Thermal Decomposition of *S*-2-Benzothiazole Thiocarbonates

C. H. Chen

Research Laboratories, Eastman Kodak Company, Rochester, New York 14650

Received May 6, 1976

Thermal decompositions of *S*-2-benzothiazole thiocarbonates have been investigated. The results are best rationalized by an Sni ion-pair return mechanism from which *S*-substituted benzothiazoles are the major products obtained. The ready ionization of the carbon-oxygen bond of thiocarbonates at elevated temperature renders a concerted Sni′ mechanism (internal substitution with allylic rearrangement) inoperative. Of particular interest is the mixed benzothiazole-2-thiol and 2-thione compound isolated from the decomposition of 2 (or 3)-halogen-substituted ethyl (or propyl) thiocarbonates. Evidence is presented that the thione **14** results from the nucleophilic opening of the cyclic intermediate, 2,3-dihydrothiazolo[2,3-*b*]benzothiazolium chloride (**20**). The latter is readily formed under the experimental condition by intramolecular cyclization of the corresponding 2-(2-chloroethyl)benzothiazole (**23**), a primary product from the decomposition of *S*-2-benzothiazole 2-chloroethylthiocarbonate (**7**).

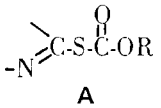
J. Heterocyclic Chem., **13**, 1079 (1976).

Introduction.

Although thiocarbonates have been reported to decompose upon heating in inert solvents at elevated temperature to give the corresponding sulfides and carbon dioxide

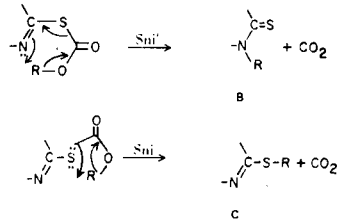
$$R'\text{-}S\text{-}\overset{\overset{O}{\|}}{C}\text{-}OR \xrightarrow{\Delta} R'SR + CO_2$$

(1,2), little is known about the thermal decomposition of thiocarbonates with *S*-substituted heterocycles containing a vinylic imino function such as those represented by structure **A**.



A

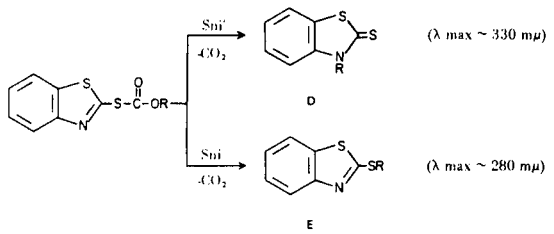
Because of the nucleophilicity of the nitrogen (3) in this system, it is of considerable interest to explore the possibility as to whether an Sni′ mechanism (internal substitution with allylic rearrangement) (4) could occur, thus giving a thermodynamically more stable thione form **B** as opposed to the usual Sni ion-pair return (1) which would be expected to give the kinetically favored isomeric form **C** (5).



The former pathway (Sni′) is of potential synthetic value in that a new *N*-substituted thione synthesis can be envisaged. Furthermore, it suggests a novel way of blocking the thione moiety. The active *N*-substituted thione heterocycles may be regenerated later at will by heat.

This paper summarizes our findings in this area. For most compounds studied, only products of structure type **C** were obtained. In a few cases where thione products were produced, they were found to result from further reactions of the primary products due to operation of an Sni ion-pair return pathway. This mechanism is consistent with that proposed by Kice and his co-workers (6,7). Where essential, independent syntheses of the products isolated from the thermal decomposition of thiocarbonates were devised for the purpose of identification and of providing further support for the proposed mechanism.

We have chosen for model studies the thermolysis of various *S*-2-benzothiazole thiocarbonates for the following reasons: benzothiazole-2-thione **D** is known to be thermodynamically more stable than its isomeric sulfide form **E** (8). Thus, an energetically more favorable Sni′ pathway may be attainable; and the unique uv absorption exhibited by the two different chromophores shown allows one to readily assign the structure of the products resulting from thermal decomposition.



Synthesis and Thermal Decomposition.

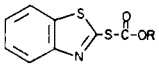
S-2-Benzothiazole thiocarbonates were synthesized from benzothiazole-2-thiol and the corresponding chloroformates in the usual manner and are listed in Table I (9). All the new compounds give satisfactory combustion analyses and their spectroscopic data (nmr, ir and uv) are in complete agreement with the assigned structure.

The thermal decomposition of *S*-2-benzothiazole thiocarbonates was performed in the presence of a small amount of powdered soft glass, without solvent. It is known that powdered soft glass, presumably due to its surface activity, in general catalyzes decarboxylation and decarbonylation reactions (11). For example, it was found that the decarboxylation of 2-(phenoxycarbonylthio)benzothiazole **2** at 180-190°, in the presence of powdered soft glass gave the corresponding sulfide **11** (Table II). The decomposition is complete within 30 minutes. Under similar conditions but without the presence of powdered glass, a considerable amount of starting thiocarbonate **2** was detected by tlc.

Table II lists the major products obtained from the thermal decomposition of the *S*-2-benzothiazole thiocar-

Table I

S-2-Benzothiazole Thiocarbonates



No.	Thiocarbonate	% Yield	M.p. (a)	Chloroform λ max
1	R = Benzyl	30 (b)	84.5-85.5°	280 mμ
2	Phenyl	89	90.2°	275
3	*iso*-Butyl	92	30-31.5°	275
4	Cholesteryl	91	155-156°	275
5	5α-Cholestan-3β-yl	90	169-170°	275
6	2,2,2-Trichloro ethyl	75 (c)	69-71°	275 335 (shoulder)
7	$-CH_2CH_2Cl$	90	101.5-102.5°	275
8	$-CH_2CH_2Br$	88	98-100°	275
9	$-CH_2CH_2CH_2Cl$	89	71.2°	275

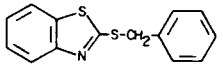
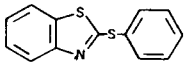
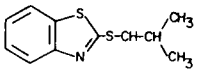
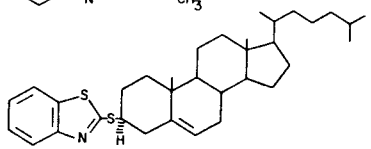
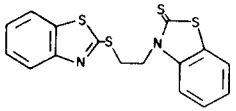
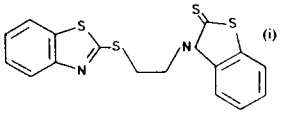
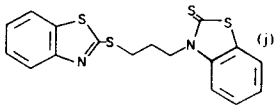
(a) M.p. was uncorrected. (b) *Ca.* 65% of decarboxylated product, 2-(benzylthio)benzothiazole (**10**) was also isolated from the reaction. (c) Nmr and tlc shown to contain *ca.* 15% impurity (δ 5.1 ppm, singlet) tentatively identified as the *N*-substituted isomer of **6**.

Table III

Compound Number	Formula	Analysis (%) Calcd. C	H	N	S	X	Found C	H	N	S	X
1	$C_{15}H_{11}NO_2S_2$	59.8	3.7	4.6	21.3		59.9	3.6	4.8	21.6	
2	$C_{14}H_9NO_2S_2$	58.5	3.2	4.9	22.3		58.6	3.3	5.1	22.7	
3	$C_{12}H_{13}NO_2S_2$	53.9	4.9	5.2	24.0		53.8	4.8	5.5	23.7	
4	$C_{35}H_{49}NO_2S_2$	72.5	8.5	2.4	11.1		72.9	8.4	2.6	11.3	
5	$C_{35}H_{51}NO_2S_2$	72.2	8.8	2.4	11.0		72.3	9.1	2.2	16.3	
6	$C_{10}H_6Cl_3NO_2S_2$	35.1	1.8	4.1	18.7	31.0	34.9	1.8	4.3	18.9	30.9
7	$C_{10}H_8ClNO_2S_2$	43.9	3.0	5.1	23.4	13.0	43.9	2.9	5.4	23.4	13.1
8	$C_{10}H_8BrNO_2S_2$	37.8	2.5	4.4	20.2	25.2	37.7	2.4	4.4	20.4	25.1
9	$C_{11}H_{10}ClNO_2S_2$	45.9	3.5	4.9	22.3	12.3	45.6	3.5	4.8	22.3	12.3
13	$C_{34}H_{49}NS_2$	76.2	9.3	2.6			76.2	9.5	2.3		
14 (15)	$C_{16}H_{12}N_2S_4$	53.3	3.4	7.7			53.0	3.4	7.4		
16	$C_{17}H_{14}N_2S_4$	54.5	3.8	7.5			54.9	3.9	7.2		

Table II

Thermal Decomposition of *S*-2-Benzothiazole Thiocarbonates

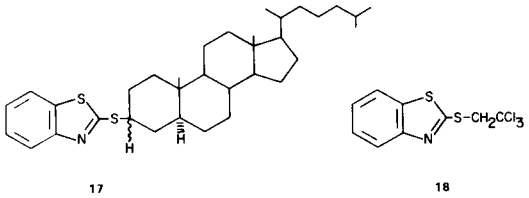
No.	Thiocarbonates	Initial t°C of Decarboxylation	Experimental Conditions	Major Product	M.p.	Chloroform λ max	Yield % (a)
10	**1** (R = Benzyl)	105°	120-150°/ 30 minutes	 (b)	---	280 mμ	95
11	**2** (-Phenyl)	160°	180-190°/ 30 minutes	 (c)	---	275 310 (weak)	95
12	**3** (-*iso*-Butyl)	160°	210-230°/ 1 hour (d)	 (e)	---	280	---
13	**4** (-Cholesteryl)	180°	185-190°/ 30 minutes		131-132°	285	52 (f)
14	**7** (-CH_2CH_2Cl)	174°	177-180°/ 1.5 hours	 (g)	146.5-147.5°	330 (strong) 270-300 (medium)	64 (h)
15	**8** (-CH_2CH_2Br)	145°	155-157°/ 30 minutes	 (i)	146.5-147.5°	330 (strong) 270-300 (medium)	66 (h)
16	**9** (-$CH_2CH_2CH_2Cl$)	150°	157-160°/ 30 minutes	 (j)	96-97°	330 (strong) 270-300 (medium)	53 (h)

(a) In the case of known compounds, the yields were estimated by nmr and tlc. (b) Literature, (10) m.p. 39.5-40.5°. (c) Literature, (12) b.p. 186-187°/3 mm. (d) Decomposition is not complete at 200-220°/30 minutes. (e) See Reference (13). (f) Among other products identified were cholesta-3,5-diene and bis-(cholesteryl)ether. (g) The major by-product was identified as 1,2-dichloroethane and a small amount of bis-(2-benzothiazole)sulfide. (h) Based on half equivalent of the starting thiocarbonate. (i) Products were identical with those obtained from decomposition of **7**, except 1,2-dibromoethane was the major by-product. (j) 1,3-Dichloropropane was the major by-product isolated. A small amount of 3,4-dihydro-2*H*-thiazino[2,3-*b*]benzothiazolium chloride, m.p. 215-216° (Literature, (14) m.p. 226°) was also detected.

bonates.

The decomposition of **5** and **6** resulted in a mixture of products from which only low yields of the corresponding *S*-substituted products, presumed to be **17** and **18**, were detected. Consequently, they were not studied further in this work.

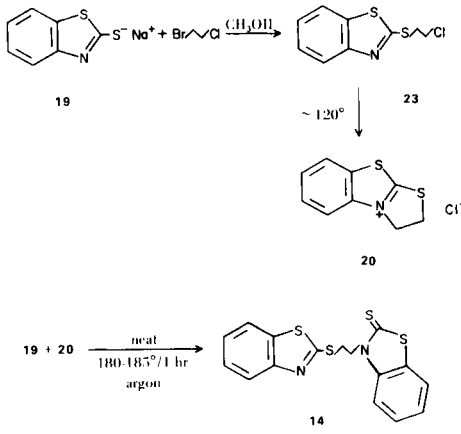
The structure of **13** was confirmed by comparison with



17 18

an authentic sample prepared in 82 percent yield by an independent synthesis from cholesteryl mercaptan, 2-chlorobenzothiazole and sodium hydride in dry THF. The stereochemistry of 3α (axial) proton in **13** was ascertained by the nmr, exhibiting a broad multiplet (1H) centered at δ 3.6 ppm (15).

Compounds **14**, (**15**) and **16** are unique in that two distinctive isomeric forms, namely, benzothiazole-2-thione and benzothiazole-2-thiol are present in one entity. The following scheme was devised as an independent synthesis of **14** *via* the intermediate 2,3-dihydrothiazolo[2,3-*b*]benzothiazolium chloride (**20**), m.p. 233.5-234.5° dec. The latter compound is prepared from 2-(chloroethylthio)benzothiazole (**23**) following a known procedure (14). The pyrolysis of dry sodium benzothiazole-2-mercaptide (**19**) (prepared from benzothiazole-2-thiol and sodium hydride in dry THF) with an equal molar amount of **20** under argon afforded 3-(2-(2-benzothiazolethio)ethyl]benzothiazole-2-thione (**14**) in about 90 percent yield.

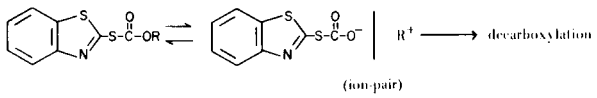


19 23 20 19 + 20 14

The uv spectrum of **14** is interesting in that it displays the characteristic chromophores for both benzothiazole-2-thiol (λ max (chloroform) ~ 280 mμ) and benzothiazole-2-thione (λ max (chloroform) ~ 330 mμ). Some overlapping of the absorption band is also observed.

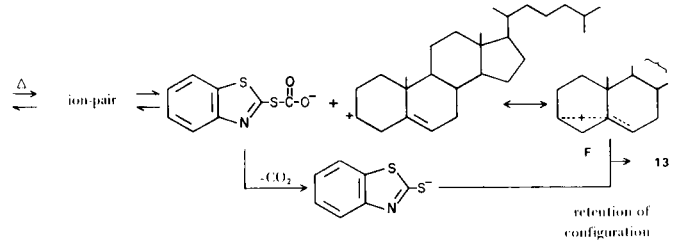
Results and Discussion.

The results of thermal decomposition of *S*-2-benzothiazole thiocarbonates are in agreement with the Sni ion-pair return mechanism proposed by Kice and his co-workers



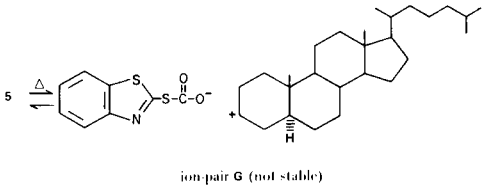
(7). The solvent dependence of the rate of decomposition suggests that the thermolysis is ionic in nature. For instance, in a separate experiment, the decomposition of 2-(2-chloroethylcarbonylthio)benzothiazole (**7**) in sulfolane in the presence of powdered soft glass was complete (giving **14**) at 170-175° within 30 minutes, while under identical conditions in 1,2,4-trichlorobenzene, a less polar solvent, the decarboxylation was less than half complete.

Table II suggests that the initial decarboxylation t°C is related to the stability of the resulting carbonium ion. The comparison of thiocarbonates **4** (R = cholesteryl) and **5** (R = 5α-cholestan-3β-yl) is of particular significance in that the former decomposes at a lower temperature (180°) and a much faster rate (t ½ = ~ 10 minutes) than that of the latter (190°; t ½ = ~ 1 hour). The stereochemistry of the product **13** from **4** suggests that a retention of configuration has resulted from the stabilization of the positive charge in the transition state due to the neighboring group participation of Δ^5-double bond (16).



4

However, such a stabilization of the bridged carbonium ion F is not attainable in the case of **5** (carbonium ion **G**),

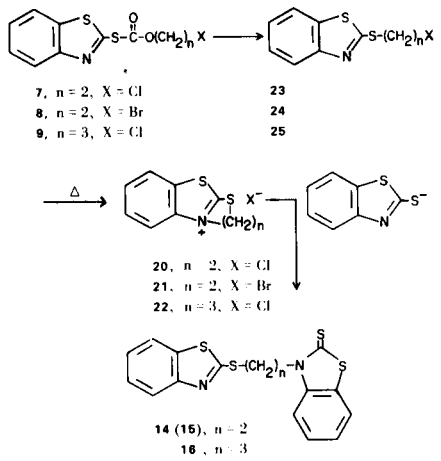


5

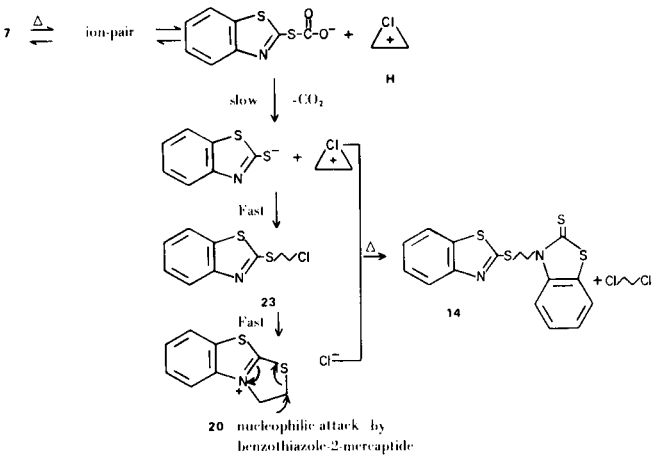
thus incurring a much higher transition state energy in the ionization step during the decomposition. This rationale would also explain the failure in obtaining a good yield of **18** from the thermal decomposition of **6** in Table I (R = $-CH_2CCl_3$).

The thiones **14**, (**15**) and **16** were shown to be secondary products resulting from nucleophilic attack of benzothi-

azole-2-mercaptide on the internal salts **20**, **21** and **22** which are readily formed from the corresponding sulfides **23**, **24** and **25** (14) under the thermolysis conditions.



To illustrate with thiocarbonate **7**, an Sni ion-pair mechanism would be expected to give the primary product **23** *via* an intermediate chloronium ion H. The sulfide **23** immediately forms an internal salt **20** under the decomposition condition. Since benzothiazole-2-mercaptide *per se* is a much better nucleophile than chloride, it quickly opens up the ring at the carbon adjacent to sulfur in **20** at elevated temperature in an irreversible process to produce the corresponding thione **14**, leaving the counter ion Cl^- which attacks the positive chloronium ion H to give 1,2-dichloroethane as the major by-product. The ionic character of the intermediate chloronium ion H and benzo-



thiazole-2-mercaptide was demonstrated by the isolation of the crossed-over product 1,2-bromochloroethane from thermal decomposition of an equal molar mixture of **7** and **8**.

EXPERIMENTAL

Melting points were taken with a Thomas-Hoover capillary melting apparatus. Microanalyses were performed by the Analytical Services Division, Research Laboratories, Eastman Kodak Company. Nuclear magnetic resonance spectra were recorded on a Varian T-60 nmr spectrophotometer and uv spectra were recorded on a Perkin-Elmer 202 spectrophotometer. Mass spectra were obtained on an AEI MS-30 mass spectrometer.

S-2-Benzothiazole thiocarbonates were synthesized from benzothiazole-2-thiol and the corresponding chloroformates following a known procedure (9). Thermal decomposition of *S*-2-benzothiazole thiocarbonates was performed in the presence of a small amount of powdered soft glass without solvent and the reaction was monitored by collecting the amount of carbon dioxide evolved. Table III lists the analytical data of all the new compounds prepared in this work.

The following experiments are illustrative.

S-2-Benzothiazole-2-chloroethylthiocarbonate (**7**).

A solution of 1.85 g. of 2-chloroethyl chloroformate in 10 ml. of methylene chloride was added dropwise to a solution of 2 g. of 2-mercaptobenzothiazole and 1.4 g. of triethyl amine in 20 ml. of methylene chloride at ambient temperature. The reaction mixture was allowed to stir overnight and worked up by pouring into ice and water, followed by extraction with methylene chloride. The organic layer was separated, dried (magnesium sulfate), and concentrated to give a solid which was recrystallized from ligroin to give 2.95 g. (90%) of pure **7**, m.p. 101.5-102.5°; uv λ max (chloroform): 275 mμ.

Thermal Decomposition of *S*-2-Benzothiazole Cholesterylthiocarbonate (**4**).

Thiocarbonate **4** (4 g.) and *ca.* 0.5 g. of powdered soft glass were heated (oil bath 180-190°) in a 15 ml. RB flask fitted with a Bantamware micro-still which was connected to a gas collector. The decomposition was essentially complete in about 30 minutes as it was followed by the subsiding of carbon dioxide evolution from the reaction mixture (total volume of carbon dioxide collected, 145 ml.). The crude product was fractionally crystallized from ethanol to give about 1.9 g. (52%) of pure 2-(3β-cholesterylthio)benzothiazole **13** as major product, m.p. 131-132°; uv λ max (chloroform): 285 mμ. The structure and stereochemistry of **13** were ascertained by comparison of its physical data with that of an authentic sample prepared by an independent synthesis. Other minor products identified from thermal decomposition of **4** were cholestadiene (m/e 368 M^+), cholesterol (m/e 386 M^+) and a solid (0.25 g., m.p. 173-174°) tentatively assigned as bischolesteryl ether.

Independent Synthesis of 2-(3β-Cholesterylthio)benzothiazole (**13**).

Cholest-5-ene-3β-thiol (2 g.) in 30 ml. of dry THF was added to a suspension of 350 mg. of sodium hydride in 10 ml. of dry THF at room temperature under argon. To the reaction mixture, after being stirred at ambient temperature for 30 minutes, was added dropwise a solution of 0.87 g. of 2-chlorobenzothiazole in 15 ml. of dry THF. After being refluxed overnight the THF was distilled and the mixture was washed with brine and extracted with ether twice. The combined ethereal extracts were dried (magnesium sulfate) and concentrated to give a brown solid, which was recrystallized (EtOH-ether) to afford 1.7 g. of pure **13**, m.p. 117.5-119°. A second crop (0.5 g.) of **13** could also be obtained from the mother liquor by concentration. This material was identical to that of the product obtained from the thermal decomposition of **4**.

Thermal Decomposition of *S*-2-Benzothiazole 2-Chloroethylthiocarbonate (**7**).

Thiocarbonate **7** (5 g.) and *ca.* 0.5 g. of powdered soft glass were heated (175-180°) for 1.5 hours in the same manner as described previously. Approximately 1.1 g. (62%) of a low boiling by-product, confirmed to be 1,2-dichloroethane (m/e 98 M^+; nmr: singlet at δ 3.8 ppm) was distilled and about 300 ml. of carbon dioxide evolved. The residue from the decomposed mixture was recrystallized from ethanol to give 2.1 g. (65%) of crystalline 3-[2-(2-benzothiazolethio)ethyl]benzothiazole-2-thione (**14**), m.p. 146.5-147.5°; m/e 360 (M^+); nmr (deuteriochloroform-TMS): 3.7 (*q*, 2, -SCH_2-), 4.8 (*q*, 2, -NCH_2-), and 7.1-8.0 (*m*, 8, Ar*H*) ppm. A small amount (0.25 g.) of bis-(2-benzothiazole) sulfide (m.p. 93-93.5°; m/e 300 M^+ for $C_{14}H_8N_2S_3$) was also isolated.

2-(2-Chloroethylthio)benzothiazole (**23**).

To a solution of 10 g. of benzothiazole-2-thiol in 50 ml. of methanol was added 1.5 g. of sodium, followed by 11 g. of 1-bromo-2-chloroethane. The mixture was refluxed overnight and worked up by stripping methanol, washed with water, and extracted (dichloromethane). The methylene chloride solution was separated, dried (magnesium sulfate), and concentrated to give a brown oil of crude **23** whose structure was confirmed by nmr (deuteriochloroform-TMS): δ 3.77 (A_2B_2 quartet, 4, -SCH_2CH_2Cl), 7.23 (*m*, 2, Ar*H*) and 7.7 (*m*, 2, Ar*H*) ppm. This material was used subsequently without further purification.

2,3-Dihydrothiazolo[2,3-*b*]benzothiazolium Chloride (**20**).

Crude 2-(2-chloroethylthio)benzothiazole (**23**) (1 g.) was heated slowly at about 120° for 2 hours. The reaction mixture which solidified on cooling, was washed with dichloromethane and filtered to give 0.5 g. of **20**, m.p. 238-239° dec. [Lit. (14) m.p. 226-228° dec.].

3-[2-(2-Benzothiazolethio)ethyl]benzothiazole-2-thione (**14**).

To a suspension of sodium hydride (130 mg.) in 10 ml. of dry THF was added 0.5 g. of 2-benzothiazolethiol under argon. The THF was removed by slow distillation, and the solid sodium mercaptide **19** thus formed was dried at room temperature by flushing under a steady stream of argon. Benzothiazolium chloride **20** (0.685 g.) and 0.2 g. of powdered soft glass were mixed with **19** and the mixture was heated to 180-185° for 1 hour under argon. On cooling, the reaction mixture was taken up in chloroform and filtered. The filtrate was concentrated *in vacuo* to give 1 g. (95%) of essentially pure **14**, m.p. 138-140°, which was found to be identical to the major product obtained from the thermal decomposition of *S*-2-benzothiazole 2-chloroethylthiocarbonate (**7**).

REFERENCES AND NOTES

(1) J. L. Kice, R. A. Bartsch, M. A. Dankleff and S. L. Schwartz, *J. Am. Chem. Soc.*, 87, 1734 (1965).

(2) J. L. Kice and M. A. Dankleff, *Tetrahedron Letters*, 1783 (1966).

(3) R. A. Bafford, F. Chanan, M. Chanon and J. Metzger, *Bull. Soc. Chim. France*, 3, 971 (1973); *Chem. Abstr.*, 79, 31975g (1973).

(4) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Hold and Co., N. Y., 1959, pp. 294-296.

(5) W. J. Humphlett, *J. Heterocyclic Chem.*, 5, 397 (1969).

(6) J. L. Kice and G. C. Hanson, *Tetrahedron Letters*, 2927 (1970).

(7) J. L. Kice, R. L. Scriven, E. Koubek and M. Barnes, *J. Am. Chem. Soc.*, 92, 5608 (1970).

(8) A. J. Halasa and G. E. P. Smith, Jr., *J. Org. Chem.*, 36, 636 (1971).

(9) A. Kapoor, *J. Pharm. Sci.*, 59, 1 (1970).

(10) L. W. Wattenberg, M. A. Page, J. L. Leong, *Cancer Res.*, 28, 2539 (1968).

(11) M. S. Newman and M. C. VanderZwan, *J. Org. Chem.*, 38, 319 (1973).

(12) P. E. Todesco and P. Vivarelli, *Gazz. Chem. Ital.*, 94, 435 (1964).

(13) W. H. Davies and W. A. Sexton, *Biochem. J.*, 43, 461 (1948).

(14) S. V. Zhuravlev, E. A. Kuznetsova and V. M. Svetlaeva, *Khim. Seraorg. Soedin. Soderzh. Neftyakh, Nefteprod.*, 8, 66 (1968); *Chem. Abstr.*, 71, 81252z (1969).

(15) K. Toir and T. Lomeno, *Tetrahedron*, 309 (1965).

(16) S. Winstein and R. Adams, *J. Am. Chem. Soc.*, 70, 838 (1948).