products directly or through other short-lived intermediates such as ketocarbenes.

Khairat M. Ibne-Rasa, Ruth H. Pater
Joseph Ciabattoni, John O. Edwards*
Department of Chemistry, Brown University
Providence, Rhode Island 02912

Received July 2, 1973

Determination of the Absolute Configuration of (+)-3-Carboxy-2,2,5,5-tetramethyl-1-pyrrolidinyloxy

Sir:

Nitroxides are paramagnetic compounds which have been widely used in recent years as spin-label reporter groups in biological systems.[1] The esr spectrum of a nitroxide depends on the polarity of its surroundings, its rotational mobility, its orientation with respect to an external magnetic field, and its proximity to other paramagnetic species. The esr spectrum of a chiral nitroxide species might therefore be sensitive to the chirality of the spin-labeled molecule's environment. Spin-label studies of enantiomeric specificity in biological systems have been limited because suitable optically pure chiral nitroxides of known absolute configuration have not been available. We wish to report here the X-ray crystallographic determination of the structure of the chiral nitroxide (+)-3-carboxy-2,2,5,5-tetramethyl-1-pyrrolidinyloxy ((+)I).

The (+) isomer of I was prepared as described previously, using *l*-(−)-α-methylbenzylamine as the resolving agent.[2] The circular dichroism spectrum of a solution of (+)-I in ethanol has maxima at 420 nm with $\Delta\epsilon_{\max}$ 0.34 M^{-1} cm^{-1} and at ~245 nm with $\Delta\epsilon_{\max}$ 0.6 M^{-1} cm^{-1}; the band at 245 nm is distorted by a strong negative band at lower wavelength.[3] The uv-visible absorption spectrum of an ethanol solution of (+)-I, which is similar to spectra reported for other aliphatic nitroxides,[4–6] exhibits two bands, one at 414 nm (ϵ 6.3 M^{-1} cm^{-1}) due to an $n \rightarrow \pi^*$ transition and one at 232 nm ($\epsilon_{\max}$ 2.3 × 10^3 M^{-1} cm^{-1}) presumably due to a $\pi \rightarrow \pi^*$ transition.

Crystals of the (+) isomer of I recrystallized from ethyl ether were found to be orthorhombic, space group $P2_12_12_1$ with a = 8.089 (16), b = 10.097 (10), and c = 12.404 (24) Å. The experimental density is 1.216 g/cm^3 compared with a calculated density of 1.221 g/cm^3, $Z = 4$.

Two axes (a, c) of diffraction data using Cu Kα radiation were collected using a Supper-Pace automated diffractometer possessing Weissenberg geometry. Following Lp corrections, the data were correlated to give the 992 independent reflections which were used in the structure determination.

Phases were obtained by direct application of the multiple tangent refinement program MULTAN.[7] An E map was calculated which clearly revealed the positions of the 13 nonhydrogen atoms. The subsequent structure-factor calculation resulted in R_1 = 0.32. Following eight cycles of refinement (R_1 = 0.11) the 16 hydrogen positions were obtained by difference synthesis. Full-matrix least-squares refinement of all positional and anisotropic thermal parameters (individual isotropic temperature factors for hydrogen) resulted in R_1 = 0.054. Final atomic positions and their estimated standard errors are given in Table I.

Table I. Atomic Positions and Estimated Standard Errors

Atom	x/a	y/b	$-z/c$
N-1	1.3586 (2)	0.2543 (3)	0.7102 (2)
C-2	1.1961 (3)	0.2543 (3)	0.6541 (2)
C-3	1.0821 (3)	0.2861 (3)	0.7516 (3)
C-4	1.1682 (4)	0.2216 (4)	0.8470 (3)
C-5	1.3536 (3)	0.2442 (3)	0.8291 (2)
O-6	1.4930 (2)	0.2554 (3)	0.6569 (2)
C-7	1.1695 (5)	0.1169 (3)	0.6049 (4)
C-8	1.1941 (5)	0.3604 (4)	0.5681 (3)
C-9	0.9067 (3)	0.2369 (3)	0.7364 (3)
O-10	0.8607 (3)	0.1283 (3)	0.7574 (5)
O-11	0.8089 (3)	0.3236 (2)	0.6914 (2)
C-12	1.4577 (4)	0.1300 (4)	0.8670 (4)
C-13	1.4157 (5)	0.3746 (4)	0.8765 (4)
H-3	1.0801 (44)	0.3796 (40)	0.7580 (35)
H-4A	1.1383 (53)	0.1308 (46)	0.8477 (37)
H-4B	1.1413 (62)	0.2653 (48)	0.9125 (48)
H-7A	1.1703 (47)	0.0497 (33)	0.6636 (32)
H-7B	1.2499 (94)	0.0862 (59)	0.5647 (64)
H-7C	1.0808 (59)	0.1161 (39)	0.5624 (41)
H-8A	1.2889 (85)	0.3287 (51)	0.5221 (51)
H-8B	1.0965 (60)	0.3692 (41)	0.5328 (42)
H-8C	1.2219 (55)	0.4492 (38)	0.6003 (37)
H-11	0.7139 (66)	0.2813 (41)	0.6884 (39)
H-12A	1.4327 (57)	0.0584 (43)	0.8340 (39)
H-12B	1.4290 (64)	0.1269 (46)	0.9428 (56)
H-12C	1.5854 (64)	0.1587 (46)	0.8614 (46)
H-13A	1.4075 (46)	0.3620 (35)	0.9619 (41)
H-13B	1.5556 (69)	0.3977 (48)	0.8477 (48)
H-13C	1.3550 (59)	0.4465 (42)	0.8571 (38)

The absolute configuration of (+)-I was determined by the direct measurement of Bijvoet differences with applied absorption corrections using a method described previously.[8] Accessible reflections with an intensity I_c greater than 2.5, calculated using the f'' values of Cromer and Liberman for oxygen, nitrogen, and carbon,[9] and a calculated $IDEL = (I_{hkl} - I_{\bar{h}\bar{k}\bar{l}})/I_c$ greater than 2.5% were ranked according to a suitability parameter $P = I_c(IDEL)^2$. The signs of the observed differences $(I_{hkl} - I_{\bar{h}\bar{k}\bar{l}})$ for the 20 reflections with the largest values of P were compared with those calculated for the S configuration. The observed signs were opposite to those calculated for all reflections, thereby establishing the configuration as R. Figure 1 is a drawing of the R configuration of (+)-I. A detailed description of the structure and absolute configuration determination will be published elsewhere.

Interatomic distances and angles and their estimated standard errors are presented in Table II. The N-1–

---

[1] H. M. McConnell and B. G. McFarland, *Quart. Rev. Biophys.*, **3**, 91 (1970).

[2] (a) K. Flohr and E. T. Kaiser, *J. Amer. Chem. Soc.*, **94**, 3675 (1972); (b) K. Flohr, Ph.D. Thesis, University of Chicago, 1973.

[3] We wish to thank Professor G. Holzwarth and Mr. A. Attiah for these measurements.

[4] Y. Brunel, H. Lemaire, and A. Rassat, *Bull. Soc. Chim. Fr.*, 1895 (1964).

[5] A. R. Forrester, J. M. Hay, and R. H. Thomson, "Organic Chemistry of Stable Free Radicals," Academic Press, New York, N. Y., 1968, p 220.

[6] E. G. Janzen, *Top. Stereochem.*, **6**, 181 (1971).

[7] P. Main, M. W. Woolfson, and G. Germain, "MULTAN: A Computer Programme for the Automatic Solution of Crystal Structures," Department of Physics, University of York, York, England, 1971.

[8] (a) J. W. Moncrief and S. P. Sims, *Chem. Commun.*, 914 (1969); (b) D. W. Engel, *Acta Crystallogr., Sect. B*, **28**, 1496 (1972).

[9] D. T. Cromer and D. Liberman, *J. Chem. Phys.*, **53**, 1891 (1970).

Table II. Bond Distances and Angles and Their Estimated Standard Errors

Atoms	Distance, Å	Angle	Degrees
N-1–C-2	1.487 (3)	C-2–N-1–C-5	116.2 (2)
N-1–C-5	1.479 (4)	C-2–N-1–O-6	120.8 (2)
N-1–O-6	1.272 (3)	C-5–N-1–O-6	122.8 (2)
C-2–C-3	1.554 (4)	N-1–C-2–C-3	99.3 (2)
C-2–C-7	1.531 (4)	N-1–C-2–C-7	108.1 (2)
C-2–C-8	1.512 (4)	N-1–C-2–C-8	109.8 (2)
C-3–C-4	1.520 (5)	C-3–C-2–C-7	114.5 (3)
C-3–C-9	1.515 (4)	C-3–C-2–C-8	113.4 (3)
C-4–C-5	1.533 (4)	C-7–C-2–C(8)	111.0 (3)
C-5–C-12	1.504 (5)	C-2–C-3–C-4	104.2 (2)
C-5–C-13	1.527 (5)	C-2–C-3–C-9	113.0 (3)
C-9–O-10	1.187 (4)	C-4–C-3–C-9	112.7 (3)
C-9–O-11	1.305 (4)	C-3–C-4–C-5	105.8 (2)
		N-1–C-5–C-4	100.4 (2)
		N-1–C-5–C-12	110.5 (3)
		N-1–C-5–C-13	108.4 (3)
		C-4–C-5–C-12	112.9 (3)
		C-4–C-5–C-13	113.2 (3)
		C-3–C-9–O-10	124.7 (3)
		C-3–C-9–O-11	113.6 (3)
		O-10–C-9–O-11	121.6 (3)

O-6 distance of 1.27 Å lies between that expected for a single bond (1.44 Å) and a double bond (1.20 Å).[10] Similar N–O distances have been observed in other *N*-oxides[11] and are indicative of a semipolar N→O bond. The conformation of the ring may be described by considering that O-6, C-3, and C-9 are displaced 0.21, −0.57, and −0.20 Å, respectively, from the least-squares plane defined by N-1, C-2, C-4, and C-5. Atoms C-2, C-5, N-1, and O-6 are nearly planar with N-1 displaced 0.03 Å from the plane of C-2, C-5, and O-6. Planarity of the C(NO)C group has also been observed in X-ray crystallographic determinations of the structures of the potassium salt and amide of a pyrrolinyl nitroxide,[12,13] but in three piperidinyl nitroxides, the N–O bonds have been found to make angles of 16, 30.5, and 18.2°, respectively, with the C–N–C planes.[11,14–16]

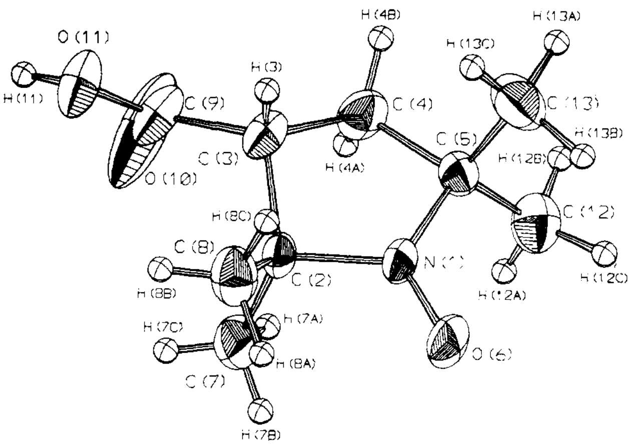

Figure 1. ORTEP II drawing of the *R* configuration of (+)-I with thermal ellipsoids representing 50% probability. Hydrogen atoms are drawn with an arbitrary radius of 0.10 Å.

Several optically active derivatives of (+)-I have been synthesized using reactions expected to proceed with retention of configuration at C-3. The *m*- and *p*-nitrophenyl esters of (+)-I prepared by coupling the acid with the corresponding nitrophenols have been employed in the investigation of enantiomeric specificity in ester hydrolysis catalyzed by α-chymotrypsin and cyclohexaamylose.[2,17] We are now using the (+)-amide, mp 198–198.5°, $[\alpha]^{25}\text{D}$ +116° (*c* 0.15, EtOH), formed by the reaction of liquid ammonia with the *p*-nitrophenyl ester of (+)-I as a precursor for the establishment of the absolute configuration of the enantiomers of 3-amino-2,2,5,5-tetramethyl-1-pyrrolidinyloxy and related derivatives, racemic forms of which have been employed in spin-label studies of many biological systems.[18]

Acknowledgment. The support of this research by a grant from the National Science Foundation (J. W. M.), by the donors of the Petroleum Research Fund, administered by the American Chemical Society (E. T. K.), by Alfred P. Sloan Foundation Fellowships (J. W. M. and E. T. K.), by an NDEA Fellowship (J. B. W.), and by a U. S. Public Health Service Medical Scientist Traineeship, GM 1939 (K. F.) and the assistance of the Emory University Computer Center are gratefully acknowledged.

---

(10) L. Pauling, "The Nature of the Chemical Bond," 3rd ed, Cornell University Press, Ithaca, N. Y., 1960.

(11) (a) J. Lajzerowicz-Bonneteau, *Acta Crystallogr., Sect. B*, **24**, 196 (1968); (b) C. Romers and B. Hesper, *Acta Crystallogr.*, **20**, 162 (1966); (c) E. L. Eichhorn, *Acta Crystallogr.*, **9**, 787 (1956).

(12) J. C. A. Boeyens and S. J. Kruger, *Acta Crystallogr., Sect. B*, **26**, 668 (1970).

(13) J. W. Turley and F. P. Boer, *Acta Crystallogr., Sect. B*, **28**, 1641 (1972).

(14) L. J. Berliner, *Acta Crystallogr., Sect. B*, **26**, 1198 (1970).

(15) P. A. Capiomont, B. Chion, and J. Lajzerowicz, *Acta Crystallogr., Sect. B*, **27**, 322 (1971).

(16) P. A. Capiomont, *Acta Crystallogr., Sect. B*, **28**, 2298 (1972).

(17) K. Flohr, R. M. Paton, and E. T. Kaiser, *Chem. Commun.*, 1621 (1971).

(18) For example, see: H. M. McConnell, *Annu. Rev. Biochem.*, **40**, 227 (1971); L. J. Berliner, Ph.D. Thesis, Stanford University, 1967.

Susan S. Ament, Joseph B. Wetherington, J. William Moncrief*
Department of Chemistry, Emory University
Atlanta, Georgia 30322

Kathleen Flohr, M. Mochizuki, E. T. Kaiser*
Searle Chemistry Laboratory, University of Chicago
Chicago, Illinois 60637

Received July 5, 1973

Organosilylhydrazyl Radicals and a Possible Triazyl Radical[1]

Sir:

Although certain triarylhydrazyls are very stable,[2] alkylhydrazyl radicals are extremely reactive, having been observed only as products of X-irradiation of the parent hydrazines in adamantane matrix.[3] We find that tris(organosilyl)hydrazyls, although less stable than triarylhydrazyls such as diphenylpicrylhydrazyl (DPPH), can be prepared and studied by electron spin resonance spectroscopy in solution at room temperature. These are apparently the first examples of organometal-substituted hydrazyls.

Tris(trimethylsilyl)hydrazyl (**1**) and tris(*tert*-butyldi-

---

(1) This work was supported by the U. S. Air Force Office of Scientific Research (NC)-OAR, USAF Grant No. AF-AFOSR-70-1904.

(2) A. R. Forrester, J. M. Hay, and R. H. Thomson, "Organic Chemistry of Stable Free Radicals," Academic Press, New York, N. Y., 1968, Chapter 4.

(3) D. E. Wood, C. A. Wood, and W. A. Lathan, *J. Amer. Chem. Soc.*, **94**, 9278 (1972).