participates in an intramolecular hydrogen bond. However, in L-aspartic acid[24] as well as in the present compound nitrogen atom N(2) participates only in intermolecular hydrogen bonding, and repulsion between the carboxyl group and the hydrogen-bond acceptor prevents the syn-planar conformation; the C-C-C O torsion angle is about −52° in both compounds.

Acknowledgments. We thank Professor K. D. Kopple for supplying the material and Professor G. N. Ramachandran for his interest.

References and Notes

(1) (a) This investigation was supported, in part, by the U.S. Public Health Service through Research Grant GM-16966 from the National Institute of General Medical Sciences, National Institutes of Health, and, in part, by the C. S. I. R., India. (b) Molecular Biophysics Unit, Indian Institute of Science. (c) Department of Organic Chemistry, Indian Institute of Science. (d) California Institute of Technology.
(2) (a) E. Sletten, *J. Am. Chem. Soc.*, **92,** 172 (1970); (b) E. Benedetti, P. Corradini, and C. Pedone, *J. Phys. Chem.*, **73,** 2891 (1969).
(3) R. Degeilh and R. E. Marsh, *Acta Crystallogr.*, **12,** 1007 (1959); R. B. Corey, *J. Am. Chem. Soc.*, **60,** 1598 (1938).
(4) (a) R. Ramani, K. Venkatesan, R. E. Marsh, and W.-J. Kung, *Acta Crystallogr., Sect. B.*, **32,** 1051 (1976); (b) E. Benedetti, M. Goodman, R. E. Marsh, H. Rapoport, and J. A. Musich, *Cryst. Struct. Commun.*, **4,** 641 (1975); (c) R. B. Von Dreele, *Acta Crystallogr., Sect. B,* **31,** 966 (1975); (d) I. L. Karle, *J. Am. Chem. Soc.*, **94,** 81 (1972).
(5) (a) K. D. Kopple and D. H. Marr, *J. Am. Chem. Soc.*, **89,** 6193 (1967); (b) K. D. Kopple and M. Ohnishi, *ibid.*, **91,** 962 (1969).
(6) C. F. Lin and L. E. Webb, *J. Am. Chem. Soc.*, **95,** 6803 (1973).
(7) E. Benedetti, R. E. Marsh, and M. Goodman, *J. Am. Chem. Soc.*, **98,** 6676 (1976).
(8) A. J. Morris, A. J. Geddes, and B. Sheldrick, *Cryst. Sturct. Commun.*, **3,** 345 (1974).
(9) M. Cotrait, M. Ptak, B. Busetta, and A. Heitz, *J. Am. Chem. Soc.*, **98,** 1073 (1976).
(10) G. Germain, P. Main, and M. M. Woolfson, *Acta Crystallogr., Sect. A,* **27,** 368 (1971); J. P. Declerq, G. Germain, P. Main, and M. M. Woolfson, *ibid.*, **29,** 231 (1973).
(11) I. L. Karle, H. Hauptman, J. Karle, and A. B. Wing, *Acta Crystallogr.*, **11,** 257 (1958).
(12) E. Benedetti, P. Corradini, and C. Pedone, *Biopolymers*, **7,** 752 (1969).
(13) E. Benedetti, D. C. Easter, and R. E. Marsh, to be published.
(14) I. Bennett, A. G. H. Davidson, M. M. Harding, and I. Morelle, *Acta Crystallogr., Sect. B,* **26,** 1722 (1970).
(15) J. Donohue and A. Caron, *Acta Crystallogr.*, **17,** 1187 (1964); J. Donohue, L. R. Lavine, and J. S. Rollett, *ibid.*, **9,** 655 (1956).
(16) T. J. Kistenmacher, D. J. Hunt, and R. E. Marsh, *Acta Crystallogr., Sect. B,* **28,** 3352 (1972).
(17) (a) J. J. Madden, E. L. McGandy, and N. C. Seeman, *Acta Crystallogr., Sect. B,* **28,** 2377 (1972); (b) J. J. Madden, E. L. McGandy, N. C. Seeman, M. M. Harding, and A. Hoy, *ibid.*, **28,** 2382 (1972).
(18) P. Edington and M. M. Harding, *Acta Crystallogr., Sect. B,* **30,** 204 (1974).
(19) M. Pfak and A. Heitz, *Org. Magn. Reson.*, **6,** 358 (1974).
(20) IUPAC-IUB Commission on Biological Nomenclature, *Biochemistry,* **9,** 3471 (1970).
(21) C. K. Johnson, "ORTEP, A Fortran Thermal Ellipsoid Program for Crystal Structure Illustrations", U.S. Atomic Energy Commission Report ORNL-3794, Oak Ridge National Laboratory, Oak Ridge, Tenn., 1965.
(22) J. D. Dunitz and P. Strickler in "Structural Chemistry and Molecular Biology", A. Rich and N. Davidson, Ed., W. H. Freeman, San Francisco, Calif., 1968, p 595.
(23) S. T. Rao, *Acta Crystallogr., Sect. B,* **29,** 1718 (1973).
(24) J. L. Derissen, H. J. Endeman, and A. J. Peerdeman, *Acta Crystallogr., Sect. B,* **24,** 1349 (1968).

Synthesis, Reactions, and Crystal and Molecular Structure of a Sulfurane with Two Apical Nitrogen-Centered Ligands: a Spirodiazasulfurane[1]

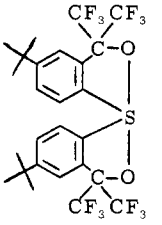
L. J. Adzima, Chian C. Chiang, Iain C. Paul,* and J. C. Martin*

Contribution from the Department of Chemistry, University of Illinois, Urbana, Illinois 61801. *Received April 18, 1977*

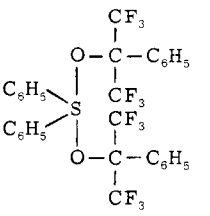
Abstract: Oxidation of bis[2-(*N*-isopropylcarbamoyl)phenyl] sulfide (**6**) with *tert*-butyl hypochlorite gives monocyclic chloroazasulfurane **7.** Treatment of **7** with potassium hydride affords spirodiaryldiamidosulfurane **4,** the first example of a sulfurane with two apical nitrogen ligands. The crystal structure of **4** reveals slightly distorted trigonal bipyramidal geometry about sulfur. The C-S-C angle is 104.8 (2)°. The S-N bond lengths, 1.899 (3) and 1.897 (3) Å, are 0.16 Å longer than the sum of the covalent radii and are among the longest reported S-N bond lengths. The calculated bond order is 0.55. The sums of the bond angles around the nitrogen atoms are 352.8 and 354.0° with the nitrogens being 0.24 and 0.22 Å out of their S-C-C planes. The crystals of **4** are monoclinic, the space group is $P2_1/c$, and there are four molecules in a unit cell of dimensions a = 13.980 (3), b = 16.091 (6), c = 9.009 (3) Å, β = 112.00(2)°. The structure was refined to an R factor of 0.059 for 2212 nonzero reflections. Comparisons of **4** with closely related structures emphasize S-N bond lengths and the geometry of nitrogen bonded to sulfur. A chloroform solution of diazasulfurane **4** hydrolyzes in seconds to sulfoxide diamide **8** upon the addition of water. Sulfurane **4** reacts with hydrogen chloride to form chloroazasulfurane **7.** Attempted oxidation of **4** with ozone or ruthenium tetroxide to form spirodiaryldiazasulfurane oxide **18** fails. We discuss the relevance of this work to earlier work on the mechanism of the facile cleavage of secondary amides in reactions with dialkoxysulfuranes.

Introduction

Sulfuranes with two apical oxygen ligands have been reported.[2] These compounds, which can be viewed as ketal analogues of sulfoxides, vary widely in their reactivities. For example, spirobicyclic sulfurane **1** is found to be inert toward acid or base hydrolysis.[2g] In contrast, acyclic sulfurane **2** reacts instantly with water to form diphenyl sulfoxide and hexafluorocumyl alcohol.[2c] Sulfurane **3** is hydrolyzed with difficulty.[2d]

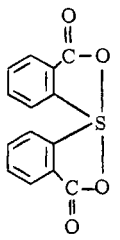


1

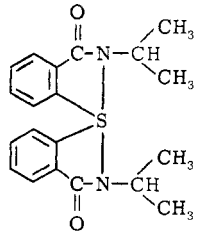


2

0002-7863/78/1500-0953$01.00/0



3



4

We report here the synthesis of the first example of a sulfurane with two apical nitrogen ligands (**4**), a new structural type, and detail various aspects of its chemistry along with a complete x-ray structure determination for **4**.

Experimental Section

Proton chemical shifts are reported on the δ scale, parts per million downfield from tetramethylsilane internal standard. The ^{1}H NMR integral ratios are rounded to the nearest whole number of nuclei. Elemental analyses of new compounds are within 0.4% of theoretical values unless otherwise stated.

Solvents. Chloroform-*d*, methylene chloride, and carbon tetrachloride were dried by passage through a column of Woelm basic alumina (activated at 150 °C for 24 h). Ether and tetrahydrofuran were dried by several additions of sodium wire until further additions caused no further hydrogen evolution.

Bis(2-carboxyphenyl) sulfide (5) was prepared using a modification of Protiva's method[3] for the preparation of the analogous monocarboxylic acid. Thiosalicylic acid (62 g, 0.4 mol) and 120 g (2.15 mol) of KOH pellets were added to 1 L of water and stirred for 10 min. Then 4 g of copper bronze and 100 g (0.4 mol) of 2-iodobenzoic acid were added and the solution was refluxed with stirring for 7 h. The solution was cooled to 25 °C and filtered and the filtrate was acidified with concentrated HCl. The precipitated diacid was filtered, washed with water, air dried, and recrystallized from glacial acetic acid to afford 97.5 g (89%) of product, mp 233.5–236 °C (lit.[4] 233–234 °C).

Anal. ($C_{14}H_{10}O_4S$) C, H, S.

Bis[2-(*N*-isopropylcarbamoyl)phenyl] Sulfide (6). Diacid **5** (27.7 g, 0.1 mol) was boiled overnight with excess thionyl chloride. The thionyl chloride was removed by vacuum and the diacid chloride was dissolved in benzene and cooled to 0 °C. Next, 52 mL (0.6 mol, excess) of isopropylamine was added with stirring. After 15 min the benzene and excess amine were removed by vacuum. The residue was dissolved in methylene chloride and filtered to remove isopropylammonium chloride. The filtrate was extracted with dilute aqueous HCl, dilute aqueous NaOH, and water and dried (Na_2SO_4) and the solvent was removed to afford crude product. Recrystallization from CH_2Cl_2–hexane gave 31.6 g (89%) of **6:** mp 182.5–184.5 °C; IR ($CHCl_3$) 3520–3400 (NH stretch), 1650 (C=O), 1540–1510 cm^{-1} (NH bend); ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.13 (d, 12, CH_3, J = 6 Hz), 4.18 (octet, 2, CH, J = 6 Hz), 6.50 (br s, 2, NH), 7.17–7.73 (m, 8, ArH); mass spectrum (70 eV) *m/e* (rel intensity) 356 (13.4, M$^+$), 299 (9.0), 213 (86.7), 184 (18.7), 120 (21.8), 58 (100), 43 (27.6).

Anal. ($C_{20}H_{24}N_2O_2S$) C, H, N, S.

1-Chloro-1-[2-(*N*-isopropylcarbamoyl)phenyl]-2-isopropyl-3-oxo-3*H*-2,1-benzazathiole (7). To a cooled solution of diamide **6** (1.33 g, 3.73 mmol) in 40 mL of CH_2Cl_2 was added dropwise by syringe 0.41 g (3.73 mmol, 0.42 mL) of *tert*-butyl hypochlorite. After stirring for 10 min at 25 °C, the solvent was removed and the white solid (**7**) was recrystallized from CH_2Cl_2–hexane, 0.77 g (53%): mp 232–234 °C; IR ($CHCl_3$) 3380 (w, broad), 2950 (s), 1719 (s), 1614 (s), 1462 (m), 1370 (m), 1290 (s), 1241 (s), 1145 (m), 963 (w), 879 (w), 790 (m), 670 cm^{-1} (m); ^{1}H NMR (220 MHz, $CDCl_3$) δ 1.454 (d, 3, CH_3, J = 6.7 Hz), 1.585 (d, 3, CH_3, J = 6.7 Hz), 1.593 (d, 3, CH_3, J = 6.7 Hz), 1.604 (d, 3, CH_3, J = 6.7 Hz), 4.46 (octet, 1, amide CH, J = 6.7 Hz), 4.82 (septet, 1, azasulfurane CH, J = 6.7 Hz), 7.56 (d, 1, ArH, J = 8 Hz), 7.75 (t, 1, ArH, J = 8 Hz), 7.89 (m, 3, ArH), 8.20 (d, 1, J = 7 Hz), 8.30 (d, 1, ArH, J = 8 Hz), 9.66 (d, 1, H ortho to S in fused ring system, J = 7.5 Hz), 11.60 (d, 1, NH); mass spectrum (70 eV) *m/e* (rel intensity) no molecular ion, 354 (4.4, M$^+$ − HCl), 339 (87.8, M$^+$ − HCl and CH_3), 254 (100), 213 (43.0), 184 (19.3), 151 (33.3), 139 (14.9), 77 (8.5).

Anal. ($C_{20}H_{21}ClN_2O_2S$) C, H, Cl, N, S.

2,2′-Bis(isopropyl)-3,3′-dioxo-1,1′-spiro[3*H*-2,1-benzazathiole] (4). All operations were conducted in a drybox. A slurry of chlorosulfurane **7** (4.65 g, 11.89 mmol) and 250 mL of dry THF was treated with about 2.5 g (62.3 mmol, excess) of potassium hydride causing vigorous evolution of H_2. After stirring for 3 h, the mixture was filtered (removing excess KH and KCl). The volume of the filtrate was reduced by high vacuum to about 50 mL. Then 125 mL of dry ether and 10–15 mL of dry THF were added, the mixture was stirred for 30 min and filtered (1.84 g), and the filtrate was cooled to −78 °C overnight. The amount of recrystallized product was 0.62 g. The mother liquor was evaporated to give 1.76 g of **4.** Total yield of diazasulfurane was 4.22 g (nearly quantitative): mp 174–175 °C; IR ($CHCl_3$) 3330 (w), 3000 (s), 1638 (s), 1584 (m), 1462 (m), 1339 (m), 1312 (w), 1256 (w), 1145 (w), 950 (w), 892 (m), 832 (w), 685 cm^{-1} (w); ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.47 (d, 6, CH_3, J = 6.7 Hz), 1.63 (d, 6, CH_3, J = 6.7 Hz), 4.11 (septet, 2, CH, J = 6.7 Hz), 7.33–7.86 (m, 6, ArH), 7.97–8.17 (m, 2, ArH, protons ortho to S); mass spectrum (70 eV) *m/e* (rel intensity) 354 (7.9, M$^+$), 339 (95.4, M$^+$ − CH_3), 281 (23.0), 254 (100), 213 (65.8), 184 (24.7), 151 (33.4), 146 (15.1), 58 (28.6).

Anal. ($C_{20}H_{22}N_2O_2S$) C, H, N, S.

Crystals of **4** were exposed to the atmosphere for 3 days. Subsequent ^{1}H NMR analysis showed that no hydrolysis had occurred.

Bis[2-(*N*-isopropylcarbamoyl)phenyl] Sulfoxide (8). A sample of 7.4 g (20.9 mmol) of sulfide **6** was dissolved in 70 mL of chloroform. Next, 4.25 g of 85% *m*-chloroperbenzoic acid (20.9 mmol of peracid) in 50 mL of $CHCl_3$ was added at 0 °C and the solution was stirred at room temperature for 2 days. The chloroform solution was then extracted twice with aqueous $NaHCO_3$ and dried (Na_2SO_4), and the chloroform was removed under high vacuum leaving a white solid. Recrystallization from CH_2Cl_2–hexane gave 7.28 g (93%) of sulfoxide **8:** mp 197–198 °C; IR ($CHCl_3$) 3330 (m, NH), 3000 (s), 1638 (s, C=O), 1547 (s), 1522 (s), 1460 (m), 1063 (m), 1022 cm^{-1} (m); ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.09 (d, 6, CH_3, J = 6.7 Hz), 1.21 (d, 6, CH_3, J = 6.7 Hz), 4.08 (octet, 2, CH, J = 6.7 Hz), 7.20–7.80 (m, 8, ArH), 8.32 (d, 2, NH, J = 7 Hz); mass spectrum (70 eV) *m/e* (rel intensity) 372 (7.4, M$^+$), 355 (45.5, M$^+$ − OH), 314 (40.1), 298 (22.3), 254 (33.1), 213 (87.6), 210 (53.1), 194 (100), 168 (68.0), 152 (60.3), 151 (84.8), 105 (31.0), 86 (49.1), 84 (76.9), 77 (49.4), 49 (99.3).

Anal. ($C_{20}H_{24}N_2O_3S$) C, H, N, S.

Reaction of 8 with Thionyl Chloride. To sulfoxide **8** (0.774 g, 2.08 mmol) in 10 mL of methylene chloride was added thionyl chloride (2 mL, excess) and the solution was stirred for 15 min. After the solvent and excess $SOCl_2$ were removed, the white solid was recrystallized from CH_2Cl_2–hexane, 0.52 g (64%), mp 238–238.5 °C. ^{1}H NMR and infrared spectra were identical with those of chloroazasulfurane **7** prepared by the earlier route.

Bis[2-(*N*-isopropylcarbamoyl)phenyl] Sulfone (11). Two equivalents of *m*-chloroperbenzoic acid (1.68 g of 85% peracid) was dissolved in 20 mL of chloroform and added over a 5-min period to a 0 °C solution of 1.51 g (4.24 mmol) of sulfide **6** in chloroform. The solution was then stirred at 25 °C overnight. The chloroform solution was extracted once with aqueous $KHCO_3$ and dried ($MgSO_4$) and the solvent was evaporated. The white solid was recrystallized from CH_2Cl_2–hexane, yielding 1.45 g (88%) of sulfone **11:** mp 169–171 °C; IR ($CHCl_3$) 3425 (m), 3020 (s), 1745 (w), 1658 (s), 1521 (s), 1465 (m), 1456 (m), 1369 (w), 1325 (m), 1230 (m), 1160 (m), 790 (s), 595 cm^{-1} (m); ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.18 (d, 12, CH_3, J = 6.7 Hz), 3.98 (octet, 2, CH, J = 6.7 Hz), 6.08 (br d, 2, NH, J = 7 Hz), 7.25–7.70 (m, 6, ArH), 7.98–8.27 (m, 2, ArH); mass spectrum (70 eV) *m/e* (rel intensity) 388 (1.8, M$^+$), 373 (2.2, M$^+$ − CH_3), 330 (35.2, M$^+$ − $NHCH(CH_3)_2$), 270 (77.5), 245 (30.6), 238 (100), 181 (28.7), 162 (23.0), 136 (43.2), 105 (30.9), 58 (99.1).

Anal. ($C_{20}H_{24}N_2O_4S$) C, H, N, S.

2-Phenylthio-*N*-isopropylbenzamide. 2-Carboxydiphenyl sulfide (14.38 g, 0.0625 mol) prepared by the method of Protiva[3] and excess thionyl chloride were refluxed overnight. The excess $SOCl_2$ was removed by vacuum leaving the acid chloride which was dissolved in benzene and cooled to 0 °C. Isopropylamine (25 mL, 0.3 mol, excess) was added with stirring. After 15 min the benzene and excess amine were removed by vacuum. The residue was dissolved in CH_2Cl_2 and filtered to remove isopropylammonium chloride. The filtrate was extracted with dilute aqueous HCl, dilute aqueous NaOH, and water and dried (Na_2SO_4) and the solvent was removed to afford crude

product. Recrystallization from CH_2Cl_2–hexane gave 14.55 g (86%) of product: mp 110 °C; IR ($CHCl_3$) 3440 (m), 3025 (s), 1660 (s), 1589 (m), 1523 (s), 1482 (m), 1468 (m), 1392 (w), 1374 (w), 1331 (w), 1286 (w), 1254 (w), 1178 (m), 1028 (w), 535 cm^{-1} (m); ^1H NMR (60 MHz, $CDCl_3$) δ 1.14 (d, 6, CH_3, J = 6.7 Hz), 4.18 (octet, 1, CH, J = 6.7 Hz), 6.26 (br s, 1, NH), 6.90–7.16 (m, 9, ArH); mass spectrum 70 eV) *m/e* (rel intensity) 271 (58.3, M^+), 213 (100), 184 (49.1), 152 (11.9), 136 (15.1), 93 (19.7), 58 (37.0).

Anal. ($C_{16}H_{17}NOS$) C, H, N, S.

1-Chloro-1-phenyl-2-isopropyl-3-oxo-3*H*-2,1-benzazathiole (13). Sufloxide **12** (0.384 g, 1.34 mmol) was treated with excess thionyl chloride and stirred for 15 min. After $SOCl_2$ was removed by vacuum, the residue was recrystallized from CH_2Cl_2–hexane and washed with ether leaving 0.258 g (63%) of **13:** mp 171–175 °C; ^1H NMR (60 MHz, $CDCl_3$) δ 1.13 (d, 3, CH_3, J = 6.7 Hz), 1.47 (d, 3, CH_3, J = 6.7 Hz), 4.63 (m, 1, CH), 7.20–8.35 (m, 8, ArH), 9.63 (m, 1, ArH, H ortho to S on disubstituted ring).

Anal. ($C_{16}H_{16}ClNOS$) C, H, Cl, N, S.

Compound **13** was also prepared by treating the sulfide (1.08 g, 3.98 mmol) in 15 mL of CH_2Cl_2 (cooled to 0 °C) with *tert*-butyl hypochlorite (0.432 g, 0.45 mL, 3.98 mmol), added by syringe. After a few minutes the solution was warmed to 25 °C and product **13** crystallized upon adding hexane, 0.592 g (49%), mp 166.5–172 °C.

Hydrolysis of Chloroazasulfurane 13. Preparation of 2-Phenylsulfinyl-*N*-isopropylbenzamide (12). A sample of **13** was dissolved in methylene chloride and extracted with aqueous KOH. The CH_2Cl_2 layer was separated and dried (Na_2SO_4) and white crystals from CH_2Cl_2–hexane were obtained: mp 156–158.5 °C; IR ($CHCl_3$) 3435 (m), 3300 (w, NH), 3010 (s), 1660 (s), 1522 (s), 1463 (m), 1389 (w), 1370 (w), 1327 (w), 1254 (m), 1174 (m), 1080 (m), 1057 (m), 1030 (s), 550 cm^{-1} (m); ^1H NMR (60 MHz, $CDCl_3$) δ 1.14 (d, 3, CH_3, J = 6.7 Hz), 1.26 (d, 3, CH_3, J = 6.7 Hz), 4.16 (octet, 1, CH, J = 6.7 Hz), 6.44 (br s, 1, NH), 7.22–7.88 (m, 8, ArH), 8.02–8.23 (m, 1, ArH); mass spectrum (70 eV) *m/e* (rel intensity 287 (53.7, M^+), 270 (17.1, $M^+ - OH$), 229 (59.0), 213 (58.3), 194 (100), 184 (65.8), 168 (41.3), 152 (91.7), 77 (36.0), 51 (21.9).

Anal. ($C_{16}H_{17}NO_2S$) C, H, N, S.

Hydrolysis of Diazasulfurane 4. A sample of diazasulfurane **4** (48 mg, 0.14 mmol) was dissolved in 0.5 mL of dry $CDCl_3$ (dried by passing through basic alumina and $MgSO_4$). ^1H NMR analysis showed that 29% of **4** had hydrolyzed to sulfoxide diamide **8.** Upon the addition of 1 drop of water of the solution, hydrolysis was complete less than 10 s.

Attempted Reaction of Diazasulfurane 4 with Methanol. A sample of diazasulfurane **4** (ca. 50 mg) was dissolved in 1 mL of dry CH_2Cl_2. Then 2.2 equiv of methanol was added. ^1H NMR analysis showed that about 6% of **4** had hydrolyzed to sulfoxide **8** after 5 min at 44 °C. After 11 h at 25 °C, no further hydrolysis was seen. The small amount of hydrolysis was probably due to trace amounts of water in the CH_3OH. There were no changes in the ^1H NMR spectrum which would indicate a reaction between **4** and methanol.

Reaction of Diazasulfurane 4 with HCl. A sample of diazasulfurane **4** was dissolved in 1 mL of dry CH_2Cl_2. This solution was then saturated with HCl gas at 25 °C. The excess HCl and CH_2Cl_2 were removed under vacuum leaving a white solid whose 60-MHz ^1H NMR spectrum was identical with that of authentic **7.**

Attempted Oxidation of Diazasulfurane 4 with Ozone and Ruthenium Tetroxide. Two samples of diazasulfurane **4** (both between 80 and 100 mg) were each dissolved in about 1 mL of dry methylene chloride. Both solutions were cooled to −78 °C and excess ozone was bubbled in. After warming to 25 °C, ^1H NMR analysis showed that partial hydrolysis to sulfoxide **8** occurred. There was no evidence for the formation of diazasulfurane oxide **18.** Each sample was then hydrolyzed completely by addition of 1 drop of water. ^1H NMR analysis showed that only sulfoxide **8** was present. There was no evidence for sulfone **11** formation due to the possible hydrolysis of diazasulfurane oxide **18.** Another sample of **4** was dissolved in dry CH_2Cl_2 and ozone was bubbled in at 25 °C. Again, ^1H NMR analysis showed that partial hydrolysis occurred but there was no evidence for sulfurane oxide formation. The addition of 1 drop of water completed hydrolysis to **8** and no sulfone could be detected.

Similar attempts at oxidation of **4** with RuO_4 also failed.

Interaction of Diazasulfurane 4 with Optically Active Solvent. To a solution of 61.5 mg (0.174 mmol) of diazasulfurane **4** in 0.5 mL of dry methylene chloride (0.35 M) was added 109.7 mg (0.62 mmol, 1.24 M) of L(−)-2,2,2-trifluoro-1-phenylethanol.[5] The 220-MHz ^1H NMR spectrum showed that one of the doublets had been split into two doublets (centered at δ 1.511 and 1.518). The other doublet (δ 1.365) was not completely resolved, showing instead a shoulder on each peak.

Interaction of Diazasulfurane 4 with Eu(fod)$_3$. A sample of **4** (39.6 mg, 0.112 mmol) was dissolved in 0.5 mL of CD_2Cl_2. The spectrum of this solution was determined before and after successive additions of Eu(fod)$_3$ (initial molarity of **4** was 0.22 M). Relative concentrations were determined through comparison of the integrals of the *tert*-butyl ligand and the methyl resonances of **4.** As Eu(fod)$_3$ was added, **4** partly hydrolyzed. At the final concentration of Eu(fod)$_3$ (0.12 M), molarities of **4** and **8** were 0.14 and 0.08 M. Plots of chemical shift vs. concentration of Eu(fod)$_3$ assigned slopes of 13.4 and 14.3 to the two doublets of **4** initially at δ 1.43 and 1.59. Slopes of 2.6 and 3.0 were assigned to the two doublets of sulfoxide **8** initially at δ 1.13 and 1.26.

X-Ray Crystallography of Diazasulfurane 4. Diazasulfurane **4** was crystallized from dry ether–THF. The crystals are white and transparent with a platelike shape. An untwinned crystal with dimensions ca. 0.4 × 0.3 × 0.2 mm was used for data collection. No special precautions were needed to protect the crystal from moisture.

Crystal Data for 4. $C_{20}H_{22}N_2O_2S$, mol wt 354.5, monoclinic, a = 13.980 (3), b = 16.091 (6), c = 9.009 (3) Å, β = 112.00 (2)°, V = 1879.0 Å^3, Z = 4, ρ_c = 1.25 g/cm^3, μ (Cu Kα) = 16.1 cm^{-1}, $F(000)$ = 752, systematic absences $0k0$ when $k = 2n + 1$ and $h0l$ when $l = 2n + 1$ establish the space group as $P2_1/c$, λ (Cu Kα) = 1.54178 Å.

Solution and Refinement of the Structure of 4. Intensity data were collected on a computer-controlled four-angle Syntex $P2_1$ diffractometer using a 2θ scan mode with variable scan speeds. A total of 3217 independent reflections was scanned in the 2θ sphere from 0 to 130° with graphite-monochromatized Cu Kα radiation (λ = 1.54178 Å). Out of these reflections, 2212 were considered to be observed at the 2σ level, as determined by counting statistics. The structure was solved by direct methods.[6] Full-matrix, least-squares refinement of the positional and anisotropic thermal parameters for the nonhydrogen atoms converged to an R factor of 0.082 and R_w of 0.099.[7] The weights were taken as $1/(\sigma(F_{obsd})^2 + (0.02F_{obsd})^2)$, where $\sigma(F_{obsd})$ is the standard deviation based on counting statistics. The positions of the hydrogens were located from a difference map. Inclusion of the hydrogen atoms with isotropic temperature factors in the least-squares refinement gave final values for R and R_w of 0.059 and 0.063, respectively, on all observed reflections. The positional and thermal parameters for the methyl hydrogen atoms, H9A, H9B, H9C, H10A, H10B, and H10C were held constant during the last few cycles of refinement since they tended to give unreasonable values. The value of $[\Sigma w(|F_{obsd}| - |F_{calcd}|)^2/m - n)]^{1/2}$, where m is the number of observations and n is the number of parameters varied, was 1.67. The analytical expression given in the International Tables of X-Ray Crystallography[8] was used to calculate the scattering factors. The final values of the atomic coordinates[9] are given in Table I.

Results

The synthetic route used to prepare diazasulfurane **4** is shown in Scheme I. Recrystallization of **4** from dry ether–THF produced white needles. The 60-MHz ^1H NMR spectrum in $CDCl_3$ shows two doublets, for diastereotopic isopropyl methyl groups, centered at δ 1.47 and 1.63.

When L(−)-2,2,2-trifluoro-1-phenylethanol[5] was added to a methylene chloride solution of **4,** one of the doublets of **4** was split into two doublets and the peaks of the other doublet were broadened due to shoulder peaks. This is evidence for a chiral sulfur center and is consistent with the pictured trigonal bipyramidal geometry.

The two aromatic protons ortho to sulfur are found in the ^1H NMR spectrum at very low field (δ 7.97–8.17). This downfield shift is highly characteristic for trigonal bipyramidal cyclic sulfuranes.[2m]

The hydrolysis of **4** is rapid in moist chloroform solution at 25 °C. In contrast, dioxasulfurane **3** is reported to hydrolyze only after boiling for 30 min in 9:1 acetone–water solvent mixture.[2d] This difference in hydrolysis rates between **4** and **3** probably reflects the different electronegativities of the

Table I. Final Coordinates for Diazasulfurane **4**. Estimated Standard Deviations in Parentheses

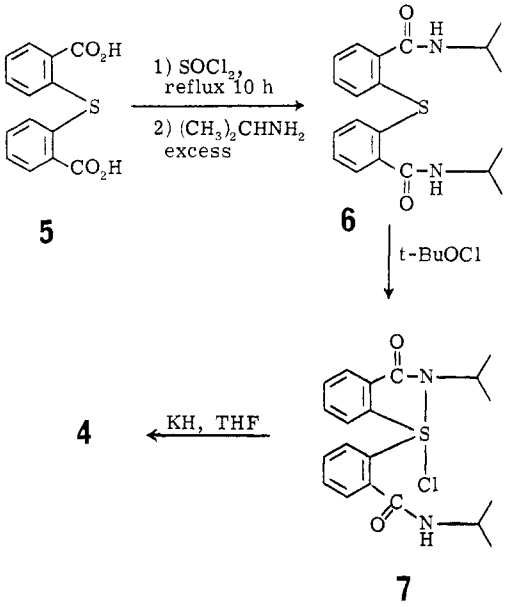
	x	*y*	*z*
S(1)	0.27350 (8)	0.07430 (6)	0.40331 (12)
C(1)	0.1563 (3)	0.1208 (2)	0.4047 (4)
C(2)	0.0590 (3)	0.1083 (3)	0.2912 (5)
C(3)	−0.0229 (4)	0.1494 (3)	0.3104 (6)
C(4)	−0.0067 (4)	0.2007 (3)	0.4396 (6)
C(5)	0.0905 (4)	0.2120 (3)	0.5535 (6)
C(6)	0.1731 (3)	0.1713 (2)	0.5355 (5)
C(7)	0.2821 (3)	0.1796 (3)	0.6471 (5)
C(8)	0.4520 (3)	0.1247 (4)	0.6679 (6)
C(9)	0.4893 (4)	0.1981 (5)	0.6099 (8)
C(10)	0.5034 (4)	0.1098 (4)	0.8426 (7)
C(11)	0.2738 (3)	−0.0296 (2)	0.4790 (5)
C(12)	0.3029 (4)	−0.0510 (3)	0.6381 (5)
C(13)	0.3009 (4)	−0.1341 (3)	0.6763 (6)
C(14)	0.2679 (4)	−0.1936 (3)	0.5568 (6)
C(15)	0.2369 (4)	−0.1716 (3)	0.3998 (6)
C(16)	0.2386 (3)	−0.0887 (2)	0.3579 (5)
C(17)	0.2093 (3)	−0.0568 (2)	0.1924 (5)
C(18)	0.2059 (4)	0.0812 (3)	0.0655 (5)
C(19)	0.3045 (6)	0.0723 (5)	0.0316 (9)
C(20)	0.1087 (6)	0.0709 (5)	−0.0825 (7)
N(1)	0.3385 (2)	0.1224 (2)	0.6093 (4)
N(2)	0.2081 (3)	0.0265 (2)	0.1973 (4)
O(1)	0.3114 (2)	0.2315 (2)	0.7558 (3)
O(2)	0.1921 (3)	−0.1024 (2)	0.0752 (4)
H(2)[a]	0.051 (3)	0.070 (3)	0.196 (5)
H(3)	−0.091 (4)	0.138 (3)	0.228 (6)
H(4)	−0.063 (4)	0.234 (3)	0.447 (5)
H(5)	0.108 (3)	0.248 (3)	0.647 (5)
H(8)	0.487 (4)	0.071 (4)	0.608 (6)
H(12)	0.328 (3)	−0.009 (3)	0.722 (5)
H(13)	0.326 (3)	−0.149 (3)	0.788 (5)
H(14)	0.273 (3)	−0.248 (3)	0.592 (5)
H(15)	0.212 (3)	−0.209 (3)	0.308 (5)
H(18)	0.209 (3)	0.135 (3)	0.103 (4)
H(19A)	0.367 (5)	0.076 (4)	0.139 (7)
H(19B)	0.295 (4)	0.110 (4)	−0.058 (7)
H(19C)	0.302 (4)	0.020 (4)	−0.020 (6)
H(20A)	0.121 (5)	0.024 (4)	−0.131 (8)
H(20B)	0.115 (4)	0.114 (4)	−0.158 (7)
H(20C)	0.050 (4)	0.074 (4)	−0.056 (7)
H(9A)[b]	0.476	0.246	0.680
H(9B)	0.446	0.212	0.488
H(9C)	0.567	0.197	0.628
H(10A)	0.484	0.051	0.867
H(10B)	0.476	0.155	0.905
H(10C)	0.583	0.117	0.880

[a] H's are given the numbers of the atoms to which they are attached. [b] The parameters for the following six hydrogen atoms were not varied in the final cycles of refinement.

diapical ligands (i.e., oxygen is more electronegative than nitrogen), since sulfuranes with more electronegative substituents are expected to have lower reactivity and greater stability.[21] Despite the great reactivity of **4** toward water in solution, crystals of **4** proved sufficiently unreactive toward atmospheric moisture to allow an x-ray crystal structure determination to be carried out on a crystal exposed to the atmosphere.

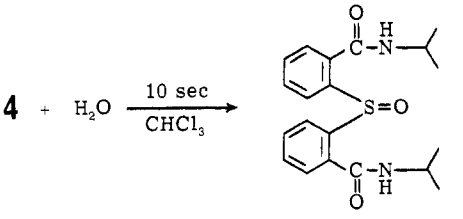
The possibility that diazasulfurane **4** would react with alcohols such as methanol to form methoxyazasulfurane **9**, which might rearrange to *N*-methyl sulfoxide **10**, was an intriguing one. However, the addition of methanol to a solution of **4** brought about no reaction at room temperature. It is clear that observable reaction of **4** with methanol is slower than with water. This may be the result of rapid and equilibrium-favored reversibility of the reaction forming **9**. Further work will be required to elucidate this point.

Scheme I



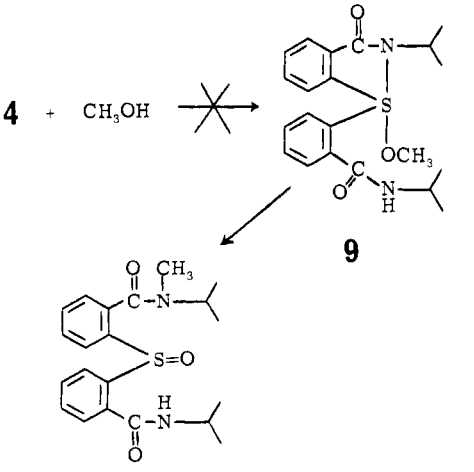
5 **6** **4** **7**

Evidence for the basic nature of **4** is provided by complexation of **4** with Eu(fod)$_3$, a strong Lewis acid.[10] The addition of increments of Eu(fod)$_3$ to a methylene chloride solution of **4** caused the two diastereotopic doublets at δ 1.43 and 1.59 to



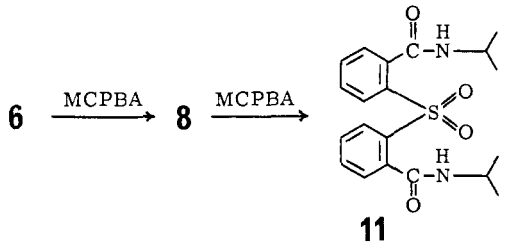
8

move progressively downfield with slopes of 13.4 and 14.3 (chemical shift vs. Eu(fod)$_3$). It should also be noted that during the study some hydrolysis of **4** to sulfoxide diamide **8** occurred. The two doublets (δ 1.13 and 1.26) due to **8** showed very much smaller slopes (2.6 and 3.0) than those seen for **4**. This suggests that Eu(fod)$_3$ complexes more strongly with sulfurane **4** than with sulfoxide **8**. Although it has not been possible to identify unambiguously the basic site in **4** responsible for this complexing, the apical nitrogen atoms represent the most probable site.



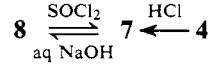
9 **10**

m-Chloroperbenzoic acid (MCPBA) oxidation of **6** provides an alternative route to **8** and to sulfone **11**.

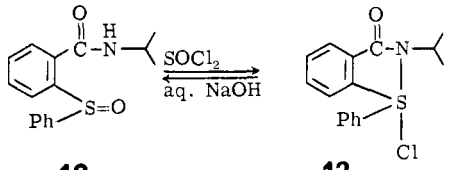


11

The reaction of diazasulfurane **4** with hydrogen chloride produces chloroazasulfurane **7.** This compound can be recrystallized from CH_2Cl_2–hexane and can be handled in air without decomposition. Compound **7** can also be produced by the reaction of diamide sulfide **6** with *tert*-butyl hypochlorite (Scheme I) and by treatment of diamide sulfoxide **8** with excess thionyl chloride. The latter reaction occurs very rapidly producing sulfur dioxide and hydrogen chloride. Treatment of **7** with aqueous base regenerates sulfoxide **8.**



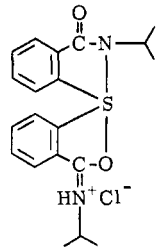
In an analogous reaction chlorosulfurane **13** is produced by reaction of sulfoxide **12** with thionyl chloride. Hydrolysis back



12 13

to sulfoxide **12** is easily accomplished. Crystalline **13** is somewhat sensitive to atmospheric moisture.

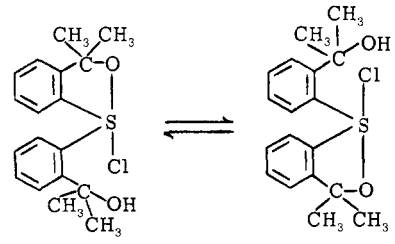
The structure suggested for compound **7** has chlorine and nitrogen atoms occupying the apical positions. However, another possible structure is **14** in which nitrogen and oxygen



14

atoms are the apical ligands with the imine nitrogen as a base to accommodate the hydrogen chloride. The 220-MHz ^1H NMR spectrum shows a total of four methyl doublets, consistent with either **7** or **14** since each structure has a chiral sulfur center. A low-field ortho proton doublet at δ 9.66 suggests that **7** is the correct structure, with the S–Cl bond being covalent. Several such chlorosulfuranes have shown this distincitive feature.[2j,n] Azasulfurane **13** shows a large downfield doublet at δ 9.43. This shift is believed to be due to the close proximity of the ortho proton to the chlorine atom covalently bonded to sulfur.[2j,n] The ortho proton peaks seem for oxasulfuranes[2l,m] have not been seen at fields lower than δ 8.7, an argument against structural hypothesis **14.** Another slightly broader absorption (doublet) in the spectrum of **7** is located at δ 11.60. We suggest that this far downfield shift is an amide N–H signal that is strongly hydrogen bonded to the chlorine ligand on sulfur and is thus at lower field than is usual for such protons.[11]

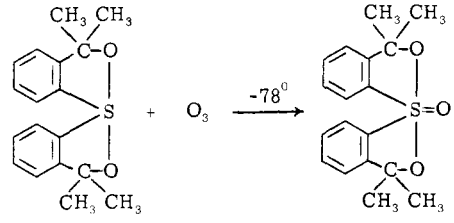
This same type of hydrogen bonding may be occurring in chlorosulfurane **15.**[12] At 25 °C, **15** undergoes a rapid degen-



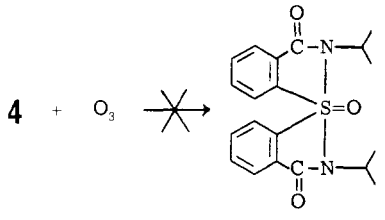
15

erate ligand exchange process as pictured. This is frozen out at −95 °C to give a slow-exchange spectrum with the signal assigned to the hydrogen bonded OH proton at δ 10.33. It is interesting that chloroazasulfurane **7** shows no evidence for such a rapid degenerate ligand exchange in its room temperature NMR.

Attempted Oxidation of Diazasulfurane. Sulfurane oxides lacking halogen ligands have only recently been reported.[2f,g,l] Since the oxidation of diazasulfurane **4** to form diazasulfurane oxide **18** would represent a new structural type, we attempted to prepare **18** by several routes. Since ozone has been used successfully to form sulfurane oxide **17** from sulfurane **16,** we



16 17



18

attempted to oxidize **4** with ozone,[2l] both at −78 and 25 °C, but with no evidence of any reaction. Treatment of **4** with ruthenium tetroxide also gave no reaction. Failure of these reagents to oxidize **4** may be the result of steric hindrance by the isopropyl groups which blocks attack on sulfur.

Structure of 4. Figure 1 shows a stereoscopic view of the molecular structure of **4,** and Figure 2 shows its crystal structure, determined in this work. Selected bond lengths (Table II), bond angles (Table III), and torsion angles (Table IV) are also provided.

Discussion

Diazasulfurane **4** is the first reported sulfurane with apical nitrogen ligands. This new structural type benefits from the added stability gained by the incorporation of the sulfur in two five-membered rings, an effect which has also been reported for cyclic diaryldioxasulfurane structures.[2g] No acyclic analogues of **4** with apical nitrogen ligands have been isolated, although they have been suggested as reactive intermediates in the cleavage of secondary amides with sulfurane **2** (Scheme II).

The choice of structure **4** over alternative structures **19** and **20** was easy for the less symmetrical **20,** which could be ruled out on the basis of the identity of the two isopropyl groups in its ^1H NMR spectra. Neither ^1H NMR spectra nor infrared spectra (strong absorption at 1638 cm^{-1})[13] provided the basis

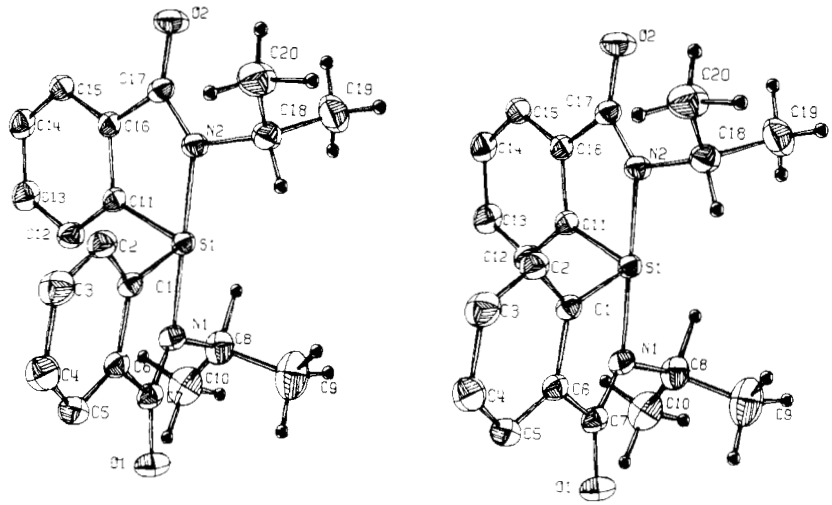


Figure 1. Stereoscopic view of diazasulfurane **4.**

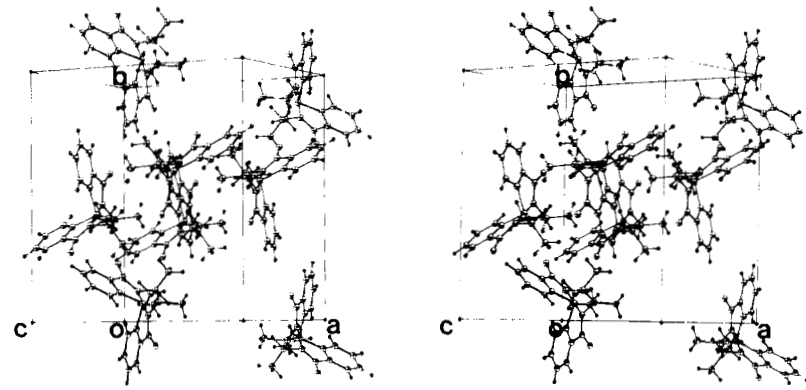


Figure 2. Stereoscopic view of the crystal structure of **4.** The bonds of the reference molecule, which is the one nearest the origin, are shaded darker than the others.

Table II. Selected Bond Lengths (Å) for **4** with Estimated Standard Deviations in Parentheses[a]

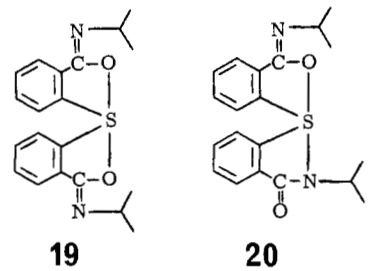
S(1)-C(1)	1.805 (4)	C(8)-C(10)	1.484 (8)
S(1)-C(11)	1.805 (4)	C(8)-N(1)	1.473 (6)
S(1)-N(1)	1.899 (3)	C(11)-C(12)	1.380 (6)
S(1)-N(2)	1.897 (3)	C(11)-C(16)	1.391 (5)
C(1)-C(2)	1.377 (6)	C(12)-C(13)	1.383 (7)
C(1)-C(6)	1.377 (5)	C(13)-C(14)	1.384 (7)
C(2)-C(3)	1.388 (8)	C(14)-C(15)	1.361 (7)
C(3)-C(4)	1.375 (8)	C(15)-C(16)	1.390 (6)
C(4)-C(5)	1.375 (8)	C(16)-C(17)	1.482 (6)
C(5)-C(6)	1.389 (7)	C(17)-N(2)	1.342 (5)
C(6)-C(7)	1.484 (6)	C(17)-O(2)	1.233 (5)
C(7)-N(1)	1.337 (6)	C(18)-C(19)	1.526 (10)
C(7)-O(1)	1.234 (5)	C(18)-C(20)	1.515 (9)
C(8)-C(9)	1.465 (9)	C(18)-N(2)	1.469 (6)

[a] A full listing of bond lengths and angles is included in the microfilm edition.[9]

Table III. Selected Bond Angles (deg) for **4** with Estimated Standard Deviations in Parentheses[a]

C(1)-S(1)-C(11)	104.8 (2)	C(12)-C(11)-S(1)	125.6 (3)
C(1)-S(1)-N(1)	85.8 (2)	C(16)-C(11)-S(1)	112.8 (3)
C(1)-S(1)-N(2)	93.9 (2)	C(17)-C(16)-C(11)	115.8 (4)
C(11)-S(1)-N(1)	94.4 (2)	C(17)-C(16)-C(15)	125.4 (4)
C(11)-S(1)-N(2)	85.8 (2)	N(2)-C(17)-O(2)	128.4 (4)
N(1)-S(1)-N(2)	179.8 (2)	N(2)-C(17)-C(16)	108.4 (4)
C(2)-C(1)-S(1)	125.6 (3)	O(2)-C(17)-C(16)	123.2 (4)
C(6)-C(1)-S(1)	112.7 (3)	C(19)-C(18)-C(20)	113.1 (5)
C(7)-C(6)-C(1)	115.8 (4)	C(19)-C(18)-N(2)	111.1 (5)
C(7)-C(6)-C(5)	124.4 (4)	C(20)-C(18)-N(2)	112.8 (4)
N(1)-C(7)-O(1)	128.0 (4)	S(1)-N(1)-C(7)	114.7 (3)
N(1)-C(7)-C(6)	108.6 (4)	S(1)-N(1)-C(8)	114.6 (3)
O(1)-C(7)-C(6)	123.4 (4)	C(7)-N(1)-C(8)	123.4 (4)
C(9)-C(8)-C(10)	114.4 (5)	S(1)-N(2)-C(17)	115.5 (3)
C(9)-C(8)-N(1)	111.8 (5)	S(1)-N(2)-C(18)	113.8 (3)
C(10)-C(8)-N(1)	113.9 (4)	C(17)-N(2)-C(18)	124.7 (4)

[a] A full listing of bond angles is included in the microfilm edition.[9]



19 **20**

for a choice between **4** and **19,** however, and it was only after the x-ray structure determination was complete that the choice of structure **4** was firm. Structure **19** places two electronegative oxygen atoms in the apical positions, a feature which might be considered favorable[14] relative to **4,** in which less electronegative nitrogen atoms occupy these positions.

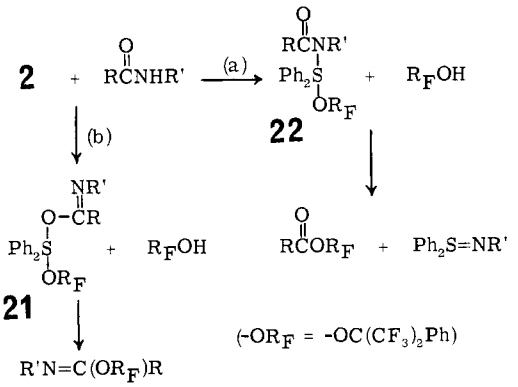
Reactions of acyclic sulfurane **2** with secondary amides have been reported[15] to follow two principal routes (Scheme II). One route (a) leads to the formation of sulfilimines via an inter-

Table IV. Selected Torsion Angles (deg) for **4**[a]

C(8)-N(1)-N(2)-C(18)	−76.0
C(8)-N(1)-C(7)-O(1)	−15.7
C(18)-N(2)-C(17)-O(2)	−13.0
C(6)-C(1)-S(1)-N(1)	6.2
C(16)-C(11)-S(1)-N(2)	5.7
S(1)-N(1)-C(7)-O(1)	−164.3
S(1)-N(2)-C(17)-O(2)	−163.9
S(1)-C(1)-C(6)-C(7)	1.3
S(1)-C(11)-C(16)-C(17)	0.9
C(7)-N(1)-N(2)-C(17)	130.7

[a] The sign of the torsion angle A-B-C-D is considered positive if, when looking along the BC bond, we must rotate atom A clockwise to eclipse atom D.

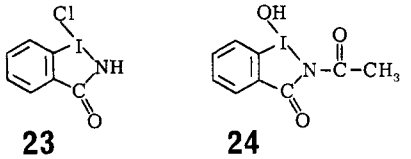
Scheme II



mediate (**22**) with a nitrogen centered ligand. The other route (b), leading to imidates, is postulated to occur via intermediate **21.** Route (b) is favored by an increase in the steric bulk of R′ (specifically for R′ = isopropyl).

This earlier evidence for the intermediacy of **21,** in which the ambident amido ligand is bonded to sulfur through its oxygen, made it difficult to rule out the analogous structure **19** until x-ray evidence for structure **4** became available.

Two iodinane models,[16] **23** and **24,** in which hypervalent

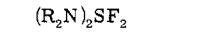


23 **24**

iodine is bonded to the nitrogen in potentially ambident amido ligands, can be cited as possible precedents for structure **4** but in neither case is the steric bulk of the other substituents on nitrogen as great as that of the isopropyl groups of **4.**

A detailed examination of acyloxysulfuranes and of acyloxyiodinanes[17] shows substantial differences in the two series in the dependence of carbonyl stretching frequencies of an apical acyloxy ligand with variations in the trans apical ligand. It is clear that **23** and **24** provide unreliable models for interpretations of features of the infrared spectrum of **4** (or **19**).

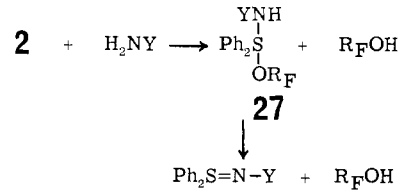
A limited number of precedents exist for sulfuranes bearing N-centered ligands. Recently, Middleton reported[18] a number of bis(dialkylamino)sulfur difluorides (**25**). These new compounds and the earlier known dialkylaminosulfur trifluorides (**26**)[19] are found to be good fluorinating agents useful in or-



25 **26**

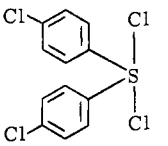
ganic synthesis.[19e,g] It is seen that **25** is similar to diazasulfurane **4** in that each contains two nitrogen ligands. But because of electronegativity differences, the two fluorine ligands of **25** would be expected to be in the apical positions, pushing the amino groups into equatorial positions.[14] In **4,** the N-centered ligands occupy apical positions.

In the reactions of acyclic sulfurane **2** with primary amines to form sulfilimines, the formation of a sulfurane intermediate with one nitrogen-centered apical ligand (**27**) has been pos-



tulated.[20] A number of isolable azasulfonium salts of considerable synthetic utility have recently been reported.[21]

X-Ray Structure of 4. The x-ray structure determination establishes the structure of **4.** The geometry about sulfur is a slightly distorted trigonal bipyramid similar to that found for other sulfuranes whose x-ray structures have been determined.[22-25] The two phenyl ligands occupy two equatorial positions and the two nitrogen ligands occupy the two apical positions. The other equatorial position is considered to be occupied by the sulfur lone pair. The N-S-N bond angle, 179.8 (2)°, is nearer collinearity than for any other sulfurane yet studied.[2k] The essentially collinear S-N bonds are very slightly bent in the direction of the equatorial phenyl rings and away from the lone pair, in the same direction as for most other sulfuranes for which structural information has been reported. Only dichlorosulfurane **28** shows the apical axis bent in the



28

other direction and in this case it is probable that crystal lattice interactions are properly invoked to explain the atypical geometry.[22]

The S-N bond lengths for **4** are 1.899 (3) and 1.897 (3) Å, significantly longer (0.16 Å) than the sum of the sulfur and nitrogen covalent radii (1.74 Å).[25] This is not surprising if one notes that these three-center four-electron bonds, when described by Musher's hypervalent bonding scheme,[23b,26] are predicted to have a bond order less than one. Pauling's correlation[27] of bond order and bond length specifies a S-N bond order of 0.55 in **4,** from the observed bond lengths.

Both N(1) and N(2) deviate considerably from the planes determined by the three groups to which they are bonded (0.24 and 0.22 Å, respectively). The sums of the angles about nitrogen are considerably less than 360° (352.8 and 354.0°, respectively). No intermolecular contacts (Figure 2) appear to be short enough to influence the molecular geometry materially.

This lack of coplanarity of the bonds to nitrogen in the amido ligands of **4** stands in contrast to the usual geometry in amides.[28] The coplanarity which might be predicted from the importance of the amide resonance structure with a double bond to nitrogen is seen in a number of amides for which x-ray structures are available, e.g., difluoroacetamide,[29] *N,N*-diphenylacetamide,[30] and γ- and β-lactams.[31]

Examples are known, however, in which the amide nitrogen is nonplanar. An extreme case is aziridinone **29** in which the sum of the angles about nitrogen is 313.8° and the nitrogen is 0.534 Å from the plane defined by its three substituents.[32] Pyramidal nitrogen is also reported for *N,N′*-diethyl-*N,N′*-

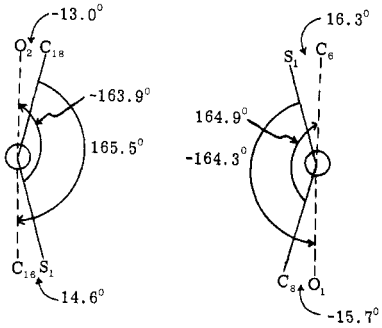
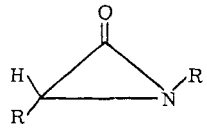
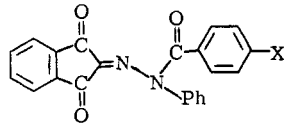


Figure 3. Torsion angles as viewed along the N-C amide bonds.



29 (R = 1-adamantyl)

diphenylurea (N atoms 0.17 and 0.19 Å from the plane)[33] and 4-diethylcarbamoylcyclohex-3-enecarboxylic acid (0.10 Å).[31c] Cephaloridine hydrochloride is reported to have a nonplanar β-lactam nitrogen (sum of the angles around N is 350.7°).[34] Several *N*-acylhydrazones (**30**) show large pyramidal distortions at amide nitrogens (0.18–0.24 Å).[35]



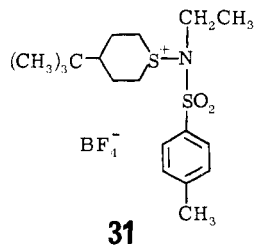
30a, X = H

30b, X = Br

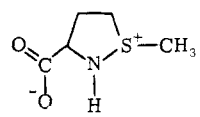
30c, X = t-Bu

Departures from planarity at amide nitrogen have generally been attributed to steric effects,[36,37] either in amides bearing bulky substituents at nitrogen[36] or in small ring lactams.[37] In the former case twisting about the carbonyl–nitrogen bond to relieve nonbonded interactions can decrease the importance of amide resonance and cause the nitrogen to move toward the pyramidal geometry appropriate for unconjugated nitrogen compounds.

The sum of the angles about nitrogen in azasulfonium salt **31**, in which the nitrogen is conjugated with a sulfonyl group,



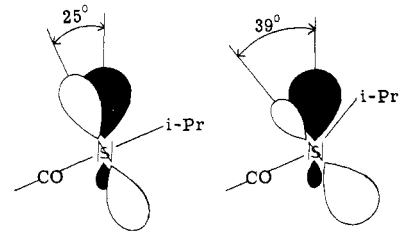
31



32

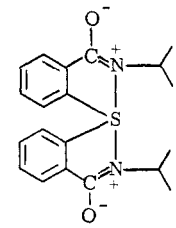
as well as with the sulfonium sulfur, is 356°,[38] with the nitrogen atom 0.19 Å out of the plane. An even greater pyramidal distortion (0.40 Å) is seen[21] for the nitrogen of dehydromethionine (**32**), an azasulfonium salt with nitrogen conjugated only with the sulfonium sulfur, although in this case the difficulties attendant to location of a hydrogen by x-ray crystallography render the uncertainties larger.

The importance of amidelike resonance in **4** (structure **4a**) is reflected in a carbonyl stretching frequency (1638 cm^{-1}) which is even lower than that for the amide (**6**) from which **4**



a **b**

Figure 4. Projection along N–S bond in **4** showing interaction of the sulfur lone pair (shaded orbital) with the lone pair orbital on nitrogen. An increase in the dihedral angle between lone pairs is seen on going from (a) planar nitrogen to (b) pyramidally distorted nitrogen, assuming the hybrid atomic orbital on the nitrogen in (b) to be directed perpendicular to the plane determined by the three atoms bonded to nitrogen.



4a

was prepared (1650 cm^{-1}). Any steric effect which we postulate to explain the pyramidal geometry about the nitrogens of **4** must therefore operate by a mechanism other than one involving a lessening of amidelike resonance.

We could invoke steric repulsion between carbonyl oxygen and the vicinal isopropyl group, which is relieved as the isopropyl group is bent out of the plane. Sizes of torsional angles around the nitrogen–carbonyl bond of **4** provide possible support for this idea. The two groups are not eclipsed (Figure 3) but form dihedral angles of 13.0 [O(2)-C-N-C(18)] and 15.7° [O(1)-C-N-C(8)].

It is noteworthy that the pyramidal distortion in **4** is such that the isopropyl group on each nitrogen is bent out of the plane in a direction which places it trans on the five-membered ring relative to the aromatic ring on the adjacent sulfur.

Two electronic effects might also be invoked to rationalize the observed deviation from coplanarity of the bonds to nitrogen. The pyramidal distortion in **4** may be a manifestation of lone-pair–lone-pair repulsions between sulfur and nitrogen. The lone pair on sulfur is considered to occupy the remaining equatorial position along a line bisecting the C–S–C angle. If the nitrogen atoms of **4** were planar the dihedral angle between the lone pair on sulfur and the occupied p orbitals on the nitrogens would be about 25°. The dihedral angle increases to about 39° for the pyramidally distorted nitrogens actually seen. The direction of distortion is such that the larger lobe of the hybrid orbital on pyramidal nitrogen is directed away from the sulfur lone pair (Figure 4). The observed pyramidal distortion at nitrogen is therefore in a direction to minimize these lone-pair–lone-pair repulsions. A somewhat related diminution of the lone-pair–lone-pair repulsion might be responsible in part for the earlier noted pyramidal distortion at the amide nitrogens in the series of compounds of structure **30**.[35]

Evidence for the energetically significant contribution of related lone-pair–lone-pair repulsions in determining conformations and the energetics of conformational equilibria for substituted hydrazines has accumulated from several laboratories.[39] Eclipsing of lone-pair orbitals on adjacent atoms provides significant destabilization.

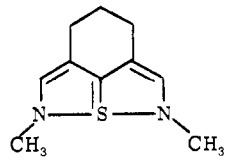
The second electronic effect which might be invoked to rationalize the pyramidal distortion at nitrogen flows from the decrease in dihedral angle between the lone pair of electrons on nitrogen and one of the equatorial C–S bonds on going from

Table V. Selected X_2AY_2 Structures

Compd	Equatorial angle, deg	Ref
2	104.4	24
28	108.6	22
$(p\text{-}CH_3C_6H_4)_2SeCl_2$	106.5	41
$(p\text{-}CH_3C_6H_4)_2SeBr_2$	108.0	41
Ph_2TeBr_2	94.4	42
$(p\text{-}ClC_6H_4)_2TeI_2$	101.1	43
1	108.1	25a
3	107.8	25b
4	104.7	This work

a to **b** in Figure 4 (from ca. 27° for **a** to ca. 13° for **b**). This would be expected to enhance hyperconjugative delocalization of the nitrogen lone pair into the antibonding C–S orbital, a bonding interaction which would lower the energy of **b** relative to **a.**

A useful comparison for diazasulfurane **4** is molecule **33,**



33

a tricoordinate sulfur(IV) species. A full x-ray structure determination of **33** has been done by Hordvik and Julshamn.[40] The N–S–N angle for **33** is 168.5 (2)°, with the bending toward the six-membered ring. This contrasts with the almost linear N–S–N angle (179.8 (2)°) seen for **4.** The nitrogens of **33** are essentially planar (360 and 359.9°, sums of angles about N) while those of **4** are distorted pyramidal. The average[40] S–N bond length in **33** (1.925 Å) is 0.028 Å longer than the S–N bonds of **4.** The relief of lone-pair repulsions which accompanies the pyramidal distortion about the nitrogens of **4** is not possible in **33.** In keeping with this the geometry about nitrogen is observed to be planar.

It has been pointed out[23] that for a number of derivatives of hypervalent chalcogens (sulfuranes, selenuranes, and telluranes, see Table V) the equatorial central C–X–C angle decreases as the difference in electronegativity between the central atom X and the apical substituents increases. This trend has also been rationalized in a discussion[44] of bonding in sulfuranes. Since nitrogen is less electronegative than oxygen (3.04 for nitrogen, 3.44 for oxygen),[45] the equatorial angle of diazasulfurane **4** might be expected to be larger than the equatorial angle of dioxasulfurane **3,** a close structural analogue. The data do not, in this case, conform to the generalization. The C–S–C angle for diazasulfurane **4** is 104.8 (2)° and for dioxasulfurane 3, 107.8° (see Table V). This apparent exception to the expected trend may be a result of the large uncertainties quoted in the structural parameters determined for **3.**

Acknowledgment. This work was supported in part by a grant to J.C.M. from the National Cancer Institute (CA 13963). The x-ray work was carried out using equipment purchased under the terms of our NSF Major Equipment Chemistry Department Grant (MPS 75-05911). The structure determination was part of a class project and we acknowledge the contributions of Lance A. Christell, Ronald L. Amey, Jim Hauske, Peter Rinaldi, and Susan Ruth Krauss. We also thank Mary K. Greensley for providing the stereodrawings, and Professors A. J. Arduengo, III, S. F. Nelsen, and I. Kapovits for helpful discussions.

Supplementary Material Available: A listing of final thermal parameters, complete bond lengths and angles, and observed and calculated structure factors (15 pages). Ordering information is given on any current masthead page.

References and Notes

(1) Part 35 in a series on sulfuranes. For part 34 in this series see L. J. Adzima and J. C. Martin, *J. Org. Chem.*, in press.
(2) (a) M. Allan, A. F. Janzen, and C. J. Willis, *Can. J. Chem.*, **46,** 3671 (1968); (b) J. I. Darragh and D. W. A. Sharp, *Angew. Chem., Int. Ed. Engl.*, **9,** 73 (1970); (c) J. C. Martin and R. J. Arhart, *J. Am. Chem. Soc.*, **93,** 2339, 2341 (1971); (d) I. Kapovits and A. Kálmán, *Chem. Commun.*, 649 (1971); (e) R. J. Arhart and J. C. Martin, *J. Am. Chem. Soc.*, **94,** 4997, 5003 (1972); (f) E. F. Perozzi and J. C. Martin, *ibid.*, **94,** 5519 (1972); (g) J. C. Martin and E. F. Perozzi, *ibid.*, **96,** 3155 (1974); (h) J. C. Martin and M. M. Chau, *ibid.*, **96,** 3319 (1974); (i) G. W. Astrologes and J. C. Martin, *ibid.*, **97,** 6909 (1975); (j) T. M. Balthazor and J. C. Martin, *ibid.*, **97,** 5634 (1975); (k) J. C. Martin and E. F. Perozzi, *Science*, **191,** 154 (1976); (l) L. J. Adzima and J. C. Martin, *J. Am. Chem. Soc.*, **99,** 1657 (1977); (m) G. W. Astrologes and J. C. Martin, *ibid.*, **99,** 4390 (1977); (n) J. C. Martin and T. M. Balthazor, *ibid.*, **99,** 152 (1977).
(3) J. Jilek, V. Seidlova, E. Svatek, and M. Protiva, *Monatsh. Chem.*, **96,** 182 (1965).
(4) H. Gilman and D. L. Esmay, *J. Am. Chem. Soc.*, **75,** 278 (1953).
(5) W. H. Pirkle, R. L. Muntz, and I. C. Paul, *J. Am. Chem. Soc.*, **93,** 2817 (1971). Burdick and Jackson Laboratories Inc., Muskegon, Mich., offer L(−)-2,2,2-trifluoro-1-phenylethanol for sale.
(6) The MULTAN series of programs was used: G. Germain, P. Main, and M. M. Woolfson, *Acta Crystallogr., Sect. A*, **27,** 368 (1971).
(7) $R = \Sigma\|F_{obsd}| - |F_{calcd}\|/\Sigma|F_{obsd}|$; $R_w = [\Sigma w\|F_{obsd}| - |F_{calcd}\|^2/\Sigma w|F_{obsd}|^2]^{1/2}$.
(8) J. A. Ibers and W. C. Hamilton, Ed., "International Tables for X-Ray Crystallography", Vol. IV, Kynoch Press, Birmingham, England, 1974, pp 99–102.
(9) See paragraph at end of paper regarding supplementary material.
(10) B. Feibush, M. F. Richardson, R. E. Sievers, and C. S. Springer, Jr., *J. Am. Chem. Soc.*, **94,** 6717 (1972).
(11) J. R. Dyer, "Applications of Absorption Spectroscopy of Organic Compounds", Prentice-Hall, Englewood Cliffs, N.J., 1965, p 85.
(12) L. J. Adzima and J. C. Martin, *J. Org. Chem.*, in press.
(13) R. M. Silverstein and G. C. Bassler, "Spectrometric Identification of Organic Compounds", 2nd ed, Wiley, New York, N.Y., 1967 pp 87, 97.
(14) E. L. Muetterties and R. A. Schunn, *Q. Rev., Chem. Soc.*, **20,** 245 (1966).
(15) J. C. Martin and J. A. Franz, *J. Am. Chem. Soc.*, **97,** 6137 (1975).
(16) W. Wolf and L. Steinberg, *Chem. Commun.*, 449 (1965).
(17) P. Livant and J. C. Martin, *J. Am. Chem. Soc.*, in press.
(18) W. J. Middleton, *J. Org. Chem.*, **40,** 574 (1975).
(19) (a) G. C. Demitras, R. A. Kent, and A. G. MacDiarmid, *Chem. Ind. (London)*, **41,** 1712 (1964); (b) G. C. Demitras and A. G. MacDiarmid, *Inorg. Chem.*, **6,** 1903 (1967); (c) S. P. von Halasz and O. Glemser, *Chem. Ber.*, **103,** 594 (1970); (d) *ibid.*, **104,** 1247 (1971); (e) L. N. Markovskij, V. E. Pashinnik, and A. V. Kirsanov, *Synthesis*, 787 (1973); (f) J. A. Gibson, D. G. Ibbott, and A. F. Janzen, *Can. J. Chem.*, **51,** 3203 (1973); (g) L. N. Markovskij and V. E. Pashinnik, *Synthesis*, 801 (1975).
(20) J. A. Franz and J. C. Martin, *J. Am. Chem. Soc.*, **97,** 583 (1975). Other types of sulfurane intermediates with nitrogen ligands are also postulated in this paper.
(21) R. S. Glass and J. R. Duchek, *J. Am. Chem. Soc.*, **98,** 965 (1976), and references cited therein.
(22) N. C. Baenziger, R. E. Buckles, R. J. Maner, and T. D. Simpson, *J. Am. Chem. Soc.*, **91,** 5749 (1969).
(23) (a) I. C. Paul, J. C. Martin, and E. F. Perozzi, *J. Am. Chem. Soc.*, **93,** 6674 (1971); (b) *ibid.*, **94,** 5010 (1972); (c) E. F. Perozzi, J. C. Martin, and I. C. Paul, *ibid.*, **96,** 6735 (1974).
(24) A. Kálmán, K. Sasvári, and I. Kapovits, *Acta Crystallogr., Sect. B*, **29,** 355 (1973).
(25) L. Pauling, "The Nature of the Chemical Bond", 3rd ed, Cornell University Press, Ithaca, N.Y., 1960, p 260.
(26) J. I. Musher, *Angew. Chem., Int. Ed. Engl.*, **8,** 54 (1969).
(27) L. Pauling, *J. Am. Chem. Soc.*, **69,** 542 (1947).
(28) J. M. Lehn, *Fortschr. Chem. Forsch.*, **15,** 311 (1970), and A. Rauk, L. C. Allen, and K. Mislow, *Angew. Chem., Int. Ed., Engl.*, **9,** 400 (1970), discuss the factors important in determining energy barrier heights for pyramidal inversion at nitrogen. Although formamide is not planar at nitrogen [C. C. Costain and J. M. Dowling, *J. Chem. Phys.*, **32,** 158 (1960)], more highly substituted amides tend to be so.[29–31]
(29) D. O. Hughes and R. W. H. Small, *Acta Crystallogr., Sect. B*, **28,** 2520 (1972).
(30) W. R. Krigbaum, R.-J. Roe, and J. D. Woods, *Acta Crystallogr., Sect. B*, **24,** 1304 (1968).
(31) (a) K. B. Birnbaum, *Acta Crystallogr., Sect. B*, **26,** 722 (1970); (b) R. Parthasarathy, *ibid.*, **26,** 1283 (1970); see, however, (c) C. Pedone, E. Benedetti, A. Immirzi, and G. Allegra, *J. Am. Chem. Soc.*, **92,** 3549 (1970).
(32) A. H.-J. Wang, I. C. Paul, E. R. Talaty, and A. E. Dupuy, Jr., *J. Chem. Soc., Chem. Commun.*, 43 (1972).
(33) P. Ganis, G. Avitabile, E. Benedetti, C. Pedone, and M. Goodman, *Proc. Natl. Acad. Sci. U.S.A.*, **67,** 426 (1970).
(34) R. M. Sweet and L. F. Dahl, *J. Am. Chem. Soc.*, **92,** 5489 (1970).
(35) S. A. Puckett, M. K. Greensley, I. C. Paul, and D. Y. Curtin, *J. Chem. Soc., Perkin Trans. 2*, 847 (1977).
(36) D. B. Pendergrass, Jr., I. C. Paul, and D. Y. Curtin, *J. Am. Chem. Soc.*, **94,** 8730 (1972).
(37) F. K. Winkler and J. D. Dunitz, *J. Mol. Biol.*, **59,** 169 (1971).

(38) R. E. Cook, M. D. Glick, J. J. Rigau, and C. R. Johnson, *J. Am. Chem. Soc.*, **93**, 924 (1971).
(39) S. F. Nelsen and G. R. Weisman, *J. Am. Chem. Soc.*, **98**, 3281 (1976); Y. Nomura, N. Masai, and Y. Takeuchi, *J. Chem. Soc., Chem. Commun.*, 288 (1974); for a review see J. B. Lambert, *Top. Stereochem.*, **8**, 19 (1971).
(40) A. Hordvik and K. Julshamn, *Acta Chem. Scand.*, **26**, 343 (1972). The S–N bond lengths of **33** are 1.901 (5) and 1.948 (5) Å. The difference (0.047 Å), more than nine times the standard deviation, is significant. We use an average S–N bond length in our comparisons. For a related structural study see F. Leung and S. C. Nyburg, *Chem. Commun.*, 707 (1970).
(41) J. D. McCullough and R. E. Marsh, *Acta Crystallogr.*, **3**, 41 (1950).
(42) G. D. Christofferson and J. D. McCullough, *Acta Crystallogr.*, **11**, 249 (1958).
(43) G. Y. Chao and J. D. McCullough, *Acta Crystallogr.*, **15**, 887 (1962).
(44) M. M. L. Chen and R. Hoffmann, *J. Am. Chem. Soc.*, **98**, 1647 (1976).
(45) A. L. Allred, *J. Inorg. Nucl. Chem.*, **17**, 215 (1961).

Kinetics of Chlorpromazine Cation Radical Decomposition in Aqueous Buffers

Hung Yuan Cheng, Patricia Holt Sackett, and Richard L. McCreery*

Contribution from the Department of Chemistry, The Ohio State University, Columbus, Ohio 43210. *Received June 2, 1977*

Abstract: The stoichiometry and kinetics of the reactions of the perchlorate salt of chlorpromazine cation radical ($CPZ^{+\cdot}$) in aqueous buffers were examined in the pH range 2–7 using electrochemistry and spectrophotometry. In phosphate and citrate media, 1 mol of radical produced 0.5 mol each of chlorpromazine and chlorpromazine sulfoxide, while in amine buffers or unbuffered solution, other products were formed. For phosphate and citrate buffers, the decay of $CPZ^{+\cdot}$ was second order in $CPZ^{+\cdot}$ first order in buffer anion concentration, inverse first order in $[H^+]$ and inverse first order in neutral chlorpromazine concentration. The kinetic data indicate the formation of a cation radical/buffer adduct which is oxidized by another molecule of $CPZ^{+\cdot}$, followed by rearrangement to the sulfoxide product. The results are inconsistent with a mechanism involving disproportionation of the radical, but rather indicate a direct reaction of cation radical with buffer components and water.

Introduction

During the last decade, there has been significant interest in the phenothiazine-based cation radicals for two fairly distinct reasons. First, the structure and reactions of the phenothiazine cation radical are similar to those of the intensely studied diphenylanthracene and thianthrene radicals. Examination of the kinetics and mechanisms of reactions of these radicals with nucleophiles has been very active.[1-6] In addition, the phenothiazine-based major tranquilizers such as chlorpromazine (CPZ) and fluphenazine are very widely used antipsychotic drugs, whose activity and metabolism are believed to involve formation of the radical cation as an intermediate.[7,8] Owing to the low stability of these radical ions in neutral aqueous environments, previous work was carried out in nonaqueous solvents, or in strong aqueous acids. It is the purpose of the present work to investigate the sulfoxidation of the CPZ cation radical under conditions which more closely approximate those in physiological fluids.

Two general mechanisms have been proposed for the reactions of nucleophiles (including water) with cation radicals, differing in the reactive form of the radical. In the first (Scheme I), the cation radical ($Ar^{+\cdot}$) is attacked directly by nucleophile (Z), then the adduct is oxidized by a second molecule of cation radical.

Scheme I

$$Ar^{+\cdot} + Z \rightleftarrows (ArZ)^{+\cdot}$$
$$(ArZ)^{+\cdot} + Ar^{+\cdot} \rightleftarrows Ar + (ArZ)^{2+}$$
$$(ArZ)^{2+} \rightarrow \text{products}$$

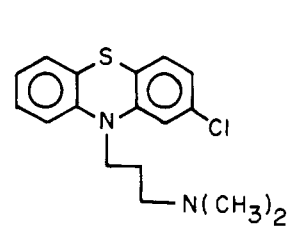
A second mechanism which must be considered involves diproportionation of the cation radical to its dication (Scheme II).

Scheme II

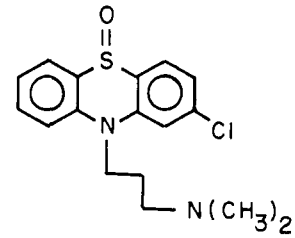
$$2Ar^{+\cdot} \rightleftarrows Ar + Ar^{2+}$$
$$Ar^{2+} + Z \rightleftarrows (ArZ)^{2+}$$
$$(ArZ)^{2+} \rightarrow \text{products}$$

While it is true that the overall stoichiometry of the two routes is identical, it should be emphasized that one mechanism involves direct reaction of the cation radical with nucleophile while the other involves a dication intermediate. Numerous examples of these types of reactions are available,[1-6] recent cases being the reaction of 10-phenylphenothiazine cation radical with pyridine[9] and thianthrene cation radical with water,[10] both using acetonitrile as a solvent. The details of the kinetics will not be repeated here, but in both cases, the kinetics indicate a direct attack of cation radical by the nucleophile, according to Scheme I. It is also interesting to note that the formation of thianthrene sulfoxide from thianthrene radical and water was accelerated in the presence of pyridine by the formation of a pyridine/radical reactive intermediate.[10]

The substantial pharmacological interest in chlorpromazine has prompted several studies of its oxidation and radical ion chemistry. In strong sulfuric acid CPZ (**1**) may be electrochemically oxidized via two one-electron processes to chlorpromazine sulfoxide (CPZO, **2**).[11,12] The hydrolysis of the



1



2

0002-7863/78/1500-0962$01.00/0