Anal. Calcd for $C_{14}H_{14}ClNO$: C, 67.88; H, 5.69; N, 5.65. Found: C, 67.93; H, 5.75; N, 5.66.

2,4-Bis(4-chlorobenzoyl)-1-methylpyrrole (11c). A solution of 10.0 g (0.045 mol) of **1c**, 5.8 mL (0.045 mol) of 4-chlorobenzoyl chloride, and 6.05 g (0.045 mol) of $AlCl_3$ in 1,2-dichloroethane was stirred for 4 h at 25 °C and then heated under reflux for 16 h. Additional portions of 4-chlorobenzoyl chloride (5.8 mL) and $AlCl_3$ (6.05 g) were added. The mixture was heated under reflux for 5 h. The mixture was poured into dilute HCl and extracted with $CHCl_3$. The $CHCl_3$ solution was decanted to separate the insoluble solid. The $CHCl_3$ solution was washed successively with *N,N*-(dimethylamino)propylamine solution, dilute HCl, and $NaHCO_3$ solution and dried ($MgSO_4$). The solvent was evaporated in vacuo. The residue (16 g) was dissolved in a smaller quantity of $CHCl_3$, the insoluble solid removed by filtration, and the solvent evaporated. The residue was recrystallized from EtOAc to give 2.0 g (12% yield) of white solid: ^1H NMR ($CDCl_3$) δ 7.80–7.46 (9 H, m), 7.10 (1 H, d, J = 1.5 Hz), 4.05 (3 H, s); UV (MeOH) δ 254 nm (ϵ 29 600), 307 (21 300).

Anal. Calcd for $C_{19}H_{13}Cl_2NO_2$: C, 63.70; H, 3.65; N, 3.90. Found: C, 63.29; H, 3.76; N, 3.90.

4-Chloro-4'-methoxybenzophenone (12). A mixture of 0.5 g (1.4 mmol) of **11c** and 0.3 mL (2.8 mmol) of anisole was heated at 95 °C in 10 g of PPA. After 1 h, 0.15 mL of anisole was added. The mixture was heated for 5 h. It was poured into water and extracted with CH_2Cl_2. The CH_2Cl_2 solution was washed with $NaHCO_3$ solution, dried ($MgSO_4$), and concentrated to dryness. The residue was chromatographed on silic-AR CC-4 with a hexane–CH_3CCl_3 step gradient as eluant. The first compound-bearing fraction, upon evaporation and recrystallization of the residue from MeOH, gave 0.091 g of **12** as a white solid: mp 125–126 °C (lit.[19] mp 125 °C); IR ($CHCl_3$) ν_{max} 3005, 1650, 1600 cm^{-1}; mass spectrum, m/e 246, 245, 218, 210, 138, 134.

The second chromatographic fraction on TLC (SiO_2; EtOAc–cyclohexane, 1:2) corresponded to a mixture of **2c** and **11c**.

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Registry No. 1a, 37496-06-3; **1b**, 62128-31-8; **1c**, 62128-32-9; **1d**, 62128-33-0; **1e**, 932-16-1; **1f**, 62128-36-3; **2a**, 62128-30-7; **2b**, 62128-43-2; **2c**, 62128-44-3; **2d**, 62128-45-4; **2e**, 932-62-7; **2f**, 62128-39-6; **3a**, 1072-83-9; **3b**, 13169-71-6; **4a**, 1072-82-8; **4b**, 62128-38-5; **5a**, 1192-58-1; **5b**, 1003-29-8; **6a**, 36929-60-9; **6b**, 7126-39-8; **7**, 62128-28-3; **8**, 62128-48-7; **9**, 76010-94-1; **11c**, 76024-67-4; **12**, 10547-60-1; 4-chloro-*N,N*-dimethylbenzamide, 14062-80-7; 1-methylpyrrole, 96-54-8; 1-methyl-5-(4-methylbenzoyl)pyrrole-2-acetate Na, 35711-34-3; 5-(4-chlorobenzoyl)-1,4-dimethylpyrrole-2-acetic acid, 33369-31-2; 1,2,5-trimethylpyrrole, 930-87-0; 4-chlorobenzoyl chloride, 122-01-0; anisole, 100-66-3; *N,N*-dimethylbenzamide, 611-74-5.

(19) P. Peterson, *Am. Chem. J.*, **46**, 339 (1913).

Linearly Fused Isoquinolines. 3.[1] Positional Effect of Substitution on Equilibrium of Tetrazole–Azide Systems. Anomalous Behavior in Trifluoroacetic Acid

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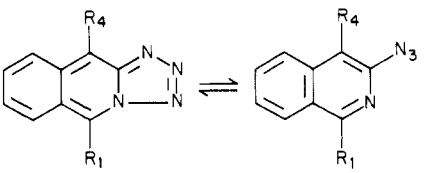
A new method for synthesis of heteroaromatic azides has been elaborated, and a series of substituted tetrazolo[1,5-*b*]isoquinoline derivatives has been synthesized. The effect of R_1 and R_4 substituents on the equilibrium between 3-azidoisoquinoline (**1b**) and tetrazol[1,5-*b*]isoquinoline (**1a**) was investigated. Only a slight difference in influence of substituents in the opposite positions R_1 and R_4 was found. In contrast to earlier examples, the equilibria discussed here are shifted to the tetrazole form in TFA!

Recently we have reported[1,2] that tetrazolo[1,5-*b*]isoquinoline (**1a**), in contrast to its two angular isomers, tetrazolo[5,1-*a*]isoquinoline and tetrazolo[1,5-*a*]quinoline, forms an equilibrium with its isomeric azido compound, 2-azidoisoquinoline (**1b**) (Scheme I). The equilibrium constants, 0.2 and 1.3 in chloroform and dimethyl sulfoxide, respectively, seemed highly suitable values for investigation of slight shifts of the equilibrium caused by different substituents or solvents. Both carbon atoms neighboring the "fusion site" of the title system can be substituted. This system is ideal for study of substituent effects exerted by R_1 or R_4 on opposite sides of the tetrazole ring fusion.

For this purpose, suitable model compounds bearing the same substituents R_1 and R_4 have been synthesized. The method reported by us[1] for the parent ring system allowed

Scheme I



1a, $R_4 = R_1 = H$ **1b**, $R_4 = R_1 = H$

the preparation of 5-methyltetrazolo[1,5-*b*]isoquinoline (**6a**).

Oxidation of 3-chloro-1-methylisoquinoline[3] with *m*-chloroperbenzoic acid led to *N*-oxide **3** which under relatively forced conditions afforded the hydrazino *N*-oxide compound **4**. The surprisingly stable 3-hydrazino-1-methylisoquinoline (**5**) was prepared by titanium tri-

(1) Part 2: Gy. Hajós and A. Messmer, *J. Heterocycl. Chem.*, **15**, 463 (1978).

(2) Gy. Hajós and A. Messmer, *J. Heterocycl. Chem.*, **13**, 882 (1976).

(3) A. Kametani et al., *Chem. Pharm. Bull.*, **15**, 704 (1967); *Chem. Abstr.*, **67**, 82074 (1967).

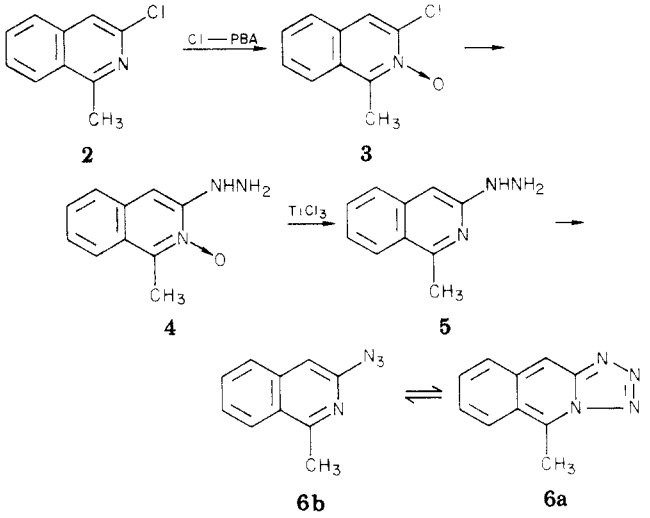
0022-3263/81/1946-0843$01.00/0

Table I.[a] Characteristic Data of Azide and Tetrazole Isomers

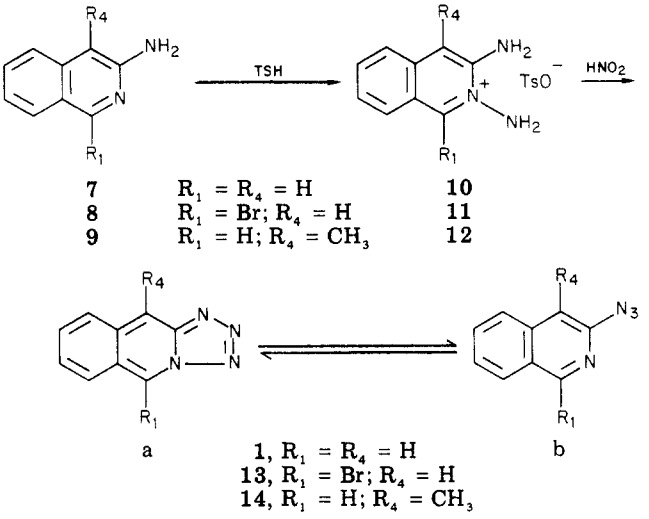
no.	R_1	R_4	mp, °C	azide band IR (KBr)	solvent	azide[b] (b) H_1	H_4	CH_3-1	CH_3-4	tetrazole[b] (a) H_1	H_4	CH_3-1	CH_3-4	$K = \frac{\text{tetrazole}}{\text{azide}}$
1	H	H	126-128	+ (weak)	D	9.2	7.4			10.3	8.9			1.5
					C	9.1	7.2			9.6	8.6			0.15
					T	9.4				10.2	8.9			10
6	CH_3	H	123-124	–	D		7.2	2.9			8.7	3.3		5
					C		7.0	2.9			8.4	3.3		1.2
					T						8.7	3.8		∞
14	H	CH_3	139-140	–	D	9.0			2.4	10.1			3.1	5
					C	9.0			2.4	9.5			3.2	1.2
					T					10.1			3.3	∞
13	Br	H	113-114	+	D		7.5							0
					C		7.1							0
					T		8.1							0
15	H	Br	133-135	+	D	9.2				10.4				0.2
					C	9.2								0
					T	9.5								0

[a] Abbreviations: D = dimethyl sulfoxide; C = chloroform; T = trifluoroacetic acid. [b] ^1H NMR chemical shifts, δ.

Scheme II



Scheme III



chloride reduction in high yield; its reaction with nitrous acid gave the methyl-substituted tetrazole–azide isomer pair (**6**) (Scheme II).

This synthetic route was, however, not applicable to preparation of the isomer with the CH_3 group in the opposite position (R_4) and neither of the desired bromo-substituted derivatives could be obtained in this way.

Interestingly, we observed formation of tetrazolo[1,5-*b*]isoquinoline (**1a**) when 2,3-diaminoisoquinolinium tosylate (**10**), prepared from 3-aminoisoquinoline (**7**) with *O*-tosylhydroxylamine (TSH),[4] was reacted with nitrous acid. In general, reactions of *N*-aminoazinium salts with nitrous acid lead to cleavage of the NH_2 group; therefore, in our case formation of 3-aminoisoquinoline (**7**) would have been expected (Scheme III).

This surprising formation of a tetrazole raised a mechanistic question. Did the N-amination (e.g., **7** → **10**) take place on the ring nitrogen? If TSH were to attack the amino nitrogen atom, instead the tosylate salt of 3-hydrazinoisoquinoline would have formed. This salt, when treated with sodium nitrite, obviously should give the tetrazole.

This possibility was, however, excluded by comparison of the tosylate salt of 3-hydrazinoisoquinoline prepared from ethanolic solutions of 3-hydrazinoisoquinoline and equivalent *p*-toluenesulfonic acid (mp 192 °C) with the crystalline product obtained from 3-aminoisoquinoline and TSH (**10**). Both infrared spectra and melting points showed that the two substances were different. The fact that diamino compound **10** could be recovered from acetic acid solution after 1 h excluded also the possibility of a rearrangement of **10** to the 3-hydrazino derivative.

Several other substituted 2,3-diaminoisoquinoline salts show the same behavior. Thus, diaminoisoquinolinium salts **11** and **12**, prepared from 3-amino-1-bromoisoquinoline (**8**) and 3-amino-4-methylisoquinoline (**9**) with TSH, reacted with nitrous acid to give the corresponding tetrazole–azide isomer pairs **13** and **14**.

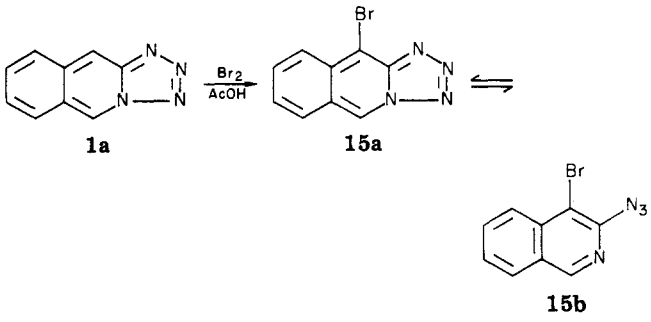
In the case of derivative **13** (R_1 = Br), which, as will be shown below, exists entirely in azido form, the synthesis is to our knowledge the first preparation of an azido compound which involves ring opening of the isomeric tetrazole: the first step is necessarily the formation of tetrazole **13a** which rapidly opens to azide **13b**.

Preparation of the counterpart of **13**, i.e., **15** (R_4 = Br), was relatively easy. Bromination of the unsubstituted tetrazole **1a** led selectively to 3-azido-4-bromoisoquinoline (**15b**, Scheme IV), as shown unambiguously by its NMR spectrum.

These five derivatives containing methyl or bromo groups as R_1 or R_4 were studied in $CDCl_3$, Me_2SO-d_6, and trifluoroacetic acid solutions by NMR and, as solid crystals, by IR. Table I summarizes the characteristic NMR shifts,

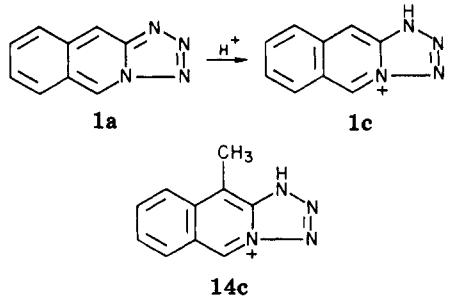
(4) E. E. Glover and K. T. Rowbottom, *J. Chem. Soc., Perkin Trans. 1*, 367 (1976).

Scheme IV



1a 15a 15b

Scheme V



1a 1c 14c

the equilibrium constants determined on the basis of integration of singlet H_1 or CH_3 signals in the NMR spectra, and appearance of the solid-state azide band in the IR spectra.

Several features detailed in Table I are in good agreement with earlier publications:[5] (i) chemical shifts of the R_1 = H proton in tetrazoles have higher δ values relative to those in the corresponding azides due to the increased ring current; (ii) the electron-releasing methyl group enhances the stability of the tetrazole form, but the electron-attracting bromo atom favors the azido isomer; (iii) in every case the tetrazole form is favored in Me_2SO relative to the equilibrium constant in $CDCl_3$.

An interesting picture can be obtained by comparison of compound pairs in Table I, i.e., between derivatives having a certain substituent as R_1 or R_4. The differences in K values caused by the position of CH_3 or Br substituents seem to be rather slight. The most remarkable difference is that while 3-azido-1-bromoisoquinoline (**13b**) does not form any tetrazole at all, the 4-bromo equilibrium (**15a** ⇌ **15b**) is shifted to the tetrazole side (**15a**) to a very small extent in Me_2SO solution. This fact seems to be in agreement with the generally accepted explanation of the cyclization of azide to tetrazoles, namely, that the lone pair[6] of the ring nitrogen favors ring closure. Therefore, the more remote the position of the substituent, the less pronounced the expected effect.

A surprising set of data was found in trifluoroacetic acid. According to the literature,[7] TFA shifts the equilibrium toward the azide isomer. We found, however, that the equilibrium constants obtained in TFA solutions are higher than those in $CDCl_3$. Methyl derivatives **6** and **14** do not contain any trace of azide component (Scheme V)!

This unusual behavior seems to be due to the linearly fused heteroaromatic ring rather than to any solvent effect. As we mentioned earlier[1] we believe that the relative instability of tetrazolo[1,5-*b*]isoquinoline (**1a**) can be attributed to its quinonoid electronic structure. This disappears, however, when the neutral ring is protonated (**1c**). The essential energetic difference between the neutral and the protonated forms, which does not exist with the angularly fused tetrazoloquinoline or tetrazolo[1,5-*a*]isoquinoline, may cause the apparent anomaly in TFA solutions.

Evidence for existence of a tetrazolium salt in TFA was supported by treatment of the TFA solution of **14** with HBF_4 and subsequently with ether. Compound **14c** was obtained in crystalline form. NMR spectra of **14c** and **14** in TFA were identical.

Experimental Section

Melting points are uncorrected. IR spectra were recorded with Unicam SP 200 equipment. NMR spectra were obtained by Varian EM-360 apparatus.

3-Aminoisoquinoline,[8] 1-bromo-3-aminoisoquinoline,[8] 3-amino-4-methylisoquinoline,[9] *O*-tosylhydroxylamine (TSH),[4] and 3-chloro-1-methylisoquinoline[2] were synthesized according to literature procedures.

3-Chloro-1-methylisoquinoline 2-Oxide (3). A mixture of 0.5 g (2.7 mmol) of 3-chloro-1-methylisoquinoline (**2**), 0.8 g (4.6 mmol) of *m*-chloroperbenzoic acid, and 8 mL of benzene was stirred until a solution formed and was allowed to stand at room temperature for 2 days. Treatment of the reaction mixture with sodium carbonate solution followed by extraction with dichloromethane afforded 0.35 g (65%) of crude product. Recrystallization from ethyl acetate yielded colorless crystals: mp 155–158 °C; NMR ($CDCl_3$) δ 8.2–7.3 (m, 5 H, H_{4-8}), 2.9 (s, 3 H, CH_3).

Anal. Calcd for $C_{10}H_8ClNO$ (mol wt 193.64): C, 62.02; H, 4.16; N, 7.23. Found: C, 62.34; H, 4.50; N, 6.98.

3-Hydrazino-1-methylisoquinoline 2-Oxide (4). A mixture of 2.3 g (11.9 mmol) of 3-chloro-1-methylisoquinoline 2-oxide, 14 mL of *n*-butanol, and 14 mL of 100% hydrazine hydrate was refluxed for 1 h. The excess hydrazine hydrate was removed from the cold reaction mixture by extraction with water. Evaporation of the organic layer gave 1.7 g (76%) of crude product which, on recrystallization from ethanol–ether, resulted in yellow needles: 0.9 g (40%); mp 155–157 °C; IR (KBr) 3600–2900, 1660, 1640, 1570, 1520 cm^{-1}; NMR (TFA) δ 7.9–7.2 (m, 4 H, H_{5-8}), 7.1 (s, 1 H, H_4), 2.8 (s, 3 H, CH_3).

Anal. Calcd for $C_{10}H_{11}N_3O$ (mol wt 189.22): C, 63.48; H, 5.86; N, 22.21. Found: C, 63.06; H, 6.02; N, 21.95.

3-Hydrazino-1-methylisoquinoline (5). 3-Hydrazino-1-methylisoquinoline 2-oxide (**4**, 0.5 g, 2.6 mmol) was treated with 6 mL of 15% titanium trichloride solution at room temperature. The pH of the resulting solution was adjusted with sodium hydroxide to a value of 10. Extraction with dichloromethane gave 0.32 g (70%) of pale yellow crystals: mp 108–110 °C; mass spectrum, m/e 173 (M^+).

Anal. Calcd for $C_{10}H_{11}N_3$ (mol wt 173.22): C, 69.34; H, 6.40; N, 24.26. Found: C, 69.12; H, 6.63; N, 24.12.

5-Methyltetrazolo[1,5-*b*]isoquinoline (6). 3-Hydrazino-1-methylisoquinoline (0.4 g, 2.3 mmol) was dissolved in a mixture of 3 mL of water and 3 mL of acetic acid and was treated with a solution of 0.2 g of sodium nitrite (2.9 mmol) in 2 mL of water. A crystalline solid separated at once which, after further addition of water, was filtered and recrystallized from water–acetonitrile (50%) to yield 0.22 g (51%) of product, mp 123–124 °C.

Anal. Calcd for $C_{10}H_8N_4$ (mol wt 184.2): C, 65.20; H, 4.38; N, 30.42. Found: C, 64.87; H, 4.62; N, 30.16.

3-Azido-4-bromoisoquinoline (15). Tetrazolo[1,5-*b*]isoquinoline (0.51 g, 3.0 mmol) was dissolved in 5 mL of acetic acid and the solution was treated with 1.45 g (9.0 mmol) of bromine dropwise at room temperature. The reaction mixture was purified from the small tarry byproduct by filtration and the yellow filtrate was neutralized by sodium hydroxide solution. A cream-colored precipitate formed which was filtered and recrystallized from methanol to give 0.45 g of product (60%): mp 133–135 °C: NMR ($CDCl_3$) δ 8.9 (s, H_1), 8.05 (m, H_5), 7.73 (m, H_6), 7.50 (m, H_7), 7.88

(5) M. Tisler, *Synthesis*, 123 (1973).
(6) L. A. Burke et al., *J. Am. Chem. Soc.*, **98**, 1685 (1976).
(7) R. N. Butler, *Adv. Heterocycl. Chem.*, **21**, 402 (1977).
(8) F. Johnson and W. A. Nasutavicus, *J. Org. Chem.*, **27**, 3953 (1962).
(9) H. Win and H. Tickelman, *J. Org. Chem.*, **32**, 59 (1967).

(m, H_8) ($J_{5,6}$ = 8.4, $J_{6,7}$ = 6.9, $J_{7,8}$ = 8.0, $J_{5,7}$ = 1.2, $J_{6,8}$ = 1.6, $J_{5,8}$ = 0.6, $J_{1,5}$ = 0.6 Hz).

Anal. Calcd for $C_9H_5BrN_4$ (mol wt 249.09): C, 43.40; H, 2.02; Br, 32.08. Found: C, 43.19; H, 2.31; Br, 31.67.

Preparation of 2,3-Diaminoisoquinolinium Salts 10-12. A solution of the requisite 3-aminoisoquinoline derivative (5.0 mmol) in 10 mL of dichloromethane was treated with a solution of 5.2 mmol of *O*-tosylhydroxylamine in 20 mL of dichloromethane at 0-5 °C. The product precipitated in crystalline form within 10 min. A further quantity of the crystals deposited on addition of a limited amount ot ether. Recrystallization from isopropyl alcohol gave rise to brilliant yellow needles.

2,3-Diaminoisoquinolinium tosylate (10): mp 160-162 °C (65%); perchlorate salt, mp 170-172 °C; NMR (TFA) δ 9.1 (s, 1 H, H_1), 8.0-7.5 (m, 4 H, H_{5-8}), 8.45 (s, 1 H, H_4).

Anal. Calcd for $C_{16}H_{17}N_3O_3S$ (mol wt 331.40): C, 57.99; H, 5.17; S, 9.68. Found: C, 57.70; H, 5.40; S, 9.61.

2,3-Diamino-4-methylisoquinolinium tosylate (12): mp 168-170 °C (67%); fluoroborate salt, mp 182-184 °C; NMR (TFA) δ 9.1 (s, 1 H, H_1), 8.05-7.4 (m, 4 H, H_{5-8}), 2.65 (s, 3 H, CH_3).

Anal. Calcd for $C_{17}H_{19}N_3O_3S$ (mol wt 345.43): C, 59.11; H, 5.54; S, 9.28. Found: C, 58.93; H, 5.80; S, 9.03.

1-Bromo-2,3-diaminoisoquinolinium tosylate (11): mp 175-177 °C (45%).

Anal. Calcd for $C_{16}H_{16}BrN_3O_3S$ (mol wt 410.31): C, 46.84; H, 3.93; N, 10.24; Br, 19.48. Found: C, 46.52; H, 3.98; N, 10.01; Br, 19.10.

Reaction of the Diaminoisoquinolinium Salts with Nitrous Acid. A solution of the 2,3-diaminoisoquinolinium derivative (3.0 mmol) in a mixture of 10 mL of acetic acid and 10 mL of water was treated with a solution of 0.35 g (5.1 mmol) of sodium nitrite in 3 mL of water at room temperature. Cryatalline precipitate deposited within few minutes which was filtered and recrystallized from the given solvent.

Tetrazolo[1,5-*b*]isoquinoline (1a). The product obtained by this procedure in 70% yield proved to be fully identical (spectroscopical data and physical constants) with that prepared by earlier methods.[1,2]

10-Methyltetrazolo[1,5-*b*]isoquinoline (14): mp 139-141 °C (EtOH); yield 65%.

Anal. Calcd for $C_{10}H_8N_4$ (mol wt 184.21): C, 65.20; H, 4.38; N, 30.42. Found: C, 64.92; H, 4.51; N, 30.18.

3-Azido-1-bromoisoquinoline (13): mp 113-114 °C (MeOH); yield 60%.

Anal. Calcd for $C_9H_5BrN_4$ (mol wt 249.09): C, 43.40; H, 2.02; Br, 32.08. Found: C, 43.28; H, 2.34; Br, 31.72.

10-Methyltetrazolo[1,5-*b*]isoquinoline HBF_4 Salt (14c). A solution of **14** in TFA was treated with a few drops of hydrofluoroboric acid (40%) and ether was added. Colorless crystals separated which were recrystallized from nitromethane; mp 174-175 °C.

Anal. Calcd for $C_{10}H_9BF_4N_4$ (mol wt 272.03): C, 44.15; H, 3.83; N, 20.60. Found: C, 43.87; H, 3.95; N, 20.31.

Registry No. **1a**, 33459-64-2; **1b**, 60877-39-6; **2**, 15787-12-9; **3**, 75949-08-5; **4**, 75949-09-6; **5**, 75949-10-9; **6a**, 75949-11-0; **6b**, 75949-12-1; **7**, 25475-67-6; **8**, 13130-79-5; **9**, 7697-66-7; **10**, 75949-14-3; **10** perchlorate salt, 75949-15-4; **11**, 75949-17-6; **12**, 75949-19-8; **12** fluoroborate salt, 75949-20-1; **13**, 75949-21-2; **14a**, 75949-22-3; **14b**, 75949-23-4; **14c**, 75949-25-6; **15a**, 75949-26-7; **15b**, 75961-48-7.

Pyrimidines. 17. Novel Pyrimidine to Pyridine Transformation Reaction. One-Step Synthesis of Pyrido[2,3-*d*]pyrimidines[1]

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A number of 2,6-dihydroxypyridines (**3**) and pyrido[2,3-*d*]pyrimidines (**9**) were prepared in one step from 1,3-dimethyluracil derivatives (**1**) via new transfragment reactions by which the N_1-C_2-N_3 fragment of **1** is displaced by the C-C-N fragment of acyclic or cyclic 1,3-ambident nucleophiles. As acyclic nucleophiles, acetamide derivatives (**2**) substituted at the α position with an electron-withdrawing R^3 group were employed. The products were 2,6-dihydroxypyridines substituted at C_3 with R^3 (**3**). 1,3-Dimethyl-4-thiouracil (**4**) could be converted into 2-hydroxy-6-mercaptonicotinamide (**5**) by treatment with malonamide. 1-Methylpyridine derivatives (**6**) could be obtained by treatment of 1,3-dimethyluracil (**1a**) with *N,N'*-dimethylmalonamide or *N*-methylcyanoacetamide. Treatment of **1a** with malononitrile in ethanolic NaOEt gave 3-cyano-2-ethoxy-6-hydroxypyridine (**7**). Derivatives of 1,3-dialkyl-6-aminouracil (**8**) were used as cyclic 1,3-ambident nucleophiles. Treatment of 5-substituted 1,3-dimethyluracil (**1**) with **8** in base afforded 1,3-dialkyl-6-substituted-pyrido[2,3-*d*]pyrimidine-2,4,7-(1*H*,3*H*,8*H*)-trione (**9**). Compound **4** was converted into 7-mercapto-1,3-dimethylpyrido[2,3-*d*]pyrimidine-2,4-(1*H*,3*H*)-dione (**10**) by treatment with 1,3-dimethyl-6-aminouracil. Treatment of 5-cyano-1,3-dimethyluracil (**1g**) with 1-*n*-butyl-6-aminouracil (**11**) afforded 1-*n*-butyl-6-cyanopyrido[2,3-*d*]pyrimidine-2,4,7(1*H*,3*H*,8*H*)-trione (**12**). Plausible mechanisms for the pyrimidine-to-pyridine and pyrimidine-to-pyrido[2,3-*d*]pyrimidine transformation reactions are proposed.

The synthesis of simple heterocyclic compounds has been approached in three different ways: (a) total synthesis by cyclization of acyclic compounds, (b) introduction or modification of functional groups on a heterocyclic ring, and (c) ring transformations of cyclic compounds.[2] For preparative purposes, the last method has rarely been employed. For example, uracil derivatives were converted into pyrazolone by treatment with hydrazine;[3] however,

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(2) For a comprehensive review of ring transformations, see: van der Plas, H. C. "Ring transformations of Heterocycles"; Academic Press: London and New York, 1973; Vol. 1 and 2.

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