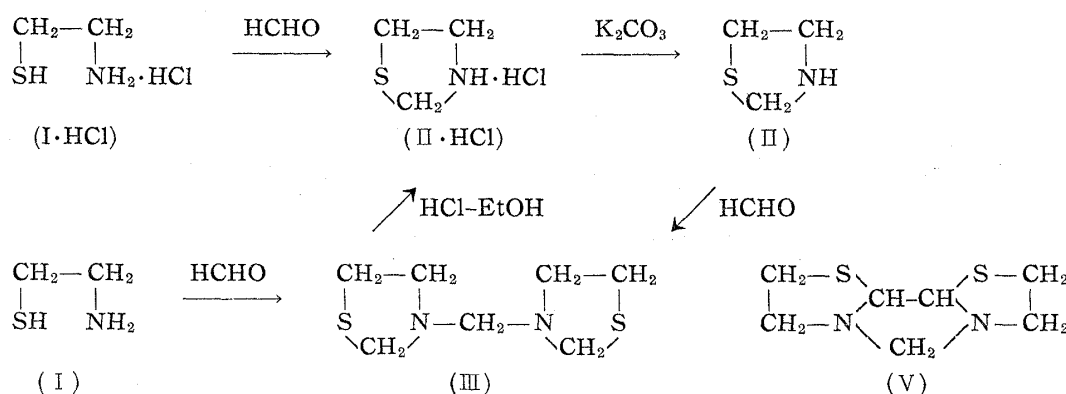


A New Development in the Formation Reaction of Thiazolidines from 2-Aminoalkanethiols and Carbonyl Compounds

It has already been reported that cysteamine (I) hydrochloride reacted with formaldehyde to give thiazolidine (II) hydrochloride.¹⁾ In the present work, the action of formaldehyde on free cysteamine (I) was examined and the reaction gave a new substance, m.p. 48~49°, which was characterized as 3,3'-methylene-dithiazoline (III) from the data of molecular weight determination (Calcd. for C₇H₁₄N₂S₂ : 190.34. Found : 183.20), elemental analyses (*Anal.* Calcd. for C₇H₁₄N₂S₂ : C, 44.17; H, 7.41; N, 14.72. Found : C, 44.14; H, 7.32; N, 14.58), and infrared spectrum (no absorption band due to -NH-), and from the formation of (II)·hydrochloride and formaldehyde on treatment with ethanolic hydrochloric acid. (III) was also formed by the action of formaldehyde on (II).

Treatment of (I) with other carbonyl compounds, such as acetaldehyde, acetone, cyclohexanone, and benzaldehyde, did not give the corresponding 3,3'-methylene-di compounds like (III), but gave the corresponding simple thiazolidines which were not converted to the 3,3'-methylene-di compounds by the action of formaldehyde.



Treatment of 2,2'-dithiazolidine²⁾ (IV) with formaldehyde yielded perhydroimidazo[1,5-*b*:4,3-*b'*]dithiazole (V), m.p. 80~81°. (*Anal.* Calcd. for C₇H₁₂N₂S₂ : C, 44.65; H, 6.42; N, 14.88. Found : C, 44.43; H, 6.31; N, 14.82. No absorption band due to -NH- in its infrared spectrum). The two condensed forms of 2-aminocyclohexanethiol (VI) and their hydrochlorides³⁾ were analogously treated with formaldehyde and gave the following products which were in parallel with the case of (I) and its hydrochloride : DL-Cyclohexa[*d*]-thiazolidine (VII)·hydrochloride, *Anal.* Calcd. for C₇H₁₃NS·HCl : C, 46.78; H, 7.85; N, 7.79. Found (*trans*-form of m.p. 211~212°) : C, 46.43; H, 7.79; N, 7.93. (*cis*-form of m.p. 204~205°). C, 46.83, H, 7.83; N, 7.90.

3,3'-Methylenebis[cyclohexa[*d*]thiazolidine] (VIII). *Anal.* Calcd. for C₁₅H₂₆N₂S₂ : C, 60.40; H, 8.72; N, 9.40. Found (*trans*-form of m.p. 97~98°) : C, 60.50; H, 8.77; N, 9.51. Found (*cis*-form of m.p. 101~102°) : C, 60.30; H, 8.78; N, 9.33. Both *trans*- and *cis*-forms of (VIII) were decomposed respectively to (*trans*- and *cis*-(VII)) hydrochlorides and formaldehyde on treatment with ethanolic hydrochloric acid.

Subsequently, the reaction of 2-aminoalkanethiols with D-glucose was examined. The condensation product of DL-*trans*-2-aminocyclohexanethiol (*trans*-(VI)) and D-glucose was

1) S. Ratner, H. T. Clarke : J. Am. Chem. Soc., **59**, 200 (1937).

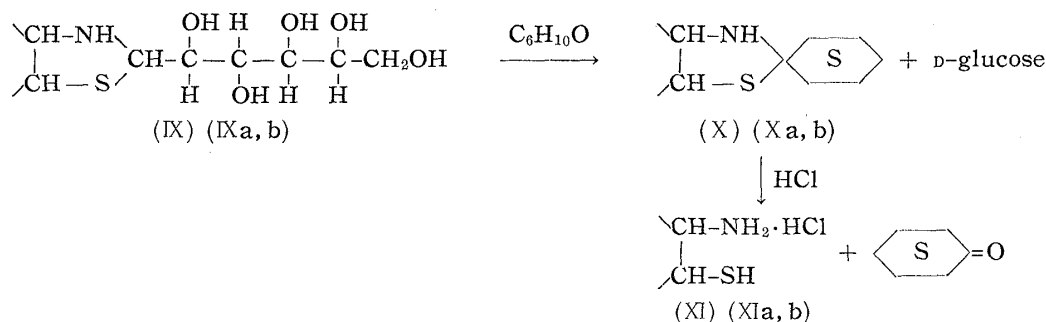
2) R. Kuhn, F. Drawert : Ann., **57**, 590 (1954).

3) T. Taguchi, M. Kojima : J. Am. Chem. Soc., **78**, 1464 (1956).

separated by recrystallization from ethanol into two products which were diastereomeric, m.p. 161~163°, $[\alpha]_D^{25} +15.6^\circ$, and m.p. 152~153°, $[\alpha]_D^{25} -61.4^\circ$ (*Anal.* Calcd. for $C_{12}H_{23}O_5NS$: C, 49.12; H, 7.90; N, 4.77. Found (for product of m.p. 161~163°): C, 49.05; H, 7.81; N, 4.74. Found (for product of m.p. 152~153°): C, 49.13; H, 7.93; N, 4.70).

Since the structure of the condensation product from 2-aminoethanethiol (I) and D-glucose has been established as 2-(D-gluco-1,2,3,4,5-pentahydroxypentyl)thiazolidine⁴⁾ (IX), it was deduced that the structure of the diastereomeric products might be 2-(D-gluco-1,2,3,4,5-pentahydroxypentyl) (+)-*trans*-cyclohexa[*d*]thiazolidine (IXa) and its (–)-isomer (IXb).

The direct derivation of the thiazolidine derivatives, (IX), (IXa), and (IXb) into 2-aminoalkanethiols (XI, XIa, and XIb) was impossible and hence the exchange of D-glucose in the



molecules with cyclohexanone was successfully effected by boiling them in cyclohexanone, thus yielding (+)-*trans*-spiro[cyclohexane-1,2'-cyclohexa[*d*]thiazolidine] (Xa) and its (–)-antipode (Xb) respectively from (IXa) and (IXb). Hydrochloride, m.p. 229~231°, $[\alpha]_D^{25} +65.6^\circ$, and m.p. 228~230°, $[\alpha]_D^{25} -65.6^\circ$ (*Anal.* Calcd. for $C_{12}H_{21}NS \cdot \text{HCl}$: C, 58.16; H, 8.95; N, 5.65. Found (for product of m.p. 229~231°): C, 58.40; H, 9.04; N, 5.67. Found (for product of m.p. 228~230°): C, 58.23; H, 9.04; N, 5.74).

(Xa) and (Xb) were easily hydrolyzed in hydrochloric acid solution to give (+)-*trans*-2-aminocyclohexanethiol hydrochloride, m.p. 215~217°, $[\alpha]_D^{25} +49.0^\circ$, and its (–)-antipode, m.p. 217~219°, $[\alpha]_D^{25} -49.1^\circ$ (*Anal.* Calcd. for $C_6H_{13}NS \cdot \text{HCl}$: C, 42.97; H, 8.41; N, 8.35. Found (for product of m.p. 215~217°): C, 43.25; H, 8.23; N, 8.64. Found (for product of m.p. 217~219°): C, 43.38; H, 8.14; N, 8.58). These experiments have established a new method for optical resolution available for other resolvable aminoalkanethiols and aminoalkanols.

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4) W. Bonner, W. Meyer: *Ber.*, **94**, 225 (1961).