI.

Treatment of the aziridine with acetic anhydride in pyridine at room temperature gave *trans*-O,N-diacetate IXb, and heating under reflux with glacial acetic acid or with ethyl formate afforded low yields of *cis*-N-monoacetate VIIIc or *cis*-N-formyl derivative VIIId, m.p. 209–210° respectively. Compound VIIId was hydrolysed with hydrochloric acid to give *cis*-alkanolamine VIIIa.

In ring-opening reactions with acids, it is considered that a low reaction temperature produces predominantly the *trans*-compound[9] and a higher reaction temperature causes epimerization to the *cis*-isomer.

TABLE 1. EFFECT OF SOLVENT AND REACTION TEMPERATURE ON AZIRIDINE FORMATION BY LAH REDUCTION OF THE KETOXIME Ib*

Solvent	Reaction condition °C	Product, % Aziridine IIa	Primary amine IIIa	Total yield, %
THF	reflux	79·0	12·1	91·1
Ether	reflux	62·4	18·9	81·3
Dioxan	reflux	59·3	12·5	71·8
Dioxan	60–70[a]	70·0	16·0	86·0
Glyme[b]	67–71[a]	83·0	10·0	93·0

* In each case, 300 mg of the oxime Ib was reduced by refluxing with 112 mg (2 molar equiv) of LAH in 10 ml of the solvent for 2 hr and the products were separated by column chromatography on SiO_2 (Merck).

[a] Inner temp of the reaction mixture.

[b] Ethyl glycol monomethyl ether.

The aziridine on treatment with carbon disulfide gave a thiazolidine 2-thione derivative IX, m.p. 260–262°, as aziridine derivatives generally do.[10]

The effects of the solvents and the reaction temperatures on aziridine formation are summarized in Table 1, which shows that THF and glyme are preferable as solvents and that the optimum temperature is about 70°.

This convenient and simple method for synthesizing certain aziridines is in agreement with similar findings on bridged systems[1,2] by Kitahonoki *et al.* Details for generalizing this method have been investigated[11] and the reaction mechanism will be reported elsewhere.

EXPERIMENTAL

All m.ps determined in capillary tubes were uncorrected. UV spectra were determined with a Hitachi EPS-2 recording spectrophotometer and IR spectra with a Nippon Bunko DS-201B spectrometer. Unless otherwise stated, solns were dried over anhyd Na_2SO_4.

LAH reduction of dibenzo[a.c]*cycloheptadien-6-one oxime* (Ib)

A soln of Ib (5·9 g, 0·0265 mole) in THF (175 ml) was added with stirring to a suspension of LAH (5·9 g, 0·155 mole) in THF (120 ml) over a period of 10 min and the mixture refluxed with stirring for 4 hr, showing colour changes from yellow → yellowish green → yellowish brown → brown. After cooling, excess LAH was destroyed with H_2O. The mixture was filtered and the filtrate evaporated to dryness under reduced press and the residue dissolved in benzene, washed with H_2O, dried and evaporated leaving a residue (5·25 g). Chromatography on SiO_2 (300 g, Merck) gave IIa as an oil (4·3 g) from the fractions eluted with Chf:MeOH (50:1). The oil showed one spot on TLC using SiO_2 and Chf:MeOH (25:1), and had the IR absorption at 3270 cm^{-1} (>NH). Trituration with ethylene glycol and recrystallization from ether afforded IIa as needles, m.p. 95–97°. (Found: C, 81·57; H, 6·98; N, 5·99. $C_{15}H_{13}N \cdot \frac{1}{2}$ | CH_2OH / CH_2OH requires: C, 81·76; H, 6·69; N, 6·04%.)

Phenylisocyanate (198 mg) and oily IIa (350 mg) in abs ether (7 ml) were stirred at room temp for 4 hr yielding a crystalline product. Evaporation of the ether, trituration of the residue with ether and recrystallization from Me_2CO-ether gave IIb (380 mg) as plates, m.p. 148–152°. Repeated recrystallization gave a pure sample, m.p. 152–153°, ν_{max}^{Nujol} 3300 (—NH—), 1668 cm^{-1} (—C(=O)—). (Found: C, 80·71; H, 5·58; N, 8·37. $C_{22}H_{18}ON_2$ requires: C, 80·95; H, 5·56; N, 8·58%.)

p-Nitrobenzoylchloride (200 mg) in abs benzene (1 ml) was added under cooling with ice to a soln of oily IIa (169 mg) and Et_3N (150 mg) in abs benzene (1·5 ml) and the mixture allowed to stand with cooling for 2 hr. The benzene was evaporated under reduced press and the residue recrystallized several times from ether–benzene to give IIc (117 mg) as needles, m.p. 193–194°; ν_{max}^{Chf} 1680 cm^{-1} (—C(=O)—). (Found: C, 74·03; H, 4·51; N, 7·59. $C_{22}H_{16}O_3N_2$ requires: C, 74·14; H, 4·53; N, 7·86%.)

Further elution with Chf:MeOH (50:1–20:1) gave IIIa (670 mg) as an oil, which was characterized as the hydrochloride needles, m.p. 261–262° (dec). (Found: C, 73·37; H, 6·69; N, 5·82; Cl, 14·45. $C_{15}H_{15}N \cdot HCl$ requires: C, 73·31; H, 6·59; N, 5·70; Cl, 14·43%.)

The picrate crystallized from EtOH as prisms, m.p. 242–244°. (Found: C, 57·68; H, 4·15; N, 12·78. $C_{21}H_{18}O_7N_4$ requires: C, 57·53; H, 4·14; N, 12·78%.)

The Leuckart reaction of dibenzo[a,c]*cycloheptadien-6-one* (Ia)

A mixture of Ia (500 mg, 0·0024 mole), $CO(NH_2)_2$ (2·3 g, 0·084 mole) and HCOOH (4·6 g, 6·1 moles) was heated at 100–110° under N_2 for 2 hr, at 120–180° for 1 hr and at 180° for 3 hr. After cooling, the reaction mixture was poured into H_2O and extracted with benzene. The benzene layer was washed with 10% Na_2CO_3, 10% HCl and H_2O. The dried benzene soln was evaporated to dryness under reduced press and the residue (495 mg) was chromatographed on neutral Al_2O_3 (5% H_2O). Elution with pet ether:

benzene (1:9), benzene only and benzene:Chf (9:1) gave crystalline fractions, which were combined and recrystallized from benzene to give pure IIIb (187 mg) as needles, m.p. 135–136°; ν_{max}^{Nujol} 3250, 1655 cm^{-1} (—NHCHO). (Found: C, 81·22; H, 6·44; N, 5·89. $C_{16}H_{15}ON$ requires: C, 80·98; H, 6·33; N, 5·90%.)

Hydrolysis of 6-formylaminodibenzo[a,c]*cycloheptadiene* (IIIb) *with hydrochloric acid*

A suspension of IIIb (550 mg) in 10% HCl (15 ml) was refluxed for 1 hr resulting in a clear soln. The mixture was shaken with benzene and the acidic layer evaporated to dryness under reduced press leaving crude IIIa—HCl (478 mg) as needles, which on recrystallization from H_2O afforded a pure substance (352 mg), m.p. 261–262° (dec), identical in all respects with that obtained by a LAH reduction of Ib.

Catalytic hydrogenation of IIa *with* PtO_2

A soln of IIa (100 mg) in glacial AcOH (4 ml) was shaken in an atm of H_2 with the Adams' catalyst (50 mg). After 5·5 hr, 1·2 molar equivs of H_2 (12·7 ml) had been absorbed. The catalyst was removed by filtration and the filtrate made basic with 10% Na_2CO_3 and extracted with benzene. The organic layer was washed with H_2O, dried and evaporated leaving a residue (86 mg) which was converted to the hydrochloride (51 mg) which crystallized as needles from EtOH–AcOEt, m.p. 261–262° (dec). The hydrochloride was identical with that of IIIa derived from IIIb.

LAH reduction of IIa *in refluxing dioxan*

A soln of crude oily IIa (300 mg) in abs dioxan (9 ml) was added with stirring over a period of 5 min to a suspension of LAH (300 mg) in abs dioxan (6 ml). The mixture was refluxed for 9 hr, allowed to stand overnight at room temp and again refluxed for 2 hr. The excess LAH was destroyed with H_2O, the resulting inorganic substance washed with ether and the filtrate combined with the ethereal washings, the organic layer evaporated to dryness under reduced press leaving a residue, which was dissolved in dil HCl, filtered, basified with 10% Na_2CO_3 and extracted with benzene. The benzene layer was washed with H_2O, dried and evaporated leaving an oily residue (216 mg), the hydrochloride of which was recrystallized from EtOH–AcOEt as needles of IIIa—HCl (150 mg), m.p. 258–260° (dec).

The Stevens-Bamford reaction of dibenzo[a.c]*cycloheptadien-6-one* (Ia)

(i) *6-Tosylhydrazino-dibenzo*[a.c]*cycloheptadiene* (IV). A soln of Ia (500 mg) and *p*-toluenesulfonylhydrazine (700 mg) in EtOH (10 ml) was refluxed for 10 min yielding on cooling a crystalline ppt which was recrystallized from EtOH and then from benzene to give pure IV (734 mg), m.p. 178–180° (dec);

ν_{max}^{Nujol} 3210 (—N—), 1340, 1162 cm^{-1} (—N—SO_2—). (Found: C, 69·92; H, 5·41; N, 7·29. $C_{22}H_{20}O_2N_2S$ requires: C, 70·18; H, 5·36; N, 7·44%).

(ii) *Action of* Na *in ethyleneglycol on* IV. Metallic Na (3·4 g) was dissolved in ethylene glycol (140 ml) in an atm of N_2 and to the soln was added the tosylhydrazone IV (13 g). The mixture was gradually heated in an oil-bath, yielding a dark purple soln. Evolution of N_2 gas occurred at 160–170° accompanied with gradual decolouration. On refluxing for 2 hr, the colour changed to yellow. The reaction mixture was poured into H_2O (860 ml) and extracted with benzene. The benzene layer was washed with H_2O, dried and evaporated *in vacuo* leaving a brown oil (6·6 g), which was chromatographed on SiO_2 (180 g, TOKAI). The fractions eluted with pet. ether:benzene (10:1) were distilled under reduced press to give oily V (3·6 g), b.p. 162–165°/10 mm; λ_{max}^{EtOH} 234·5, 251·5 (shoulder), 296 mμ (ε 7300, 2670, 256). (Found: C, 93·82; H, 6·41. $C_{15}H_{12}$ requires: C, 93·71; H, 6·29%.)

(iii) *Addition of bromine to the triene* V. Bromine (50 mg) in glacial AcOH (0·1 ml) was added to a soln of V (50 mg) in glacial AcOH (0·2 ml) and the mixture allowed to stand at room temp for 1 hr, then treated with H_2O (1·5 ml) and extracted with ether. The ethereal extract was washed with H_2O, dried and evaporated leaving an oil (94 mg), which was chromatographed on SiO_2 (3 g, TOKAI). The fractions eluted with pet. ether:benzene (5:1) were allowed to stand overnight in a refrigerator and the crystalline dibromide recrystallized from MeOH, m.p. 91–93° as prisms (Ref 4, m.p. 90–91°). (Found: C, 51·40; H, 3·58; Br, 45·02. $C_{15}H_{12}Br_2$ requires: C, 51·16; H, 3·44; Br, 45·39%.)

Addition of iodine isocyanate to the triene V

While light and moisture were avoided, a soln of I_2 in abs ether (10 ml) was added dropwise with stirring to a suspension of V (1·0 g) and fresh AgCNO (1·13 g) in abs ether (5 ml) with cooling in an ice-salt bath. The reaction mixture was stirred at −15°– −10° for 3 hr and at 0° for 19 hr and filtered to remove AgI

which was washed with ether. The filtrate and the ethereal washings were combined, washed with 10% $NaHSO_3$ and H_2O and dried and evaporated to dryness leaving a crystalline substance (1·2 g) which was washed with a small amount of pet. ether and VIa recrystallized as prisms from abs ether, m.p. 120–121°; ν_{max}^{Nujol} 2275 cm^{-1} (—NCO). (Found: C, 53·28; H, 3·40; N, 4·29; I, 34·87. $C_{16}H_{12}ONI$ requires: C, 53·20; H, 3·35; N, 3·88; I, 35·14%.)

Refluxing of the iodoisocyanate derivative VIa *with* EtOH

A soln of VIa (30 mg) in abs EtOH (1·5 ml) was refluxed for 1 hr. On standing at room temp, crystals (34 mg) precipitated and recrystallization from EtOH gave pure VIb, m.p. 163–164° (dec); ν_{max}^{Nujol} 3300 (—NH—), 1693 cm^{-1} (—NHCOOEt). (Found: C, 53·28; H, 4·63; N, 3·55; I, 31·28. $C_{18}H_{18}O_2NI$ requires: C, 53·08; H, 4·45; N, 3·44; I, 31·17%.)

Ring closure of the iodourethane derivative VIb *with* EtOH–KOH

A soln of VIb (200 mg) in 3% ethanolic KOH (6 ml) was refluxed for 1 hr. The mixture was poured into H_2O and extracted with benzene. The benzene layer was washed H_2O, dried and evaporated to give a crude residue (106 mg), which on chromatography over SiO_2 (4 g, TOKAI) gave a crude product from the fractions eluted with benzene:Chf (1:1) and Chf only. The crude product was treated with phenylisocyanate to give the corresponding N-phenylcarbamoyl derivative, m.p. 150–151° which was identical with IIb described above in m.p., mixed m.ps and IR spectra. Furthermore, addition of 10% HCl to the crude product dissolved in ether yielded after evaporation to dryness *in vacuo* the hydrochloride which recrystallized from EtOH–AcOEt, m.p. 242–243° (dec). This product was identical with the hydrochloride of the chloroamine derivatives VII, described in the following experiment. From these results, the crude product was proved to be the aziridine IIa.

Action of HCl *on* IIa

The oily aziridine IIa (450 mg) was dissolved in 10% HCl and the mixture evaporated to dryness *in vacuo*. Trituration with acetone and recrystallization from EtOH–AcOEt gave the hydrochloride of the chloroamine VII (458 mg), m.p. 242–243° (dec) as needles. (Found: C, 64·25; H, 5·62; N, 5·01; Cl, 25·14. $C_{15}H_{14}NCl \cdot HCl$ requires: C, 64·31; H, 5·39; N, 4·99; Cl, 25·30%.) The picrate recrystallized from EtOH-ether, m.p. 189–190° (dec). (Found: C, 54·10; H, 4·08; N, 11·49; O, 23·79. $C_{15}H_{14}NCl \cdot C_6H_3O_7N_3$ requires: C, 54·34; H, 3·63; N, 11·85; O, 23·69%.)

Action of 5% *sulfuric acid on* IIa

The oily aziridine IIa (2·8 g) was refluxed in 5% H_2SO_4 (180 ml) for 1 hr. After cooling, the mixture was made basic with 10% Na_2CO_3 and extracted with benzene. The benzene layer was washed with H_2O, dried and evaporated to dryness *in vacuo* to give the residue (2·5 g) which was chromatographed on neutral Al_2O_3 (95 g, woelm). The fractions eluted with benzene were recrystallized from benzene as needles of *trans*-IXa (263 mg), m.p. 217–218°. (Found: C, 80·75; H, 6·84; N, 6·43; O, 6·94. $C_{15}H_{15}ON$ requires: C, 79·97; H, 6·71; N, 6·22; O, 7·10%.) The fractions eluted with benzene only and benzene: Chf (7:1)–Chf:MeOH (5:1) were combined to leave a crystalline residue (903 mg) which was recrystallized from benzene as plates of pure *cis*-VIIIa, m.p. 158–159°. (Found: C, 80·26; H, 6·80; N, 6·14. $C_{15}H_{15}ON$ requires: C, 79·97; H, 6·71; N, 6·22%.)

cis-O,N-*Diacetate* VIIIb *and* O-*monoacetate* VIIIc

cis-Alkanolamine VIIIa (500 mg) was acetylated with Ac_2O (5 ml) and pyridine (15 ml) at room temp. Working up in a usual manner, the residue (611 mg) was recrystallized as needles of *cis*-VIIIb (580 mg), m.p. 205–206°; ν_{max}^{Nujol} 3320 (—NH—), 1750 (—OAc), 1652 cm^{-1} (—NHAc). (Found: C, 74·06; H, 6·27; N, 4·57. $C_{19}H_{19}O_3N$ requires: C, 73·76; H, 6·19; N, 4·53%.) *cis*-VIIIb (500 mg) in 1% ethanolic KOH (50 ml) was allowed to stand for 3 hr. The mixture was poured into H_2O to give a crystalline substance which was separated by filtration. The filtrate was extracted with benzene and the benzene extract washed with H_2O, dried and evaporated to dryness to give the residue which was combined with the above separated substance and recrystallized as needles from acetone to give *cis*-VIIIc (347 mg), m.p. 223–224°; ν_{max}^{Nujol} 1640 cm^{-1} (—NHAc). (Found: C, 76·30; H, 6·45; N, 5·39. $C_{17}H_{17}O_2N$ requires: C, 76·38; H, 6·41; N, 5·24%.)

trans-O,N-*Diacetate* IXb *and* O-*monoacetate* IXc

trans-O,N-Diacetate IXb (200 mg) was treated with Ac_2O (2 ml) and pyridine (6 ml) at room temp for

19 hr. Working up in a usual manner, the reaction mixture gave crude *trans*-IXb (265 mg) which was recrystallized as needles from benzene to yield pure IXb (237 mg), m.p. 230–231°; ν_{max}^{Nujol} 3274 (—NH—), 1741 (OAc), 1640 cm^{-1} (—NHAc). (Found: C, 73·76; H, 6·29; N, 4·94; O, 15·63. $C_{19}H_{15}O_3N$ requires: C, 73·76; H, 6·19; N, 4·53; O, 15·52%.) *trans*-IXb (237 mg) in 1% ethanolic KOH (24 ml) was allowed to stand at room temp for 3 hr. Working up in an analogous manner and recrystallization from acetone gave needles of *trans*-IXc (170 mg), m.p. 210–211°; ν_{max}^{Nujol} 3255 (—NH—), 1655, 1634 cm^{-1} (—NHAc). (Found: C, 76·14; H, 6·38; N, 5·30. $C_{17}H_{17}O_2N$ requires: C, 76·38; H, 6·41; N, 5·24%.)

Chromic acid oxidation of cis- *and* trans-N-*monoacetates*, VIIIc *and* IXc

To a soln of *cis*-VIIc (50 mg) in acetone (5 ml) aqueous 8 N-chromic acid (0·2 ml) was added dropwise. The mixture was stirred at room temp for 24 hr, poured into H_2O and extracted with ether. The ethereal extract was washed with H_2O, dried and evaporated to dryness leaving X (40 mg) which recrystallized as needles (25 mg) from acetone, m.p. 170–171°; ν_{max}^{Nujol} 3330 (—NH—), 1693 (—C—), 1648 cm^{-1} (—NHAc);

λ_{max}^{EtOH} 237, 255 (shoulder), 300 mμ (ε 24,400, 9920, 1920). (Found: C, 76·46; H, 5·89; N, 5·26. $C_{17}H_{15}O_2N$ requires: C, 76·96; H, 5·70; N, 5·28%.) *trans*-IXc (50 mg) in acetone (5 ml) was oxidized with aqueous 8N-chromic acid (0·2 ml) at room temp for 3·5 hr. After working up, the residue (32 mg) was subjected to preparative TLC using SiO_2 (GF_{254}) and Chf:MeOH (20:1). The starting material (10 mg) and crude ketone (16 mg) were separated. The crude X was recrystallized from acetone as needles, m.p. 171–172° and was identical in all respects with that obtained from the *cis*-isomer.

Treatment of cis-*alkanolamine* VIIIa *with phosgen in pyridine*

To a soln of 30% phosgen in toluene (15 ml) at −45°, *cis*-VIIIa (150 mg) in Chf (3·5 ml) and pyridine (3 ml) was added and the mixture kept at −45– −25° for 0·5 hr and at room temp for 22 hr. Under cooling with ice, the mixture was poured into H_2O and extracted with toluene. The toluene extract was washed with H_2O, dried and evaporated to dryness *in vacuo* leaving 138 mg which on chromatography over SiO_2 (6 g) gave XI (85 mg) as plates, m.p. 196–197°; ν_{max}^{Chf} 3422 (>NH), 1768 cm^{-1} (>C=O). (Found: C, 76·30; H, 5·37; N, 5·70. $C_{16}H_{13}O_2N$ requires: C, 76·47; H, 5·22; N, 5·57%.)

Hydrolysis of the oxazolidone XI *with* 5% EtOH–KOH

A soln of XI (29 mg) in 5% EtOH–KOH (3 ml) was refluxed for 2·5 hr. The mixture was evaporated to dryness *in vacuo*, poured into H_2O and extracted with benzene. The benzene extract was washed with H_2O, dried and evaporated under reduced press leaving 26 mg which recrystallized from benzene (13 mg), m.p. 155–156° and was identical with *cis*-VIIIa.

Isomerization of trans-*alkanolamine* IXa *to* cis-*isomer* VIIIa

trans-IXa (0·6 mg) in 5% H_2SO_4 (0·5 ml) was refluxed for 3 hr. The mixture was basified with 10% Na_2CO_3 and extracted with AcOEt. The organic extract was washed with H_2O, dried and evaporated to dryness leaving 0·6 mg which were examined on TLC using SiO_2 and Chf:MeOH (5:1) and showed in almost equal intensity two spots corresponding to *cis*-VIIIa and *trans*-IXa. Isomerization of *cis*-isomer to *trans*-isomer did not occur.

Treatment of the aziridine IIa *with* Ac_2O *and pyridine*

The oily IIa (200 mg) was treated with Ac_2O (2 ml) and pyridine (6 ml) at room temp for 17 hr. The mixture was evaporated to dryness *in vacuo* and extracted with benzene. The benzene extract was washed with H_2O, 10% $NaHCO_3$, 5% HCl, H_2O, dried and evaporated leaving 198 mg from which a crystalline product was mechanically separated and recrystallized from benzene yielding *trans*-IXb (20 mg) as needles, m.p. 228–230°. The mother liquor was not further investigated.

Refluxing of the aziridine IIa *with* AcOH

The oily aziridine IIa (150 mg) was refluxed in glacial AcOH (4 ml) for 3·5 hr. The mixture was evaporated to dryness *in vacuo* leaving 154 mg which recrystallized from acetone giving *cis*-VIIIc (32 mg), m.p. 223–224°. Further investigation of other products was not performed.

Heating of the aziridine IIa *with* HCOOEt

A mixture of the oily aziridine IIa (314 mg) and HCOOEt (2·07 g) was heated at 100° in a sealed tube for 3 hr. The mixture was evaporated leaving 390 mg which were chromatographed on neutral Al_2O_3 (12 g, woelm). The fractions eluted with Chf:MeOH (20:1–10:1) were recrystallized as needles of *cis*-VIIId (41 mg), m.p. 209–210°; ν_{max}^{Nujol} 3380 (—OH), 3200 (—NH—), 1640 cm^{-1} (—NHCHO). (Found: C, 75·59; H, 6·12; N, 5·58. $C_{16}H_{15}O_2N$ requires: C, 75·87; H, 5·97; N, 5·53%). *cis*-VIIId (70 mg) was refluxed with 10% HCl (4 ml) for 1·5 hr. The mixture was evaporated to dryness under reduced press leaving a residue which was recrystallized from EtOH–AcOEt as needles of the hydrochloride of *cis*-VIIIa (36 mg), m.p. 261–262° (dec). (Found: C, 68·85; H, 6·32; N, 5·39; Cl, 13·95. $C_{15}H_{15}ON \cdot HCl$ requires: C, 68·82; H, 6·16; N, 5·35; Cl, 13·55%.)

Reaction of the aziridine IIa *with* CS_2

The oily aziridine IIa (300 mg) and CS_2 (1·5 ml) was heated in a sealed tube in a boiling water-bath for 6 hr. The mixture was evaporated to dryness *in vacuo* and the residue was washed with ether. The residual substance (310 mg) was chromatographed on SiO_2 (10 g, Merck) and crystalline fractions were eluted with benzene. The fractions were combined and recrystallized from AcOEt as leaflets of pure XII (90 mg), m.p. 260–262°; ν_{max}^{Chf} 3376 cm^{-1} (—NH—). (Found: C, 67·52; H, 4·68; N, 4·96; S, 22·55. $C_{16}H_{13}NS_2$ requires: C, 67·81; H, 4·62; N, 4·74; S, 22·63%.)

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