Figure 1. Comparative rates of metabolism of 4-C^{14}-androst-4-ene-3,17-dione and 4-C^{14}-estradiol by *Nocardia restrictus*.

androst-4-ene-3,17-dione was rapidly metabolized by *N. restrictus* whereas practically all of the radioactivity could be recovered either as 4-C^{14}-estrone or 4-C^{14}-estradiol after incubation of 4-C^{14}-estradiol with *N. restrictus*.

With this information available, it appeared desirable to synthesize 19-hydroxycholest-4-en-3-one (I). If the organism cleaves the side chain first to yield 19-hydroxy-androst-4-ene-3,17-dione, the latter compound should be converted into estrone which then should accumulate. When I (1.2 g.) was incubated with *N. restrictus*, an 8% yield[11] of estrone (65 mg.) was indeed obtained, m.p. 257–259°, identical (mixture melting point and infrared spectrum) with an authentic sample. When 1.2 g. of I was exposed to CSD-10,[12] 230 mg. of estrone (30%) was obtained.[13] Similarly, 19-hydroxy-β-sitost-4-en-3-one (II) was also converted into estrone by CSD-10 in 10% yield.[13]

I

II
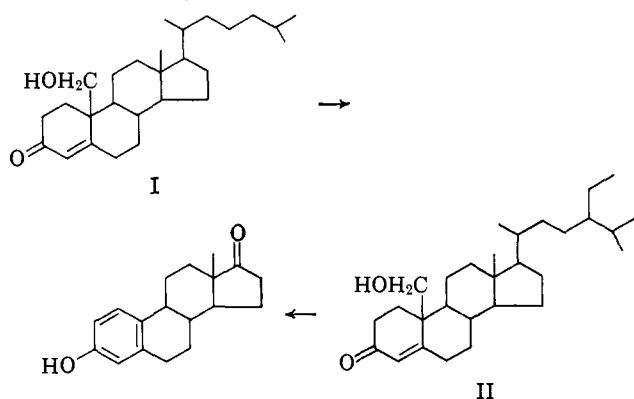
Cholestenone is not only a very poor inducer of the steroid 1-dehydrogenase and the 9α-hydroxylase but also it is a very poor substrate for these enzymes when compared to androst-4-ene-3,17-dione.[14,15] Thus it is

(11) The major portion of the remaining 92% can be accounted for as unmetabolized substrate and phenolic acids.

(12) CSD-10 is an organism isolated from soil utilizing cholesterol as a sole carbon source.

(13) Practically all the steroidal material was recovered in these fermentations, the main portion being unmetabolized substrate.

(14) C. J. Sih and R. E. Bennett, *Biochim. Biophys. Acta*, **56**, 584 (1962).

(15) F. N. Chang and C. J. Sih, *Biochemistry*, **3**, 1551 (1964).

unlikely that ring fission preceded side-chain cleavage. All these results support the view that the major pathway of sterol breakdown among microorganisms involves first the removal of the sterol side chain to yield C-19 steroids. The reason for the nonaccumulation of C-19 steroidal intermediates from cholesterol is due to their rapid metabolism *via* the conventional 9,10-seco pathway, for when the A ring is first aromatized estrone accumulates, and practically all of the steroidal material is recovered.[16]

In view of the accessibility of I and II from cholesterol and β-sitosterol, respectively,[17] this appears to be an attractive route for the synthesis of estrone from these readily available sterols.[18]

Acknowledgment. We wish to thank Mr. Y. Y. Tsong and Mr. F. N. Chang for their technical assistance.

(16) The compound, A-nor-3,5-secocholestan-5-on-3-oic acid can be visualized as the product resulting from the action of oxygenases on cholestenone in a manner similar to peracids. However, we have not been able to detect this compound in our fermentations. Since practically all of the steroidal material can be recovered in forms other than this compound, it appears to us this alternate mechanism advanced by Turfitt (ref. 4) is a minor side reaction rather than a major degradative pathway. This explanation is supported by the fact that A-nor-3,5-seco-androstan-5-on-3-oic acid is very poorly metabolized by these organisms.

(17) J. Kalvoda, K. Heusler, H. Ueberwasser, G. Anner, and A. Wettstein, *Helv. Chim. Acta*, **46**, 1361 (1963).

(18) This investigation was supported in part by research grants from the National Institutes of Health (AM-4874 and AM-6110).

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Valence Tautomerism in Cyclooctatetraene–Iron Carbonyl Complexes

Sir:

The concept of facile valence tautomerism has been invoked to rationalize apparently conflicting physical data recently obtained for several organometallic π-complexes. For example, although X-ray data suggest[1] a structure of cyclooctatetraene–iron tricarbonyl (I) in which the $Fe(CO)_3$ residue is bonded to only four carbon atoms of the C_8 ring, nonetheless the n.m.r. spectrum of the complex indicates all eight protons to be equivalent.[2] A diene–iron tricarbonyl formulation with rapid rotation of the $Fe(CO)_3$ group about the ring, to produce equivalent valence-tautomeric structures (Ia, etc.), would reconcile these data.

Analogous degenerate valence tautomerism has been proposed to occur in the $C_7H_7Fe(CO)_3$[3] and $C_7H_7Fe_2(CO)_6$ cationic systems,[4] and similar behavior is indicated for a cyclopentadienyl–cycloheptatrienyl–Mo(CO)$_2$ complex.[5]

In each of these systems the valence tautomers possess the same type of metal–ligand electronic

(1) B. Dickens and W. N. Lipscomb, *J. Chem. Phys.*, **37**, 2084 (1962).

(2) (a) T. A. Manuel and F. G. A. Stone, *J. Am. Chem. Soc.*, **82**, 366 (1960). (b) M. D. Rausch and G. N. Schrauzer, *Chem. Ind.* (London), 957 (1959). (c) We have not been able to find evidence for the broadening of this peak at temperatures as low as −60°.

(3) J. E. Mahler, D. A. K. Jones, and R. Pettit, *J. Am. Chem. Soc.*, **86**, 3589 (1964).

(4) G. F. Emerson, J. E. Mahler, R. Pettit, and R. Collins, *ibid.*, **86**, 3590 (1964).

(5) R. B. King, *Tetrahedron Letters*, 1137 (1963).

$$I \quad\longrightarrow\quad Ia \qquad\qquad II$$
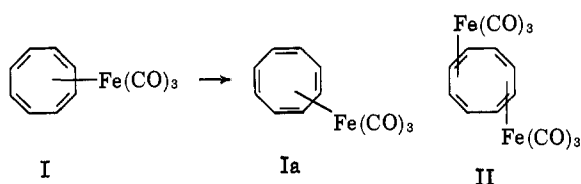
structure.[6] We now wish to present evidence for the occurrence of a novel type of valence tautomerism in which the valence tautomers possess different types of metal–ligand bonding, and one which serves to further demonstrate the high degree of bond mobility possible in organometallic complexes.

In addition to cyclooctatetraene–iron tricarbonyl (I) we have found that reaction of cyclooctatetraene with $Fe_2(CO)_9$ produces three isomeric complexes of formula $C_8H_8Fe_2(CO)_6$. One of these three is identical with the material isolated from the reaction of cyclooctatetraene with $Fe(CO)_5$[2a,b] for which the structure II is suggested from X-ray studies.[1] The other two complexes,[3] hereafter referred to as III and IV, can be separated by chromatography on alumina; they each form orange-red crystals from pentane and each melts in the range 90–93° (m.m.p. 72–85°). *Anal.* Calcd. for $C_8H_8Fe_2(CO)_6$: C, 43.80; H, 2.10; Fe, 29.10. Found (for IIII): C, 44.01; H, 2.21; Fe, 28.86; (for IV): C, 43.98; H, 2.20; Fe, 29.09. The three $Fe_2(CO)_6$ complexes can also be formed upon reaction of I with $Fe_2(CO)_9$.

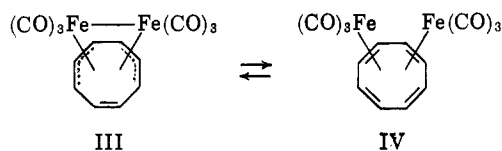The n.m.r. spectrum of complex III (Figure 1a) shows four regions of absorption of equal areas at τ 4.2, 5.4, 5.9, and 7.5. The complex shows a strong band at 772 cm.$^{-1}$ in its infrared spectrum suggestive of a *cis* double bond. The Mössbauer spectrum[7] indicates both iron nuclei to be chemically equivalent and the high dipole moment (3.9 D.) points to a structure having both iron atoms on the same side of the C_8 ring. These data are consistent with a bis (π-allyl–$Fe(CO)_3$) formulation (III) analogous to other triene–$Fe_2(CO)_6$ complexes recently reported.[4]

$$III \quad\rightleftarrows\quad IV$$

Complex IV, on the other hand, shows only two proton resonances at τ 5.0 and 6.0 in the n.m.r. spectrum (Figure 1b); the spectrum is similar to that of the complex II (two regions of absorption at τ 4.2 and 6.7). The infrared spectrum of IV indicates the absence of a noncomplexed *cis* double bond while the Mössbauer spectrum again shows the two iron atoms to be chemically equivalent. We propose that IV has the structure shown; each iron atom is considered bonded to the ring by means of a diene–iron tricarbonyl structural unit as in complex II but with both iron atoms being on the same side of the ring.

The n.m.r. spectrum of solutions of III slowly changes upon standing; the original four peaks decrease uni-

Figure 1. N.m.r. spectra of (a) complex III (upper curve); (b) complex IV (middle curve); (c) complex V (lower curve).

formly in intensity and two new peaks corresponding to complex IV begin to appear. Likewise, the spectrum seen when pure IV is dissolved also changes with time; the two original peaks decrease in intensity, and the four peaks corresponding to complex III appear.

These data indicate that III and IV are in equilibrium[8] in solution and from the n.m.r. spectra it appears that the equilibrium constant is approximately unity.

The n.m.r. spectra of III and IV undergo a further change upon more prolonged standing; the six regions of absorption slowly disappear and finally become replaced by one sharp singlet at τ 5.33 (Figure 1c). Shiny black crystals are deposited from solution at this time. The black crystalline material, which is very rapidly formed when III or IV are heated for a few seconds in CCl_4 or benzene, is responsible for the single peak in the n.m.r. spectrum. The black material analyses to be a $C_8H_8Fe_2(CO)_5$ complex[9] and displays the same sharp proton signal at τ 5.33 just mentioned. The infrared spectrum suggests the presence of a bridging carbonyl group in the complex (band at 1803 cm.$^{-1}$) as well as the absence of free *cis*-olefinic groups (no absorption in the region 680–780 cm.$^{-1}$); the Mössbauer spectrum indicates a structure with two equivalent iron atoms.

We propose then that this complex has the structure Va and, in order to account for the single peak in the n.m.r. spectrum, it is suggested that rapid valence tautomerism to the equivalent structure Vb is occurring

(6) Rapid valence tautomerism has also been proposed to occur in such σ-bonded cyclopentadienyl complexes as σ,σ-dicyclopentadienyl-mercury and σ,π-dicyclopentadienyl–iron dicarbonyl (G. Wilkinson and T. S. Piper, *J. Inorg. Nucl. Chem.*, **2**, 32 (1956); **3**, 104 (1956)).

(7) The Mössbauer spectra were kindly provided by Professor R. Collins.

(8) The equilibration appears complete after 3 hr. at 35° starting with either of the pure isomers.

(9) The properties of this material bear a strong resemblance to those reported for a "$C_8H_8Fe_2(CO)_7$" complex isolated from the reaction of cyclooctatetraene with $Fe(CO)_5$ (see ref. 2a).

in solution. Thus, a rapid rotation of the Fe–Fe bond about 45° would render all protons equivalent.

Va → Vb etc.

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The Stable Conformation of 1,1,4,4-Tetrafluorobutadiene

Sir:

The n.m.r. spectra of I,[1] II,[2] and *cis-* and *trans*-III[2] reveal that the long-range fluorine–fluorine spin–spin

I   II

III

coupling constant $J_{FF'}$ has a large value (20–30 c.p.s.) when the fluorine atoms are spatially close to each other. The large magnitude of $J_{FF'}$ in these cases has been attributed to a "through space" spin–spin interaction.[2,3]

Servis and Roberts[4] have studied the n.m.r. fluorine spectrum of $F_2C=CH—CH=CF_2$ in the liquid phase. $J_{FF'}$ is 36.6 c.p.s. in this case also. Based on the large value of $J_{FF'}$ and on the assumption of a "through space" contribution to the spin–spin coupling it would seem that $CF_2=CH—CH=CF_2$ exists in a cisoid form.

In theory at least this molecule can have two geometric configurations, *cis* and *trans* (see Figure 1).

cis, μ = 2.0 D.   *trans*, μ = 0.0 D.

Figure 1. Geometrical isomers of 1,1,4,4-tetrafluorobutadiene.

Because of the partial conjugation of the single C–C bond, rotation about this bond will be hindered (probably about 10 kcal./mole). Lide has studied the rotational spectrum of isoprene[5] and of fluoroprene.[6]

(1) H. S. Gutowsky and V. D. Mochel, *J. Chem. Phys.*, **39**, 1195 (1963).
(2) S. Ng and C. H. Sederholm, *ibid.*, **40**, 2090 (1964).
(3) L. Petrakis and C. H. Sederholm, *ibid.*, **35**, 1243 (1961).
(4) K. Servis and J. D. Roberts, *J. Am. Chem. Soc.*, **87**, 1339 (1965). The author is greatly indebted to Servis and Roberts for furnishing their n.m.r. results prior to publication.
(5) D. R. Lide, Jr., and M. Jen, *J. Chem. Phys.*, **40**, 252 (1964).
(6) D. R. Lide, Jr., *ibid.*, **37**, 2074 (1962).

In both cases Lide has been able to detect only the spectrum of the *trans* isomer and has estimated that the increase in free energy going from *trans* to *cis* must be at least 1 kcal./mole. He also was unable to find the microwave spectrum of butadiene and 2,3-dimethylbutadiene. The dipole moment of the *cis* form would be small ($\sim$0.4 D.), so that the intensity of absorption lines is low. In fact, there is no conclusive spectroscopic evidence for the existence of a *cis* isomer of any butadiene.

The stable geometric forms can best be determined by searching for the microwave spectrum. Because the intensities of pure rotational transitions are proportional to the square of the dipole moment, μ, and because the dipole moment of the *trans* species is zero by symmetry, a microwave spectrum is allowed only for the *cis* isomer. Here the latter would have a large dipole moment ($\sim$2 D.) and a dense and intense b-type spectrum. Hence a qualitative examination for the presence of a pure rotational spectrum will in itself confirm the presence or absence of large concentrations of the *cis* form. These results will be more sensitive than Lide's negative results with fluoroprene where the spectrum could be obscured by the spectra of the *trans* form, or with isoprene where the estimated dipole moment of the *cis* form, if present, is very small ($\sim$0.4 D.).

A 99% pure sample of $CF_2=CHCH=CH_2$ was generously offered by Servis and Roberts. The microwave region from 18 to 22 kMc. and from 24.5 to 25.0 kMc was thoroughly searched. The sample pressure was about 30 μ, and the Stark voltage was kept between 500 and 1000 v. No pure rotational spectrum was found for this molecule; hence the molecule must exist primarily in the *trans* form. From intensity considerations, a concentration of 3% *cis* in the sample should easily have been detected. An equilibrium concentration of 3% corresponds to ΔF (*cis-trans*) $\simeq$ 2.5 kcal.

Since in the *trans* isomer only the fluorine atoms on the same carbon are close to each other, at least in 1,1,4,4-tetrafluorobutadiene a "through space" interaction cannot account for the large long-range spin–spin coupling constant. These results render the "through space" explanation for large $J_{FF'}$ long-range coupling constants in other molecules doubtful. If the n.m.r. determination of the geometric forms of any other molecule is based on the magnitude of the long-range coupling constants, these results should best be confirmed by other means.

(7) Consultant at the Jet Propulsion Laboratory.

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