**quinoxaline (27a).**—A mixture of 3.00 g of **9** and 1.40 g of *p*-nitrobenzaldehyde in 70 ml of dry toluene was refluxed with vigorous stirring for 75 min. Most of the solvent was evaporated and the residue was treated with a small amount of 95% EtOH. The mixture was filtered to give 3.46 g (79.7%) of **27a**. Four recrystallizations from $CH_3CN$ gave **27a** decomposing at 178–181° with considerable darkening of **27a** near the decomposition point.

*Anal.* Calcd for $C_{28}H_{20}N_4O_5$: C, 68.29; H, 4.09; N, 11.37. Found: C, 68.05; H, 4.26; N, 11.54.

**1,2-Dihydro-1,2,4-triphenyl-3aH-oxazolo[3,2-*a*]quinoxaline (28).**—A mixture of 1.00 g of **11** and 0.358 g of benzaldehyde in 30 ml of toluene was refluxed with stirring for 1 hr. The solvent was evaporated and the oily residue was induced to crystallize by warming in 95% EtOH. Filtration gave 0.390 g (29%) of **28**. Recrystallization three times from $CH_3CN$ gave **28**, mp 151.6 dec.

*Anal.* Calcd for $C_{28}H_{22}N_2O$: C, 83.55; H, 5.51; N, 6.96. Found: C, 83.68; H, 5.53; N, 7.03.

**1,2-Dihydro-1-(*p*-nitrophenyl)-2,4-diphenyl-3aH-oxazolo[3,2-*a*]quinoxaline (29).**—A mixture of 3.00 g of **9** and 1.40 g of benzaldehyde in 70 ml of dry toluene was refluxed with vigorous stirring for 90 min. The reaction mixture was worked up as for **28** to give 2.33 g (59%) of **29**. Recrystallization once from toluene and thrice from $CH_3CN$ gave **29**, mp 178–180°.

*Anal.* Calcd for $C_{28}H_{21}N_3O_3$: C, 75.15; H, 4.73; N, 9.39. Found: C, 74.75; H, 4.95; N, 9.68.

**6a,6b,12b,13-Tetrahydro-13-*p*-nitrophenyl-6-phenylacenaphtho[1′,2′:3,4]pyrrolo[1,2-*a*]quinoxaline (19).**—A mixture of 2.05 g of **9** and 1.00 g of acenaphthylene in 50 ml of dry toluene was refluxed for 1 hr with vigorous stirring. The reaction mixture was cooled and filtered to give 2.06 g of crude **19**. Five crystallizations from *p*-xylene gave **19** decomposing at 231–233°. The product darkens considerably near the decomposition point. This reaction was also carried out in 1-propanol with comparable yields.

*Anal.* Calcd for $C_{33}H_{23}N_3O_2$: C, 80.31; H, 4.70; N, 8.51. Found: C, 80.45; H, 4.79; N, 8.25.

**Preparation of 6a,6b,12b,13-tetrahydro-6,13-diphenylacenaphtho[1′,2′:3,4]pyrrolo[1,2-*a*]quinoxaline** was prepared the same way as **19** with 0.592 g of **11**, 0.304 g of acenaphthylene in 10 ml of toluene. Recrystallization of the product from 50:50 EtOH–$C_6H_6$ gave material decomposing at 207–210°. A molecular weight determination by mass spectroscopy gave a value of 448.

*Anal.* Calcd for $C_{33}H_{24}N_2$: C, 88.36; H, 5.39; N, 6.25. Found: C, 88.31; H, 5.35; N, 6.16.

**Hydrolysis of 6 to *p*-Nitrobenzyl Phenyl Diketone.**—To 5 ml of cold concentrated $H_2SO_4$ was added 300 mg of **6**. The mixture was poured over 200 g of ice and allowed to stand overnight and filtered. A yield of 0.261 (94.7%) of the diketone was obtained. It was converted into **12** by reaction with *o*-phenylenediamine. The hydrolysis of **7** and **8** were carried out analogously and the resulting $\alpha$ diketones reacted with *o*-phenylenediamine to give the known quinoxalines **30** and **31**.

**Registry No.**—**6**, 18039-27-5; **7**, 18039-28-6; **8**, 18039-29-7; **9**, 18039-30-0; **10**, 18039-31-1; **11**, 18039-32-2; **12**, 18039-33-3; **14**, 18039-34-4; **16**, 18039-35-5; **17**, 18067-01-1; **18**, 18039-36-6; **19**, 18067-02-2; **27a**, 18039-37-7; **28**, 18039-38-8; **29**, 18039-39-9; **30**, 18039-40-2; 6a, 6b, 12b, 13-tetrahydro-6,13-diphenylacenaphtho[1′,2′,3,4]pyrrolo[1,2-*a*]quinoxaline, 18039-41-3.

**Acknowledgment.**—We thank Professor Den-Itsu Shiho of the University of Toyama for a copy of the infrared spectrum of compound **15**, Cecil C. Langham of the Chemical Abstracts Service for assistance in nomenclature and the National Institutes of Health for Grant CA-10015.

# 1,2,3-Oxathiazolidines—a New Heterocyclic System[1]

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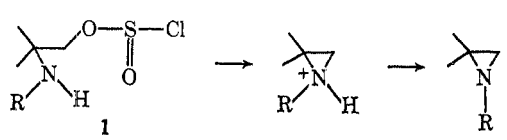
*Received August 2, 1968*

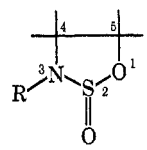
The reactions of $\beta$-amino alcohols with thionyl chloride in the presence of base leads to 2-oxo-1,2,3-oxathiazolidines (a previously unreported heterocyclic system) in good to excellent yields. Evidence is presented for the general structure of these compounds. The existence of the asymmetry at sulfur in these compounds is discussed and the anisotropic nature of the S–O bond is used to assign stereochemistry.

The conversion of $\beta$-amino alcohols to $\beta$-haloamines followed by base-catalyzed cyclization (Gabriel synthesis) constitutes one of the more useful routes to aziridines.[2] Our desire to develop milder routes to functionally substituted aziridines has prompted us to investigate alternative techniques for ring closure of amino alcohols. A possible modification of the Gabriel synthesis consisted of the reaction of amino alcohols with thionyl chloride in the presence of base. Our hope was that conditions could be derived which would be favorable to initial formation of a chlorosulfite ester (**1**) and its subsequent intramolecular decomposition to an aziridine.



**1**

We have prepared a variety of amino alcohols which have bulky or electron-withdrawing groups on nitrogen. These compounds were treated with thionyl chloride in the presence of tertiary amines in nonpolar solvents. The products from these reactions clearly did not correspond to the desired aziridines. In each case, elemental and mass spectral analysis revealed that the products contained, in addition to those atoms expected for the aziridine, the elements of $SO_2$. We have assigned to these products the 2-oxo-1,2,3-oxathiazolidine structure (**2**). This structure constitutes



**2**

the first example of the 1,2,3-oxathiazolidine heterocyclic ring system.[3,4] For this reason we would like to

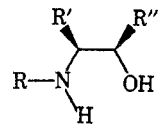
(1) Support of this work by the National Science Foundation Grants GP-5531 and GP-8044 is gratefully acknowledged.

(2) P. E. Fanta in "Heterocyclic Compounds with Three- and Four-Membered Rings," Part 1, A. Weissberger, Ed., Interscience Publishers, New York, N. Y., 1964, p 528.

(3) McCombie and Parkes reported the preparation of 2-oxo-1,2,3-oxathiazoles (the unsaturated analog of **2**) from thionyl chloride and certain $\alpha$-amino ketones.[4]

(4) H. McCombie and J. W. Parkes, *J. Chem. Soc.*, **101**, 1991 (1912).

TABLE I
AMINO ALCOHOLS



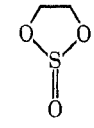
| Compd no. | Method | R | R′ | R″ | Time, hr | Temp, °C | Yield, % | Bp (mm) or mp, °C | Mol wt[a] | Calcd, % C | Calcd, % H | Calcd, % N | Found, % C | Found, % H | Found, % N |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **3** | B | *t*-Bu | H | H | 20 | 25 | 77 | 42–43 | 117 | *b* | | | | | |
| **4** | B | *t*-Bu | H | $CH_3$ | 20 | 25 | 84 | 58 (2.5) | 131 | *c* | | | | | |
| **5** | A | *t*-Bu | $CH_3$ | H | 20 | 25 | 93 | 40–42 | 131 | *d* | | | | | |
| **6** | B | *t*-Bu | H | $C_6H_5$ | 5 | 65 | 65 | 86–87 | 193 | 74.59 | 9.90 | 7.24 | 74.33 | 9.84 | 7.38 |
| **7** | A | *t*-Bu | $C_6H_5$ | H | 20 | 25 | 87 | 61–62 | 193 | 74.59 | 9.90 | 7.24 | 74.71 | 10.06 | 7.11 |
| **8** | B | *t*-Bu | H | $(C_6H_5)_2$ | 48 | 65 | 91 | 99–100 | 269 | 80.25 | 8.60 | 5.20 | 80.52 | 8.47 | 5.35 |
| **9** | A | Ph | Ph | $CO_2Et$ | | | | 73–74 | 285 | *e* | | | | | |
| **10** | A | 3-*t*-Butylaminopropanol | | | 3 | 35 | 89 | 67–69 | 131 | *g* | | | | | |

[a] Molecular weight determinations were made by analysis of the mass spectra. [b] S. J. Childress, M. G. Cordasco, O. J. Plekss, and L. Reiner, *J. Amer. Chem. Soc.*, **76**, 3988 (1954); R. E. Holmen, *ibid.*, **73**, 1859 (1951). [c] J. L. Boivin, *Can. J. Chem.*, **36**, 1405 (1958). [d] H. Wollweber and R. Hiltmann, German Patent 1,176,152 (1964); *Chem. Abstr.*, **61**, P13192*e* (1964). [e] V. F. Martynov and G. Olman, *Zh. Obsch. Khim.*, **27**, 1881 (1957). The structure assigned by these authors on the basis of chemical degradation was R′ = $CO_2Et$, R″ = Ph. We have reversed this assignment because **9** shows a parent peak at *m/e* 182 ($PhCH{=}N^+HPh$). This structural reassignment removes the inconsistency which the reactions of aryl-substituted glycidic esters posed to the accepted mechanistic picture of epoxide reactions.[f] [f] A. Rosowsky in "Heterocyclic Compounds with Three- and Four-Membered Rings," Part I, A. Weissberger, Ed., Interscience Publishers, New York, N. Y., 1964, p 323. [g] v. F. Wille, L. Saffer, and W. Weisskopf, *Ann. Chem.*, **568**, 34 (1950).

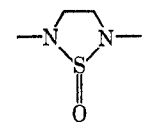
present the details of its preparation as well as evidence for its structure and stereochemistry. In future articles we shall describe additional aspects of the synthesis, structure and reactions of this and related heterocyclic systems.

The amino alcohols used in our study were prepared from the reactions of amines with epoxides (method A) and by lithium aluminum hydride reduction of α-amino esters (method B). The yields and physical properties of these amino alcohols are summarized in Table I.

The transformation of these amino alcohols to 2-oxo-1,2,3-oxathiazolidines was accomplished by their reaction with thionyl chloride in dry hexane or benzene. A slight excess of triethylamine or pyridine was used as the proton acceptor. The products of these reactions and their physical properties are indicated in Tables II and III. Evidence for the assignment of general structure **2** to these compounds was obtained from their mass spectra which revealed efficient loss of $SO_2$ from the molecular ion and its fragments. The absence of rearrangement in ring closure and additional support for structure **2** was obtained by acid-catalyzed hydrolysis of **15a** and **17** to their precursor amino alcohols **6** and **9**.[5] Cyclization of **1** to **2** is given additional credence by the similar formation of cyclic sulfites (**18**)[6] and 1-oxo-1,2,5-thiadiazolidines (**19**)[7]

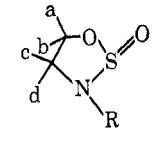


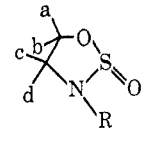
**18**



**19**

from the reaction of thionyl chloride with diols and diamines, respectively. An examination of Table II reveals that amino alcohols **4**, **5**, **6**, and **7** each yielded a pair of isomeric 2-oxo-1,2,3-oxathiazolidines. Existence of isomeric pairs requires that these heterocyclic compounds possess a noncarbon dissymmetric center. This conclusion is reinforced by the spectral properties of oxathiazolidines **11** and **16**. Although these compounds lack carbon asymmetry, their nmr spectra clearly reveal the magnetic nonequivalence of the two ring faces. Ample precedence exists for the configurational stability of trisubstituted sulfur. This precedence extends to the analogous cyclic sulfites **18**.[6] For this reason we ascribe this asymmetric nature of the 2-oxo-1,2,3-oxathiazolidines to asymmetry at sulfur. No evidence is available concerning the hybridization of nitrogen. Either planar or rapidly inverting tetrahedral geometry would be consistent with the failure to observe additional isomerism attributable to asymmetry at both nitrogen and sulfur.





It is possible to assign the substituent geometry of the isomeric pairs by means of nmr spectroscopy. The sulfoxide bond is known to have acetylenic-like anisot-

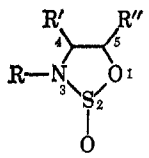
(5) In contrast to the acid lability, these compounds were quite stable to base (see Experimental Section). This observation suggests that these heterocyclic compounds might be useful as protective groups for amino alcohols.

(6) (a) H. F. van Woerden, C. F. van Valkenburg, and G. M. van Woerkom, *Rec. Trav. Chim. Pays-Bas*, **86**, 601 (1967); (b) H. F. van Woerden and E. Havinga, *ibid.*, **86**, 341, 353 (1967); (c) Y. Y. Samitov, *Dokl. Akad. Nauk SSSR*, **164**, 347 (1965); *Proc. Acad. Sci. USSR, Chem. Sect.*, **164**, 877 (1965); (d) P. B. D. de la Mare, W. Klyne, D. J. Millen, J. G. Pritchard, and D. Watson, *J. Chem. Soc.*, 1813 (1956); (e) C. A. Bunton, P. B. D. de la Mare, P. M. Greasely, D. R. Llewellyn, H. H. Pratt, and J. G. Tillett, *ibid.*, 4751 (1958); (f) C. A. Bunton, P. B. D. de la Mare, and J. G. Tillett, *ibid.*, 4754 (1958); (g) C. A. Bunton, P. B. D. de la Mare, A. Lennard, D. R. Llewellyn, R. B. Pearson, J. G. Pritchard, and J. G. Tillett, *ibid.*, 4761 (1958); (h) E. D. Davies and J. G. Tillett, *ibid.*, 4766 (1958); (i) J. G. Tillett, *ibid.*, 37 (1960); (j) J. G. Tillett, *ibid.*, 5138 (1960); (k) J. G. Pritchard and P. C. Lauterbur, *J. Amer. Chem. Soc.*, **83**, 2105 (1961); (l) W. W. Carlson and L. H. Cretcher, *ibid.*, **69**, 1952 (1947); (m) P. C. Lauterbur, J. G. Pritchard, and R. L. Vollmer, *J. Chem. Soc.*, 5307 (1963); (n) J. G. Pritchard and P. T. Funke, *J. Heterocycl. Chem.*, **3**, 209 (1966); (o) D. G. Hellier, J. G. Tillett, H. F. van Woerden, and R. F. M. White, *Chem. Ind.* (London), **50**, 1956 (1963); (p) H. F. van Woerden, *Tetrahedron Lett.*, 2407 (1966); (q) C. G. Overberger, T. Kurtz, and S. Yaroslavsky, *J. Org. Chem.*, **30**, 4363 (1965); (r) R. S. Edmundson, *Tetrahedron Lett.*, 1649 (1965); (s) J. G. Pritchard and R. L. Vollmer, *J. Org. Chem.*, **28**, 1545 (1963).

(7) S. Melamed and W. L. Croxall, U. S. Patent 2,624,729 (1953); *Chem. Abstr.*, **47**, 11256*d* (1953).

Table II

2-Oxo-1,2,3-oxathiazolidines from β-Amino Alcohols



| Compd no. | Precursor amino alcohol | R | R′ | R″ | Confign | Solvent | Yield, % | Bp (mm) or mp, °C | Method of purifcn | Mol wt[a] | Calcd, % C | Calcd, % H | Calcd, % N | Found, % C | Found, % H | Found, % N |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 11 | 3 | *t*-Bu | H | H | | Benzene | 71 | 70–75 (0.3) | Distn | 163 | 44.17 | 8.03 | 8.58 | 44.25 | 8.04 | 8.56 |
| 12a | 5 | *t*-Bu | $CH_3$ | H | *cis* | Hexane | 19 | 70–80 (0.2) | Distn | 177 | 47.44 | 8.54 | 7.90 | 47.55 | 8.68 | 7.97[a] |
| 12b | 5 | *t*-Bu | $CH_3$ | H | *trans* | Hexane | 26 | 70–80 (0.2) | Distn | 177 | | | | | | |
| 13a | 4 | *t*-Bu | H | $CH_3$ | *cis* | Benzene | 15.5 | 70–80 (0.2) | Distn | 177 | 47.44 | 8.54 | 7.90 | 47.26 | 8.58 | 8.05[b] |
| 13b | 4 | *t*-Bu | H | $CH_3$ | *trans* | Benzene | 17.5 | 70–80 (0.2) | Distn | 177 | | | | | | |
| 14a | 7 | *t*-Bu | $C_6H_5$ | H | *cis* | Hexane | 37 | 89–90 | Fractnl crystn | 239 | 60.22 | 7.16 | 5.86 | 60.40 | 7.35 | 5.76 |
| 14b | 7 | *t*-Bu | $C_6H_5$ | H | *trans* | Hexane | 50 | 105–110 | Fractnl crystn | 239 | 60.22 | 7.16 | 5.86 | 60.91 | 7.41 | 6.13 |
| 15a | 6 | *t*-Bu | H | $C_6H_5$ | *cis* | Hexane | 44 | 110–111.5 | Fractnl crystn | 239 | 60.22 | 7.16 | 5.86 | 60.28 | 7.21 | 5.98 |
| 15b | 6 | *t*-Bu | H | $C_6H_5$ | *trans* | Hexane | 44 | 130 (0.1) | Fractnl crystn | 239 | 60.22 | 7.16 | 5.86 | 60.51 | 7.29 | 6.14 |
| 16 | 8 | *t*-Bu | H | $(C_6H_5)_2$ | | Hexane | 97 | 102–103.5 | Crystn | 315 | 68.56 | 6.70 | 4.44 | 68.47 | 6.90 | 4.55 |
| 17 | 9 | Ph | Ph | $CO_2Et$ | *c* | Benzene | 99 | 112.5–114 | Crystn | 331 | 61.65 | 5.17 | 4.23 | 61.58 | 5.14 | 4.23 |

[a] Mass spectral. [b] Analysis as a *cis–trans* mixture. [c] R′ and R″ are *cis* to each other. Only one isomer was formed and thus the relative geometry of the S–O group is not known.

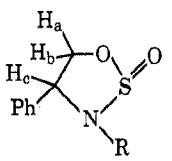
Table III

Spectral Properties of 2-Oxo-1,2,3-oxathiazolidines

| Compd no. | Confign | R | R′ | R″ | Ir (S=O), $cm^{-1}$ | Nmr data, δ, ppm: $H_a$ | $H_b$ | $H_c$ | $H_d$ | R′, R″ | $C(CH_3)_3$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 11 | | *t*-Bu | H | H | 1158 | m 4.0–4.9 | | m 3.0–3.7 | | | 1.37 |
| 12a | *cis* | *t*-Bu | $CH_3$ | H | 1165 | m 4.2–4.7 | | | 3.58 | 1.42 | 1.33 |
| 12b | *trans* | *t*-Bu | $CH_3$ | H | 1153 | 4.73 | 3.89, 3.74 | | | 1.17 | 1.40 |
| 13a | *cis* | *t*-Bu | H | $CH_3$ | 1153 | | 4.53 | 2.7–3.7 | | 1.53 | 1.33 |
| 13b | *trans* | *t*-Bu | H | $CH_3$ | 1153 | 5.08 | | 2.7–3.7 | | 1.37 | 1.33 |
| 14a | *cis* | *t*-Bu | $C_6H_5$ | H | 1169 | Complex multiplet | | 4.3–4.9 | | m 7.1–7.7 | 1.23 |
| 14b | *trans* | *t*-Bu | $C_6H_5$ | H | 1158 | 5.07 | 4.13 | 4.67 | | 7.23 | 1.27 |
| 15a | *cis* | *t*-Bu | H | $C_6H_5$ | 1152 | | 5.38 | m 3.2–3.8 | | m 7.42 | 1.38 |
| 15b | *trans* | *t*-Bu | H | $C_6H_5$ | 1152 | 5.93 | | 3.83 | 3.82 | 7.28 | 1.33 |
| 16 | | *t*-Bu | H | $(C_6H_5)_2$ | 1154 | | | 3.91 | 4.12 | 7.28<br>7.31 | 1.33 |
| 17 | | Ph | Ph | $CO_2C_2H_5$ | *a* | 5.92[b] | | | 5.55 | *c* | |

[a] Several bands in the expected region. [b] $J$ = 7 Hz. [c] 3.77 (2 H, complex multiplet); 1.87 (3 H, triplet).

ropy.[8,9] In terms of our five-membered heterocyclic rings, this results in the deshielding of ring substituents which are *cis* to the sulfoxide bond. In the 4- and 5-methyl-substituted oxathiazolidines, the *cis* configuration was assigned to isomers (**12a** and **13a**), respectively, which showed the most deshielded methyl group (Table III). The 5-phenyl isomers could be differentiated on the basis of the C-5 proton. This C-5 proton in the *trans* isomer (**15b**) appeared at δ 5.38 and in the *cis* isomer (**15a**) further downfield at 5.93. In the 4-phenyl isomers the complexity of the spectra inhibited direct identification of the C-4 proton. Stereochemical assignment could be made, however, on the basis of a complete nmr spectral analysis of the *trans* isomer **14a**. The more deshielded of the methyl-



**14a**

$J_{ac}$ = 7 Hz, $\delta_a$ 5.08
$J_{ab}$ = 8 Hz, $\delta_b$ 4.13
$J_{bc}$ = 1.5 Hz, $\delta_c$ 4.67

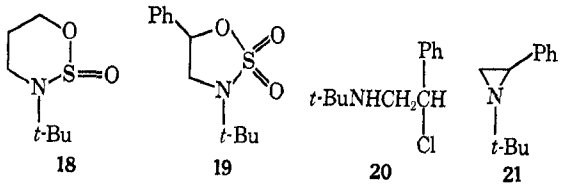
ene protons, $H_a$, was identified as *cis* to $H_c$ by $J_{ac}$ and thus a *trans* relationship is established for the S–O bond and in the phenyl ring. Since only one isomer of **17** was found, no stereochemical assignment could be made.

Finally, in order to explore the generality and scope of the cyclization, two modifications were investigated. The first of these resulted in the demonstration that these cyclizations were extendable to larger rings. Thus **10** could be converted into 2-oxo-3-*t*-butyl-1,2,3-

(8) A. B. Foster, J. M. Duxbury, T. D. Inch, and J. M. Webber, *Chem. Commun.*, 881 (1967), and references cited therein.

(9) K. W. Buck, A. B. Foster, W. D. Pardoe, M. H. Qadir, and J. M. Webber, *ibid.*, 759 (1966), and references cited therein.

tetrahydrooxathiazine (**18**).[10] A second modification was the attempted synthesis of 2,2-dioxo-1,2,3-oxathiazolidine by the reaction of **6** with sulfuryl chloride and triethylamine in hexane. The expected product, **19**, was not found. Open-chain material, presumed to be the amino chloride **20**, was obtained and converted in an attempted chromatographic purification into aziridine **21**.




**18** **19** **20** **21**

## Experimental Section

Melting points and boiling points are uncorrected. Liquid samples of less than 5 g were molecularly distilled using a hot air bath and the boiling point reported was the temperature of the air bath. Routine infrared spectra were recorded on a Perkin-Elmer 137 spectrophotometer and the expanded infrared spectra were run on a Perkin-Elmer 337 spectrophotometer. All nmr spectra were recorded on a Varian A-60-A spectrometer. Chemical shifts of nmr spectra run in organic solvents are reported in parts per million downfield from internal tetramethylsilane ($\delta$). Chemical shifts of nmr spectra run in $D_2O$ are reported in parts per million downfield from a point 4.99 ppm upfield from the DOH peak. Mass spectra were obtained on a RMU 6E mass spectrometer. Fragments are reported as *m/e* (relative intensity). Microanalyses were obtained from Galbraith Laboratories, Inc., Knoxville, Tenn.

**Amino alcohols** were prepared either by the lithium aluminum hydride reduction of amino esters or by the reaction of oxiranes with primary amines.

**Amino Esters.**—Methyl 3-*t*-butylaminopropionate was prepared from the reaction of an equimolar amount of *t*-butylamine and methyl acrylate in an equal volume of methanol at room temperature for 12 hr. The resultant reaction mixture was evaporated to a crude oil which gave pure amino ester upon distillation. $\alpha$-Amino esters were synthesized from the reaction of $\alpha$-bromo esters with a 10% molar excess of *t*-butylamine in an equal volume of alcohol at reflux temperature for 24 hr. Evaporation of the crude reaction mixtures followed by distillation gave the pure amino esters. Ethyl $\alpha$-bromopropionate was commercially available and methyl $\alpha$-bromophenylacetate was prepared by the method of Edwards and coworkers.[11] Physical parameters of these reactions are listed in Table IV.

**Reduction of Amino Esters with Lithium Aluminum Hydride. Method A.**—Amino esters in ether solution (1 g in 2–3 ml) were added to an equimolar quantity of lithium aluminum hydride suspended in ether (1 g in 40–50 ml) and stirred 3–30 hr. Excess lithium aluminum hydride was destroyed, the ether solution filtered, and the residual aluminum salts were washed with several portions of ether. The combined filtrate and washings were evaporated and the crude amino alcohol was distilled or recrystallized. Physical parameters and yields of these compounds are listed in Table I.

Oxiranes.—Ethylene and propylene oxides were commercially available. 2,2-Diphenyloxirane was prepared by the method of Corey and Chaykovsky.[12]

**Ring Opening of Oxiranes with Primary Amines. Method B.**—The oxirane and primary amine were added to an equal volume of methanol (the cheaper or more volatile material was usually in 5–10% excess). Volatile oxiranes were allowed to stand overnight at room temperature while the less volatile and more highly substituted oxiranes were refluxed until the oxirane had been consumed. Evaporation yielded a crude product which was purified by crystallization or distillation. Physical parameters of these reactions are listed in Table I.

**2-Oxo-1,2,3-oxathiazolidines from $\beta$-Amino Alcohols. General Method.**—A solution of thionyl chloride (5% molar excess) in hexane or benzene (1 ml in 10–20 ml) was added over a period of 10–20 min to a solution of the amino alcohol in hexane or benzene (1 g in 25–50 ml) with a slight excess (usually 10–15%) of 2 equiv of triethylamine. The reaction was stirred overnight at room temperature, then washed with several portions of water, dried ($K_2CO_3$), and evaporated to a crude mixture of the two diastereomeric oxathiazolidines.

In most reactions, two isomers were produced and could usually be separated by crystallization, distillation or chromatography. The chemical shift of the *t*-butyl groups in the nmr spectra of the 4-substituted oxathiazolidine mixtures permitted evaluation of the relative abundance of the two isomers. With 5-substituted oxathiazolidines, the relative amount of the two isomers was determined by integration of the lower field ring protons. In most case, both diastereomers were produced in close to equal amounts. The spectral properties of these compounds are listed in Table III, the yields and elemental analyses are given in Table II. The yields reported are for that particular oxathiazolidine and the total yield of oxathiazolidines in a given reaction is the sum of the *cis* and *trans* isomers. The phenyl-substituted oxathiazolidine mixtures were separated by fractional crystallization in hexane. The 4- and 5-methyloxathiazolidines did not separate on an alumina column and were purified by distillation and examined as a mixture of isomers.

**Reaction of 1-Phenyl-2-*t*-butylaminoethanol (6) with Sulfuryl Chloride in Hexane.**—Sulfuryl chloride (16 ml, 10% wt/total volume in benzene, 11.8 mmol) was added to a solution of 1-phenyl-2-*t*-butylaminoethanol (**6**, 2.0 g, 10.4 mmol) and triethylamine (2.5 g, 3.5 ml, 25 mmol) in 150 ml of hexane with stirring at 0° over a 15-min period. The reaction was stirred overnight at room temperature, then washed with two 50-ml portions of water, dried ($K_2CO_3$), and evaporated to a paste. Recrystallization from hexane gave the original amino alcohol **6** (0.5 g, 25%). The filtrate was evaporated to an oil which gave an nmr spectrum that showed no aziridine. This oil was separated on a column of deactivated alumina which was packed in hexane and eluted with hexane. Fractions of 50 ml were collected. Fractions 5–9 were evaporated to an oil (0.4 g, 23%) which was distilled and identified as 1-*t*-butyl-2-phenylaziridine (**21**), bp 50° (0.1 mm).

*Anal.* Calcd for $C_{12}H_{17}N$: C, 82.26; H, 9.78; N, 7.99. Found: C, 82.41; H, 10.00; N, 8.29.

**2-Oxo-3-*t*-butyl-1,2,3-tetrahydrooxanthiazine (18).**—A solution of thionyl chloride in benzene (50 ml, 10% wt/total volume, 42 mmol) was added over a period of 0.5 hr with stirring to a solution of 3-*t*-butylaminopropanol (**10**, 5 g, 38 mmol) and triethylamine (14 ml, 100 mmol) in 500 ml of hexane at 5–10°. After stirring overnight at room temperature, the reaction mixture

TABLE IV

AMINO ESTERS

| Compound | Yield, % | Bp (mm) or mp, °C | Ir (C=O), cm$^{-1}$ | Mol wt[a] | Calcd, % C | Calcd, % H | Calcd, % N | Found, % C | Found, % H | Found, % N |
|---|---|---|---|---|---|---|---|---|---|---|
| Ethyl 2-*t*-butylaminopropionate | 80 | 58–59.5 (10) | 1730 | 173 | [b] | | | | | |
| Methyl 3-*t*-butylaminobutyrate | 96 | 57 (3.5) | 1730 | 159 | 60.36 | 10.76 | 8.80 | 60.52 | 10.72 | 8.96 |
| Methyl 2-*t*-butylamino-2-phenylacetate | 82 | 75–76 (0.1) | 1735 | 221 | 70.56 | 8.66 | 6.34 | 70.43 | 8.66 | 6.43 |

[a] Molecular weights were determined by analysis of the mass spectra. [b] H. Wollweber and R. Hiltmann, German Patent 1,176,152 (1964); *Chem. Abstr.*, **61**, P13192*e* (1964).

(10) In the absence of base, $\gamma$-amino alcohols are converted into the $\gamma$-amino chloride hydrochloride, *e.g.*, N. J. Leonard and D. A. Durand, *J. Org. Chem.*, **33**, 1323 (1968).

(11) B. K. Edwards, A. A. Goldberg, and A. H. Wragg, *J. Pharm. Pharmacol.*, **12**, 179 (1960).

(12) E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1345, 1353 (1965).

was washed with two 200-ml portions of water, dried ($K_2CO_3$), and evaporated to a crude oil (3.5 g, 52%) which was distilled to give pure 2-oxo-3-*t*-butyl-1,2,3-tetrahydrooxathiazine (**18**), bp 60–65° (0.02 mm).

*Anal.* Calcd for $C_7H_{15}NSO_2$: C, 47.47; H, 8.53; N, 7.90. Found: C, 47.58; H, 8.49; N, 7.94.

**Acid Hydrolysis of *cis*-2-Oxo-3-*t*-butyl-5-phenyl-1,2,3-oxathiazolidine (15a).**—The oxathiazolidine **15a** (100 mg, 0.42 mmol) and hydrochloric acid (0.5 g, 5.2 mmol) were dissolved in 10 ml of tetrahydrofuran and 10 ml of water. After stirring overnight, the reaction mixture was made basic with sodium hydroxide and evaporated to yield a solid which was extracted with 20 ml of carbon tetrachloride and 10 ml of water. The organic layer was dried ($K_2CO_3$) and evaporated to a solid (60 mg, 75%) which was identified as 1-phenyl-2-*t*-butylaminoethanol (**6**) by analysis of the nmr spectrum and comparison with the nmr spectrum of an authentic sample.

**Acid Hydrolysis of 17.**—The oxathiazolidine **17** (300 mg, 0.81 mmol) was dissolved in 7 ml of EtOH and 3 ml of water, and 2 ml of concentrated hydrochloric acid added. This mixture was allowed to stand at room temperature for 1 week. It was evaporated and, after basification, extracted into chloroform. The dried chloroform extracts were evaporated to give 126 mg (47%) of solid which was identical by thin layer and nmr spectral comparison with **9**.

**Attempted Base Hydrolysis of *cis*-2-Oxo-*t*-butyl-5-phenyl-1,2,3-oxathiazolidine (15a).**—Oxathiazolidine **15a** (320 mg, 1.34 mmol) and sodium hydroxide (0.20 g, 5.0 mmol) were dissolved in 10 ml of tetrahydrofuran and 10 ml of water. After stirring overnight at room temperature, the reaction mixture was evaporated to a paste and extracted with 20 ml of ether and 10 ml of water. The ether layer was dried ($K_2CO_3$) and evaporated to give the starting oxathiazolidine **15a** (by analysis of the nmr spectrum) as a solid (240 mg, 75% recovery). The recovered oxathiazolidine **15a** (190 mg, 0.79 mmol) and sodium hydroxide (0.40 g, 10 mmol) were dissolved in 10 ml of tetrahydrofuran and 10 ml of water. After refluxing overnight, the reaction mixture was flash evaporated to a paste and extracted with 20 ml of ether and 15 ml of water. The ether layer was dried ($K_2CO_3$) and evaporated to give the starting oxathiazolidine **15a** (by analysis of the nmr spectrum) as a solid (125 mg, 66% recovery).

**Attempted Base Hydrolysis of *cis*-2-Oxo-3-*t*-butyl-4-phenyl-1,2,3-oxathiazolidine (14a).**—Oxathiazolidine **14a** (100 mg, 0.42 mmol) and sodium hydroxide (0.35 g, 8.8 mmol) were dissolved in 10 ml of tetrahydrofuran and 10 ml of water and stirred for 12 hr at room temperature. The reaction mixture was evaporated to a paste which was extracted with 10 ml of water and 20 ml of carbon tetrachloride. The carbon tetrachloride layer was dried ($K_2CO_3$) and evaporated to solids (100 mg, 100% recovery) which gave an nmr spectrum identical with that of the starting oxathiazolidine.

**Registry No.**—**3**, 4620-70-6; **4**, 18366-38-6; **5**, 18366-39-7; **6**, 18366-40-0; **7**, 18366-41-1; **8**, 6071-99-4; **9**, 18366-43-3; **10**, 18366-44-4; **11**, 18366-45-5; **12a**, 18366-46-6; **12b**, 18366-79-5; **13a**, 18366-80-8; **13b**, 18366-81-9; **14a**, 18366-82-0; **14b**, 18366-83-1; **15a**, 18366-84-2; **15b**, 18366-85-3; **16**, 18366-47-7; **17**, 18366-86-4; **18**, 18366-48-8; **21**, 18366-49-9; ethyl 2-*t*-butylaminopropionate, 18366-50-2; methyl 3-*t*-butylaminobutyrate, 18366-51-3; methyl 2-*t*-butylamino-2-phenylacetate, 18366-52-4.

# 1,5-Benzodiazocines

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The syntheses of 2-(3-aminopropylamino)-5-chlorobenzophenones **2** and **9** and their intramolecular dehydrations to give 8-chloro-1,2,3,4-tetrahydro-6-phenyl-1,5-benzodiazocines **3** and **10** were effected. A procedure purported to yield a 8-chloro-3,4-dihydro-1,5-benzodiazocin-2-one has been found in fact to give a dimer. This procedure has been successfully utilized in the synthesis of 8-chloro-3,4-dihydro-1-methyl-6-phenyl-1,5-benzodiazocin-2(1H)-one **19**, which has been structurally related to **10**. A rationale for the anomalous results of this reaction is offered.

As a result of our continuing interest in the syntheses of medium-sized heterocycles, we wish to report the preparation of some 1,5-benzodiazocines. Although the syntheses of 1,6- and 2,5-benzodiazocines have by now been well documented,[1] the recorded examples of the 1,5 system are limited to the hexahydrobenzodiazocines of Shiotani and Mitsuhashi[2] and the 3,4-dihydro-1,5-benzodiazocin-2-one claimed by Sulkowski.[3]

Of particular interest was the 6-phenyl-2,3,4,5-tetrahydro-1,5-benzodiazocine system, exemplified by compound **3** (Scheme I). As the result of another study,[4] 9-chloro-1,2,3,5-tetrahydro-7-phenylpyrimido[1,2-*a*]-[1,4]benzodiazepine (**1**) was available. Acid hydrolysis of **1** gave the desired substituted benzophenone **2** which was quite resistant to dehydration attempts, but was converted into a crystalline product on prolonged heating in pyridine. Intramolecular dehydration was inferred from the mass spectrum (*m/e* 270) and the elemental analysis. Since no transannular reaction would be anticipated and since the spectrophotometric results suggested the presence of both amine and imine moieties,[5] the 1,5-benzodiazocine structure **3** was assigned.

For practical reasons, an alternate synthetic procedure to **3** was desired. Compound **4**,[4] the precursor of **1**, was also available and was hydrolyzed in good yield to the substituted benzophenone **5a**. The reaction of **5a** with ethanolic ammonia gave a mixture which contained the open amine **2** as well as the cyclized product **3**. The high ratio of **3** to **2** resulting from these reaction conditions may be due to the addition of ammonia to the benzophenone carbonyl and increased susceptibility of the resultant quaternary carbon to nucleophilic attack,[6] or by actual formation of the

(1) See, for example, W. Schroth and B. Streckenbach, *Z. Chem.*, **3**, 465 (1963), and T. S. Sulkowski, M. A. Wille, A. Mascitti, and J. L. Diebold, *J. Org. Chem.*, **32**, 2180 (1967).

(2) S. Shiotani and K. Mitsuhashi, *Yakugaku Zasshi*, **84**, 656 (1964).

(3) T. S. Sulkowski, U. S. Patent 3,294,782 (1966).

(4) M. E. Derieg, R. I. Fryer, R. M. Schweininger, and L. H. Sternbach, *J. Med. Chem.*, **11**, 912 (1968).

(5) The ir absorptions (KBr) were at 3265 (NH) and 1610 $cm^{-1}$ (>C=N—) and the uv maxima (2-propanol) were at 223 mμ (infl) (ε 22,500), 248 (17,300), 267 (infl) (13,500) and 365 (2700).

(6) For a discussion of the role of carbinolamine intermediates in the formation of Schiff bases, see R. L. Rieves in "The Chemistry of the Carbonyl Group," S. Patai, Ed., Interscience Publishers, New York, N. Y., 1966, pp 608–614.