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# THE REACTION OF THIAZOLO[3,2-b]PYRIDAZINIUM PERCHLORATES WITH HYDRAZINES. FORMATION OF 1,4-BIS-(2-VINYL-3-PYRIDAZINYLIDENE)TETRAZENES

Kazue SATOH and Tadashi MIYASAKA*
School of Pharmaceutical Sciences, Showa University
Hatanodai 1-5-8, Shinagawa-ku, Tokyo 142

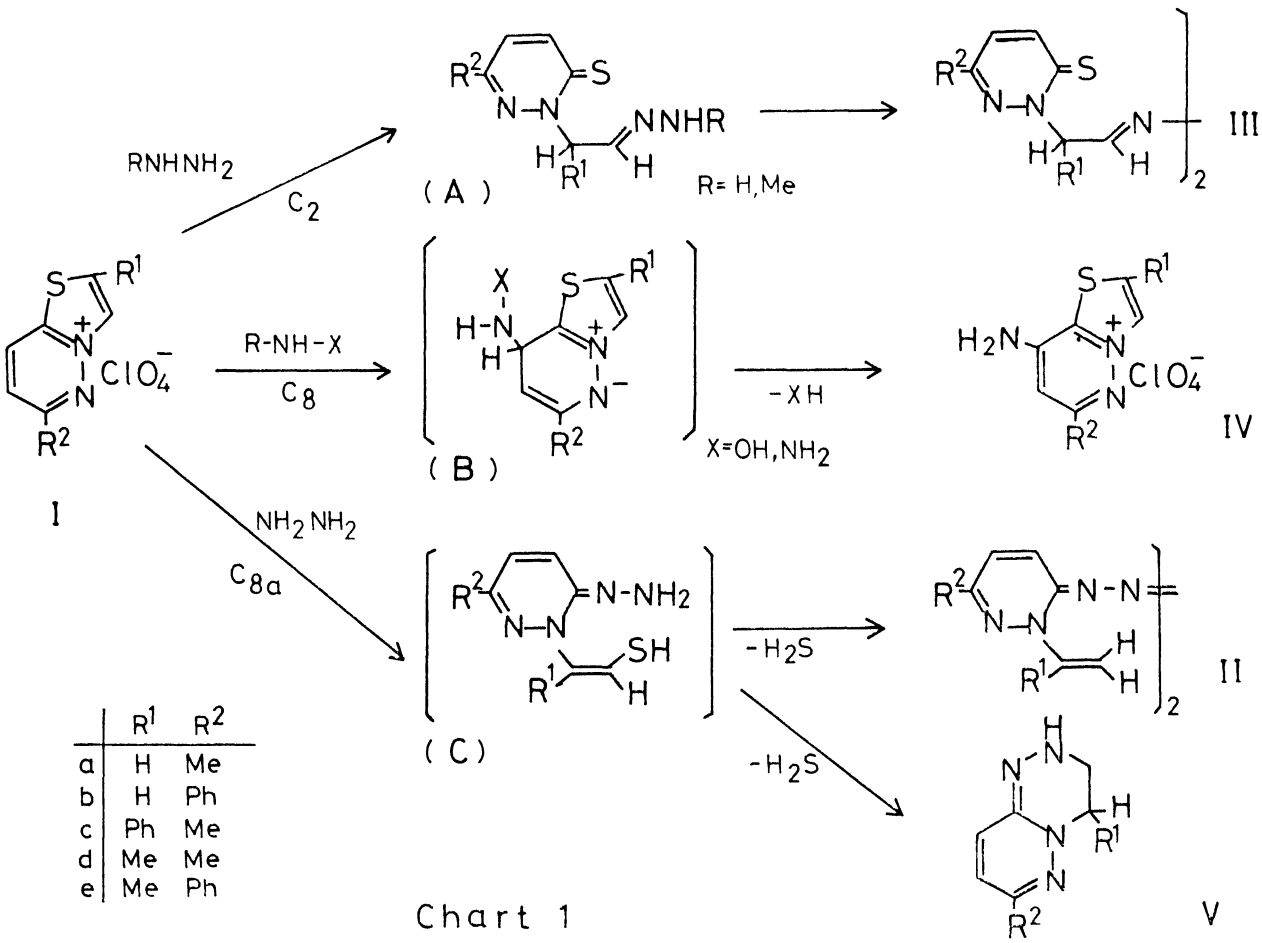
Treatment of thiazolo[3,2-b]pyridazinium perchlorates with hydrazine hydrate in acetonitrile afforded the title compounds and several products depending upon its reaction time and temperature and difference of substituent. Catalytic reduction of the tetrazenes gave 2H-3,4-dihydropyridazino[6,1-c]triazines. Oxidation with 30% $H_2O_2$ yielded pyridazino[6,1-c]-3-triazinones.

In the course of our studies on the synthesis and the reaction of pi-deficient condensed azolium salts,[1] almost all of C-, O-, S- and N-nucleophiles were revealed to attack at $C_{8a}$, the most electron-deficient position of oxazolo[3,2-b]pyridazinium salts.[2] However, in the case of the thiazolo[3,2-b]pyridazinium salts (I), C- and S-nucleophiles were proved to attack at $C_7$- and/or $C_8$-position to furnish ylide- and/or enamine-quinoid type compounds through a new nucleophilic substitution reaction with participation of triplet oxygen.[3] In this communication, we present a reaction of the salts (I) with hydrazines as N-nucleophile to furnish new heterocyclic systems.

When a solution of 6-phenylthiazolo[3,2-b]pyridazinium perchlorate (Ib) was treated with 3 equivalent hydrazine hydrate (100%) in refluxing acetonitrile, orange-red prisms of 1,4-bis-(6-phenyl-2-vinyl-3-pyridazinylidene)tetrazene (IIb)[$C_{24}H_{20}N_8$; Mass (m/e): 420 ($M^+$), 171 (corresponding to 3-amino-6-phenylpyridazine); UV $\lambda$ max ($CHCl_3$, nm): 234.5, 275.0, 320.0][4] and N,N'-bis-[2-(6-methylpyridazin-3-thion)yl-phenylacetoaldimine](IIIb) [mp 217-218°(d); NMR $\delta$ ($CDCl_3$, ppm): 5.61 (2H, d, J=4Hz, coupled with a peak at $\delta$ 7.83 ppm), 7.44 (1H, d, J=9Hz), 7.83 (1H, m), 7.88 (1H, d, J=9Hz); Mass (m/e): 456 ($M^+$), 213 ($1/2M^+$-NH), 188 (6-phenylpyridazin-3-thione)] were obtained with evolution of hydrogen sulfide. In addition to IIc and IIIc [mp 190-195°], similar treatment of Ic furnished 7-methyl-4-phenylpyridazino[6,1-c]triazinium perchlorate (VII).

Heating of tetrazene (IIc) with hydrazine hydrate and perchloric acid (5 and 2 equivalents each) in acetonitrile for 3 hours gave 6-methyl-3-phenylimidazo[1,2-b]-pyridazine (VI) [20%; picrate mp 209-210°; Mass (m/e): 209 ($M^+$); NMR $\delta$ ($CDCl_3$, ppm): 2.60 (3H, s), 6.93 (1H, d, J=9Hz), 7.87 (1H, d, J=9Hz), 7.94 (1H, s, $C_2$-H)] and colorless flakes of VII [35%; mp 225-227°; NMR $\delta$ (DMSO-$d_6$, ppm): 2.76 (3H, s), 7.93 (1H, d, J=10Hz), 8.55 (1H, d, J=10Hz), 8.82 (1H, s, $C_3$-H)] (Chart 2).

Reaction of the perchlorates ($R^1$=Me; Id,e) with hydrazine hydrate gave 8-amino-thiazolo[3,2-b]pyridazinium perchlorates (IVd,e) as colorless needles instead of the




| | $R^1$ | $R^2$ |
|---|---|---|
| a | H | Me |
| b | H | Ph |
| c | Ph | Me |
| d | Me | Me |
| e | Me | Ph |

Chart 1

corresponding tetrazenes (Table I and III). 8-Amino-compounds (IVd,e) were also obtained by the reaction of Id,e with hydroxylamine hydrochloride and potassium hydroxide in dimethyformamide at room temperature. However, similar treatment of the salts with a phenyl substituent at $C_3$ or of those without any substituent at $C_3$ (Ia,b,c) gave an intractable mixture. By conducting the reaction of I with hydrazine hydrate at room temperature, red crystals of 2H-3,4-dihydropyridazino[6,1-c]triazines (Va-e) were isolated instead of the tetrazenes (II) or 8-amino-compounds (IV).

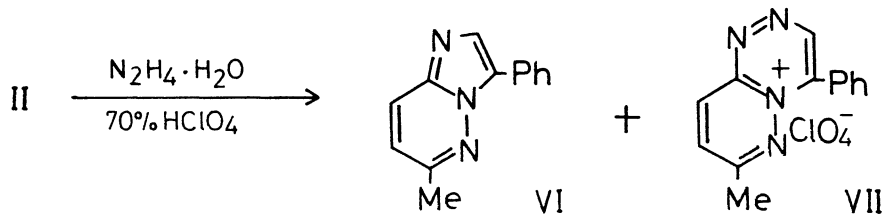



Chart 2

Catalytic reduction of tetrazene (IIb) with 5% palladium charcoal in acetic acid afforded red prisms of pyridazinotriazine (Vb) in 63% yield. Catalytic reduction of tetrazenes gave reportedly two moles of amines with evolution of nitrogen.[5] Formation of Vb by catalytic reduction of IIb seems to induced by cyclization due to nucleophilicity of the N-vinyl moiety during the reduction. By heating the tetrazene (IIb) with 30% $H_2O_2$ at 50° for 45 minutes, 3,4-dihydropyridazino[6,1-c]-3-triazinone

Table I. Products from reaction of I with hydrazine hydrate

| I | Reaction condition: molar ratio | react.temp. (°C) | time (hr.) | Products and yield (%): I | II | III | IV | V | VII |
|---|---|---|---|---|---|---|---|---|---|
| a | 3 | reflux* | 1 | - | 28 | 9 | - | - | - |
| a | 5 | r.t. | 24 | - | - | 9 | - | 53 | - |
| a | 10 | r.t. | 6 | - | 10 | 18 | - | 28 | - |
| b | 3 | reflux | 1 | - | 48 | 7 | - | - | - |
| b | 10 | r.t. | 24 | - | - | 41 | - | 33 | - |
| c | 3 | reflux | 1 | 5 | 18 | 21 | - | - | 28 |
| c | 10 | r.t. | 20 | - | 25 | 24 | - | 17 | - |
| c | 10 | r.t. | 42 | - | 17 | 10 | - | 34 | - |
| d | 3 | reflux | 4 | - | - | 19 | 54 | - | - |
| d | 10 | r.t. | 44 | 26 | - | 7 | - | 21 | - |
| e | 10 | reflux | 1 | - | - | 18 | 35 | - | - |
| e | 10 | r.t. | 26 | - | - | - | - | 27 | - |

*) Solvent: $CH_3CN$

(VIIIb) [mp 182-192°; IR $\nu$max(KBr $cm^{-1}$): 1650 (sh), 1640; NMR $\delta$ ($CDCl_3$, ppm): 4.72 (2H, s, $C_4$-$\underline{CH}_2$); Mass (m/e): 226 ($M^+$), 197 ($M^+$-29)] was obtained. By oxidation of IIa and IIc in the same manner, VIIIa [42%; mp 193-196°(d)] and VIIIc [49%; mp 237-247° (d)] were obtained, respectively. VIIIa was also obtained by heating of Va with 30% $H_2O_2$ in acetic acid at 50° for 30 minutes (Chart 3).

A plausible mechanism is shown in Chart 1. Nucleophilic addition of the hydrazine at $C_2$ of I gives III through the intermediate (A). Isolation of (A) was successful as the $\underline{N}$-methyl derivative [(A), R=$R^2$=Me, $R^1$=Ph; mp 114-115.5°] by treatment of Ic with methyhydrazine. 8-Amino-compound (IV) is formed by the initial attack of the hydrazine or hydroxylamine at $C_8$ and followed by elimination of ammonia or water. When the hydrazine attacks at $C_{8a}$, the labile intermediate (C) which is not isolated but detected by thin-layer chromatography, suffers either oxidative dimerization to form II with concomitant elimination of hydrogen sulfide or reductive recyclization to give V. The salt (I) bearing a methyl substituent at $C_3$ gives IV as a result of preferential attack of the reagent at $C_8$ instead of $C_{8a}$ due to stabilization of the thiazole $\underline{N}$-imine type intermediate (B) by hyperconjugation of the methyl group. The mechanism for the formation of II and V is not

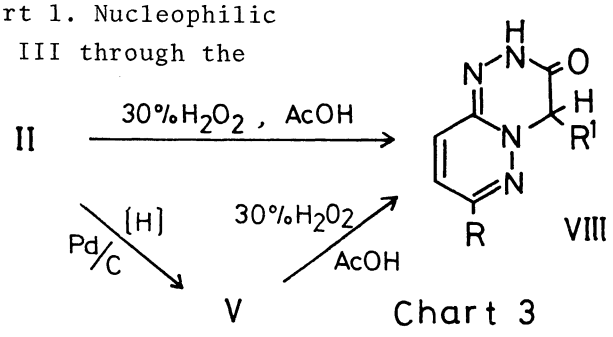


Chart 3

Table II. Tetrazenes (II)

| Compd. No. | $R^1$ | $R^2$ | Mp (°C (d)) | NMR $\delta$ (ppm in $CDCl_3$): Ha | Hb | Hc | $C_4$-$\underline{H}$ | $C_5$-$\underline{H}$ |
|---|---|---|---|---|---|---|---|---|
| IIa | H | $CH_3$ | 225-227.5 | 3.65(q) | 4.24(d,d) | 4.57(d,d) | 6.20(d) | 6.54(d) |
| | | | | | Ja,b=3.4Hz,Jb,c=5.9Hz, | Ja,c=12.7Hz | | J4,5=9.3Hz |
| IIb | H | $C_6H_5$ | 211-213 | 3.82(q) | 4.46(d,d) | 4.75(d,d) | 6.73(d) | 6.54(d) |
| | | | | | Ja,b=3Hz, | Jb,c=6Hz, Ja,c=13Hz, | | J4,5=10Hz |
| IIc | $C_6H_5$ | $CH_3$ | 210-211 | 4.72(d) | 5.32(d), | 6.98-7.24 | 5.72(d) | 6.04(d) |
| | | | | | Ja,b=2Hz, | (arom. 5H) | | J4,5=10Hz |

Table III. 8-Aminothiazolo[3,2-b]pyridazinium perchlorates (IV)

| Compd. No. | $R^1$ | $R^2$ | Mp (°C) | NMR δ (ppm)* $C_2$-H | $C_7$-H | $C_8$-$NH_2$# | IR ν KBr max ($cm^{-1}$) NH | | $NH_2$ |
|---|---|---|---|---|---|---|---|---|---|
| IVd | $CH_3$ | $CH_3$ | 239-241 | 8.44(s) | 6.92(s) | 8.24(s) | 3430<br>3340 | 3240<br>3100 | 1650<br>1580 |
| IVe | $CH_3$ | $C_6H_5$ | 285-286 | 8.43(s) | 7.40(s) | 8.31(s) | 3400<br>3340 | 3240<br>3120 | 1650<br>1580 |

* Solvent:DMSO-$d_6$ # $D_2O$ exchangeable

Table IV. 3,4-Dihydropyridazino[6,1-c][1,2,4]triazines (V)

| Compd. No. | $R_1$ | $R^2$ | Mp (°C) | NMR δ (ppm in $CDCl_3$) $C_3$-H | $C_4$-H | $C_8$-H | $C_9$-H |
|---|---|---|---|---|---|---|---|
| Va | H | $CH_3$ | 57- 58 | 3.15(2H,t) | 3.47(2H,t) | 6.14(1H,d) | 6.46(1H,d) |
| | | | | $J_{3,4}$=4.5Hz | | $J_{8,9}$=10Hz | |
| Vb | H | $C_6H_5$ | 124-125 | 3.28(2H,t) | 4.15(2H,t) | 6.65(1H,d) | 6.84(1H,d) |
| | | | | $J_{3,4}$=4.5Hz | | $J_{8,9}$=10Hz | |
| Vc | $C_6H_5$ | $CH_3$ | 185-186 | 3.27(2H,d) | 5.12(1H,m)<br>7.28(5H,s) | 6.16(1H,d) | 6.59(1H,d) |
| | | | | $J_{3,4}$=2.8Hz | | $J_{8,9}$=10Hz | |
| Vd | $CH_3$ | $CH_3$ | 202(pic.) | 3.02(2H,d) | 4.12(1H,m)<br>1.48(3H,d) | 6.15(1H,d) | 6.53(1H,d) |
| | | | | $J_{3,4}$=2.9Hz, 6.3Hz | | $J_{8,9}$=10Hz | |
| Ve | $CH_3$ | $C_6H_5$ | 122-123 | 3.10(2H,d) | 4.29(1H,m)<br>1.57(3H,d) | 6.63(1H,d) | 6.73(1H,d) |
| | | | | $J_{3,4}$=3Hz, 6Hz | | $J_{8,9}$=10Hz | |

yet completely elucidated. Presumably S- and C-nucleophiles attack at $C_7$ and/or $C_8$ as soft base, while O- and N-nucleophiles attack at $C_{8a}$ as hard base.

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