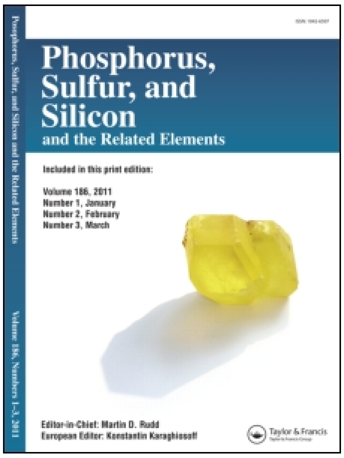


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

ISOLATION AND SINGLE-CRYSTAL X-RAY DIFFRACTION ANALYSIS OF *N*-BENZYL-3-THIA-7-AZABICYCLO[3.3.1]-NONAN-9,9-DIOL PERCHLORATE, A NOVEL HYDRATE FORMED FROM REACTION OF *N*-BENZYL-3-THIA-7-AZABICYCLO[3.3.1]-NONAN-9-ONE WITH PERCHLORIC ACID

Bruce R. Bailey III[a]; K. Darrell Berlin[a]; Elizabeth M. Holt[a]
[a] Department of Chemistry, Oklahoma State University, Stillwater, OK

To cite this Article Bailey III, Bruce R. , Berlin, K. Darrell and Holt, Elizabeth M.(1984) 'ISOLATION AND SINGLE-CRYSTAL X-RAY DIFFRACTION ANALYSIS OF *N*-BENZYL-3-THIA-7-AZABICYCLO[3.3.1]-NONAN-9,9-DIOL PERCHLORATE, A NOVEL HYDRATE FORMED FROM REACTION OF *N*-BENZYL-3-THIA-7-AZABICYCLO[3.3.1]-NONAN-9-ONE WITH PERCHLORIC ACID', Phosphorus, Sulfur, and Silicon and the Related Elements, 20: 2, 131 — 137

To link to this Article: DOI: 10.1080/03086648408077620

URL: http://dx.doi.org/10.1080/03086648408077620

Phosphorus and Sulfur, 1984, Vol. 20, pp. 131–137
0308-664X/84/2002-0131/$18.50/0

ISOLATION AND SINGLE-CRYSTAL X-RAY DIFFRACTION ANALYSIS OF *N*-BENZYL-3-THIA-7-AZABICYCLO[3.3.1]-NONAN-9,9-DIOL PERCHLORATE, A NOVEL HYDRATE FORMED FROM REACTION OF *N*-BENZYL-3-THIA-7-AZABICYCLO[3.3.1]-NONAN-9-ONE WITH PERCHLORIC ACID

BRUCE R. BAILEY, III, K. DARRELL BERLIN* and
ELIZABETH M. HOLT*

Department of Chemistry, Oklahoma State University, Stillwater, OK 74078

(*Received February 28, 1984; in final form March 23, 1984*)

We report the isolation and single crystal X-ray diffraction analysis of *N*-benzyl-3-thia-7-aza-bicyclo[3.3.1]nonan-9,9-diol perchlorate which is the hydrate obtained from reaction of *N*-benzyl-3-thia-7-azabicyclo[3.3.1]nonan-9-one with perchloric acid. Synthesis of the ketone precursor of the diol involved reaction of 4-thianone with excess paraformaldehyde in the presence of benzylamine in methanol/acetic acid. An X-ray diffraction analysis was performed on a single crystal of the hydrate. There are two molecules in the unit cell of the perchlorate in space group $P\bar{1}$. Unit cell dimensions (at 27°C) are: $a = 15.720(16)$, $b = 17.425(14)$, $c = 6.917(6)$ Å; $\alpha = 78.77(7)$, $\beta = 90.35(7)$, $\gamma = 62.13(6)°$, $Z = 4$. The system is confirmed to be a chair–chair conformer in the solid state with little ring distortion near the gem diol group in the molecule.

INTRODUCTION

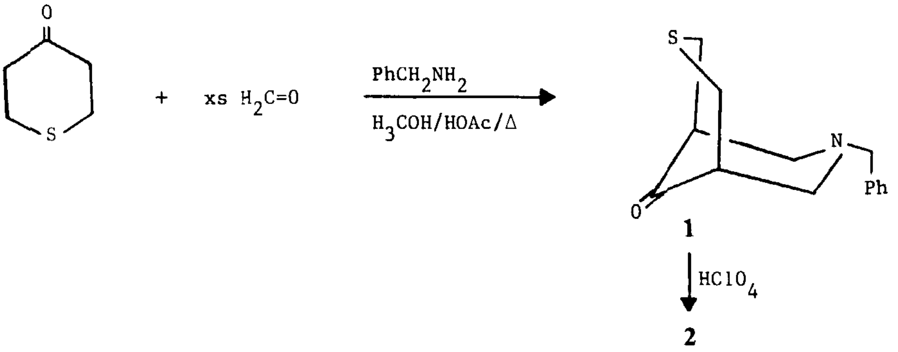
Hydrates of 1-hetera-4-cyclohexanones have been recorded for members of the piperidones,[1] the phosphorinanones,[2] and for *N*-benzyl-3-oxa-7-azabicyclo-[3.3.1]nonan-9-one hydroperchlorate[3] but no structural analysis of a single crystal could be found in the literature. Although the precursor ketone **1** is known,[4] we report herein the isolation and crystal structure of *N*-benzyl-3-thia-7-azabicyclo[3.3.1]nonan-9,9-diol perchlorate (**2**) which is formed from reaction of **1** with perchloric acid.

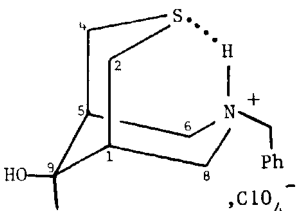
RESULTS AND DISCUSSION

The synthesis of **2** followed the pathway illustrated from 4-thianone in a Mannich type of condensation.[4,5] All spectral data support the structure of **2** including the ^{13}C NMR profile. Interestingly, a comparison of the ^{13}C resonance for the bridge carbon [C(9)] in **2** with signals for the corresponding carbons in a number of six-membered heterocyclic relatives reveals a pattern (Table I) which places the absorbance

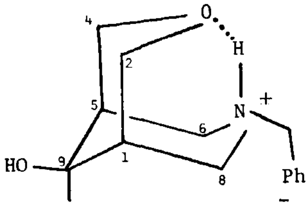
---

*Author to whom all correspondence should be addressed.

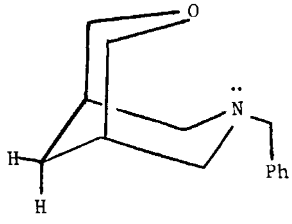




2



3



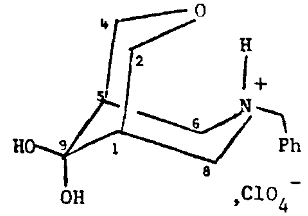
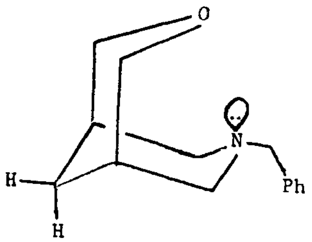
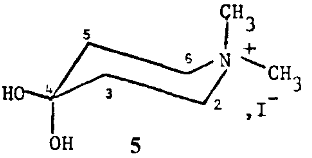
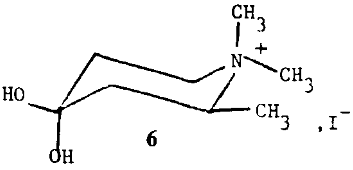
4

between approximately 88–102 ppm from TMS. It is clear that not only the heteroatom present but substitution on the ring is also important for determining the chemical shift for the gem-diol carbon. The comparison with the oxygen analog **3** is particularly interesting in that the chemical shifts for C(1,5) are still slightly downfield from the counterparts in **2** but the shift for C(9) is *upfield* in **3** compared to that in **2**. No single crystal X-ray diffraction analysis of **3** has ever been reported. Consequently, it is not possible to determine unequivocally whether or not the upfield resonance of C(9) in **3** is due to a chair–boat form (with the ring oxygen atom in a boat conformer) or to perhaps intermolecular H-bonding as well as intramolecular H-bonding in the chair–chair form. An examination of the ^{13}C spectrum of the closest relative available, namely **4**,[3] showed the signal for C(2,4) at 70.6 ppm and that for C(6,8) at 57.6 ppm. One might suspect this suggests that **3** exists as a chair–boat form since C(2,4) absorbs at a much higher field than in **4**, but this can not be substantiated at this time. We do note in passing that the signal for C(2,6) [which is comparable to C(6,8) in **2** and **3**] is about the same in the hydrates (or gem diols) of the simple piperidones **5**–**8** (Table I) compared with that in **3** which lends credence to the supposition that these systems all possess chair forms for the nitrogen-containing rings. The C(9) resonances are also quite similar in **6**–**8** as well as in the phosphorus systems **9** and **10**, again suggesting that distortion at the diol end of the molecule is minimal regardless of the nature of the heteroatom three bonds removed from C(9). The large downfield shift for C(9) in piperidone **5** has no rationale which is immediately obvious since all data for **5**–**8** were taken on aqueous solutions.

The crystal data for **2** are in Table II and the bond angles and bond distances are in Table III. A projection drawing of **2** (Figure 1) clearly shows the system to be a chair–chair form in the solid state. Figure 2 shows the orientations of the two

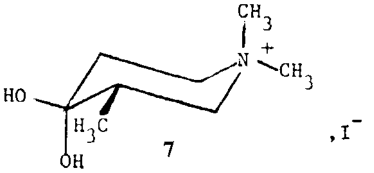
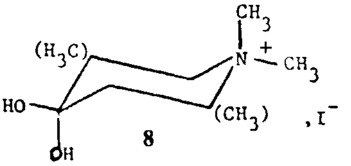
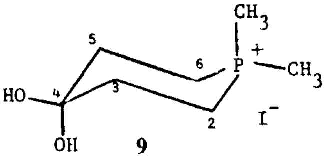
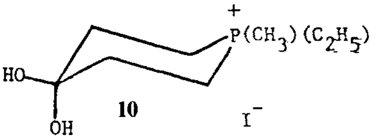
TABLE I

^{13}C NMR chemical shifts for **2** and related gem-diol systems (from TMS in ppm)

Compound	C(1)	C(2)	C(4)	C(5)	C(6)	C(8)	C(9)
2 (DMSO-d_6)	37.3	29.0	29.0	37.3	54.7	54.7	92.9
 **3** [DCCl$_3$]	39.0*	55.5	55.5	39.0	61.8	61.8	88.5
 **4**	30.2[a]	70.6	70.6	30.2	57.6	57.6	30.2
	C(3) [C(1)]	C(2) [C(8)][d]		C(5) [C(5)]	C(6) [C(6)][d]		C(4) [C(9)][d]
 **5**	33.1[b]	61.1		33.1	61.1		101.7
 **6**	42.8[b]	66.2		35.5	66.4		89.9

molecules of the asymmetric unit. From Table III, there are no exceptional structural details. The C—S bond distances in molecule **A** and molecule **B** are, respectively, 1.823(7) and 1.810(8) Å and are comparable to that found by Sutton (average 1.817 Å) for the C—S distance in a number of paraffinic C—S compounds.[6] The chair–chair conformer has two molecules per asymmetric unit with a donated hydrogen bond to sulfur [H(7)...S(3), 2.22(10) Å in molecule **A**: 2.20(6) Å in molecule B]. The average C—N (ring) distance was found to be 1.508(9) Å which is very near to that found for the N—C (ring) distance (1.506 and 1.512 Å) in 7-benzyl-3-thia-7-azabicyclo[3.3.1]nonane hydroperchlorate.[4] This again supports the contention for the lack of ring deformation in the nitrogen-containing portion of the title molecule.

TABLE I (*Continued*)

Compound	C(1)	C(2)	C(4)	C(5)	C(6)	C(8)	C(9)
 **7**	39.4[b]	67.0		35.9	62.2		92.7
 **8**	43.0[b]	67.0		39.8	68.0		92.3
	C(3) [C(1)][d]	C(2) [C(2)]		C(5) [C(5)]	C(6) [C(4)][d]		C(4) [C(9)][d]
 **9**	33.5[c]	19.6		33.5	19.5		94.3
 **10**	33.5[a]	17.5		33.5	17.5		94.4

[a] Reference 3.

[b] Reference 1.

[c] Reference 2.

[d] The bottom row of numbers are for comparable positions in **2** and **3**.

TABLE II

Crystal data for $C_{14}H_{20}NO_2S \cdot ClO_4$ (**2**)

Formula	$C_{14}H_{20}ClNO_6S$
MWT	365.8
a	15.720(16) Å
b	17.425(14)
c	6.917(6)
α	78.77(7)°
β	90.35(7)
γ	62.13(6)
V	1632.7(24) Å^3
F(000)	768
μMoK_α	4.12 cm^{-1}
λMoK_α	0.71069 Å
D_{calc}	1.49 g · cm^{-3}
Z	4
Obs. refl.	4735
R	6.5%
Space group	P$\bar{1}$

TABLE III

Bond angles (°) and distances (Å) for $C_{14}H_{20}NO_2S \cdot ClO_4$ (**2**)

	Molecule A	Molecule B		Molecule A	Molecule B
C1–C2	1.527(10)	1.538(10)	C6–N7–C11	112.9(6)	114.1(5)
C2–S3	1.825(6)	1.818(7)	C8–N7–C11	110.6(6)	110.7(6)
S3–C4	1.820(8)	1.803(9)	N7–C8–C1	110.6(6)	110.7(6)
C4–C5	1.508(10)	1.518(10)	C8–C1–C2	112.8(6)	114.6(6)
C5–C9	1.535(7)	1.533(7)	C8–C1–C9	111.2(6)	111.4(3)
C5–C6	1.513(12)	1.513(11)	C2–C1–C9	111.8(7)	109.5(6)
C6–N7	1.510(10)	1.503(11)	C1–C9–C5	109.4(5)	108.9(6)
N7–C8	1.503(7)	1.514(7)	C1–C9–O100	107.9(6)	106.9(6)
C8–C1	1.512(13)	1.497(11)	C1–C9–C101	112.9(6)	113.6(5)
C1–C9	1.509(11)	1.513(11)	O100–C9–O101	109.7(5)	110.4(6)
C9–O100	1.400(10)	1.418(8)			
C9–O101	1.406(8)	1.394(9)	C5–C9–C100	110.6(5)	110.8(4)
N7–C11	1.506(12)	1.502(11)	C5–C9–C101	106.3(6)	106.3(6)
C11–C12	1.500(9)	1.521(9)	N7–C11–C12	110.8(8)	111.0(7)
C12–C13	1.357(13)	1.357(13)	C11–C12–C17	120.3(7)	120.1(8)
C13–C14	1.406(13)	1.399(12)	C11–C12–C13	120.8(7)	118.0(6)
C14–C15	1.336(21)	1.357(20)	C13–C12–C17	118.8(7)	121.8(7)
C15–C16	1.365(18)	1.337(23)	C12–C13–C14	119.3(10)	119.7(9)
C16–C17	1.396(11)	1.399(14)	C13–C14–C15	120.3(12)	118.4(12)
C17–C12	1.365(12)	1.357(11)	C14–C15–C16	121.9(9)	121.5(10)
S3–H7	2.22(10)	2.20(6)	C15–C16–C17	117.6(10)	121.0(11)
Cl1–O11	1.426(6)		C16–C17–C12	112.0(9)	117.6(10)
Cl1–O12	1.395(8)				
Cl1–O13	1.411(8)		O11–Cl1–O12	108.6(4)	
Cl1–O14	1.430(6)		O11–Cl1–O13	110.2(4)	
Cl2–O21	1.423(6)		O11–Cl1–O14	107.7(5)	
Cl2–O22	1.422(6)		O12–Cl1–C13	110.1(5)	
Cl2–O23	1.416(7)		O12–Cl1–C14	111.4(4)	
Cl2–O24	1.384(9)		O13–Cl1–C14	108.9(4)	
C1–C2–S3	114.3(4)	115.1(4)	O21–Cl2–O22	107.0(4)	
C2–S3–C4	99.6(3)	99.7(3)	O21–Cl2–O23	109.6(4)	
S3–C4–C5	114.0(6)	113.3(6)	O21–Cl2–O24	110.5(4)	
C4–C5–C6	114.7(6)	114.3(6)	O22–Cl2–O23	111.0(4)	
C4–C5–C9	110.6(6)	111.7(5)	O22–Cl2–O24	108.9(4)	
C6–C5–C9	109.4(6)	110.0(6)	O23–Cl2–O24	109.9(5)	
C5–C6–N7	112.4(6)	112.3(5)			
C6–N7–C8	111.2(5)	111.2(6)			

EXPERIMENTAL

General data. All melting points are uncorrected and have been taken on a Thomas–Hoover apparatus. All ^1H and ^{13}C NMR data were obtained on a Varian XL-100(15) or a Varian XL-300 NMR spectrometer with chemical shifts measured from internal TMS. The XL-100(15) spectrometer was equipped with a Nicolet TT-100 PFT accessory. Single frequency, off-resonance spectra were gathered by irradiating with a continuous wave frequency at about δ −5 compared to TMS in the proton spectrum. IR spectral data were obtained on a Perkin–Elmer unit, model 681. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tennessee. 4-Thianone was purchased (Aldrich) or prepared by published procedures.[8] Benzylamine (Eastman, bp 182–185°C) was used without further purification.

N-Benzyl-3-thia-7-azabicyclo[3.3.1]nonan-9-one (**1**). Benzylamine (0.46 g, 4.3 mmol), paraformaldehyde (1.00 g, 33.0 mmol), and 15 mL of methyl alcohol were mixed and treated with acetic acid (0.38 g, 6.3 mmol). 4-Thianone (0.50 g, 0.004 mol) was added and the procedure was similar to that reported.[4] The yield was 0.4 g (38%), mp 91–92°C. The IR, ^1H, and ^{13}C spectral data have been recorded[4] or can be found in Table I.

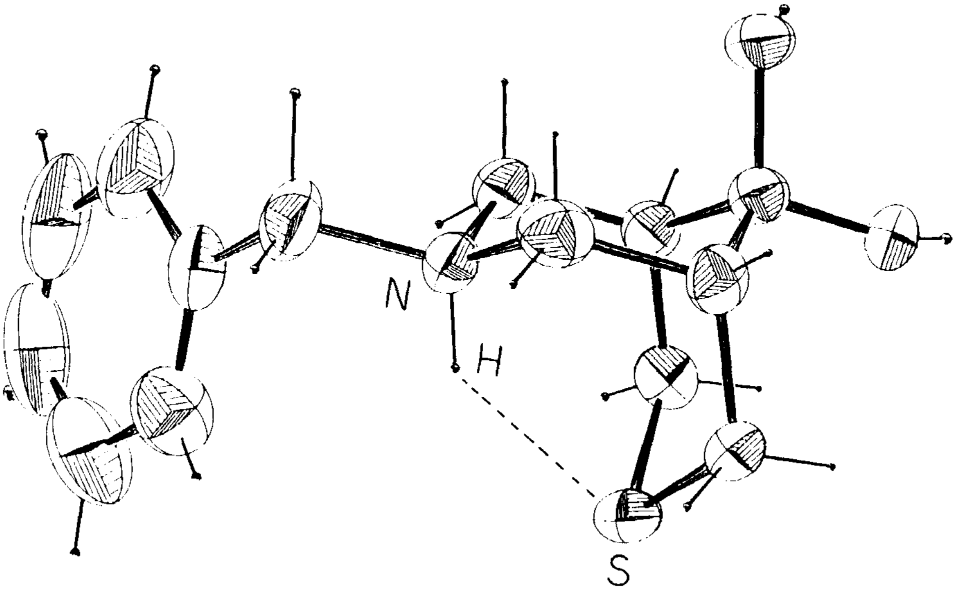


FIGURE 1 A projection drawing for diol **2**.

N-Benzyl-3-thia-7-azabicyclo[3.3.1]nonan-9,9-diol perchlorate (**2**). The solution of **1** (0.30 g, 0.001 mol) in 30 mL of H_2O : ethanol (1 : 1) was treated in a dropwise manner with 1 mL of $HClO_4$ (60%, Baker reagent) over a 5-min period. After heating the solution for about one minute, it was treated with decolorizing charcoal and then filtered while hot. The remaining procedure was similar to that reported;[4] mp 214–115°C; yield 0.32 g (76%). The spectral properties can be found in Table I or have been recorded[4] although **2** was not totally identified previously.[4]

Experimental data for crystal structure **2**. A crystal of $C_{14}H_{20}NO_2S \cdot ClO_4$ (**2**) was sealed in a capillary and mounted on a Syntex P3 automated diffractometer. Unit cell dimensions (Table II) were determined by least squares refinement of the best angular positions for 15 independent reflections ($2\theta > 15°$) during normal alignment procedures using monochromated molybdenum radiation (λ = 0.71069 Å). Data (9221 points) were collected at room temperature using a variable scan rate, a θ–2θ scan mode and a scan width of 1.2° below $K\alpha_1$ and 1.2° above $K\alpha_2$ to a maximum 2θ value of 116°. Background were measured at each side of the scan for a combined time equal to the total scan time. The intensities of three standard reflections were remeasured after every 97 reflections, and because those intensities showed less than 8%

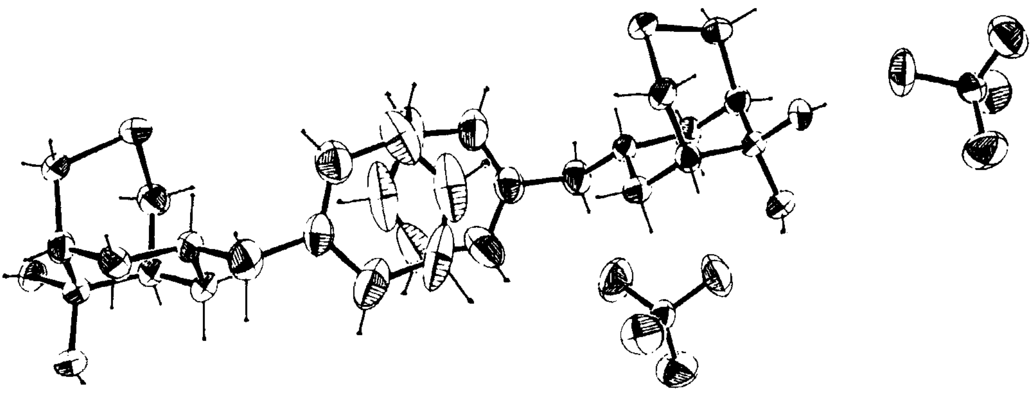


FIGURE 2 Three-dimensional drawing of the two molecules of the asymmetric unit in the cell of **2**.

variation, corrections for decomposition were deemed unnecessary. Data were corrected for Lorentz, polarization and background effects. After removal of redundant and space group forbidden data, 4635 reflections were considered observed $[I > 3.0\sigma(I)]$. The structure was solved by direct methods using MULTAN80.[9] Refinement of scale factor, positional and anisotropic thermal parameters for all non-hydrogen atoms was carried out to convergence.

Hydrogen positional parameters were determined from a difference Fourier synthesis.[10] These hydrogen positional parameters were refined along with non-hydrogen parameters in the final cycles of refinement. The final cycle of refinement [Function minimized $\Sigma(|F_0| - |F_c|)^2$] led to a final agreement factor, $R = 6.5\%$ $[R = (\Sigma||F_0| - |F_c||/\Sigma|F_0|) \times 100]$. Scattering factors were taken from Cromer and Mann.[11] Unit weights were used throughout.[12]

ACKNOWLEDGMENTS

The authors very gratefully acknowledge the partial support of this work in the form of salary (KDB) by the College of Arts and Sciences, Oklahoma State University. One of us (BRB) gratefully acknowledges a Fellowship from the Scottish Rites Organization of 1982–1983. We gratefully acknowledge partial support by the American Heart Association–Oklahoma Affiliate, Incorporated, grant. OK-83-G-2. We (KDB) are extremely grateful for partial support by the National Institutes of Health of the DHHS via a grant from the National Heart, Lung, and Blood Institute, HL 32191-01.

REFERENCES AND NOTES

1. A. J. Jones and M. M. A. Hassan, *J. Org. Chem.*, **37**, 2332 (1972).
2. J. J. Breen, S. O. Lee and L. D. Quin, *J. Org. Chem.*, **40**, 2245 (1975).
3. P. Arjunan, K. D. Berlin, C. L. Barnes and D. van der Helm, *J. Org. Chem.*, **46**, 3196 (1981).
4. B. R. Bailey, III, K. D. Berlin, E. M. Holt, B. J. Scherlag, R. Lazzara, J. Brachmann, D. van der Helm, D. R. Powell, N. S. Pantaleo and P. C. Reunitz, *J. Med. Chem.*, **27** (1984), in press.
5. R. Jeyaraman and S. Avila, *Chem. Rev.*, **81**, 149 (1981).
6. L. E. Sutton, "Tables of Interatomic Distance," The Chemical Society, London (1965), S 22s.
7. K. D. Berlin and E. M. Holt, unpublished results.
8. P. Y. Johnson and G. A. Berchtold, *J. Org. Chem.*, **35**, 584 (1970). See also M. E. Garst, B. J. McBride and A. T. Johnson, *J. Org. Chem.*, **48**, 8 (1983).
9. P. Main, S. J. Fiske, S. E. Hull, L. Lessinger, G. Germain, J.-P. Declercq and M. M. Woolfson, MULTAN 80. A system of computer programs for the automatic solution of crystal structures from X-ray diffraction data, University of York, England and Louvain-la-Meuve, Belgium.
10. J. M. Stewart, Ed., "The XRAY System-Version of 1980," Technical Report TR446 of the Computer Center, University of Maryland, College Park, Maryland.
11. D. T. Cromer and I. B. Mann, *Acta Cryst.*, **24**, 321 (1968).
12. Crystallographic data have been deposited with the Cambridge Crystallographic Data Center, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Requests should be accompanied by the full literature citation for this paper.