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The Syntheses of *N*-Arylaziridines

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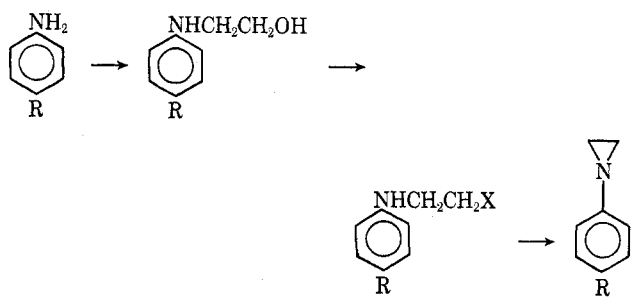
A number of *N*-arylaziridines were prepared by cyclization of the corresponding 2-bromo-, 2-chloro-, or 2-tosyloxyethylanilines. Sodium hydride in dimethyl sulfoxide was used for the ring closure. The parent 2-arylaminoethanols were prepared by the reaction of the anilines with ethylene chlorohydrin or ethylene oxide. Another approach utilized the formation and reductive cleavage of *N*-aryl-2-oxazolidone. This reduction was accomplished with lithium aluminum hydride or potassium borohydride. The oxazolidone may be converted directly to the arylaminoethyl bromide hydrobromide by treatment with 48% HBr. Synthesis of 2,2′-dideuterio-*N*-arylazirdine was possible by cyclization of *N*-(2,2′-dideuterio-2-tosyloxyethyl)aniline, and the parent alcohol could be made by the reduction of *N*-phenylglycine ethyl ester with lithium aluminum deuteride. The *N*-arylaziridines are unstable and are best stored over KOH in a nitrogen (or better, argon) atmosphere.

The control of insects by flooding the insect population with sterile males is a well-known technique. Certain aziridine compounds have been found to be quite effective as chemosterilants.[2-4] Chemosterilant and carcinostatic[5] activity may be related to the effectiveness of aziridines as alkylating agents, which is related to the ease of opening of the aziridine ring. The aziridines in the present study were prepared in order to evaluate the effect of aromatic substituents on the rate of aziridine ring opening.[6] The compounds prepared will be screened for chemosterilant activity.

Of the numerous reported syntheses of aziridine compounds, the general procedure developed by Heine, *et al.*,[7,8] was chosen. The preparation of each *N*-arylaziridine consisted of a three-step synthesis as illustrated (Scheme I).

Heine used sodium hydroxide in approximately 80% aqueous ethanol to cyclize the *N*-(2-bromoethyl)anilines to the corresponding *N*-arylaziridines. The procedure[9] is quite tedious. In addition, not all of the phenyl substituents are stable to hydrolysis under these conditions. Thus, it was necessary to find an alternate method of ring closure.

SCHEME I



Results and Discussion

Preparation of *N*-Arylaziridines.—The use of sodium hydride in a nonprotonic solvent at room temperature to cyclize the various 2-chloro-, -bromo-, and -tosyloxyethylanilines was one way to avoid hydrolysis of the aziridines formed. Dimethyl sulfoxide (DMSO) as a reaction solvent was found to give the best results. The great solubility of the amine salts in DMSO allowed for an easily controlled dropwise addition of the amine solutions to the sodium hydride in the reaction vessel. The DMSO was easily removed from the product by extraction with water. The aziridines were not subject to further reaction under these conditions.

The *p*-OCH_3, *p*-CH_3, *p*-H, *p*-F, *p*-Cl, *p*-Br, *p*-CN, and *p*-NO_2 *N*-phenylaziridines were prepared from aryl-

(1) Predoctoral Assistantship, Entomology Research Division, Agricultural Research Service, USDA, in cooperation with North Dakota State University.

(2) E. F. Knipling, *Science*, **130**, 902 (1959).

(3) A. B. Borkovec, *ibid.*, **137**, 1034 (1962).

(4) A. B. Borkovec, *Residue Rev.*, **6**, 87 (1964).

(5) T. H. Goodridge, W. T. Huntress, and R. T. Bratzel, *Cancer Chemother. Rep.*, **26**, 407 (1963).

(6) The kinetics of ring opening of *N*-arylaziridines will be reported elsewhere.

(7) H. W. Heine, B. L. Kapur, and C. Mitch, *J. Amer. Chem. Soc.*, **76**, 1173 (1954).

(8) H. W. Heine, B. L. Kapur, J. B. Bove, R. W. Greiner, K. H. Klinger, and C. Mitch, *ibid.*, **76**, 2503 (1954).

(9) R. Adams and J. B. Segur, *J. Amer. Chem. Soc.*, **45**, 785 (1923).

aminoethyl halides and tosylates in excellent yields by using the DMSO–sodium hydride method. Generally, a 1 *M* solution of the amine in DMSO was allowed to react with 5% molar excess of sodium hydride. (A concentrated solution of the 2-arylaminoethyl bromides can result in the formation of *N*,*N*′-diarylpiperazines.[10]) The *N*-(*p*-acetylphenyl)aziridine was prepared by using tetrahydrofuran as the solvent and 1 equiv of sodium hydride, since the corresponding arylaminoethyl halide was found to decompose spontaneously in DMSO. Of the nine *N*-arylaziridines prepared, only the *p*-CH_3, *p*-H, and *p*-F compounds had been previously reported.[7,8,11]

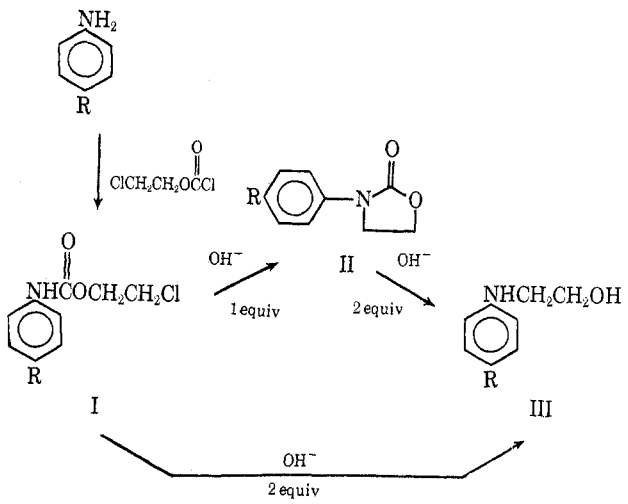
Preparation of the 2-Arylaminoethanols.—The most useful procedure reported for the preparation of the 2-arylaminoethanols is the reaction of the various anilines with ethylene oxide or 2-chloroethanol.[7,8,10,12–14] The *p*-OCH_3, *p*-CH_3, *p*-Br, *p*-Cl, *p*-CN, and *p*-F anilinoethanols were all prepared according to the general procedure of Heine, *et al.*,[8] using 1 equiv of the 2-chloroethanol or 2-bromoethanol and 2 equiv of the corresponding para-substituted aniline. An attempt to prepare the *N*-(2-hydroxyethyl)-*p*-aminoacetophenone according to this procedure resulted in the formation of considerable amounts of a *p*-aminoacetophenone imine dimer and only trace amounts of the desired product. When 1.5 equiv of *N*,*N*-dimethylaniline was added, the imine was not formed, and an improved but poor yield of the *N*-(2-hydroxyethyl) compound was obtained. It should be noted that the above procedure yields a mixture of the aniline and the mono- and bisanilinoethanols, which involves a tedious separation problem.

The method of Oprzadek,[15] which utilizes the reaction of ethanolamine with *p*-nitrochlorobenzene, was used to prepare *N*-(2-hydroxyethyl)-*p*-nitroaniline.

There are two methods of preparing 2-arylaminoethanols that we did not consider until very late in our synthetic program; both of these should give improved yields with much less effort. In 1923 Adams and Segur[9] showed that 2-arylaminoethanols can be prepared from 3-aryl-2-oxazolidones as illustrated in Scheme II; 2 equiv of the aniline and 1 equiv of 2-chloroethylchloroformate were used to prepare the 2-chloroethyl carbanilide I. The unreacted aniline was easily removed by means of its hydrochloride salt. All intermediates (I and II) were very stable compounds which were readily distilled or recrystallized, and the overall yields from the aniline to the *N*-(2-hydroxyethyl)aniline compound (III) were in the 70–75% range.

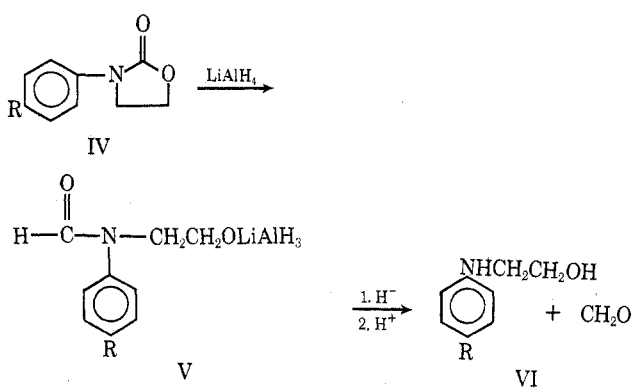
Since not all phenyl substituents are stable in hot aqueous alkali, the method of Palopoli and Feil,[16] using sodium hydride in acetone to induce alkylation of a secondary arylamide with an alkyl halide, was used to close the 2-chloroethylphenylcarbonate I to the *N*-aryl-2-oxazolidone II. The cyclization of 2-chloroethyl-*p*-acetylphenyl carbonate to *N*-(*p*-acetylphenyl)-2-oxazolidone occurred upon using a slight excess of sodium

SCHEME II



hydride, and gave a 98% yield. Since lithium aluminum hydride reduced *N*-methylformanilide[17] to *N*-methylaniline and formaldehyde, it was concluded that metal hydrides should reduce IV (Scheme III) to

SCHEME III



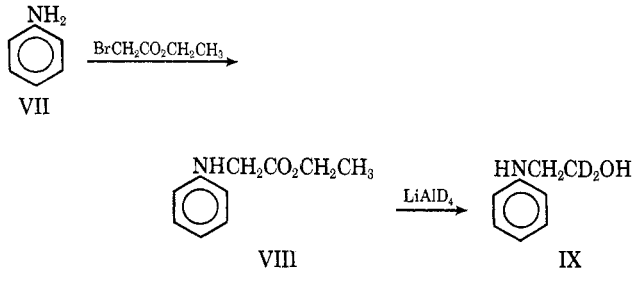
the 2-arylaminoethanol VI *via* intermediate V. Both lithium aluminum hydride and lithium borohydride reduced *N*-(*p*-methoxyphenyl)-2-oxazolidone to *N*-(2-hydroxyethyl)-*p*-anisidine. In the lithium aluminum hydride reduction, approximately 0.2 equiv of formaldehyde was isolated by means of a derivative with 5,5-dimethyl-1,3-cyclohexanedione.[18]

The other method of preparing 2-arylaminoethanols is the metal hydride reduction of *N*-arylglycine ethyl esters (VIII). The reaction sequence used for the preparation of the dideuterio compound is shown in Scheme IV, and gave an overall conversion of about 80%.

Preparation of 2-Arylaminoethyl Halides and *p*-Toluenesulfonates.—The second step in each synthesis of the *N*-arylaziridines is the conversion of the *N*-(2-hydroxyethyl)anilines into 2-halides or tosylates. The *p*-CH_3, *p*-F, *p*-Cl, *p*-Br, *p*-CH_3CO, and *p*-H 2-anilinoethanols were converted to the corresponding *N*-(2-bromoethyl)aniline hydrobromides by the action of hot 48% hydrobromic acid according to a procedure analogous to Pearman's.[19] The *N*-(2-chloroethyl)-*p*-anisidine hydrochloride was prepared in good yield from the

(10) W. Pearlman, *J. Amer. Chem. Soc.*, **70**, 871 (1948).
(11) U. F. Bystrowa, O. A. Yuzhalova, and R. G. Kostzanouskii, *Dokl. Akad. Nauk SSSR*, **147**, 843 (1962); *Chem. Abstr.*, **59**, 2625*d* (1963).
(12) L. Knorr, *Ber.*, **22**, 2092 (1889).
(13) W. J. Jacobs and M. Heidelberger, *J. Biol. Chem.*, **21**, 421 (1915).
(14) R. K. Summerbell and D. R. Berger, *J. Amer. Chem. Soc.*, **79**, 6504 (1957).
(15) B. Oprzadek, *Lodz. Tow. Nauk. Wydz. III, Acta Chim.*, **8**, 785 (1923).
(16) F. P. Palopoli and V. J. Feil, U. S. Patent 3,247,252 (1966).
(17) F. Weygand and H. Linden, *Angew. Chem.*, **66**, 174 (1954).
(18) A. I. Vogel, "A Textbook of Practical Organic Chemistry," 34th ed, Wiley, New York, N. Y., 1960, pp 332–334.
(19) W. Pearlman, *J. Amer. Chem. Soc.*, **70**, 870 (1948).

SCHEME IV

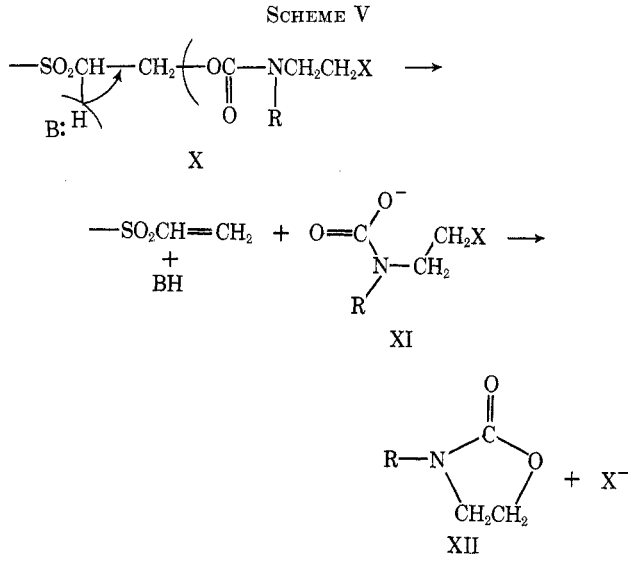


corresponding anilinoethanol by the addition of excess HCl dissolved in *N*,*N*-dimethylformamide and 1.5 equiv of thionyl chloride. Both *N*-(2-hydroxyethyl)-*p*-nitroaniline and *N*-(2-hydroxyethyl)-*p*-aminobenzonitrile were converted to the corresponding *N*-(2-tosyloxyethyl) compounds by reaction with *p*-toluenesulfonyl chloride in pyridine.

A more convenient method of preparing the *N*-(2-bromoethyl) compounds by the action of hydrobromic acid on *N*-aryl-2-oxazolidones[20] was discovered late in this work. The *N*-(*p*-acetylphenyl)-2-oxazolidone was easily converted to the corresponding *N*-(2-bromoethyl) compound by using 48% hydrobromic acid.

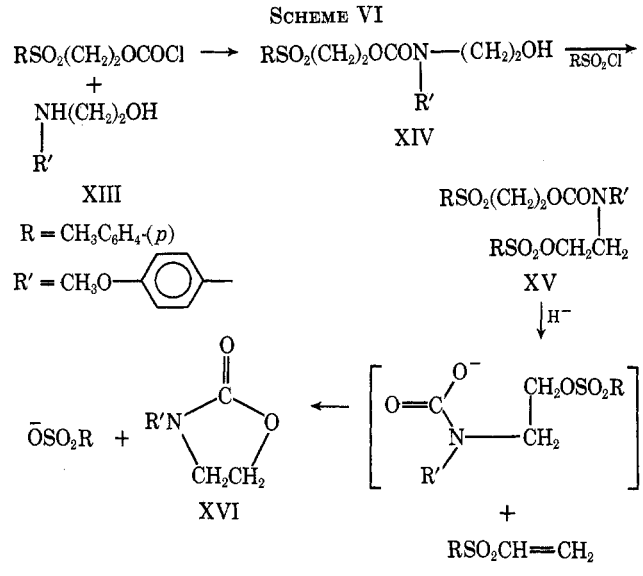
A Novel Synthesis of an *N*-Aryl-2-oxazolidone.—The preparation of 2-oxazolidones has been achieved by several methods.[21] Of general application has been the reaction of a 2-amino alcohol with carbonic acid derivatives and the base-induced cyclization of a 2-haloalkyl carbonate. The formation of the carboxylate ion XI (Scheme V) during the base-induced removal of the

SCHEME V



2-*p*-tolylsulfonylethoxycarbonyl group X used for the protection of amines[22] suggested a novel way for the preparation of 2-substituted 2-oxazolidones. Thus, a suitably substituted ethylamino compound (X) would undergo base-induced cyclization to yield a 3-substituted 2-oxazolidone (XII). This method was used to prepare *N*-(*p*-methoxyphenyl)-2-oxazolidone. The *N*-(2-hydroxyethyl)-*p*-anisidine (XIII) was allowed to react with 2-*p*-tolylsulfonylethyl chloroformate to yield *N*-(2-hydroxyethyl)-*N*-(2-*p*-tolylsulfonylethoxycarbonyl)-*p*-anisidine (XIV); treatment of XIV with *p*-toluenesulfonyl chloride gave the tosylate XV, which, upon treatment with sodium hydride, yielded *N*-(*p*-methoxyphenyl)-2-oxazolidone (XVI) (Scheme VI).

SCHEME VI



Experimental Section

Melting points and boiling points are uncorrected. All infrared spectra were obtained on a Perkin–Elmer Model 337 spectrophotometer.[23] The nmr spectra were run on a Varian Associates Model A-60A in solutions as indicated with respect to TMS. Unless otherwise indicated, reagents and solvents were used as received. Microanalyses were carried out by the Huffman Laboratories, Inc., Wheatridge, Colo., and by the Midwest Microlab Inc., Indianapolis, Ind.

Preparation of *N*-Arylaziridines.—The procedure for the preparation of *N*-(*p*-nitrophenyl)aziridine will be given in detail. The pertinent data for the other aziridines are given in Table I. When the acid salts of the anilines were used, 2 equiv of sodium hydride was employed.

***N*-(*p*-Nitrophenyl)aziridine.**—To a flame-dried 500-ml three-necked flask equipped with a drying tube, mechanical stirrer, and argon inlet adapter was added 100 ml of dry DMSO (percolated through alumina and stored over molecular sieve) and 5.04 g (0.21 mol, 8.69 g of a 58% mineral oil dispersion) of sodium hydride. The flask was placed in an oil bath at room temperature and 67.7 g (0.2 mol) of *N*-(2-tosyloxyethyl)-*p*-nitroaniline in 150 ml of DMSO was added dropwise with stirring. When the vigorous evolution of hydrogen had ceased, the flask was heated to 40°. A spot test using 4-(*p*-nitrobenzyl)pyridine[24] was developed to follow both the disappearance of the tosylate and the appearance of the aziridine.

A. Procedure for Tosylate (or Displaceable Halide).—(1) Spot a piece of filter paper with a drop of reaction mixture. (2) Spray paper until wet with a 2% solution of 4-(*p*-nitrobenzyl)-pyridine in acetone. (3) Heat with a stream of warm air (heat gun) for 1–2 min. (4) Spray with a 1.0 *M* solution of sodium carbonate.

B. Procedure for Aziridine.—(1) Repeat steps 1 and 2. (2) Spray with a 1.0 *M* solution of *p*-toluenesulfonic acid. (3) Repeat steps 3 and 4.

A positive test is the development of a blue spot. When the spot test for the tosylate had become negative, the reaction was stopped (about 4 hr). After cooling, the mixture was slowly poured into a separatory funnel containing ice-cold ether (300 ml) and 0.1 *M* NaOH (500 ml). After mixing, the aqueous layer was removed and the ether solution was extracted with 0.1 *M* NaOH (four 200-ml portions), washed with saturated NaCl

(20) T. F. Wood, *Chem. Abstr.*, **47**, 11255*i* (1953).
(21) R. C. Elderfield, "Heterocyclic Compounds," Vol. 5, Wiley, New York, N. Y., 1957, pp 396–400.
(22) A. T. Kader and C. J. M. Stirling, *J. Chem. Soc.*, 258 (1964).
(23) Mention of a proprietary product or company name does not necessarily imply endorsement of product or name by the USDA.
(24) J. G. Pomonis, R. F. Severson, and P. J. Freeman, *J. Chromatog.*, **40**, 78 (1969).

TABLE I

PROPERTIES OF AZIRIDINES AND AZIRIDINE PRECURSORS[a]

No.	R	Bp, °C (mm), or mp, °C	Yield, %	n_D (°C)	Ir, cm^{-1}	Nmr chemical shift, δ (in CCl_4 except where noted)
		CH_2 / CH_2 — NC_6H_4R-(*p*)				
1	H	80.5–81 (17) [lit.[b] 70–70.5 (13)]	78			
2	NO_2	83–83.5	85		KBr, ν 3075, 3000 (CH_2); 1320.6 (CN)	2.17 (s, 4, CH_2CH_2)
3	CN	84–85	77		KBr, ν 3071, 2944 (CH_2); 1336, 1339 (CN)	2.11 (s, 4, CH_2CH_2)
4	F	85–86 (18) [lit.[c] 73–74 (15)]	76			
5	Br	76.5–77 (0.27)	86	1.5828 (23.5)	CCl_4, ν 3067, 2995 (CH_2); 1317 (CN)	1.98 (s, 4, CH_2CH_2)
6	Cl	63.5–64 (0.28)	86	1.5652 (25)	CCl_4, ν 3067, 2997 (CH_2); 1326.2 (CN)	1.98 (s, 4, CH_2CH_2)
7	CH_3O	63–63.5 (0.42)	70	1.5507 (25)	CCl_4, ν 3066, 2993 (CH_2); 1294 (CN)	1.90 (s, 4, CH_2CH_2); 2.19 (s, 3, OCH_3)
8	CH_3	62.5–63 (2.8) [lit.[b] 76–77 (8)]	78			
9	CH_3CO	70–71	43		CCl_4, ν 3068, 2976 (CH_2); 1333.1 (CN)	2.08 (s, 4, CH_2CH_2); 2.42 (s, 3, $COCH_3$)
10	H, 2-d_2	80–81 (18)	44	1.552 (21)	CCl_4, ν 3060, 2990 (H); 2310, 2170 (D); 1320 (CN)	1.95 (s, 2, CH_2CD_2)
		$CH_3C_6H_4SO_2OCH_2CH_2NHC_6H_4R$-(*p*)				
11	NO_2	128.5–130.5	90		KBr, ν 3400 (NH); 1365, 1183 (SO); 1015 (COS)	DMSO-d_6, 2.33 (s, 3, CH_3); 3.48 (t, 2, J = 5.0 Hz, CH_2N); 4.17 (t, 2, J = 5.0 Hz, CH_2O); 7.26 (broad s, 1, NH)
12	CN	104.5–106	63		KBr, ν 3410 (NH); 1345, 1179 (SO); 1010 (COS)	$CDCl_3$, 2.41 (s, 3, CH_3); 3.41 (t, 2, J = 5.5 Hz, CH_2N); 4.18 (t, 2, J = 5.5 Hz, CH_2O); 4.53 (s, 1, NH)
		$[XCH_2CH_2NH_2C_6H_4R$-(*p*)$]^+X^-$				
	R	X	Mp, °C	Yield, %	Ir, cm^{-1}	Nmr chemical shift, δ (in DMSO-d_6 and acetone-d_6)
13	CH_3O	Cl	157–160	80	KBr, ν 2450–2910 (NH_2^+) and 778 (CCl)	DMSO-d_6, 3.62 (t, 2, J = 5.2 Hz, CH_2N); 3.79 (s, 3, OCH_3); 3.95 (t, 2, J = 5.2 Hz, CH_2Cl); 7.66 (broad s, 2, $-NH_2^+$)
14	H	Br	134–137 (lit.[d] 136–139)	54		
15	CH_3	Br	180.5–182 (lit.[b] 180–181)	72		
16	F	Br	128–130 (lit.[c] 128.5–129)	45		
17	Br	Br	149.5–151	34	KBr, ν 2440–2920 (NH_2^+) and 570 (CBr)	DMSO-d_6, 3.55 (t, 4, CH_2CH_2) and 7.73 (s, 2, NH_2)
18	Cl	Br	151–153	47	KBr, ν 2440–2920 (NH_2^+) and 570 (CBr)	Acetone-d_6, 3.98 (s, 4, CH_2CH_2) and below 12.0 (s, 2, NH_2)
19	CH_3CO	Br	165–166.5	23	KBr, ν 2440–2910 (NH_2^+) and 565 (CBr)	DMSO-d_6, 2.42 (s, 3, CH_3CO); 3.60 (s, 4, CH_2CH_2Br); 6.65 (w, 2, NH_2)

[a] Satisfactory analytical values (±0.30% for C, H, and N) were reported for the following new compounds, namely **2**, **3**, **5–7**, **9**, **11–13**, and **18**. Satisfactory analytical values for sulfur or halogen were reported for **5**, **6**, **11–13**, and **18** (for chlorine). Ed. Calcd for **17**: C, 26.29; Br, 66.61. Found: C, 27.68; Br, 65.92. Calcd for **19**: C, 37.18; Br, 49.48. Found: C, 38.02; Br, 48.81. [b] Reference 8. [c] Reference 11. [d] Reference 10.

(200 ml), and dried (anhydrous Na_2SO_4). The ether solution was treated with charcoal and filtered, and the solvent was removed under reduced pressure to yield an oily solid. The solid was washed with petroleum ether (bp 30–60°) and recrystallized from CCl_4 to yield 27.2 g (0.17 mol, 85%), mp 83–83.5°, of the aziridine.

Preparation of 2-Arylaminoethyl-*p*-toluenesulfonates. *N*-(2-Tosyloxyethyl)-*p*-nitroaniline.—A solution of 57.3 g (0.3 mol) of *N*-(2-hydroxyethyl)-*p*-nitroaniline in 200 ml of dry pyridine was placed in an ice–salt bath and allowed to cool. Freshly purified *p*-toluenesulfonyl chloride was added with stirring at such a rate that the reaction temperature never exceeded −5°. When the

TABLE II

2-ARYLAMINOETHANOLS

No.	Compd	Method	Yield, %	Bp, °C (mm), or mp, °C
20	*N*-(2-Hydroxyethyl)aniline	1[a]	98	150–152 (10)
21	*N*-(2-Hydroxyethyl)-*p*-nitroaniline	2[b]	38	109–110 (lit.[b] 110–111)
22	*N*-(2-Hydroxyethyl)-*p*-aminobenzonitrile	3[c]	46	91–92 (lit.[d] 92.5–93)
23	*N*-(2-Hydroxyethyl)-*p*-fluoroaniline	3[c]	70	117–119 (0.15) [lit.[e] 145–146 (2.5)]
24	*N*-(2-Hydroxyethyl)-*p*-bromoaniline	3[c]	62	79–81 (lit.[f] 93)
25	*N*-(2-Hydroxyethyl)-*p*-chloroaniline	3[c]	74	76–77 (lit.[b] 77–77.5)
26	*N*-(2-Hydroxyethyl)-*p*-methoxyaniline	3,[c] 4[g]	92	40–50 bp 150–152 (0.15) [lit.[h] 188–191 (8)]
27	*N*-(2-Hydroxyethyl)-*p*-toluidine	3[c]	45	130–132 (0.36) [lit.[i] 155–157 (8)]
28	*N*-(2-Hydroxyethyl)-*p*-aminoacetophenone	3[c]	22	105–107
29	*N*-(2-Hydroxyethyl-2-d_2)aniline	1[a]	98	

[a] Method 1 (Scheme IV): reduction of *N*-arylglycine ethyl ester. [b] Method 2: reaction of ethanolamine and *p*-nitrochlorobenzene (ref 15). [c] Method 3 (Scheme I): reaction of arylamine and 2-chloroethanol or 2-bromoethanol (ref 8). [d] A. Purenas and J. Degutis, *Kauno Politech. Inst. Darb.*, **6**, 191 (1957); *Chem. Abstr.*, **54**, 5551*f* (1960). [e] Reference 11. [f] F. B. Dains, *J. Amer. Chem. Soc.*, **47**, 1981 (1925). [g] Method 4 (Scheme III): reaction of *N*-aryloxazolidone with $LiAlH_4$ or KBH_4. [h] References 13, 14. [i] Reference 8.

addition was complete, the reaction mixture was allowed to stir for 2 hr. During this time it was warmed to 0°. The mixture was poured into 500 ml of ice–water containing 0.3 mol of potassium carbonate. The crude product was collected, washed with cold water, and dried under vacuum. The tosylate was recrystallized from 1:4 absolute ethanol–benzene to yield 90 g of product (0.27 mol, 90%), mp 128.5–130.5°. *N*-(2-Tosyloxyethyl)-*p*-aminobenzonitrile was prepared by a similar method.

Preparation of 2-Arylaminoethyl Halides. *N*-(2-Chloroethyl)-*p*-anisidine Hydrochloride.—A flask containing 100 ml of dry dimethylformamide (DMF), which had been percolated through alumina and stored over molecular sieve, and 50 g (0.3 mol) of *N*-(2-hydroxyethyl)-*p*-anisidine under argon was placed in an ice bath. Dry HCl gas was bubbled through the solution for a few minutes and then 53.4 g (0.45 mol) of freshly distilled thionyl chloride was added slowly with stirring. When the addition was complete, the ice bath was removed and the solution was stirred at room temperature for 3 hr. The mixture was poured into 300 ml of $CHCl_3$ and extracted with saturated NaCl (three 300-ml portions). The solvent was removed under reduced pressure to yield a solid hydrochloride. The solid amine hydrochloride was recrystallized from hot 5:1 chloroform–hexane to yield 53.7 g (0.24 mol), 80%, mp 157–160°.

Most of the 2-arylaminoethylbromide hydrobromides were prepared by the action of hot 48% HBr on the corresponding 2-arylaminoethanol according to Pearlman's procedure.[19]

***N*-(2-Bromoethyl)-*p*-aminoacetophenone.**—A 200-ml portion of 48% HBr was heated to approximately 80°, and 12.3 g (0.06 mol) of *N*-acetylphenyl)-2-oxazolidone was added at such a rate that time was allowed for the previously added portion to dissolve. The mixture was concentrated to 100 ml on the steam bath, and the residual acid was removed under reduced pressure to yield a red mass. The solid was neutralized with 5% sodium carbonate and extracted into ether (three 150-ml portions). The ether extract was washed with 5% sodium carbonate solution and saturated NaCl and dried, and the solvent was removed to yield a black solid. The solid was recrystallized from warm CCl_4 to yield 11.0 g (0.046 mol, 77%) of the amine, mp 89–93°. The product should be used immediately, since it decomposes to a tar upon standing. The hydrobromide was prepared by reaction of the alcohol and 48% HBr.[19] Its physical properties are listed in Table I.

Preparation of 2-Arylaminoethanols.—The 2-arylaminoethanols were prepared, unless otherwise indicated, by reacting 1 equiv of the aniline and 2 equiv of 2-chloroethanol according to the procedure of Heine, *et al.*[8] Yields and methods of preparation are summarized in Table II. The preparation of *N*-(2-hydroxyethyl)-*p*-aminoacetophenone is given in detail.

***N*-(2-Hydroxyethyl)-*p*-aminoacetophenone.**—Ten grams (0.074 mol) of *p*-aminoacetophenone, 9.75 g (0.078 mol) of 2-bromoethanol, and 12.1 g (0.1 mol) of *N*,*N*-dimethylaniline were heated with stirring under argon at 60° for 20 hr. The mixture was neutralized with K_2CO_3 and steam distilled to remove the *N*,*N*-dimethylaniline. The residue was extracted with $CHCl_3$ and the solvent was removed to yield an oil which solidified upon standing. The mixture was separated by column chromatography, using 15 g of Woelm basic aluminum oxide activity grade one per gram of mixture. After elution with 220 ml of ether, all of the *p*-aminoacetophenone had been removed from the column. At 270 ml the product appeared, and it was eluted off with 2:1 chloroform–absolute ethanol. The solvent was removed and the resulting solid was recrystallized from hot benzene to give a 22% yield of product: mp 105–107°; ir (KBr) 3280 (OH), 3370 (NH), and 1072 cm^{-1} (CO); nmr ($CDCl_3$) 2.48 (s, 3, CH_3O), 3.33 (t, 2, J = 5.8 Hz, NCH_2–), 3.85 (t, 2, J = 5.8 Hz, CH_2O), 4.22 (broad s, 1, OH), 4.75 (broad s, 1, NH), 6.56 [d, 2, J = 9.0 Hz, $(CH)_2N$], and 7.79 ppm [d, 2, J = 9.0 Hz, $(CH_2)_2CO$].

Anal. Calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found: C, 67.29; H, 7.37; N, 7.84.

Reduction of 3-(*p*-Methoxyphenyl)-2-oxazolidone.—A solution of 0.1 g (5.2×10^{-4} mol) of 3-(*p*-methoxyphenyl)-2-oxazolidone in 5 ml of dry tetrahydrofuran was added dropwise to 0.01 g (2.6×10^{-4} mol, 1 equiv of hydride) of $LiAlH_4$ in 5 ml of tetrahydrofuran at 0°. The reaction was protected from moisture by means of a drying tube and from the atmosphere by passing through a stream of argon.

The reaction mixture was stirred at 0° for 3 hr. The reaction mixture was hydrolyzed with H_2O and a solution of 5,5-dimethylcyclohexane-1,3-dione (2 equiv) was added in 10 ml of 50% ethanol. A drop of piperidine was added, and the mixture was heated until all of the tetrahydrofuran was removed. The mixture was then placed in an ice bath, and the crystals formed were collected to yield 0.2 equiv of the formaldehyde derivative, mp 188° after two recrystallizations from 50% ethanol (lit.[17] 189°). The mother liquor was extracted with ether, the organic layer was washed with saturated NaCl and dried with anhydrous Na_2SO_4, and the solvent was removed under reduced pressure to yield an oil. A study of nmr, ir, and thin layer chromatography (basic alumina) indicated almost complete conversion of the oxazolidone to *N*-(2-hydroxyethyl)-*p*-anisidine. A similar experiment with $LiBH_4$ gave comparable results except that no attempt was made to isolate the formaldehyde.

Preparation of *N*-Aryl-2-oxazolidones. *N*-[(2-Chloroethoxy)carbonyl]-*p*-aminoacetophenone.—A 97% yield of this compound was prepared according to the method of Najen[25] using $CHCl_3$ as the reaction solvent. The solid product was crystallized from hot benzene, mp 125–128° (lit.[25] 127°).

***N*-(*p*-Acetylphenyl)-2-oxazolidone.**—Dry acetone (100 ml) and 13.1 g (0.054 mol) of *N*-[(2-chloroethoxy)carbonyl]-*p*-aminoacertophenone were placed in an oil bath at room temperature under argon. Sodium hydride (2.32 g, 0.057 mol of 58% mineral oil dispersion) was added at such a rate that time was allowed for the vigorous reaction accompanying the previous addition to subside. The resulting mixture was poured into ice-cold H_2O and placed in the cold. The crystals which had formed were collected and dried to yield 10.7 g (0.052 mol, 98%) of the product, mp 149.5–150.5° (lit.[25] 152°).

(25) H. Najen, P. Chabrien, R. Giudicelle, and P. Mobille, *Bull. Soc. Chim. Fr.*, 471 (1957).

N-(2-Hydroxyethyl)-*N*-(2-*p*-tolylsulfonylethoxycarbonyl)-*p*-anisidine.—A solution of 10.6 g (0.06 mol) of *N*-2-hydroxyethyl-*p*-anisidine and 6.08 g (0.03 mol) of freshly distilled triethylamine in 40 ml of $CHCl_3$ (purified by percolating through anhydrous alumina) were cooled to 0° in an ice bath (the flask was protected against moisture by means of a drying tube). A solution of 13.75 g (0.06 mol) of 2-(*p*-tolylsulfonyl)ethylchloroformate[22] in 25 ml of $CHCl_3$ was added dropwise with stirring. When addition was complete, the ice bath was removed, and the mixture was stirred at room temperature for 2 hr. With the addition of 50 ml of ethyl ether, a solid formed, and the triethylamine hydrochloride that precipitated was removed. The organic layer was extracted with 5% HCl (three 150-ml portions), washed with 5% $NaHCO_3$, and dried ($NaSO_4$), and the solvent was removed under reduced pressure to yield an oil (XIV), 19.44 g (0.05 mol, 83%). All attempts to crystallize the product failed: ir (neat, KBr) 3490 (OH), 1720 (C=O), and 1320, 1290, and 1420 cm^{-1} (SO_2); nmr ($CDCl_3$) 2.43 (s, 3, CH_3), 3.52 (broad s, 1, OH), 3.39 (t, 2, J = 6 Hz, $-SO_2CH_2$), 3.72 (broad s, 4 NCH_2CH_2O), 3.79 (s, 3, $-OCH_3$), 4.39 ppm (t, 2, J = 6 Hz, CH_2OCO).

N-(2-Tosyloxyethyl)-*N*-(2-tolylsulfonylethoxycarbonyl)-*p*-anisidine.—A solution of 19.4 g (0.05 mol) of XIV (crude oil) in 10 ml of anhydrous pyridine was cooled to 0° in an ice bath. A solution of 9.88 g (0.053 mol) of *p*-toluenesulfonyl chloride was added slowly with stirring and cooling. The mixture was placed in the refrigerator overnight and then poured into 200 ml of cold 1 *N* HCl and extracted with 20 ml of $CHCl_3$. The $CHCl_3$ was washed with 1 *N* HCl (three 150-ml portions) and dried (sodium sulfate), and the solvent was removed under reduced pressure to yield an oil. The oil was placed under vacuum for 10 hr to yield 25.3 g (0.049 mol, 98%) of product XV.

After 2 months, a small amount of product crystallized from benzene. The product, as analyzed by nmr, formed approximately a 1:1 compound with benzene, mp 80–81°. Drying at 75° under high vacuum removed most of the benzene, mp 104–105.5°. An acceptable analysis could not be obtained: ir (KBr) 1720 (C=O), 1320, 1290, and 1140 (SO_2 in SO_2CH_2) and 1370 and 1175 cm^{-1} (SO_2 in SO_2O); nmr (acetone) 2.29 (s, 3, *p*-CH_3–), 2.39 (s, 3, *p*-CH_3–), 3.54 (t, 2, J = 6.4 Hz, $-SO_2CH_2$), 3.64 (t, 2, J = 5.5 Hz, $-NCH_2$), 3.78 (s, 3, *p*-CH_3O–), 4.38 (t, 2, J = 6.4 Hz, $-CH_2OCO$), 4.42 ppm (t, 2, J = 5.5 Hz, $-CH_2CH_2OSO_2$).

3-(*p*-Methoxyphenyl)-2-oxazolidone.—To a solution of 24 g of crude XV in 60 ml of dry THF at 0° under argon, 2.08 g of a 58% NaH mineral oil dispersion (equivalent to 0.05 mol of hydride) was added slowly with stirring and cooling. When addition was complete, the ice bath was removed, and the mixture was stirred at room temperature for 2 hr. The sodium *p*-toluenesulfonate that had precipitated was removed by filtration and the solvent was removed under reduced pressure to yield an oily solid. The solid was recrystallized from benzene to yield 8.7 g (0.045 mol, 91%) of the oxazolidone: mp 108–109° (lit.[26] 109–110);[26] ir (KBr) 1740 cm^{-1} (C=O); nmr (acetone-d_6) 3.80 (s, 3, OCH_3 and 4.28 ppm (m, 4, CH_2CH_2–).

Registry No.—**2**, 30855-79-9; **3**, 30855-80-2; **5**, 30855-81-3; **6**, 28192-05-4; **7**, 27347-09-7; **9**, 30855-84-6; **10**, 30855-85-7; **11**, 30855-86-8; **12**, 30855-87-9; **13**, 27347-07-5; **17**, 30858-75-4; **18**, 23482-29-3; **19**, 30858-77-6; **20**, 122-98-5; **28**, 30858-79-8; XIV, 30858-80-1; XV, 30858-81-2 *N*-(2-tosyloxyethyl)-*p*-nitroaniline, 30855-86-8; *N*-(2-chloroethyl)-*p*-anisidine HCl, 27347-07-5; 3-(*p*-methoxyphenyl)-2-oxazolidone, 5198-48-1.

(26) A. F. McKay and R. V. Braun, *J. Org. Chem.*, **16**, 1829 (1951).

Aziridines. XXIV. Reactions of Derivatives of 2-Vinylaziridine

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1-(*p*-Nitrocarbobenzoxy)-2-vinylaziridine (**1**) was converted in refluxing decalin into predominantly 1-*p*-nitrocarbobenzoxy)-2-pyrroline (**2**) along with some 1-(*p*-nitrocarbobenzoxy)-3-pyrroline. Reaction of 2-vinylaziridine with phenyl isothiocyanate in ether at 0° gave 2-anilino-4,7-dihydro-1,3-thiazepine (**6**). 2-(*p*-Chlorophenyl)-4,7-dihydro-1,3-thiazepine (**7**) was formed when 2-vinylaziridine was treated with *p*-chlorothiobenzoylthioglycolate.

Previous studies on the thermolysis of aziridines bearing an unsaturated group on the 1 position and a vinyl group on the 2 position of the ring have demonstrated that such compounds undergo ring expansion to either seven-membered or five-membered rings. Thus, 1-[1,2-bis(trifluoromethyl)]vinyl-2-vinylaziridine, 1-*p*-bromophenyl-2-isopropenylaziridine, and 1-*p*-nitrobenzoyl-2-vinylaziridine isomerized upon heating into the seven-membered ring systems, 2,3-bistrifluoromethyl-3,4-dihydro-7*H*-azepine,[1] 7-bromo-4-methyl-2,5-dihydro-1*H*-1-benzazepine,[2] and 2-*p*-nitrophenyl-4,7-dihydro-1,3-oxazepine,[3] respectively. On the other hand, 1-carbethoxy-2-methyl-2-vinylaziridine when subjected to gas chromatography at 100° rearranged into 1-carbethoxy-3-methyl-3-pyrroline.[4] Various 3-(2-vinylaziridinyl)benzoxazolinones although not substituted at the 1 position of the aziridine ring with an unsaturated moiety also, when heated in decalin, rearrange to 3-pyrrolines.[5]

(1) E. L. Stogryn and S. J. Brois, *J. Amer. Chem. Soc.*, **89**, 605 (1967).
(2) P. Scheiner, *J. Org. Chem.*, **32**, 2628 (1967).
(3) P. G. Mente, H. W. Heine, and G. R. Scharoubim, *ibid.*, **33**, 4547 (1968).
(4) A. Mishra, S. N. Rice, and W. Lwowski, *ibid.*, **33**, 481 (1968).

In this paper several new examples of ring expansions of 2-vinylaziridine derivatives into five-membered and seven-membered ring systems are reported. We wish to describe first the thermolysis of 1-(*p*-nitrocarbobenzoxy)-2-vinylaziridine (**1**) in decalin. In contrast to the gas chromatographic behavior of 1-carbethoxy-2-methyl-2-vinylaziridine which rearranges to a 3-pyrroline,[4] compound **1** rearranges predominantly to 1-(*p*-nitrocarbobenzoxy)-2-pyrroline (**2**).

We also wish to describe the reactions of 2-vinylaziridine with phenyl isothiocyanate and sodium *p*-chlorothiobenzoylthioglycolate. Presumably in these reactions 1-thiocarboxanilide-2-vinylaziridine and 1-(*p*-chlorothiobenzoyl)-2-vinylaziridine form and spontaneously isomerize to 4,7-dihydro-1,3-thiazepines.

Results and Discussion

Thermolysis of **1** in refluxing decalin resulted in a mixture of 1-(*p*-nitrocarbobenzoxy)-2-pyrroline (**2**) and 1-(*p*-nitrocarbobenzoxy)-3-pyrroline (**3**) in overall yields of 63–75% (Scheme I).

(5) (a) R. S. Atkinson and C. W. Rees, *Chem. Commun.*, 1232 (1967); (b) R. S. Atkinson and C. W. Rees, *J. Chem. Soc. C*, 778 (1969).