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Synthesis of Zwitterionic Pyridazine Derivatives. I

Takao Yamazaki, Masanori Nagata, Fujio Nohara, and Siro Urano

Faculty of Pharmaceutical Sciences, University of Toyama[1]

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Anhydro 4-hydroxy-pyrido[1,2-*b*]pyridazinium hydroxide derivatives were prepared starting with ethyl 2-piperidine-carboxylate (I).

I was, *via* the N-nitroso compound (II), converted into the corresponding N-amino derivative (III), which was condensed with ethyl acetoacetate to give ethyl 1-(ethoxy-carbonyl-isopropylidene)amino-2-piperidine carboxylate (IV) in a good yield. The Dieckmann condensation of IV led to the corresponding cyclic compound (V), mp 152—153°, contaminated with a small amount of a 4-hydroxy-pyrido[1,2-*b*]pyridazinium hydroxide derivative (VI), mp 135—136° (anhydronium base).

V and VI are transmutable each other by oxido-reduction. VI was readily hydrolysed to the corresponding carboxylic acid (VII), which was decarboxylated to anhydro 4-hydroxy-2-methyl-5,6,7,8-tetrahydro-pyrido[1,2-*b*]pyridazinium hydroxide (VIII), mp 142°. The C_3-position of VIII was subject to both the electrophilic and the nucleophilic attacks; VIII was readily brominated with bromine to give the 3-bromo compound (IX) which led, *via* the corresponding thiouronium bromide, to the 3-mercapto compound (XII), and to the anilino derivative (X) reacted with aniline. Furthermore, VIII was treated with hydrogen peroxide to give 3-hydroxy derivative (XV). The above synthesis has been applicable to a general method for the preparation of anhydro 1-substituted or 1,6-disubstituted 5-hydroxy-pyridazinium hydroxides, a type of zwitterionic heterocyclic compounds.

Lately there has been considerable concern with zwitterionic heterocyclic compound including mesoionic compound.[2] We are now going to describe a synthesis of anhydro 4-hydroxy-pyrido[1,2-*b*]pyridazinium hydroxide derivatives, which has been applicable[3] to a general method for the preparation of anhydro 1-substituted or 1,6-disbustituted 5-hydroxy-pyridazinium hydroxides, a type of zwitterionic heterocyclic compounds, relatively unknown except for anhydro 5-hydroxy-1-methyl-pyridazinium hydroxide.[4]

The synthetic procedures were as follows.

Ethyl 2-piperidine-carboxylate (I) was treated with nitrous acid in a usual manner, giving the corresponding nitroso compound (II), bp_3 126—131°, which was reduced with an excess of zinc dust and acetic acid at 20—25° to give a hydrazine derivative (III), bp_3 88—91°, whose piperonylidene derivative melted at 64—65°. III, giving a positive Fehling's test, was reacted with ethyl acetoacetate in the presence of catalytic amount of acetic acid to afford ethyl 1-(ethoxycarbonyl-isopropylidene)amino-2-piperidinecarboxylate (IV), $bp_{0.05}$ 138—142°, in a good yield. The Dieckmann condensation of IV with sodium ethoxide in anhydrous benzene led to a mixture of two 4-azaquinolizine derivatives, (V), mp 152—153° and (VI), mp 135—136° (hydrate, mp 57—58°) in a ratio of 2:1, which was increased when condensed under nitrogen. The separation of V from VI was successful through fractional recrystallization of the crude reaction product from alcohol, because VI was highly soluble compared with V.

1) Location: *Gofuku-3190, Toyama.*
2) W. Baker, W.D. Ollis, and V.D. Poole, *J. Chem. Soc.*, **1949**, 307; F.H.C. Stewart, *Chem. Rev.*, **64**, 129 (1964); J.C.E. Simpson, "Condensed Pyridazine and Pyrazine Rings," 1953, p. 119; E.J. Alford and K. Schofield, *J. Chem. Soc.*, **1953**, 1811.
3) Ready to be published in a near future by the authors.
4) K. Eichenberger, R. Rometsch, and J. Druey, *Helv. Chim. Acta*, **39**, 1755 (1956).

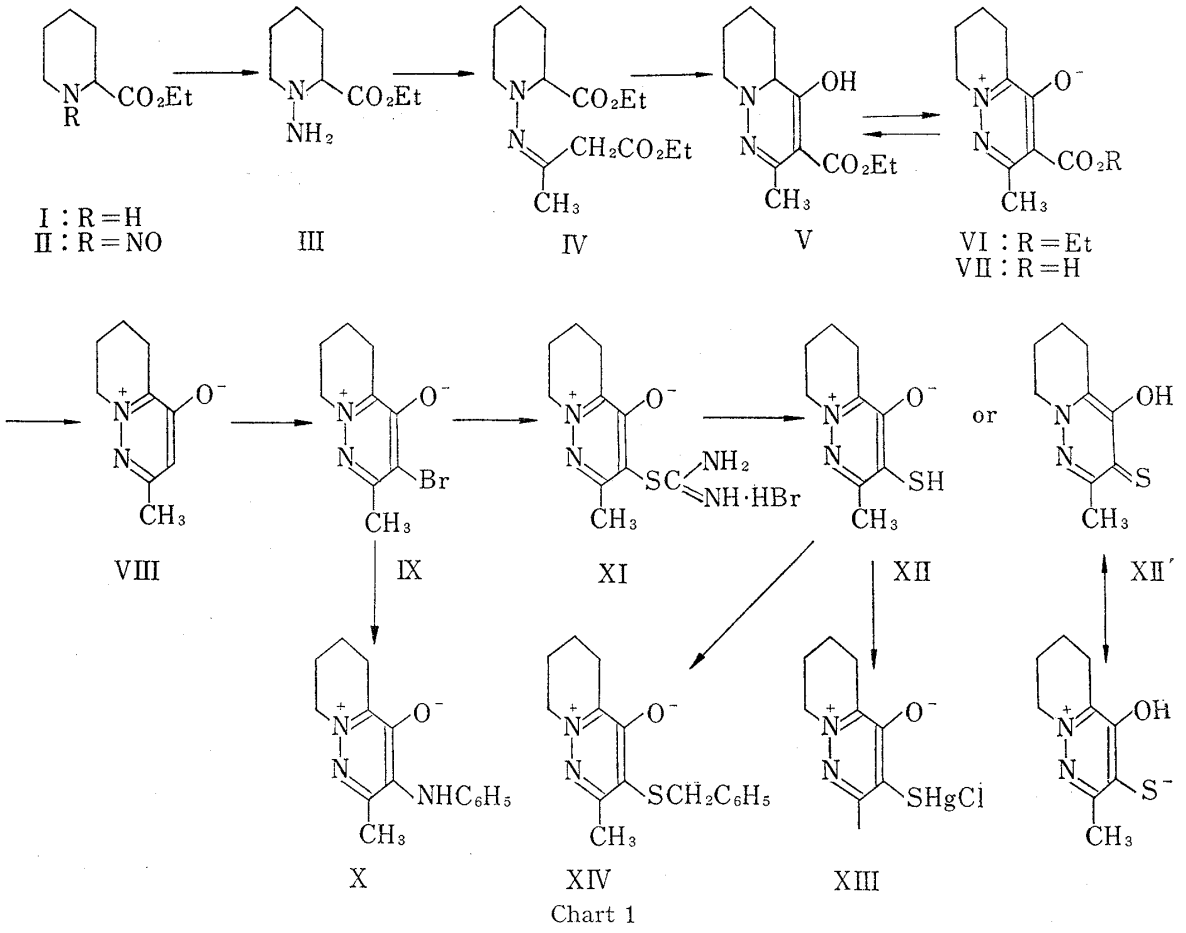


Chart 1

The compound V gave a positive ferric chloride test and the infrared (IR) absorptions at 2800 cm^{-1}—2600 cm^{-1} and 1640 cm^{-1} in dilute chloroform solution (Fig. 1), which suggested intramolecular hydrogen bonding between 4-hydroxyl and 3-ethoxycarbonyl groups. The nuclear magnetic resonance (NMR) signals (in $CDCl_3$, 100 Mc) associated with 4-hydroxyl and 4a-H protons were also observed at $-1.5\ \tau$ (s) and $7.2\ \tau$ (m) respectively.

In contrast with V, the compound VI exhibited no longer either a positive ferric chloride test or 4-hydroxy and 4a-H proton magnetic resonance signals, and the IR absorptions due to the intramolecular hydrogen bonding observed for V disappeared, while the IR absorption by the oridinary aromatic estercarbonyl being observed at 1700 cm^{-1} (Fig. 1). VI was reduced to V over platinum oxide catalyst, and the latter in high dilution reversely underwent spontaneous dehydrogenation to the former in a few days, which was cofirmed by the time dependency of the ultraviolet (UV) absorption by the latter. The above conversion was most conveniently effected by mercuric acetate oxidation, or by treating V with platinum oxide in alcohol, which was accompanied by a vigorous evolution of hydrogen. The compound VI has in addition, two UV absorption maxima at 262 mμ (log ε, 3.31) and 323 mμ (log ε, 3.51) analogous to anhydro 5-hydroxy-1-methyl-pyridazinium hydroxide[4,5] (Table I). All of these chemical and physical data are thus consistent with the structures given to V and VI. Hydrolysis of VI with acid or alkali afforded the carboxylic acid (VII), decomp. 190—191°, which was decarboxylated to anhydro 4-hydroxy-2-methyl-5,6,7,8-tetrahydropyrido[1,2-*b*]pyridazinium hydroxide (VIII), mp 142°, upon thermal decomposition or boiling with 20% hydrochloric acid. pK_a value for this latter compound determined by spectrophotometric measurement

5) D. E. Metzler and E. E. Snell, *J. Am. Chem.*, **77**, 2431 (1955); K. Eichenberger, R. Rometsch, and J. Druey, *Helv. Chem. Acta*, **39**, 1755 (1956).

was 2.77 at 20°, (Fig. 2, Table II) suggesting that the base is fairely weak, though it formed a stable hydrochloride, decomp. 256° and *o*-methiodide, mp 176°. It is of great interest that the 3-position has been subject to both the electrophilic and the nucleophilic substitutions.

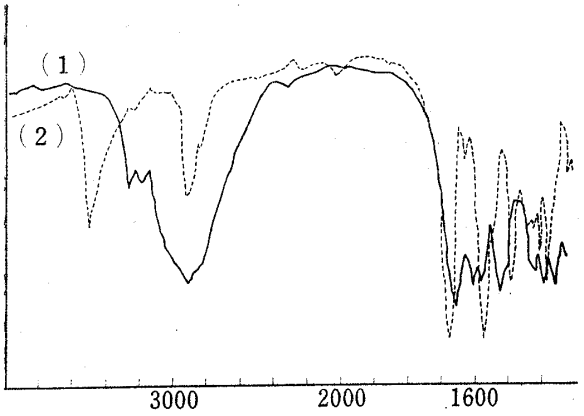


Fig. 1. Infrared Spectra
(1): V, (2): VI (KBr)

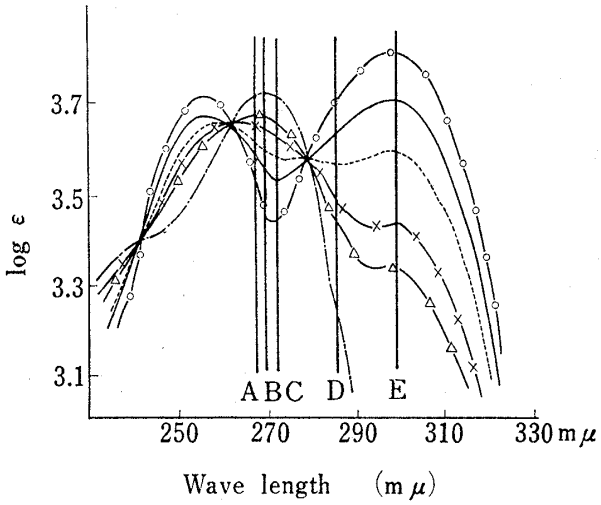


Fig. 2. Absorption Spectra of VII of in Different Solvent

———: PH 3.20 ----------: PH 2.90
—×—×: PH 2.58 —△—△: PH 2.43
———: PH 1.51 —○—○: PH >7.00

TABLE I. UV Spectral Data

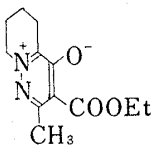
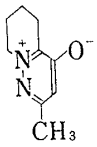
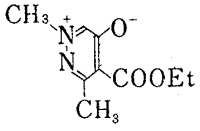
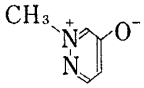
Compound / Solvent								
	λ max	log ε	λmax	log ε	λmax	log ε	λmax	log ε
EtOH	262	3.31	260	3.43	260	3.25	258	3.64
	323	3.51	311	3.44	325	3.23	311	3.36
H_2O			257	3.33			254	3.60
			298	3.43			302	3.27
2N HCl			240	3.15			234	3.25
			270	3.28			270	3.27
0.1N NaOH			255	3.18			253	3.61
			297	3.37			303	3.28

TABLE II

	mμ	H+ pH= 1.51	β pH=> 7.00	pH=3.20 −log[a] T_{obs}	pH=3.20 pK_a	pH=2.90 −log[a] T_{obs}	pH=2.90 pK_a	pH=2.58 −log[a] T_{obs}	pH=2.58 pK_a	pH=2.43 −log[a] T_{obs}	pH=2.43 pK_a	Mean value
A	268	0.648	0.390	0.454	2.72	0.500	2.77	0.553	2.81	0.572	2.81	2.78
B	270	0.657	0.347	0.423	2.71	0.480	2.78	0.542	2.81	0.565	2.81	2.78
C	272	0.644	0.339	0.414	2.79	0.471	2.81	0.533	2.82	0.555	2.82	2.78
D	286	0.199	0.623	0.523	2.69	0.451	2.74	0.367	2.76	0.328	2.79	2.77
E	300	0.015	0.800	0.620	2.70	0.489	2.75	0.335	2.79	0.267	2.82	2.76

a) $pK_a = pH - \log \frac{\varepsilon_{\beta H^+} - \varepsilon_{obs}}{\varepsilon_{obs} - \varepsilon_{\beta}} = pH - \log T$

VIII was quantitatively brominated with bromine in sodium carbonate solution or with NBS[6] in chloroform to afford 3-bromo compound (IX), mp 165°, showing no NMR signal at 3.55 τ (s) associated with C_3-H proton observed in case of VIII. Furthermore, the 3-bromo compound was subject to nucleophilic attacks; IX was converted into 3-anilino compound (X), mp (hydrobromide), 185°, treated with aniline, and into 3-mercapto compound (XII), mp 171° *via* thiouronium bromide (XI), mp 152°, treated with thiourea.

It may be reasonable that the 3-mercapto compound should be represented as XII', though it formed the corresponding chloromercurithio compound (XIII), mp 255° and S-benzyl derivative (XIV), mp 96°, whose methiodide melted at 175°. Whether the compound (XIV) is really of a S-benzyl derivative or of an O-benzyl one, and accordingly the methiodide derived from it is an O-methyl iodide or a S-methyl iodide, is open to controversy. One of the purposes of the authers, however, lies in the study on the chemical activity at the C_3-position. A conclusive discussion on this matter was therefore left undone in the present paper.

The above mentioned electrophilic and nucleophilic substitutions at the C_3-position may be attributed to the negatively charged oxygen at the C_4-position and to the positively charged pyridazine ring or the bridgehead nitrogen respectively.

The synthesis of the above compound VIII and its chemical behaviours may thus be applicable[3] to a general synthesis of various anhydro 1-substituted or 1,6-disubstituted 5-hydroxypyridaznium hydroxides starting with the corresponding aminoesters, and to the chemical reactions of the resultant anhydronium bases.

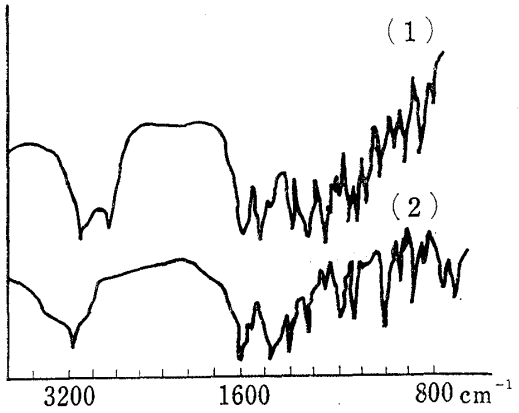


Fig. 3. Infrared Spectra (KBr)
(1): XV (2): VIII

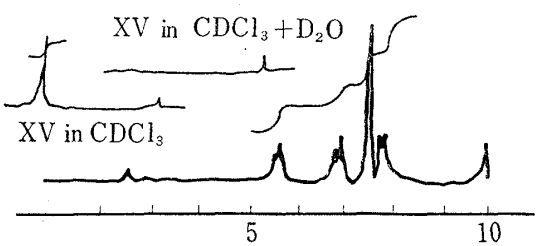


Fig. 4. NMR Spectrum of XV in $CDCl_3$ (60 Mc)

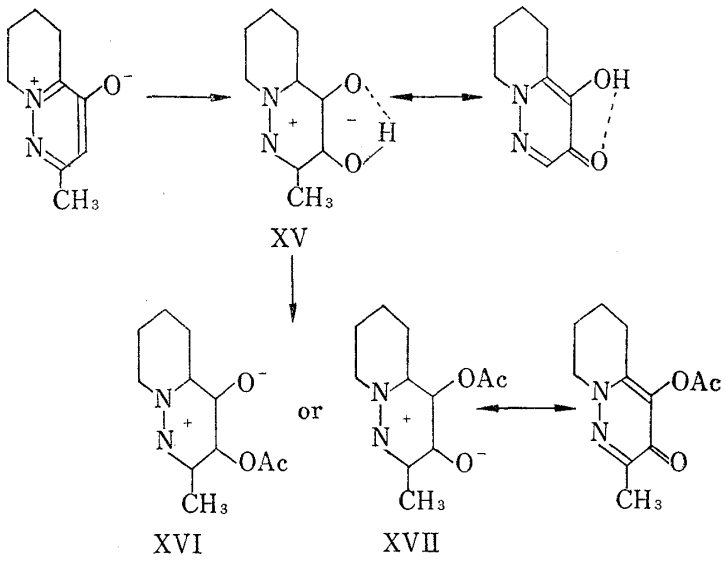


Chart 2

Finally it remains, in addition, to be reported that VIII, reacted with hydrogen peroxide in acetic acid, was converted into the 3-hydroxy compound (XV), mp 214°, in a fairly good yield. XV showed a positive ferric chloride test, a typical deep bluepurple coloration, and the IR absorptions at 2800 cm^{-1}—2600 cm^{-1}, both associated with the intramolecular hydro-

6) Mechanism for the bromination of VIII with NBS, ionic or radical, is to be elucidated in a near future.

gen bonding between the 3-hydroxyl group and the 4-oxygen anion. (Fig. 3, Chart 2). In addition, the structure of XV was verified by the three facts that a NMR signal at 0.45 τ (s) (Fig. 4) associated with the intramolecular hydrogen bonding mentioned above was newly observed, while the NMR signal at 3.55 τ (s) associated with the C_3-H proton of VIII disappearing, and the other signals remaining unchanged at all, the above signal at 0.45 τ (s) completely disappeared when treated with deuterium oxide, which was reminiscent of a phenolic hydroxyl group, and the hydroxyl compound, XV, treated with acetic anhydride, gave the corresponding acetoxy compound (XVI or XVII) whose IR spectrum showed a sharp absorption at 1780 cm^{-1} characteristic of a phenol acetate derivative.

The structure of the reaction product from VIII with hydrogen peroxide was thus elucidated.

Experimental[7]

Ethyl 1-Nitroso-2-piperidinecarboxylate (II)——To a solution of ethyl 2-piperidinecarboxylate (69 g) in 10% HCl (252 ml) was added dropwise 33% aqueous solution of $NaNO_2$ (190 g) with stirring at 5°. After standing at room temperature over night, the mixture was extracted with ether. The extract was satisfactory washed with saturated aqueous solution of urea, dried over $MgSO_4$, and distilled to give 1-nitroso compound II (61 g), bp_3 126—131°, which gave positive Liebermann test. *Anal.* Calcd. for $C_8H_{14}O_3N_2$: C, 51.61; H, 7.52; N, 15.05. Found: C, 51.06; H, 7.80; N, 15.06. IR $\nu_{max}^{Liq.}$ cm^{-1}: 1450 (N–NO), 1730 (COOEt).

Ethyl 1-Amino-2-piperidinecarboxylate (III)——To a suspension of zinc dust (100 g) and II (41 g) in glacial AcOH (158 g), was added dropwise 108 g of water at 10—15° over a period of 2 hr. The reaction mixture was then stirred at room temperature for 3 hr. The resulting solid mass was filtered off and washed several time with benzene. The filtrate and the washings were combined, washed with saturated NaCl solution, then with $NaHCO_3$ solution to remove acetic acid, and dried over Na_2SO_4. The benzene extract was distilled to give a colorless oil (29.8 g), bp_3 88—91°, which reduced Fehling's solution on warming. The hydrochloride of III was prepared with EtOH–HCl and recrystallized from EtOH to give colorless prisms, mp 214—216° (decomp.). *Anal.* Calcd. for $C_8H_{16}O_2N_2$–HCl: C, 45.68; H, 8.55; N, 13.41. Found: C, 45.25; H, 8.77; N, 13.22. The ethanolic solution of III was heated with an equivalent mole of piperonal to give the corresponding Schiff's base mp 64—65°. *Anal.* Calcd. for $C_{17}H_{22}O_3N_2$: C, 63.14; H, 6.62; N, 9.21. Found: C, 63.16; H, 6.53; N, 9.07.

Ethyl 1-(Ethoxycarbonyl-isopropylidene)amino-2-piperidinecarboxylate (IV)——A solution of III (34.4 g), ethyl acetoacetate (26 g), a glacial AcOH (1 ml) in anhydrous benzene (150 ml) was refluxed for 8 hr. The benzene layer was dried over $MgSO_4$ and distilled to leave a pale yellow oil (50 g), $bp_{0.05}$ 138—142°. *Anal.* Calcd. for $C_{14}H_{24}O_4N_2$: C, 59.72; H, 8.55; N, 10.13. Found: C, 59.55; H, 8.45; N, 9.86. IR $\nu_{max}^{Liq.}$ cm^{-1}: 1640, 1720 (CO), 1600 (C=N).

Ethyl 4-Hydroxy-2-methyl-5,6,7,8-tetrahydro-4aH-pyrido[1,2-*b*]pyridazine-3-carboxylate (V)——To a suspension of EtONa, obtained from sodium metal (35.5 g) and absolute EtOH (13 ml), in anhydrous toluene (100 ml) was added IV (32 g) with stirring over a period of 35 min.

The mixture was heated under nitrogen at 100—115° for 2 hr. The reaction mixture was, after cool, treated with cold water, and the water layer, saturated with CO_2, was extracted with $CHCl_3$. The $CHCl_3$ extract, dried over $MgSO_4$, gave 23 g of crude solid mass, after distilling off the solvent. Recrystallization from EtOH gave colorless needles V (18.1 g), mp 152—153°. *Anal.* Calcd. for $C_{12}H_{18}O_3N_2$: C, 60.48; H, 7.61; N, 11.76. Found: C, 60.33; H, 7.48; N, 11.66. IR ν_{max}^{KBr} cm^{-1}: 3240, 3200 (OH), 1680 (CO). UV λ_{max}^{EtOH} mμ (log ε): 228 (3.89), 260 (3.76), 302 (3.37), 326 (3.35). NMR (10% solution in $CDCl_3$) τ: 7.8 (3H, s, $-C\underline{H}_3$), 5.6 (2H, q, $-COOC\underline{H}_2-CH_3$), 8.7 (3H, t, $-COOCH_2-C\underline{H}_3$), −1.5 (1H, s, O$\underline{H}$), 7.2 (1H, m, $=C\underline{H}-$), 6.84 (6H, m), 7.66 (2H, q, $-C\underline{H}_2-$). The mother liquor of the recrystallization was condensed to give a yellowish oil, which was eluted through alumina with benzene to afford VI (2.6 g) as colorless needles, mp 135—136° (hydrate, mp 57—58°). *Anal.* Calcd. for $C_{12}H_{16}O_3N_2$: C, 61.79; H, 6.79; N, 11.86. Found: C, 61.75; H, 6.99; N, 11.86. IR ν_{max}^{KBr} cm^{-1}: 1700 (CO). UV λ_{max}^{EtOH} mμ (log ε): 262 (3.31), 323 (3.51). NMR (10% solution in $CDCl_3$) τ: 7.7 (3H, s, $-CH_3$), 5.6 (2H, q, $-COOC\underline{H}_2-CH_3$), 8.65 (3H, s, $-COOCH_2-C\underline{H}_3$), 6.95, (3H, t), 8.0 (4H, t), 5.6 (2H, t, $-C\underline{H}_2-$).

Anhydro 3-Ethoxycarbonyl-4-hydroxy-2-methyl-5,6,7,8-tetrahydropyrido[1,2-*b*]pyridazinium Hydroxide (VI)——a) Dehydrogenation with Platinum Oxide: A mixture of V (3.41 g) and PtO_2 catalyst (0.2 g) in absolute EtOH (100 ml) was refluxed for 4 hr with stirring. The resultant Pt-black was filtered off and washed with warm EtOH.

7) All melting points were uncorrected.

The filtrate and washings were combined and evaporated *in vacuo* to leave a crude crystal mass, which was recrystallized from isopropylether–EtOH (1:1) to give 2.8 g of VI as colorless needles, mp 57—58° (hydrate). This product was identical with the minor product, VI, obtained by the Dieckmann condensation of IV, which was confirmed by the admixture and IR spectrum.

b) Dehydrogenation with Mercuric Acetate: The mixture of V (3.56 g) and $Hg(AcO)_2$ (9.55 g) in EtOH (200 ml) was heated at 45—50° for 2 hr with stirring. The resultant precipitate was filtered off and washed with warm EtOH. The filtrate and washings were combined and saturated with H_2S. The alcoholic solution, after removing mercuric sulfide, was evaporated *in vacuo* to leave a crude crystal mass, which was recrystallized from isopropylether–EtOH (1:1) to give 2.6 g of VI.

c) Hydrogenation of VI: A solution of VI (2.0 g) in absolute EtOH (20 ml) was shaken with PtO_2 catalyst (0.2 g) under hydrogen for 30 min, and the solution, after the removal of Pt catalyst, was evaporated *in vacuo* under nitrogen atmosphere to leave a crude solid mass (1.8 g). Recrystallization from EtOH gave colorless needles mp 152—153°. The IR and mp were identical with those of V.

Anhydro 4-Hydroxy-3-hydroxycarboxy-2-methyl-5,6,7,8-tetrahydropyrido[1,2-*b*]pyridazinium Hydroxide (VII)——A solution of VI (23.6 g) in 10% NaOH (100 g) was heated for 30 min on a water bath. The solution was acidified with 10% HCl, and the resultant precipitate of VII was collected by filtration and recrystallized from EtOH to give colorless prisms, mp 190—191° (decomp.). *Anal.* Calcd. for $C_{10}H_{12}O_3N_2$: C, 57.69; H, 5.17; N, 13.46. Found: C, 57.67; H, 5.07; N, 13.46. IR ν_{max}^{KBr} cm^{-1}: 1700 (CO).

Anhydro 4-Hydroxy-2-methyl-5,6,7,8-tetrahydropyrido[1,2-*b*]pyridazinium Hydroxide (VIII)——A solution of VII (16 g) in 20% HCl (100 g) was refluxed until the evolution of CO_2 subsided. The reaction solution was, after basifying with 10% Na_2CO_3, extracted with $CHCl_3$, dried over $MgSO_4$ and evaporated *in vacuo* to leave a crude crystal mass. Recrystallization from ethyl acetate gave VIII (9.5 g), mp 142° (hydrate mp 67—68°). *Anal.* Calcd. for $C_9H_{12}ON_2$: C, 68.58; H, 7.32; N, 17.07. Found: C, 65.48; H, 7.32; N, 17.10. NMR (10% solution in $CDCl_3$): 7.7 (1H, t, $-CH_3$), 3.55 (1H, s, aromatic H), 6.95 (2H, t), 8.0 (4H, t), 5.7 (2H, t, $-CH_2-$). The picrate had mp 179°. *Anal.* Calcd. for $C_9H_{12}ON_2 \cdot C_6H_3O_7N_3$: C, 45.82; H, 3.89; N, 17.81. Found: C, 45.40; H, 3.91; N, 17.97. The hydrochloride had mp 256° (decomp.) after recrystallization from EtOH. *Anal.* Calcd. for $C_9H_{12}ON_2$–HCl: C, 53.77; H, 3.91; N, 13.74. Found: C, 53.87; H, 6.48; N, 13.96.

Anhydro 3-Bromo-4-hydroxy-2-methyl-5,6,7,8-tetrahydropyrido[1,2-*b*]pyridazinium Hydroxide (IX)——To a solution of VIII (0.5 g) in $CHCl_3$ (20 ml) was added dropwise a solution of Br_2 (0.5 g) diluted with a small amount of $CHCl_3$. The reaction mixture was allowed to stand at room temperature to afford a precipitate of yellowish needles. Recrystallization from EtOH gave a crystal whose mp 206°. *Anal.* Calcd. for $C_9H_{11}ON_2Br \cdot HBr$: C, 33.33; H, 3.71; N, 8.67. Found: C, 33.07; H, 3.67; N, 8.62. The free base, IX, was readily given by neutralization of the hydrobromide with 10% Na_2CO_3 or by adding equivalent amount of bromine to an alkaline solution of VIII at room temperature, immediately separating out in theoretical yield. Recrystallization from EtOH gave pale yellow needles, mp 165°. *Anal.* Calcd. for $C_9H_{11}ON_2Br$: C, 44.44; H, 4.53; N, 11.52. Found: C, 44.53; H, 4.66; N, 11.23. Method of bromination with NBS: A solution of VIII (0.5 g) and NBS (0.6 g) in $CHCl_3$ (15 ml) was heated on a water bath for 30 min. The solid mass, separating out from the reaction mixture, was filtered off, and the $CHCl_3$ solution was washed with dilute NaOH solution, dried over K_2CO_3, and evaporated to afford a yellow solid mass. Recrystallization from EtOH gave IX, which was identical with the compound obtained by the previous procedure.

Anhydro 3-Anilino-4-hydroxy-2-methyl-5,6,7,8-tetrahydropyrido[1,2-*b*]pyridazinium Hydroxide (X)——A solution of IX (0.5 g) in toluene (50 ml) was reacted with aniline (0.2 g) under reflux for 8 hr. The solution was evaporated under reduced pressure to dryness to give a crude crystal mass. Recrystallization from EtOH gave pure X-HBr as yellow prisms, mp 185°. *Anal.* Calcd. for $C_{15}H_{17}ON_3$–HBr: C, 52.17; H, 5.50; N, 12.17. Found: C, 52.27; H, 5.39; N, 12.05.

Anhydro 4-Hydroxy-2-methyl-3-thiouroniumbromide-5,6,7,8-tetrahydropyrido[1,2-*b*]pyridazinium Hydroxide (XI)——To a solution of IX (0.3 g) in EtOH (20 ml) was added thiourea (0.23 g), and the reaction mixture was heated under reflux for 10 min and then evaporated *in vacuo* to afford a glutinous substance. Recrystallization from EtOH gave XI as pale yellow needles, mp 152°. *Anal.* Calcd. for $C_{10}H_{15}ON_4SBr$: C, 37.62; H, 4.70; N, 17.55. Found: C, 37.53; H, 4.97; N, 17.61. IR $\nu_{max}^{Liq.}$ cm^{-1}: 3320, 3190 (NH). UV λ_{max}^{EtOH} $m\mu$ (log ε): 240 (4.28), 319 (3.99).

Anhydro 4-Hydroxy-2-methyl-3-mercapto-5,6,7,8-tetrahydropyrido[1,2-*b*]pyridazinium Hydroxide (XII)——To a solution of XI (0.5 g) in EtOH (20 ml was added thiourea (0.23 g), and the mixture was heated under reflux for 3 hr, evaporated to give a viscous mass. The viscous mass was added to 10% NaOH (20 ml) and was heated at 100° for 20 min. The solution was after cool neutralized with 10% HCl to yield a solid mass, which was extracted with benzene, dried over Na_2SO_4 and evaporated to leave XII as yellow needles, mp 171°. *Anal.* Calcd. for $C_9H_{12}ON_2S$: C, 55.10; H, 6.12; N, 14.29. Found: C, 54.93; H, 6.38; N, 14.02. UV λ_{max}^{EtOH} $m\mu$ (log ε): 241 (3.64), 366 (3.93). NMR (10% solution in $CDCl_3$) τ: 5.74 (2H, t, $\equiv\overset{+}{N}-CH_2-$), 7.05 (2H, t, $-CH_2-$), 7.4 (3H, s, $-CH_3$), 8.0 (4H, t, $-CH_2-CH_2-$).

Anhydro 3-Chloromercurithio-4-hydroxy-2-methyl-5,6,7,8-tetrahydropyrido[1,2-*b*]pyridazinium Hydroxide (XIII)——A mixture of XII (0.5 g) and $HgCl_2$ (0.5 g) in EtOH (10 ml) was refluxed until clear solution was obtained and then allowed to stand at room temperature.

The resulting yellow precipitate was collected and recrystallization from DMF gave pale yellow needles, mp 255°. *Anal.* Calcd. for $C_9H_{11}ON_2SHClg$: C, 25.12; H, 2.56; N, 6.51. Found: C, 24.97; H, 2.69; N, 6.50.

Anhydro 3-Benzylthio-4-hydroxy-2-methyl-5,6,7,8-tetrahydropyrido[1,2-*b*]pyridazinium Hydroxide (XIV)——To a mixture of XII (0.5 g) and MeONa (0.1 g) in MeOH (20 ml) was added benzylchloride (0.3 g), and the mixture was refluxed for 3 hr, NaCl separated out being rejected by filtration. The filtrate was concentrated and the residue was extracted well with $CHCl_3$, dried over Na_2SO_4 and evaporated to give a yellow viscous oil, which was crystallized with EtOH–isopropylether. Recrystallization from EtOH gave yellow needles, mp 96°. *Anal.* Calcd. for $C_{16}H_{18}ON_2S$: C, 67.13; H, 6.29; N, 9.78. Found: C, 67.06; H, 6.46; N, 9.71. UV λ_{max}^{EtOH} mμ (log ε): 260 (3.73), 353 (3.81). NMR (10% solution in $CDCl_3$): 5.74 (2H, t, =N–C$\underline{H}_2$–), 7.05 (2H, t, –Ç–C$\underline{H}_2$–), 7.4 (3H, s, –C$\underline{H}_3$), 8.0 (4H, t, –C$\underline{H}_2$–C$\underline{H}_2$–). The hydrochloride was prepared by treating XIV with EtOH–HCl and recrystallized from EtOH to give yellowish needles, mp 175°. *Anal.* Calcd. for $C_{16}H_{18}ON_2S\cdot HCl$: C, 59.63; H, 5.90; N, 7.82. Found: C, 59.39; H, 6.16; N, 8.52. The menthiodide was prepared by treating XIV with MeI in MeOH to give yellow needles, mp 175°. *Anal.* Calcd. for $C_{16}H_{18}ON_2S\cdot CH_3I$: C, 47.66; H, 4.91; N, 6.54. Found: C, 47.35; H, 4.73; N, 6.68.

Anhydro 3,4-Dihydroxy-2-methyl-5,6,7,8-tetrahydropyrido[1,2-*b*]pyridazinium Hydroxide (XV)——To a solution of VIII (2.4 g) in glacial AcOH (9 ml) was added 30% H_2O_2 (1.5 ml), and the solution was heated for 3 hr at 80—90°. An additional 30% H_2O_2 (1.1 ml) was added to the reaction mixture, which was maintained at 100° for further 2 hr. The reaction mixture was then evaporated *in vacuo* to almost dryness. The residue was purified using column chromatography (alumina, solvent $CHCl_3$), affording XV as a solid mass. Recrystallization from EtOH gave colorless granules, mp 214°. *Anal.* Calcd. for $C_9H_{12}O_2N_2$: C, 59.98; H, 6.71; N, 15.55. Found: C, 59.93; H, 6.80; N, 15.51. UV λ_{max}^{EtOH} mμ (log ε): 305 (4.12). IR λ_{max}^{KBr} cm^{-1}: 2800—2400 (–OH---O–). NMR (10% solution in $CDCl_3$): 7.65 (3H, s, –C$\underline{H}_3$), 0.45 (1H, s, –O$\underline{H}$), 5.85 (2H t), 7.05 (2H t), and 7.95 (4H, t, –C$\underline{H}_2$–).

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