maintaining the temperature below 30°, to a volume of 20 ml. and filtered again to remove additional methylenebis(dimedone); the filtrate was again concentrated at 1 mm. to remove the remaining water. The residue (1.10 g.), a tacky solid, on trituration with an acetone–ethanol mixture gave a crystalline solid (0.30 g., m.p. 158–165°); recrystallization from acetonitrile gave colorless needles, m.p. 170–171°; infrared (Nujol mull): 3.15, 3.27, 3.45, 5.95, 6.50, 6.95, 7.15, 7.27, 7.57, 8.60, 8.80, 9.07, 9.55, 9.72, 10.07, 11.50, 12.35 μ.

Anal. Calcd. for $C_5H_6N_2O_2$: C, 35.3; H, 5.95; N, 27.40; CH_2O (total), 58.64; mol. wt., 102. Found: C, 35.06; H, 6.07; N, 27.11; CH_2O (total), 58.64; mol. wt., 104.6 ± 10.

Tetrahydro-3,5-bis(methoxymethyl)-4*H*-1,3,5-oxadiazin-4-one (II). A. Method of Kadowaki.[2]—This procedure gave a liquid which on distillation *in vacuo* through a 6-in. Vigreux column gave 101.7 g. of product. (54%), b.p. 127–137° at 4 mm., $n^{25}D$ 1.4675; infrared (film): 2.95, 3.42, 3.55, 6.02, 6.70, 6.87, 7.20, 7.50, 7.75, 8.57, 9.35, 9.80, 10.35, 10.75, 11.05, 11.87, 12.42, 12.95, 13.32, 14.27 μ.

Anal. Calcd. for $C_7H_{14}N_2O_4$: C, 44.20; H, 7.42; N, 14.74; CH_3O, 32.60; CH_2O (total), 63.05. Found: C, 44.05; H, 7.49; N, 14.61, CH_3O, 37.16; CH_2O (total), 57.8; CH_2O (free), none.

B. Isolation by Vapor Phase Chromatography.—Samples (50 μl.) of the reaction mixture prepared by the Kadowaki procedure were injected into an F&M Model 500 gas chromatograph containing a 12-ft. column packed with 20% silicon gum rubber on Chromosorb W, a flux calcined diatomaceous earth, while using a helium flow rate of 50 ml. per minute. The temperature conditions were maintained as follows: injection part, 270°, block, 300°, and column, 200°. Using these conditions it was found that pure II ($n^{25}D$ 1.4705) had a retention time of 15.4 min. (peak height); samples of II were collected in a tube cooled to −60°; infrared (film): 3.37, 3.50, 5.97, 6.66, 6.82, 7.20, 7.50, 7.75, 8.57, 9.32, 9.80, 10.32, 10.75, 11.05, 12.45, 13.35, 14.25 μ.

Anal. Calcd. for $C_7H_{14}N_2O_4$: C, 44.20; H, 7.42; N, 14.74; CH_3O, 32.60; CH_2O (total), 63.05. Found: C, 44.04; H, 7.39; N, 14.76; CH_3O, 32.49; CH_2O (total), 63.66.

Tetrahydro-3,5-dimethyl-4*H*-1,3,5-oxadiazin-4-one (III).—An amount of 95.1 g. (0.50 mole) of II was dissolved in sufficient methanol to make 400 ml. of solution. The solution was charged to a 1-l. stainless steel autoclave together with 15 g. of Raney nickel and shaken at 150–165° for 10 min. and at 200° for 8 hr.; the autoclave was then cooled to room temperature and vented.

The methanolic solution on concentration *in vacuo* gave 59.8 g. of crude product which on analysis by vapor phase chromatography showed three components; the last component was identified as starting material.

Distillation of the crude product under reduced pressure gave five fractions boiling over a range of 74–90° at less than 1 mm.; vapor phase analysis of each fraction showed that no clear-cut separation was obtained. However, the second fraction (6.4 g., b.p. 74–77° at less than 1 mm.) had the greatest concentration of the first component. When this fraction was cooled at −60° to induce crystallization and twice recrystallized from ether at −60°, the resulting solid (m.p. 36.4°, $n^{26}D$ 1.4808) was found to be chromatographically pure and identified as III; infrared (film): 3.40, 3.47, 6.05, 6.60, 6.82, 7.00, 7.15, 7.57, 7.95, 8.17, 9.05, 9.25, 9.65, 10.35, 12.40, 13.32 μ.

Anal. Calcd. for $C_5H_{10}N_2O_2$: C, 46.10; H, 7.74; N, 21.55; CH_2O (total), 46.1. Found: C, 45.90; H, 7.75; N, 21.45; CH_2O (total), 46.8.

The second component was not isolated; it is believed to be tetrahydro-1,3,5-trimethyl-4*H*-1,3,5-triazin-4-one because the addition of pure tetrahydro-1,3,5-trimethyl-4*H*-1,3,5-triazin-4-one to the crude product greatly increased the peak height of the second component.

Tetrahydro-1,3,5-trimethyl-4*H*-1,3,5-triazin-4-one.—An amount of 17.6 g. (0.20 mole) of 1,3-dimethylurea was dissolved in 33.2 g. (0.41 mole) of 37% formaldehyde and 31.0 g. (0.40 mole) of 40% aqueous methylamine was added dropwise while maintaining the temperature below 35°. The reaction mixture was refluxed for 18 hr. and concentrated at 15 mm. to remove the water. The residue (29.0 g.) was distilled at 0.30 mm. through a micro Vigreux column and the fraction (7.35 g.) boiling at 65–67° was collected and identified as tetrahydro-1,3,5-trimethyl-4*H*-1,3,5-triazin-4-one.

Anal. Calcd. for $C_6H_{13}N_3O$: C, 50.39; H, 9.09; N, 29.35. Found: C, 50.33; H, 9.09; N, 29.35.

1,3-Dimethyl-1-methoxymethylurea (IV).—The procedure used was that described by Becher and Griffel.[4] Distillation of the crude material through a 5-in. Vigreux column gave 75.3 g. (65%) of a colorless liquid (b.p. 99–100° at 1 mm., $n^{25}D$ 1.4626); infrared (film): 2.98, 3.40, 3.55, 6.10, 6.53, 7.10, 7.30, 7.73, 8.0, 8.15, 8.52, 8.70, 9.20, 9.35, 9.70, 10.32, 10.57, 11.06, 11.85, 12.55, 13.00 μ.

Anal. Calcd. for $C_5H_{12}O_2$: C, 45.4; H, 9.15; N, 21.2; CH_3O, 23.45; CH_2O (total), 22.7. Found: C, 46.1; H, 9.33; N, 21.64; CH_3O, 24.19; CH_2O (total), 23.2.

Acknowledgment.—The authors wish to thank Dr. Jessie Gove for the infrared data, and Dr. James Parsons for assistance with the vapor phase chromatography. They also wish to thank the late Mr. Oliver Sundberg and Mr. John Kobliska, and their associates, for the microanalyses.

Polyfunctional Aliphatic Compounds. IV. The Cyclization of Nitriles by Halogen Acids. A New Synthesis of Thiazoles

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α-Cyanoalkyl thiocyanates, prepared from α-chloroalkyl and α-(4-toluenesulfonyloxy)alkyl cyanides, are shown to undergo cyclization to derivatives of 2-bromo-4-aminothiazole by means of hydrogen bromide. Hydrogen chloride is unsatisfactory as a cyclizing agent whereas hydrogen iodide causes further reduction and leads directly to derivatives of the previously inaccessible 4-aminothiazoles. Attempts to apply this synthesis to the preparation of selenazoles were unsuccessful.

In earlier papers,[1,2] we have shown that the cyclization reaction of α,ω-dinitriles can be used effectively for the synthesis of pyridine and isoquinoline compounds. For example, 3-hydroxyglutaronitrile is cyclized to 2-amino-6-bromopyridine hydrobromide by hydrogen bromide and 2-cyanobenzyl cyanide with the same reagent leads exclusively to 3-amino-1-bromoisoquinoline hydrobromide.

All previous work[3] dealing with the action of anhydrous hydrogen halides on dinitriles of the type under discussion has been devoted largely to systems in which the two nitrile groups were joined by a carbon

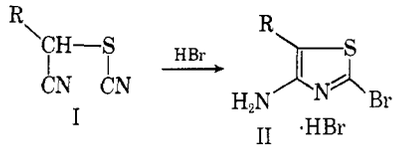
(1) Part II, F. Johnson, J. P. Panella, A. A. Carlson, and D. H. Hunneman, *J. Org. Chem.*, **27**, 2473 (1962).

(2) Part III, F. Johnson and W. A. Nasutavicus, *ibid.*, **27**, 3953 (1962).

(3) This has been summarized in part II (ref. 1).

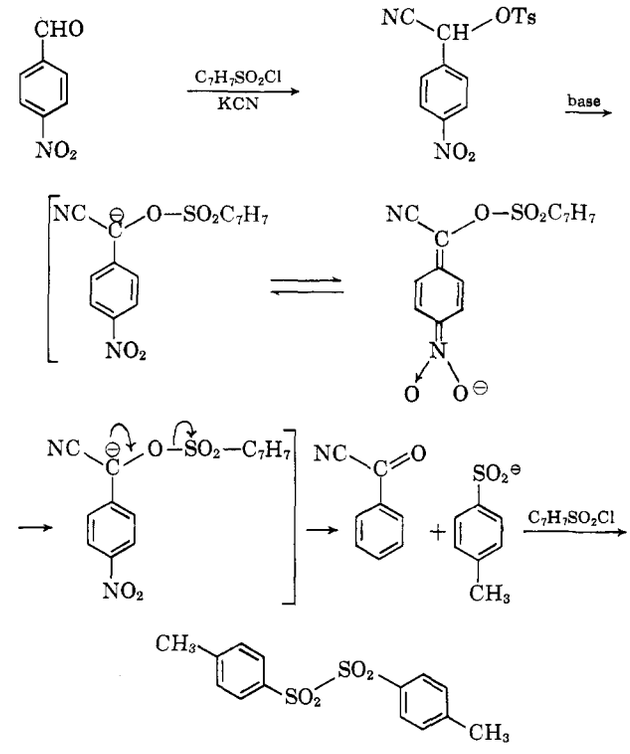
chain.[4] We now report studies where the latter has been modified by the incorporation of a heteroatom, namely sulfur or selenium.

In view of the fact that the electron-accepting and electron-donating effect of divalent sulfur appear to be similar to those of a 1,2-phenylene group, it seemed likely that the cyclization of the appropriate cyano thiocyanates also might proceed in one specific direction. In addition, if the cyclization were to be analogous to that of 2-cyanobenzyl cyanide then α-cyanoalkyl thiocyanates should lead to derivatives of the essentially inaccessible 4-aminothiazoles. We now report that this is the case and that the reaction of these dinitriles (I) with anhydrous hydrogen bromide proceeds exclusively to give 4-amino-2-bromothiazole hydrobromides (II).



Cyanoalkyl Thiocyanates.—Of the required starting materials (I) only those where R = H or C_6H_5 were known in the previous literature. The former compound had been reported[5] to be of use as a solvent for polyacrylonitrile (no preparative details were given), while Brintzinger and Schmahl[6] had described it as a solid, m.p. 96–98°. They claimed its preparation by the action of potassium cyanide on chloromethylsulfenyl chloride in acetic acid. The phenyl homolog (I, R = C_6H_5) had been prepared[7,8] twice previously by the action of ammonium thiocyanate on α-bromobenzyl cyanide in alcohol. This latter method, obviously capable of much wider application, had the disadvantage of requiring α-halonitriles, materials often having disagreeable properties. Nevertheless, Taylor[9] has pointed out that the analogous α-cyanoalkyl arylsulfonates are handled more easily and can be used as effectively as α-haloalkylnitriles in substitution reactions. As they also seemed to have the added benefit of easy preparation[10] from the corresponding aldehydes, these at first appeared to be our starting materials of choice.

However, although we were able to prepare the previously known α-cyanoalkyl 4-toluenesulfonates, the method[10] failed completely to give solid products when applied to 2-methoxy-, 2,4-dimethoxy-, 4-chloro-, 3- and 4-nitro-, or 4-acetaminobenzaldehyde, terephthaldehyde, cinnamaldehyde, or furfural. The use of methanesulfonyl chloride or benzenesulfonyl chloride in place of 4-toluenesulfonyl chloride in the reaction with 4-chlorobenzaldehyde was equally unsuccessful. In most of these cases a noncrystallizable viscous sirup was isolated and only when using 4-nitrobenzaldehyde could any solid material be obtained. This, however, proved to be 4-tolyl disulfone, undoubtedly formed by the following sequence.



Properties of this material were in good agreement with those previously recorded[11,12] for this substance. The base-catalysed elimination of sulfinate ion from sulfonate esters of this type has been well documented by Loudon[10] and by Taylor.[9] However disulfone formation has not been observed previously, and the above reaction represents an alternate pathway for the disappearance of sulfinate anion. In the case of 4-chlorobenzaldehyde, further treatment of the crude reaction mixture with ammonium thiocyanate did give a very small amount of the required α-cyano-4-chlorobenzyl thiocyanate. This, however, was the only example of the aldehydes listed previously, where any conversion to the desired product could be achieved.

In those instances where the preparation of the α-cyanoalkyl 4-toluenesulfonate failed, recourse had to be made to the α-chloroalkyl cyanides. These were prepared by the action of thionyl chloride on the cyanohydrins of a selection of the preceding aldehydes according to known procedures.[13,14]

Whereas it was possible to convert the α-chloroalkylnitriles and α-cyanoalkyl 4-toluenesulfonates to the α-cyanoalkyl thiocyanates with thiocyanate ion in boiling alcohol, it was found that usually anhydrous dimethylformamide was a much more suitable solvent. Using this medium, the reactions were complete inside thirty minutes at room temperature, and the products, generally obtained in high yield, required little purification.

(4) The only exceptions are thiocyanogen [A. Söderback, *Ann.*, **419**, 217 (1919); **465**, 184 (1928)] and the N,N′-dicyanoguanidines [D. W. Kaiser, U. S. Patent 2,630,433 (1953); J. J. Roemer and D. W. Kaiser, U. S. Patent 2,658,893 (1953)].

(5) R. C. Houtz (to E. I. du Pont de Nemours and Co.), U. S. Patent 2,404,727 (1946).

(6) H. Brintzinger and H. Schmahl, *Chem. Ber.*, **87**, 314 (1954).

(7) A. Kretov and A. Panchenko, *J. Russ. Phys. Chem. Soc.*, **61**, 1975 (1929); *Chem. Abstr.*, **24**, 4769.

(8) D. G. Coe, M. M. Gale, R. P. Linstead, and C. J. Timmons, *J. Chem. Soc.*, 123 (1957).

(9) E. C. Taylor, G. A. Berchtold, N. A. Goeckner, and F. G. Stroehmann, *J. Org. Chem.*, **26**, 2715 (1961).

(10) J. D. Loudon and I. Wellings, *J. Chem. Soc.*, 1780 (1959).

(11) T. P. Hilditch, *ibid.*, 1524 (1908).

(12) E. v. Meyer, R. Nacke, and M. Gmeiner, *J. prakt. Chem.* **63**, [ii] 167 (1901).

(13) W. H. Davies, A. W. Johnson, and H. A. Piggott, *J. Chem. Soc.*, 352 (1945).

(14) A. H. Cook, J. Downer, and B. Hornung, *ibid.*, 502 (1941).

TABLE I

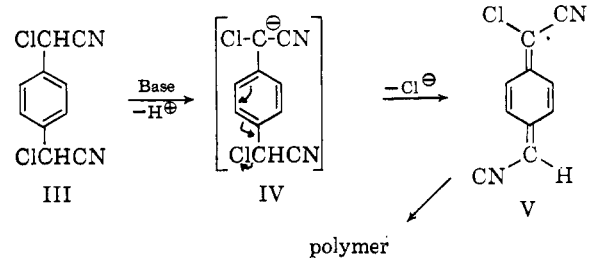
PREPARATION OF α-CYANOALKYL THIOCYANATES USING DIMETHYLFORMAMIDE AS REACTION MEDIUM

RCH(CN)SCN

R	Cryst. from[a]	M.p., °C.	Yield, %	Formula	Analyses: Calcd. C	Calcd. H	Calcd. N	Calcd. S	Found C	Found H	Found N	Found S
C_6H_5	E–P	78–80	83	$C_9H_6N_2S$[b]	..	...	..	..	..	...	..	..
2-ClC_6H_4	E–P	86–88	89	$C_9H_5ClN_2S$	51.8	2.4	13.4	15.4	51.8	2.4	13.4	15.3
4-ClC_6H_4	E–P	78–80	83	$C_9H_5ClN_2S$	51.8	2.4	13.4	15.4	51.8	2.0	13.3	15.4
2,4-$Cl_2C_6H_3$	MC–P	136–138	96	$C_9H_4Cl_2N_2S$	44.5	1.7	11.5	13.2	44.2	1.6	11.4	13.3
2-$CH_3OC_6H_4$	MC–P	104–105	91	$C_{10}H_8N_2OS$	58.8	3.9	13.7	15.7	58.8	3.9	13.5	15.9
2-$NO_2C_6H_4$	MC–P	87–89	74	$C_9H_5N_3O_2S$	49.3	2.3	19.2	14.6	49.1	2.3	19.1	14.7
4-$CH_3CONHC_6H_4$	...	136–140	49	$C_{11}H_9N_3OS$[c]	..	...	..	..	..	...	..	..

[a] Solvent key: E = ether; P = petroleum ether (b.p. 30–60°); MC = methylene chloride. [b] Known compound; yield when ethanol used as solvent was 45%. [c] This material resisted purification by crystallization and was used as such for further work.

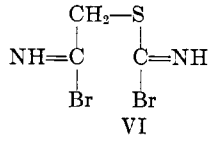
A few failures were observed. α-Cyano-β-phenylethyl 4-toluenesulfonate reacted with ammonium thiocyanate in boiling ethanol to give a dark red solid which lacked a band in its infrared spectrum for the –SCN group, and from the same reaction in dimethylformamide only traces of starting material could be isolated. The reaction of α,α′-dichlorobenzene-1,4-bisacetonitrile (III) with ammonium thiocyanate in dimethylformamide was accompanied by some vivid color changes and the deposition of ammonium chloride, but only an extremely insoluble amorphous brown powder was obtained. The latter showed nitrile but no thiocyanate absorption in the infrared spectrum. It is possible that this product is polymeric in nature having been formed from the *p*-xylylene derivative (V) shown below.

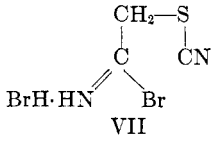


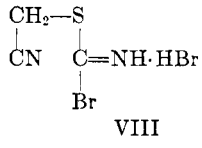
Finally, the parent compound (I, R = H) deserves some attention. It was prepared easily by refluxing chloroacetonitrile with ammonium thiocyanate in ethanol for a few hours, and proved to be a highly mobile liquid which could not be induced to crystallize at room temperature. Besides giving good elemental analytical data, its infrared spectrum showed bands at 4.40 and 4.57 μ in agreement with structure I (R = H). As Brintzinger, *et al.*,[6] claimed this material to be a solid, we repeated their experiments. Although it was possible to isolate some yellow crystals of m.p. 160–170° (with effervescence) which had no infrared absorption bands in the 4–5-μ region, we were unable to obtain any compound corresponding to that of these authors.

Table I lists the α-cyanobenzyl thiocyanates prepared for cyclization studies.

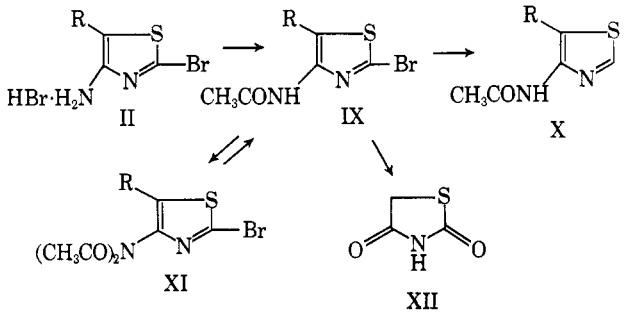
Thiazoles.—The reaction of the α-cyanoalkyl thiocyanates with hydrogen bromide in an inert solvent (usually acetic acid or ether) occurred quite readily, in most instances a highly crystalline salt being obtained. These hydrolyzed rapidly in moist air but were found to be stable indefinitely at room temperature in a dry atmosphere. The product (II, R = H) from I (R = H), to which most attention was given, had a good analysis for a compound containing two bromine atoms. That this is indeed the hydrogen bromide salt of a bromoaminothiazole and not an open chain analog such as VI, VII, or VIII, is suggested by the evidence that its infrared spectrum shows no absorption in the 4–5-μ region but does show considerable similarity to the hydrobromide salt of 3-amino-1-bromoisoquinoline around 3 μ. In addition, structure VI seems unlikely, as previous attempts[15] to isolate the monohydrobromide adducts of simple nitriles have failed. If formed at all, they appear to disproportionate into nitrile and







the nitrile dihydrobromide. Treatment of II (R = H) with acetic anhydride containing pyridine afforded a bromoacetaminothiazole (IX) which on hydrogenation led to 4-acetaminothiazole (X, R = H). The physical properties of the latter agreed well with those published[16] for this compound, and by direct comparison, were completely dissimilar to those of 2-acetaminothiazole. Clearly then the cyclization of I (R = H) by hydrogen bromide leads to 4-amino-2-bromothiazole hydrobromide and not to the alternate 2-amino-4-bromothiazole salt, a result in agreement with the corresponding cyclization[2] of 2-cyanobenzyl cyanide. By analogy, similar structural assignments were made to those cyclized products prepared from

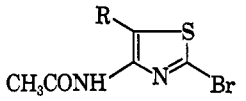


(15) F. Klages and W. Grill, *Ann.*, **594**, 21 (1956).

(16) H. Erlenmeyer and D. Markees, *Helv. Chim. Acta*, **29**, 1229 (1946).

TABLE II

PREPARATION OF 4-ACETAMINO-2-BROMOTHIAZOLES



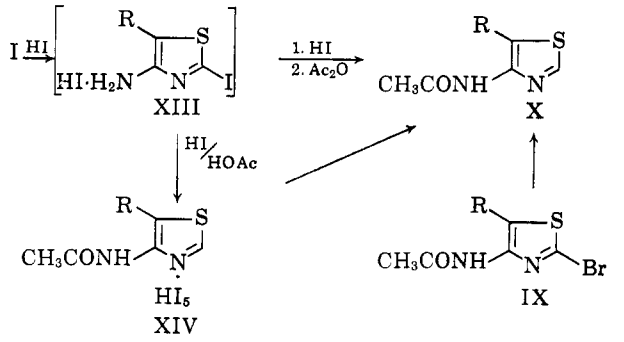
R	Method	Cryst. from[a]	M.p., °C.	Yield, %	Formula	Analyses: Calcd. C	H	Br	N	S	Found C	H	Br	N	S
H	A	A-P	165	86	$C_5H_5BrN_2OS$	27.2	2.3	36.1	12.7	14.5	27.1	2.0	35.9	12.7	14.7
C_3H_7	B	MC-P	107–109	43	$C_8H_{11}BrN_2OS$	36.5	4.2	30.4	10.6	12.2	36.6	3.9	30.3	10.6	12.3
C_6H_5	C	EE	160–162	74	$C_{11}H_9BrN_2OS$	44.5	3.1	26.9	9.4	10.8	44.5	3.0	27.1	9.2	10.7
2-ClC_6H_4	B	EE	120–121	55	$C_{11}H_8BrClN_2OS$	39.8	2.4	..	8.4	9.7	39.5	2.3	..	8.4	9.7
4-ClC_6H_4	B	EE	182–183	80	$C_{11}H_8BrClN_2OS$	39.8	2.4	24.1	8.4	9.7	39.7	2.4	24.3	8.4	9.8
2,4-$Cl_2C_6H_3$	B	EE-P	134–136	94	$C_{11}H_7BrCl_2N_2OS$	36.3	2.0	..	7.7	8.8	36.0	1.7	..	7.7	8.9
2-$CH_3OC_6H_4$	C	EE	143–145	83	$C_{12}H_{11}BrN_2O_2S$	44.0	3.4	24.4	8.6	9.8	43.6	3.4	24.2	8.4	9.7
2-$NO_2C_6H_4$	A	EE	118–120	20	$C_{11}H_8BrN_3O_3S$	38.6	2.4	23.4	12.3	9.4	38.4	2.1	23.8	12.1	9.3
4-$CH_3CONHC_6H_4$	C	ET	229–233	88	$C_{13}H_{12}BrN_3O_2S$	44.1	3.4	22.6	11.9	9.1	43.9	3.3	22.4	12.0	8.8

[a] Solvent key: A = acetone; ET = ethanol; EE = ethyl acetate; others as in Table I.

I where R = alkyl or aryl. In general, these materials were characterized as their 4-acetamino derivatives by treatment with acetic anhydride, and the latter are listed in Table II. In some cases, if base was excluded during the acetylation step and the mixture heated, an N,N-bisacetylamino compound (XI) could be isolated as the sole product. This was converted easily to the monoacetyl compound by a mild basic hydrolysis.

Some solvolysis reactions of II (R = H) also were examined and appear to be rather complex. Treatment with water almost immediately led to a very insoluble substance which was unaffected by acetic anhydride in the presence of hydrogen bromide and acetic acid. Its elemental analysis corresponds well with that required by $C_3H_5BrN_2OS$, and from its infrared spectrum and the fact that it releases bromide ion on treatment with sodium hydrogen carbonate we have assigned to it the structure 4-imino-2-oxothiazolidine hydrobromide. Treatment of II (R = H) with sodium hydrogen carbonate solution gave a bright yellow insoluble material which within minutes began to decompose, changing eventually to a mottled purple substance which could not be recrystallized without further decomposition. If following the subsidence of effervescence, the moist material was immediately transferred to an excess of acetic anhydride in pyridine, a highly crystalline product could be isolated, which, from its elemental analysis is assigned the empirical formula $C_8H_{13}BrN_4O_6S_2$. Further work on the material is continuing. Lastly, boiling II (R = H) with hydrochloric acid led to thiazolidine-2,4-dione (XII), identified by comparison with an authentic sample.[17]

The action of other halogen acids on I also was examined. The reaction of hydrogen iodide was more complex than that of hydrogen bromide. Thus, I (R = H) treated with hydrogen iodide in acetic acid initially gave a brown solid which quickly redissolved with the liberation of iodine. Addition of acetic anhydride after one hour then afforded 4-acetaminothiazole directly. When acetic anhydride was omitted and the reaction mixture was allowed to stand overnight, a black crystalline precipitate was formed. From its elemental analysis and its conversion by a basic solution of sodium thiosulfate to 4-acetaminothiazole, it appears to be a hydrogen iodide periodide (XIV, R = H) of the latter substance. Presumably these reactions proceed through a 4-amino-2-iodothiazole salt (XIII, R = H) which then undergoes reductive deiodination[18] by the excess of hydrogen iodide present. Reductive cleavage



of the thiocyanate group also occurs for besides the expected 4-acetaminothiazole (X, R = 2, 4-$Cl_2C_6H_3$), hydrogen iodide treatment of I (R = 2, 4-$Cl_2C_6H_3$) affords some 2,4-dichlorobenzyl cyanide.[19] The former product was identified by hydrogenation of 4-acetamino-2-bromo-5-(2,4-dichlorophenyl)thiazole (IX, R = 2, 4-$Cl_2C_6H_3$) using a palladium catalyst, which removed only bromine from the molecule.

By contrast, hydrogen chloride treatment of I (R = H) in acetic acid did not lead to the desired 4-amino-2-chlorothiazole compounds. A precipitate did appear but acetylation with acetic anhydride afforded only a small amount of a compound containing no chlorine, whose elemental analysis is in agreement with that of $C_5H_6N_2SO_2$. The infrared spectrum of the material showed bands at 3.05, 3.22, 5.90, and 6.17 μ which suggests that it may be 4-acetamino-2-oxo-4-thiazoline. No further work was done with this compound.

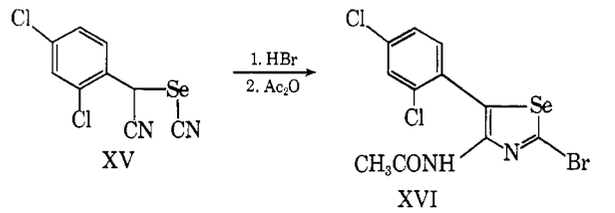
Selenazoles.—An attempt was made to extend the above cyclization procedures to the preparation of 1,3-selenazoles. Cyanomethyl selenocyanate, prepared from potassium selenocyanate and chloroacetonitrile in boiling alcohol, when treated with hydrogen bromide

(17) W. Davies, J. A. Maclaren, and L. R. Wilkinson, *J. Chem. Soc.*, 3491 (1950).

(18) Such facile deiodination in the thiazole series is not unprecedented. Y. Garreau [*Compt. rend.*, **230**, 448 (1950)] observed that 2-amino-4-iodo-5-methylthiazole was reduced to 2-amino-5-methylthiazole by a mixture of hydrogen chloride and allyl alcohol.

(19) P. B. Russell and G. H. Hitchings, *J. Am. Chem. Soc.*, **73**, 3763 (1951).

in ether, deposited selenium. After treatment of the reaction mixture with acetic anhydride, no 4-acetamino-2-bromoselenazole could be isolated. α-Cyano-2,4-dichlorobenzyl selenocyanate (XV) behaved in much the same manner. However, in this case a trace of a substance was obtained after acetylation whose infrared spectrum resembled that of the corresponding thiazole (IX, R = 2, 4-$Cl_2C_6H_3$). Unfortunately, insufficient material was obtained for analysis but it does appear to be the required XVI. Hydrogen chloride in the case of



XV XVI

XV caused selenium deposition and did not lead to any selenazole compound.

The reactions presented in this paper represent a new approach to the synthesis of thiazoles and in particular to 4-aminothiazoles. Although a number of 2,4-diaminothiazoles are known,[17,20-24] only a few derivatives of 4-aminothiazole itself have been reported. The previously mentioned 4-acetaminothiazole and its precursor 4-acetamino-2-chlorothiazole were prepared by Erlenmeyer and Markees[16] while 4-amino-2,5-diphenylthiazole, the only known free 4-aminothiazole, was synthesized by Taylor, *et al.*[25] Nevertheless, no general synthetic pathway to these materials has been described before, and the methods presented here now make them easily available.

Further reactions of these compounds will be presented in a later paper.

Experimental

Melting points were determined on a Fisher-Johns melting point block and are not corrected. Infrared spectra were recorded on a Baird spectrophotometer Model no. 4-55 as films or as Nujol mulls. Hydrogen bromide (30–33%) in acetic acid was used as supplied by Eastman Kodak.

α-Chloro-2-methoxybenzyl Cyanide.—2-Methoxybenzaldehyde (82 g.) was added to a solution of sodium bisulfite (100 g.) in water (750 ml.). The mixture which became homogeneous almost immediately was cooled to 12° and treated with a solution of potassium cyanide (45 g.) in water (100 ml.), with stirring during 30 min. This reaction solution was then extracted with ether (two 200-ml. portions) and organic phase dried over anhydrous magnesium sulfate. After removal of the latter, pyridine (5 ml.) was added, followed by a solution of thionyl chloride (80 g.) in ether (100 ml.). The second reagent was added during 40 min. at room temperature and thereafter the mixture was refluxed for 6 hr. The ether layer was removed by decantation, washed twice with water (two 100-ml. portions), and, after drying over anhydrous magnesium sulfate, evaporated to give a brown oil (79 g.). Distillation of this liquid under reduced pressure afforded only one fraction (45.4 g.), b.p. 113° (0.5 mm.), $n^{25}D$ 1.5430, which solidified after standing at room temperature for two weeks, m.p. 40–42°. A sample redistilled for analysis boiled at 123° (3.3 mm.), $n^{25}D$ 1.5429.

Anal. Calcd. for C_9H_8ClNO: C, 59.5; H, 4.4; Cl, 19.5; N, 7.7. Found: C, 59.7; H, 4.5; Cl, 19.4; N, 7.7.

α-4-Dichlorobenzyl Cyanide.—The procedure used was exactly the same as that of the preceding example. From 4-chlorobenzaldehyde (21.1 g.) there was obtained a crude brown oil (24.5 g.) which when distilled under reduced pressure afforded pure α,4-dichlorobenzyl cyanide (17.5 g.), b.p. 85–87° (0.18 mm.), $n^{25}D$ 1.5575.

Anal. Calcd. for $C_8H_5Cl_2N$: C, 51.6; H, 2.7; Cl, 38.1; N, 7.5. Found: C, 51.5; H, 2.8; Cl, 38.2; N, 7.5.

4-Acetamino-α-chlorobenzyl Cyanide.—4-Acetamino-α-cyanobenzyl alcohol, m.p. 80°, was prepared in quantitative yield from 4-acetaminobenzaldehyde according to the procedure of Buck.[26] It exhibited bands in the infrared spectrum at 2.95 (-OH) and 6.01 μ (acetamino). Nitrile absorption was not apparent between 4 and 5 μ, but this is not unusual with α-hydroxynitriles. This material (7.6 g.) was suspended in dry ether (50 ml.), and triethylamine (4.1 g.) added, followed by a solution of thionyl chloride (15 g.) in ether (20 ml.). The latter was added dropwise during 20 min. and the suspended solid turned a yellow color but not dissolve. The mixture was refluxed for 1.5 hr. and water then added, whereupon all solid present went into solution. The ether phase was separated, washed with water, dried over anhydrous magnesium sulfate, and evaporated to dryness. The resulting brown material was crystallized from methylene chloride–ether (with charcoal decolorizing) to give a yellow solid, m.p. 120–122° (4.15 g.). A sample recrystallized for analysis had m.p. 124–127°.

Anal. Calcd. for $C_{10}H_9ClN_2O$: C, 57.6; H, 4.3; Cl, 17.0; N, 13.4. Found: C, 57.8; H, 4.1; Cl, 17.0; N, 13.4.

α,α′-Dichlorobenzene-1,4-bisacetonitrile.—Terephthalaldehyde (6.5 g.) was added to liquid hydrogen cyanide (50 ml.). After stirring for 1 min., the mixture became homogeneous, then within 3 min. a solid began to precipitate. Two hours later, the excess hydrogen cyanide was removed *in vacuo* and the residual solid, presumed to be terephthalaldehyde biscyanohydrin, suspended in ether (25 ml.). Thionyl chloride (18 g.) in ether (25 ml.) was added dropwise and the mixture refluxed for 2 hr. The solution was washed with water (five 10-ml. portions), dried over magnesium sulfate, and the ether removed by distillation. The resulting solid (8.5 g.), m.p. 100–120°, when crystallized from methylene chloride–carbon tetrachloride afforded crystals (2.1 g.), m.p. 132–135°. Recrystallization from ether–petroleum ether (b.p. 30–60°) led to the pure material, m.p. 139–141°. Its infrared spectrum showed a band at 4.41 μ.

Anal. Calcd. for $C_{10}H_6Cl_2N_2$: C, 53.4; H, 2.7; Cl, 31.5; N, 12.4. Found: C, 53.1; H, 2.6; Cl, 31.3; N, 12.4.

α-Cyano-β-phenylethyl 4-Toluenesulfonate.—Phenyl acetaldehyde (24 g.) in 50% ethanolic solution was poured onto 4-toluenesulfonyl chloride (19 g.) and to this paste was added potassium cyanide (6.5 g.) in water (25 ml.) with cooling and stirring. After standing 5° overnight, the solid (12 g.) which had precipitated was removed by filtration and recrystallized from ethanol to give pure α-cyano-β-phenylethyl 4-toluenesulfonate (2.7 g.), m.p. 77–78°.

Anal. Calcd. for $C_{16}H_{15}NO_3S$: N, 4.6; S, 10.6. Found: N, 4.7; S, 10.9.

4-Tolyl Disulfone.—4-Nitrobenzaldehyde (15 g., 0.1 mole) and 4-toluenesulfonyl chloride (19 g., 0.1 mole) were dissolved in dioxane (100 ml.) and the resulting solution treated dropwise with potassium cyanide (6.5 g., 0.1 mole) in water (25 ml.). After standing overnight the mixture was diluted with a large volume of water and extracted with methylene chloride (two 100-ml. portions). This extract was dried over magnesium sulfate and evaporated to small bulk. Dilution with acetone then afforded a white crystalline precipitate (1.4 g.), m.p. 205–206°. Several recrystallizations raised the melting point to 210–211° (reported[11] m.p. 212°). The infrared spectrum of this substance showed bands at 7.46 and 8.79 μ, characteristic of a sulfone group.

Anal. Calcd. for $C_{14}H_{14}O_4S_2$: C, 54.2; H, 4.55; S, 20.7. Found: C, 54.3; H, 4.2; N, 20.9.

α-Cyanoalkyl Thiocyanates (I).—The requisite α-chloroalkyl cyanide or α-cyanoalkyl 4-toluenesulfonate (0.02 mole) was dissolved in anhydrous dimethylformamide (10 ml.) and a solution of dry sodium or ammonium thiocyanate (0.021 mole) in the same solvent (10 ml.) added in one portion at room temperature.

(20) K. Gapanathi and A. Venkataraman, *Proc. Ind. Acad. Sci.*, **22A**, 359 (1945).

(21) S. C. De and P. K. Datta, *Sci. Cult.* (Calcutta), **11**, 150 (1945); *Chem. Abstr.*, **40**, 1804 (1946).

(22) A. H. Land, C. Ziegler, and J. M. Sprague, *J. Org. Chem.*, **11**, 617 (1946).

(23) R. M. Dodson and H. W. Turner, *J. Am. Chem. Soc.*, **73**, 4517 (1951).

(24) B. H. Chase and J. Walker, *J. Chem. Soc.*, 4443 (1955).

(25) E. C. Taylor, J. A. Anderson, and G. A. Berchtold, *J. Am. Chem. Soc.*, **77**, 5444 (1955).

(26) J. S. Buck, *ibid.*, **55**, 3388 (1933).

In most cases precipitation of ammonium or sodium chloride or the corresponding 4-toluenesulfonate salt was complete in half an hour. The mixture was then filtered into ice–water and the precipitate collected and crystallized from the appropriate solvent.

Cyanomethyl Thiocyanate.—To a solution of sodium thiocyanate (40.5 g., 0.5 mole) in methanol (250 ml.) there was added chloroacetonitrile (37.75 g., 0.5 mole) in one portion. The mixture was refluxed for 22 hr., with good stirring and the sodium chloride (28 g.) then removed by filtration. The filtrate was evaporated under reduced pressure to remove methanol and the water-soluble residue taken up in methylene chloride, dried over calcium chloride, and stirred with decolorizing charcoal. The methylene chloride was then evaporated under reduced pressure. This procedure was necessary to remove traces of basic inorganic salts which, if still present when the crude product was distilled, led to an explosion.

The pale brown liquid was twice distilled through a 6-in. Vigreux column to give pure cyanomethyl thiocyanate, b.p. 100–101° (1.5 mm.) (30.9 g., yield 62.0%). A sample redistilled for analysis boiled at the same temperature and pressure and had $n^{25}D$ 1.5088.

Anal. Calcd. for $C_3H_2N_2S$: C, 36.7; H, 2.1; N, 28.6; S, 32.7. Found: C, 36.6; H, 1.9; N, 28.6; S, 32.9.

1-Cyanobutyl Thiocyanate.—To a mixture of butyraldehyde (21.6 g., 0.3 mole) and benzenesulfonyl chloride (53 g. 0.3 mole) there was added dropwise with stirring a solution of potassium cyanide (19.5 g., 0.3 mole) in water (45 ml.). After stirring for 2 hr., the reaction mixture was poured into methylene chloride and water. The organic layer was separated, washed with water, dried over anhydrous magnesium sulfate, and the solvent removed under reduced pressure. The residual sirup (64 g.) was added to a solution of ammonium thiocyanate (18 g., 0.245 mole) in ethanol (120 ml.) and the whole stirred at 40° for 4 hr. A yellow solid (7 g.) which had separated was removed by filtration (this material was not investigated), and the filtrate concentrated under reduced pressure. The semisolid residue was stirred vigorously with ether and the undissolved solid removed by filtration. The ethereal extract was washed three times with water, dried over anhydrous magnesium sulfate, and the ether removed evaporatively. The liquid thus obtained was distilled and that fraction (11.6 g.) distilling at 85–98° (0.5 mm.) collected. Redistillation at the same pressure afforded pure 1-cyanobutyl thiocyanate (10.6 g., yield 25%), b.p. 95°, $n^{25}D$ 1.4805. Its infrared spectrum showed absorption bands at 4.45 and 4.60 μ.

Anal. Calcd. for $C_6H_8N_2S$: C, 51.4; H, 5.8; N, 20.0; S, 22.9. Found: C, 51.5; H, 5.8; N, 19.9; S, 23.0.

Cyanomethyl Selenocyanate.—A solution of potassium selenocyanate (30 g.) in water (90 ml.) was added, in one portion, to chloroacetonitrile (31.5 g.) in methanol (250 ml.) and the mixture refluxed overnight. The solvents were removed under reduced pressure, and the residual sludge of oil and salt extracted with methylene chloride. The extract was stirred with anhydrous magnesium sulfate, and the methylene chloride and excess chloroacetonitrile then removed under reduced pressure. The dark red oily product was fractionally distilled and that portion (15.4 g.) boiling at 131–134° (0.45 mm.) collected. Refractionation of this material through a 4-in. Vigreux column gave a fairly pure sample of cyanomethyl thiocyanate (13.3 g.), b.p. 118° (0.3 mm.). Its infrared spectrum showed bands at 4.44 (nitrile) and 4.62 μ (selenocyanate).

Anal. Calcd. for $C_3H_2N_2Se$: C, 24.8; H, 1.4; N, 19.3. Found: C, 25.0; H, 1.6; N, 19.4.

A later fraction (3.6 g.), b.p., 138–140° (0.45 mm.) obtained from the first distillation showed only a single band (at 4.44 μ) in its infrared spectrum and we consider this to be biscyanomethyl selenide derived undoubtedly from some potassium selenide impurity in the potassium selenocyanate.

2,4-Dichloro-α-cyanobenzyl Selenocyanate.—2,4-Dichloro-α-cyanobenzyl 4-toluenesulfonate (6.05 g.) dissolved in dimethylformamide (50 ml.) was treated with solution of potassium selenocyanate (2.5 g.) in water (7.5 ml.). The mixture was allowed to stand at room temperature for 20 hr. and then poured into ice–water. The solid precipitate was removed by filtration and dried (4.3 g., 89%). A sample recrystallized from methylene chloride–ether had m.p. 151–152° (softening at 142°). Its infrared spectrum showed absorption bands at 4.45 (–CN) and 4.62 μ (–SeCN).

Anal. Calcd. for $C_9H_4Cl_2N_2Se$: C, 37.3; H, 1.4; N, 9.7. Found: C, 37.2; H, 1.4; N, 9.6.

Cyclization of Dinitriles with Hydrogen Bromide. Method A.—The α-cyanoalkyl thiocyanate was dissolved in ten to twenty times its weight of dry ether, and anhydrous hydrogen bromide passed through the solution at 0° for 1.5 hr., or until precipitation of the solid appeared complete. The solid was removed by filtration under a dry atmosphere and then added to an excess of a 2:1 mixture of acetic anhydride–pyridine. After 2 hr. at room temperature, the mixture was poured into 20% aqueous sodium acetate and stirred for a short period. The resulting solid was removed by filtration, washed with water, and dried, then recrystallized from the appropriate solvent.

Treatment of cyanomethyl thiocyanate (3 g.) in this way led to the immediate deposition of a faintly yellow crystalline solid (6.6 g.) with no definite melting point. It decomposed slowly at 140–180°. Its infrared spectrum showed bands at 3.25, 3.88, 6.40, and 6.65 μ. 3-Amino-1-bromoisoquinoline hydrobromide had corresponding bands in the same regions.

Anal. Calcd. for $C_3H_4Br_2N_2S$: C, 13.9; H, 1.6; Br, 61.5; N, 10.8; S, 12.3. Found: C, 13.8; H, 1.7; Br, 61.0; N, 10.6; S, 12.4.

Method B.—The α-cyanoalkyl thiocyanate was dissolved in three times its weight of glacial acetic acid and added to a solution of acetic acid containing three equivalents of hydrogen bromide with stirring at 10°. After 2 hr., a fivefold excess of acetic anhydride was added at the same temperature, and 2 hr. later the mixture poured into water containing a little pyridine. The precipitate was then treated as under method A.

Method C.—This was identical with method B, except that a 3:1 mixture of acetic anhydride–pyridine was used to effect acetylation.

4-(N,N-Bisacetylamino)-2-bromo-5-phenylthiazole.—α-Cyanobenzyl thiocyanate (1.0 g.) in benzene (30 ml.) was treated with hydrogen bromide for 45 min. and the precipitate collected and added to acetic anhydride (5 ml.). After heating for 30 min. at 100°, the product was isolated in the usual way. Recrystallization from ethyl acetate gave the pure compound (1.59 g., 82%), m.p. 150–151°. Its infrared spectrum showed a band at 5.80 μ.

Anal. Calcd. for $C_{13}H_{11}BrN_2O_2S$: Br, 23.6; N, 8.3; S, 9.5. Found: Br, 23.6; N, 8.3; S, 9.3.

4-(N,N-Bisacetylamino)-2-bromo-5-(4-chlorophenyl)thiazole.—Using exactly the same procedure as before α-cyano-4-chlorobenzyl thiocyanate (1.3 g.) was converted to the title compound in 92% yield. The product was recrystallized from ethyl acetate, m.p. 202–204°.

Anal. Calcd. for $C_{13}H_{10}BrClN_2O_2S$: C, 41.8; H, 2.7; N, 7.5; S, 8.6. Found: C, 41.7; H, 2.5; N, 7.7; S, 8.5.

A sample (1.0 g.) of this material in ethanol (35 ml.) was refluxed for 30 min. with sodium hydrogen carbonate (0.23 g.) in water (10 ml.). Evaporative removal of the ethanol followed by dilution with water led to 4-acetamino-2-bromo-5-(4-chlorophenyl)thiazole (0.8 g.) identical in all respects with the material prepared as described earlier.

4-Acetaminothiazole.—A solution of 4-acetamino-2-bromothiazole (0.22 g.) in ethanol (75 ml.) containing sodium acetate (84 mg.) was stirred in an atmosphere of hydrogen with a 10% palladium-on-charcoal catalyst (50 mg.) for 3 hr. At the end of this time, hydrogen absorption ceased and the catalyst and solvent were removed in the usual way. Extraction of the residue led to 4-acetaminothiazole (0.12 g.), m.p. 176–178° (reported[16] m.p. 175–176°), which crystallized as flat blades from carbon tetrachloride. The infrared spectrum of this material with bands at 3.10 and 5.94 μ was completely different from that of a specimen of 2-acetaminothiazole of m.p. 203°.

Anal. Calcd. for $C_5H_6N_2OS$: C, 42.2; H, 4.3; N, 19.7; S, 22.6. Found: C, 42.1; H, 4.2; N, 19.4; S, 22.5.

The Action of Hydrogen Iodide on Cyanomethyl Thiocyanate. (a).—A solution of cyanomethyl thiocyanate (2.0 g.) in acetic acid (10 ml.) was added dropwise to 13% hydrogen iodide in acetic acid (50 ml.). The dark brown solid that appeared quickly redissolved and after 1 hr. acetic anhydride (10 ml.) was added and the solution stirred for 2 hr. Isolation of the product by dilution with water and methylene chloride extraction afforded 4-acetaminothiazole (0.7 g.), m.p. 174–178°, identical with a specimen prepared by the procedure described previously.

(b).—When reaction was carried out as in method A but the addition ofacetic an hydride was omitted, and the reaction allowed to proceed for 24 hr., a highly crystalline black precipitate formed

(4.7 g.). This was removed by filtration and washed with methylene chloride.

Recrystallization proved difficult and the material was analyzed as such.

Anal. Calcd. for $C_5H_7I_3N_2OS$: C, 7.7; H, 0.9; I, 81.6; N, 3.6. Found: C, 7.7; H, 0.6; I, 79.6; N, 4.1.

A specimen (0.5 g.) of this material treated with a mixture of sodium hydrogen carbonate and sodium thiosulfate solutions afforded 4-acetaminothiazole (82 mg., 91%), m.p. 175–178°.

4-Acetamino-5-(2,4-dichlorophenyl)thiazole. (a).—To α-cyano-2,4-dichlorobenzyl thiocyanate (1.2 g.) suspended in glacial acetic acid (10 ml.) there was added dropwise at 5° a solution (12 g.) of hydrogen iodide (10–12%) in the same solvent. After an additional 30 min. at this temperature, acetic anhydride (3 ml.) was added and the liquid allowed to stand for 2 hr. at room temperature, then poured into 20% sodium acetate solution. Extraction with methylene chloride afforded a noncrystallizable gum which was redissolved in methylene chloride and percolated through a silica gel (5 g.) column. The initial eluate yielded an oil which slowly crystallized affording 2,4-dichlorobenzyl cyanide (50 mg.), m.p. 57–58° (reported[19] m.p. 58–59°). The infrared spectrum of this material had a band at 7.07 μ characteristic of a methylene group in a benzyl cyanide system.

Further elution of the column with ethyl acetate led to a second oil which when recrystallized from methylene chloride–ether afforded 4-acetamino-5-(2,4-dichlorophenyl)thiazole (0.35 g.), m.p. 115–116°. This material did not depress the melting point of a specimen prepared according to the procedure following.

Anal. Calcd. for $C_{11}H_8Cl_2N_2OS$: C, 46.0; H, 2.8; Cl, 24.7; N, 9.8; S, 11.2. Found: C, 46.0; H, 2.6; Cl, 24.5; N, 9.7; S, 11.2.

(b).—4-Acetamino-2-bromo-5-(2,4-dichlorophenyl)thiazole (1.0 g.) was dissolved in ethanol (60 ml.) containing potassium hydroxide (0.23 g.) and the resulting solution stirred under hydrogen in the presence of a 10% palladium-on-charcoal catalyst (0.15 g.). Hydrogen absorption had almost ceased after 2 hr. and the catalyst and solvent were removed by the usual methods. The residue was extracted with methylene chloride, and the extract concentrated and diluted with ether. Cooling to 5° caused crystallization of the product (0.45 g., 59% yield). A further crystallization from ethyl acetate gave the pure substance, m.p. 116–117°. Its infrared spectrum was identical with that of the material prepared by method a.

The Action of Hydrogen Chloride on Cyanomethyl Thiocyanate.—Cyanomethyl thiocyanate (0.1 g.) in ether (5 ml.) was saturated at room temperature with hydrogen chloride. After 1 hr. the yellow precipitate was removed and heated with acetic anhydride (~5 ml.) until solution was complete. The mixture was then poured into sodium acetate solution and the product isolated by methylene chloride extraction. Crystallization of the latter from acetone–petroleum ether (b.p. 66–67°) led to fine white needles, m.p. 202–206° (20 mg.).

Anal. Calcd. for $C_5H_6N_2O_2S$: C, 38.0; H, 3.8; N, 17.7; S, 20.3. Found: C, 38.1; H, 3.6; N, 17.5; S, 20.3.

Solvolysis Experiments with 4-Amino-2-bromothiazole Hydrobromide. (a).—The hydrobromide (1.0 g.) was stirred vigorously with water (15 ml.) for 15 min. and the undissolved solid removed by filtration and dried (0.5 g.), m.p. >280°. Its infrared spectrum showed bands at 5.92 and 6.20 μ.

Anal. Calcd. for $C_3H_5BrN_2OS$: C, 18.3; H, 2.6; Br, 40.6; N, 14.2; S, 16.3. Found: C, 18.4; H, 2.5; Br, 40.4; N, 14.1; S, 16.0.

(b).—The hydrobromide (4.0 g.) was added, with stirring, in one portion to 10% sodium hydrogen carbonate solution (200 ml.). As soon as effervescence had subsided, the solid was removed and, while still damp, added to a mixture of pyridine (20 ml.) and acetic anhydride (20 ml.) and the resulting mixture stirred for 1 hr. The clear solution was poured into water and the product isolated by methylene chloride extraction. The resulting brown gum crystallized easily from methanol and gave a highly crystalline solid (1.0 g.), m.p. 178–180° (effervesces at 110–120°). Two further crystallizations afforded the pure material, m.p. 184–185°, as large diamonds. Its infrared spectrum showed absorption at 2.97, 3.05, 3.11, 3.12, 5.92, and 6.52 μ.

Anal. Calcd. for $C_8H_{13}BrN_4O_6S_2$: C, 23.7; H, 3.2; Br, 19.7; N, 13.8; S, 15.8. Found: C, 23.5; H, 3.2; Br, 20.0; N, 13.8; S, 16.0.

(c).—The hydrobromide (0.5 g.) was refluxed with 5 *N* hydrochloric acid (10 ml.) for 3 hr. Evaporation of the solution to dryness followed by crystallization of the residue from ether–petroluem ether (b.p. 30–60°) afforded colorless prisms of thiazolidine-2,4-dione, m.p. 126–127° undepressed on admixture with an authentic specimen.

The Action of Hydrogen Bromide on α-Cyano-2,4-dichlorobenzyl Selenocyanate.—The selenocyanate (0.4 g.) was suspended in glacial acetic acid (4 ml.) and stirred while hydrogen bromide in acetic acid (1 g., 30% hydrogen bromide) was added dropwise. The reaction mixture immediately became homogeneous and turned a dark brown color. After 30 min., an excess of acetic anhydride was added and the solution then allowed to stand a further 3 hr. The mixture was poured into 20% sodium acetate solution and deposited selenium removed by filtration. The filtrate was processed by methylene chloride extraction which led to a small amount of a sirup. On standing in the refrigerator, this deposited crystals (6 mg.), m.p. 170° (softening at 160°). Its infrared spectrum showed bands at 3.09 and 6.00 μ.

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Hydrogenation of Diels–Alder Adducts of Anthracene[1]

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In the presence of ruthenium catalyst, hydrogen attacks selectively only one aromatic ring in 9,10-dihydroanthracene-9,10-endo-α,β-succinic anhydride (I). Several diesters and an N-substituted imide were prepared from the resulting hydrogenation product (II). In the presence of Raney nickel, the action of hydrogen on I is nonselective. In contrast to I, hydrogenation of 11-methylol-9,10-dihydro-9,10-ethanoanthracene in the presence of ruthenium catalyst proceeds with attack on both aromatic rings. This difference is attributed to steric effects.

The Diels–Alder condensation of anthracene with dienophiles is a reversible, temperature-dependent reaction.[2] At higher temperatures, usually above 200°, the equilibrium is shifted in favor of the polycyclic hydrocarbon.[3] Pyrolysis of anthracene adducts has been suggested as a means of purifying anthracene or unsaturated alcohols.[4] The low thermal stability of these adducts excludes their use as potential starting materials for the preparation of polymers. It was thought that hydrogenation of one or both benzene

(1) Paper presented before the Division of Fuel Chemistry, 143rd National Meeting of the American Chemical Society, Cincinnati, Ohio, January, 1963.

(2) For numerous references, see M. C. Kloetzel, *Org. Reactions*, **4**, Chap. 1 (1948).

(3) (a) W. E. Bachmann and M. C. Kloetzel, *J. Am. Chem. Soc.*, **60**, 481 (1938); (b) R. Norman Jones, C. J. Gogek, and R. W. Sharpe, *Can. J. Research*, **26B**, 719 (1948).

(4) C. W. Smith and R. T. Holm, U. S. Patent 2,761,883 (1956).