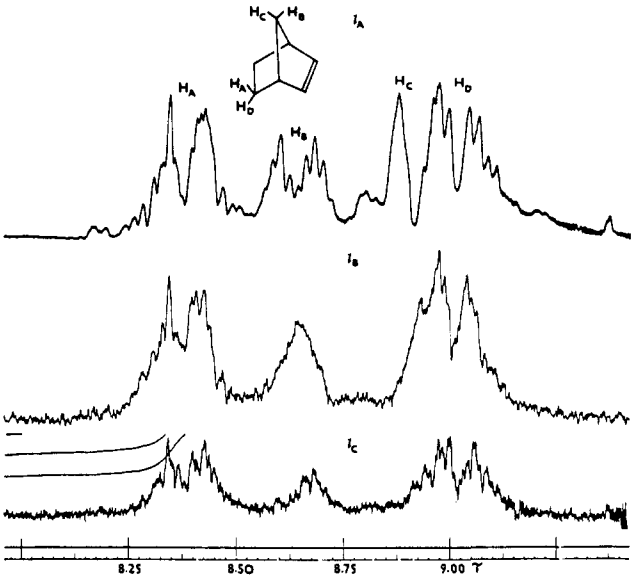
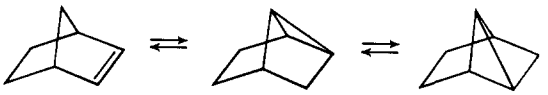


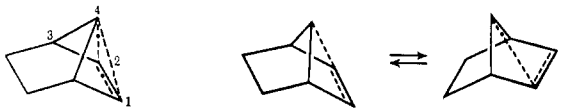
Figure 1. Nmr spectra at 100 Mc: (I_A) norbornene; (I_B) *anti*-7-deuterionorbornene from *anti*-bromide; (I_C) *anti*-7-deuterionorbornene from *syn*-bromide.

action of a cyclopropylcarbinyl radical at a carbon which does not have radical character. The steric factor is too small, and there is no precedent for reaction of the latter type. Either VII or equilibrating nonclassical radicals VIII can accommodate the result.



VI

In systems without a rigid framework, structures like VII are expected to be favored,[2] but rigid systems are



VII VIII

also stabilized by including 1,4 overlap along with 2,4 overlap.[15]

Results of application of the kinetic criterion for delocalization, in this and in other systems, will be reported soon.

(15) The numbering system used for VII emphasizes the homoallylic portion of the molecule.

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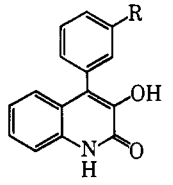
Received December 4, 1967

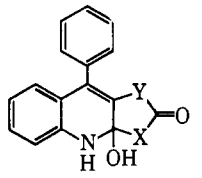
The Synthesis of Cyclopenin[1]

Sir:

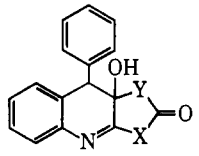
Cyclopenin, $C_{17}H_{14}N_2O_3$, a metabolite first isolated[2] from *Penicillium cyclopium* and later[3] from *Penicillium viridicatin*, in dilute acid solution loses its optical activity with concomitant appearance in high yield of 3-hydroxy-4-phenyl-2-quinolone (viridicatin, I, R = H),[2-4] carbon dioxide, and methylamine. To accommodate these observations, a quinolinooxazolidinone structure (IIa or IIIb) was assigned[2] to cyclopenin; fusion at the 3,4 positions of the quinoline also was postulated.[5] In each case, the isomer with the oxygen and N–CH_3 interchanged was also a contender.



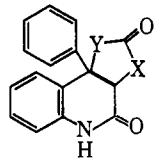
I



IIa, X = NCH_3; Y = O
b, X = O; Y = NCH_3

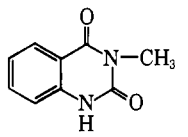


IIIa, X = NCH_3; Y = O
b, X = O; Y = NCH_3

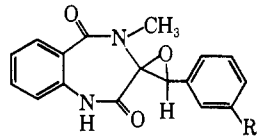


IVa, X = NCH_3; Y = O
b, X = O; Y = NCH_3

Reinvestigation[3,4,6] showed that a phenolic metabolite, cyclopenol, accompanied cyclopenin and that cyclopenol is also labile to mild acid, yielding 3′-hydroxyviridicatin (I, R = OH). Oxidation of cyclopenin[4] with hydrogen peroxide–acetic acid gave anthranilic acid, benzoic acid, benzaldehyde, and in particular 3-methyl-2,4-quinazolinedione (V). Biosynthetic studies[4,7] showed that anthranilic acid and phenylalanine were incorporated into cyclopenin, that the carbon dioxide evolved in the viridicatin transformation derived from the anthranilic acid carboxyl, and that this carbon remained in the quinazoline V. None of the previous proposals (II, III, and IV) is compatible with these data, and a new structural proposal,[4] the benzodiazepine VI, was made for cyclopenin. Further support was provided by the strong amide absorption in the ir and the one proton singlet at δ 4.04 in the nmr, assigned to the benzylic hydrogen.



V



VI

Although a strong case can be made for VI, some anomalies remained. Particularly striking was the

(1) Supported in part by the U. S. Army Research Office, Durham, N. C.

(2) A. Bracken, A. Pocker, and H. Raistrick, *Biochem. J.*, 57, 587 (1954).

(3) J. H. Birkinshaw, M. Luckner, Y. S. Mohammed, K. Mothes, and C. E. Stickings, *ibid.*, **89**, 196 (1963).

(4) Y. S. Mohammed and M. Luckner, *Tetrahedron Letters*, 1953 (1963).

(5) J. T. Edward, *Ann. Rept. Progr. Chem.* (Chem. Soc. London), **51**, 247 (1954).

(6) M. Luckner and Y. S. Mohammed, *Tetrahedron Letters*, 1987 (1964).

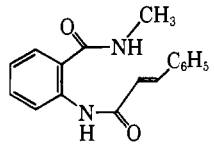
(7) M. Luckner and K. Mothes, *ibid.*, 1035 (1962); *Arch. Pharm.*, **296**, 18 (1963).

facile loss of carbon dioxide and rearrangement necessary in transforming cyclopenin (VI, R = H) to viridicatin (I, R = H) and not required of the previous proposals (II, III, and IV) which contained the viridicatin skeleton intact. Synthesis of the postulated structure was undertaken to resolve these doubts.

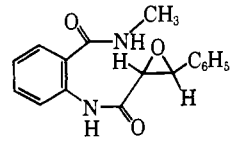
2-Amino-N-methylbenzamide with *trans*-cinnamoyl chloride gave 2-(N-methylcarboxamido)-*trans*-cinnamanilide (VII) (mp 187°)[8] which was epoxidized with *m*-chloroperbenzoic acid to the glycidamide VIII (mp 166–167°). Excess potassium *t*-butoxide in *t*-butyl alcohol (to form the diamidate anion) lead to ring closure to 3,4-dihydro-3-hydroxybenzyl-4-methyl-1H-1,4-benzodiazepin-2,5-dione (IXa) (mp 199°); only one of the two possible diastereomers was obtained. A small amount of dehydroxybenzylated product, X,[9] was produced, presumably from IXa by a retroaldol reaction.

Acetylation of IXa provided the O-acetyl derivative IXb (mp 233–235°) which thermally underwent elimination to 3-benzylidene-3,4-dihydro-4-methyl-1H-1,4-benzodiazepine-2,5-dione (XI) (mp 208–209°); over-all yield from VII to XI was 58%. Only one stereoisomer of the benzylidene compound XI was isolated; it was assigned the *trans* configuration shown on the following evidence.

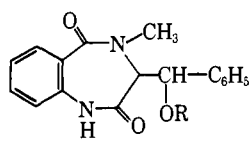
The *trans*-cinnamate retained its configuration during amide formation and epoxidation as indicated by the coupling constants for the vinyl protons of VII (J = 16 cps) and the α and β hydrogens of the β-phenylglycidamide VIII (J = 2.5 cps). A single diastereomer was



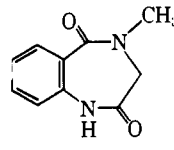
VII



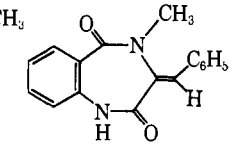
VIII



IXa, R = H
b, R = $COCH_3$



X



XI

obtained for IXa and its configuration is unchanged by acetylation. Pyrolytic *cis* elimination then yields the *trans*-benzylidene XI. Confirmation for this assignment was obtained by isolation of both isomers from condensation of X and benzaldehyde.[10] The major isomer (identical with XI) had N-methyl and vinyl hydrogen resonances at δ 3.2 and 6.95, respectively, while in the minor isomer they were at δ 3.5 and 6.72. The upfield shift for the N-methyl signal in the *trans* isomer is due to shielding from the benzene ring π cloud; the downfield shift of the vinyl hydrogen signal in the *trans* isomer is due to deshielding by the carbonyl.[11]

(8) Satisfactory elemental analyses were obtained for all compounds in the synthetic sequence, and in each case the spectroscopic data (uv, ir, nmr) supported the assigned structures.

(9) P. M. Carabateas and L. S. Harris, *J. Med. Chem.*, 9, 6 (1966).

(10) J. L. Wong, unpublished work, this laboratory.

(11) Similar observations have been made with 2-acetyl-5-benzylidenecreatinine [A. R. Frasca and E. B. Dennler, *Chem. Ind.* (London), 509 (1967)].

The epoxidation of XI was complicated by adverse steric and electronic factors, and no precedent exists for epoxidation of a double bond so substituted. A large variety of methods gave no reaction, overoxidation, or traces of epoxide. Finally, conditions were found (*m*-chloroperbenzoic acid, room temperature, 14 days) which gave a 37% yield of epoxide. That this material was *dl*-cyclopenin (VI, R = H) (mp 194–195°) was established by comparison with natural *l*-cyclopenin [mp 179–180°, $[\alpha]^{23}_{5462}$ −301° (*c* 1.0, methanol)].[12] The ir ($CHCl_3$), uv (C_2H_5OH), and nmr ($CDCl_3$) spectra of the two compounds were identical, the R_f's on tlc were the same, and both gave viridicatin with acid. This synthesis establishes the structure of cyclopenin beyond doubt and confirms the previous proposal.[4] It also allows the assignment of relative stereochemistry as shown in VI.

(12) Prepared from a crude isolate obtained by H. R. while a guest in the laboratory of Dr. H. Raistrick in March 1956.

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Received January 12, 1968

Hydrogen–Deuterium Exchange in a Cobalt–Nitrogen Complex

Sir:

The recently reported nitrogen complexes of cobalt[1–5] are useful models for the nitrogen-binding site of the nitrogenase enzyme.[6] The activation energies for coordination of N_2 are very low, and the relative affinities for N_2, H_2, and NH_3[4] seem to be similar to those of the enzyme. Therefore, it was of interest to study the exchange of D_2 with the hydridonitrogen complex, $HCo(N_2)(PPh_3)_3$.[5]

Surprisingly, when benzene solutions of $HCo(N_2)(PPh_3)_3$ were allowed to equilibrate with deuterium gas at 25°, the amount of hydrogen introduced into the gas far exceeded the amount available by exchange with the lone Co–H. Indeed, the extent of exchange corresponded to roughly 19 hydrogens per mole of cobalt complex. For example, the gases from incubation of 5.1×10^{-5} mol of $HCo(N_2)(PPh_3)_3$ with 6.5×10^{-5} mol of D_2 (25°, 24 hr) contained 88% H_2, 11% HD, and 0.5% D_2. The calculated values for random statistical exchange of 19 H's are 87% H_2, 12% HD, and 1% D_2. This result suggests that not only the Co–H but also six aryl H's per phosphine ligand exchange with the D_2 atmosphere.

The extent and position of aromatic deuteration were confirmed by the following experiment. A solution of 1.0 mmol of $HCo(N_2)(PPh_3)_3$ in 50 ml of benzene was stirred with 21 mmol of D_2 at 25° for 6 days.

(1) A. Misono, Y. Uchida, and T. Saito, *Bull. Chem. Soc. Japan*, 40, 700 (1967).

(2) A. Yamamoto, S. Kitazume, L. S. Pu, and S. Ikeda, *Chem. Commun.*, 79 (1967).

(3) A. Sacco and M. Rossi, *ibid.*, 316 (1967).

(4) A. Yamamoto, L. S. Pu, S. Kitazume, and S. Ikeda, *J. Am. Chem. Soc.*, 89, 3071 (1967).

(5) J. A. Ibers, *Chem. Commun.*, 96 (1968).

(6) R. W. F. Hardy and R. C. Burns, *Ann. Rev. Biochem.*, in press.