ACTA CHEMICA SCANDINAVICA 24 (1970) 179–188

Derivatives of Hydrazine

VII. Structure and Reactions of 5,5-Dialkyl-1,3,4-thiadiazolidine-2-thiones

UFFE ANTHONI, CHARLES LARSEN and PER HALFDAN NIELSEN

Chemical Laboratory II (General and Organic Chemistry), University of Copenhagen, The H. C. Ørsted Institute, DK 2100 Copenhagen, Denmark

The structure of the products from the reaction between aliphatic ketones and hydrazinium dithiocarbazates has been investigated. Chemical, IR, and ^{1}H NMR spectroscopic evidence supports that the products are 1,3,4-thiadiazolidine-2-thiones rather than alkylidenedithiocarbazic acids. Treatment with potassium hydroxide or methyl iodide leads in some cases to a ring-opening reaction giving, respectively, salts and methyl esters of the alkylidenedithiocarbazic acids.

A number of alkylidenedithiocarbazic esters (Fig. 1, structure A, R^4=alkyl), derived from alkylhydrazines (R^3=alkyl) and aliphatic and aromatic aldehydes and ketones (R^1 and R^2=H, alkyl or aryl), have recently been prepared by Sandström.[1] In the case of R^3=H (Fig. 1, structure 1) it was pointed out that alternative formulations as imidothioles (2) or thiadiazolidines (3) were equally possible. However, from the ultraviolet absorption spectra it was concluded that the isomer 1 was predominant in all cases and very likely the only isomer present.

As a continuation of our studies of dithiocarbazic acids[2] and their derivatives[3] a determination of the structure of alkylidenethiocarbazic acids (Fig. 1, structure A, R^4=H) became of interest. A structural problem related to that discussed by Sandström exists for these compounds which can have either the dithioacid structure (Fig. 1, structure 4) or the isomeric 1,3,4-thiadiazolidine-2-thione structure (5). The present paper reports chemical and spectroscopic investigations of aliphatic members of this class of compounds. Our results have led to a conclusion contrasting to that made in the case of the esters, namely, that the cyclic form (5) is the predominant molecular species in both the solid state and in solution.

Several substituted 1,3,4-thiadiazolidine-2-thiones (5) have recently been reported by Heugebart and Willems,[4] and assigned the cyclic (5) rather than the open-chain structure (4). However, these authors report that the 3,5,5-

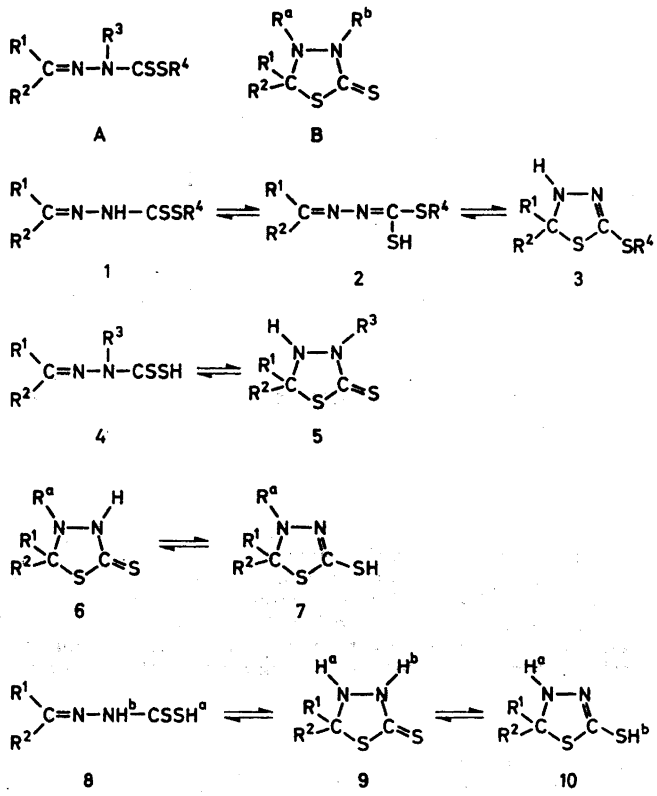
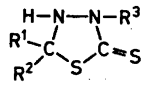


Fig. 1.

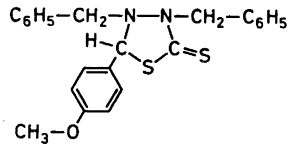
trisubstituted 1,3,4-thiadiazolidine-2-thiones (5) react with potassium hydroxide commenting, that since this compound contains no enolizable thioxo group a rearrangement of an alkyl group might occur. Since an equilibrium with a cyclic thiol form (analogous to the equilibrium 6⇌7) is excluded because of the substituent in the 3-position this result can most reasonably be explained by invoking the presence of the equilibrium (4⇌5) in solution. Also, since spectroscopic data were not included in the investigation by Heugebart and Willems [4] it was decided to reinvestigate some of these compounds. The results are listed in Tables 1 and 2 which also include the results for some compounds with related structures.

For reference purposes it was clearly of interest to include some substituted 1,3,4-thiadiazolidine-2-thiones in the investigation (Fig. 1, structure B). In cases where both R^a and R^b are different from hydrogen, isomeric structures are excluded. An example of such compounds is 5-*p*-methoxyphenyl-3,4-dibenzyl-1,3,4-thiadiazolidine-2-thione which has been shown to have the thiadiazolidinethione structure by Karle and Karle [5] from an X-ray diffraction study.

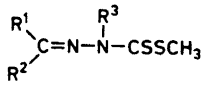
Table 1. Physical constants for compounds with the structure:



Compound	R^1	R^2	R^3	Lit.	Mp.°C	Yield %	Formula	Analyses (C, H, N)
I	CH_3	CH_3	H	3	119—120	85		
II	C_2H_5	CH_3	H	3	66—67	20		
III	C_2H_5	C_2H_5	H	—	85—86	70	$C_6H_{12}N_2S_2$	Found: 40.90 6.72 15.79 Calc.: 40.87 6.86 15.89
IV	$-(CH_2)_4-$		H	3	120—121	40		
V	$-(CH_2)_5-$		H	3	134—136	80		
VI	$-(CH_2)_6-$		H	—	86—87	20	$C_8H_{14}N_2S_2$	Found: 47.59 6.93 14.01 Calc.: 47.49 6.97 13.85
VII	CH_3	CH_3	CH_3	3	80—81	80		
Ia	CD_3	CD_3	H	—	119—120	85		
VIIa	CD_3	CD_3	CH_3	—	80—81	80		

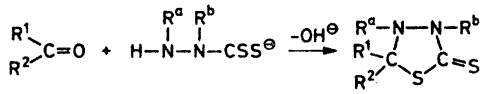


3,4,5,5-Tetramethyl-1,3,4-thiadiazolidine-2-thione (Fig. 1, structure B, $R^1=R^2=R^a=R^b=CH_3$) was selected as a more convenient reference compound. In line with the reasoning outlined above the compound proved insoluble in potassium hydroxide. Taeger and El-Hewehi [6] have prepared a number of 3-unsubstituted compounds (Fig. 1, structure B, $R^b=H$) as examples of 1,3,4-thiadiazolidine-2-thiones capable of isomerization. It was concluded by Taeger and El-Hewehi that they may exist in both the thioamide (6) and in the imidothiol form (7) because they form a potassium salt with potassium hydroxide. Finally, 1,3,4-thiadiazolidine-2-thiones of the type 9, which may isomerize in either of two different ways (to 8 or 10), will be discussed below.

Table 2. Physical constants for compounds with the structure: 

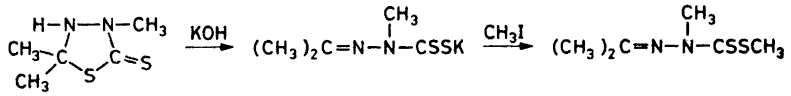
Compound	R^1	R^2	R^3	Mp.°C	Yield %	Formula	Analyses (C, H, N and S)
VIII	CH_3	CH_3	H	117–118	85	$C_5H_{10}N_2S_2$	Found: 37.02 6.25 17.27 39.20 Calc: 37.01 6.21 17.27 39.51
IX	CH_3	CH_3	CH_3	48–49	70	$C_6H_{12}N_2S_2$	Found: 41.00 6.98 16.05 Calc.: 40.87 6.86 15.89
X	CH_3	CH_3CH_2	H	62–63	80	$C_6H_{12}N_2S_2$	Found: 40.78 6.92 16.11 Calc.: 40.87 6.86 15.89
XI	$-(CH_2)_4-$		H	145–146	80	$C_7H_{12}N_2S_2$	Found: 44.71 6.42 14.94 Calc.: 44.64 6.43 14.88
XII	$-(CH_2)_5-$		H	100–101	80	$C_8H_{14}N_2S_2$	Found: 47.42 6.94 13.86 Calc.: 47.49 6.97 13.85
XIII	$-(CH_2)_6-$		H	115–116	85	$C_9H_{16}N_2S_2$	Found: 49.85 7.50 13.10 Calc.: 49.96 7.46 12.95
VIIIa	CD_3	CD_3	H	117–118	80		
IXa	CD_3	CD_3	CH_3	48–49	70		

The general procedure for the preparation of 1,3,4-thiadiazolidine-2-thiones with aliphatic substituents in the 3, 4, and 5 positions is the reaction between an aliphatic aldehyde or ketone and a hydrazinium dithiocarbazate (for simplicity structure B is given for the product):



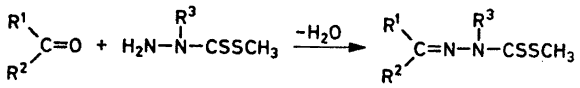
DISCUSSION OF THE STRUCTURE

Chemical evidence. All the 1,3,4-thiaadiazolidine-2-thiones I—VII listed in Table 1 are easily soluble in triethylamine or potassium hydroxide. By adding hydrochloric acid to the basic solutions the compounds were re-precipitated with unchanged melting points and IR spectra identical with those of the starting materials. The solubility of the compounds I—VI in base can be explained by assuming the compounds to be in equilibrium with the thiol form, (Fig. 1, 9⇌10) or the dithioacid form, (Fig. 1, 9⇌8). However, a tautomeric equilibrium (9⇌10) is excluded for compound VII. The only alternative is the ring opening (4⇌5) indicating that the potassium salt of VII possesses the acyclic structure. By dissolving VII in ethanolic potassium hydroxide and subsequently adding methyl iodide, VII was converted to methyl 2-methyl-3-isopropylidenedithiocarbazate (IX).[1]



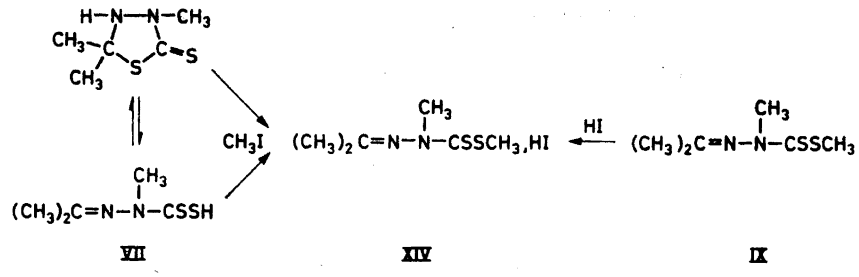
VII IX

In the same way the other compounds I—VI were converted to the corresponding esters given in Table 2. The structure of the products VIII—XII was established by synthesis from the ketone and methyl dithiocarbazate [7] or methyl 2-methyldithiocarbazate.[8]



In all cases the esters formed in the two different ways were shown to be identical. The infrared and ^{1}H NMR spectra (see below definitely showed the esters VIII—XIII to have analogous acyclic structures.

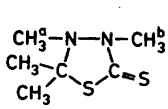
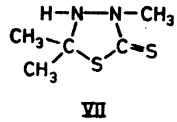
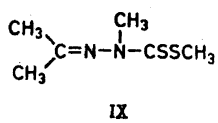
Attempts were made to synthesize a cyclic methiodide of VII. Compound VII, when dissolved in an excess of methyl iodide, gave the methiodide (XIV). This, however, was acyclic since it proved to be identical with the hydroiodide (XIV) of $(CH_3)_2C{=}N{-}N(CH_3){-}CSSCH_3$ prepared above. Treatment with CH_3I and KOH are therefore followed by ring-opening of the thiadiazole ring.



Although a cyclic structure (9 or 10) is the most likely [6] for the compounds I—VII since they are formed from a ketone and hydrazinium dithiocarbazate, an equilibrium with the acyclic alternative (8) in solution (as presented in the scheme above) is indicated on the basis of the data presented above. Since acyclic products are formed both from the reaction of VII with CH_3I and with KOH, the ring opening cannot be due to base catalysis alone. From the evidence discussed so far, it is probable that, in CH_3I solution at least, an equilibrium exists between the two structures.

^1H NMR spectroscopic evidence. As the structure of 3,4,5,5-tetramethyl-1,3,4-thiadiazolidine-2-thione is unambiguous, it was used as spectroscopic reference. The ^1H NMR spectrum of this compound was recorded in deuteriochloroform, carbon tetrachloride, and benzene at 40°C. The chemical shifts of the methyl protons (Table 3) are solvent dependent showing an upfield shift of the signals with change of solvent from deuteriochloroform to carbon tetrachloride or benzene, possibly reflecting the change in solvent polarity.

Table 3. Chemical shifts (τ, ppm) of the CH_3 protons in 3,4,5,5-tetramethyl-1,3,4-thiadiazolidine-2-thione, 3,5,5-trimethyl-1,3,4-thiadiazolidine-2-thione, and methyl 3-isopropylidene-2-methyldithiocarbazate.

Solvent				 VII		 IX	
	$(CH_3)_2C$	$CH_3{}^a-N$	$CH_3{}^b-N$	$(CH_3)_2C$	CH_3-N	$(CH_3)_2C$	CH_3-N
$CDCl_3$	8.36	7.28	6.49	8.31	6.41	8.06 7.82	6.33
CCl_4	8.37	7.54	6.56	8.34	6.50	8.11 7.87	6.41
C_6H_6	8.93	8.01	6.92	8.88	6.80	8.89 8.44	6.62

^{1}H NMR spectra of VII were recorded in the same three solvents and almost the same positions were observed for the methyl proton signals (Table 3). The difference in chemical shifts between compound VII and 3,4,5,5-tetramethyl-1,3,4-thiadiazolidine-2-thione, does not exceed 3.0 Hz for the $(CH_3)_2C$ signal and 4.1 Hz for the CH_3N signal. Furthermore the same solvent dependence is observed for identical groups in the two compounds. These observations strongly indicate compound VII to possess the cyclic structure (B).

If an open chain structure A is assumed for VII a potential rotation barrier about the C=N bond of the same order of magnitude as that in $(CH_3)_2C=N-N(CH_3)-CSSCH_3$ (IX) would be expected. Since the structure of IX has been established (see above) the ^{1}H NMR spectra of this compound were recorded in the same three solvents (Table 3). The $(CH_3)_2C$ signal was observed as a doublet at $\tau=8.06$ ppm and $\tau=7.82$ ppm with the two peaks of equal intensity, showing the two methyl groups to be nonequivalent in the chemical shift sense because of the C=N bond. The spacing of the two signals is almost unchanged in the interval 0°C—45°C. At 50°C a broadening of the two lines starts, and when the temperature is raised above 58°C, which is the coalescence temperature, only an averaged signal at $\tau=7.94$ ppm is observed. In addition, although the temperature at which the signals due to the two methyl groups of IX coalesced was rather high (58°C) the ^{1}H NMR spectrum of VII, recorded at low temperature (−30°C), showed no splitting of the $(CH_3)_2C$ signal. From these observations it must be concluded that either the difference in height of the rotation barrier between IX and the open form of VII is appreciable or the cyclic structure of VII is verified.

In order to investigate whether a concentration dependent equilibrium between the open chain and the cyclic structure of VII exists in solution, the ^{1}H NMR spectrum of VII was recorded with 0.5 mg substance dissolved in 500 µl deuteriochloroform; again, however, only one single $(CH_3)_2C$ signal was observed. The most probable explanation that account for the appearance of a singlet for the $(CH_3)_2C$ signal of VII is that the two methyl groups are equally shielded, in accordance with the cyclic structure B for VII. The appearance of a $(CH_3)_2C$ signal as a singlet in three solvents make the eventuality of accidental chemical shift coincidence negligible.

Compound (I) is only slightly soluble in $CDCl_3$, CCl_4, and C_6H_6, however, on recording the ^{1}H NMR spectrum of a saturated solution of (I) in $CDCl_3$ only one methyl proton signal was observed at $\tau=8.25$ ppm. The $(CH_3)_2C$ protons of $(CH_3)_2C=N-NH-CSSCH_3$ (VIII) showed two peaks at $\tau=8.02$ ppm and $\tau=7.92$ ppm ($CDCl_3$, 40°C). The coalescence temperature for the two lines was 46°C. These observations, together with a comparison of the τ values given in Table 3, indicate that compound (I) possesses the cyclic structure B. The ^{1}H NMR spectra of the other compounds II—VI gave no information which opposed their assignments as cyclic structures.

IR spectroscopic evidence. In the infrared spectra, recorded in KBr, of each of the compounds given in Table 1 neither absorption in the C=N stretching region nor in the SH stretching region could be found. These observations are only consistent with a cyclic structure for the compounds.

In the case of the compounds given in Table 2 one or two bands were observed in the region 1605—1655 cm^{-1} when the IR spectra of each compound were recorded in KBr or $CHCl_3$. One of these bands is assigned to the C=N stretching vibration. At least three explanations can be advanced to account for the second band. (1) *cis-trans* Isomerism, (2) association effects, (3) a combination or overtone mode. *cis-trans* Isomerism is excluded as the doubling is found in the compounds VIII and IX where *cis-trans* isomerism is impossible. As the extra band occurs in both the solid state and in solution, association effects cannot reasonably be held responsible for its appearance. The most probable interpretation is therefore the third alternative. To verify this by isotopic substitution the reaction sequence leading to VIII and IX was repeated using acetone-d_6 instead of acetone to give VIIIa and IXa. The infrared spectra were recorded and Table 4 summarizes the absorption in the C=N stretching region, determined for the compounds VIII, VIIIa, IX, and IXa.

The IR spectrum of VIII displayed a strong band at 822 cm^{-1} in KBr and 820 cm^{-1} in $CHCl_3$ which are assigned to a skeletal stretching vibration. The band at 1655 cm^{-1} in KBr and 1640 cm^{-1} in $CHCl_3$ in the IR spectrum of VIII (Table 4) is proposed to be an overtone of this skeletal vibration. In the IR spectrum of IX the band at 1605 cm^{-1} (both in KBr and $CHCl_3$) is similarly assigned to an overtone of the band observed at 802 cm^{-1} in KBr and 804 cm^{-1} in $CHCl_3$.

Table 4. Characteristic IR absorptions in the C=N stretching region of the compounds VIII, IX and their analogous compounds perdeuterated in the isopropylidene group.[a]

	VIII	VIIIa	IX	IXa
KBr (cm^{-1})	1635 s 1655 s	1630 s —	1605 s 1635 s	1610 s —
$CHCl_3$ (cm^{-1})	1620 m 1640 m	1620 —	1605 w 1635 s	1615 s —

[a] The following abbreviations have been used: s=strong, m=medium, w=weak.

The deuterated compounds VIIIa and IXa only exhibited one absorption in the C=N stretching region, and in line with the proposal suggested above the skeletal band was displaced outside the region 800—850 cm^{-1}, which appeared blank in the IR spectra of these compounds. From the combined IR spectral data it can furthermore be concluded that no combination mode can adequately explain the appearance of the extra band in the C=N stretching region.

Since the band (or the bands) between 1600—1655 cm^{-1} has only been observed in compounds with an acyclic structure B it seems to be useful as an indication of such a structure. In the potassium salt of VIII the C=N absorption was observed at 1615 cm^{-1} in KBr and on this basis an acyclic structure was assigned to this salt. Heugebart and Willems have prepared the

silver salt of some 1,3,4-thiadiazolidine-2-thiones and since these salts are stable they conclude the salts to be cyclic. Our result with the potassium salt indicate that this is probably not correct.

The mass spectra of the compounds given in Tables 1 and 2 will be published separately in a full paper.[9] The cyclic structures exhibited a fragmentation path different from that of the acyclic structures. In all cases the molecular weight was found to be in agreement with the postulated formulas.

EXPERIMENTAL

Analyses were carried out at the Microanalyses Department of this laboratory using a Perkin Elmer 240 Elemental Analyzer for C, H, N analyses. The melting points were determined on a Mettler FP Melting Point Apparatus and were not corrected. Conditions and equipment used for recording the IR spectra were reported in part I of this series.[10] The proton magnetic resonance spectra were recorded on a Varian A 60A Spectrometer equipped with a Varian V-6040 Variable Temperature Probe and Temperature Controller using TMS as internal reference.

The starting materials. Methylhydrazine and acetone-d_6 (99 %) were commercial products. 1,2-Dimethylhydrazine was available from the stock of chemicals of this laboratory.[11]

5,5-Dimethyl-1,3,4-thiadiazolidine-2-thione (*I*). Hydrazinium dithiocarbazate [7] (5 g) was suspended in acetone (50 ml). The suspension was heated to the boiling point and kept at this temperature for one minute. After filtration the solution was cooled in an ice bath and (I) was precipitated with pentane. All the compounds given in Table 1 were prepared in this way. Elemental analyses proved the compounds, with the exception of IV and VI, to be essentially pure. The compounds IV and VI were dissolved in chloroform and re-precipitated with pentane, in order to remove a contamination with the corresponding azine. Recrystallization was not necessary to obtain a pure product.

3,4,5,5-Tetramethyl-1,3,4-thiadiazolidine-2-thione. This compound was prepared from 1,2-dimethylhydrazinium dithiocarbazate following the directions given above. The yield was 60 %, m.p. 99—100°C. (Found: C 40.60; H 6.74; N 15.75. Calc. for $C_6H_{12}N_2S_2$: C 40.87; H 6.86; N 15.89).

The alkylidene derivatives of methyl- and 2-methyldithiocarbazate. The compounds given in Table 2 were all prepared according to the directions given by Sandström [1] for methyl 3-isopropylidenedithiocarbazate. Absolute ethanol or pentane was used for recrystallization.

The conversion of I—VII to alkylidene derivatives of methyldithiocarbazate and 2-methyldithiocarbazate. Potassium hydroxide (0.01 mol) was dissolved in absolute ethanol (15 ml) and an equimolar amount of one of the compounds I—VII was dissolved in this solution. Methyl iodide (0.01 mol) was added dropwise and the mixture left for 2 h at room temperature. The precipitated potassium iodide was filtered off, and the filtrate was evaporated to dryness. The crystalline residue was recrystallized from pentane. The yields were 70—80 % of colourless crystals. Identity of these products with those given in Table 2 was confirmed from identical IR spectra and by mixture melting points.

Methyl 3-isopropylidene-2-methyldithiocarbazate hydroiodide. (*XIV*). 3,5,5-Trimethyl-1, 3,4-thiadiazolidine-2-thione (0.01 mol) was dissolved in methyl iodide (5 ml) at room temperature. A few minutes later a crystalline product separated which was filtered off and washed with pentane (10 ml). A nearly quantitative yield of (XIV), m.p. 126—127°C, was obtained as yellowish crystals. (Found: C 23.48; H 4.28; N 9.36. Calc. for $C_6H_{13}IN_2S_2$: C 23.69; H 4.31; N 9.21). This compound exhibited a melting point and IR and PMR spectra identical with a sample prepared in the following way: Dry hydrogen iodide prepared from 48 % aqueous hydrogen iodide and P_2O_5 [12] was passed through a solution of methyl 3-isopropylidene-2-methyldithiocarbazate (0.05 mol) in pentane (30 ml). The yield was 60 % of yellow crystals with a melting point of 125—126°C.

The C deuterated materials used for the IR- investigations were prepared in a manner identical to that described for the undeuterated compounds, except that acetone-d_6 was used.

The potassium salt of I. 5,5-Dimethyl-1,3,4-thiadiazolidine-2-thione (0.01 mol) was dissolved in an equimolar amount of ethanolic potassium hydroxide. The potassium salt was precipitated with ether. (Found: C 25.31; H 4.06; N 14.73. Calc. for $C_4H_7KN_2S_2$: C 25.78; H 3.79; N 15.04). The yield was almost quantitative. M.p. 75—150°C, with slow destruction.

REFERENCES

1. Sandström, J. *Acta Chem. Scand.* **17** (1963) 937.
2. Anthoni, U. *Acta Chem. Scand.* **20** (1966) 2742.
3. Anthoni, U., Dahl, B. M., Larsen, Ch. and Nielsen, P. H. *Acta Chem. Scand. In press.*
4. Heugebart, P. C. and Willems, J. F. *Tetrahedron* **22** (1966) 913.
5. Karle, I. L. and Karle, J. *Tetrahedron Letters* **47** (1964) 3579.
6. Taeger, V. E. and El-Hewehi, Z. *J. prakt. Chem.* (4) **18** (1962) 255.
7. Busch, M. and Starke, M. *J. prakt. Chem.* (2) **93** (1916) 59.
8. Sandström, J. *Arkiv Kemi* **9** (1956) 255.
9. Larsen, Ch. *To be published.*
10. Anthoni, U., Larsen, Ch. and Nielsen, P. H. *Acta Chem. Scand.* **21** (1967) 1201.
11. Jensen, K. A., Anthoni, U., Kägi, B., Larsen, C. and Pedersen, C.Th. *Acta Chem. Scand.* **22** (1968) 1.
12. Brauer, G. *Handbuch der präparativen anorganischen Chemie I*, p. 262, Ferdinand Enke Verlag, Stuttgart 1960.

Received June 17, 1969.