

The Synthesis of Sulfur-Containing Pyridazines. I.
Benzylthiolation with a Subsequent Selective Debenzylation on
4,5-Dihalo-3-Pyridazines.

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Treatment of 4,5-dichloro- (I) or 4,5-dibromo-3-pyridazone (I') with sodium benzylthiolate or benzylisothiuronium chloride in aqueous alkaline alcoholic solution gives 4,5-bis(benzylthio)-3-pyridazone (II_a) in a reasonable yield. However, I is allowed to react with an excess of sodium benzylthiolate in the presence of sodium amide in dry toluene, by heating them under reflux for ten hours, to yield 4-mercapto-5-benzylthio-3-pyridazone (III_a) as a by-product, together with the main product, II_a. Similar results are observed in the reactions of I' with sodium benzylthiolate, with sodium 2-furfurylthiolate, and with 2-thenylthiolate, yielding III_a, 4-mercapto-5-(2-furfurylthio)-3-pyridazone (III_b), and 4-mercapto-5-(2-thenylthio)-3-pyridazone (III_c), respectively, besides the main products, corresponding 4,5-bis(benzylthio)-3-pyridazines under the similar reaction conditions. The courses of these reactions are confirmed by independent experiments and the structures of the products are established by unambiguous methods.

During the course of the study on the synthesis of sulfur-containing pyridazine derivative,³⁾ the present paper deals with an interesting result obtained from a reaction of 4,5-dihalo-3-pyridazone with an excess of sodium benzylthiolate or analogous reagents in the presence of sodium amide in dry toluene, by heating them under reflux for 10 hours, in attempts to prepare a series of 4,5-bis(benzylthio)-3-pyridazines.

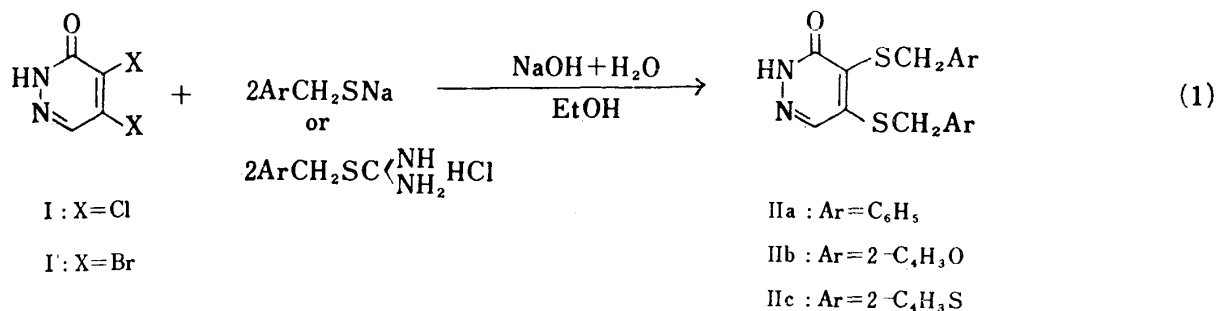
General procedure for preparation of this type of compounds, such as 4,5-bis(benzylthio)-3-pyridazone (II_a), 4,5-bis(2-furfurylthio)-3-pyridazone (II_b), and 4,5-bis(2-thenylthio)-3-pyridazone (II_c), may be classified as follows: (1) Benzylthiolation or arylmethylthiolation of 4,5-dihalo-3-pyridazines (I : X=Cl and I' : X=Br) in basic media; (2) Benzylation or arylmethylation of 4,5-dimercapto-3-pyridazone in basic media; (3) Stepwise method composed of procedure 1 and 2, for example, I or I' is converted to 4-halo-5-mercapto-3-pyridazone (IV : X=Cl or IV' : X=Br) or 4-halo-5-benzylthiopyridazone (V_a : X=Cl, Ar=C₆H₅-; V_a' : X=Br, Ar=C₆H₅-; V_b : X=Cl, Ar=2-C₄H₃O-; or V_c : X=Cl, Ar=2-C₄H₃S-) from which directly or via 4-mercapto-5-benzylthio-3-pyridazone (III_a : Ar=C₆H₅-; III_b : Ar=2-C₄H₃O-; or III_c :

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Ar=2-C₄H₃S-), the purpose compound (II_a, II_b or II_c) is producible.

4,5-Dichloro-3-pyridazone reacted with sodium benzylthiolate or benzylisothiuronium chloride in aqueous alkaline ethanolic solution, by heating them for a few hours, to give 4,5-bis(benzylthio)-3-pyridazone (II_a) in a good yield and almost similar results were observed in the preparation of the II_b and II_c, in such a reaction condition. (Eqn. 1 and TABLE 1)



The reaction is formulated as the equation 1 and the products are shown in the TABLE 1.

TABLE 1 4,5-Bis(benzylthio)-3-pyridazones

Comd. No.	Ar	M. P., °C*	Yield, %	Formula	Analysis					
					Calcd.			Found.		
					C	H	N	C	H	N
II _a	C ₆ H ₅	160	94.0	C ₁₈ H ₁₆ ON ₂ S ₂	63.32	4.74	8.23	63.63	4.73	8.59
II _a			92.0					63.48	4.72	8.40
II _b	2-C ₄ H ₃ O	97	43.8	C ₁₄ H ₁₂ O ₃ N ₂ S ₂	52.32	3.68	8.72	52.42	3.97	9.17
II _c	2-C ₄ H ₃ S	121	86.1	C ₁₄ H ₁₂ ON ₂ S ₄	47.69	3.43	7.94	47.96	3.60	8.34

* All melting points are uncorrected.

On the contrary, I reacted with an excess of sodium benzylthiolate (R) (I : R = 1 : 4 (molar ratio) or two equivalents of R required by I) in the presence of sodium amide in dry toluene, by heating them under reflux for ten hours, to produce 4(or 5)-mercapto-5(or 4)-benzylthio-3-pyridazone, (III_a), (m. p., 186°, yield, 20%) together with the main product, II_a, (m. p., 160°, yield, 48.5%). And almost similar results were also noticed as expected in the cases in which I' and an excess of R, and analogous reagents, were allowed to react in a similar reaction condition as above; viz., the by-products were III_a (yield, 18%), 4-(or 5)-mercapto-5(or 4)-(2-furfurylthio)-3-pyridazone, (III_b), (m. p., 145°, yield, 19%) and 4(or 5)-mercapto-5(or 4)-(2-thenylthio)-3-pyridazone, (III_c), (m. p., 153°, yield, 5.9%), corresponding to the main products II_a, II_b (m. p., 97°, yield, 40.6%), and II_c (m. p., 121°, yield, 71.8%).

The reaction is expressed in the equation 2 and the results are shown in the TABLE 2.

Each of III type compounds, easily converted by benzylation to the corresponding II, appears in greenish yellow crystals and shows the characteristic frequencies, ν_{S-H} in 2500 cm⁻¹ and $\nu_{C=O}$ in a region of 1620 (III_a), and 1630 cm⁻¹ (III_b and III_c), in I.R. absorption spectra. On the contrary, all II type compounds are almost colorless in pure states, and similar in $\nu_{C=O}$ in 1630 cm⁻¹ to, however, different in lack of the

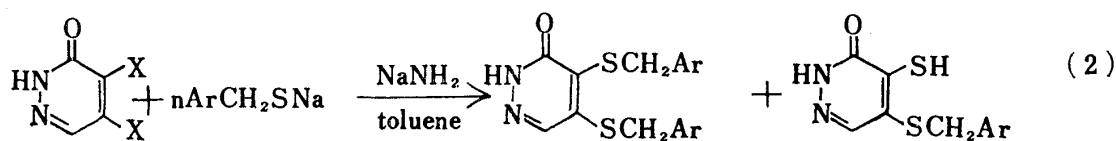
IIa : Ar = C₆H₅IIIa : Ar = C₆H₅IIb : Ar = 2-C₄H₃OIIIb : Ar = 2-C₄H₃OIIc : Ar = 2-C₄H₃SIIIc : Ar = 2-C₄H₃S

TABLE 2. Products from a reaction of 4,5-Dihalo-3-Pyridazone with an excess of Sodium Benzylthiolate in the presence of sodium amide in dry toluene (Eqn 2)

Exp. No.	4(or 5)-Mercapto-5(or 4)-benzylthio-3-pyridazone							4,5-Bis(benzylthio)-3-pyridazone			Total Yield, %				
	Compd. No.	Ar	M. P., °C*	Yield, %	Formula	Analysis			Compd. No.	M. P., °C		Yield, %			
						Calcd.							Found		
						C	H	N	C	H	N				
1	III _a	C ₆ H ₅	186	20.0	C ₁₁ H ₁₀ ON ₂ S ₂	52.77	4.03	11.19	52.81	4.01	11.03	II _a	160	48.5	68.5
2	III _a	C ₆ H ₅		18.0					52.83	4.01	11.20	II _a	160	59.0	77.0
3	III _b	2-C ₄ H ₃ O	145	19.0	C ₉ H ₈ O ₂ N ₂ S ₂	44.98	3.36	11.65	44.85	3.46	11.62	II _b	97	40.6	59.0
4	III _c	2-C ₄ H ₃ S	153	5.9	C ₉ H ₈ ON ₂ S ₃	42.62	3.15	10.93	42.40	3.45	11.02	II _c	121	71.8	77.7

* All melting points are uncorrected.

characteristic frequency in 2500cm⁻¹ from, the III type ones.

Although it was experimentally revealed that the III type compound, partly debenzylated product always formed together with the II type compound, under the reaction condition as mentioned above, it is still difficult to say directly about the structure the II type compound or the reaction mechanism. For all that, the formation of the mercaptans by C—S bond cleavage of benzyl-, other aralkyl- or alkylthio compounds, by using sodium in liquid ammonia, lithium in demethylamine, aluminium tribromide, or aluminium trichloride, in toluene, has been well known.

In the circumstances, prior to a direct structural proof of the III type compound, on the assumption that the compound III, should be assignable to 4-mercapto-5-benzylthio-3-pyridazone (III_i), a stepwise method of preparing the compounds, III_i and II, as shown in the Chart 1, was attempted to carry out. In the chart, the compounds(IV or IV'), and(V_i), are written postulationaly, likewise III_i, as 4-halo-5-mercapto- and 4-halo-5-benzylthio-3-pyridazone, respectively.

Following the scheme in the chart 1, the three kinds of the compounds III_i were prepared by thiolation of the corresponding X_i (4-chloro-5-benzylthio-(m. p., 197°), 4-bromo-5-benzylthio-(m. p., 197°), 4-chloro-(2-furfurylthio)-(m. p., 133°), or 4-chloro-(2-thenylthio)-3-pyridazone (m. p., 170°)) with sodium hydrosulfide, by heating them in aqueous ethanolic solution, and any one of III_i's compounds proved identical in any respect with the corresponding compound (III_a, III_b, or III_c) formed as by-product in the reaction 2.

In the course of preparing four kinds of the V_i type compound, all of them were easily formed by direct benzylthiolation of I (or I') in a rather moderate reaction condition, or a short time contact of I (or I')

with the corresponding sodium benzylthiolate in aqueous alkaline ethanolic solution at room temperature, and they were also prepared by S-benylation of the IV or IV', in a similar moderate condition as mentioned (TABLE 4).

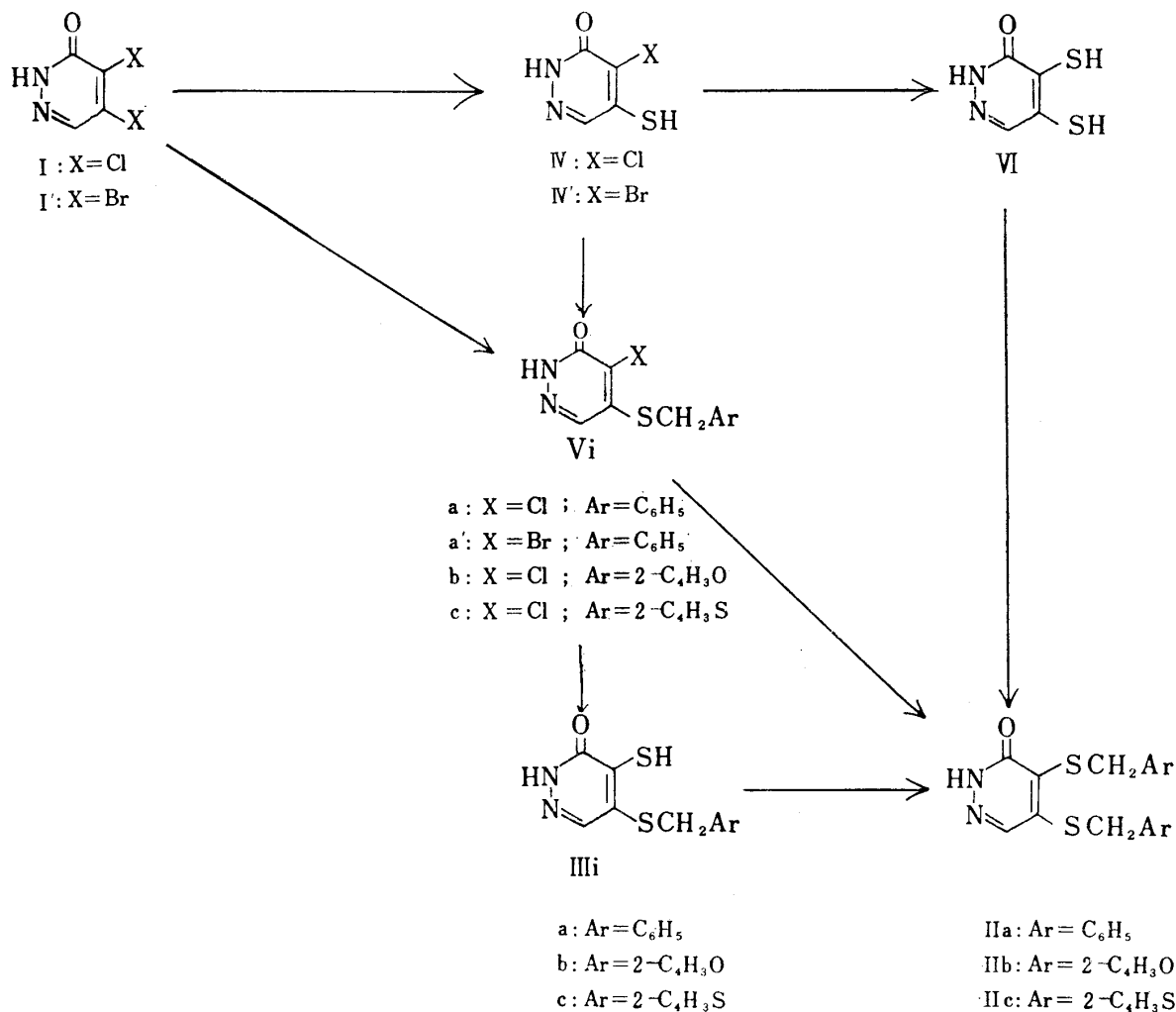


chart 1

The compound IV, or IV', one of the most important key compounds in the scheme, derived from I or I', respectively, by thiolation with sodium hydrosulfide in aqueous ethanolic solution at a room temperature, is comparatively unstable, particularly to heat, acid or light, in the presence or absence of a polar solvent, to produce dipyridazo[4,5-b:4,5-e]-1,4-dithiin-1,6-dione.^{9,10)}

Each of four kinds of the compound VI_i, obtained from the IV or IV' by benzylation, or directly from I or I' by appropriate benzylation, was easily converted by an additional benzylation to the corresponding II compound. In this connection, the compound II was also formed by di-benylation of crude 4,5-dimercapto-3-pyridazone (IV) derived from IV or IV' by additional thiolation with sodium hydrosulfide in aqueous ethanolic solution, by heating them under pressure. (TABLE 5)

All of the compounds IV, IV', and IV, show the similar characteristic frequency of stretching vibration of S-H group in the region of 2500~2550cm⁻¹ in the I.R. absorption spectra, likewise as in the compounds of

TABLE 3 4-Mercapto-5-benzylthio-3-pyridazones (III_i)

Ar	M. P., °C ^{*1}	Nujol		Yield, % based on the V _i
		I, R. S-H	$\nu(\text{cm}^{-1})$ C=O	
C ₆ H ₅	186	2500	1620	75.0
C ₆ H ₅ ^{*2}				88.0
2-C ₄ H ₃ O	145	2500	1630	68.8
2-C ₄ H ₃ S	153	2500	1630	73.2

*1 All melting points are uncorrected.

*2 Bromo derivative, and in other cases chloro derivative, was used as V_i.

TABLE 4 4-Halo-5-benzylthio-3-pyridazones (V_i)

Ar	X	M. P. ^{*1} , °C	Yield, %		Formula	Analysis, %					
			Method† A	Method† B		Calcd.			Found		
						C	H	N	C	H	N
C ₆ H ₅	Cl	197	27.0	41.3 ^{*2}	C ₁₁ H ₉ ON ₂ SCl	52.28	3.59	11.09	52.34	3.65	11.39
C ₆ H ₅	Br	197	28.7	45.4 ^{*2}	C ₁₁ H ₉ ON ₂ SBr	44.45	3.05	9.43	44.66	3.14	9.67
2-C ₄ H ₃ O	Cl	133	37.0 ^{*2}		C ₉ H ₇ O ₂ N ₂ SCl	44.54	2.91	11.59	44.78	3.14	12.00
2-C ₄ H ₃ S	Cl	170	23.3	60.0 ^{*2}	C ₉ H ₇ ON ₂ S ₂ Cl	41.77	2.73	10.83	41.78	2.83	11.08

*1 All melting points are uncorrected.

*2 Analytical values shown are for the products prepared by the methods with asterisks.

† Method A : Benzylthiolation of I or I'. Method B : Benzylation of IV or IV'.

TABLE 5 Yields of 4,5-Bis(benzylthio)-3-pyridazones (II) prepared by various methods

Ar	Yield, %		
	Method A†	Method B ₁ †	Method B ₂ †
C ₆ H ₅	69.1, 88.2 [*]	80.0	60.0
2-C ₄ H ₃ S	63.7	35.4	70.0

* Bromo derivative, and in other cases chloro derivative, was used as starting material in Method A.

† Method A: Benzylthiolation of V_i. Method B₁: Benzylation of III_i. Method B₂: Dibenylation of VI

III, which is rather weak in intensity but well-defined, and completely disappeared when these compounds are S-benzylated.

Subsequent to the above fact, a direct structural proof of III_a for the compound, 4-mercapto-5-benzylthio-3-pyridazone, as a representative of the III_i type compounds, was carried out as follows: The compound, V_{i=a} or V'_{i=a}, whose structure was tentatively presumed to be 4-halo-5-benzylthio-3-pyridazone as described above, from which the compound III_a being derivable, was easily converted to 4 (or 5)-morpholino-5(or 4)-benzylthio-3-pyridazone (m. p., 191°, yield, 79.0%) (VII), by heating under reflux with an excess

of morpholine, and this compound was desulfurized by heating with Raney-nickel in dimethylformamide to form 4-morpholino-3-pyridazine (m. p., 175°, yield, 44.2%) (VIII). Structural assignment of the compound to VIII is attributed to the isomerism relationship between VIII and 5-morpholino-3-pyridazine (m. p., 257°) (XI) (chart 2). The structure of XI is unambiguous because this compound is derived from 4-chloro-5-morpholino-¹¹⁾ (m. p., 236°) (IX) or 4-bromo-5-morpholino-3-pyridazine (m. p., 157°) (IX'), as well as from 3-chloro-4-morpholino-6-pyridazine (m. p., 200°) (XIV), by catalytic dechlorination with palladium on charcoal. (chart 3)

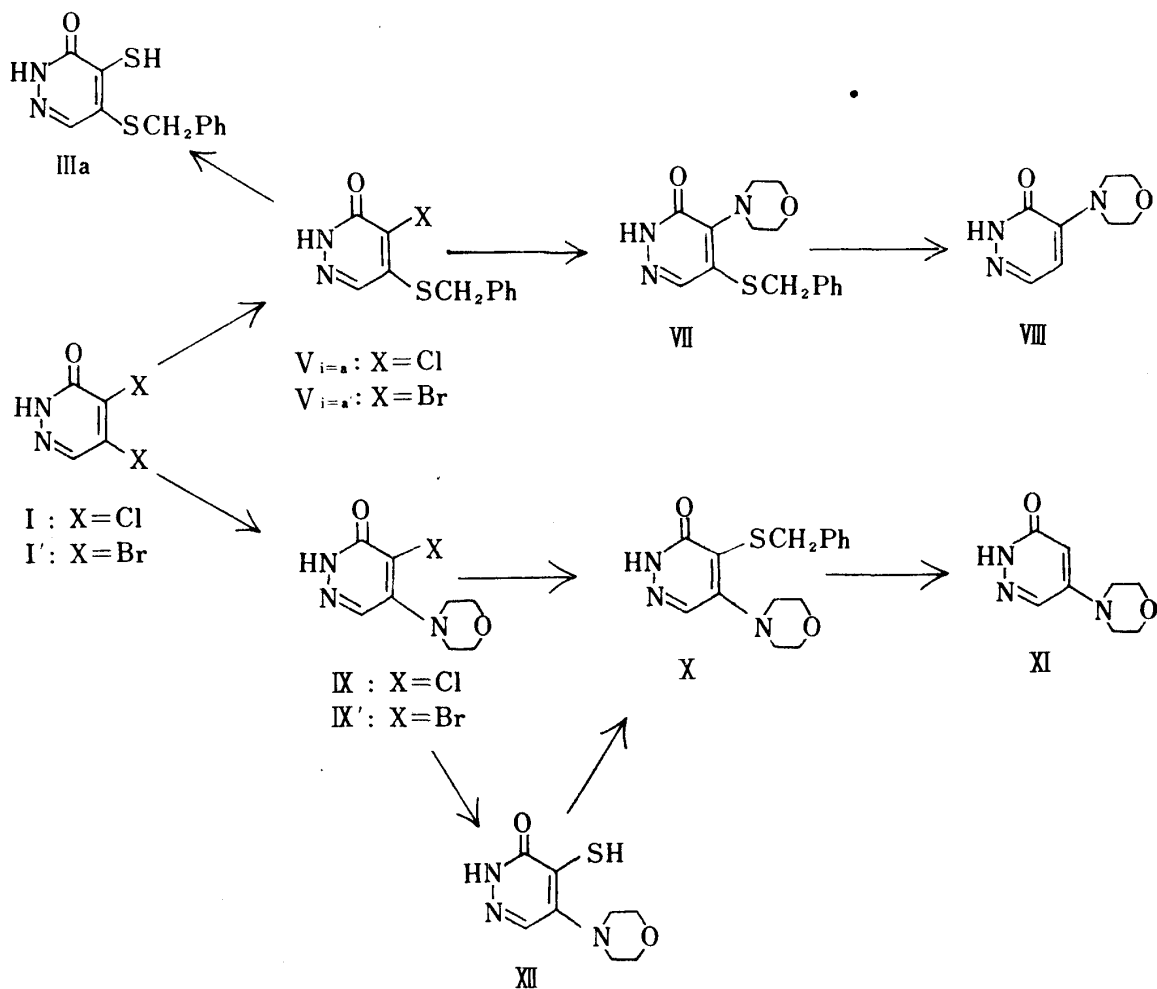


chart 2

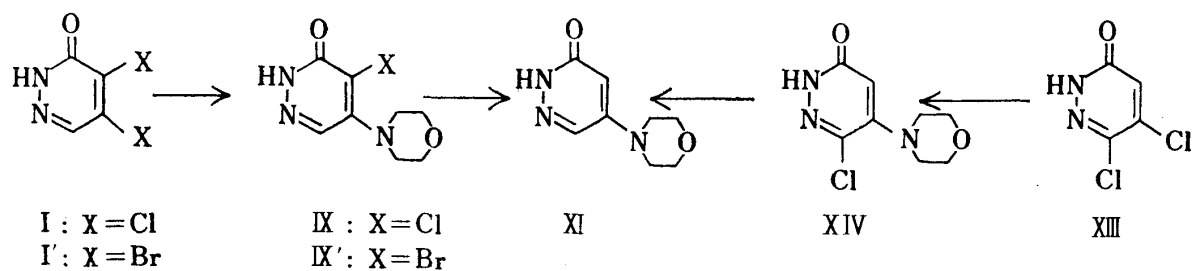


chart 3

By the way, the compound IX or XIV was prepared by heating I or 3,4-dichloro-6-pyridazone, (XIII)¹³⁾, respectively, with morpholine in ethanol. The compound XI was also formed by desulfurization of 4-benzylthio-5-morpholino-3-pyridazone (X) (m. p., 201°) by heating with Raney-nickel in dimethylformamide, and the latter was obtained from IX or IX', by benzylthiolation or via 4-mercapto-5-morpholino-3-pyridazone XII (m. p., 171°) derived from IX or IX', by S-benylation. (chart 2)

Furthermore to ascertain an isomerism relationship between the two compounds VIII and XI, each of them was converted to the same compound, 4-morpholino-pyridazine (m. p., 89°) (XVI), by way of chlorination followed by catalytic dechlorination with palladium on charcoal, viz., via 4-morpholino-3-chloropyridazine (m. p., 122°) (XV) and 5-morpholino-3-chloropyridazine (m. p., 115°) (XVII), respectively, as shown in the chart 4.

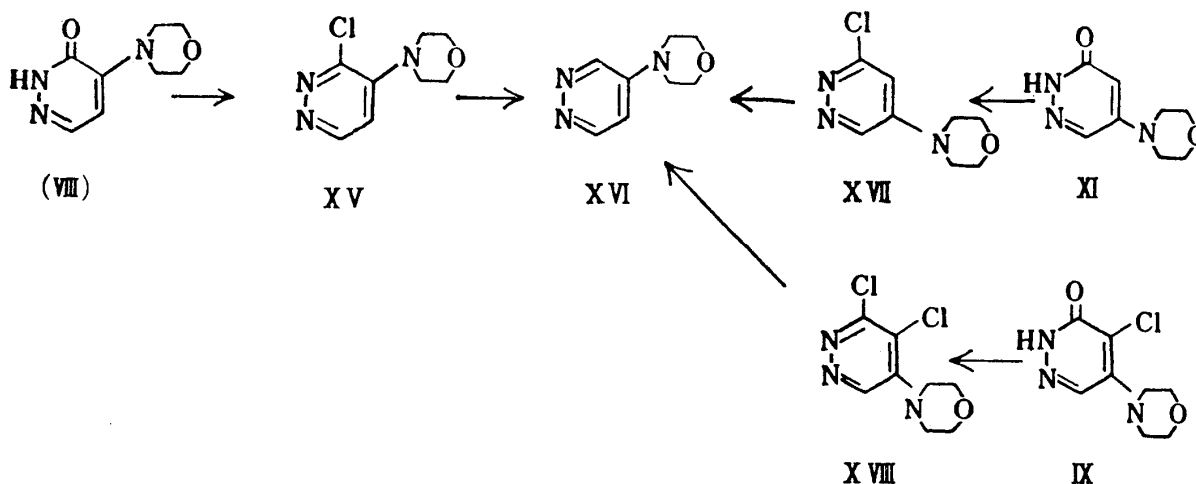
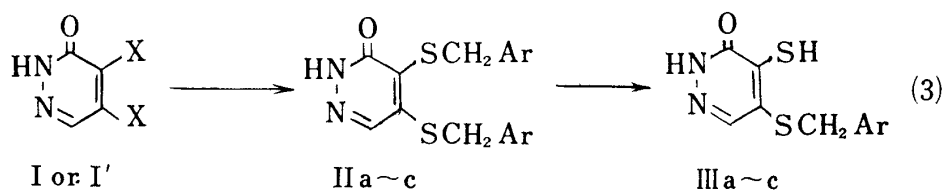


chart 4

The compound XVI, was also derived by catalytic dechlorination of 3,4-dichloro-5-morpholino pyridazine (m. p., 107.5°) (XVIII) prepared by chlorinating IX, from which XI being derivable.

On the basis of the experimental facts mentioned hitherto, it may be reasonable to assign the compounds, IV, IV', V_{i=a}, and V'_{i=a'} to 4-chloro-5-mercapto-, 4-bromo-5-mercapto-, 4-chloro-5-benzylthio-, and 4-bromo-5-benzylthio-3-pyridazone, respectively, and consequently the compound III_a to 4-mercapto-5-benzylthio-3-pyridazone. It seems also reasonable, by analogical inference, to assume the compounds III_b and III_c being assignable to 4-mercapto-5-(2-furfurylthio)-3-pyridazone and 4-mercapto-5-(2-thenylthio)-3-pyridazone, respectively, and each of the compounds III_{a~c} formed as by-products in the reaction (Eqn. 2) being derived presumably by the selective debenylation from the corresponding one of the compounds II_{a~c} initially formed in the course of the reaction.

Finally in order to confirm whether such debenylation really occurs in the course of the reaction, II_a was subjected to the reaction with an excess of sodium benzylthiolate in a similar reaction condition as mentioned above, to produce III_a, in a rather lower yield, but undoubtedly. (Eqn. 3)



It is concluded that a reaction of 4,5-dihalo-3-pyridazone with an excess of sodium benzylthiolate in the presence of sodium amide in dry toluene, by heating them under reflux for a rather longer time, always forms 4-mercapto-5-benzylthio-3-pyridazone together with 4,5-bis(benzylthio)-3-pyridazone, in other words, in the course of the reaction, the benzylthiolation never fails to be followed by the debenzylation which occurs selectively on the benzylthiol group attached to the position 4, not on that to the position 5, of the pyridazone ring.

Further work is in progress on the reaction of 4,5- and 4,6-dihalo-N²-substituted-3-pyridazones with sodium benzylthiolate, and will be reported at a later date.

Experimental

I. A reaction of 4,5-dihalo-3-pyridazone with sodium benzylthiolate in aqueous alkaline ethanolic solution.

A. 4,5-Bis(benzylthio)-3-pyridazone (II_a)¹¹⁾ — a) 4,5-Dichloro-3-pyridazone (0.82g) was added to sodium benzylthiolate solution containing benzylisothiuronium chloride (2.02g) in a mixture of 5% sodium hydroxide solution (20ml.) and ethanol (20ml.), and the mixture was heated under reflux for 3 hours. On cooling the resulted solution, it was acidified with hydrochloric acid to precipitate crude 4,5-bis(benzylthio)-3-pyridazone (II_a)¹¹⁾ (m. p. 157°, 1.7g) which was collected, washed with water and dried. Purification was effected by recrystallization from ethanol to form almost colorless crystals (m. p. 160°, 1.6g) Anal. for II_a . (TABLE 1) I. R. $\text{cm}^{-1} : \nu_{c=0}$ 1630

b) Starting from 4,5-dibromo-3-pyridazone (1.27g) and sodium benzylthiolate in an aqueous alkaline ethanolic solution, and treating them in a similar manner as described above, II_a (mp. 160°, 1.56g) was obtained. Anal for II_a (TABLE 1)

B. 4,5-Bis(2-furfurylthio)-3-pyridazone (II_b)⁴⁾ — 4,5-Dichloro-3-pyridazone (0.82g) was allowed to react with sodium furfurylthiolate consisted of 2-furfurylmercaptan (1.14g) in a mixture of 5% sodium hydroxide solution (20ml) and ethanol (20ml), under an almost similar condition as described on the A, to yield 4,5-bis(2-furfurylthio)-3-pyridazone (mp. 97°, almost colorless crystals, 0.7g or 43.8% in yield). I. R. $\text{cm}^{-1} : \nu_{c=0}$ 1630. Anal. for II_b . (TABLE 1)

C. 4,5-Bis(2-thenylthio)-3-pyridazone (II_c)⁴⁾ — 4,5-Dichloro-3-pyridazone (1.65g) was added to the sodium thiolate solution containing 2-thenylisothiuronium chloride (4.17g) in a mixture of 5% sodium hydroxide solution (40ml) and ethanol (40ml), and the whole was allowed to react and treated similarly as

described above. 4,5-Bis(2-thenylthio)-3-pyridazone, recrystallized from ethanol (m.p. 121°, almost colorless crystals, 3.00g or 86.1% in yield) was obtained. I. R. cm^{-1} : $\nu_{\text{C=O}}$ 1630. Anal. for II_c. (TABLE 1)

II. *A reaction of 4,5-dihalo-3-pyridazone with an excess of sodium benzylthiolate in the presence of sodium amide in dry toluene by heating them under reflux for a rather long time.*

A. *A reaction of 4,5-dichloro-3-pyridazone with sodium benzylthiolate* a) — 4,5-dichloro-3-pyridazone (3.30g) was added to sodium benzylthiolate suspension in toluene previously prepared by heating benzylmercaptan (9.94g) with powdered sodium amide (3.50g) in dry toluene (200ml) for 30 minutes, and the mixture was heated under reflux for ca. 10 hours.

Reaction mixture was concentrated in a vacuum to dryness, residual solid was treated with water (70ml), and the residual solid (A) was separated by filtration from the filtrate (B). The solid (A) was suspended in water and acidified with concd. hydrochloric acid to pH=ca.1. Collected solid was washed with water, dried, and recrystallized from ethanol to give 4,5-bis(benzylthio)-3-pyridazone (3.30g or 48.5% in yield), almost colorless crystals m.p. 160° underpressed on admixture with an authentic specimen.

The alkaline filtrate (B) was acidified with concd. hydrochloric acid to precipitate a solid which was collected, washed with water, and recrystallized from ethanol to give 4-mercapto-5-benzylthio-3-pyridazone (III_a) (1.00g or 20.0% in yield), greenish yellow crystals, m.p. 186° underpressed by admixture with the compound (m.p., 186°) derived from 4-chloro-5-benzylthio-3-pyridazone (VI_{i=a}). I. R. cm^{-1} : $\nu_{\text{C=O}}$ 1620; $\nu_{\text{S-H}}$ 2500. Anal. for III_a. (TABLE 2)

b) The two compounds, 4,5-bis(benzylthio)-3-pyridazone (m.p., 160°, 2.00g or 59.0% in yield) and 4-mercapto-5-benzylthio-3-pyridazone (m.p., 186°, 0.45g or 18% in yield) were obtained, starting from 4,5-dibromo-3-pyridazone (2.53g) by a similar treatment as described on the Method II, A-a.

B. *Reaction of 4,5-dibromo-3-pyridazone with sodium 2-furfurylthiolate* — 4,5-Bis(2-furfurylthio)-3-pyridazone (II_b) (m.p., 97°, 7.80g or 40.6% in yield) and 4-mercapto-5-(2-furfurylthio)-3-pyridazone (III_b) (m.p. 145°, greenish-yellow crystals, 2.70g or 19.1% in yield) were obtained by treatment of 4,5-dibromo-3-pyridazone (15.24g) with the sodium thiolate suspension, prepared from 2-furfurylmercaptan (27.36g) and sodium amide (10.50g) in dry toluene (600ml), similarly as described on the Method II, A-a.

Anal. Calcd. for C₁₄H₁₂O₃N₂S₂ (320.388): C, 52.32; H, 3.68; N, 8.72. Found: C, 52.40; H, 3.72; N, 8.83. M.p., 97° (II_b) was underpressed on admixture with a sample prepared by the Method I-A. IR for II_b cm^{-1} : $\nu_{\text{C=O}}$ 1630.

Anal. for III_b (TABLE 2) M.p. 145° (III_b) was underpressed admixture with a sample derived from 4-chloro-5-(2-furfurylthio)-3-pyridazone (VI_{i=b}). I. R. for III_b cm^{-1} : $\nu_{\text{C=O}}$ 1630, $\nu_{\text{S-H}}$ 2500.

C. *Reaction of 4,5-dibromo-3-pyridazone with sodium 2-thenylthiolate* — 4,5-Bis(2-thenylthio)-3-pyridazone (II_c) (m.p., 121°, 5.10g or 71.8% in yield) and 4-mercapto-5-(2-thenylthio)-3-pyridazone (III_c) (m.p., 153°, greenish-yellow crystals, 0.30g or 5.9% in yield), were obtained by treating 4,5-dibromo-3-pyridazone (5.08g) with the sodium thiolate, prepared from 2-thenylmercaptan (10.40g) and sodium amide (3.50) in dry toluene (200ml), similarly as described on the Method II-A.

Anal. Calcd. for $C_{14}H_{12}ON_2S_4$ (352.516) : C, 47.69; H, 3.43; N, 7.94. Found : C, 47.73; H, 3.63; N, 8.10 m. p. 121°C (III_c) showed no depression on admixture with a sample prepared by the Method I-C. I. R. for II_c cm^{-1} : $\nu_{\text{C=O}}$ 1630.

Anal. for III_c (TABLE 2) M. p. 153° (III_c) was undepressed on admixture with a sample prepared from 4-chloro-5-(2-thenylthio)-3-pyridazone (VI_c). I. R. for III_c cm^{-1} : $\nu_{\text{C=O}}$ 1630; $\nu_{\text{S-H}}$ 2500.

III. A reaction of 4,5-dihalo-3-pyridazone with sodium hydrosulfide in ethanol at a room temperature.

A. 4-Chloro-5-mercapto-3-pyridazone (IV) — 4, 5-Dichloro-3-pyridazone (8.25g) was added to the solution containing 32% aq. sodium hydrosulfide solution (26.3g) in ethanol (50ml), and the whole was stirred at a room temperature. Spontaneous evolution of heat was noticed, while stirring deposited sodium chloride increased the amount and stirring was continued for 2 hr.

Reaction mixture was filtered to remove deposited salt, the filtrate (yellow sol.) was concentrated in a vacuum, the residue was dissolved in water (50ml.) and acidified with concentrated hydrochloric acid (ca. 12ml.) to pH=ca. 1 to precipitate the product which was collected, washed with a small amount of water and dried in a vacuum desiccator. Crude 4-chloro-5-mercapto-3-pyridazone (m. p. $>300^\circ$ and almost colorless crystals) amounted 6.8g. (83.6% in yield). Purification was effected by alternate dissolving in an alkaline solution and precipitating by acidification with concentrated hydrochloric acid.

Anal. Calcd. for $C_4H_3ON_2\text{SCl}$ (162.603) : C, 29.54; H, 1.86; N, 17.23: Found. C, 29.84; H, 1.93; N, 17.41. I. R. cm^{-1} : $\nu_{\text{S-H}}$ 2550 and $\nu_{\text{C=O}}$ 1650

B. 4-Bromo-5-mercapto-3-pyridazone (IV') — This compound (m. p. $>300^\circ$ and almost colorless crystals, 8.6g or 84.1% in yield) was obtained, starting from 4,5-dibromo-3-pyridazone (12.7g.) by treating similarly as described above.

Anal. Calcd. for $C_4H_3ON_2\text{SBr}$ (207.066) : C, 23.40; H, 1.47; N, 12.53. Found: C, 23.56; H, 1.37; N, 13.76. I. R. cm^{-1} : $\nu_{\text{S-H}}$ 2550 and $\nu_{\text{C=O}}$ 1650.

IV. 4-Halo-5-(benzylthio)-3-pyridazones (VI)

A. 4-Halo-5-benzylthio-3-pyridazone (VI_a and VI_a') — a) 4,5-Dichloro-3-pyridazone (3.3g.) was dissolved in an alkaline solution consisted of 5% sodium hydroxide sol. (80ml.) and concd. aq. ammonia (64ml.) and to the solution benzylmercaptan (4.97g.) in ethanol (150ml.) was added. The mixture was stirred at a room temperature for 2 hr.

Reaction mixture was acidified with a mixed acid (glacial acetic acid and concd. hydrochloric acid) and concentrated in a vacuum. Precipitated solid was collected, washed with water, and dried. Dried material was recrystallized twice from ethanol to give 4-chloro-5-benzylthio-3-pyridazone (m. p. $191-193^\circ$, 1.4g. or 27.0% in yield) (VI_a). Further purification was effected by recrystallization again from ethanol to yield an analytical specimen, m. p. 197° , unchanged by admixture with a sample prepared by the method IV, A-b.

Anal. Calcd. for $C_{11}H_9ON_2\text{SCl}$ (252.721) : C, 52.28; H, 3.59; N, 11.09. Found: C, 52.23; H, 3.75; N, 11.31.

b) Benzyl chloride (7.54g.) was added to the sodium thiolate solution containing 4-chloro-5-mercapto-3-pyridazone (7.80g.) (IV) in a mixture of 5% sodium hydroxide sol. (93ml.), concd. aq. ammonia (90ml.)

and ethanol (183ml.) and the whole was stirred at a room temperature for 2 hr.

Reaction mixture was filtered and an alkaline filtrate was treated almost similarly as the Method IV A-a to give 4-chloro-5-benzylthio-3-pyridazone (m. p. 193-194°, 5.0g, or 41.3% in yield) ($V_{i=a}$). Analytical specimen melted at 197° (from ethanol) and mixed m. p. by admixture with a sample prepared by the Method IV, A-a was unchanged. Anal. for this product. (TABLE 4).

a') 4-Bromo-5-benzylthio-3-pyridazone (m. p. 197°, 1.7g. or 28.7% in yield) ($V_{i=a'}$) was obtained by benzylthiolation of 4,5-dibromo-3-pyridazone (5.8g) with sodium benzylthiolate solution (benzylmercaptan, 4.97g.) in a similar manner as described on the Method IV, A-a. Mixed m. p. on admixture with a sample prepared by the Method IV, A-b' was 197°.

b') 4-Bromo-5-benzylthio-3-pyridazone (m. p. 197°, 2.7g. or 45.4% in yield) ($V_{i=a'}$) was obtained by benzylating 4-bromo-5-mercapto-3-pyridazone (4.14g) with benzylchloride (2.53g.) in a similar way as described in the case IV, A-b. Anal. for this product (TABLE 4). Mixed M. p. by admixture with a sample prepared by the method IV, A-a' was 197°.

B. 4-Chloro-5-(2-furfurylthio)-3-pyridazone ($V_{i=b}$) — The compound ($V_{i=b}$) (m. p. 133°, 4.5g. or 37.0% in yield) was obtained by furfurylthiolation of 4,5-dichloro-3-pyridazone (8.25g.) with sodium 2-furfurylthiolate solution (2-furfurylmercaptan, 11.4g.) similarly as in the case of IV, A-a. Anal. for the product (TABLE 4).

C. 4-Chloro-5-(2-thenylthio)-3-pyridazone ($V_{i=c}$) — a) The compound ($V_{i=c}$) (m. p. 170°, 0.6g. or 23.3% in yield) was obtained by thenylthiolation of 4,5-dichloro-3-pyridazone (1.65g.) with sodium 2-thenylthiolate solution (2-thenylisothiuronium chloride (4.2g) in a mixture of 5% sodium hydroxide sol. (40ml.), concd. aq. ammonia (30ml.) and ethanol (40ml.), similarly as the case of IV, A-a. Mixed m. p. by admixture with a sample prepared by the method IV, C-b was 170°.

b) — The compound ($V_{i=c}$) (m. p. 170°, 3.1g. or 60.0% in yield) was obtained by thenylation of 4-chloro-5-mercapto-3-pyridazone (3.25g.) with 2-thenyl chloride (5.30g.) in a similar manner as described on the method IV, A-b. Anal. for the product. (TABLE 4) Mixed m. p. by admixture with a sample prepared by the method IV, C-a was 170°.

V. 4-Mercapto-5-benzylthio-3-pyridazones (III_i)

A. 4-Mercapto-5-benzylthio-3-pyridazone (III_{i=a}) — a) 4-chloro-5-benzylthio-3-pyridazone ($V_{i=a}$) (0.5g.) was added to the sodium hydrosulfide solution containing 32% aq. sodium hydrosulfide sol. (0.7g.) in ethanol (30ml.) and the mixture was heated under reflux for 5 hr. Excess of ethanol was removed in a vacuum, residual solid was treated with water and filtered. Filtrate was acidified with concd. hydrochloric acid to pH=ca.1. Precipitated solid was collected by filtration, washed with water and recrystallized from ethanol to give 4-mercapto-5-benzylthio-3-pyridazone (III_{i=a}) (m. p. 186°, 0.35g. or 75.0% in yield) in greenish yellow crystals. Mixed m. p. by admixture with a sample (m. p. 186°) (III_a) formed as a by-product in the reaction 2 was 186°.

Anal. Calcd. for $C_{11}H_{10}ON_2S_2$ (250.338) : C, 52.77; H, 4.03; N, 11.19. Found : C, 52.90; H, 3.93; N, 11.08.

b) 4-Bromo-5-benzylthio-3-pyridazone ($V_{i=a'}$) (1.49g) was allowed to react with sodium hydrosulfide solution in a similar manner as described on the method V, A-a, to produce the compound $III_{i=a}$ (1.10g or 88.0% in yield), m.p. 186° undepressed on admixture with an authentic specimen, in greenish yellow crystals.

B. 4-Mercapto-5-(2-furfurylthio)-3-pyridazone ($III_{i=b}$)

4-Chloro-5-(2-furfurylthio)-3-pyridazone ($V_{i=b}$) (1.10g) was allowed to react with sodium hydrosulfide solution (32% NaSH sol. (1.70g) in ethanol (75ml)) similarly as in the case of the V, A-a, to form 4-mercapto-5-(2-furfurylthio)-3-pyridazone ($III_{i=b}$) (0.75g or 68.8% in yield), m.p. 145° undepressed on admixture with a sample (III_b) formed as a by-product in the reaction 2, in greenish yellow crystals.

C. 4-Mercapto-5-(2-thenylthio)-3-pyridazone ($III_{i=c}$)

By treating 4-chloro-5-(2-thenylthio)-3-pyridazone ($V_{i=c}$) (1.29g) with sodium hydrosulfide solution (32% NaSH sol. (11.70g) in ethanol (75ml)), similarly as described on the method V, A-a, 4-mercapto-5-(2-thenylthio)-3-pyridazone ($III_{i=c}$) (0.9g or 73.2% in yield), m.p. 153° undepressed on admixture with a sample (III_c) formed as a by-product in the reaction 2, in greenish yellow crystals, was obtained.

VI. 4,5-Bis(benzylthio)-3-pyridazones by other miscellaneous preparations.

A. 4,5-Bis(benzylthio)-3-pyridazone — a) 4-Chloro-5-benzylthio-3-pyridazone ($V_{i=a}$) (0.51g) was added to sodium benzylthiolate solution containing benzylmercaptan (0.30g) in a mixture of 5% sodium hydroxide solution (4ml) and ethanol (4ml), and the whole was heated under reflux for 3 hours.

Reaction mixture was acidified with concd. hydrochloric acid, precipitated product was collected, washed with water, dried and recrystallized from ethanol. 4,5-Bis(benzylthio)-3-pyridazone (0.47g or 69.1% in yield), m.p. 160°C undepressed on admixture with a sample prepared by the method V A-c, was obtained.

b) 4,5-Bis(benzylthio)-3-pyridazone (0.60g or 88.2% in yield), m.p. 160°, was obtained by treating 4-bromo-5-benzylthio-3-pyridazone ($V_{i=a'}$) (0.59g) with sodium benzylthiolate, in a similar manner as described on the Method V, A-a.

c) 4-Mercapto-5-benzylthio-3-pyridazone (III_a) (0.50g) was dissolved in a mixture of 5% sodium hydroxide solution (4ml) and ethanol (7ml) and to the solution was added benzylchloride (0.28g) with stirring.

The mixture was kept stirred at room temperature for 5 hours, and colorless crystals separated meanwhile increased gradually. Reaction mixture was acidified with concd. hydrochloric acid and precipitated solid were collected, washed with water, dried, and recrystallized from ethanol. 4,5-Bis(benzylthio)-3-pyridazone, m.p. 160° undepressed on admixture with a sample prepared by the method VI, A-a, 0.55g or 80% in yield, was obtained.

Calcd. for $C_{18}H_{16}ON_2S_2$ (340.456) : C, 63.32; H, 4.74; N, 8.23. Found: C, 63.63; H, 4.73; N, 8.59.

d) A mixture of 4-chloro-5-mercapto-3-pyridazone (IV) (0.81g), 32% aq. sodium hydrosulfide (1.70g) and ethanol (75ml) were placed in a closed glass tube and heated in a boiling water bath for 10 hours. Reaction mixture was concentrated in a vacuum to dryness, residual solid was dissolved in water and filtered. Alkaline filtrate was acidified with concd. hydrochloric acid to precipitate crude 4,5-dimercapto-3-pyridazone

(VI) (m. p. $> 300^{\circ}$, pale yellow crystals, 0.58g). Starting from 4-bromo-5-mercapto-3-pyridazone (IV') (1.04g) and similarly treating as above, the same product (VI) (0.57g) was obtained.

Crude 4,5-dimercapto-3-pyridazone (0.68g) was dissolved in 5% sodium hydroxide solution (16ml) and to the solution was added benzylchloride (1.26g) in ethanol (16ml) with stirring. The mixture was stirred at room temperature for 3 hours, and then acidified with concd. hydrochloric acid. Precipitated product was collected, washed with water, dried, and recrystallized from ethanol to give 4,5-bis(benzylthio)-3-pyridazone (0.85g or 60.0% in yield), m. p. 160° showed no depression on admixture with a authentic specimen.

Anal. Calcd. for $C_{18}H_{16}ON_2S_2$ (340.456) : C, 63.32; H, 4.74; N, 8.23. Found : C, 63.44; H, 4.83; N, 8.35.

B. 4,5-Bis(2-thenylthio)-3-pyridazone (II_c) — a) 4-Chloro-5-(2-thenylthio)-3-pyridazone (VI=c) (0.52g) was heated with sodium 2-thenylthiolate solution containing 2-thenylisothiuronium chloride (0.84g) in a mixture of 5% sodium hydroxide solution (8ml) and ethanol (8ml), under reflux for 3 hours.

Reaction mixture was acidified with glacial acetic acid, precipitated solid was collected, washed with water, dried, and recrystallized from ethanol. 4,5-Bis(2-thenylthio)-3-pyridazone (0.45g or 63.7% in yield) melted at 121° undepressed on admixture with an authentic specimen prepared by the method on the reaction 1, was obtained.

b) 2-Thenylchloride (0.30g) was added to the sodium thiolate solution containing 4-mercapto-5-(2-thenylthio)-3-pyridazone (III_{i=c}) (0.30g) in a mixture of 5% sodium hydroxide solution (4ml) and ethanol (4ml) and the whole was allowed to stand, with occasionally shaking, at room temperature for 1 hour.

Almost similarly treating the reaction mixture as described above, 4,5-bis(2-thenylthio)-3-pyridazone (0.15g or 35.4% in yield) melting at 121° undepressed on admixture with an authentic specimen, was obtained.

VII. 4-(4-Morpholino)-3-pyridazone (VIII) and 5-(4-morpholino)-3-pyridazone (XI)

A. 4-(4-Morpholino)-5-benzylthio-3-pyridazone (VII) — 4-Bromo-5-benzylthio-3-pyridazone (VI=a') (0.63g) and morpholine (4.35g) were heated together at $150-160^{\circ}$ (bath temperature) for 4 hours. On cooling the reaction mixture, it was diluted with water (30ml) to precipitate colorless solid which was collected, washed with water, and recrystallized from ethanol. 4-(4-morpholino)-5-benzylthio-3-pyridazone (VII) (0.6g or 79.2% in yield) melted at 191° and shaped in pale yellow crystals.

Anal. Calcd. for $C_{15}H_{17}O_2N_3S$ (303.376) : C, 59.38; H, 5.65; N, 13.85. Found : C, 59.33; H, 5.78; N, 14.02.

The same compound, (VII) (m. p., 191° , 2.60g or 87.1% in yield) was also obtained, starting from 4-chloro-5-benzylthio-3-pyridazone (VI=a) (2.53g), by the similar treatment as described above.

B. 4-(4-Morpholino)-3-pyridazone (VIII) — 4-(4-Morpholino)-5-benzylthio-3-pyridazone (VII), (1.00g) was added to a mixture of Raney-nickel (4.0g), dimethylformamide (5ml) and water (1ml) and the whole was heated to $120-140^{\circ}$ (bath temperature). Heating within the temperature range was continued for 16 hours. Reaction mixture was filtered while hot, residual solid was washed with hot ethanol several times and alcoholic washings were combined to the filtrate. Combined solution was concentrated in a vacuum to dryness

and the residue was recrystallized from ethanol to give 4-(4-*morpholino*)-3-*pyridazone* (VIII) (m. p., 176°, 0.22g or 36.8% in yield) in colorless crystals.

Anal. Calcd. for $C_8H_{11}O_2N_3$ (181.192) : C, 53.03; H, 6.12; N, 23.19. Found : C, 52.84; H, 6.18; N, 23.37.

C. 4-*Benzylthio*-5-(4-*morpholino*)-3-*pyridazone* (X) — 4-Chloro-5-(4-*morpholino*)-3-*pyridazone* (IX) (2.16g) and 32% aq. sodium hydrosulfide solution (7.00g) were placed in a closed glass tube and it was heated in a boiling water bath for 10 hours.

On cooling the reaction mixture, deposited solid was collected, dissolved in water (80ml) and filtered. Alkaline filtrate was acidified with concd. hydrochloric acid (2ml), precipitated product was collected, washed with water and recrystallized from ethanol. 4-*Mercapto*-5-(4-*morpholino*)-3-*pyridazone* (XII), m. p. 171°, yellowish green crystals, was obtained. Yield, 1.68g (78.8%).

Anal. Calcd. for $C_8H_{11}O_2N_3S$ (213.258) : C, 45.05; H, 5.19; N, 19.71. Found : C, 44.96; H, 5.27; N, 19.88.

I. R. cm^{-1} : ν_{S-H} 2505; $\nu_{C=O}$ 1630

The same compound (XII) (1.25g) was also prepared by treating 4-*bromo*-5-(4-*morpholino*)-3-*pyridazone* (IX') (2.60g) in a similar manner as described above.

Benzylchloride (0.76g) was added to the sodium thiolate solution containing 4-*mercapto*-5-(4-*morpholino*)-3-*pyridazone* (XII) (0.64g) in a mixture of 5% sodium hydroxide solution (4.8ml), 28% aq. ammonia (4.8ml) and ethanol (10ml) and the whole was allowed to stand at room temperature with occasionally skaking for 1.5 hours.

Reaction mixture was acidified with concd. hydrochloric acid to precipitate the product which was collected, washed with water, dried, and recrystallized from ethanol. 4-*Benzylthio*-5-(4-*morpholino*)-3-*pyridazone* (X) (m. p. 201°, 0.7g or 77.0%) was obtained and this was identical in any respect with the compound (X) (m. p. 201°) prepared by benzylthiolation of 4-*bromo*-5-(4-*morpholino*)-3-*pyridazone* (IX') in an anhydrous reaction condition (sodium amide in dry toluene) at rather elevated temperature.

Anal. Calcd. for $C_{15}H_{17}O_2N_3S$ (303.376) : C, 59.38; H, 5.65; N, 13.85. Found : C, 59.44; H, 5.89; N, 14.11.

I. R. cm^{-1} : $\nu_{C=O}$ 1630

D. 5-(4-*Morpholino*)-3-*pyridazone* (XI) — a) A mixture of 4-*bromo*-5-(4-*morpholino*)-3-*pyridazone* (IX') (1.30g), sodium hydroxide (0.40g) in water (70ml) and 5% palladium on charcoal (0.50g) was hydrogenated at a room temperature and atmospheric pressure. When theoretical amount of hydrogen was absorbed, the catalyst was removed by filtration from the reaction mixture, washed with water and the washings were combined to the filtrate. Combined alkaline solution was neutralized with glacial acetic acid and concentrated in vacuo to dryness. Residual solid was collected, washed with a small amount of water and recrystallized from ethanol to give 5-(4-*morpholino*)-3-*pyridazone* (XI) (m. p. 260°, 0.40g) in colorless crystals. Mixed melting point on admixture with 4-(4-*morpholino*)-3-*pyridazone* (m. p. 176°) (VIII) showed a marked depression, although no depression in melting point was observed in admixture of any pair of the derivatives, the compound derived from IX or IX', the one from 3-chloro-4-(4-*morpholino*)-6-*pyridazone* (XIV) and the one from 4-(benzylthio)-5-(4-*morpholino*)-3-*pyridazone* (X).

Anal. Calcd. for $C_8H_{11}O_2N_3$ (181.192) : C, 53.03; H, 6.12; N, 23.19. Found : C, 52.77; H, 6.12; N, 23.20.

The same compound XI, (0.15g) was obtained by catalytic dechlorination of 4-*chloro*-5-(4-*morpholino*)-3-*pyridazone* (IX) (0.7g) in a similar manner.

b) By catalytic dechlorination of 3-*chloro*-4-(4-*morpholino*)-6-*pyridazone* (XIV) (0.40g), 5-(4-*morpholino*)-3-*pyridazone* (XI) (0.18g) was also obtained.

Anal. Calcd. for $C_8H_{11}O_2N_3$ (181.192) : C, 53.03; H, 6.12; N, 23.19. Found : C, 52.83; H, 6.07; N, 23.09.

c) 4-*Benzylthio*-5-(4-*morpholino*)-3-*pyridazone* (X) (1.0g) was desulfurized by heating with Raney-nickel (3.0g) in a mixture of dimethylformamide (5ml) and water (1ml), likewise as described on the VII-B, to produce 5-(4-*morpholino*)-3-*pyridazone* (XI), (0.1g), m. p., 260° undepressed on admixture with any sample prepared by the method VII-D-a or VII-D-b.

VIII. 4-(4-*Morpholino*)-*pyridazine* (XVI)

A. *Dechlorination of 3-chloro-4-(4-morpholino)-pyridazine (XV) to 4-(4-morpholino)-pyridazine (XVI) by catalytic hydrogenation* — 4-(4-*Morpholino*)-3-*pyridazone* (VIII) (1.0g) in phosphorous oxychloride (5ml) was heated at 110-115° (bath temperature) for 3 hours. On cooling the reaction mixture, it was poured onto crushed ice, resulted mixture was neutralized with 10% sodium hydroxide solution, alkaline solution was extracted with chloroform and the extract was dried over anhydrous sodium sulfate. Dried chloroform solution was concentrated in a vacuum to dryness and residual solid was recrystallized from ethyl acetate. 3-*Chloro-4-(4-morpholino)-pyridazine* (XV), m. p. 123° (0.55g or 50.0% in yield), colorless crystals, was obtained.

Anal. Calcd. for $C_8H_{10}ON_3Cl$ (199.641) : N, 21.05; Found : N, 21.21.

To a solution of 3-*chloro-4-(4-morpholino)-pyridazine* (XV) (0.37g) in a mixture of 5% sodium hydroxide solution (3ml) and ethanol (25ml), 5% palladium on charcoal (0.2g) was added and the mixture was hydrogenated at a room temperature and atmospheric pressure. When absorption of hydrogen stopped, the catalyst was removed by filtration from the reaction mixture, the filtrate was acidified with concd. hydrochloric acid, and acidic solution was concentrated in a vacuum. Concentrated solution was basified again with dilute sodium hydroxide solution, extracted with chloroform and the extract was dried over anhydrous sodium sulfate. Chloroform solution was concentrated in vacuo to dryness and the residue was recrystallized from ethyl acetate. 4-(4-*Morpholino*)-*pyridazine* (XVI) *hemi-hydrate*, m. p. 89° undepressed on admixture with any sample prepared from 3-*chloro-5-(morpholino)-pyridazine* (XVII) or from 3,4-*dichloro-5-(morpholino)-pyridazine* (XVIII) by catalytic dechlorination, weighed 0.16g (37.9% in yield).

This compound formed a picrate (m. p. 191°).

Anal. Calcd. for $C_8H_{11}ON_3 \cdot \frac{1}{2}H_2O$ (174.202) : C, 55.15; H, 6.97; N, 24.12. Found : C, 54.70; H, 6.86; N, 24.39.

Anal. Calcd. for $C_{14}H_{14}O_8N_6$ (394.302) : C, 42.64; H, 3.58; N, 21.32. Found : C, 42.94; H, 3.58; N, 21.14.

B. *Dechlorination of 3-chloro-5-(4-morpholino)-pyridazine (XVII) to 4-(4-morpholino)-pyridazine (XVI) by catalytic hydrogenation.* — 5-(4-*Morpholino*)-3-*pyridazone* (XI) (2.0g) was chlorinated,

similarly in the case of the compound VIII, by heating with phosphorous oxychloride (10ml) to produce 3-chloro-5-(4-morpholino)-pyridazine (XVII), m. p. 114°, 1.0g (45.7% in yield) in colorless crystals.

Anal. Calcd. for $C_8H_{10}ON_3Cl$ (199.641) : C, 48.13; H, 5.05; N, 21.05. Found : C, 48.44; H, 5.24; N, 20.90.

3-Chloro-5-(4-morpholino)-pyridazine (XVII) (0.85g) was dechlorinated in a similar manner as described on the compound XV, 4-(4-morpholino)-pyridazine (XVI) *hemi-hydrate* (m. p. 89°), 0.40g was obtained. Either this compound or its picrate (m. p., 191°) was identical with the corresponding sample prepared from the compound XV, respectively.

Anal. Calcd. for $C_8H_{11}ON_3 \cdot \frac{1}{2}H_2O$ (174.202) : C, 55.15; H, 6.97; N, 24.12. Found : C, 54.84; H, 6.83; N, 24.02.

Anal. Calcd. for $C_{14}H_{14}O_8N_6$ (394.302) : C, 42.64; H, 3.58; N, 21.32. Found : C, 42.85; H, 3.70; N, 21.47.

C. *Dechlorination of 3,4-dichloro-5-(4-morpholino)-pyridazine (XVIII) to 4-(4-morpholino)-pyridazine (XVI) by catalytic hydrogenation.* — 4-Chloro-5-(morpholino)-3-pyridazone (IX) (8.0g) was chlorinated by heating with phosphorous oxychloride (40ml), in a similar manner as described on the method VIII-A, 3,4-dichloro-5-(4-morpholino)-pyridazine (XVIII), m. p. 107.5°, 4.02g, was obtained.

Anal. Calcd. for $C_8H_9ON_3Cl_2$ (234.090) : C, 41.04; H, 3.88; N, 17.95. Found : C, 41.29; H, 4.14; N, 18.02.

3,4-Dichloro-5-(Morpholino)-pyridazine (XVIII) (1.0g) was dechlorinated by catalytic hydrogenation, in a similar manner as described on the compound XV, 4-(4-morpholino)-pyridazine (XVI) *hemi-hydrate*, (0.3g) m. p. 89° undepressed on admixture with a sample prepared from the compound (XV), was produced and its picrate (m. p., 191°) was also identical with an authentic specimen.

Anal. Calcd. for $C_8H_{11}ON_3 \cdot \frac{1}{2}H_2O$ (174.200) : C, 55.15; H, 6.97; N, 24.12. Found : C, 55.34; H, 6.72; N, 24.12.

Anal. Calcd. for $C_{14}H_{14}O_8N_6$ (394.302) : C, 42.64; H, 3.58; N, 21.32. Found : C, 42.84; H, 3.64; N, 21.22.

IX. *A reaction of 4,5-bis(benzylthio)-3-pyridazone with sodium benzylthiolate in the presence of sodium amide in dry toluene.*

4,5-Bis(benzylthio)-3-pyridazone (3.40g) was added to the sodium benzylthiolate suspension in toluene, prepared by heating benzylmercaptan (2.48g) with sodium amide (0.88g) in dry toluene (50ml) under reflux for 30 minutes, and the whole was heated under reflux for ca. 10 hours. Reaction mixture was concentrated in a vacuum to dryness, to the residual cake water (40ml) was added and the mixture was fully triturated. Residual solid was separated by filtration, washed with water (40ml) and washings were combined to the alkaline filtrate.

The residual solid was suspended in water (50ml) and acidified with concd. hydrochloric acid, recollected by filtration, washed with water, dried, and recrystallized from ethanol. 4,5-Bis(benzylthio)-3-pyridazone (II_a) (m. p., 160°C), 2.60g, was recovered. The alkaline filtrate was acidified with concd. hydrochloric acid to precipitate solid which was washed with water, dried, and recrystallized from ethanol. 4-Mercapto-5-benzylthio-3-pyridazone (III_a) obtained weighed 0.10g (4.0% in yield) and melted at 186° undepressed on admixture with an authentic specimen.

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大野武男, 森逸男: クロロフルオレスセインの水銀反応について

Takeo Ohno, Itsuo Mori: Mercuration of Chlorofluoresceins

Mercuration of eight kinds of chlorofluorescein (2'-Cl, 4'-Cl, 2',4'-Cl, 4',5'-Cl, 2',7'-Cl, 2',5'-Cl, 2',4',5'-Cl, 2',4',7'-Cl-fl) was discussed and sterilizing effect of mercurichlorofluorescein was compared here.

フタレイン類の水銀化 (以下 Hg 化と略記) 反応に関しては古く White¹⁾ が fluorescein (以下 fl. と略記), Bromofl. (以下 Brfl. と略記) の Hg 化反応を報告し, 長瀬²⁾ 大野 は mercurochrome の製造条件について詳しく検討した. またフタレイン類の化合物の Hg 化合物の殺菌効果については Candeli³⁾ が eosin と Hg(OAc)₂ の反応生成物について, Petrilli, Rohatgi⁴⁾ らが数種の Brfl. の Hg化合物について報告している. しかるに Clfl.