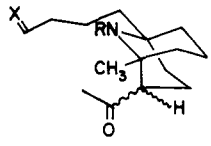
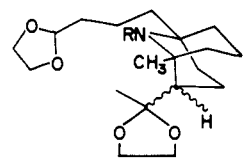
10% HCl, neutralization, and back extraction into ether, resulted in the formation of the monocyclic enamine **11** in 90% yield: found for **11**, ir(max) (neat) 1710 and 1640 cm^{-1}; pmr peaks (CCl_4) at δ 2.05 (s, 6 H, $CH_3C{=}O$ and $CH_3C(N){=}C$), 2.5 (s, 3 H, CH_3N), 4.05 (m, 1 H, HC=CN), and 4.8–6.0 (m, 3 H, vinyl). Treatment of **11** wth 5 equiv of isopropenyl acetate and 1.3 equiv of *p*-toluenesulfonic acid in benzene at reflux for 48 hr (under a Soxhlet extractor containing molecular sieves 5 Å) produced the bicyclic amine **12** in 45% yield after chromatography on silica gel (R_f = 0.5, ether–methanol 1:1): found for **12**, ir(max) (neat) 1705 cm^{-1}; pmr peaks (CCl_4) at δ 1.05 (s, 3 H, CH_3), 2.10 (s, 3 H, $CH_3C{=}O$), 2.20 (s, 3 H, CH_3—N), 2.8–3.0 (m, 1 H, CCHC=O), and 4.8–6.0 (m, 3 H, vinyl).[12] The orientation of the acetyl group in this intermediate was not of particular significance at this stage because of subsequent stereo equilibration.

Treatment of **12** with 10 equiv of Collins' reagent in methylene chloride for 72 hr afforded the bicyclic amide **13** in 80% yield.[13] The $>C{-}CH_3$ singlet which occurred at δ 1.05 in the pmr spectrum of the amine **12** was shifted to δ 1.60 in **13** indicating that the methyl protons are in the deshielding cone of the formyl group, further confirming the structural assignments.

Cleavage of the *N*-formyl olefin **13** with osmium tetroxide–sodium metaperiodate[14] in *tert*-butyl alcohol–water (3:1) afforded **14** in good yield (ir(max) (neat): 1730, 1710, 1667 cm^{-1}). The aldehyde–ketone was immediately treated with excess ethylene glycol in refluxing benzene containing a catalytic amount of *p*-toluenesulfonic acid to give the ketal–acetal **15** (85% yield) which afforded the amine **16** in 85% yield after



12, R = CH_3, X = CH_2
13, R = CHO, X = CH_2
14, R = CHO, X = O



15, R = CHO
16, R = H

reaction with 3 *N* KOH in absolute ethanol in a degassed sealed tube at 110° for 72 hr. As expected, the $>C{-}CH_3$ protons in the pmr spectrum of **16** were shifted back to δ 1.20. As in the monocyclic case (**7** → **11**), extraction of **16** into 10% HCl, neutralization, and back extraction into ether afforded the tricyclic enamine **17** as an unstable foam (85% yield):[15] found for **17**, ir(max) (neat) at 1705 and 1640 cm^{-1}; pmr peaks (CCl_4) at δ 1.15 (s, 3 H, CH_3), 2.11 and 2.18 (singlets, ratio 7:1, 3 H, $CH_3C{=}O$) (indicative of two epimers about the carbon bearing $CH_3C{=}O$), 2.6–2.9 (m, 1 H, CCH-C=O), 4.3 (m, 1 H, NC=CH), and 6.0 (bd, J = 9 Hz, 1 H, NCH=C).

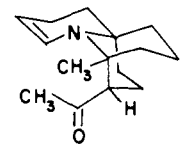
(12) Lower yields were obtained in this process if molecular sieves were not used. The reaction is regarded as a Mannich type process proceeding *via* the enol acetate of the conjugate acid (iminium ion) of 11. Cyclization could also be effected using pyrrolidine-*p*-toluenesulfonic acid reagent, but the yield of 12 was inferior.

(13) A. Cave, C. Kan-Fan, P. Potier, J. LeMen, and M.-M. Janot, *Tetrahedron*, 23, 4691 (1967).

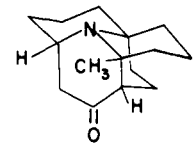
(14) R. Pappo, D. S. Allen, Jr., R. U. Lemieux, and W. S. Johnson, *J. Org. Chem.*, 21, 478 (1956).

(15) F. Bohlmann, H. J. Muller, and K. Schumann, *Chem. Ber.*, 106, 3026 (1973).

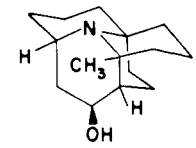
The fourth and final ring of the porantherine skeleton was closed simply by exposure of **17** to 10 equiv of *p*-toluenesulfonic acid monohydrate in toluene at reflux for 3 hr. The tetracyclic amine **18** was isolated as a crystalline solid (mp 109–112°) after chromatography on alumina (R_f = 0.7, ether) (yield 45%): found for **18**, ir(max) (CCl_4) at 1705 cm^{-1}; pmr peaks at δ 0.95 (s, 3 H, CH_3) and 3.4–3.7 (b, 1 H, >CHN). Reduction of the carbonyl group of **18** with sodium borohydride in methanol at room temperature afforded the alcohol **19**



17



18



19

in 92% yield (mp 159–164°): found for **19**, ir(max) ($CHCl_3$) at 3605 cm^{-1}; pmr peaks at δ 1.45 (s, 3 H, CH_3), 3.45–3.7 (b, 1 H, NCH), and 4.1 (m, 1 H, >CHOH). The position of the methyl peak at δ 1.45 in the pmr spectrum indicates that the reduction occurred exclusively to form the axial alcohol as indicated in **19**. Finally, elimination of water from **19** was accomplished by reaction in pyridine with 5 equiv of thionyl chloride at room temperature for 90 min. (±)-Porantherine (**1**) was isolated as a colorless oil in 55% yield after chromatography on alumina. The synthetic product was identical with natural porantherine by thin-layer chromatographic, pmr, ir, and mass spectral comparison. The rich and highly characteristic ir spectra of synthetic and plant-derived **1**·HCl were also identical.

The synthetic approach outlined in Scheme I (among others) was also suggested by LHASA-10,[4] the Harvard program for computer-assisted synthetic analysis.[16,17]

(16) We are indebted to Dr. J. A. Lamberton of CSIRO, Australia, for providing a reference sample of plant-derived porantherine.

(17) Financial assistance by the National Institutes of Health and the National Science Foundation is gratefully acknowledged.

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Nucleic Acid Hydrolysis. I. Isomerization and Anomerization of Pyrimidic Deoxyribonucleosides in an Acidic Medium

Sir:

The mechanism of the acidic hydrolysis of nucleosides, which has been proposed by Kenner[1a] and Dekker,[1b] is based on the transient formation of an unstable Schiff base, subsequent to the etheral oxygen protonation.[2] Proton transfer, from a conjugated acid protonated on the base, to annular oxygen has also been suggested.[1b] However, these hypotheses, which involved the ring oxygen opening in a similar

(1) (a) G. W. Kenner in "The Chemistry and Biology of Purines," G. E. W. Wolstenholme and C. M. O'Connor, Ed., Little, Brown and Co., Boston, Mass, 1957, p 312; (b) C. A. Dekker, *Annu. Rev. Biochem.*, 29, 453 (1960).

(2) T. L. V. Ulbricht, *Compr. Biochem.*, 8, 196 (1963); E. R. Garrett J. K. Seydel, and A. J. Sharpen, *J. Org. Chem.*, 31, 2219 (1966).

Scheme I

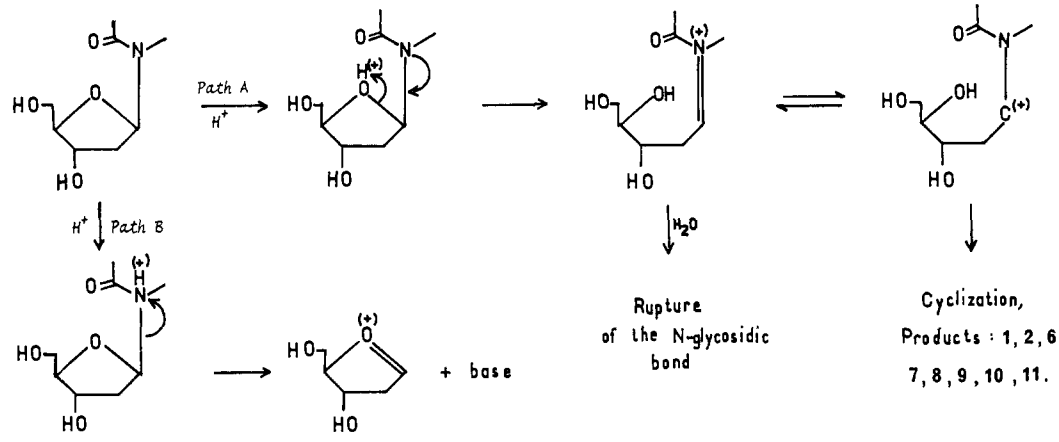


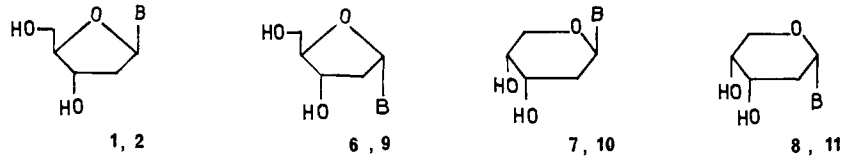
Table I. R_f Values and Yields of the Isomers Produced by the Warming of 0.1 *M* Deoxyribonucleosides in 2 *M* HClO, at 90°

	R_f		% [a]				
			Time[b] (min)				
	Solvent I	Solvent II	15	30	60	90	120
Thymidine (**1**)	0.37	0.52	88.9	73.2	39.0	21.8	9.0
1-(2-Deoxy)-α-D-*erythro*-pentofuranosyl)thymine (**6**)	0.37	0.46	3.2	6.4	10.5	8.5	7.6
1-(2-Deoxy-β-D-*erythro*-pentopyranosyl)thymine (**7**)	0.48	0.49	1.1	2.8	6.7	7.4	8.5
1-(2-Deoxy-α-D-*erythro*-pentopyranosyl)thymine (**8**)	0.39	0.34	0.4	0.8	1.4	2.0	2.1
Thymine (**5**)	0.55	0.66	6.4	16.8	42.4	60.3	72.8
2′-Deoxyuridine (**2**)	0.28	0.44	92.6	83.6	68.1	52.6	43.6
1-(2-Deoxy-α-D-*erythro*-pentofuranosyl)uracil (**9**)	0.28	0.41	2.1	4.8	8.8	10.6	8.7
1-(2-Deoxy-β-D-*erythro*-pentopyransol)uracil (**10**)	0.33	0.42	0.9	1.9	4.1	4.3	4.8
1-(2-Deoxy-α-D-*erythro*-pentopyranosyl)uracil (**11**)	0.29	0.33	0.5	0.8	1.7	2.4	2.7
Uracil (**12**)	0.36	0.46	3.9	8.9	17.3	30.1	40.2

[a] The yields were measured by ^{14}C liquid scintillation counting. [b] Thymidine and 2′-deoxyuridine were purified prior the reaction and appeared free of any impurities.

way to the mechanism of glycosylamine acidic solvolysis,[3] have been recently questioned,[4] mainly for the absence of known concurrent anomerization reactions. An A_1 mechanism consistent with kinetic and thermodynamic data has been hypothesized.[4,5,6]

We wish to report that the treatment of thymidine (**1**) and deoxyuridine (**2**) with 2 *M* $HClO_4$ in the conditions of usual hydrolysis gave rise to formation of the corresponding α-furanosidic and pyranosidic isomers.



B = Thymin-1-yl **1, 6, 7, 8**

B = Uracil-1-yl **2, 9, 10, 11**

This isomerization reaction, so far unknown, is in favor of the Kenner and Dekker mechanism[1] which must thus occur to a significant extent, at least for some pyrimidic deoxyribonucleosides, according to Scheme I (path A).

The four pyranoside and furanoside anomers and the base derivatives of 2′-deoxyuridine were separated by two-dimensional tlc[7] on silicagel MN-S-HR (solvent 1, $CHCl_3$–CH_3OH–H_2O (4:2:1) to which 5% of methanol was added to the lower phase; solvent 2, ethyl acetate–2-propanol–water (75:16:9)).

The acidic solvolysis of the $^{14}C_2$ nucleosides, thymidine (**1**), 2′-deoxyuridine (**2**), 5-bromo-2′-deoxyuridine (**3**), and 2′-deoxycytidine[8] (**4**), in 2 *M* $HClO_4$ at 90° was monitored thanks to this thin-layer chromatography system.[9] The warming of 0.1 *M* thymidine (**1**) in 2 *M* $HClO_4$ at 90° gave rise to the release of thymine (**5**)

(3) H. S. Isbell, and H. L. Frush, *J. Org. Chem.*, **23**, 1309 (1958).
(4) (a) R. Shapiro and S. Kang, *Biochemistry*, **8**, 1806 (1969); (b) B. Capon, *Chem. Rev.*, **69**, 407 (1969); (c) J. A. Zoltewicz, D. F. Clark, T. W. Sharpless, and G. Grahe, *J. Amer. Chem. Soc.*, **92**, 1741 (1970).
(5) R. Shapiro and M. Danzig, *Biochemistry*, 11, 23 (1972).
(6) J. A. Zoltewicz, and D. F. Clark, *J. Org. Chem.*, **37**, 1193 (1972); R. P. Panzica, R. J. Rousseau, R. K. Robins, and L. B. Townsend, *J. Amer. Chem. Soc.*, **94**, 4708 (1972); L. Hevesi, E. Wolfson-Davidson, J. B. Nagy, O. B. Nagy, and A. Bruylants, *ibid.*, **94**, 4715 (1972); E. R. Garrett and P. J. Mehta, *ibid.*, **94**, 8532 (1972).
(7) J. Cadet and R. Teoule, *J. Chromatogr.*, **76**, 407 (1973).
(8) The four isomers of deoxycytidine could not be separated by our chromatographic solvent systems. The compounds have been deaminated in order to obtain the corresponding uracil derivatives.
(9) The reactional mixture was neutralized by adding K_2CO_3 solution. After the elimination of the inorganic salts, an aliquot (1–2 μl) of the ethanolic filtrate was submitted for analysis.

and to the production of three new nucleosidic derivatives which might be located by the cysteine spray reagent. The two nucleosides, which have an α-diol group,[10] have been shown to be respectively 1-(2-deoxy-β-D-*erythro*-pentopyranosyl)thymine (**7**) and 1-(2-deoxy-α-D-*erythro*-pentopyranosyl)thymine (**8**). The last nucleosidic compound has been identified as 1-(2-deoxy-α-D-*erythro*-pentafuranosyl)thymine (**6**).

The acid solvolysis of 0.1 *M* 2′-deoxyuridine produced similar corresponding compounds, *i.e.*, 1-(2-deoxy-α-D-*erythro*-pentofuranosyl)uracil (**9**), 1-(2-deoxy-β-D-*erythro*-pentopyranosyl)uracil (**10**), 1-(2-deoxy-α-D-*erythro*-pentopyranosyl)uracil (**11**), and uracil (**12**). All these nucleosides have been characterized by ir, uv, CD, mass spectrometry, and by comparison with authentic samples.[11,12]

On the other hand, the acid hydrolysis of 5-bromo-2′-deoxyuridine and of 2′-deoxycytidine gave only the rupture of the *N*-glycosidic bond.

The quantitative importance of the rearrangement and of the cleavage reactions has been measured and is shown in Table I.

The electronic shifts (pathway A) from the pyrimidic moiety to the annular oxygen were important, and it is worth noting that the yield of the isomerization decreased in the expected order, thymidine > 2′-deoxyuridine > 5-bromo-2′-deoxyuridine.[13] Hydrolysis of the acyclic Schiff base partially explained the release of thymine and uracil.

In conclusion, different mechanisms (A_1 mechanism, C–O rupture) as previously suggested by Capon[4b] may be involved in the nucleosidic acid hydrolysis.

Acknowledgments. The authors are indebted to Mrs. Georges and Miss Pouchot for their skillful assistance throughout this work.

(10) The periodic oxidation of the two nucleosides gave corresponding "dialdehydic nucleosides."

(11) G. Etzold, R. Hintsche and P. Langen, *Chem. Ber.*, **101**, 226 (1968); M. Hoffer, *Chem. Ber.*, **93**, 2777 (1960); M. Prystas, J. Farkas, and D. Sörm, *Collect. Czech. Chem. Commun.*, 3123 (1965); E. Wittenburg, *Chem. Ber.*, **101**, 3132 (1968).

(12) J. Cadet, *Tetrahedron Lett.*, 867 (1974); J. Cadet and R. Teoule, *Carbohyd. Res.*, **29**, 345 (1973); H. Quelo, J. Cadet, and R. Teoule, *C. R. Acad. Sci., Ser. C*, **275**, 1137 (1972); J. Ulrich, J. Cadet, and R. Teoule, *Org. Mass Spectrom.*, **7**, 543 (1973).

(13) The easier ring oxygen isomerization of the 5-bromo-6-hydroxy-5,6-dihydrothymidine and of the 5,5-dibromo-6-hydroxy-5,6-dihydro-2′-deoxyuridine[12] in acidic medium was correlated with the increase of the basicity of N_1 atom.

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Addition of Nitrosonium Ion to Mercaptide-Bridged Binuclear Iron(II) and Cobalt(II) Complexes

Sir:

The mercaptide-bridged iron(II) dimer of *N,N′*-dimethyl-*N,N′*-bis(β-mercaptoethyl)ethylenediamine, $(FeL)_2$ (**1**), has been shown to have a distorted geometry with a short nonbonded Fe ··· Fe distance of 3.206 (5) Å attributable to ligand constraints.[1] This compound is highly reactive. Here we report its reaction with nitrosonium salts to form the novel nitrosyl bridged dimeric cation **2**.

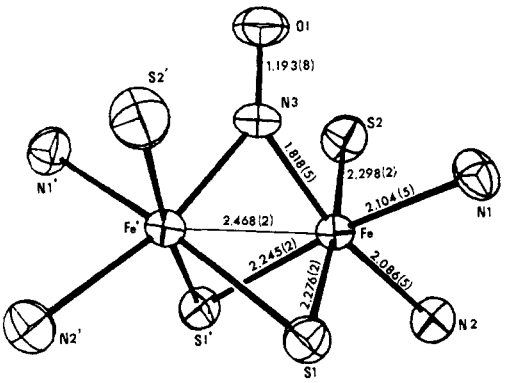

Figure 1. The inner coordination sphere of $[(FeL)_2NO]PF_6 \cdot$ acetone showing the 40% probability thermal ellipsoids. Selected bond angles are (deg): Fe–N3–Fe′, 85.5 (3); Fe–N3–O1, 137.2 (1); Fe–S1–Fe′, 66.2 (1); N3–Fe–S1, 90.6 (1); N3–Fe–S1′, 91.6 (1); S1–Fe–S1′, 80.6 (1); S1–Fe–N1, 84.8 (1); N1–Fe–N2, 84.6 (2); N2–Fe–S2, 84.3 (1); N3–Fe–N2, 168.5 (2); N1–Fe–S1′, 165.3 (1); S1–Fe–S2, 175.3 (1).

$$\underset{\mathbf{1}}{(FeL)_2} + (NO)^+ \longrightarrow \underset{\mathbf{2}}{[(FeL)_2NO]^+}$$

Addition of methylene chloride under nitrogen to a solid mixture of **1** and either $(NO)PF_6$ or $(NO)BF_4$ produced a dark brown solution containing **2**. Purification was effected by fractional crystallization from CH_2Cl_2–EtOAc.[2,3] The infrared spectrum of **2** (Nujol mull) shows a peak of medium intensity at 1553 cm^{-1} which may be assigned to the stretching vibration of a bridging nitrosyl ligand.[4] The 77°K Mössbauer effect spectrum of the BF_4^- salt of **2** exhibits a single quadrupole split doublet with δ = 0.29 mm/sec relative to natural iron foil and ΔE_q = 1.54 mm/sec, consistent with chemically equivalent iron atoms. Thus the nitrosonium cation adds to the mercaptide-bridged bimetallic center in **1** and now bridges the two iron atoms.

This interpretation has been confirmed by a single-crystal X-ray structure determination. Crystals of $[(FeL)_2NO]PF_6 \cdot$acetone, obtained upon recrystallization from acetone–ethanol, belong to the orthorhombic space group $Ama2$-C_{2v}^{16} with cell dimensions a = 24.18 (2) Å, b = 15.670 (7) Å, c = 8.011 (4) Å, ρ_{obsd} = 1.66 (2) g/cm³, ρ_{calcd} = 1.657 g/cm³ for four formula units per unit cell. The structure was solved by the heavy atom method using 1345 independent reflections ($2\theta < 55°$, $F^2 > 3\sigma(F^2)$) collected on a four-circle automated diffractometer using monochromatized Mo Kα radiation. Refinement by full-matrix least-squares methods yielded final values for the usual agreement factors $R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ and $R_2 = [\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2]^{1/2}$ of 0.032 and 0.037, respectively. During refinement the acetone molecule was treated as a rigid

(1) W. J. Hu and S. J. Lippard *J. Amer. Chem. Soc.*, **96**, 2366 (1974).

(2) *Anal.* (Galbraith Laboratories) Calcd for $C_{16}H_{36}N_8S_4OPF_6Fe_2$: C, 27.47; H, 5.19; N, 10.01; S, 18.34; F, 16.30; P, 4.43. Found: C, 27.20; H, 5.06; N, 9.80; S, 18.20; F, 16.12; P, 4.30. Calcd for $C_{16}H_{36}N_8S_4OBF_4Fe_2$: C, 29.97; H, 5.65; N, 10.92; S, 20.00; B, 1.69. Found: C, 29.60; H, 5.65; N, 10.20; S, 19.17; B, 1.78.

(3) The complex **2** is also produced in high yield using nitronium salts, *e.g.*, $(NO_2)PF_6$, instead of nitrosonium salts (*cf.* A. N. Nesmeyenov, K. N. Anisimov, N. E. Kolobova, and L. L. Krasnoslobodskaya, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 860 (1970)).

(4) R. B. King and M. B. Bisnette, *Inorg. Chem.*, **3**, 791 (1964).