0.025 G/deg ($CHCl_3$). Unlike biradical I, however, the S resonances tend to broaden slightly with decreasing temperature.

For biradical III, flexing should consist only of limited rotation about the C_4'–N bond and of flexing in the five- and six-membered rings. Accordingly, we observe no broadening of the S resonance lines up to 200° in xylene or down to −60° in carbon disulfide. The twisting amplitude about the C_4'–N bond should be sufficiently large, such that it should have a quite drastic effect on the direct overlap of the unpaired electron distributions. Unless this motion is fast over the entire temperature range examined and therefore results in an average exchange, these observations again indicate that simple direct exchange is of little importance. In contrast to I or II, we observe for III a nearly linear *increase* in J with increasing temperature of 0.08 G/deg in xylene (20–200°), 0.074 G/deg in chloroform (20–150°), and 0.092 G/deg in carbon disulfide (−60 to 20°). For all three biradicals studied here, the small changes in J with temperature could be due to rapid conformational changes in the molecules. However, one must also consider the possibility that these changes reflect changes in solvation with temperature, since solvent is important in determining the exchange energy.

These results support the idea that the exchange energy in a biradical is strongly influenced by the chemical nature of the connecting bridge in a manner not simply related to the distance between the nitroxyl groups or their relative orientation. For biradical III the results appear to be inconsistent with either a simple indirect (through bond) or direct (through space) exchange mechanism since one would expect the exchange to increase with the electron density on nitrogen (*i.e.*, with increasing a) as is seen for I and II. The exchange thus seems a complex function of the biradical structure.

Acknowledgment. This work was supported, in part, by the U. S. Atomic Energy Commission.

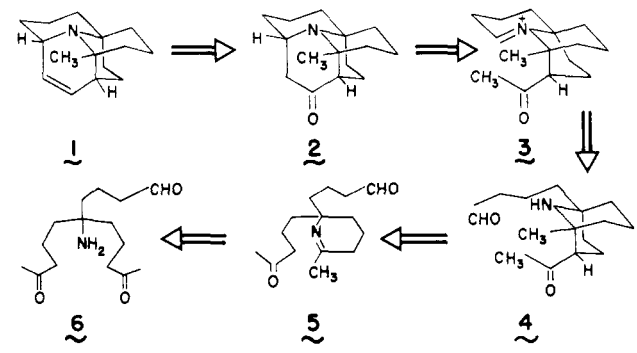
E. Kurt Metzner,* Louis J. Libertini, M. Calvin
Laboratory of Chemical Biodynamics
Lawrence Berkeley Laboratory, University of California
Berkeley, California 94720
Received July 3, 1974

A Total Synthesis of (±)-Porantherine

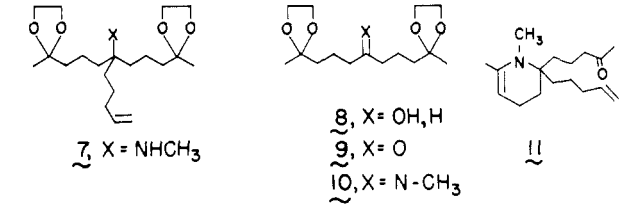
Sir:

Porantherine, the major alkaloid of the low, woody shrub, *Poranthera corymbosa*, has been shown by X-ray crystallography to possess structure **1**.[1,2] We describe here a synthesis of this interesting tetracyclic structure, the first known natural product with a bridged 9b-azaphenalene network.[3] The overall plan of synthesis, derived by antithetic (retrosynthetic) analysis,[4] and unusually simple for such a complex molecule, involves structures **2**, **3**, **4**, **5**, and **6** (or equivalents) as key intermediates as shown in Scheme I.

Scheme I



Following this general outline, the synthesis of the symmetric tertiary carbinamine **7** was undertaken. The addition of 2 equiv of the Grignard reagent derived from 5-chloro-2-pentanone ethylene ketal[5] to ethyl formate in tetrahydrofuran (THF) at reflux gave the desired secondary alcohol **8**[6] (95% yield). Oxidation to the ketone **9** was easily accomplished in 93% yield with 6 equiv of Collins' reagent at room temperature in methylene chloride.[7] Treatment of the ketone in a sealed tube with 2 equiv of methylamine in toluene containing molecular sieves 4 Å[8] at 110° for 18 hr afforded a quantitative yield of the imine **10**. Finally, four cycles of reaction of **10** with 1-lithio-4-pentene[9] in benzene at room temperature,[10] gave, after column chromatography on silica gel (R_f = 0.2, ether–methanol 1:1), the desired tertiary carbinamine **7** in 65% yield:[11] found for **7**, ir(max) (neat) 1635, 1225, and 1060 cm^{-1}; pmr peaks (CCl_4) at δ 1.25 (s, 6 H, CH_3), 2.2 (b, 3 H, CH_3N), 3.85 (s, 8 H, ketal), and 4.8–6.0 (m, 3 H, vinyl). Extraction of the tertiary carbinamine **7** into



7, X = $NHCH_3$ — **8**, X = OH,H; **9**, X = O; **10**, X = N-CH_3 — **11**

(1) W. A. Denne, S. R. Johns, J. A. Lamberton, and A. McL. Mathieson, *Tetrahedron Lett.*, 3107 (1971).

(2) An ambiguous stereochemical formulation of porantherine given in ref 1 and an erroneous stereo formula appearing in a later publication [W. A. Denne, S. R. Johns, J. A. Lamberton, A. McL. Mathieson, and H. Suares, *Tetrahedron Lett.*, 1767 (1972)] have been superseded by a correction; see Erratum, *ibid.*, 794 (1973).

(3) A group of structurally related polycyclic amines has recently been isolated from various insect species. See (a) B. Tursch, D. Daloze, M. DuPont, J. M. Pasteels, and M. C. Tricot, *Experientia*, **27**, 1380 (1971); (b) B. Tursch, D. Daloze, M. DuPont, C. Hootele, M. Kaisin, J. M. Pasteels, and D. Zimmermann, *Chimia*, **25**, 307 (1971); (c) B. Tursch, D. Daloze, and C. Hootele, *ibid.*, **26**, 74 (1972); (d) M. C. Tricot, J. M. Pasteels, and B. Tursch, *J. Insect Physiol.*, **18**, 499 (1972).

(4) See, for example, E. J. Corey, *Quart. Rev., Chem. Soc.*, **25**, 455 (1971), and papers therein cited.

(5) Cl. Feugeas and H. Normant, *Bull. Soc. Chim. Fr.*, 1441 (1963).

(6) Satisfactory proton magnetic resonance (pmr) and infrared (ir) spectra and analytical data (exact mass or elemental analysis) have been obtained for all intermediates.

(7) R. Ratcliffe and R. Rodehorst, *J. Org. Chem.*, **35**, 4000 (1970).

(8) J. Szmuszkovicz, *Advan. Org. Chem.*, **4**, 11 (1963).

(9) The lithium reagent was prepared from 5-bromo-1-pentene and lithium (1% sodium) wire in ether at 0°. The solvent was then evaporated *in vacuo* and replaced by benzene.

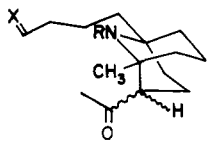
(10) In each cycle 1 equiv of the lithium reagent was added to the imine, the reaction was stirred for 1 hr at room temperature and quenched with 1 equiv of 0.4 *N* HCl in benzene. This sequence, which was repeated four times in the same flask without intermediate operations, was used because of the occurrence of proton transfer to the lithium reagent in competition with C=N addition.

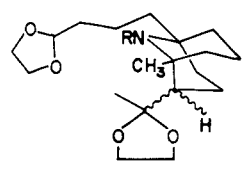
(11) (a) J. Heut, *Bull. Soc. Chim. Fr.*, 952 (1964); (b) J. Pornet, *Tetrahedron Lett.*, 967 (1971); (c) L. Miginiac and B. Manze, *Bull. Soc. Chim. Fr.*, 3832 (1968).

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).

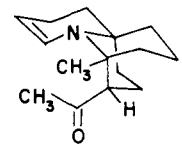
(12) Lower yields were obtained in this process if molecular sieves were not used. The reaction is regarded as a Mannich type process proceeding *via* the enol acetate of the conjugate acid (iminium ion) of **11**. Cyclization could also be effected using pyrrolidine-*p*-toluenesulfonic acid reagent,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

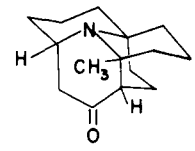
(14) R. Pappo, D. S. Allen, Jr., R. U. Lemieux, and W. S. Johnson, *J. Org. Chem.*, 21, 478 (1956).

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

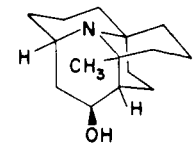
The fourth and final ring of the porantherine skeleton was closed simply by exposure of **17** to 10 equiv of *p*-toluenesulfonic acid monohydrate in toluene at reflux for 3 hr. The tetracyclic amine **18** was isolated as a crystalline solid (mp 109–112°) after chromatography on alumina (R_f = 0.7, 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.

E. J. Corey,* Richard D. Balanson
Department of Chemistry, Harvard University
Cambridge, Massachusetts 02138
Received July 5, 1974

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).