(silica gel, 1:1 ethyl acetate/pentane) gave 0.04 g (51%) of **28**: IR 2950, 1700, 1415 $cm^{-1}$; NMR $\delta$ 1.1 (m, 3 H), 2.0 (m, 4 H), 2.3–2.5 (m, 3 H), 3.2–3.4 (m, 4 H), 5.1 (s, 2 H), 7.3 (s, 5 H); mass spectrum, (20 eV), 275 ($M^+$), 91 (base); high-resolution mass spectrum, obsd $m/z$ 275.151 795, $C_{16}H_{21}NO_3$ requires 275.152 09.

A solution containing 0.16 g ($5.82 \times 10^{-4}$ mol) of **28**, 0.8 g of 10% of Pd/C, and 2 drops of 70% aqueous perchloric acid in 10 mL of absolute methanol was stirred under 101 kPa of hydrogen for 2 h. This solution was passed through a small pad of activated basic alumina (Brockman) with ether to afford 0.056 g (78% yield) of **29** and **30**. GC analysis on 3% Dexsil indicated that **30** and **29** were in a 3:2 ratio, with the lower boiling **30** eluting first. A picrate salt was formed directly: 0.146 g (91% yield); mp 228–239 °C; NMR $\delta$ 1.14 (d, $J$ = 5 Hz), 1.23 (d, $J$ = 6 Hz), 1.78 (brd m),2.15 (brd m), 2.35 (brd m), 2.64 (brd m), 2.82 (brd m), 2.98 (brd m), 3.12 (brd m), 3.68 (brd m), 3.90 (brd m), 4.04 (brd m), 4.28 (brd m), 4.40 (brd m), 8.89 (s);[50] GC/MS [using a 3% SE-30 column at 110 °C for 2 min and then programmed at 20 °C/min] (70 eV), for $t_R$ = 2 min (from $Et_2O$), $m/z$ 125 ($M^+$), 97, 83 (base), 55,[48] for $t_R$ - 2.5 min, $m/z$ 125 ($M^+$), 97, 83 (base), 55.[48] In a separate experiment, part of the product was converted to the picrates, which were combined with the above and repeatedly crystallized from methanol, enriching **29**: mp 239–241 °C (lit.[36] mp (**29**) 243–244 °C; mp (**30**) 234–236 °C); GC/MS, $t_R$ = 2.5 min, mass spectrum identical with that above. The pooled methanol mother liquors were evaporated, and the residue was crystallized from ethanol to yield mainly **30**: mp 229–231 °C; GC/MS, $t_R$ = 2.0 min, mass spectrum identical with that above.

(50) We are grateful to Ms. Victoria Roberts for obtaining this 360-MHz spectrum. Unfortunately, the exceptionally broad, ill-defined multiplets precluded meaningful decoupling experiments.

**Acknowledgment.** We are grateful for NIH Grant CA 22238 for support of this work. The low-resolution mass spectra were obtained on an instrument purchased by NIH Shared Instrument Grant GM 27583; some of the high-resolution spectra were recorded at the Biomedical Mass Spectrometry Resource, Berkeley, CA, supported by NIH Grant RR 00719.

**Registry No.** **1**, 4383-26-0; **2**, 80662-79-9; **3**, 5279-23-2; **4**, 80662-80-2; **5**, 78805-03-5; **6**, 80662-81-3; **7**, 80662-82-4; **8**, 25070-76-2; **9**, 80662-83-5; **10**, 80662-84-6; **11**, 80662-85-7; **11** diacetate, 80662-86-8; **12**, 34637-22-4; **12** monoacetate, 80662-87-9; **13**, 25630-24-4; **14**, 80662-88-0; **15**, 80662-89-1; **16**, 80662-90-4; **17**, 80248-99-3; **18**, 80249-00-9; **19**, 80662-91-5; **20**, 80662-92-6; **21**, 80662-93-7; **22**, 80662-94-8; **26**, 643-20-9; **26** picrate, 14129-07-8; **27**, 13618-93-4; **27** picrate, 5210-66-2; (±)-**28**, 80662-95-9; (±)-**29**, 17463-81-9; (±)-**29** picrate, 17463-80-8; (±)-**30**, 76548-10-2; (±)-**30** picrate, 76548-11-3; *N*-(Z-propenyl)-*N*-(3-butenyl)amine, 80662-96-0.

# New Heterocyclic Rearrangement: Transformation of 1-Substituted 4-(Alkylamino)-1*H*-pyrrolo[3,2-*c*]pyridines into 1-Substituted 4-(Alkylamino)-1*H*-pyrrolo[2,3-*b*]pyridines (5-Aza- to 7-Azaindoles)

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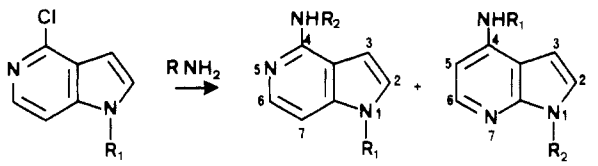
Substitution of 1-alkyl-4-chloro-1*H*-pyrrolo[3,2-*c*]pyridines by primary alkylamines in excess afforded the expected 1-alkyl-4-(alkylamino)-1*H*-pyrrolo[3,2-*c*]pyridines and their 1-alkyl-4-(alkylamino)-1*H*-pyrrolo[2,3-*b*]pyridine isomers resulting from the reversible isomerization of the preceding compounds.

In 1970 we described[1] a synthesis of 1-substituted 4-chloro-1*H*-pyrrolo[3,2-*c*]pyridines (5-azaindoles). Nucleophilic displacement of the chlorine atom was then reported to give the expected 4-substituted products, and this reaction was used to prepare various 4-anilino-1*H*-pyrrolo[3,2-*c*]pyridines.[2] The structure of a derivative of 1-benzyl-4-amino-1*H*-pyrrolo[3,2-*c*]pyridine obtained by reduction of the corresponding hydrazine was established by X-ray crystallography,[3] and the structure of various 4-substituted 1-alkyl-1*H*-pyrrolo[3,2-*c*]pyridine derivatives seemed to be unambiguous.

Surprisingly, a recent experiment showed that substitution of 1-methyl-4-chloro-1*H*-pyrrolo[3,2-*c*]pyridine by benzylamine and other primary alkylamines can afford a mixture of two isomeric compounds. Reinvestigation of this reaction allowed us to establish conditions which lead to normal substituted 1*H*-pyrrolo[3,2-*c*]pyridines and their 1*H*-pyrrolo[2,3-*b*]pyridine (7-azaindoles) isomers and to specify in what cases isomerization can be observed.

Substitution of 1-methyl-4-chloro-1*H*-pyrrolo[3,2-*c*]-pyridine (**1**) by various primary alkylamines in excess takes place by boiling the mixture in 2-methoxy- or 2-ethoxyethanol (Scheme I). For completion of the reaction, heating with benzylamine, 2-hydroxypropylamine, and 3-hydroxypropylamine required at least 1 week. In every

Scheme I[a]




**1** **2** **3**

[a] a, $R_1 = CH_3$, $R_2 = CH_2C_6H_5$; b, $R_1 = CH_3$, $R_2 = CH_2CH(OH)CH_3$; c, $R_1 = CH_3$, $R_2 = CH_2CH_2CH_2OH$; d, $R_1 = R_2 = CH_2C_6H_5$.

† Laboratoire de Synthèse Organique.
‡ Unité 219 de l'Inserm.

(1) Bisagni, E.; Bourzat, J. D.; André-Louisfert, J. *Tetrahedron* **1970**, *26*, 2087.
(2) Bisagni, E.; Bourzat, J. D.; Marquet, J. P.; Labrid, C.; Delort, P.; Le Ridant, A. *Chim. Ther.* **1973**, *5*, 559.
(3) (a) Ducrocq, C.; Bisagni, E.; Lhoste, J. M.; Mispelter, J.; Defaye, J. *Tetrahedron* **1976**, *32*, 773. (b) Ducruix, A.; Riche, C.; Pascard, C. *Tetrahedron Lett.* **1976**, 51.
(4) Ducrocq, C.; Bisagni, E.; Rivalle, C.; Mispelter, J. *J. Chem. Soc, Perkin Trans. 1* **1979**, 135.
(5) Marquet, J. P.; Montagnier, L.; Gruest, J.; Bourzat, J. D.; André-Louisfert, J.; Bisagni, E. *Chim. Ther.* **1971**, *6*, 427.
(6) Schneller, S. T.; Luo, J. K. *J. Org. Chem.* **1980**, *45*, 4045.

0022-3263/82/1947-1500$01.25/0 

Table I. 1*H*-Pyrrolo[3,2-*c*]pyridine (2a–d) and 1*H*-Pyrrolo[2,3-*b*]pyridine (3a–d) Characteristic $^1$H NMR Chemical Shifts[a] at 100 MHz in $Me_2SO$-$d_6$

| | chemical shift[b,c] | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| compd | N1 $CH_3$ | N1 $CH_2$ | H2 | H3 | N4 $CH_2$ | N4 $CH_3$ | H5 | H6 | H7 | $J_{3,7}$[b] |
| 2a | 3.69 (s) | | 7.08 (3.1) | 6.68 | 4.70 (d, 6) | | | 7.63 (6.1) | 6.67 | 0.8 |
| 3a | | 5.36 (s) | 7.16 (3.6) | 6.55 | | 2.85 (d, 4.9) | 6.11 (5.5) | 7.88 | | |
| 2b | 3.69 (s) | | 7.08 (3) | 6.62 | 3.33 (m) | | | 7.60 (6) | 6.66 | 0.8 |
| 3b | | 4.04 (s) | 7.10 (3.5) | 6.47 | | 2.84 (d, 4.9) | 6.08 (5.5) | 7.84 | | |
| 2c | 3.67 (s) | | 7.06 (3.2) | 6.59 | 3.48 (m) | | | 7.61 (6) | 6.63 | 0.8 |
| 3c | | 4.19 (t) | 7.10 (3.5) | 6.49 | | 2.84 (d, 5) | 6.08 (5.5) | 7.85 | | |
| 2d | | | 7.2-7.3 | 6.73 | 4.68 (d) | | | 7.57 | 6.69 | 0.5 |
| 3d | | 5.36 (s) | 7.2 (3.4) | 6.66 | 4.48 (d, 6) | | 6.10 (5.5) | 7.80 | | |

[a] Chemical shifts in parts per million from $Me_4Si$ as an internal reference. [b] $J_{3,7}$ represents the zig-zag coupling between H3 and H7 in hertz. Other coupling constants between vicinal protons are given in parentheses in hertz. [c] s, singlet; d, doublet; t, triplet; m, multiplet.

case, purification by alumina column chromatography affords two compounds corresponding to the normal substituted products **2a–d** and to their 1*H*-pyrrolo[2,3-*b*]pyridine isomers **3a–d**, respectively.

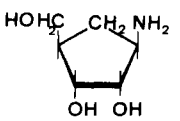
The structures of the 1*H*-pyrrolo[3,2-c]pyridine **2** and 1*H*-pyrrolo[2,3-*b*]pyridine derivatives **3** have been assigned on the basis of $^1$H NMR data. As shown on Table I, the existence of a small coupling constant between 3-H and 7-H results from a zig-zag coupling which is characteristic of the 1*H*-pyrrolo[3,2-c]pyridine system. Further evidence of the two structures comes from the methyl proton signals which appear as a sharp singlet at 3.67–3.69 ppm in 1*H*-pyrrolo[3,2-*c*]pyridine derivatives **2** and as a doublet at 2.84–2.85 ppm [$J$(NH–$CH_3$) = 4.9–5 Hz] in 1*H*-pyrrolo-[2,3-*b*]pyridine compounds **3**. As expected, this doublet becomes a singlet by exchange with $D_2O$. The comparison of chemical shifts and coupling constants of the other protons of the molecules is in full agreement with these assignments (Table I). Additional clear distinction between the two ring systems is provided by their UV spectra (Table II).

The presence of 1*H*-pyrrolo[2,3-*b*]pyridine derivatives **3** in the resulting mixture starting from 1-methyl-4-chloro-1*H*-pyrrolo[3,2-*c*]pyridine (**1**) shows that a secondary reaction takes place by opening and subsequent closing of the pyrrole nucleus of intermediate products **2**.

In order to specify the required conditions of this new rearrangement, we have examined the possible transformation of compounds **2** and **3** with primary amines in the presence and absence of water and/or hydrochloric acid.

No rearrangement could be observed by boiling the amine in methoxy ethanol plus water or aqueous hydrochloric acid solution. On the contrary, heating of the hydrochlorides of **2** and **3** with primary amines (conditions which are closely related to those of the direct substitution of compound **1**) allowed us to observe the rearrangements **2** → **3** and **3** → **2**. In every case, the reaction leads to an equilibrium indicating that the isomerization is a reversible one. However, although the primary amine brings about the transformation of the studied 4-amino-1*H*-pyrrolo-[3,2-*c*]pyridines **2** or 4-amino-1*H*-pyrrolo[2,3-*b*]pyridine (**3**) hydrochlorides, it acts only as a "catalyst". Thus, reaction of **2c**·HCl with benzylamine gave a mixture of **2c** and **3c** and no traces of benzyl-substituted compounds.

Nevertheless, probably due to the weak stability of amine 4[7] under the reaction conditions necessary to promote the expected substitution and isomerization, this reaction was not applicable to the synthesis of a 1*H*-pyrrolo[2,3-*b*]pyridine nucleoside analogue.



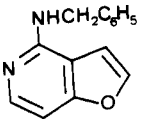
4

Table II

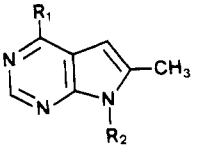
| compd[a] | UV,[b] λ nm (ε) | yield,[d] % | mp,[e] °C |
|---|---|---|---|
| 2a | 277 (17 550) | 43 | 94 (C) |
| 3a | 271 (11 700), 295 (15 500), 304 (13 400) | 23 | 180 (C) |
| 2b | 277 (15 000) | 50.6 | 116 (T) |
| 3b | 271 (9400), 295 (12 700), 304 (10 600) | 16.9 | 128 (C) |
| 2c | 277 (16 500) | 45.2 | 120 (T) |
| 3c | 271 (9400), 295 (13 500), 304 (11 800) | 4.3 | 144 (T) |
| 2d | 277 (21 180) | 25.1 | 152-153.5 (E) |
| 3d[c] | 273 (11 600), 297 (16 200), 306 (14 400) | 28 | 197 (X) |

[a] Satisfactory analytical data (±0.4% for C, H, N, and Cl) were obtained for all compounds listed in the table. [b] Absorption spectra were recorded on samples dissolved in ethanol. [c] Only the hydrochloride of compound **3d** could be crystallized. [d] Indicated yields correspond to substitution experiments (method A in Experimental Section). [e] Solvent: C, cyclohexane; T, toluene; E, ethanol; X, xylene.

We also tried to isomerize the hydrochlorides of 4-(benzylamino)furo[3,2-*c*]pyridine (**5**) and 4-(benzylamino)-6-methyl-7-(2,3-dihydroxypropyl)-7*H*-pyrrolo[2,3-d]pyrimidine (**6a**) and its isomer **6b**. In neither case was a reaction observed. TLC (ethyl acetate-ethanol 8-2 v:v) showed no transformation of the starting compound.



5



6

a $R_1$ = $NHCH_2$-$C_6H_5$ ; $R_2$ = $CH_2$-CHOH-$CH_2OH$

b $R_1$ = $NHCH_2$-CHOH-$CH_2OH$ ; $R_2$ = $CH_2$-$C_6H_5$

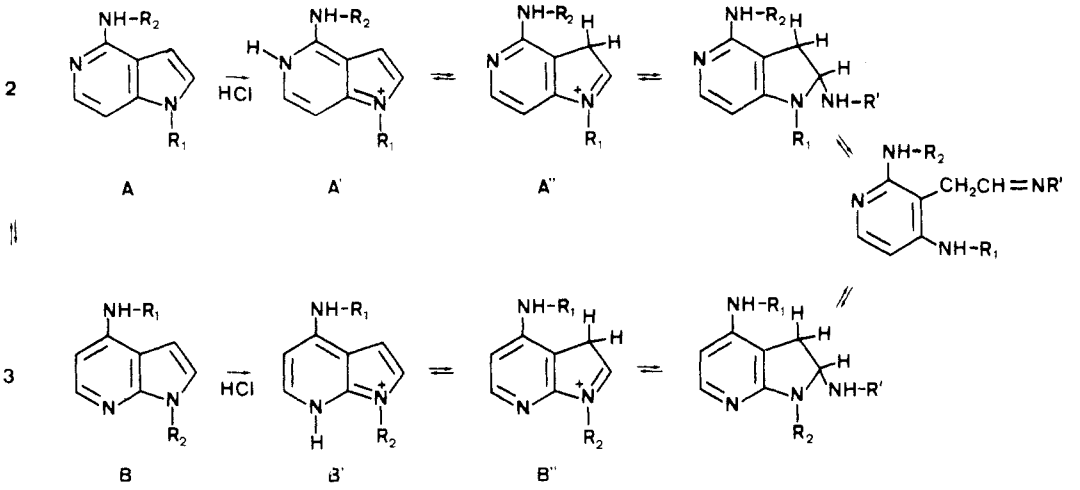
c $R_1$ = Cl ; $R_2$ = $CH_2$-CHOH-$CH_2OH$

d $R_1$ = Cl ; $R_2$ = $CH_2$-$C_6H_5$

For interpretation of this new reversible isomerization, we propose the mechanism shown in Scheme II. Pro-

(7) Shealy, Y. F.; Clayton, J. D. *J. Am. Chem. Soc.* **1969**, *91*, 3075.

Scheme II



tonation exchange experiments carried out with A and B in $D_2O$–DCl solution showed that the deuteration of the pyridine heterocycle occurred immediately, giving A′ and B′, which present characteristic $^1H$ NMR chemical shifts ($\delta$) and coupling constants (hertz): **2c**, 6.98 (6-H), 6.50 (7-H), $J_{6,7}$ = 7.2 Hz; **3c**, 6.20 (5-H), 7.59 (6-H), $J_{5,6}$ = 7.4 Hz.

On the other hand, a slow exchange of 3-H was observed, leading to totally 3-deuterated starting compounds (half-life 90 min in **2c** and 60 min in **3c**). This is consistent with the postulated intermediates A″ and B″ and the proposed mechanism. With furo[3,2-*c*]pyridine derivative **5**, no deuteriation of 3-H was observed. In this case, the absence of an intermediate able to react with the nucleophile might explain why no rearrangement could be observed. From this viewpoint it is more surprising that no rearrangement could be detected with pyrrolo[2,3-*d*]pyrimidines although 5-H was exchangeable (half-life 40 min). We have not found a satisfactory interpretation for this result.

To our knowledge, such an opening (and ring closure) reaction of a pyrrole nucleus has not previously been reported. However, the ring opening of certain quaternarized pyridines by primary amines[4] and the well-known Dimroth rearrangement of various purine and pyrimidine derivatives, which proceeds by a N–C bond cleavage, can be compared to this new transformation. In view of our present results, we have reexamined the structure of various 4-amino-1*H*-pyrrolo[3,2-*c*]pyridine derivatives already described. All 1-methyl-4-anilino-1*H*-pyrrolo-[3,2-*c*]pyridines[2] as well as 4-amino-1*H*-pyrrolo[3,2-*c*]-pyridine derivatives resulting from the substitution by secondary amines such as pyrrolidine, morpholine, and piperidine[1] correspond to the published structures. Only the compounds previously reported in ref 1 and 5 as **2a** and **2d** were misformulated and correspond to their **3a** and **3d** isomers, respectively. The compounds **2a** and **2d**, which were not then isolated, are now described in this paper.

In summary, this work showed that two compounds previously described as 4-(alkylamino)-1*H*-pyrrolo[3,2-*c*]pyridines **2** were misformulated. It established the possibility of transformation of 1-substituted 4-(alkylamino)-1*H*-pyrrolo[3,2-*c*]pyridines **2** into their 1*H*-pyrrolo[2,3-*b*]pyridine isomers **3**. This reversible reaction was observed with four 4-(alkylamino)-1*H*-pyrrolo[3,2-*c*]-pyridine hydrochlorides and primary alkylamines, but the required conditions of this new rearrangement ruled out its possible application to unstable (or only slightly stable) primary alkylamines. This isomerization seems to be limited to the 1-substituted 4-(alkylamino)-1*H*-pyrrolo[3,2-*c*]pyridines as starting materials. Nevertheless, it could be useful for synthesis of some new 4-aminopyrrolo[2,3-*b*]pyridine derivatives of type **3** which have been recently reported as inaccessible by substitution of the corresponding chloro derivatives.[6]

## Experimental Section

Elemental analyses were performed by the Service Central d'Analyse, CNRS, Vernaison, France. Nuclear magnetic resonance spectra were recorded with a Varian XL-100 at 100 MHz in $Me_2SO$-$d_6$ with $Me_4Si$ as an internal standard. UV spectra were taken on a Cary Model 118C. Column chromatography was done on neutral alumina from Prolabo. Melting points were determined on a Koefler apparatus and are not corrected.

**Method A (Substitutions).** All substitutions were performed by boiling the 1-alkyl-4-chloro-1*H*-pyrrolo[3,2-*c*]pyridines (6 mmol) with various amines (12 mmol) in 2-methoxyethanol (15 mL) for 8 days. The mixture was then evaporated under reduced pressure. The residue was taken up in an aqueous solution of sodium hydroxide (20 mmol) and extracted with chloroform (2 × 50 mL). The viscous residue which contained the two isomers (7-azaindole and 5-azaindole) was then chromatographed on an alumina column (50 g; 1.5 × 44 cm) with chloroform for **2a** and **3a**, with ethyl-acetate–ethanol (95:5 v/v) for **2b,c** and **3b,c**, and with toluene–ethylacetate (9:1 v/v) for **2d** and **3d**.

**Method B (Isomerizations).** Rearrangements of 1*H*-pyrrolo[3,2-*c*]pyridines into 1*H*-pyrrolo[2,3-*b*]pyridines and vice versa were performed as follows. The starting compound (2 mmol) was dissolved in concentrated hydrochloric acid (10 mL), and the mixture was evaporated under reduced pressure and dried by evaporation in the presence of absolute ethanol. It was then refluxed in 15 mL of 2-ethoxyethanol for 8 days in the presence of 2 mmol of the primary amine corresponding to the 4-substituent of 1*H*-pyrrolo[3,2-*c*]pyridines **2a–d** or to the 1-substituent of 4-(alkylamino)-1*H*-pyrrolo[2,3-b]pyridines **3a–d**. The resulting mixture was treated as described above (method A), and the two isomers were separated by chromatography. The ratio of the rearranged compound vs. the starting compound was always near 1. One must mention that rearrangement assays starting with **2** or **3** and using benzylamine led exclusively to **3** and **2**, respectively.

4-(Benzylamino)furo[3,2-*c*]pyridine (**5**) was synthesized as already described.[8]

**4-Chloro-6-methyl-7-(2,3-dihydroxypropyl)-7*H*-pyrrolo-[2,3-*d*]pyrimidine (6c).** A solution of 2.05 g (1 mmol) of 5-acetonyl-4,6-dichloropyrimidine[9] in water (30 mL) was stirred at 100 °C for 4 h with 1.81 g (2 mmol) of 3-amino-1,2-propanediol. Cooling of the resulting mixture left **6c** as a solid which was

(8) Bourzat, J. D.; Bisagni, E. *Bull. Soc. Chim. Fr.* **1971**, 1727.
(9) Bisagni, E.; Marquet, J. P.; Andrê-Louisfert, J. *Bull. Soc. Chim. Fr.* **1969**, 4338.

recristallized from ethanol (91%); mp 154 °C. Anal. Calcd for $C_{10}H_{11}N_3O_2Cl$ (mol wt 241.67): C, 49.69; H, 5.00; N, 17.38; Cl, 14.66. Found: C, 49.68; H, 5.14; N, 17.36; Cl, 15.02.

**4-(Benzylamino)-6-methyl-7-(2,3-dihydroxypropyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (6a).** A solution of **6c** (1 g, 4.1 mmoles) in 2-methoxyethanol (40 mL) was stirred for 4 h under reflux with 877 mg (8.2 mmol) of benzylamine. After evaporation of the mixture under reduced pressure, the residue was cristallized twice in water yielding **6a**: 66%; mp 155 °C. Anal. Calcd for $C_{17}H_{20}N_4O_2$ (mol wt 312.36): C, 65.36; H, 6.45; N, 17.94. Found: C, 65.34; H, 6.34; N, 18,23.

**7-Benzyl-6-methyl-4-[(2,3-dihydroxypropyl)amino]-7*H*-pyrrolo[2,3-*d*]pyrimidine (6b).** A solution of **6d**[9] in 2-methoxyethanol was treated as described above with 3-amino-1,2-propanediol. An analytical sample of **6b** was obtained by crystallization from ethanol, giving colorless crystals: mp. 194 °C; 74%. Anal. Calcd for $C_{17}H_{20}N_4O_2$ (mol wt 312.34): C, 65.36; H, 6.45; N, 17.94. Found: C, 65.18; H, 6.38; N, 18.04.

**Acknowledgment.** This investigation was supported in part by funds from the "Institut National de la Santé et de la Recherche Médicale" (CRL No. 813013.

**Registry No. 1a**, 27382-01-0; **1d**, 35636-10-3; **2a**, 27382-09-8; **2a**·HCl, 80765-61-3; **3a**, 80765-62-4; **3a**·HCl, 80765-63-5; **2b**, 80765-64-6; **2b**·HCl, 80765-65-7; **3b**, 80765-66-8; **3b**·HCl, 80765-67-9; **2c**, 80765-68-0; **2c**·HCl, 80765-69-1; **3c**, 80765-70-4; **3c**·HCl, 80765-71-5; **2d**, 35801-12-8; **2d**·HCl, 80765-72-6; **3d**·HCl, 80765-73-7; **5**, 46802-94-2; **6a**, 80765-74-8; **6b**, 80765-75-9; **6c**, 80765-76-0; **6d**, 26035-89-2; 5-acetonyl-4,6-dichloropyrimidine, 26035-69-8; 3-amino-1,2-propanediol, 616-30-8.

# Bufadienolides. 32. Selenium Dioxide Dehydrogenation of 14-Dehydrobufalin[1a]

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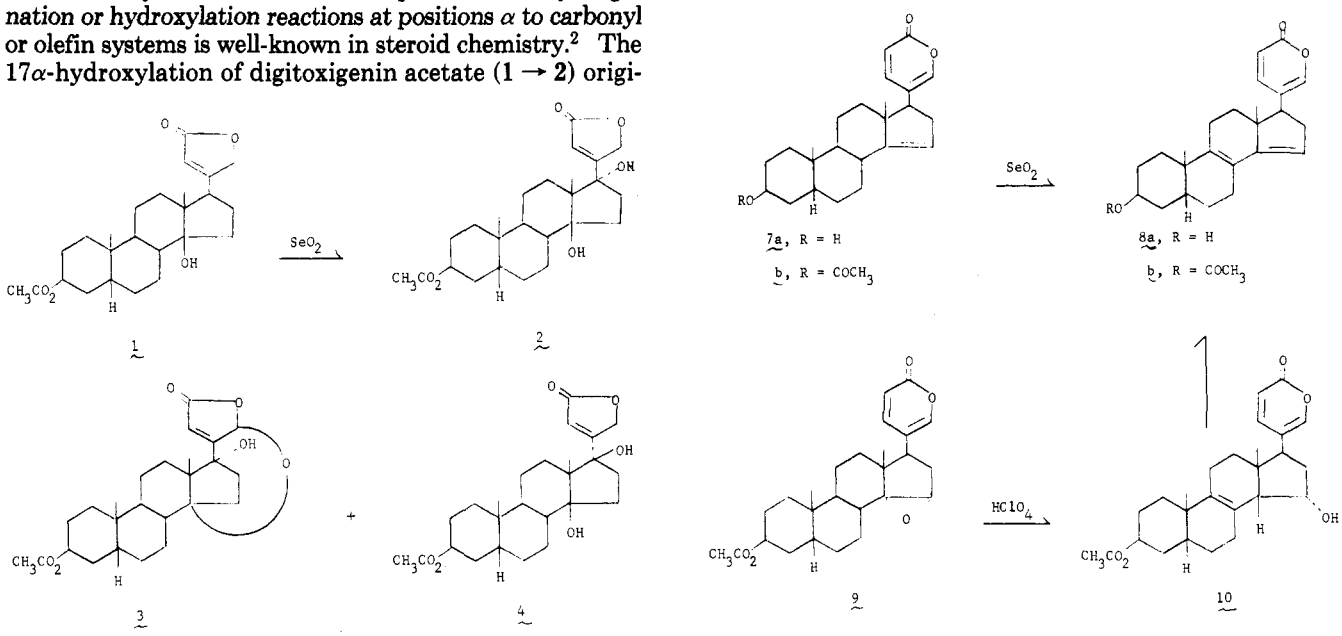
*Received June 5, 1981*

Unlike digitoxigenin acetate (**1**), bufalin acetate (**5a**), resibufogenin acetate (**6a**), and cinobufagin acetate (**6b**) were found to be resistant to selenium dioxide hydroxylation (e.g., **1** → **2**). However, under similar conditions selenium dioxide was found to dehydrogenate 14-dehydrobufalin (**7a**) to 3β-hydroxy-5β-bufa-8,14,20,22-tetraenolide (**8a**). An analogous dehydrogenation reaction was observed by employing 14-dehydrobufalin acetate (**7b** → **8b**). The structure of tetraene **8** was confirmed by dehydration of alcohol **10** to yield the same tetraene (**8b**). In turn, the structure of alcohol **10** prepared from α-epoxide **9** was substantiated by an X-ray crystallographic study of *o*-nitrobenzoate derivative **11**.

The utility of selenium dioxide promoted dehydrogenation or hydroxylation reactions at positions α to carbonyl or olefin systems is well-known in steroid chemistry.[2] The 17α-hydroxylation of digitoxigenin acetate (**1** → **2**) originally observed by Sondheimer and colleagues[3] provides an interesting illustration of such reactions. Subsequently, strophanthidin acetate was found to undergo the same 17α-hydroxylation reaction,[4] and the allyl oxidation of digitoxigenin acetate (**1**) with selenium dioxide was studied in detail by the Repke group.[5] In the latter investigation,

Scheme I




(1) (a) For part 31 and "Steroids and Related Natural Products. 98" refer to Y. Kamano, G. R. Pettit, M. Inoue, M. Tozawa, and Y. Komeichi, *J. Chem. Res., Miniprint*, *M*, 0837 (1977); G. R. Pettit, E. G. Thomas, and C. L. Herald, *J. Org. Chem.*, **46**, 4167 (1981). (b) Department of Chemistry, Faculty of Science, Tokyo Metropolitan University, Fukazawa, Setagaya Ku, Tokyo 158, Japan. (c) Department of Physical Chemistry, University of Cape Town, Cape Town, South Africa.

(2) cf. C. Djerassi, "Steroid Reactions", Holden-Day, San Francisco, 1963.

(3) N. Danieli, Y. Masur, and F. Sondheimer, *Tetrahedron*, **23**, 715 (1967).

(4) R. K. Ruzieva, M. B. Gorovits, and N. K. Abubakirov, *Khim. Prir. Soedin.*, 57 (1968).

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