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AZIRIDINE RING EXPANSION SEQUENCES
A NEW SYNTHESIS OF 2-OXAZOLIDONES[1a]

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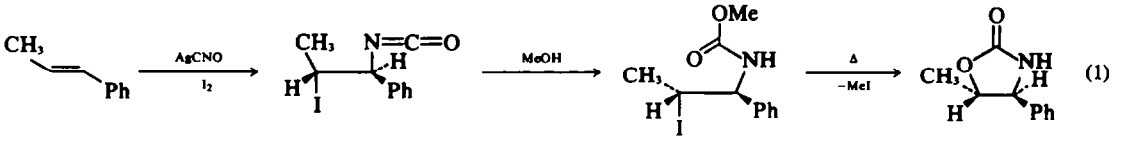
Abstract—β-Chloroamine hydrochlorides, produced stereospecifically and regiospecifically from aziridines with anhydrous hydrogen chloride in ether, are condensed with sodium carbonate in dry DMSO to afford isomerically pure 2-oxazolidinones.

Although many synthetic routes are available to the industrially and pharmaceutically important 2-oxazolidones relatively few afford stereochemically and regiochemically pure compounds.[2-4] Some years ago we reported that iodine isocyanate addition to olefins, followed by alcoholysis and pyrolysis, resulted in the production of isomerically pure 2-oxazolidones[5] (Eq 1). The stereoselectivity of these reactions has been confirmed by other workers.[6]

We have now developed a complementary route, one which affords derivatives of equal stereochemistry but opposite regiochemistry, and which takes advantage of the facile synthesis of aziridines from olefins via hydride reduction of iodine azide adducts[7] (Eq 2).



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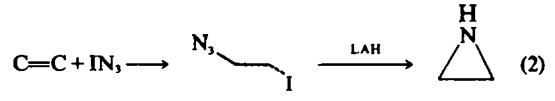

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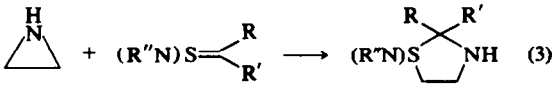

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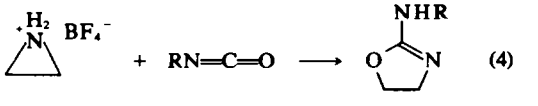

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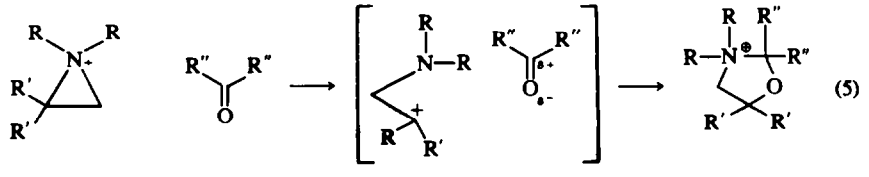
Aziridines are well known to undergo ring expansion with a variety of unsaturated nucleophiles of nitrogen and sulfur[8,9] (Eq 3). The enlargement normally proceeds stereospecifically with inversion.

Aziridinium salts will expand with carbonyl derivatives as well.[9] Aziridinium tetrafluoroborate reacts with isocyanates yielding alkylamino oxazolines after base workup[9,10] (Eq 4) while 1,1,2,2 tetrasubstituted aziridinium perchlorates form oxazolidinium perchlorates via a 1,3 dipolar cycloaddition with aldehydes and ketones[11] (Eq 5).

The analogous reaction with carbon dioxide or one of its derivatives would appear to provide a ready synthesis of 2-oxazolidones, but this has not been accomplished. Ethyl chloroformate reacts with aziridine to give the simple carbamate[12] (Eq 6).

However a few reports in the literature, including the first synthesis of the parent 2-oxazolidone[13] (Eq 7) and the kinetic study of the reaction of aqueous bicarbonate with 2,2-dichlorodiethylamine,[14] which appeared while this work was in progress, indicated that carbon dioxide might react with β-haloamines to yield oxazolidones. While β-haloamines **6** are relatively unstable with respect to the aziridinium salts,[5] their hydrogen halide salts **2** are quite stable in the absence of moisture. They are readily and cleanly produced from the aziridine, **1**. Consequently a series of experiments was undertaken to assess the synthetic utility of the sequence aziridine **1** → β-haloamine **6** $\xrightarrow{CO_2}$ 2-oxazolidone **3**.



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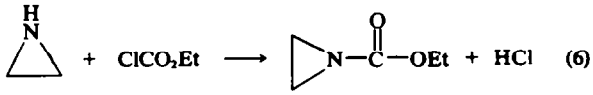
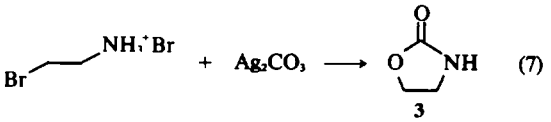
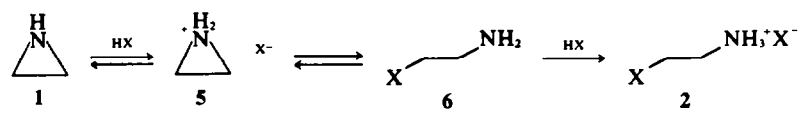


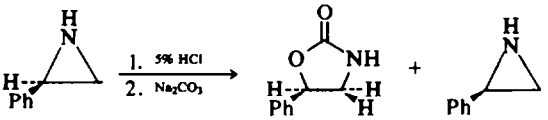


and $NaHCO_3$ in a variety of solvents. In water, 80% EtOH, MeOH, DMF, and CH_3CN the results were disappointing, but in DMSO and HMPA a significant yield of oxazolidone **3a**, was obtained, along with some recovered aziridine **1a**. DMSO was selected for further work since it could be separated from the products without excessive difficulty via an aqueous workup. Reaction of **2a** with Na_2CO_3 in DMSO gave **3a** in 61% yield. *cis*-5-Phenyl-4-methyl-2-oxazolidone (**3a**) was identified by its spectra, m.p., and hydrolysis to dl-norephedrine HCl (**4a**).



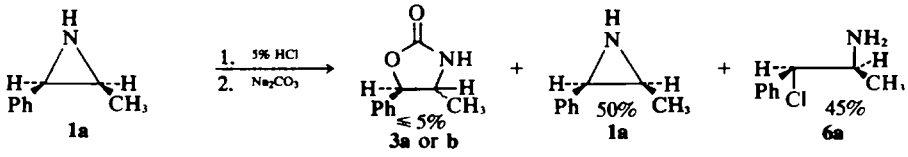
RESULTS

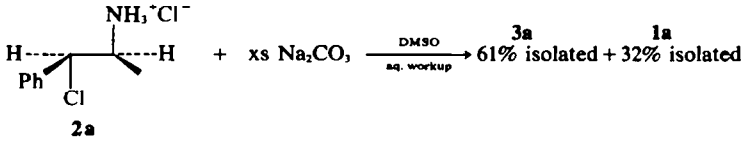
Initially 2-phenylaziridine (**1g**) was simply stirred with 5% aqueous HCl and neutralized with Na_2CO_3 to produce a 70% conversion to 5-phenyl-2-oxazolidone **3g**. None of the isomeric 4-phenyl-2-oxazolidone, the product previously reported from the iodocarbamate pyrolysis, was produced. With this satisfactory indication of the regiospecificity of the reaction we commenced a study of the stereochemistry of the process using *cis*-2-phenyl-3-methylaziridine **1a**. However, under the same conditions, aziridine **1a** gave $\leq$ 5% of an oxazolidone, as indicated by the absence of signals attributable to **3a** or **3b** in the NMR and the presence of merely a weak 1760cm^{-1} carbonyl band in the IR. The NMR showed instead an approximately 1:1 mixture of aziridine **1a** and 1-chloro-1-phenyl-2-aminopropane **6a**. The anticipated intermediate,



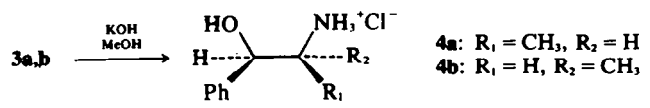
Similarly the *erythro*-chloroamine hydrochloride **2b**, prepared in 88% yield, gave *trans*-oxazolidone **3b** in 69% yield along with 17% of *trans* aziridine **1b**. Hydrolysis of the *trans* oxazolidone **3b** gave dl-norpseudoephedrine HCl (**4b**).

cis-Oxazolidone **3a** was also obtained from the reaction of chloroamine hydrochloride **2a** with excess $NaHCO_3$ though in somewhat poorer yields (52%), and from the reactions of Na_2CO_3 or $NaHCO_3$ with the neutral chloroamine **6a**. Chloroamine **6a** is easily obtained from aqueous





threo - 1 - chloro - 1 - phenyl - 2 - propyl ammonium chloride **2a**, was prepared in 90% yield from **1a** with anhydrous HCl in ether and reacted with Na_2CO_3 bicarbonate neutralization of **2a**. However no oxazolidone whatever, as proven by the absence of a 1760 cm^{-1} band in the IR spectrum of the product,



was formed when aziridine **1a** was stirred with a large excess of Na_2CO_3 in DMSO and CO_2 was vigorously bubbled thru. When chloroamine **6a** was stirred with fewer than 100 equivalents of $NaHCO_3$ the yield of oxazolidone **3a** decreased while the yield of aziridine **1a** increased (Fig 1). Furthermore oxazolidone formation could not be effected when gaseous carbon dioxide was bubbled through a DMSO solution of chloroamine **6a** containing an equivalent of LiH. The NMR of the product showed 60% aziridine **1a**, 40% chloroamine **6a**.

When chloroamine **6a** was stirred with 50 equivalents of NaN_3, (partially soluble in DMSO) and 50 equivalents of $NaHCO_3$ the product mixture contained 27% oxazolidone **3a** and 66% aziridine **1a** by NMR, with a maximum of 7% of a compound containing azide as indicated by a 2120 cm^{-1} band. Reaction with 100 equivalents of NaN_3 and no $NaHCO_3$ produced an oil exhibiting a stronger 2120 cm^{-1} band but containing 71% aziridine **1a** by NMR. Addition of a single drop of water to an otherwise standard preparation of oxazolidone **3a** in DMSO decreased its yield to 30%.

Attempts to utilize the corresponding bromide

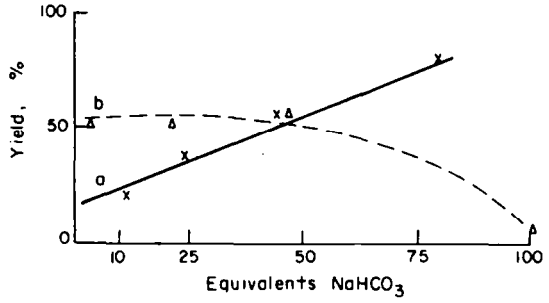
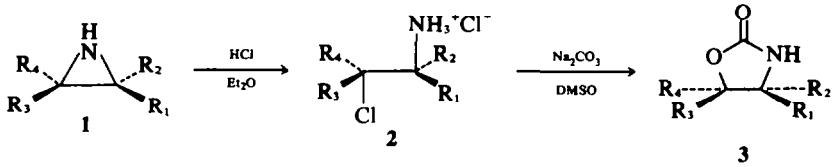


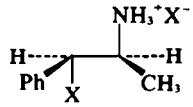
Fig 1. Percent yield of oxazolidone **3a** and aziridine **1a** from chloroamine **6a** as a function of equivalents $NaHCO_3$ employed. a. unbroken line: yield of oxazolidone **3a**; b. broken line: yield of aziridine **1a**.

Table 1. Conversion of aziridines 1 to oxazolidones 3 via 2



Aziridine 1	Chloroamine hydrochloride 2			Oxazolidone 3		
	% yield[a]	m.p.	% (aq)[b]	% (vacuum)[c]	m.p.	% overall[d]
(a) *cis*-Phenyl methyl $R_3 = Ph, R_1 = Me, R_2 = R_4 = H$	90	198–203°	61	78	148–8·5°	51
using hydrobromide salt:	60	190–93·5°	..	20	148–8·5°	9
(b) *trans*-Phenyl methyl $R_3 = Ph, R_2 = Me, R_1 = R_4 = H$	88	174–177°	73	76	119–121°	48
(c) *cis*-Diphenyl $R_3 = R_1 = Ph, R_4 = R_2 = H$	90	228–229°	50	46	192–193°	40
(d) *trans*-Diphenyl $R_3 = R_2 = Ph, R_4 = R_1 = H$	46	202–205°	..	93	159–162	29
(e) *cis*-Dimethyl $R_3 = R_1 = Me, R_4 = R_2 = H$	25[e]	158–158·5°	..	57	109–110°	13
(f) *trans*-Dimethyl $R_3 = R_2 = Ph, R_4 = R_1 = H$	65[e]	174–175·5°	7	90	105–108°	52
(g) Phenyl $R_3 = Ph, R_1 = R_2 = R_4 = H$	76	168–172°	67	94	90–91°	27
(h) Cyclohexyl $R_3 = R_1 = (CH_2)_4, R_4 = R_2 = H$	47[e]	208–210°	..	31	...	12
(i) t-Butyl $R_1 = tBu, R_2 = R_3 = R_4 = H$	65[e]	232–234°	..	61	110–111°	30
(j) Diphenyl methyl $R_3 = R_4 = Ph, R_1 = Me, R_2 = H$	51[f]	154–156°	..	0	...	0

[a] Yield based on aziridine unless otherwise indicated. [b] Yield based on 2 using an aqueous workup. [c] Yield based on 2 using a vacuum workup. [d] Overall yield of oxazolidone from olefin by most direct route. [e] Yield based on iodoazide. [f] Of **5j** not **2j**.



7a: X = Br
7b: X = I

and iodide derivatives were generally less successful. The hydrobromide **7a** afforded a 20% yield of **3a** using a vacuum workup; the remainder of the starting material is presumed to have reverted to aziridine **1a** which codistilled with the DMSO. The iodide salt **7b** turned brown immediately on dissolution in DMSO and gave an undistinguishable mixture of products containing < 5% of **3a**.

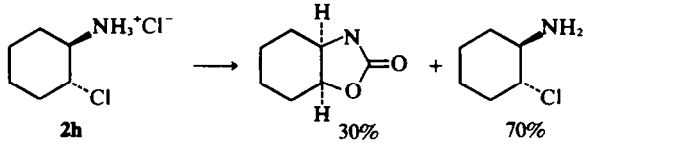
A number of other derivatives were prepared as shown in Table 1. Because of the low yield of the water soluble lower molecular weight dimethyl oxazolidones **3e** and **3f** during an aqueous workup, an alternative nonaqueous workup procedure was developed. The crude reaction mixture was diluted with $CHCl_3$ to facilitate filtration of the excess carbonate, and filtered. Solvents were removed in vacuum (*ca* 1mm) and the solid product was crystallized. Since, generally, superior yields of oxazolidones, free of aziridine and almost free of DMSO, were obtained in this fashion, the technique was used for the majority of the cases reported here. Stereospecificity was observed in every case; the expected regiochemistry was again observed in the case of the 5-phenyl-oxazolidone **3g**.

The oxazolidones were produced in conversions ranging from 31–95%; *cis*-diphenyl and *cis*-dimethyl oxazolidones **3c** and **3d** were obtained in significantly lower yields than their respective *trans*-isomers **3a** and **3f**. *trans*-2-Chlorocyclohexylammonium chloride **2h** failed to lead to complete ring closure. A product mixture obtained via aqueous workup contained, in addition to the 30% of *cis*-oxazolidone **3h**, 70% of neutral chloramine **6h**.

5,5-Diphenyl-4-methyl-2-oxazolidone **3j** was not accessible because the corresponding chloroamine hydrochloride **2j** could not be isolated.[15] Aziridinium salt **5j** gave quantitatively aziridine **1j** and no detectable amount of oxazolidone.

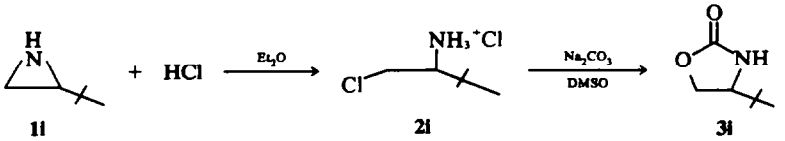
DISCUSSION

A. HCl Ring opening of Aziridines. Ring opening reactions of aziridines by hydrogen halides, water, and other nucleophiles are among the oldest known reactions of aziridines[16] and have been studied extensively, although only a few data on unsymmetrically substituted aziridines are available.[9,17] In the past such a ring-opening has not been considered to have preparative value, since the aziridines themselves were most commonly prepared by closure of the haloamine derivatives. However, with the availability of newer efficient syntheses of aziridines, ring opening of the latter becomes a route to β-halo amines. The kinetics, regiochemistry, and stereochemistry observed in the reaction have been discussed in terms of an S_N1-S_N2 continuum depending on the extent of bond-making and bond-breaking in the transition state. A modified S_N1 mechanism, which allows for the preservation of stereochemistry, was advanced for aziridines possessing tertiary or benzylic carbon centers. At the same time an S_N2 mechanism explains the direct preference for ring-opening at primary carbon exhibited by 2,2 dimethyl aziridine.[9] In accord with expectation, *cis*-2-phenyl-3-methyl aziridine **1a** was opened with HCl in ether to give exclusively *threo*-1-chloro-1-phenyl-2-propylammonium chloride **2a**. Likewise *trans*-2-phenyl-3-methylaziridine **1b** gave the *erythro*-chloroamine salt. The NMR spectra of the two salts and the stereo-chemical purity of the derived oxazolidones demonstrate the absence of any isomerization. Ring-opening occurred with stereochemical inversion at the carbon most capable of stabilizing a positive charge. Similarly the *cis*-and *trans*-diphenyl, -dimethyl and cyclohexyl aziridines **1c, d, e, f,** and **h**, have all been shown to open with inversion. 2-Phenylaziridine **1g** opens



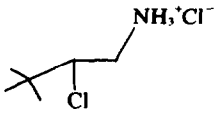
2h **3h** 30% **6h** 70%

2-t-Butylaziridine **1i** was opened regiospecifically by HCl to 1-chloro-3,3-dimethyl-2-butylammonium chloride **2i** which with carbonate produced 4-t-butyloxazolidone **3i**.



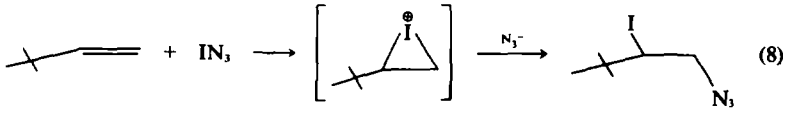
1i **2i** **3i**

with substitution exclusively at the benzylic carbon.[9] The chloroamine hydrochloride derived from 2-t-butylaziridine **1i**, m.p. 218°, has been formulated in the literature[18] as the primary alkylamine regioisomer **2k**, yet hydrogen chloride treatment of **1i**



2k

would be predicted to occur with nucleophilic attack by chloride on the primary carbon in accord with the analogous opening of the iodonium ion

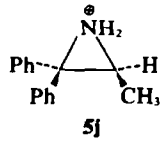


(8)

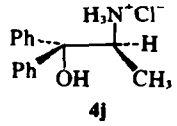
opening in the formation of the iodine azide adduct from which it was derived.[7] (Eq 8)

Indeed the ms of the product showed prominent ions at *m/e* 86 and 80/78 corresponding to ions of structure C_4H_9—$CH{=}\overset{+}{N}H_2$ and $\overset{+}{N}H{=}CH_2CH_2Cl$, confirming the expected regiochemistry as in **2i**.

2,2-Diphenyl-3-methylaziridine **1j** was inconvertible to an oxazolidone. It was even impossible to obtain a stable chloroamine derivative **2j**; instead, as reported by F. N. Campbell *et al.*[15] we isolated either the aziridinium chloride **5j** or the corresponding amino alcohol hydrochloride **4j**. Presumably the benzhydrylic chloride **2j** is too labile, and it either ring closes to **5j** or is solvolyzed to **4j** with water.



5j

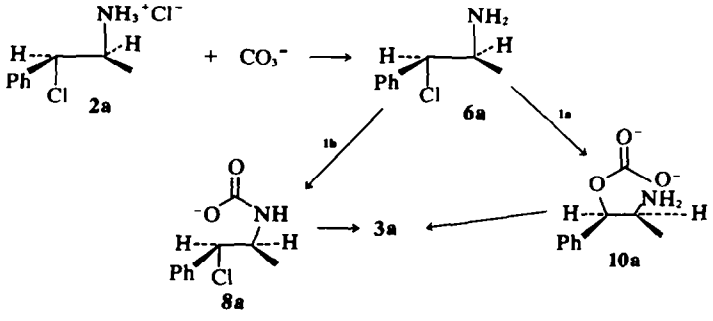


4j

B. Oxazolidone formation A number of mechanisms might be envisioned for oxazolidone formation from **2**, the more prominent being shown in Schemes 1 and 2. Carbonate neutralization of the ammonium salt **2** can be followed by either carbonate displacement of chloride in **6a** and ring closure to **3** (Scheme 1a) or by carbamate salt formation and closure of **6a** (Scheme 1b). Alternatively the chloroamine **6a** might ring-close to an aziridine **1a** via an aziridinium salt **5a**, followed by condensation with carbonate and ring expansion of **9a** to **3a** via front side displacement (Scheme 2), perhaps with solvent assistance from the rear. S_N2 opening of the aziridinium ion **5a** with carbonate is excluded by the stereochemical results since it would produce *threo*-**10b** which would ring close to *trans*-oxazolidone **3b**.

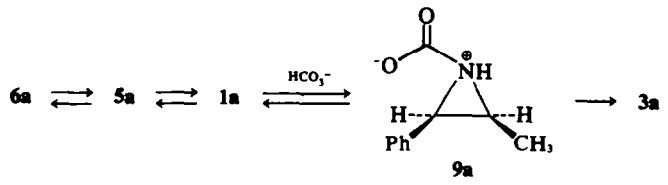
A scheme similar to 1 but with carbonate displacement of chloride preceeding neutralization of the ammonium salt **2a** is unlikely since acid-base reactions are normally very fast. Similar sequences with the intervention of carbonium ions are easily rejected on the basis of the evident stereospecificity of the reaction. Clean Walden inversion is observed throughout in both the aziridine ring opening and the oxazolidone ring closure. The ready neutralization of chloroamine hydrochloride **2a** in water, the isolation of recovered aziridine **1** in the reaction **2**→**3**, and the demonstration that *cis*-chloroamine **6a** gives *cis*- oxazolidone **3a** require a chloroamine **6** as an intermediate.

That a ring closed aziridinium salt **5** (Scheme 2) is not an intermediate leading to **3** may be inferred from several sources. As discussed above aziridines and aziridinium salts usually open with inversion at the reacting site, but the intervention of an intermediate such as **9a** would require a front side displacement with retention.[19] 2,2-Diphenyl-3-methylaziridinium salt **5j** failed to give any oxazolidone **3j**. Reaction of Na_2CO_3 with impure batches of chloroamine salt **2**, the major impurity being the intermediate aziridinium salt **5**, always



2a **6a** **8a** **10a**

SCHEME 1.



SCHEME 2.

gave reduced yields of oxazolidone **3** with correspondingly increased recovery of aziridine **1**. When aziridine **1a** was submitted to the reaction conditions even with the added factor of excess carbon dioxide no oxazolidone **3a** was formed, although it has been shown [20] that primary amines and relatively unhindered secondary amines react essentially instantaneously with carbon dioxide in alkaline aqueous solution to form carbamate salts. The above results suggest that **9a** is not an intermediate on the path to **3a** in DMSO solution.

The observation that the yield of oxazolidone **3a** depends on the number of equivalents of carbonate salt employed (Fig 1), in amounts far exceeding the solubility of Na_2CO_3 in DMSO, implicates the surface area of the salt as a critical variable. That no oxazolidone **3a** was formed from chloroamine **6a** and carbon dioxide in the presence of one equivalent of base confirms this.

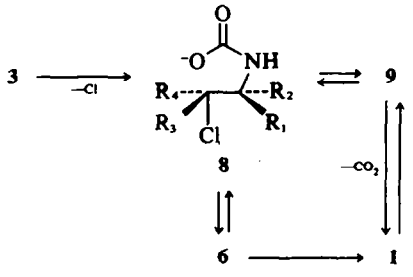
Possibly DMSO solvates the sodium ion at the solvent-solid interface allowing the amine to coordinate by hydrogen bonding with the carbonate. Other hydroxylic solvents would compete with the amine for the carbonate sites, thus quenching the reaction. Indeed formation of **3a** did not proceed in water, ethanol or methanol and addition of water to DMSO reduced the yield.

Clearly there is a competition between ring closure of chloroamine **6** to aziridine **1** and its reaction with carbonate leading to oxazolidone **3**. The presence of a base in solution, such as Na_2CO_3 in hydroxylic solvents or NaN_3 in DMSO, increased the yield of aziridine **1a**.

Substitution of bromide **7a** for chloride in **2a** reversed the percentage of oxazolidone **3a** and aziridine **1a**. In fact β-bromoamines undergo ring closure to aziridines 100 times faster in water than the corresponding β-chloroamines.[9]

It is more difficult to choose between paths **1a** and **1b**. Since the key step is demonstrably occurring at the solid surface, the fact that azide ion displacement of chloride failed to compete with oxazolidone formation despite azide's superior nucleophilicity,[21] still does not exclude carbonate displacement of chloride (to form **10a**) on the carbonate surface.

The fate of chlorocarbamate ion **8** is expected to be sensitive to subtle substituent and solvent

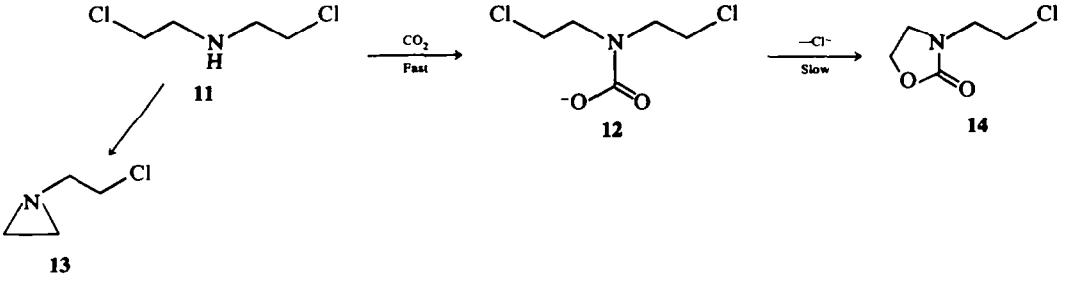


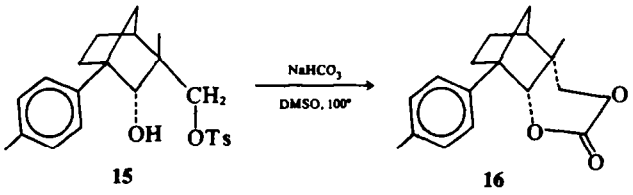
SCHEME 3.

effects. Intermediate **8** can either revert to chloroamine **6** or ring close to a 3 or a 5 membered ring (Scheme 3).

In general closure of 5-membered rings occurs more quickly than closure of 3-membered rings, but *cis* interactions are more severe in the former than in the latter.[22,23] Indeed we observed that *cis*-diphenyl chloroamine hydrochlorides **2c** and **2e** gave relatively more aziridines **1c** and **1e** than did their respective *trans* isomers. Some difficulty in ring closure in either sense would be expected for *trans*-2-chlorocyclohexylamine hydrochloride **2h** since flipping to a *trans*-diaxial conformer[24] is required. In fact, large amounts of unreacted *trans*-2-chlorocyclohexylamine **6h** were isolated.

Further if path **1a** were being followed greater differences in the rate of the reaction, dependent on





15 16

the primary, secondary, or benzylic nature of the chloride, might be expected. Thus we prefer path **1b** but cannot exclude path **1a**.

It is interesting to compare this surface reaction in DMSO with the reaction in aqueous solution. Robinson and Herbrandson[14] showed that the slow step of the reaction of **11** was ring closure of the carbamate anion **12** to **14** but with a rate 50 times faster than formation of **13**. Presumably chloroamine hydrochloride **2g**, which gave oxazolidone **3g** in aqueous solution, underwent a similar process; however, addition of a single Me group (**2a**) diverted the aqueous reaction to aziridine **1a**. H-bonding of chloroamine **6a** to a carbonate surface allows condensation with carbonate to compete more successfully with aziridine ring closure.

Recently Bosworth and Magnus reported the formation of the cyclic carbonate **16** from tosylate **15** during an attempted Kornblum oxidation.[25] Since this reaction is entirely analogous to ours, it may also occur on the carbonate surface, thus calling into question the conclusion that bicarbonate is necessarily a better nucleophile than DMSO.

The reaction sequence described also serves as a regiospecific and stereospecific synthesis of β-amino alcohols, as indicated by the formation of norephedrine **4g** and norpseudoephedrine **4b** in 51% and 49% yields respectively by base catalyzed hydrolysis of oxazolidones **3a** and **3b**.

EXPERIMENTAL*

General. trans- **1b**, *cis*-and *trans*- **1e** and **1f**, **1h**, and **1i** were prepared via LAH reduction of the iodine azide adduct of the olefin.[7] *cis*-aziridines **1a** and **1c** were prepared from the respective *trans*-olefins by LAH reduction of the derived azirine.[26] *trans*- **1d** was produced by LAH reduction of the aziridinyl phosphonate.[27] Compound **1g** was prepared from styrene via the iodine isocyanate adduct,[28] and **1j** was obtained by addition of PhMgBr to the appropriate azirine.[29]

General procedure for the ring opening of aziridines

Preparation of chloroamine hydrochlorides **2**. A soln of **1** (0·05 mole) in 50–100ml anhyd ether was added slowly to 200ml anhyd ether/1% EtOH previously saturated with anhyd HCl and cooled in ice. The initially formed oily ppt redissolved with stirring and the clear solution was stirred for 2 h while warming to 25°, or until reprecipitation occurred. The mixture was refrigerated for at least 3 h and the crystals of **2** (Table 1) were collected by filtration and rinsed with ether. The physical properties of **2a**,[30] **2b**,[31] **2c**,[32] **2d**† **2e**,[7] **2f**,[7] **2g**,[34] **2h**,[28] **2i**,[18] and **2j**,[15] were identical to those reported (Table 1).

General Procedure for oxazolidone formation aqueous workup

A soln of **2** (0·01 mole) in 200ml dry DMSO was stirred vigorously 4–20 hr at 25° with 106g anhyd Na_2CO_3 (1·0 mole). The mixture was diluted with 800–1000ml of cold $CHCl_3$, filtered through a layer of Celite, and washed with 4–6 liters cold water. After Na_2SO_4 drying and filtration solvent was removed *in vacuo* leaving oxazolidone **3** and aziridine **1**, if any. This workup is not suitable for the lower molecular weight oxazolidones (eg. **3e**, **3f**, **3h**, **3i**) because of their solubility in water.

cis-5-Phenyl-4-methyl-2-oxazolidone **3a** Compound **2a** (1·425g) afforded a $CHCl_3$ soln which was further washed with 5% HCl before drying. The non-basic portion yielded 0·753g of **3a** (61%). The acidic washes were basified and extracted to yield 0·298g of **1a** (95% pure) as a colorless oil (32% recovery of **1a**).

trans-5-Phenyl-4-methyl-2-oxazolidone **3b** From **2b** (2·06g) after washing with 5% HCl one obtained 1·86g (73%) pale yellow solid. Neutralization and extraction of the acid layer gave *trans*- **1b** (0·277g; 17%)

cis-4,5-Diphenyl-2-oxazolidone **3c** From **2c** (2·5g) was obtained 1·910g of a white solid, 60% **3c**, 40% **1c** by NMR. After washing with 5% HCl the residue was recrystallized affording **3c**.[35–37] Neutralization and extraction of the acid layer afforded *cis*-**1c** (0·315g; 17%).

trans-4,5-Dimethyl-2-oxazolidone **3f** From **2f** (1·44g; 0·01 mole) was obtained 0·067g (6%) of a liquid whose spectra agreed with those of **3f**.[37]

5-Phenyl-2-oxazolidone **3g** From **2g** (1·598g) 0·910g of a yellow solid **3g**[38] was obtained.

General procedure for oxazolidone formation vacuum workup

Compound **2** (0·01 mole) was dissolved in 200ml dry DMSO and stirred vigorously for 4h with 106g anhyd Na_2CO_3 (1·0 mole). The mixture was drowned in 800ml cold $CHCl_3$ and filtered through a layer of Celite. Solvent was removed from the clear filtrate (rotovap, then 40–60°/0·02mm) until dryness (solid products) or until no further liquid distilled (liquid products). The residue was dissolved insofar as possible in 200ml of acetone or $CHCl_3$, dried, (Na_2SO_4), and filtered. Solvent removal gave **3** (Table 1) contaminated only with traces of DMSO with one exception. *cis*-**3c** was found to be contaminated with 37% of **1c**. The IR, NMR, and mass spectra and/or

*All m. ps were recorded on a Fisher-Johns block and are uncorrected. IR spectra were recorded on a Perkin-Elmer Model 457 infrared spectrometer; mass spectra were recorded on a Varian M.A.T. CH-5 instrument. NMR spectra were obtained using a Varian A-60A spectrometer with TMS as internal standard. Microanalysis was performed by Atlantic Microlabs, Atlanta, Georgia.

†Although the salt **2d** has not been reported, the neutral chloroamine has been prepared.[33]

the m.ps of these products were identical to those reported.[2,28,35-38] Preparative GLC (20% BDS on GasChrom P, 175°) of the DMSO contaminated samples of **3e** and **3f** gave the pure products.

4-t-Butyl-2-oxazolidone **3i** *vacuum workup.* **2i** (1·72g, 0·01 mole) afforded 0·986g of an oily solid, NMR (DMSO-D_6): 2·18 (bs, disappears in D_2O, 1), 5·80 (complex m, 2), 6·48 (4 band m, a further 1·5 Hz splitting disappears in D_2O, 1), 9·18 (s, 9), in addition to a small peak for DMSO (61% yield), recrystallized (Et_2O/hexane) m.p. 110–111°; IR (KBr): 3240, 1730 cm^{-1}; ms:m/e 143 (M^+; 4·16%), 128 (2·00, M^+-CH_3), 87 (100·00%, M^+-$(CH_3)_2C=CH_2$), 86 (22·02), 57 (77·11, tBu^+). *Found*: C, 58·81, H, 9·20; N, 9·76. *Calc.* for $C_7H_{13}NO_2$: C, 58·72; H, 9·15; N, 9·78.

Attempted formation of 5,5-diphenyl-4-methyl-2-oxazolidone **3j** *vacuum workup.* Compound **5j** (1·41g, 0·005 mole) afforded 1·183g of a yellow oil, 94% aziridine **1j**, 6% DMSO by NMR. The IR showed no bands between 2900 and 1600 cm^{-1}.

threo-1-Bromo-1-phenyl-2-propylamine hydrobromide **7a** The general procedure for HCl ring opening was followed, with *cis*-**1a**,[25] substituting gaseous HBr for HCl and affording 8·85g white powder, m.p. 190–193·5° (60%) IR (KBr): 2870, 2500, 2480, 1950, 1590, 1510 cm^{-1} NMR (DMSO-D_6): 1·69t (bs, 3, disappears in D_2O), 4·47 (d, J = 9, 1, PhC**H**-Br), 5·84 (d of q, J = 9, 7, 1, C**H**CH_3), 8·82 (d, J = 7, 3, $CHCH_3$); ms: *m/e* 171, 169 (6·29, 6·41%, PhCHBr), 134 (21·97%, Ph-$\overset{+}{C}H$-$\overset{+}{N}H_2$), 81, 79 (17·41, 17·62%, Br^+), 44 (87·80%, $CH_3\overset{+}{C}H=\overset{+}{N}H_2$. *Found*: C, 36·55; H, 4·50; N 4·68. *Calc.* for $C_9H_{13}Br_2N$: C, 36·63; H 4·45; N 4·75.

Oxazolidone **3a** *from bromide salt* **7a** Hydrobromide **7a** (2·95g, 0·01 mole) by vacuum workup afforded 0·819g yellow oily solid, 25% *cis*- **3a**, 75% DMSO by NMR integration (20% yield oxazolidone).

threo-1-Iodo-1-phenyl-2-propylamine hydroiodide **8a** To *cis*-**1a** (1·33; 0·01 mole) dissolved in 250 ml acetone was added 50 ml of 50% HI. After 1 hr of stirring solvent was removed *in vacuo*. The residue was recrystallized (95% EtOH/Et_2O) to yield 0·50g luminescent white plates (13%) which turned brown immediately on dissolution in DMSO-D_6. The NMR spectrum taken 45 min later showed a 3:1 mixture of 2 compounds possessing high field doublets, neither of which was starting material **1a**. In the presence of Na_2CO_3 a brown liquid was obtained which contained no **3a** by NMR.

Oxazolidone **3a** *from chloride salt* **2a** *with* $NaHCO_3$. Hydrochloride **2a** (0·206g, 0·001 mole) was treated as above (vacuum workup) with 8·4g (0·1 mole) $NaHCO_3$ to give 0·109g of an oil containing 52% of *cis*-**3a** by NMR.

Oxazolidone **3a** *from chloride salt* **2a**. Effect of added water Hydrochloride **2a** (0·20g, 0·001 mole) was treated as above (vacuum workup) with the addition of one drop water, affording 0·054g of oxazolidone **3a** (30%).

threo-1-Hydroxy-1-phenyl-2-propylamine hydrochloride **4a** (*dl-norephedrine hydrochloride*). A soln of **3a** (0·665g) in 20 ml 0·85 N methanolic KOH and 5 ml H_2O was refluxed under N_2 for 10·5 h. Solvent was removed and the residue was dissolved insofar as possible in ether. After $MgSO_4$ drying and filtration, dry HCl gas was bubbled into the filtrate and 0·320g white crystals were collected m.p. 192–193·5° (Merck, 190–194°)

erythro-1-Hydroxy-1-phenyl-2-propylamine hydrochloride **4b**. Oxazolidone **3b** (0·084g) treated as described under **4a**, produced 0·038g of white solid, m.p. 175–6° (Merck 169–171°), mixed with an authentic sample (K&K). m.p. 171–179°.

threo-1-Chloro-1-phenyl-2-propylamine **6a**. To a soln of **2a** (1·03g, 0·005 mole) in 10 ml water was added 50 ml sat $NaHCO_3$ aq, followed by 25 ml CH_2Cl_2. After 5 min of shaking the layers were separated and the aqueous phase washed with an additional 20 ml CH_2Cl_2. The organic layers were dried ($MgSO_4$) and solvents removed *in vacuo* yielding 0·792g of **6a** as a yellow oil (93%), NMR ($CHCl_3$): 2·58t (s, 5, Ph), 5·29 (d, J = 7, 1, Ph C**H**(Cl)—, 6·65 (qn, J = 7, 1, $CHCH_3$), 8·35 (s, 2, NH, disappears in D_2O), 8·99 (d, J = 7, 3, $CHCH_3$); IR (neat): 3380, 3300, 1600 cm^{-1}; ms: *m/e* 171, 169 (M^+), 132 (Ph-$\overset{+}{C}$(=NH)-), 127, 125 (PhC$\overset{+}{H}$Cl), 44 ($CH_3CH=\overset{+}{N}H_2$).

Oxazolidone **3a** *from chloroamine* **6a**. Chloroamine **6a** (0·170g, 0·001 mole) was treated as above with Na_2CO_3 (10·6g; 0·1 mole) (vacuum workup) to give 0·078g solid *cis*-**3a**, pure by NMR (46%). Similar treatment with $NaHCO_3$ (8·4%; 0·1 mole) gave 0·141g white solid **3a**, (80%). Use of 0·05 mole $NaHCO_3$ and an aqueous workup afforded 0·138g of an oil, 50% **3a**, 50% **1a** by NMR (89% total); 0·025 mole $NaHCO_3$ afforded 0·123g of an oil, 40% **3a**, 60% **1a** (81%); 0·01 mole $NaHCO_3$ resulted in 0·105g of an oil, 30% **3a**, 70% **1a** by NMR (72%).

When this reaction was carried out using 50 equivts NaN_3 and 50 of $NaHCO_3$, aqueous workup gave 0·138g of an oil, IR: 3260, weak 2120, 1745, 1605 cm^{-1}. The NMR showed 27% oxazolidone **3a**, 66% aziridine **1a**, allowing a mazimum 7% of an azide compound.

A similar experiment with 100 equivts of NaN_3 and no $NaHCO_3$ gave an oil whose IR exhibited a 2120 cm^{-1} azide band and whose NMR showed 71% **1a**.

Dry CO_2 gas was bubbled through a soln of **6a** (0·170g; 0·001 mole) in 20 ml DMSO. After 5 min a portion of lithium hydride (0·004g; 0·001 mole) was added, and after 30 min the remainder was added. Bubbling was continued for 6 h and aqueous workup gave an oil whose IR showed a very weak 1755 cm^{-1} CO and whose NMR showed 40% **6a**, 60% **1a**.

Attempted formation of oxazolidone **3a** *from aziridine* **1a**

A soln of *cis*-**1a** (1·33g; 0·01 mole) in 100 ml DMSO was stirred with 53g Na_2CO_3 for 4 h while 100 equivts CO_2 was bubbled through (106g Na_2CO_3, aq HCl). An aqueous workup gave 1·632g of **1a** (by NMR and IR).

Solubility of Na_2CO_3 *in DMSO*

A slurry of 25·00g Na_2CO_3 in DMSO was stirred for 4 h and filtered. The cake was washed with $CHCl_3$ and dried leaving 24·824g Na_2CO_3. A liter of $CHCl_3$ was added to the initial DMSO filtrate yielding a clear soln; no precipitation occurred.

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