tion[3] unless a number of resonance structures is hybridized. However, the LCAO orbitals are reasonable, and indicate that the compound has filled valence orbitals. Local hybridization is conveniently assumed to be sp along the BCl direction. The eight sp orbitals pointing inward form two strongly bonding orbitals and, in the one-electron approximation, a vacant doubly degenerate pair which may interact with the lone pairs on the Cl atoms.[4] The π orbitals of the boron atoms form six pairs of bonding orbitals, thus giving a total of eight bonding pairs for the B . . . B interactions. A more detailed discussion of the structure determination and valence theory will be presented elsewhere. This molecule, like other known boron hydrides and halides, has high enough symmetry to prevent reactive regions, and low enough symmetry that unfilled electronic levels do not occur near the highest filled levels. The occurrence of this new polyhedron has suggested a study, now under way, of LCAO molecular orbitals in other polyhedra, and a comparison with orbitals in $Mo(CN)_8^{-4}$, which also has D_{2d} symmetry.[5]

We wish to thank Dr. M. Atoji for his help in the early stages, and to thank the Office of Naval Research, the Office of Ordnance Research and the Computing Center of the University for aid in this investigation. We are also indebted to the Shell Oil Company for a fellowship to Robert Jacobson.

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SCHOOL OF CHEMISTRY
UNIVERSITY OF MINNESOTA
MINNEAPOLIS 14, MINNESOTA

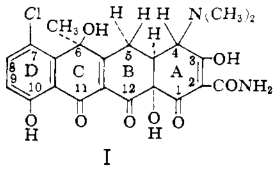
ROBERT A. JACOBSON
WILLIAM N. LIPSCOMB

RECEIVED AUGUST 25, 1958

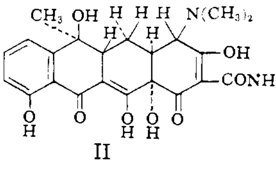
TWO NEW TETRACYCLINE-RELATED COMPOUNDS: 7-CHLORO-5a(11a)-DEHYDROTETRACYCLINE AND 5a-*epi*-TETRACYCLINE. A NEW ROUTE TO TETRACYCLINE

Sir:

We wish to report the isolation, characterization, and structure proof of two new tetracycline-related compounds: 7-chloro-5a(11a)-dehydrotetracycline (I), accumulated by *Streptomyces aureofaciens* Duggar mutant S-1308, and 5a-*epi*-tetracycline (II), prepared from I by catalytic hydrogenation.[1]



I



II

7-Chloro-5a(11a)-dehydrotetracycline hydrochloride: $[\alpha]^{25}D$ +15.5° (0.65% in 0.03N HCl); λ_{max} 221 mμ, ϵ 27,500; λ_{max} 251 mμ, ϵ 23,000; λ_{max} 375 mμ (very broad), ϵ 4,300. *Anal.* Found for $C_{22}H_{22}N_2Cl_2O_8$: C, 51.23; H, 5.12; N, 5.21; Cl, 13.82; 0 (Unterzaucher), 24.54; loss on drying, 0; ash, 0. The origin and composition of I implied a close relationship to 7-chlorotetracycline. Upon catalytic hydrogenation (Pd–C), I rapidly absorbed two moles of hydrogen, yielding two chlorine-free organic products. They were tetracycline and II, an isomer of tetracycline differing from tetracycline, on the basis of the ultraviolet absorption spectrum (300–400 mμ), in the Rings B–C–D chromophore region. 5a-*epi*-Tetracycline hydrochloride monohydrate: $[\alpha]^{25}D$ +147° (0.50% in 0.1 *N* H_2SO_4); λ_{max} 220 mμ, ϵ 15,000; λ_{max} 265 mμ, ϵ 19,200; λ_{max} 336 (broad), ϵ 12,000. *Anal.* Found for $C_{22}H_{25}N_2ClO_8.H_2O$: C, 53.12; H, 5.33; N, 5.36; Cl, 7.41; 0 (Unterzaucher), 28.75; loss on drying, 3.43; ash, 0. The hydrogen uptake, the fact that tetracycline is a major reduction product, and the difference between the ultraviolet absorption spectrum of I and of 7-chlorotetracycline, especially in the region attributed solely to the Rings B-C-D chromophore (300–400 mμ), suggested that I is a dehydrochlorotetracycline, the additional unsaturation being associated with the Rings B-C-D chromophore. The presence in I of non-hydrogen-bonded carbonyl absorption in the infrared (5.8 μ) favors 5a(11a) as the position of the additional double bond.

The isomeric relationship of II and tetracycline was established by analysis and by the conversion of II in essentially quantitative yield under established dehydration conditions to anhydrotetracycline. These facts, together with the fact that tetracycline and II maintain their different identities under conditions expected to bring about tautomeric equilibrium, established II as 5a-*epi*-tetracycline.

Further confirmation of the relationship between tetracycline and II was found in their relative rates of dehydration. In 1*N* sulfuric acid at 100°, the half reaction times for dehydration of tetracycline and II were <1 min. and 67 min., respectively. This is consistent with the structural assignment of 5a(α)H,6(β)OH (therefore *trans*) for tetracycline[1] and 5a(β)H,6(β)OH (therefore *cis*) for II.

Paper chromatography gave these R_f values for I in the systems: 0.3*M* sodium phosphate (*p*H 3.0)/*n*-butanol, 0.49; MacIlvaine's buffer (*p*H 4.7)/ethyl acetate, 0.87; 0.3*N* phosphoric acid, 0.1% trichloroacetic acid/9:1 chloroform-*n*-butanol, 0.39. II ih the phosphate/butanol system had an R_f value of 0.65.

The organism, S-1308, accumulating I is a mutant descended from the original 7-chlorotetracycline-producing *S. aureofaciens* A-377 soil isolate of Duggar.

Neither 7-chloro-5a(11a)-dehydrotetracycline nor 5a-*epi*-tetracycline possesses *in vitro* antibacterial activity toward *Staphylococcus aureus* in excess of 0.5% that of 7-chlorotetracycline.

It is now known that the antibacterial activity of tetracycline (toward *S. aureus*) is substantially unaltered by replacement of 5-H with OH, of 6-CH_3 with H, or of 7-H with Cl or Br. In contrast, other small changes reducing this antibacterial activity

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(1) The configurations in this paper are based on the stereochemistry suggested by Hochstein, *et al.* (THIS JOURNAL, **75**, 5467 (1953)) for 5-hydroxytetracycline.

of tetracycline by twenty-fold or greater are 2-carboxamide to nitrile, epimerization at C.4, epimerization at C.5a, and dehydrogenation at C.5a(11a).

J. R. D. McCORMICK
LEDERLE LABORATORIES PHILIP A. MILLER
AMERICAN CYANAMID COMPANY JOHN A. GROWICH
PEARL RIVER, NEW YORK NEWELL O. SJOLANDER
ALBERT P. DOERSCHUK

RECEIVED AUGUST 18, 1958

STUDIES[1] INVOLVING ISOTOPICALLY LABELLED FORMIC ACID AND ITS DERIVATIVES. IV. DETECTION OF CYANIDE (CN^-) IN A MIXTURE OF FORMIC ACID AND NITROGEN IN THE MASS SPECTROMETER

Sir:

During mass spectrometric studies of formic acid,[1] a research spectrometer[2] was modified for examining ion-molecule reactions. An essentially field-free region was set up between the ionization chamber and the first accelerating plate. Ions produced from one gas in the ionization chamber are passed at low energy through neutral molecules of another gas introduced into the field-free space. As the 10-fold higher pressure[3] in the chamber permits little back diffusion from the field-free region, it is possible to determine which of two species furnishes the ion in an ion-molecule reaction by inverting the mode of addition of two gases and noting the effect on the relative abundance of a production.

Ionization of formic acid in the chamber by electrons having an indicated energy[4] of 2.3 e.v. produced $HCOO^-$ ions[1] and essentially no positive ions.[5]

With nitrogen gas in the field-free region, a negative ion of mass 26 was detected. Its mass was not affected by substitution of DCOOH for the formic acid. Substitution of either $HC^{13}OOH$ for formic acid or nitrogen-N^{15} for nitrogen shifted the mass of this ion to 27. Use of both $HC^{13}OOH$ and nitrogen-N^{15} in the same experiment caused mass 28 to appear. When carbon monoxide or carbon dioxide was substituted for formic acid the ion of mass 26 failed to appear. We conclude that this negative ion is CN^-. Since the positive peaks known to arise from hydrogen cyanide and cyanogen[6] were absent even with the electron energy raised to 75 e.v., neither of these substances is a likely precursor. Inversion of the mode of addition—that is introduction of nitrogen into the ionization chamber and formic acid into the field-free region—resulted in a 10-fold reduction in abundance of the CN^- ion.

When, in a subsequent experiment, an equimolar mixture of nitrogen and formic acid at 2 mm. pressure was subjected to a spark discharge, 1% hydrogen cyanide was found in the product mixture.

In the mass spectrometric study, some active species produced from formic acid in the ionization chamber apparently reacts with nitrogen molecules to give rise to the CN^- ions. The active species is probably the negative ion,[7] $HCOO^-$, although we cannot rule out all other possibilities. Were the present reaction between $HCOO^-$ and N_2 molecules, this would presumably be the first mass-spectrometric observation of a negative[8] ion-molecule reaction of this type.

The present results indicate some similarity between the reactions produced by the electric discharge and those effected by the 2.3 e.v. electrons in the mass spectrometer. The results also may be significant because of a current interest in nitrogen fixation by ionizing radiations.

Helpful discussions with Russell Baldock, John Burns and P. S. Rudolph are acknowledged.

[1] Previous study, G. A. Ropp and C. E. Melton, THIS JOURNAL, **80**, 3509 (1958).

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[7] The low energy of the ionizing electrons makes it improbable that a positive ion is the precursor of the CN^- ion. A free-radical precursor is unlikely at the low pressures employed since a three-step process would be required: (a) electron impact with formic acid to produce a radical, (b) reaction of the radical with nitrogen, and (c) conversion of the resulting species to CN^-.

[8] A number of positive ion-molecule reactions are known: see H. S. Johnston in *Annual Reviews of Physical Chemistry*, **8**, 252–3 (1957). However, see E. E. Muschlitz, Jr., *J. Appl. Phys.*, **28**, 1414 (1957).

[9] Operated by Union Carbide Corporation for the U. S. Atomic Energy Commission.

CHEMISTRY DIVISION[9] C. E. MELTON
OAK RIDGE NATIONAL LABORATORY
OAK RIDGE, TENNESSEE GUS A. ROPP

RECEIVED JULY 25, 1958

A NOVEL SYNTHESIS OF METAL CARBONYLS USING TRIETHYLALUMINUM AS THE REDUCING AGENT[1]

Sir:

We wish to report a novel method for preparing transition metal carbonyls, one that is of particular value for the less accessible metal carbonyls. The method consists essentially of a reductive carbonylation[2] reaction of an appropriate salt of the transition metal with triethylaluminum and carbon monoxide. The reaction generally is carried out in an ether solvent at elevated temperature and pressure. The triethylaluminum appears to function in this reaction as a selective reducing agent for the transition metal, permitting carbonylation to occur at a rate greater than the rate of reduction to the free metal.

The method differs from the conventional Grignard methods[3–7] in that (1) it is applicable to the

[1] Reductive Carbonylation Synthesis of Metal Carbonyls. I.

[2] The term "reductive carbonylation" as used here denotes overall reduction and carbonylation of the transition metal in a compound or intermediate in which the metal has a formal positive charge of one or greater.

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