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# Studies of Heterocyclic Compounds. X.[1] The Reaction of the Thiazolo-[3,2-*b*]pyridazinium Perchlorates with Potassium Cyanide

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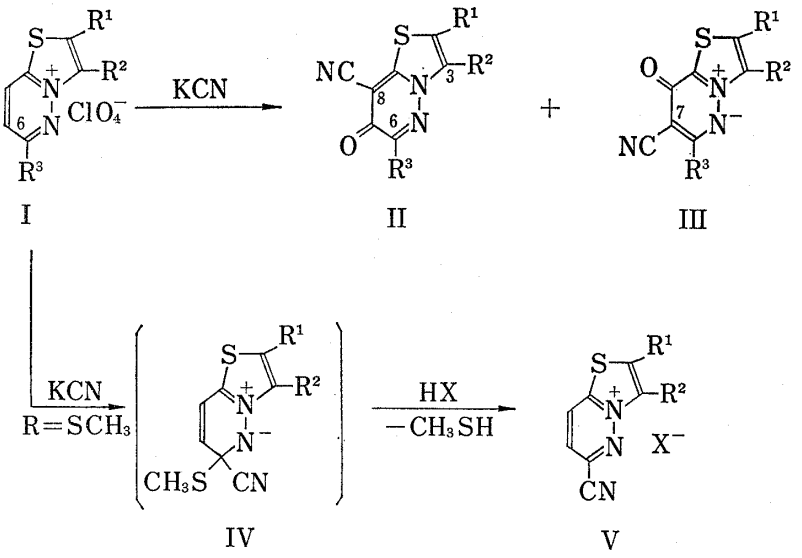
Treatment of thiazolo[3,2-*b*]pyridazinium perchlorates (I) with potassium cyanide in water-acetonitrile furnishes 8-cyano-4,7-dihydrothiazolo[3,2-*b*]pyridazine-7-ones (II) and anhydro-7-cyano-5,8-dihydro-8-oxothiazolo[3,2-*b*]pyridazinium hydroxides (III), the structure of which are elucidated by chemical properities, infrared, nuclear magnetic resonance, ultraviolet and mass spectrometry, and elemental analysis. Examination of the reaction by conducting under nitrogen or oxygen stream and with or without water as the solvent and by monitoring the presence of organic free radical by means of electron spin resonance spectroscopy suggests that the reaction is initiated by the nucleophilic attack of the cyanide either at $C_8$- or $C_7$-position of the pi-deficient thiazolo[3,2-*b*]pyridazinium system (I), followed by incorporation of the atmospheric oxygen to form hydroperoxide *via* radical anion species.

**Keywords**——nucleophilic addition; thiazolopyridazine derivatives; radical induced oxidative substitution; mass; NMR; ESR

We have reported the synthesis of 3,6-disubstituted thiazolo[3,2-*b*]pyridazin-4-ium perchlorates (I) and their chemical properties toward the hydroxide ion in the preceeding paper.[1] With respect to the reactivity of 3-mercaptothiazolo[3,2-*b*]pyridazinium salts and ylides, it was already presented to resist to electrophiles.[3] Now we wish to report the reaction of I with potassium cyanide which afforded unexpected products.

A large excess of potassium cyanide was added to 3,6-dimethylthiazolo[3,2-*b*]pyridazinium perchlorate (Ib) in the mixed solvent of acetonitrile and water (1 : 1 v/v), and the mixture was stirred at room temperature. After 6 hours' stirring, the thin-layer chromatography (TLC)




I II III IV V

Chart 1

1) Part IX: K. Arakawa, T. Miyasaka, K. Satoh, *Chem. Parm. Bull.* (Tokyo), **25**, 299 (1977).
2) Location: *Hatanodai, Shinagawa-ku, Tokyo.*
3) Y. Iwai, Dissertation for the Master's Degree, Showa University.

indicated that the spot of the starting material disappeared and the new spots were observed at *Rf* 0.57 and 0.35 (5% methanol–chloroform). The mixture was efficiently separated by column chromatography on silica gel. It was found by elemental analysis that rapidly eluting product (*Rf*=0.57) A (mp 238—238.5°) and slowly eluting product (*Rf*=0.35) B (mp 289—290°) had the same composition $C_9H_7ON_3S$. The infrared (IR) spectra of these products did not show remarkable differences; A showed bands at 2215 and 1595 $cm^{-1}$. The nuclear magnetic resonance (NMR) spectrum of A displayed a doublet signal at 2.44 (H–C=C–C$\underline{H}_3$, $J$=1.1 Hz) coupled with a multiplet at 7.33 ppm ($\underline{H}$–C=C–$CH_3$), and B displayed a doublet signal at 2.59 and a multiplet signal at 8.23 ppm in the lower field than A. These spectra lacked signals of the typical AB-pattern due to $C_7$– and $C_8$–protons in the perchlorate (I), but one aromatic proton as a singlet in the lower field. The above NMR spectral data indicated that the thiazole nucleus remained and either $C_7$ or $C_8$–proton on the pyridazine ring was occupied. The ultraviolet (UV) spectrum of the compound A in tetrahydrofuran showed the absorption maximum at 309 mμ which shifted to a little bit shorter wave length at 305 mμ in methanol. However, the compound B in tetrahydrofuran had the absorption maxima at 365 and 354 mμ,

Table I. The Reaction of Ia—i with Cyanide Ion

| Compd. No. | $R^1$ | $R^2$ | $R^3$ | React. solvent | Time (hr) | II mp (°C) | II Yield (%) | III mp (°C) | III Yield (%) |
|---|---|---|---|---|---|---|---|---|---|
| Ia | H | H | $CH_3$ | $H_2O$ | 20 | 231.5—232.5 | 39 | >300 | 13 |
| Ib | H | $CH_3$ | $CH_3$ | $CH_3CN$–$H_2O$ | 6 | 238 —238.5 | 48 | 289—290 | 26 |
| Ic | H | $C_6H_5$ | $CH_3$ | $CH_3CN$–$H_2O$ | 1 | 245 —248 | 32 | 300 | 12 |
| Id | –$(CH_2)_4$– | | $CH_3$ | $CH_3CN$–$H_2O$ | 20 | 233 —234 | 56 | 237—238 | 31 |
| Ie | H | H | $C_6H_5$ | MeOH–$H_2O$ | 2 | 206 —207 | 25 | 264—266 | 46 |
| If | H | $CH_3$ | $C_6H_5$ | MeOH–$H_2O$ | 3 | 211.5—214 | 26 | 291—294 | 34 |
| Ig | H | $C_6H_5$ | $C_6H_5$ | MeOH–$H_2O$ | 20 | 277 —279 | 31 | — | — |
| Ih | H | $CH_3$ | $SCH_3$ | MeOH–$H_2O$ | 4 | >300 | 27 | >300 | 13 |
| Ii | H | $C_6H_5$ | $SCH_3$ | MeOH–$H_2O$ | 4 | 292 —293 | 22 | 296—297 | 12 |

Table II. Analytical Data of II and III

| | Molecular formula | Analysis (%) Calcd. C | Calcd. H | Calcd. N | Found C | Found H | Found N |
|---|---|---|---|---|---|---|---|
| IIa | $C_8H_5ON_3S$ | 50.25 | 2.64 | 21.98 | 50.31 | 2.65 | 22.31 |
| IIb | $C_9H_9ON_3S$ | 52.67 | 3.44 | 20.47 | 52.40 | 3.49 | 20.12 |
| IIc | $C_{14}H_9ON_3S$ | 62.91 | 3.39 | 15.72 | 62.81 | 3.67 | 16.20 |
| IId | $C_{12}H_{11}ON_3S$ | 58.77 | 4.52 | 17.14 | 58.48 | 4.36 | 16.99 |
| IIe | $C_{13}H_7ON_3S$ | 61.65 | 2.79 | 16.59 | 61.83 | 2.83 | 16.44 |
| IIf | $C_{14}H_9ON_3S$ | 62.91 | 3.39 | 15.72 | 62.68 | 3.67 | 15.56 |
| IIg | $C_{19}H_{11}ON_3S$ | 69.28 | 3.37 | 12.76 | 68.89 | 3.62 | 12.32 |
| IIh | $C_9H_7ON_3S$ | 45.55 | 2.97 | 17.71 | 45.25 | 3.08 | 17.86 |
| IIi | $C_{14}H_9ON_3S$ | 56.17 | 3.03 | 14.04 | 55.87 | 2.97 | 14.54 |
| IIIa | $C_8H_5ON_3S$ | 50.25 | 2.64 | 21.98 | 49.96 | 2.51 | 22.31 |
| IIIb | $C_9H_9ON_3S$ | 52.67 | 3.44 | 20.47 | 52.37 | 3.49 | 20.36 |
| IIIc | $C_{14}H_9ON_3S$ | 62.91 | 3.39 | 15.72 | 63.04 | 3.31 | 15.81 |
| IIId | $C_{12}H_{11}ON_3S$ | 58.77 | 4.52 | 17.14 | 58.83 | 4.39 | 17.34 |
| IIIe | $C_{13}H_7ON_3S$ | 61.65 | 2.79 | 16.59 | 61.74 | 2.88 | 16.50 |
| IIIf | $C_{14}H_9ON_3S$ | 62.91 | 3.39 | 15.72 | 62.62 | 3.39 | 15.36 |
| IIIh | $C_9H_7ON_3S$ | 45.55 | 2.97 | 17.71 | 45.78 | 3.12 | 17.90 |
| IIIi | $C_{14}H_9ON_3S$ | 56.17 | 3.03 | 14.04 | 56.40 | 2.89 | 14.30 |

and the remarkable blue shift was observed at 348 mμ in methanol. From the above mentioned spectral data the compound A was assigned as 8-cyano-4,7-dihydro-3,6-dimethylthiazolo[3,2-*b*]pyridazine-7-one (IIb) and B was assigned as anhydro-7-cyano-5,8-dihydro-3,6-dimethyl-8-oxothiazolo[3,2-*b*]pyridazinium hydroxide (IIIb).

The reaction of the quaternary ammonium perchlorates (Ia—i) with potassium cyanide proceeded in a similar manner as Ib. For example, in case of Ih, i ($R^3=SCH_3$) it is predicted that the substitution reaction would occur at $C_6$–position to yield 6-cyanothiazolopyridazinium salt (V) *via* the intermediate (IV) as shown in Chart 1. In practice, however, the addition of the cyanide occurred at $C_7$– or $C_8$–carlon and gave the enamine quinoids (IIh, i) and the ylide quinoids (IIIh, i), respectively.

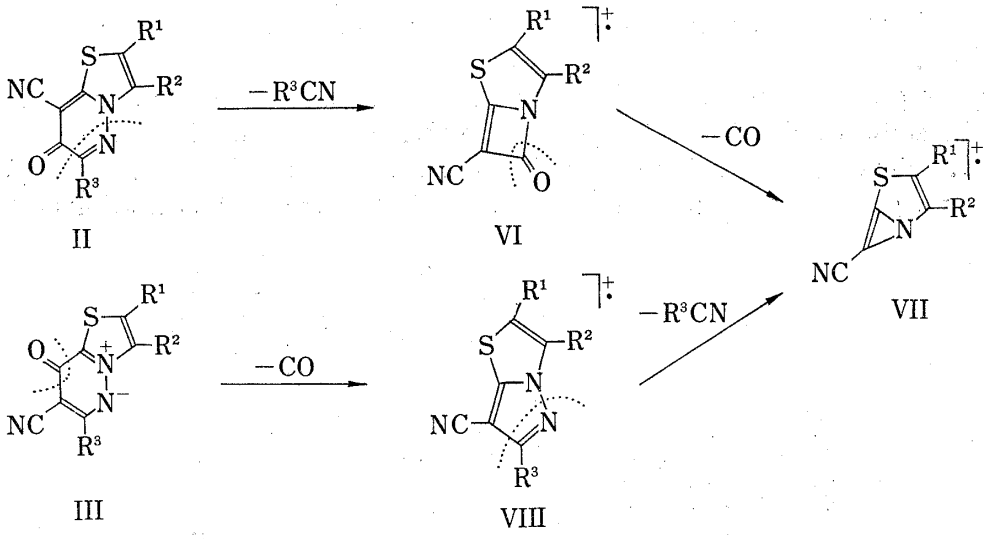
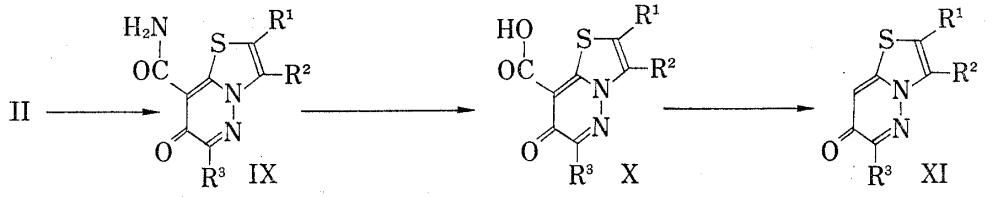


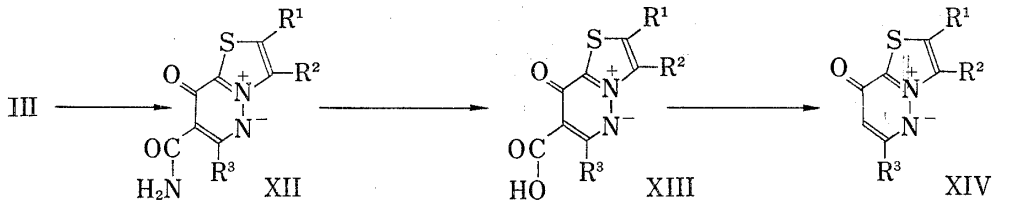

Chart 2




| | $R^1$ | $R^2$ | $R^3$ | mp (°C) | (%) |
|---|---|---|---|---|---|
| IXa : | H | H | $CH_3$ | 285—287 | 83 |
| IXb : | H | $CH_3$ | $CH_3$ | >300 | 85 |
| IXc : | H | $C_6H_5$ | $CH_3$ | 296—298 | 85 |
| IXd : | $-(CH_2)_4-$ | | $CH_3$ | >300 | 60 |

$R^1=H$
$R^2=R^3=CH_3$

XIa : $R^1=H, R^2=R^3=CH_3$
XIb : $R^2=H, R^2=CH_3$, $R^3=C_6H_5$




$R^1=H$
$R^2=R^3=CH_3$

Chart 3

In the mass spectrum of the enamine quinoid (II) the fragmentation involving loss of $R^3CN$ was first observed next to the molecular ion peak and was formulated as VI. The subsequent fragmentation was a loss of carbon monoxide to give the cyanoazirinothiazole ion (VII). A primary loss of carbon monoxide from the molecular ion was observed in the spectrum of the ylide quinoid (III) and was given as VIII, and subsequent loss of $R^3CN$ led to the peak corresponding to VII. These main fragmentation pathways are illustrated in Chart 2. Other fragmentations represented the usual decomposition pattern of thiazoles.[4] These observations further supported the assigned quinoid structure of both products II and III.

Because the quaternary salts (I) were hardly soluble in water, acetonitrile or methanol was used to increase the solubility of I. For example, the reaction of Ib with potassium cyanide in water as solvent took three days to give IIb in 34% yield and IIIb in 24% yield, and it also took two days in acetonitrile as solvent to give IIb in 41% yield and IIIb in 5% yield. Each reaction in a simple solvent needed more time than in mixed solvents and gave the products in lower yields.

The cyano group of the quinoids compounds II and III behaved normally and were hydrolyzed with sulfuric acid at room temperature to give the corresponding amides IX and XII, respectively. Heating of IXb in refluxing concentrated hydrochloric acid or 50% sulfuric acid for 2 hours gave the corresponding carboxylic acid (X), and further heating of it afforded

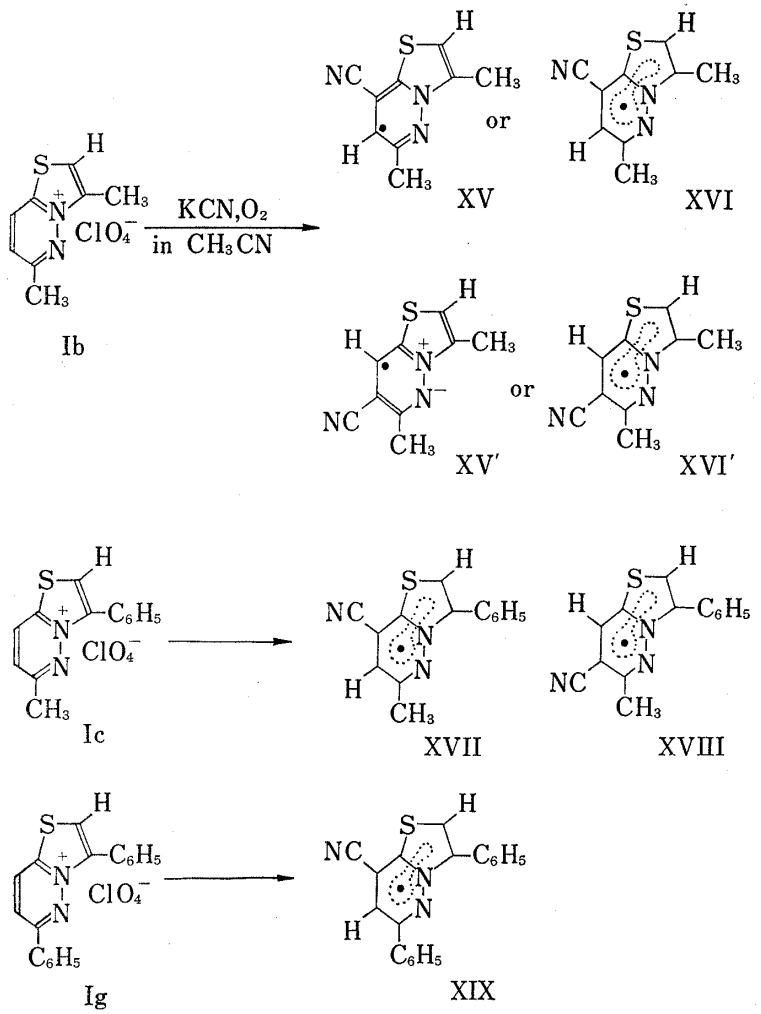



Chart 4

4) Q.N. Porter, J. Baldas, "Mass spectroscopy of Heterocyclic Compounds" Wiley-interscience, New York, 1970, p. 532.

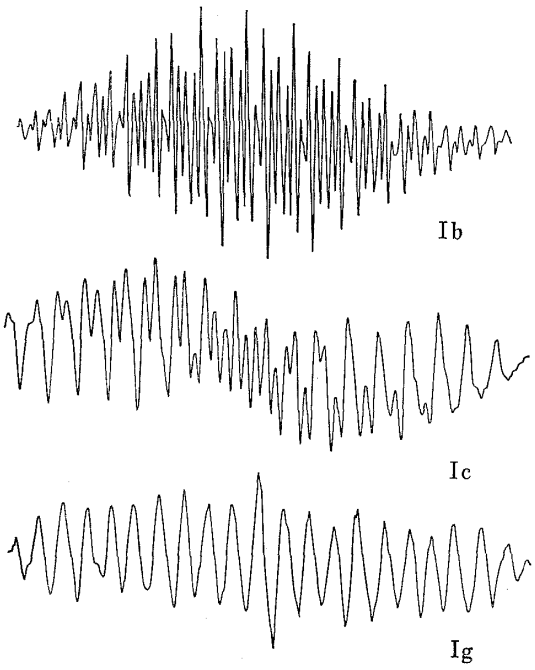



Fig. 1

the quinoid compound (XI) by way of decarboxylation. Similar heating of XII in 50% sulfuric acid gave the quinoid (XIV) *via* the corresponding carboxylic acid (XIII) which was not isolated. The NMR spectrum of the compound (XIa) in deuteriochloroform showed a singlet at $\delta$ 6.78 ppm ($C_8$–H) and the compound (XIV) showed a signal at $\delta$ 6.45 ppm ($C_7$–H). The carbonyl group of both quinoids II and III did not react with 2,4-dinitrophenylhydrazine and so it seemed to have the characteristic properties of a carbonyl ketone like a $\gamma$-pyridone.[5]

Although the reaction was conducted in anhydrous acetonitrile as solvent, osygenated product II and III were formed as well. When the reaction of Ib was carried out under nitrogen stream, the compounds (IIb) and (IIIb) were not isolated at all. However, when the reaction mixture was shaken under oxygen stream, the reaction proceeded with absorption of equimolar amount of oxygen to give IIb in 39% and IIIb in 15% yield, respectively. A similar reaction of Ib in water ceased after absorbing 1 mole of oxygen during 20 hours' shaking to give IIb in 17% and IIIb in 20% yield together with the amide (IXb) in 5% yield formed by hydrolysis. These facts demonstrated that atmospheric oxygen was incorporated into the substrate during the reaction. Examination of the electron spin resonance (ESR) spectroscopy of the reaction mixture proved the intervention of organic radical species which might be formed from the cyano adduct and triplet oxygen. After shaking the compound (Ib, c, g) with

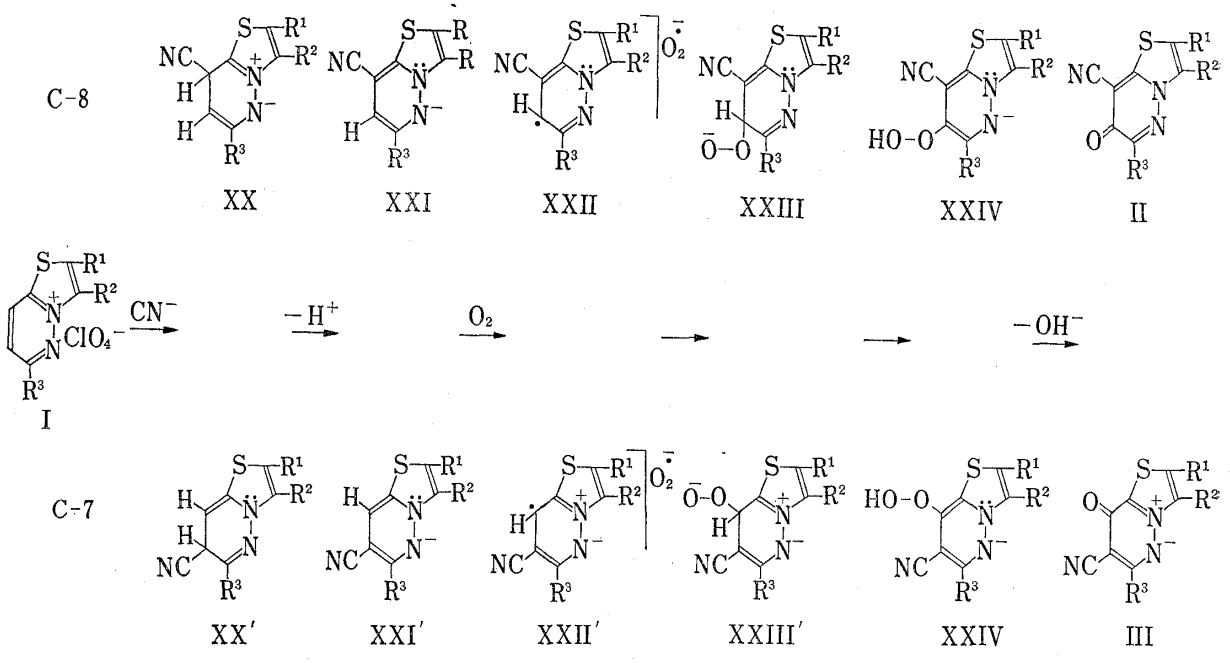



Chart 5

5) H.F. Andrew and C.K. Bradsher, *J. Heterocyclic Chem.*, 4, 577 (1967).

potassium cyanide in acetonitrile for 30 minutes, the ESR measurement was carried out and the *hfs* as shown in Table III was observed. In case of Ib, the radical intermediates can be assigned to the formulae such as XV, or XVI and XV′ or XVI′ (Chart 4). The interaction of the odd electron with hydrogen and nitrogen nuclei in the molecule had complicated the spectral pattern of Ib.

Possible mechanisms for the formation of the quinoid (II) from I and cyanide in the presence of oxygen are proposed in Chart 5. The initial attack of the cyanide at the $C_8$–position of the quaternary salts (I) gave XX, which was deprotonated in the basic medium to give the anion (XXI). Radical coupling of the pi-sufficient anion (XXI) with atmospheric oxygen furnished XXII, which was detected by ESR spectroscopy. Prototropy and the elimination of the hydroxide ion from XXIV afforded the enamine quinoid (II). In case of the attack of the cyanide at $C_7$–position, similar reaction mechanism was considered.

Recent work by Bisson and a coworker predicted the presence of a radical species in the reaction of the isobutylidene azlactone with oxygen in weakly basic media.[6] Russel and a coworker have demonstrated a radical species in the reaction of carbanions with oxygen in strongly basic media by means of ESR spectroscopy.[7] The above envisaged reaction path (Chart 5) seems reasonable and not incompatible with these literatures.

## Experimental[8]

**General Procedure for the Reaction of Thiazolo[3,2-*b*]pyridazin-4-ium Perchlorates (Ia—Ii) with Potassium Cyanide, Formation of 8-Cyano-4,7-dihydrothiazolo[3,2-*b*]pyridazine-7-ones(II) and Anhydro-7-cyano-5,8-dihydro-8-oxothiazolo[3,2-*b*]pyridazinium Hydroxides (III)**——Into a solution of I (1.000 g) in 20 ml of a mixture of acetonitrile and water (1 : 1) there was added while stirring at room temperature 1.5 g of KCN. The mixture became dark colored and gradually deposited precipitate, which was collected by filtration after 6 hrs' stirring. After drying the solid over KOH in an exicator it was submitted to silica gel chromatography to afford 8-cyano-4,7-dihydrothiazolo[3,2-*b*]pyridazine-7-one (II) as firstly eluting substance and anhydro-7-cyano-5,8-dihydro-8-oxothiazolo[3,2-*b*]pyridazinium hydroxide (III) as the secondly eluting substance.

**Reaction of 3,6-Dimethylthiazolo[3,2-*b*]pyridazin-4-ium Perchlorate (Ib) with KCN**——Into a solution of Ib (1.000 g) in 20 ml of a mixture of acetonitrile–water (1 : 1) there was added 1.5 g of KCN while stirring at room temperature. The mixture became dark colored and gradually deposited precipitate. After stirring for further 6 hr the precipitate was collected by filtration and dried in an exicator (KOH) overnight. The light brown crystalline solid was chromatographed on silica gel. Elution with 5% MeOH–$CHCl_3$ afforded first 8-cyano-4,7-dihydro-3,6-dimethylthiazolo[3,2-*b*]pyridazine-7-one (IIb) (mp 238—238.5° after recrystallization from MeOH, 370 mg, 48% yield) UV $\lambda_{max}^{MeOH}$ mμ (log ε): 214 (4.10), 237 (4.10), 306 (4.23). Mass Spectrum *m/e*: 205 ($M^+$), 164 ($M^+-CH_3CN$), 136 (164—C=O). From the next eluate, anhydro-7-cyano-5,8-dihydro-3,6-dimethyl-8-oxothiazolo[3,2-*b*]pyridazinium hydroxide (IIIb) (mp 289—290°, after recrystallization from MeOH, 200 mg, 26% yield) was obtained. UV $\lambda_{max}^{MeOH}$ mμ (log ε): 233.5 (4.13), 239.5 (4.14), 262.5 (3.90), 269.5 (3.98), 348 (4.16). Mass Spectrum *m/e*: 205 ($M^+$), 177 ($M^+-C=O$), 136 ($177-CH_3CN$).

**General Procedure for the Hydrolysis of 8-Cyano-4,7-dihydrothiazolo[3,2-*b*]pyridazine-7-ones (II), Formation of 8-Carboxamido-4,7-dihydrothiazolo[3,2-*b*]pyridazine-7-one (IXa—IXd)**——After a solution of 100 mg of IIa—IId in 1 ml of conc. $H_2SO_4$ was allowed to stand at room temperature for 15—30 hr, the mixture was poured onto ice water. The precipitated crystals were collected by filtration and recrystallized from a mixture of MeOH–$H_2O$ (8 : 2) to give colorless crystals (60—85% yield).

**General Procedure for the Hydrolysis of Anhydro-7-cyano-5,8-dihydro-8-oxothiazolo[3,2-*b*]pyridazinium Hydroxides (III), Formation of Anhydro-7-carboxamido-5,8-dihydro-8-oxothiazolo[3,2-*b*]pyridazinium Hydroxides (XII)**——After a solution of 60 mg of IIIb in 0.6 ml of conc. $H_2SO_4$ was allowed to stand at room temperature for a week, the mixture was poured onto ice water to deposit white crystals. Recrystallization

6) R. Bisson, R.B. Yeats, and E.W. Warnhoff, *Can. J. Chem.*, **50**, 2851 (1972).
7) *a*) G.A. Russel, E.T. Strom, E.R. Talaty, and S.A. Weiner, *J. Am. Chem. Soc.*, **88**, 1998 (1966); *b*) G.A. Russell and H. Malkus, *ibid.*, **89**, 160 (1967).
8) Melting points were measured in capillary tubes and also on the Yanagimoto micro melting point apparatus. All melting points were uncorrected. NMR spectra were measured by Hitachi R-20 60MC and R-22 90MC NMR spectrophotometer, using tetramethylsilane as the internal reference. IR and UV spectra were measured on a JASCO IRA-I spectrophotometer and on a Hitachi EPS-3 UV spectrophotometer, respectively. Mass spectra were recorded on a Hitachi RMS-4 instrument. ESR spectra were measured on a JEOL JES-PE-IX spectrometer.

from MeOH gave colorless cubes (mp over 300°, 50 mg, 78% yield). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1665 (sh), 1603, 1520, 1438. *Anal.* Calcd. for $C_9H_9O_2N_3S$: C, 48.43; H, 4.06; N, 18.83. Found: C, 48.28; H, 3.99; N, 18.38.

**Hydrolysis of 4,7-Dihydro-3,6-dimethyl-7-oxothiazolo[3,2-*b*]pyridazine-8-carboxylic Acid (X)**——A mixture of IXb (150 mg) in conc. HCl (3 ml) was heated under reflux for 2 hr. After cooling the reaction mixture was neutralized with $K_2CO_3$ to deposit crystals, which were collected by filtration and were recrystallized from EtOH. Colorless crystals were obtained, which melted at 193—195° (50 mg, 33% yield). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3420 (OH), 1715, 1695, 1580, 1500, 1385. NMR $\delta$ ppm (in DMSO-$d_6$): 2.47 (3H, s), 2.50 (3H, d), 7.52 (1H, q). *Anal.* Calcd. for $C_9H_8O_3N_2S$: C, 48.21; H, 3.60; N, 12.49. Found: C, 48.12; H, 3.97; N, 12.48.

**Decarboxylation of 4,7-Dihydro-3,6-dimethyl-7-oxothiazolo[3,2-*b*]pyridazine-8-carboxylic Acid (X), Formation of 4,7-Dihydro-3,6-dimethyl-7-oxothiazolo[3,2-*b*]pyridazine (XIa)**——A mixture of X (100 mg) in conc. HCl (4 ml) was heated under reflux for 6 hr. After cooling the reaction mixture was basified with $K_2CO_3$ to give colorless crystals, which, after recrystallization from benzene, melted at 206—207° (40 mg, 50% yield). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1580, 1500, 1450, 1430, 1380, 1345, 1310, 1240. NMR $\delta$ ppm (in $CDCl_3$): 2.45 (6H, s), 6.48 (1H, m), 6.78 (1H, s). *Anal.* Calcd. for $C_8H_8ON_2S$: C, 53.31; H, 4.47; N, 15.54. Found: C, 53.49; H, 4.36; N, 15.52.

**Hydrolysis and Decarboxylation of 8-Cyano-4,7-dihydro-3-methyl-6-phenylthiazolo[3,2-*b*]pyridazine-7-one (IIf), Formation of 4,7-Dihydro-3-methyl-6-phenylthiazolo[3,2-*b*]pyridazine-7-one (XIb)**——After a solution of IIf (150 mg) in conc. $H_2SO_4$ (1.5 ml) was allowed to stand at room temperature for 24 hr, the mixture was poured onto ice water. The precipitated crystals were collected by filtration and its solution in conc. HCl (15 ml) was heated under reflux for 4 hr. After cooling the reaction mixture was basified with $K_2CO_3$ to deposit colorless crystals, which, after recrystallization from benzene–*n*-hexane, melted at 167—168° (40 mg, 30% yield). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1595, 1475, 1360. NMR $\delta$ ppm (in $CDCl_3$): 2.51 (3H, d, $J$=1.1 Hz), 6.54 (1H, q), 6.97 (1H, s), 7.35—7.60 (3H, m), 8.10—8.35 (2H, m). *Anal.* Calcd. for $C_{13}H_{10}ON_2S$: C, 64.44; H, 4.16; N, 11.56. Found: C, 64.30; H, 4.30; N, 12.04.

**Hydrolysis and Decarboxylation of Anhydro-7-cyano-5,8-dihydro-3,6-dimethylthiazolo[3,2-*b*]pyridazinium Hydroxide (IIIb), Formation of Anhydro-5,8-dihydro-3,6-dimethyl-8-oxothiazolo[3,2-*b*]pyridazinium Hydroxide (XIV)**——After a solution of IIIb (150 mg) in conc. $H_2SO_4$ (3 ml) was allowed to stand at room temperature for a week, the mixture was diluted with $H_2O$ (3 ml) and was heated under reflux for 5 hr. After cooling the reaction mixture was basified with $K_2CO_3$ to deposit colorless crystals, which were collected by filtration and recrystallized from benzene. The colorless crystals melted at 177—180° (60 mg, 46% yield). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1680, 1570, 1485. NMR $\delta$ ppm (in $CDCl_3$): 2.50 (3H, s), 2.68 (3H, d, $J$=1.1 Hz), 6.45 (1H, s), 7.43 (1H, m). *Anal.* Calcd. for $C_8H_8ON_2S$: C, 53.31; H, 4.47; N, 15.54. Found: C, 53.43; H, 4.44; N, 15.32.

**Attempted Reaction of KCN and 3,6-Dimethylthiazolo[3,2-*b*]pyridazin-4-ium Perchlorate (Ib) under Nitrogen Stream**——1) A solution of Ib (265 mg, 1 mmole) in $CH_3CN$ (2 ml) was added to a stirred suspension of KCN (500 mg) in $CH_3CN$ (10 ml) under nitrogen stream. After stirring for 2 hr separation of any crystalline product was not observed and the presence of neither IIb or IIIb was observed by the detection of the reaction mixture by TLC. The starting material Ib was not isolated from the reaction mixture.

2) The above described procedure was repeated in water in stead of $CH_3CN$ as solvent. After stirring of 2 hr the presence of neither IIb nor IIIb was observed by the detection of the reaction mixture by TLC.

**Reaction of KCN and 3,6-Dimethylthiazolo[3,2-*b*]pyridazin-4-ium Perchlorate (Ib) under Oxygen Stream**——1) A solution of Ib (265 mg, 1 mmole) in $CH_3CN$ (2 ml) was added to a stirred suspension of KCN (500 mg) in $CH_3CN$ (10 ml) under oxygen stream. The sluggish up-take of oxygen ceased after absorbing 22 ml of oxygen during 20 min. The reaction mixture did not show the presence of the starting material on the TLC plate any more. After evaporating the solvent, water (5 ml) was added to the residue to deposit crystals, which were collected by filtration. The filtrate was extracted with $CHCl_3$ and the organic layer was dried over $MgSO_4$, filterd and evaporated to dryness under reduced pressure to give crystals. The combined crystals were purified by column chromatography through silica gel in 5% MeOH–$CHCl_3$ to give IIb (80 mg, 39% yield) and IIIb (30 mg, 15% yield).

2) The above described procedure was repeated in water instead of $CH_3CN$ as solvent to give IIb (35 mg, 17% yield), IIIb (40 mg, 20% yield) and the amide (IXb) (10 mg, 4% yield).

3) A solution of Ib (265 mg, 1 mmole) in $CH_3CN$ (2 ml) was added to a stirred suspension of KCN (500 mg) in $CH_3CN$ (10 ml) under nitrogen stream. The reaction mixture did not show the presence of IIb and IIIb on the TLC plate after stirring for 2 hr. After the evaporation of the solvent, water (5 ml) was added to the residue to deposit crystals, which were collected by filtration. The filtrate was extracted with $CHCl_3$ and the organic layer was dried over $MgSO_4$, filtered and evaporated to dryness under reduced pressure to give crystals. The combined crystals were purified by column chromatography through silica gel in 5% MeOH–$CHCl_3$ to give IIb (50 mg, 24% yield) and IIIb (45 mg, 22% yield).

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