yield: ^{1}H NMR ($CDCl_3$) δ 1.45 (d, 12 H), 1.31 (t, 12 H), 4.22 (m, 8 H). Rate constants in s^{-1} 135.1 °C (1.64×10^{-4}), 140.15 °C (2.64×10^{-4}), 145.1 °C (4.75×10^{-4}), 150.3 °C (7.40×10^{-4}), and 155.14 °C (1.21×10^{-3}).

2-Propynyl 2-Bromo-2-methylpropanoate (3). To a solution of the α-bromoisobutyryl bromide (**2**) (103 g, 0.45 mol) in 200 mL of anhydrous ether cooled to 0 °C under nitrogen was added a solution of 30.0 g (0.53 mol) of propargyl alcohol and 43 g (0.53 mol) of pyridine in 150 mL of dry ether. The reaction mixture was allowed to warm to room temperature and to stir overnight. The product mixture was washed with water (2 × 50 mL), 5% bicarbonate (3 × 75 mL)8 5% HCl (2 × 50 mL), and brine (50 mL), dried over $MgSO_4$, and concentrated. Distillation provided 65 g (0.32 mol, 63%) of the ester: bp 84–87 °C (20 mm) [lit.[9] bp 59–60 °C (3 mm)]; ^{1}H NMR ($CDCl_3$) δ 1.97 (s, 6 H), 2.17 (t, 1 H), 4.71 (d, 2 H); IR (neat) 3290, 2180, 1735 cm^{-1}.

2,2-Dimethyl-3,4-pentadienoic Acid (4). The general method of Walker and Baldwin was used.[9,10] Activated zinc dust (45 g) was placed in flame-dried glassware with 90 mL of dry benzene under argon gas. The stirred suspension was heated to reflux and 10.2 g (50 mmol) of ester **3** in 60 mL of dry benzene was slowly added over a time period of 1.5 h. After addition, heating was maintained for 2 h. The product mixture was then cooled to room temperature and 50 mL of 6 M sulfuric acid was added. After 1 h the unreacted zinc was filtered and the acidic layer was removed and extracted with ether (3 × 30 mL). The combined organic phases were then washed with saturated bicarbonate (4 × 40 mL) and water (30 mL). The basic extracts were made acidic with concentrated sulfuric acid and extracted with ether (4 × 30 mL). The etheral solution was dried over $MgSO_4$, filtered, and concentrated to a clear light yellow liquid. Distillation provided 2.0 g (16 mmol, 32%) of the colorless product: bp 81–84 °C (2 mm) [lit.[10] 66–70 °C (0.8 mm)]; ^{1}H NMR ($CDCl_3$) δ 1.35 (s, 6 H), 4.83 (d, 2 H), 5.41 (t, 1 H), 11.63 (br, 1 H); IR (neat) 1950 and 1710 cm^{-1}.

1,1-Dimethyl-2,3-butadienylamine·Hydrochloride (7). To dry glassware was added a mixture of 5.8 g (46 mmol) of allenic acid **4**, 30 mL of $CHCl_3$, and dropwise 8.0 g (67 mmol) of thionyl chloride. After stirring at reflux for 8 h, the solvent and unreacted $SOCl_2$ were distilled from the acyl chloride, which was used without further purification in the next step: ^{1}H NMR ($CDCl_3$) δ 1.42 (s, 6 H), 4.9 (d, 2 H), 5.3 (t, 1 H); IR (neat) 1955 and 1790 cm^{-1}.

Sodium azide (6.0 g, 92 mmol) was added portionwise to a solution of the previously prepared acyl chloride in 20 mL of acetone cooled to 0 °C. Sufficient water was added to dissolve the NaN_3 and the mixture was stirred for 1 h. The reaction mixture was then poured into a separatory funnel and extracted with ether (4 × 30 mL). The etheral solution was dried over $MgSO_4$, filtered, and concentrated to the acyl azide, a clear liquid; IR (neat) 2125, 1958, and 1680 cm^{-1}. The acyl azide was taken up in benzene and stirred under reflux for 18 h. An infrared spectrum of a concentrated 1-mL aliquot of the product solution indicated the azide had completely decomposed to isocyanate; IR (neat) 2255 and 1958 cm^{-1}. Hydrolysis of the isocyanate to the amine was accomplished by heating the benzene solution with 10% HCl for 12 h. The reaction mixture was then cooled to room temperature, the aqueous layer drawn off, and the organic layer extracted with 5% HCl (3 × 10 mL). The combined acidic extracts were made basic by the addition of K_2CO_3 and then extracted with CH_2Cl_2 (5 × 30 mL). Continuous extraction for 24 h of the aqueous phase with CH_2Cl_2 provided an additional small amount of amine. The amine **7** was purified as the hydrochloride salt (2.12 g, 18 mmol; 39% based on the starting allenic acid) by recrystallization from ethanol–ethyl acetate: mp 171–172 °C; ^{1}H NMR ($CDCl_3$) δ 1.57 (s, 6 H), 5.0 (d, 2 H), 5.43 (t, 1 H), 8.50 (br, 3 H; exchangeable with D_2O); IR ($CHCl_3$) 3380 and 1950 cm^{-1}.

Anal. Calcd for $C_6H_{12}NCl$: C, 53.95; H, 8.99; N, 10.50. Found: C, 54.15; H, 9.15; N, 10.35.

***N,N'*-Bis(1,1-dimethyl-2,3-butadienyl)sulfamide (8).** The amine hydrochloride **7** (1.0 g, 8.4 mmol) was taken up in 5 mL of 10% NaOH and the free amine was extracted with CH_2Cl_2 (5 × 5 mL). The solution was dried over KOH for 2 h, decanted into a dry flask containing 0.85 g (8.4 mmol) of triethylamine under argon, and cooled to −30 °C. A solution of 0.57 g (4.2 mmol) of sulfuryl chloride in 20 mL of CH_2Cl_2 was added slowly over approximately 30 min. After addition the reaction was kept at dry ice temperature for 2 h and then allowed to warm to room temperature and stir overnight. The product mixture was washed with 5% HCl (3 × 20 mL), dried over $MgSO_4$, filtered, and concentrated to a white solid, which was recrystallized from pentane to give 0.84 g, (3.1 mmol, 74%): mp 69–70 °C; ^{1}H NMR ($CDCl_3$) δ 1.45 (s, 12 H), 4.32 (br, 2 H), 4.90 d, 2 h), 5.48 (m, 2 H).

Anal. Calcd for $C_{12}H_{20}N_2O_2S$: C, 56.22; H, 7.88; N, 10.93. Found: C, 56.39; H, 7.71; N, 10.79.

***N,N'*-Bis(1,1-dimethyl-2,3-butadienyl)diazene (1m).** A two-phase mixture of hexane and a solution of 60 mL of bleach and NaOH (1.80 g) was cooled to 0 °C. The sulfamide **8** (0.50 g, 2 mmol) and 3 drops of Aliquot 336 (phase-transfer catalyst) were added to the mixture. After 6 h at 0 °C, the reaction had reached completion as evidenced by the disappearance of the starting material. The two layers were separated and the hexane solution was washed with water (30 mL), 5% HCl (2 × 15 mL), and water (10 mL), followed by drying over $MgSO_4$. The solution was then passed through a short column of Florisil. Removal of the solvent under vacuum provided 0.10 g (1.1 mmol, 53%) of the diazene, a light yellow liquid. Further purification was accomplished via sublimation: ^{1}H NMR ($CDCl_3$) δ 1.29 (s, 12 H) 4.79 (d, 4 H), 5.39 (t, 2 H); ^{13}C NMR ($CDCl_3$) 25.46, 68.48, 96.96, 206.6 ppm; IR (neat) 1950 cm^{-1}; UV (cyclohexane) λ_{max} 364 (ϵ 38.7).

Registry No. **1b**, 93605-35-7; **1d**, 93605-36-8; **1f**, 7336-02-9; **1m**, 93605-37-9; **2**, 20769-85-1; **3**, 40630-86-2; **4**, 4058-53-1; **4** (acid chloride), 93605-44-8; **5**, 93605-40-4; **6**, 93605-41-5; **7**·HCl, 93605-42-6; **8**, 93605-43-7; ·$C(CH_3)_2SO_2CH_3$, 4853-78-5; ·$C(CH_3)_2SO_2C_6H_5$, 93605-38-0; ·$C(CH_3)_2P(O)(C_2H_5O)_2$, 85971-71-7; ·$C(CH_3)_2CH{=}C{=}CH_2$, 93605-39-1; ·$CH{=}CH_2$, 2669-89-8; ·CN, 2074-87-5; ·C≡CH, 2122-48-7; ·NCO, 22400-26-6; ·CH_3, 2229-07-4; $HC{\equiv}CCH_2OH$, 107-19-7; *N,N'*-bis[dimethyl(methylthio)methyl]diazene, 40889-01-8; *N,N'*-bis[dimethyl(phenylthio)methyl]diazene, 26307-20-0.

(8) Levin, Y. A.; Gozman, I. P.; Abul'khanov, A. G.; Ivanov, B. E. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1975**, *4*, 983.
(9) Walker, J. A. Ph.D. Dissertation, Massachusetts Institute of Technology, Cambridge, MA, 1973.
(10) Baldwin, J. E.; Walker, J. A. *J. Chem. Soc., Chem. Commun.* **1973**, 117.

Cycloadditions of 5-Nitropyrimidines with Ynamines. Synthesis and Crystal Structure of a 2,2a-Dihydroazeto[2,3-*d*]-3,5-diazocine, a Novel Heterocycle[1]

A. T. M. Marcelis and H. C. van der Plas*

Laboratory of Organic Chemistry, Agricultural University, De Dreijen 5, 6703 BC Wageningen, The Netherlands

S. Harkema

Laboratory of Chemical Physics, Twente University of Technology, 7500 AE Enschede, The Netherlands

Received July 13, 1984

In a previous paper we have reported that 5-nitropyrimidine is able to undergo [4 + 2]-cycloaddition reactions with electron-rich enamines.[2] This reaction proceeds through an addition of the enamine to the 1 and 4 positions of the pyrimidine, followed by loss of HCN and amine, resulting in formation of 2,3,5-trisubstituted pyridine derivatives. In contrast, the cycloaddition of the ynamine 1-(diethylamino)propyne with methyl pyrimidine-5-carboxylate takes place across C-2 and C-5 to afford, after

(1) Part 32 on Ring transformations of heterocycles with nucleophiles; for part 31, see: Smit P.; Stork G. A.; van der Plas, H. C. *Recl. Trav. Chim. Pays-Bas* **1983**, *102*, 453.
(2) Charushin, V. N.; van der Plas, H. C. *Tetrahedron Lett.* **1982**, *23*, 3965.

0022-3263/85/1950-0270$01.50/0

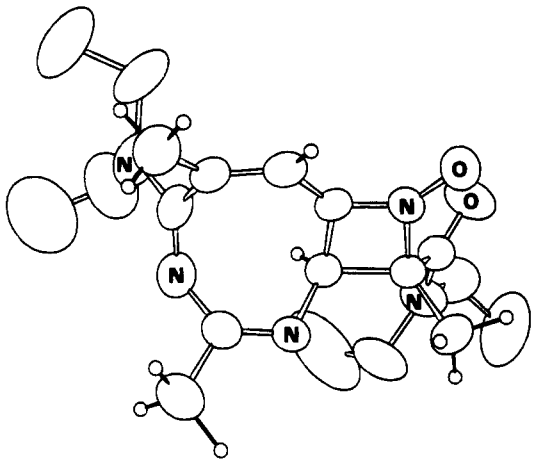


Figure 1. ORTEP[14] view of molecule **5b**.

loss of HCN, a 3,4,5-trisubstituted pyridine derivative.[3] This result prompted us to examine the reaction of 5-nitropyrimidine with 1-(diethylamino)propyne. Earlier attempts to isolate the product of this reaction were unsuccessful,[2] and on the basis of the ^1H NMR spectrum of the crude reaction product it was assumed that the product was a cycloadduct, formed by addition of 1-(diethylamino)propyne to the 1,4 position of 5-nitropyrimidine.[2] We now report the isolation and characterization of this product and of some derivatives obtained from 2-substituted 5-nitropyrimidines.

Some nitro(hetero)aromatics and nitroalkenes have been found to react with ynamines to form a variety of products. *N*-(Hetero)aryl-*C*-carbamoylnitrones may be formed from nitro(hetero)aromatics.[4] Furthermore, a [2 + 2]-cycloaddition across the carbon–carbon double bond leading to a cyclobutene may occur or a [4 + 2]-addition to yield a cyclic six-membered nitronate. The last mentioned compounds are usually unstable and are converted into either isoxazolidines or four-membered cyclic nitrones.[5]

Results and Discussion

Reaction of 5-nitropyrimidine (**1a**) and its 2-methyl (**1b**), 2-phenyl (**1c**), and 2-methoxy derivatives (**1d**) with an excess of 1-(diethylamino)propyne in dry chloroform gave products (yields 50–70%), which according to their mass and ^1H and ^{13}C NMR data must be considered as addition products between the 5-nitropyrimidines and the ynamine in a ratio of 1:2.

Because the structure of these compounds was not evident from their spectroscopic data, a crystal structure analysis was undertaken of the crystalline product obtained in the reaction of **1b** with 1-(diethylamino)propyne (see Figure 1).

The molecule consists of a 1,3-diazocine ring fused to a four-membered cyclic nitrone, being to our knowledge the first example of an azetodiazocine ring system. The double bonds in the diazocine ring are all cis, and the conformation of the diazocine can be described as boat-like. The diethylcarbamoyl group and the diazocine nitrogen are on opposite faces of the dihydroazete ring.

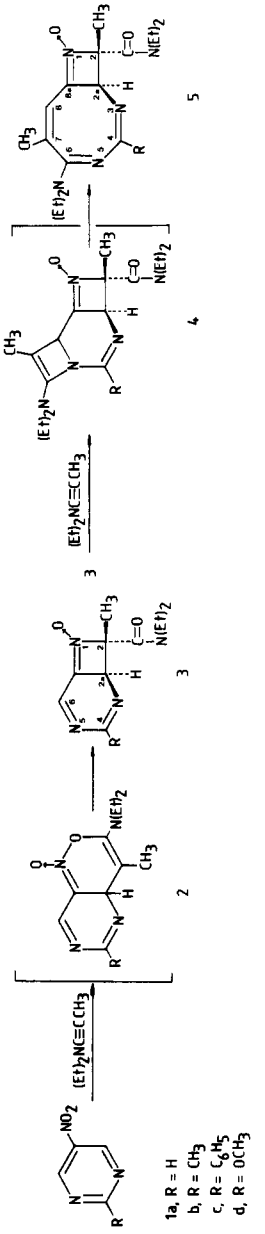
The spectroscopic data of the products are tabulated in Table I. H-8 shows coupling with H-2a (J = 1.0 Hz) and the CH_3 at C-7 (J = 1.6 Hz). Furthermore, H-4 in **5a** couples with H-2a (J = 2.1 Hz). The ^{13}C NMR data of the dihydroazete oxide part of **5** agree well with those found

Table I. Spectral Properties of 5

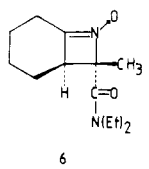
	MS, m/e found; formula (M^+, m/e calcd)	^1H NMR ($CDCl_3$), δ				^{13}C NMR ($CDCl_3$), δ							
no.		R	H-8	H-2a	CH_3–C-2	CH_3–C-7[a]	C-4[b]	C-6[c]	C-7	C-8	C-8a	C-2a	C-2	CH_3–C-2	C=O
5a	347.232; $C_{18}H_{29}N_5O_2$ (347.232)	7.83[d]	6.43	4.48	1.82	2.03	158.3	156.7	137.5	115.9	147.6	58.5	87.6[g]	16.2	168.3
5b	361.248; $C_{19}H_{31}N_5O_2$ (361.248)	2.01[f]	6.38	4.34	1.74	1.90	167.5	154.6	137.0	115.9	148.0	59.5	87.4	15.9	168.5
5c	423.263; $C_{24}H_{33}N_5O_2$ (423.263)	[g]	6.38	4.67	1.94	1.90	164.6	156.9	137.4	115.5	147.8	59.6	87.7	15.9	168.4
5d	377.243; $C_{19}H_{31}N_5O_3$ (377.243)	3.74	6.42	4.37	1.78	2.00	162.5	159.1	136.4	115.5	147.9	57.7	87.4	15.5	168.3

[a] Doublet, J = 1.6 Hz. [b] Doublet, J = 153 Hz. [c] Doublet, J = 163 Hz. [d] Doublet, J = 2.1 Hz. [e] Doublet, J = 194 Hz. [f] Doublet, J = 1.0 Hz. [g] Phenyl absorptions.

Scheme I



(3) Neunhofer, H.; Werner, G. *Liebigs Ann. Chem.* **1974**, 1190.
(4) Reinhoudt, D. N.; Kouwenhoven, C. G. *Recl. Trav. Chim. Pays-Bas* **1976**, *95*, 67.
(5) Pennings, M. L. M.; Reinhoudt, D. N. *J. Org. Chem.* **1982**, *47*, 1816.



6

Figure 2.

for a series of *N,N*-diethyl-2,3-dihydro-2-azetecarboxamide 1-oxides.[5] Also, the chemical shifts of the methyl groups at C-2 in **5** of about 16 ppm agree well with the shift of a methyl group in a cyclic nitrone being fused to cyclohexane, i.e., **6** (Figure 2), and having the diethylcarbamoyl group and the hydrogen on the same face of the four-membered ring, as in the compounds being obtained in this study. The assignments of the ^{13}C NMR resonances of the diazocine ring follow from comparison of the data of the different compounds and from ^{13}C–^{1}H coupling constants.

The formation of **5** can be rationalized as follows (see Scheme I). It involves in the early stages of the reaction as one of the intermediates the cyclic nitronic ester **2**. Although the formation of **2** formally results from a [4 + 2]-cycloaddition, the reaction probably proceeds via a 1,4-dipolar intermediate.[5]

The ring contraction of **2** into the dihydroazeto[2,3-*d*]-pyrimidine **3** probably occurs in a stereospecific fashion, involving a 1,3-sigmatropic shift of the nitrogen of the nitronate. The conformation of the nitronate, imposed by the dihydropyrimidine part of the molecule, determines the stereochemistry of the resulting dihydroazete oxide, which is the same as in the cyclic nitrone **6** obtained from reaction of 1-nitrocyclohexene with 1-(diethylamino)-propyne.[5]

When noncyclic nitroalkenes are used, the resulting cyclic nitrones have the diethylcarbamoyl groups and the substituent at C-3 on the same face of the dihydroazete ring.[5,6]

Intermediate **3** reacts further by a [2 + 2]-cycloaddition of 1-(diethylamino)propyne to the pyrimidine skeleton, followed by isomerization into the diazocine **5**. A [2 + 2]-cycloaddition of an ynamine to the C=N bond of a dihydroazaaromatic has been observed before,[7,8] but addition of an ynamine to the C=N bond, forming a part of a dihydropyrimidine, is an unknown process. 1,3-Diazocines have been found upon rearrangement of products obtained from the photocycloaddition of uracil with alkynes.[9]

Alternatively, the [2 + 2]-cycloaddition and ring expansion may precede the nitronate or nitrone formation. However, such a process seems less likely, because the N-5–C-6 bond in the intermediate nitronic ester **2** or the azeto[2,3-*d*]pyrimidine **3** is probably more electron deficient then the N-3–C-4 bond in the 5-nitropyrimidines **1** and is also no longer part of an aromatic system. Therefore, this bond can be expected to be more prone to form a [2 + 2]-cycloadduct with the ynamine. Attempts to study the formation of intermediates by performing the reaction in a 1:1 ratio at low temperature were unsuccessful. Only unreacted 5-nitropyrimidine and the 1:2 reaction product were observed. When the reaction was carried out in an NMR tube at −40 °C, again only unreacted starting material and the 1:2 reaction product were observed, indicating that any intermediate must be very liable to further reaction.

The dihydroazeto[2,3-*d*]-3,5-diazocine is thermally quite stable but decomposes readily under acidic conditions.

Experimental Section

Melting points are uncorrected. The ^{1}H NMR spectra ($CDCl_3$) were recorded with a Varian EM-390 90-MHz spectrometer using tetramethylsilane (Me_4Si) as internal reference. ^{13}C NMR spectra were recorded with a Bruker CXP-300 spectrometer. Mass spectra were obtained with a JEOL JMS-D-100 spectrometer. 5-Nitropyrimidine[10] and 2-substituted 5-nitropyrimidines[11] were prepared as described in the literature.

General Procedure for the Reactions of the 5-Nitropyrimidines 1a–d with 1-(Diethylamino)propyne. A solution of 2.2 mmol of 1-(diethylamino)propyne in 5 mL of dry $CHCl_3$ was added dropwise to a stirred solution of the 5-nitropyrimidines **1a–d** (1 mmol) in 20 mL of $CHCl_3$ at 0–5 °C. The reaction is exothermic. After stirring the solution for 0.5 h, the solvent was removed under reduced pressure and the product isolated by column chromatography or TLC using silica gel and ether/methanol (4:1) as eluent. The products **5** (yields 50–70%) were obtained as viscous oils except **5b**, which was obtained as a solid and could be recrystallized from diisopropyl ether/hexane: light yellow crystals; mp 139–140 °C. Anal. Calcd for $C_{19}H_{31}N_5O_2$ (M_r 361.48): C, 63.13; H, 8.64. Found: C, 63.04; H, 8.44.

X-ray Crystal Structure Analysis of 5b. Crystals of **5b** belong to the monocyclic space group *C2/c*, with cell constants a = 27.424 (2) Å, b = 8.270 (1) Å, c = 21.140 (2) Å, β = 119.51 (1)°; d_c = 1.15 g cm^{-3}; Z = 8. Intensities were measured at 274 K with a Philips PW 1100 diffractometer, using graphite monochromated Mo K_α radiation. (ω–2θ scan mode; scan speed (ω) 0.1° s^{-1}; scan width (ω) (1.8 + 0.1 tan ω)°; $4 < \omega < 25°$); 3740 reflections have been measured, of which 2778 with $I > \sigma(I)$ have been used in the solution[12] and refinement[13] of the structure. After refinement of the heavy atoms with anisotropic thermal parameters, the hydrogen atoms of the ring atoms and the methyl groups attached to the ring systems could be found from a difference Fourier synthesis. These hydrogen atoms were included in the refinement with isotropic thermal parameters. The final R factor was 11.0%. From the results of the refinement depicted in Figure 1,[14] a relatively large thermal motion in both diethylamino groups of the molecule is apparent, explaining the difficulty of locating the hydrogen atoms in this part of the molecule. The most prominent features in the final difference Fourier synthesis can be interpreted on the basis of statistical disorder of two of the diethylamino methyl groups. As the main interest of this study was the elucidation of the structure of the ring system, the disorder has not been studied in more detail and was not included in the refinements.

Acknowledgment. We are indebted to Dr. C. A. Landheer and Mr. C. J. Teunis for the mass spectroscopic measurements, to Mr. H. Jongejan for performing the microanalysis, and to Dr. H. A. J. Holterman and Mr. A. van Veldhuizen for the ^{13}C NMR measurements.

Registry No. **1a**, 14080-32-1; **1b**, 14080-34-3; **1c**, 68906-00-3; **1d**, 14001-69-5; **5a**, 93644-98-5; **5b**, 93644-99-6; **5c**, 93683-22-8; **5d**, 93645-00-2; 1-(diethylamino)propyne, 4231-35-0.

Supplementary Material Available: Tables of atomic coordinates, thermal parameters, bond distances, and bond angles (6 pages). Ordering information is given on any current masthead page.

(6) de Wit, A. D.; Pennings, M. L. M.; Trompenaars, W. P.; Reinhoudt, D. N.; Harkema, S.; Nevestveit, O. *J. Chem. Soc., Chem. Commun.* **1979**, 993.
(7) Fuks, R.; Viehe, H. G. *Chem. Ber.* **1970**, *103*, 573.
(8) Abramovitch, R. A.; More, K. M.; Shinkai, I.; Srinivasan, P. C. *Heterocycles* **1976**, *5*, 95.
(9) Kaminski, V. V.; Comber, R. N.; Wexter, A. J.; Swenton, J. S. *J. Org. Chem.* **1983**, *48*, 2337.
(10) van der Plas, H. C.; Jongejan, H.; Koudijs, A. *J. Heterocycl. Chem.* **1978**, *15*, 485.
(11) Barczynski, P.; van der Plas, H. C. *J. Org. Chem.* **1982**, *47*, 1077.
(12) Germain, G.; Main, P.; Woolfson, M. M. *Acta Crystallogr., Sect. A* **1971**, *27*, 368–376. Main, P. In "Computing in Crystallography"; Schenk, H., Ed.; Delft University Press: The Netherlands, 1978.
(13) Busing, W. R.; Martin, K. O.; Levy, H. A. ORFLS, Report ORNL-TM-305, Oak Ridge National Laboratory, TN, 1962.
(14) Johnson, C. K. ORTEP, Report ORNL-3794, Oak Ridge National Laboratory, TN, 1965.