Tri(hetero)substituted Carbonium Ions. VIII. The Hydride Reduction of Cyclic and Open-chain Dithiocarbamidium Salts

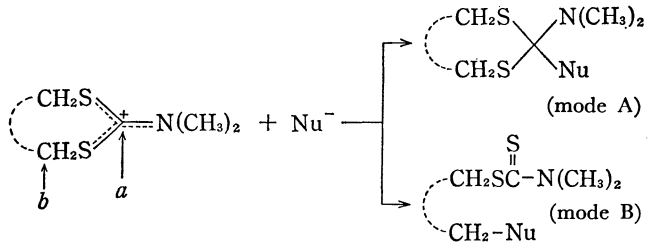
Kazuhisa HIRATANI, Takeshi NAKAI, and Makoto OKAWARA

Research Laboratory of Resources Utilization, Tokyo Institute of Technology, Ookayama, Meguro-ku, Tokyo 152

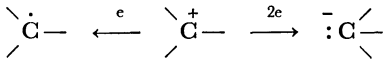
(Received June 20, 1973)

Studies were carried out on the hydride reduction of the following five stable *N,S,S*-tri(hetero)substituted carbonium ions: *N,N,S,S'*-tetramethyldithiocarbamidium ion (**1a**), 2-dimethylamino-1,3-dithiolanylium ion (**1b**), 2-dimethylamino-1,3-dithianylium ion (**1c**), 2-methylthio-3-methyl-4,5-dihydrothiazolium ion (**1d**), and 2,3,5,6-tetrahydrothiazolo[2,3-*b*]thiazolium ion (**1e**). Sodium dihydrobis(methoxyethoxy)aluminate (RDB) was found to be a suitable reducing agent. The RDB reduction of the carbonium ions at −5 °C gave the corresponding formamide thioacetals (**2**) in moderate yields. This provides a practical method for the synthesis of formamide thioacetals. The RDB reduction of **1d** at higher temperature, however, yielded abnormal products, thiazolin-2-thione (**3**) and thiazolidine (**4**) instead of the formamide thioacetal (**2d**). The mechanism for the formation of **3** and **4** has been discussed in terms of the ambident character of the cation (**1d**). Pyrolytic reactions of the thioacetals (**2**) and unsuccessful attempts to abstract the methine proton of **2b** by various bases are also described.

In previous studies[1-5] we established that (i) dithiocarbamidium ions (**1**) have two electrophilic sites (the ambident character) and (ii) in general, hard nucleophiles attack selectively site at *a* (mode A) while soft nucleophiles react at site *b* (mode B).



Reduction reactions of carbonium ions have recently drawn much attention since one- and two-electron reductions of carbonium ions might lead to carbon radical and carbanion frameworks, respectively. Although papers have appeared on the reduction of stable carbonium ions,[6] little information has been available on the reduction of stable tri(hetero)carbonium ions.



In this work, the hydride reduction (two-electron reduction) of cyclic and acylic dithiocarbamidium ions by means of metal hydride has been studied. On the basis of the selectivity rule it is anticipated that hydride ion, one of the hardest nucleophiles, attacks specifically at site *a* giving formamide thioacetals. The present paper describes the hydride reductions of the dithiocarbamidium ions which give the corresponding formamide thioacetals in moderate yields.

Results and Discussion

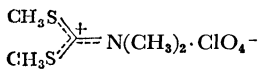
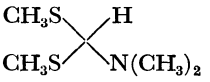
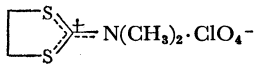
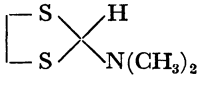
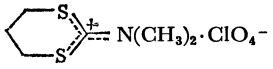
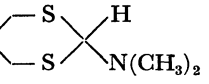
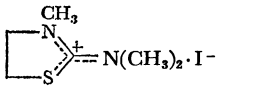
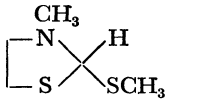
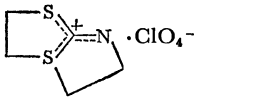
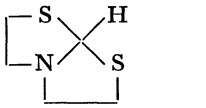
Hydride Reductions of the Carbonium Salts. The following dithiocarbamidium salts were used: *N,N,-S,S'*-tetramethyldithiocarbamidium perchlorate (**1a**),[4] 2-dimethylamino-1,3-dithiolan-2-ylium perchlorate (**1b**),[1] 2-dimethylamino-1,3-dithian-2-ylium perchlorate (**1c**),[3] 2-methylthio-3-methyl-4,5-dihydrothiazolium iodide (**1d**),[5] and 2,3,5,6-tetrahydrothiazolo[2,3-*b*]thiazolium perchlorate (**1e**).[5] Metal hydrides examined were sodium hydride, sodium borohydride (SBH), lithium aluminium hydride (LAH) and a 64% benzene solution of sodium dihydrobis(2-methoxyethoxy)aluminate (RDB).

In order to find the best reducing agent, the reactions of **1b** with the above four metal hydrides were carried out in tetrahydrofuran (THF) or ether in the range from −10 °C to room temperature for 2—4 hr. In most cases except for RDB, both reactants were almost insoluble in the solvents. It was found that sodium hydride can not reduce the cation under the conditions. The reduction using SBH and LAH gave the expected product 2-dimethylamino-1,3-dithiolane (**2b**) in *ca.* 30% and *ca.* 20%, respectively. The optimum yield (71%)was obtained by using RDB in THF at −5—0 °C. The result shows that RDB has an advantage over SBH and LAH presumably due to the greater solubility of RDB in organic solvents such as ether and THF. Thus, the hydride reductions of the other dithiocarbamidium salts were undertaken by means of RDB under similar conditions. The yields and physical properties of the formamide thioacetals thus obtained are summarized in Table 1. Their elemental analysis and NMR spectra are given in Table 2.

It should be noted that there is a well-defined trend for the absorption due to the methine proton in the formamide thioacetals to shift remarkably to a lower field in the order: **2a** (acyclic), **2c** (six-membered), and **2b** (five-membered) although their N-CH_3 signals were essentially independent of the ring size (Table 2). In view of the fact that the inductive effect on the me-

1) T. Nakai, Y. Ueno, and M. Okawara, This Bulletin, **43**, 156 (1970).
2) T. Nakai and M. Okawara, *ibid.*, **43**, 1864 (1970).
3) T. Nakai, Y. Ueno, and M. Okawara, *ibid.*, **43**, 3175 (1970).
4) T. Nakai and M. Okawara, *ibid.*, **43**, 3528 (1970).
5) T. Nakai, K. Hiratani, and M. Okawara, *ibid.*, in press.
6) K. Okamato, *Kogyo Kagaku Zasshi*, **69**, 825 (1969) (a review); F. A. Carey and H. S. Tremper, *J. Org. Chem.*, **34**, 4 (1969); H. M. Bell and H. C. Brown, *J. Amer. Chem. Soc.*, **88**, 1473 (1966); S. D. McGregor and W. M. Jones, *ibid.*, **90**, 123 (1968).

Table 1. Hydride reductions of the carbonium salts by RDB

	Carbonium salts	Formamide thioacetals	Bp(mmHg), °C [Lit.]	n_D (20°) [Lit.]	Yield %
1a		**2a** 	62—63° (5.5) [80—82° (10)][a]	1.521 [1.525][a]	38
1b		**2b** 	57—58° (1.5) [60° (0.1)][b]	1.567 [1.564][b]	71
1c		**2c** 	90—91° (2.5)	1.568	34
1d		**2d** 	59—61° (1.5)	1.561	36
1e		**2e** 	83—85° (1.0)	1.614	57

a) H. Boehme and J. Roer, *Ann. Chem.*, **648**, 21 (1961). b) C. Feugeas and D. Olschwang, *Bull. Soc. Chim. Fr.*, **1969**, 332.

Table 2. NMR data of formamide thioacetals (**2**)

	δ ppm (multiplicity)				
	≡C-H	=N-CH_3	-S-CH_3	-S-CH_2-	others
2a	4.64(s)	2.34(s)	2.06(s)	—	—
2b	6.01(s)	2.25(s)	—	3.11(m)	—
2c	5.13(s)	2.39(s)	—	2.81(t)	[-$CH_2CH_2CH_2$-] 1.6—2.1(m)
2d	4.97(s)	2.35(s)	2.04(s)	2.7—3.1(m)	[-N-CH_2-] 3.2—3.5(m)
2e	5.83(s)	—	—	[-S-CH_2CH_2-N=] 3.16(m)	

thine proton is nearly constant in the system concerned, two possible explanations can be suggested; (i) the ring-size effect on the conformation of the thioacetal ring[7] and (ii) the ring-size effect on the extent of the 3p–3d interaction between the two sulfur atoms in the ring recognized in UV spectra for cyclic thioacetals and orthothioformates.[8] At the present stage, however, it is difficult to determine which factor is more operative since no information is available on the conformational analysis and acidity of cyclic formamide thioacetals. Our attampts to abstract the methine proton of **2b** by various bases were unsuccessful.

Thus, the hydride reduction of the stable carbonium salts, which were readily prepared by the previously-reported method,[1,3–5] may provide a practical method[9] for the synthesis of formamide thioacetals which have recently attracted much attention as a synthetic intermediate.[10]

The Ambident Behavior of the Cation ***1d*** *in the Hydride Reduction.* During the course of our search for the optimum reduction conditions for the cation **1d**, we found that a change in reaction temperature from −5 °C to room temperature resulted in a complete change of the product structure; the reduction of **1d** at −5 °C gave the normal product **2d** while the reduction at room temperature (15—20 °C) yielded 3-methylthiazolidin-2-thione (**3**) and 3-methylthiazolidine (**4**) in 12% and 30% yields, respectively. The thin layer chromatogram of the crude mixture excluded any possibility of the presence of a product other than **3** and **4**. Product **3** was identical with an authentic sample.[11] The other product **4** was identified by elemental analysis and IR and NMR spectroscopic methods.

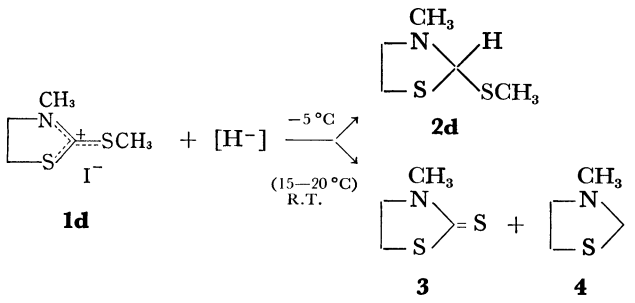
7) C. H. Bushweller, "Mechanisms of Reactions of Sulfur Compounds", ed. by N. Kharasch, Vol. 5, Intra-Science Research Foundation, Santa Monica, Calif., 1970, p. 75.

8) Y. Yano and S. Oae, *ibid.*, Vol. 4, p. 167 (1969).

9) For a recent review on synthetic methods for formamide thioacetals, see J. Gloede, L. Haase, and H. Gross, *Z. Chem.*, **9**, 201 (1969).

10) Review: R. H. DeWoefe, "Carboxylic Ortho Acid Derivatives-Preparation and Synthetic Applications," Academic Press, New York and London, 1970, Chapter 7.

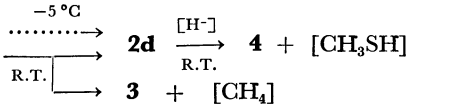
11) J. W. Batty and B. C. Weedon, *J. Chem. Soc.*, **1949**, 786.



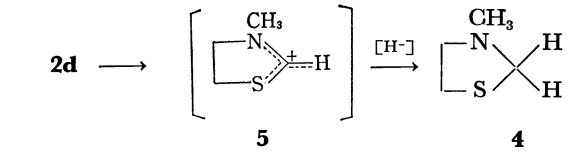
1d **2d** **3** **4**

The abnormal behavior of **1d** is in contrast to the reductions of the other carbonium salts in which the corresponding formamide thioacetals were formed in the range from −10 °C to room temperature. The effect of reaction temperature on product structure is of particular interest in connection with the ambident behavior of the tri(hetero)carbonium ions. The mechanisms for the formation of **3** and **4** in the RDB reduction of **1d** were investigated in some detail.

In order to ascertain whether the normal product **2d** is an intermediate for the formation of the abnormal products, **2d** was treated with RDB at room temperature. Only 3-methylthiazolidine (**4**) was obtained, and product **3** was not detected in the reaction mixture. Furthermore, it was found that **3** did not react with RDB under the same conditions and was recovered unchanged. The result of the control experiments led us to suggest that **4** is formed *via* hydride reduction of **2d** and that **3** is not formed *via* **2d** but directly *via* the reaction between the cation **1d** and hydride ion as follows.

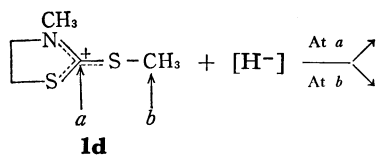


Formation of **4** *via* **2d** can be easily explained as the result of an initial reductive cleavage of the C–SMe bond followed by hydride reduction of the 3-methyl-4,5-dihydrothiazolium ion (**5**); a similar reductive cleavage of C–S bonds by hydride ion has been established for thiazolidines[12] and α-dimethylaminobenzylsulfides.[13]



5 **4**

Formation of **3**, on the other hand, can be best explained in terms of a direct attack at site *b* by hydride ion (mode B). This indicates that a change in reaction temperature from −5 °C to room temperature resulted in a partial shift of the reaction course from mode A to mode B.



1d

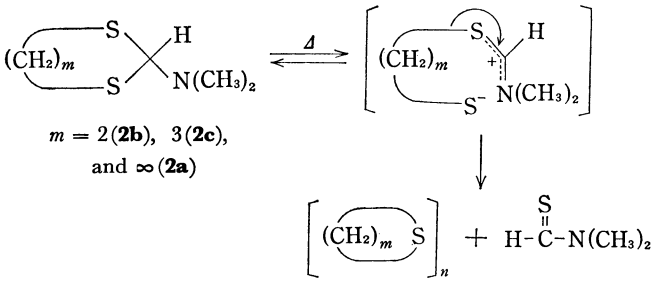
2d → **4** ····· mode A

3 ····· mode B

12) E. L. Eliel, E. W. Della, and M. M. Rogic, *J. Org. Chem.*, **27**, 4712 (1962).

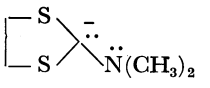
This is the first example demonstrating the important role played by the reaction temperature in determining the reaction course of ambident electrophiles such as dithiocarbamidium ions. In view of our previous findings that the reaction course for the tri(hetero)-carbonium ions depends mainly upon the nucleophilicity and bulkness of an attacking reagent and upon the stability of the cations concerned, it might be concluded that external factors such as reaction temperature should also be taken into account as an additional factor determining the reaction course for some ambident electrophiles.

Reactions of Formamide Thioacetals. Pyrolytic reactions of the formamide thioacetals were studied. When **2b** was heated in bulk at 160—170 °C for 12 hr under nitrogen atmosphere, *N*,*N*-dimethylthioformamide (**6**) was obtained as a major product along with polymeric ethylene sulfide. Both products were identified through agreement of their IR spectra with those of authentic samples. Pyrolysis of **2a** and **2c** under similar conditions also yielded **6** as a major product. Formation of **6** in these reactions can be explained by assuming an initial thermal cleavage of the C–S bond reported for the thermal reactions of ortho(thio)carbonate derivatives.[14] In contrast, **2d** was more easily pyrolyzed under the conditions to yield the cyclic thione **3** with retention of the ring structure along with a small amount of 3-methylthiazolidin-2-one.



m = 2(**2b**), 3(**2c**), and ∞(**2a**)

Attempts were made to abstract the methine proton of **2b** with various bases. When **2b** was treated with *n*-butyllithium followed by addition of deuterium oxide, it was found by IR and NMR spectroscopy that no deuterium was incorporated in the resulting thioacetal. Attempts with other bases under various conditions were also unsuccessful. In view of the ease to abstract 2-hydrogens in 1,3-dithianes by *n*-butyllithium, difficulty to abstract the methine proton in **2b** suggests that the resulting carbanion (**7**) is very unstable due to large repulsion between its sp^3 nonbonding electrons and the lone pair of electrons on the nitrogen atom.



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13) W. M. Schbert and Y. Motoyania, *J. Amer. Chem. Soc.*, **87**, 5507 (1965).

14) Y. Ueno, T. Nakai, and M. Okawara, This Bulletin, **43**, 162, 168 (1970).

15) E. D. Bergmann and A. Kaluszyner, *Rec. Trav. Chim., Pays-Bas*, **78** 289 (1959).

Experimental

General. All melting and boiling points are uncorrected. IR and UV spectra were recorded with Hitachi EPI-S2 and EPS-3T spectrophotometers, respectively. NMR spectra were obtained with a Japan Electron Optics JNN H-100 spectrometer. Chemical shifts are given in ppm with tetramethylsilane as an internal standard. All carbonium salts were prepared according to the literature methods.

*Reactions of the salt **1b** with Metal Hydride.* *a) With RDB*: A suspension of 68 g (0.27 mol) of **1b**[1] in 150 ml of THF was placed in a 500-ml three-necked flask equipped with a mechanical stirrer, dropping funnel and thermometer, and was then cooled to −5 °C. To the stirred mixture was added dropwise 8.5 g (0.27 mol) of a 64% benzene solution of RDB[16] over a period of 2 hr. The reaction mixture was then stirred at −5—0 °C for 4 hr. After removal of THF at room temperature under reduced pressure, ether and water were added to the resulting mixture. The ethereal layer was separated and dried over anhydrous sodium sulfate. After removal of the drying agent followed by distillation of ether, distillation of the liquid residue gave 28.5 g (71%) of **2b**.

Found: C, 40.16; H, 7.43; N, 9.25%. Calcd for $C_5H_{11}NS_2$: C, 40.23; H, 7.42; N, 9.38%.

b) With LAH: In a similar manner, the reaction of **1b** (3.0 g, 12 mmol) with LAH (1.0 g, 27 mmol) in 50 ml of ether at 0 °C gave 0.4 g (22%) of **2b**.

c) With SBH: In a similar manner, the reaction of **1b** (15 g, 61 mmol) with SBH (4 g, 110 mmol) in 100 ml of ether at 0 °C yielded 3.0 g (33%) of **2b**. When ethanol was used as the solvent in place of ether, a similar reaction of **1b** (75 g, 0.3 mol) with SBH (1.0 mol) gave 27 g (60%) of **2b**.

RDB Reductions of Other Carbonium Salts. By the same procedure as in the case of RDB reduction of **1b**, 35 g (0.14 mol) of **1a**[4] and 47 g (0.14 mol) of the RDB solution gave 8.0 g (38%) of **2a**.

Found: C, 39.75; H, 8.76; N, 9.25%. Calcd for $C_5H_{12}NS_2$: C, 39.70; H, 8.66; N, 9.25%.

In a similar fashion, the RDB reductions of **1c**,[3] **1d**[5], and **1e**[5] gave the corresponding formamide thioacetals (**2**) in 34%, 36%, and 57% yields, respectively.

2c, Found: C, 44.56; H, 8.12; N, 8.46%. Calcd for $C_6H_{13}NS_2$: C, 44.13; H, 8.02; N, 8.58%.

2d, Found: C, 39.98; H, 7.38; N, 9.31%. Calcd for $C_5H_{11}NS_2$; C, 40.23; H, 7.43; N, 9.38%.

2e, Found: C, 39.87; H, 6.25; N, 9.26%. Calcd for $C_5H_9NS_2$: C, 40.78; H, 6.16; N, 9.51%.

*The RDB Reduction of **1d** at Room Temperature (15—20 °C).* To a suspension of 5.5 g (0.02 mol) of **1d** in 40 ml of THF was added dropwise 5.8 g (0.02 mol) of the RDB solution at room temperature. After the mixture was stirred at room temperature, THF was removed by distillation. Ether and water were added to the residue and the ethereal layer was separated. The ethereal solution was dried over anhydrous sodium sulfate and the ether was evaporated under reduced pressure. The thin layer chromatogram (silica gel, chloroform) of the oily residue showed two spots which were assigned to *N*-methylthiazolin-2-thione (**3**) and *N*-methylthiazolidine (**4**) by comparison of the R_f values with those of authentic samples. Distillation of the residue under reduced pressure gave 0.60 g (30%) of 3-methylthiazolidine (**4**), 39—41 °C/4 mmHg, n_D (20 °C) 1.518 (lit,[15] bp 151—152 °C/760 mmHg, n_D (25 °C) 1.520), and a solid residue which was then recrystallized from water giving 0.32 g (12%) of 3-methylthiazolidin-2-thione (**3**), mp 68—69 °C (lit,[11] 69.5 °C).

4: NMR ($CDCl_3$); 2.22 (s, 3H, NCH_3), 2.87 (m, 4H, SCH_2CH_2N) and 3.90 (s, 2H, SCH_2N). Found: C, 47.48; H, 9.06; N, 13.39%. Calcd for C_4H_9NS: C, 46.59; H, 8.80; N, 13.58%.

Control Experiments. *a) Reaction of the Formamide Thioacetal (**2d**) with RDB*: A mixture of 0.3 g of **2d** and 0.7 g of the RDB solution in 10 ml of benzene was stirred at room temperature for 24 hr. Water was then added to the mixture and the solution was extracted with ether. The ethereal solution was dried over anhydrous sodium sulfate and the ether was evaporated completely to give 0.27 g of an oily residue. The oil was found to consist of **4** and unreacted **2d** by IR and NMR spectroscopy and thin layer chromatography.

*b) Reaction of **3** with RDB*: A mixture of 1.35 g of **3** and 3.0 g of the RDB solution in 30 ml of THF was stirred at room temperature for 3 hr. The mixture was poured into cold water followed by extraction with ether. The ether solution was dried over anhydrous sodium sulfate and the ether was evaporated completely giving 1.32 g of unchanged **3**.

Pyrolyses of the Formamide Thioacetals. 1.0 g of **2a** was placed in a 10 ml flask equipped with a reflux condenser and gas inlet. The flask was dipped in an oil bath heated at 150 °C and allowed to stand for 24 hr at 130—150 °C under nitrogen atmosphere. After cooling, the mixture was subjected to column chromatography (silica gel). Two products were obtained; the major product (*ca.* 30% yield) was identical (IR and UV) with an authentic sample of *N,N*-dimethylthioformamide (**6**) prepared by method in literature;[17] the minor product was identified to be methyl *N,N*-dimethylthiolcarbamate by comparison of its IR spectrum with that of an authentic sample.[4]

In a similar manner, pyrolysis of **2b** (1.5 g) at 160—170 °C for 12 hr gave an oil along with a white solid on the wall of the reflux condenser. The oil was dissolved in chloroform and chromatographed on silica gel. Elution with chloroform gave 0.57 g (64%) of the thioformamide (**6**). The white solid was identified as polymeric ethylene sulfide by IR spectroscopy and elemental analysis. No further identification was made.

The pyrolysis of **2c** (0.5 g) at 150 °C for 12 hr also gave **6** as a major product.

Pyrolysis of **2d**, (0.5 g, 3.4 mmol) at 160 °C was complete after only 3 hr. After the resulting mixture had been cooled, it was subjected to column chromatography (silica gel) to give 0.3 g (66%) of 3-methylthiazolidin-2-thione (**3**) and 0.1 g of 3-methylthiazolidin-2-one.[5] The structures of the products were determined by comparison of their IR spectra and physical properties with those of the corresponding authentic sample.

*Reaction of **2b** with n-Butyllithium.* A solution of 3.0 g (0.02 mol) of **2b** in 50 ml of THF was placed in a 100 ml three-necked flask equipped with a magnetic stirrer, gas inlet tube and thermometer. The mixture was stirred at −70 °C under nitrogen atmosphere and then 8.0 g of a 15% *n*-hexane solution of *n*-butyllithium was added dropwise to the mixture. After the mixture was stirred at −70 °C for 3 hr, 0.5 g of deuterium oxide was added and the mixture was allowed to stand until the temperature rose to room temperature. The white precipitates formed were filtered and the solvents were removed from the filtrate under reduced pressure at room temperature to give an oily residue. The IR and NMR

16) Purchased from Wako Pure Chemical Industries, Ltd.

17) R. Willstaetter, *Chem. Ber.*, **42**, 1921 (1909).

spectra of the oil agreed with those of **2b**.

A similar reaction with *n*-butyllithium-*N*,*N*,*N*′,*N*′-tetramethylethylene diamine complex resulted in the recovery of **2b** unchanged.

An attempt to abstract the methine proton in **2b** with *t*-BuOK—*t*-BuOD was unsuccessful.