Synthesis of 2-Dialkylamino-5-hydroxy-1, 3-dithian-2-ylium Perchlorates and Their Intramolecular Rearrargements by Use of Bases[1)†]

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Abstract

2-Dialkylamino-5-hydroxy-1, 3-dithian-2-ylium perchlorates (2) could be synthesized by reaction of 2-alkyl-1-chloro-2,3-epoxypropane derivertives (4) with aqueous dialkylammonium N, N-dialkyldithiocarbamates (5), followed by treatment with $NaClO_4$ in methanol. Reaction of 2 with bases gave 2, 3-epithiopropyl N,N-dialkylthiolcarbamates (8). In these cases, the reaction pathway involving intramolecular rearrrangement of 2 via formation of intermediate, heterobridged bicyclo compound, was proposed.

Introduction

Formation and reaction of a heterocyclic carbonium ion, 1, 3-dithian-2-ylium ion, have been described by Nakai et al.,[2)] and W. C. Doyle, Jr.[3a-c)]. That is, 2-dimethylamino-1,3-dithian-2-ylium perchlorate (1) has been obtained by the reaction of 1,3-dichloropropane with sodium N, N-dimethyldithiocarbamate, followed by treatment with $NaClO_4$.

In the present paper, we wish to report the syntheses of several 2-dialkylamino-5-hydroxy-1,3-dithian-2-ylium perchlorates (2) analogous to **1** by reaction of 2-alkyl-3-chloro-2-hydroxypropyl N,N-dialkyldithiocarbamates (3) with $NaClO_4$ in methanol, and also report an interesting intramolecular rearrangement of 2 by use of base, involving formation of intermediate heterobridged bicyclo compounds which contained S, S, and O atoms in their ring systems.

Results and Discussion

In general, derivatives 3 were obtained by reaction of 2-alkyl-1-chloro-2,3-epoxypropane derivatives (4) with aqueous dialkylammonium N,N-dialkyldithiocarbamates (5), which have been easily prepared from aqueous dialkylamines and CS_2 at room temperature (Eq. (1)). In these cases, by use of a large excess of CS_2, by-produced dialkylamines have been also converted to 5.

When methanolic solution of $NaClO_4$ was added to an oily product 3-chloro-2-hydroxypropyl N, N-dimethyldithiocarbamate (3a) in methanol and then the mixture was stirred at 60°C, NaCl was gradually precipitated from the solution. After about 3h, the precipitated NaCl was filtered off and the filtrate was concentrated *in vacuo* to afford 2-dimethylamino-5-hydroxy-1, 3-dithian-2-ylium perchlorate (2a). The com-

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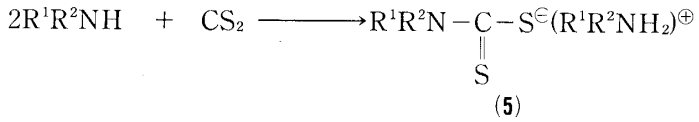
pound 2a was identified by its elemental analysis and NMR spectrum (D_2O, 20%). As described above, derivatives 2 were generally obtained by the reaction of 3 with $NaClO_4$ in methanol at 60°C (Eq. (2)) (only 2e was prepared from 3e and KI). Experimental results are summarized in Table 1.



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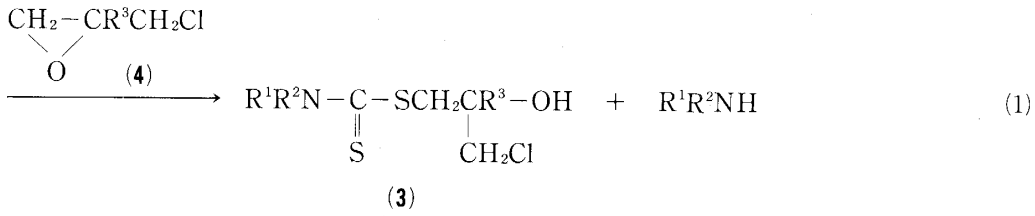

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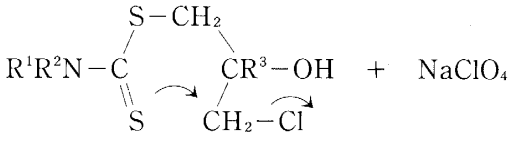

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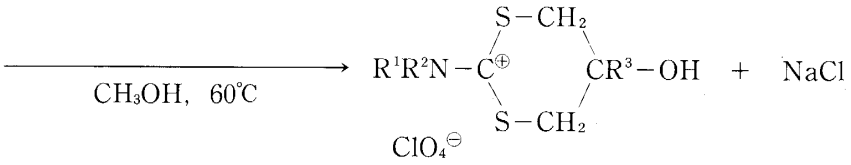

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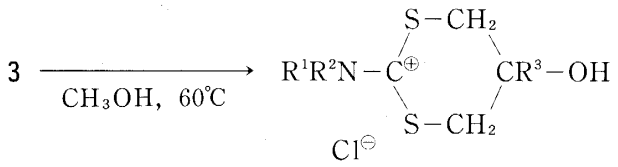
(2)

Table 1 Preparation of 2

Compd.	R^1	R^2	R^3	Yield (%)	Mp (°C)
2a	CH_3	CH_3	H	74	94–95
2b	C_2H_5	C_2H_5	H	95	97–98
2c			H	83	182–184
2d			H	43	154–156
2e[a]	CH_3	CH_3	CH_3	25	138–140
2f	C_2H_5	C_2H_5	CH_3	68	113–114
2g			CH_3	73	161–162
2h			CH_3	31	154–156

a) 2e was obtained as iodide salt.

On the other hand, by heating the devivatives 3 in methanol at 60°C for 15-20 min, 2-dialkylamino-1, 3-dithian-2-ylium chlorides (6) were obtained (Eq. (3)). However, these salts were so hygroscopic that we could not isolate them in pure states.



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(6)

The reaction of 2 with aqueous $NaHCO_3$, sodium alkoxides in alcohols, and sodium thioalkoxides in acetonitrile, gave 2, 3-epithiopropyl N, N-dialkylthiolcarbamates (8) in good yields, respectively. Experimental results are summarized in Table 2.

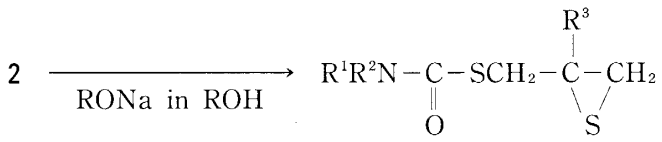

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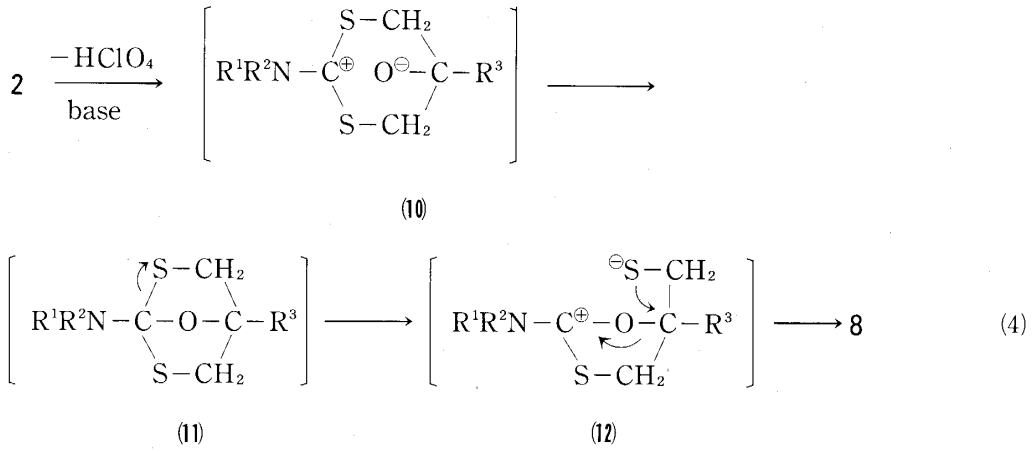
Table 2 Preparation of 8

Compd.	R^1	R^2	R^3	Yield(%)	Bp(℃)/mmHg (Mp(℃))
8a	CH_3	CH_3	H	97	84-85/2
8b	C_2H_5	C_2H_5	H	99	86-87/2
8c			H	95	114-115/2
8d			H	95	(72-73)
8e	CH_3	CH_3	CH_3	91	87-88/2
8f	C_2H_5	C_2H_5	CH_3	89	88-89/2
8g			CH_3	89	114-115/12
8h			CH_3	93	(60-61)

Explanation for the formation of 8 by reaction of 2 with sodium alkoxides or sodium thioalkoxides in nonaqueous solvent can be offered by an intramolecular rearrangement of 2. That is, these reagents should act as bases instead of nucleophiles, and lead 2 to intermediate heterobridged bicyclo compounds (11) containing S, S, and O atoms in their ring systems *via* alkoxide ions (10). Then, by cleavage of the bridged linkage 11 will be led into products 8 via 1, 3-oxathiolan-2-ylium ion (12) in the following manner (Eq. (4))[4].

Some rearrangements induced by hetero-atom bridging have been reviewed[5]. However, any report on intramolecular rearrangement involving formation of novel

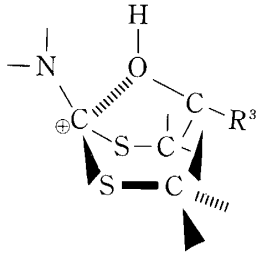


(10)

(11) (12)

heterobridged bicyclo compounds such as 11 has never appeared.

From the above behavior of derivatives 2 with bases, we presume that 2 may be formed in a boat form which is stabilized by interaction between the cationic center and nonbonded electron pair of the oxygen atom of OH group as shown in Fig. 1. Such derivatives 2 will be easily led to 11 with the aid of dases.



2

Fig. 1

Experimental

All the melting points uncorrected. The NMR spectra were recorded on a JEOL-MH-100 spectrometer. IR spectra were measured as nujol paste or neat on a Nippon Bunko IR-A spectrometer.

Synthesis of 2a. A Typical Procedure for 2 : To the mixture of aqueous dimethylamine Solution (40%, 33g, 0.3mol) and water (30 ml) was added carbon disulfide (34g, 0.45mol) below 20°C. 1-Chloro-2, 3-epoxypropane (28g, 0.3mol) was added dropwise to the above mixture at the same temperature, and then stirred for 30 min. The organic layer was separated to give oily product 3-chloro-2-hydroxypropyl N, N-dimethyldithiocarbamate (3a) ; 63g (98%). (Because 3a was very sensitive to heat, its analitical data were not obtained).

To the solution of 3a (63g, 0.3mol) in methanol (120ml) was added sodium perchlorate monohydrate (42g, 0.3mol) and the mixture was stirred for 3h at 60°C. The precipitated NaCI was filtered off and the filtrate was concentrated *in vacuo* to afford colorless crystals 2a : 62g (74%) ; mp 94-95°C (from methanol). IR (nujol) : 1075 (ClO_4) , 1575(C=N), 3460cm^{-1} (OH). ^1H NMR (D_2O) δ=3.12, 3.52 (4H,two dd, $J_{4,4'}=J_{6,6'}$ =14 Hz, $J=_{4,5}=J_{4',5}=J_{6,5}=J_{6',5}$=5Hz, 4-, 4'-, 6- and 6'-H), 3.56 (6H, s, N $(CH_3)_2$), 4.68 (1H, quintet,

5-H). Found : C, 26.06 ; H, 4.42 ; N, 5.02%. Calcd for $C_6H_{12}NClO_5S_2$: C, 25.94 ; H, 4.35 ; N, 5.04%.

2b : IR (nujol) 1080 (ClO_4), 1548 (C=N),3440 cm^{-1} (OH) ; Found : C, 31.63 ; H, 5.62 ; N, 4.75%. Cacld for $C_8H_{16}NClO_5S_2$: C, 31.42 ; H, 5.27 ; N, 4.58%.

2c : IR (nujol) 1080 (ClO_4), 1556 (C=N), 3530 cm^{-1} (OH) ; Found : C, 31, 69 ; H, 4.71 ; N, 4.52%. Calcd for $C_8H_{14}NClO_5S_2$: C, 31.63 ; H, 4.65 ; N, 4.61%.

2d : IR (nujol) 1080 (ClO_4), 1550 (C=N), 3550 cm^{-1} (OH) ; Found : C, 30.37 ; H, 4.58 ; N, 4.67%. Calcd for $C_8H_{14}NClO_6S_2$: C, 30.05 ; H, 4.41 ; N, 4.38%.

2e : IR (nujol) 1565 (C=N), 3550 cm^{-1} (OH) ; ^1H NMR (D_2O) δ = 1.54 (3H, s, CH_3), 3.18, 3.36 (4H, two d, $J_{4,4'}=J_{6,6'}$= 14 Hz, 4-, 4'-, 6- and 6'-H), 3.53 (6H, s, $N(CH_3)_2$) ; Found : C, 26.71 ; H, 4.78 ; N, 4.54%. Calcd for $C_7H_{14}NIOS_2$: C, 26.34 ; H, 4.42 ; N, 4.39%.

2f : IR (nujol) 1080 (ClO_4), 1550 (C=N), 3500 cm^{-1} (OH) ; ^1H NMR (D_2O) δ = 1.34 (6H, t, J= 7 Hz, $N(CH_2\underline{CH_3})_2$), 1.53 (3H, s, CH_3), 3.16, 3.33 (4H, two d, $J_{4,4'}=J_{6,6'}$= 14 Hz, 4-, 4'-, 6- and 6'-H), 3.93 (4H, q, $N(\underline{CH_2}CH_3)$; Found : C, 34.11 ; H, 5.92 ; N, 4.45%. Calcd for $C_9H_{18}NClO_5S_2$: C, 33.80 ; H, 5.67 ; N, 4.41%.

2g : IR (nujol) 1080 (ClO_4), 1550 (C=N), 3500 cm^{-1} (OH) ; ^1H NMR (D_2O) δ = 1.52 (3H, s, CH_3), 2.04~2.22 (4H, m, $N(CH_2\underline{CH_2})_2$), 3.15, 3.32 (4H, two d, $J_{4,4'}=J_{6,6'}$= 14 Hz, 4-, 4'-, 6 - and 6'-H), 3.66~3.90 (4H, m, $N(\underline{CH_2}CH_2)_2$) ; Found : C, 34.12 ; H, 5.26 ; N,4.44%. Calcd for $C_9H_{16}NClO_5S_2$: C, 34.01 ; H, 5.07 ; N, 4.41%.

2h : IR (nujol) 1075 (ClO_4), 1540 (C=N), 3510 cm^{-1} (OH) ; ^1H NMR (D_2O) δ = 1.53 (3H, s, CH_3), 3.21, 3.37 (4H, two d, $J_{4,4'}=J_{6,6'}$= 14 Hz, 4-, 4'-, 6- and 6'-H), 3.40~3.72 (4H, m, $N(\underline{CH_2}CH_2)_2O$), 3.80~3.98, 4.04~4.16 (4H, two m, $N(CH_2\underline{CH_2})_2O$) ; Found : C, 32.35 ; H, 5.12 ; N, 4.20%. Calcd for $C_9H_{16}NClO_6S_2$: C, 32.38 ; H, 4.83 ; N, 4.20%.

Synthesis of **8a**. By uses of aqueous $NaHCO_3$: To the aqueous $NaHCO_3$ solution (13%, 25 ml, 0.04 mol) was added the solution of **2a** (7.5 g, 0.027 mol) in water (10 ml) at room temperature and the mixture was stirred until CO_2 was no more generated. The oily product obtained was extracted with ether, dried with $MgSO_4$ and concentrated *in vacuo* to give slight yellow oil **8a** ; 4.4 g (92%) ; bp 84-85 °C/2 mmHg. IR (neat) : 1665 cm^{-1} (C=O). ^1H NMR ($CDCl_3$) δ = 2.29, 2.50 (2H, two d, $J_{3,2}=J_{3',2}$= 5 Hz, 3- and 3'-H), 2.94, 3.34 (2H, two dd, $J_{1,1'}$= 12 Hz, $J_{1,2}$= 7 Hz, $J_{1',2}$= 4 Hz, 1- and 1'-H), 3.00 (6H, s, $N(CH_3)_2$), 3.00~3.24 (1H, m, 2-H). Found : C, 40.77 ; H, 6.47 ; N, 8.05%. Calcd for $C_6H_{11}NOS_2$: C, 40.64 ; H, 6.25 ; N, 7.90%.

By use of sodium alkoxide : To the solution of **2a** (9.7 g, 0.035 mol) in dry methanol (30 ml) was added the solution of sodium methoxide (2 g, 0.035 mol) in dry methanol (20 ml) at room temperature and the mixture was stirred for 15 min. The methanol was removed *in vacuo* to give an oily residue. The residue was carried out as described above to afford **8a** ; 5.2 g (84%) ; bp 84-86 °C/2 mmHg.

By use of sodium thioalkoxide : The solution of sodium thiophenolate (5.3 g, 0.04 mol) in acetonitrile (20 ml) was added to the solution of **2a** (9.7 g, 0.035 mol) in acetonitrile (15 ml) at room temperature. The reaction mixture was worked up as described above to give **8a** ; 5.0 g (80%) ; bp 84-85 °C/2 mmHg.

8b : IR (neat) 1650 cm^{-1} (C=O) ; ^1H NMR ($CDCl_3$) δ = 1.17 (6H, t, J= 6 Hz, $N(CH_2\underline{CH_3})_2$), 2.30, 2.51 (2H, two d, $J_{3,2}=J_{3',2}$= 5 Hz, 3- and 3'-H), 2.92, — (2H, two dd, $J_{1,1'}$= 12 Hz, $J_{1,2}$ = 7 Hz, $J_{1',2}$=—Hz, 1-and 1'-H), 3.00~3.24 (1H, m, 2-H),3.36 (4H, q, $N(\underline{CH_2}CH_3)_2$) ; Found : C, 46.62 ; H, 7.42 ; N, 6.86%. Calcd for $C_8H_{15}NOS_2$: C, 46.79 ; H, 7.36 ; N, 6.82%.

8c : IR (neat) 1650 cm^{-1} (C=O) ; ^1H NMR ($CDCl_3$) δ = 1.88 (4H, br. s, $N(CH_2\underline{CH_2})_2$), 2.25, 2.42 (2H, two d, $J_{3,2}=J_{3',2}$= 5 Hz, 3- and 3'-H), 2.74, — (2H, two dd, $J_{1,1'}$= 12 Hz, $J_{1,2}$= 7 Hz, $J_{1',2}$=-Hz, 1- and 1'-H), 2.9～ — (1H, m, 2-H), 3.10～3.56 (4H, m, $N(\underline{CH_2}CH_2)_2$) ; Found : C, 47.59 ; H, 6.57 ; N, 7.07%. Calcd for $C_8H_{13}NOS_2$: C, 47.26 ; H, 6.45 ; N, 6.89%.

8d : IR (nujol) 1640 cm^{-1} (C=O) ; ^1H NMR ($CDCl_3$) δ = 2.25, 2.52 (2H, two d, $J_{3,3'}$= 5 Hz, 3- and 3'-H), 2.98, 3.34 (2H, two dd, $J_{1,1'}$= 12 Hz, $J_{1',2}$= 7 Hz, $J_{1,2}$= 4 Hz, 1- and 1'-H), 3.0-3.24 (1H, m, 2-H), 3.4～3.7 (8H, m, $N(CH_2CH_2)_2O$) ; Found : C, 44.28 ; H, 5.97 ; N, 6.38%. Calcd for $C_8H_{13}NO_2S_2$: C, 43.81 ; H, 5.97 ; N, 6.39%.

8e : IR (neat) 1655 cm^{-1} (C=O) ; ^1H NMR ($CDCl_3$) = 1.63 (3H, s, CH_3), 2.37, 2.56 (2H, two s, 3- and 3'-H), 2.99 (6H, s, $N(CH_3)_2$), 3.25, 3.38 (2H, two d, $J_{1,1'}$= 13 Hz, 1- and 1'-H). Found : C, 44.06 ; H, 6.73 ; N, 7.33%. Calcd for $C_7H_{13}NOS_2$: C, 43.94 ; H, 6.85 ; N, 7.32%.

8f : IR (neat) 1650 cm^{-1} (C=O) ; ^1H NMR ($CDCl_3$) δ = 1.14 (6H, t, J=6 Hz, $N(CH_2\underline{CH_3})_2$), 1.57 (3H, s, CH_3), 2.27, 2.48 (2H, two s, 3- and 3'-H), 3.11, 3.29 (2H, two d, $J_{1,1'}$= 14 Hz, 1- and 1'-H), 3.28 (4H, q, $N(\underline{CH_2}CH_3)_2$) ; Found : C, 49.43 ; H, 8.11 ; N, 6.48%. Cacld for $C_9H_{17}NOS_2$: C, 49.28 ; H, 7.81, N, 6.42%.

8g : IR (neat) 1655 cm^{-1} (C=O) ; ^1H NMR ($CDCl_3$) δ = 1.58 (3H, s, CH_3), 1.7～2.1 (4H, br. m, $N(CH_2\underline{CH_2})_2$), 2.26, 2.51 (2H, two s, 3- and 3'-H), 3.10, 3.26 (2H, two d, $J_{1,1'}$= 13 Hz, 1- and 1'-H), 3.1～3.5 (4H, br. m, $N(\underline{CH_2}CH_2)_2$) ; Found : C, 49.95 ; H, 7.16 ; N, 6.63%. Calcd for $C_9H_{15}NO_2S_2$: C, 49.73 ; H, 6.96 ; N, 6.44%.

8h : IR (nujol) 1645 cm^{-1} (C=O) ; ^1H NMR ($CDCl_3$) δ = 1.64 (3H, s, CH_3), 2.40, 2.58 (2H, two s, 3- and 3'-H), 3.39 (2H, s, 1- and 1^1-H), 3.44～3.80 (8H, m, $N(CH_2CH_2)_2O$) ; Found : C, 46.54 ; H, 6.72 ; N, 5.93%. Calcd for $C_9H_{15}NO_2S_2$) : C, 46.32 ; H, 6.47 ; N, 6.00%.

Acknowledgment

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References and Notes

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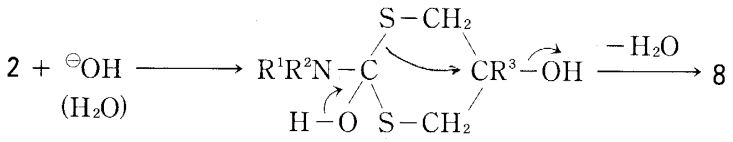
3) a) W. C. Doyle, Jr., U. S. Patent 3510290 (1970) ; Chem. Abstr., **73**, 35210c (1970). b) W. C. Doyle, Jr., U. S. Patent 3561949 (1971) ; Chem. Abstr., **74**, 87809v (1971). c) W. C. Doyle, Jr. U. S. Patent 3728371 (1973) ; Chem. Abstr., **79**, 5246a (1973).

4) In the case of using aqueous $NaHCO_3$ or aqueous NaOH, nucleophilic attack of OH^- (or H_2O) to the cationic center of **2** could explain the formation of **8** as shown in the following scheme. This mechanism, however, cannot be applied to account for the formation of **8** from **2** and sodium alkoxide or sodium thioalkoxide in nonaqueous solvent.



5) For instance, see, D. J. Cram and G. S. Hammond, "Organic Chemistry", McGrow-Hill, New York (1964), P. 484-488