5.3 g (60%) of the product, mp 202–203° (reported for *trans*-2,3-diphenyl-2,3-dihydropyrazine, mp 202–203° [1]).

**Registry No.**—1, 16635-95-3; 4, 951-87-1; 8, 31819-61-1; 9, 31819-62-2; glyoxal, 107-22-2.

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## Pyridazines. XLII. Tetrazolo–Azido Isomerizations of Isomeric Pyridotetrazolo[1,5-*b*]pyridazines

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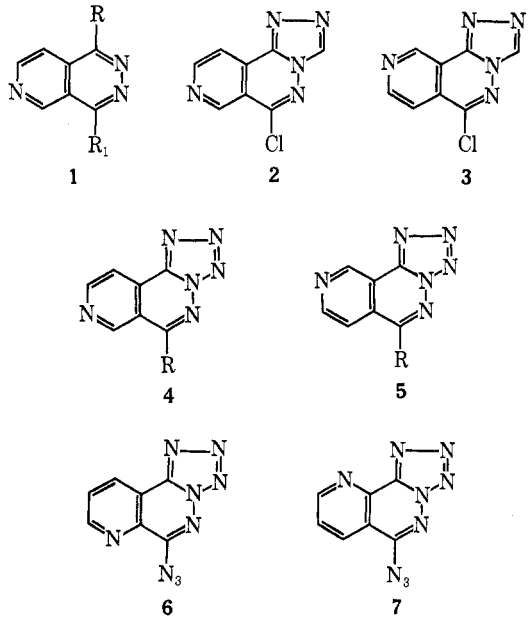
Our previous investigations on tetrazolo–azido isomerizations of several heterocyclic systems[1-8] prompted an investigation of this phenomenon on 6-azidopyrido[4,3-*d*]tetrazolo[1,5-*b*]pyridazine (**4**, R = $N_3$) and 6-azidopyrido[3,4-*d*]tetrazolo[1,5-*b*]pyridazine (**5**, R = $N_3$). The synthesis of both isomers was accomplished from the corresponding 1-chloro-4-hydrazinopyrido[3,4-*d*]pyridazine (**1**, R = Cl; $R_1$ = $NHNH_2$)[9] or its isomer (**1**, R = $NHNH_2$; $R_1$ = Cl) as starting compounds. These were converted either to the isomeric pyrido-*s*-triazolo[4,3-*b*]pyridazines (**2** and **3**) or into tetrazolo analogs **4** and **5** (R = Cl). Upon hydrazinolysis and subsequent nitrosation the isomeric azido compounds **4** and **5** (R = $N_3$) were obtained. Moreover, the isomer **4** (R = $N_3$) is obtainable in a direct synthetic approach from 1,4-dichloropyrido[3,4-*d*]pyridazine and sodium azide. The structures of both isomers were established by the nmr spectra. The singlet for $H_{10}$ of compound **5** (R = $N_3$) appears at lower field than that for $H_7$ of compound **4** (R = $N_3$), as observed with similar polycyclic systems.[10,11] It was also observed that isomer **5** (R = $N_3$), when crystallized from ethanol, is transformed into the thermodynamically more stable isomer **4** (R = $N_3$).

In dimethyl sulfoxide-$d_6$ an equilibrium is established at 70°, consisting of about 33% of **5** (R = $N_3$) and 67% of **4** (R = $N_3$), whereas for the isomeric pair of 6-azidopyrido[3,2-*d*]tetrazolo[5,1-*b*]pyridazine (**6**) and 6-azidopyrido[2,3-*d*]tetrazolo[5,1-*b*]pyridazine (**7**)[1] the equilibrium mixture consisted of 42% of **6** and 58% of **7**. The determined enthalpy changes, $\Delta H$, for these isomerizations, which follow first-order kinetics, were calculated as −2.2 kcal/mol for **5** → **4** (R = $N_3$) and −1.3 kcal/mol for **6** → **7**, respectively. The Arrhenius activation energies, $E_a$, calculated from the rate constants, are 25.2 kcal/mol (**5** → **4**, R = $N_3$) and 27.8 kcal/mol (**6** → **7**), respectively. As anticipated, they are somewhat higher than those observed with the corresponding azidotetrazolo[1,5-*b*]pyridazines,[1] whereas the enthalpy changes are lower. The calculated $\Delta S^*$ values were −2 eu for **5** → **4** (R = $N_3$) and +7 eu for **6** → **7**.




### Experimental Section

Melting points were determined on a Kofler micro hot stage and are corrected. Infrared spectra were recorded on a Perkin-Elmer 137 Infracord as KBr disks, and nmr spectra were taken on a JEOL JNM-C-60HL spectrometer using tetramethylsilane as internal standard.

1-Chloro-4-hydrazinopyrido[3,4-*d*]pyridazine and 4-chloro-1-hydrazinopyrido[3,4-*d*]pyridazine were prepared according to Matsuura and Okui.[9] They formed the corresponding benzylidene derivatives: **1** (R = Cl; $R_1$ = NHN=CHPh), mp 283–284° (from EtOH and DMF, 3:1).

*Anal.* Calcd for $C_{14}H_{10}ClN_5$: C, 59.26; H, 3.55; N, 24.69. Found: C, 59.20; H, 3.46; N, 24.83.

The benzylidene derivative of the other isomer (**1**, R = NHN=CHPh; $R_1$ = Cl) had mp 252° (from EtOH and DMF, 3:1).

*Anal.* Calcd for $C_{14}H_{10}ClN_5$: C, 59.26; H, 3.55; N, 24.69. Found: C, 59.00; H, 3.41; N, 24.74.

**6-Chloropyrido[3,4-*d*]-*s*-triazolo[4,3-*b*]pyridazine (3).**—Compound **1** (R = Cl; $R_1$ = $NHNH_2$) (0.3 g) and diethoxymethyl acetate (1 ml) were gently heated until solution occurred and then boiled for 3 min. Upon cooling the separated product (0.26 g) was recrystallized from DMF and EtOH (1:3): mp 254° (it sublimes above 200°); nmr (DMSO-$d_6$) $\delta$ 9.52 (s, $H_3$), 8.28 (d, $H_7$), 9.25 (d, $H_8$), 9.88 (s, $H_{10}$), $J_{7,8}$ = 5.6 Hz.

*Anal.* Calcd for $C_8H_4ClN_5$: C, 46.73; H, 1.96; N, 34.07. Found: C, 46.45; H, 2.08; N, 34.33.

**6-Chloropyrido[4,3-*d*]-*s*-triazolo[4,3-*b*]pyridazine (2).**—The compound was prepared in the same way from compound **1** (R = $NHNH_2$; $R_1$ = Cl) (0.2 g) (yield 0.17 g): mp 260° (from EtOH and DMF, 1:3); nmr (DMSO-$d_6$) $\delta$ 9.50 (s, $H_3$), 9.40 (s, $H_7$), 9.25 (d, $H_8$), 8.45 (d, $H_{10}$), $J_{9,10}$ = 5.6 Hz.

*Anal.* Calcd for $C_8H_4ClN_5$: C, 46.73; H, 1.96; N, 34.07. Found: C, 47.10; H, 2.22; N, 34.26.

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**6-Chloropyrido[3,4-*d*]tetrazolo[1,5-*b*]pyridazine (5, R = Cl).**—An ice-cold solution of compound **1** (R = Cl; $R_1$ = $NHNH_2$) (0.5 g) in HCl (6 ml of 2 *N*) was treated under stirring with a cold aqueous solution of $NaNO_2$ (0.2 g in 3 ml of water). The product which separated was crystallized from EtOH (0.32 g): mp 177°; nmr ($CDCl_3$) $\delta$ 8.20 (d, $H_7$), 9.28 (d, $H_8$), 10.1 (s, $H_{10}$), $J_{7,8}$ = 6.0 Hz.

*Anal.* Calcd for $C_7H_3ClN_6$: C, 40.69; H, 1.46; N, 40.68. Found: C, 40.79; H, 1.83; N, 40.84.

**6-Chloropyrido[4,3-*d*]tetrazolo[1,5-*b*]pyridazine (4, R = Cl)** was prepared as described above for **5** (R = Cl) in 75% yield: mp 184° (from EtOH); nmr ($CDCl_3$) $\delta$ 9.66 (s, $H_7$), 9.28 (d, $H_9$), 8.55 (d, $H_{10}$), $J_{9,10}$ = 5.7 Hz.

*Anal.* Calcd for $C_7H_3ClN_6$: C, 40.69; H, 1.46; N, 40.68. Found: C, 40.42; H, 1.62; N, 40.59.

**6-Hydrazinopyrido[4,3-*d*]tetrazolo[1,5-*b*]pyridazine (4, R = $NHNH_2$).**—A mixture of **4** (R = Cl) (0.2 g), ethanol (5 ml), and hydrazine hydrate (1 ml of 80%) was heated under reflux for 15 min. The product was recrystallized from DMF and EtOH (3:1) (0.16 g), mp 290–293° dec.

*Anal.* Calcd for $C_7H_6N_8$: C, 41.58; H, 2.99; N, 55.43. Found: C, 41.90; H, 3.15; N, 55.49.

**6-Hydrazinopyrido[3,4-*d*]tetrazolo[1,5-*b*]pyridazine (5, R = $NHNH_2$).**—The compound was prepared as described above for the isomer **4** (R = $NHNH_2$) in 66% yield, mp 286–288° dec (from DMF and EtOH, 3:1).

*Anal.* Calcd for $C_7H_6N_8$: C, 41.58; H, 2.99; N, 55.43. Found: C, 41.35; H, 3.09; N, 55.09.

**6-Azidopyrido[4,3-*d*]tetrazolo[1,5-*b*]pyridazine (4, R = $N_3$).**

**A.**—Compound **4** (R = $NHNH_2$) (0.2 g) was dissolved in HCl (4 ml of 2 *N*) and under stirring the ice-cold solution was treated with a cold solution of aqueous $NaNO_2$ (80 mg in 1 ml) dropwise, yield 0.16 g. For recrystallization the azide was dissolved in a minimum amount of EtOH at 40°, some charcoal was added, and, after stirring a few minutes at this temperature, the obtained filtrate was cooled to about −20° and the separated product was collected: mp 146–147°; ir 2155 $cm^{-1}$ ($N_3$); nmr (DMSO-$d_6$) $\delta$ 9.46 (s, $H_7$), 9.37 (d, $H_9$), 8.53 (d, $H_{10}$), $J_{9,10}$ = 5.9 Hz.

*Anal.* Calcd for $C_7H_3N_9$: C, 39.44; H, 1.42; N, 59.14. Found: C, 39.31; H, 1.63; N, 59.24.

**B.**—A suspension of 1,4-dichloropyrido[3,4-*d*]pyridazine (1 g) and sodium azide (0.65 g) in ethanol (20 ml) was heated under reflux for 1 hr and evaporated then to half of the original volume. The residue was poured into ice (10 g) and the separated product (0.81 g) was collected. For analysis the compound was crystallized from ethanol, mp 146–147°. The compound was found to be identical in all respects with the product obtained as described under A.

**6-Azidopyrido[3,4-*d*]tetrazolo[1,5-*b*]pyridazine (5, R = $N_3$).**—This compound was prepared in a similar manner as described for the isomer **4** (R = $N_3$) under A, yield 83%, mp 163° (crystallization was performed as described above under A). If crystallization was attempted from boiling ethanol, the isomeric azide (**4**, R = $N_3$) was obtained. Also, when melted, upon solidification the isomer **4** (R = $N_3$) is formed: ir 2151 $cm^{-1}$ ($N_3$); nmr (DMSO-$d_6$) $\delta$ 8.06 (d, $H_7$), 9.20 (d, $H_8$), 9.93 (s, $H_{10}$), $J_{7,8}$ = 5.7 Hz.

*Anal.* Calcd for $C_7H_3N_9$: C, 39.44; H, 1.42; N, 59.14. Found: C, 39.14; H, 1.68; N, 59.08.

**Rate Constants and Equilibria.**—For the determination of rate constants and equilibria measurements, nmr spectra of dimethyl sulfoxide-$d_6$ solutions were performed and the constants were calculated as described previously.[1]

For the system **5** → **4** (R = $N_3$) the values are as follows: $\Delta H$ = −2.2 ± 0.2 kcal/mol; rate constants, $k_1$ = 1.27 × $10^{-3}$ $sec^{-1}$ (at 60°), $k_2$ = 3.45 × $10^{-3}$ $sec^{-1}$ (at 80°); $E_a$ = 25.2 ± 0.2 kcal/mol; $\Delta S$ = −2 eu.

For the system **6** → **7** the values are: $\Delta H$ = −1.3 ± 0.2 kcal/mol; rate constants, $k_1$ = 8.0 × $10^{-4}$ $sec^{-1}$ (at 60°), $k_2$ = 1.39 × $10^{-3}$ $sec^{-1}$ (at 70°), $k_3$ = 2.5 × $10^{-3}$ $sec^{-1}$ (at 80°); $E_a$ = 27.8 ± 0.2 kcal/mol; $\Delta S^*$ = +7 eu.

**Registry No.**—**1** (R = Cl; $R_1$ = NHN=CHPh), 31767-04-1; **1** (R = NHN=CHPh; $R_1$ = Cl), 31767-05-2; **2**, 31767-06-3; **3**, 31767-07-4; **4** (R = Cl), 31767-08-5; **4** (R = $NHNH_2$), 31767-09-6; **4** (R = $N_3$), 31767-10-9; **5** (R = Cl), 31821-50-8; **5** (R = $NHNH_2$), 31767-11-0; **5** (R = $N_3$), 31767-12-1.

# A New Synthesis of Alkyl Oximinoglyoxylates and the Corresponding Acid and Hydroximoyl Chlorides

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A number of syntheses of oximinoglyoxylate esters, HON=$CHCO_2R$, have been reported: the reaction of alkyl gloxylates[1] or the corresponding hemiacetal[2] or alkoxybromo esters[3] with hydroxylamine, the reaction of acetoacetic esters with nitrosylsulfuric acid,[4] and the alkylation of silver oximinoglyoxylate.[5] All these methods suffer from unavailability of starting materials or low overall yields.

Nitrile oxides, derived from hydroximoyl chlorides by treatment with base,[6] have been shown to be useful cross-linking agents for unsaturated polymers.[7] We have now discovered what appears to be a simple, direct synthesis of alkyl oximinoglyoxylates (I) and the corresponding hydroximoyl chlorides (II). The method involves the reaction of ketene with nitrosyl chloride, followed by treatment with excess alcohol to yield the oximino ester; chlorination then yields the hydroximoyl chloride. The conditions which ultimately

$$CH_2{=}C{=}O \xrightarrow[2.\ ROH]{1.\ NOCl} \underset{\textbf{I}}{HON{=}CHCO_2R} \xrightarrow{Cl_2} \underset{\textbf{II}}{\overset{Cl}{\overset{|}{HON{=}CCO_2R}}}$$

proved to be most successful for the preparation of oximinoglyoxylates consisted of first condensing a measured quantity of ketene in the desired solvent at −78°. One equivalent of nitrosyl chloride then was added slowly to the cold solution followed by an excess of alcohol. The reaction mixture was warmed to room temperature and stirred for several hours. Yields of 65–78% of methyl, ethyl, and *n*-butyl oximinoglyoxylates were obtained with this procedure. Both cis and trans isomers of the oximino esters were detected by gas chromatographic analysis. By-products in the ethyl system, which was studied most thoroughly, included diethyl oxalate, ethyl diethoxyacetate, hydrazine hydrochloride, and, probably, ethyl chloroacetate. All identifications except that of ethyl chloroacetate were firm and were made by comparison of purified samples with authentic materials, either commercially available or prepared by an independent route.

In order to obtain good yields of oximinoglyoxylates from the reaction of ketene, NOCl, and alcohols, several variables must be controlled carefully. First, the reaction temperature must be kept low, not only to prevent decomposition of the ketene–NOCl adduct but also to prevent ketene dimerization. Second, nitrosyl chloride

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