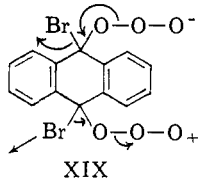
demonstrated a solvent effect in 9,10-dibromoanthracene, and possibly in anthracene itself. They have suggested initial electrophilic ozone attack to XII, followed by nucleophilic attack, intramolecularly to XIII. Alternatively, they too have conceived of nucleophilic attack by a second ozone molecule to give adducts such as XIX which would go to quinonoid products *via* the indicated electron distribution and loss of bromine, without oxidative workup. It is significant to note that in the four



XIX

instances[37,41] in which type ii attack is presumed to occur, considerably less than 50% ozone could be accounted for on one molar equivalent ozone absorption. In the case of 9,10-dibromoanthracene, a 79–80% yield of anthraquinone was obtained on absorption of *two* molar equivalents of ozone. These facts are nicely accommodated by the formation of such intermediates as XVII and XIX *via* pathways a or b, or the oxidation of XVI by a second molecule of ozone.

Finally, the ozonolysis of II/III and IV must involve cleavage of partially localized double bonds which no longer fully participate in the aromatic system by virtue of quinone formation. These localized double bonds would be expected to be more susceptible to ozonolysis than the completely aromatic I.

Carcinogenicity and the Ozone Reaction.—Recently we noted a decrease in reactivity at the L-region toward ozone as an electrophilic reagent in the series anthracene > benz[a]anthracene > dibenz[a,h]-anthracene which was approximately paralleled by a corresponding increase in reactivity at the K-region toward ozone as a double bond reagent.[4d] This order which corresponded to a progressive increase in carcinogenic activity suggested that the strongly carcinogenic I, devoid of an L-region and with a very active K-region, should react strongly with ozone at the K-region. No such strong reaction was observed. Thus there seems to be no simple correlation between carcinogenicity and K- and L-region additivity toward ozone. It may be significant, however, that ozone does attack both carcinogens dibenz[a,h]anthracene (++)[57] and I[58] at those positions which are metabolically oxidized on elimination from test animals.

(57) P. M. Bhargava and C. Heidelberger, *J. Am. Chem. Soc.*, **78**, 3671 (1956).

(58) A. H. Conney, E. C. Miller and J. A. Miller, *J. Biol. Chem.*, **228**, 753 (1957).

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY OF THE UNIVERSITY OF WISCONSIN, MADISON, WISC., AND OF STANFORD UNIVERSITY, STANFORD, CALIF.]

The Proton Magnetic Resonance Spectra of Some α-Acetoxy Ketones

BY KENNETH L. WILLIAMSON AND WILLIAM S. JOHNSON

RECEIVED JUNE 19, 1961

An examination of the n.m.r. spectra of six isomeric α-acetoxy ketones (2α-, 2β-, 4α- and 4β-acetoxycholestane-3-one and 3α- and 3β-acetoxycholestane-2-one) has revealed coupling constants for adjacent *cis* and *trans* protons (on tetrahedral carbons) larger than most of those previously reported, presumably because of the conformational rigidity of the A-ring. The use of larger parameters in the Karplus equation relating the dihedral angle between adjacent protons to the coupling constant has allowed the calculation of mutually consistent dihedral angles for these compounds from which it appears that 2β-acetoxycholestane-3-one exists in the twist conformation, a conclusion confirmed by optical rotatory dispersion measurements. In addition it has been found that the chemical shifts of equatorial protons are not always found downfield from their axial counterparts.

In order to apply nuclear magnetic resonance spectroscopy to the solution of stereochemical problems, two phenomena must be considered: namely, the field independent coupling constants and the field dependent chemical shifts of individual protons. From studies made on fourteen acetylated sugars and on two isomeric dimethoxycyclohexyl acetates, Lemieux, Kullnig and Moir[1] found that $J_{ae} = J_{ee} = 2$ to 3.5 c.p.s. and $J_{aa} = 5$ to 9 c.p.s. Karplus[2] has calculated the variation of the coupling constant of protons on adjacent carbon atoms as a function of the dihedral angle, ϕ, between these protons, and has obtained a reasonable correlation with the data of Lemieux, *et al.* The dihedral angles of the adjacent protons in these acetylated sugars were calculated on the assumption that the ring adopted a single chair conformation, a premise which may be open to question (see below). In all of these compounds the chemical shifts for equatorial protons were found at lower fields than were the shifts for axial protons.[3]

With this work in mind we examined the proton magnetic resonance spectra of six isomeric α-acetoxy ketones (2α-, 2β-, 4α- and 4β-acetoxycholestane-3-one and 3α- and 3β-acetoxycholestane-2-one) to gain some insight into the conformation of the A-ring in these compounds.

The resonance lines associated with the proton on the acetate-bearing carbon atom are displaced downfield from the other 47 protons in these keto-acetates because of the combined unshielding effects of both the adjacent carbonyl group and the acetate group. In 2α-acetoxycholestane-3-one (see Fig. 1),

(1) R. U. Lemieux, R. K. Kullnig and R. Y. Moir, *J. Am. Chem. Soc.*, **80**, 2237 (1958).

(2) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).

(3) (a) A. Novak and E. Whalley, *Can. J. Chem.*, **36**, 1116 (1958); (b) R. U. Lemieux, R. K. Kullnig, H. J. Bernstein and W. G. Schneider, *J. Am. Chem. Soc.*, **80**, 6098 (1958).

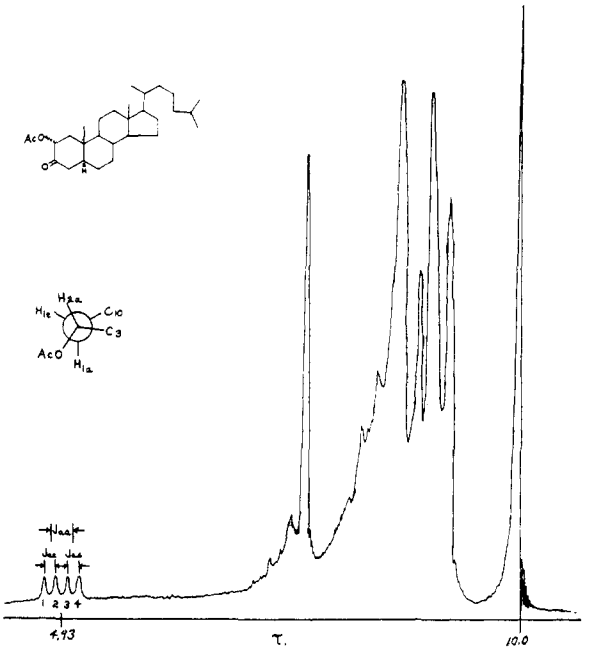


Fig. 1.

for example, the resonance of the axial proton on carbon-2 appears as a quartet due to the X proton in an ABX system.[4] Since the chemical shift (4.93 τ) is large in comparison with that of the protons on carbon-1, the spacing between lines 1 and 4 can be taken as $J_{ae} + J_{aa}$. Unless the chemical shifts of the protons on carbon-1 happen to coincide, the spacing between lines 1 and 2 or 3 and 4 can be taken as J_{ae}, and the spacing between lines 1 and 3 or 2 and 4 can be taken as J_{aa}. Since 2α-bromocholestane-3-one gives virtually the same coupling constants, it seems reasonable to conclude that the chemical shifts of the protons on carbon-1 are not identical. The X portion of the spectrum with the associated chemical shifts and coupling constants for each of the six isomers is shown in Table I.[5] It is immediately evident that the spectra of the 2-acetoxy-3-keto compounds are much simpler and thus better resolved than those of the other four isomers. The complexity of the spectra of these four compounds is probably due to additional spin–spin couplings, through the bonds, involving γ and even to some extent δ protons. This may be a transmitted coupling, *e.g.*, an ABCD· · ·X system, and/or a long-range effect of the type recently observed by Davis, Lutz and Roberts.[6] From the observed line shapes, however, it appears that the AX and ABX coupling patterns still predominate. It is evident that significant coupling does not take place across the carbonyl group because in the 2-acetoxy compounds, with simple three-proton systems, the spectra are clearly resolved.

(4) (a) G. A. Williams and H. S. Gutowsky, *J. Chem. Phys.*, **25**, 1288 (1956); (b) H. J. Bernstein, J. A. Pople and W. G. Schneider, *Can. J. Chem.*, **35**, 65 (1957); (c) H. S. Gutowsky, C. H. Holm, A. Saika and G. A. Williams, *J. Am. Chem. Soc.*, **79**, 4596 (1957).

(5) The symbols and presentation of n.m.r. spectra used herein conform to the recommendations set forth in *Proc. Chem. Soc.*, 403 (1960).

(6) D. R. Davis, R. P. Lutz and J. D. Roberts, *J. Am. Chem. Soc.*, **83**, 246 (1961).

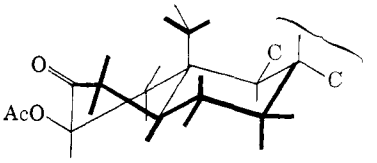


Fig. 2.

The coupling constants (J_{ae} = 6.6 c.p.s. and J_{aa} = 13.1 c.p.s.) for 2α-acetoxycholestane-3-one are much larger than the values that would be calculated from the Karplus equation[2] (J_{ae} = 1.7 c.p.s. and J_{aa} = 9.2 c.p.s.) assuming dihedral angles of 60° and 180° between the coupling protons. This discrepancy may be due to the increased rigidity of the A-ring of cholestanone which, because of the AB-*trans* ring fusion, cannot adopt any other chair form. In contrast to cholestanone, the monocyclic sugar acetates with which the Karplus equation is in better agreement do not have conformational rigidity, and consequently the coupling constants are smaller.[7] Since 2α-bromocholestane-3-one exhibits the same coupling constants as the 2α-acetoxy compound, it is unlikely that the electronic nature of the 2-substituent has any great effect on the coupling constant.[8] By making the reasonable assumptions that carbon-1 in 2α- and 2β-acetoxycholestane-3-one and carbon-4 in 3α- and 3β-acetoxycholestane-2-one have normal tetrahedral angles and that the dihedral angles separating the geminal protons on these carbons are therefore 120°, and by substituting different parameters in the Karplus equation, it is possible to arrive at a revised expression which gives mutually consistent dihedral angles for the four compounds[10]

$$J_{HH'} \begin{cases} 10\cos^2\phi & 0° \leq \phi \leq 90° \\ 16\cos^2\phi & 90° \leq \phi \leq 180° \end{cases} \quad (1)$$

From the coupling constants observed in the present work, it can be calculated that J is 16 c.p.s. when ϕ is 180° and J is 10 c.p.s. when ϕ is 0°. These values are in close agreement with the observations of Bothner-By and Naar-Colin for the coupling of *trans* and *cis* protons in olefins and with the observations of Elvidge and Jackman[11] for the

(7) J. I. Musher, *ibid.*, **83**, 1146 (1961).

(8) 2α- and 4α-acetoxycholestane-3-one form an inseparable 1:1 molecular complex (see ref. 9). It was hoped that the nuclear magnetic resonance spectrum of this complex might reveal in some way the nature of the forces responsible for complex formation. However, the observed spectrum was an exact 1:1 superposition of the separate spectra of 2α- and 4α-acetoxycholestane-3-one.

(9 (a) L. F. Fieser and M. A. Romero, *J. Am. Chem. Soc.*, **75**, 4716 (1953); (b) K. L. Williamson and W. S. Johnson, *J. Org. Chem.*, **26**, Nov. (1961).

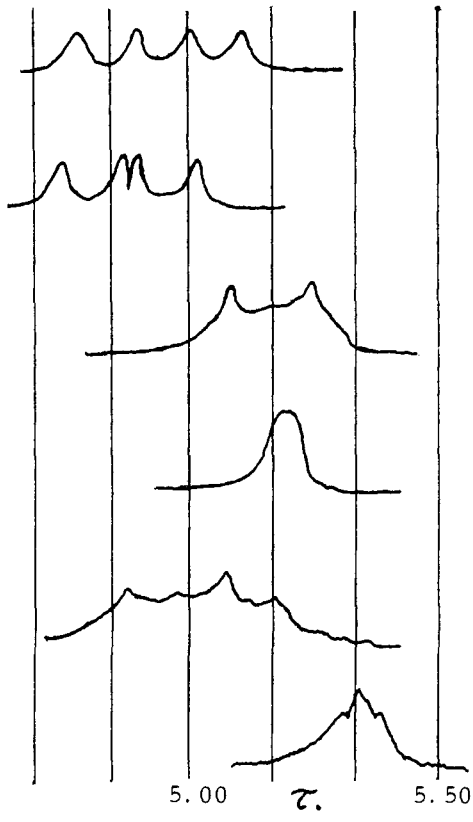
(10) In thirty monosubstituted ethyl and isopropyl derivatives, coupling constants for protons on adjacent carbon atoms of 5.98 to 7.37 c.p.s. were found (R. E. Glick and A. A. Bothner-By, *J. Chem. Phys.*, **25**, 362 (1956)). These values were later interpreted by A. A. Bothner-By and C. Naar-Colin, *J. Am. Chem. Soc.*, **83**, 231 (1961), as averages over all possible dihedral angles between coupling protons such that when ϕ = 180°, $J \simeq$ 16–18 c.p.s. and when ϕ = 0°, $J \simeq$ 8–9 c.p.s. However, rotational isomerism in these compounds makes an exact calculation of angular dependence impossible. In a series of dichlorinated and dibrominated ethanes, rotational isomerism is evidently reponsible for an even wider range of coupling constants between adjacent protons as observed by N. Sheppard and J. J. Turner, *Proc. Roy. Soc.* (*London*), **A252**, 506 (1959). The coupling constants J_{aa} = 12.35 c.p.s. and J_{ae} = 4.25 c.p.s. have been observed by J. I. Musher, *J. Chem. Phys.*, **34**, 594 (1961).

(11) J. A. Elvidge and L. M. Jackman, *Proc. Chem. Soc.*, 89 (1959).

TABLE I

N.M.R. DATA FOR SOME ACETOXYCHOLESTANONES

Compound	J_{ae}, c.p.s.	J_{aa}, c.p.s.	τ	φ°,
2α-Acetoxycholestane-3-one	6.6	13.1	4.93	34°, 154°
2β-Acetoxycholestane-3-one	7.4	9.5	4.88	133°, 13°
4α-Acetoxycholestane-3-one	11.6		5.16	148°
4β-Acetoxycholestane-3-one	4.7[a]		5.20	47°
3β-Acetoxycholestane-2-one	6.2	13.0	5.02	154°, 38°
3α-Acetoxycholestane-2-one	2.5	2.5[b]	5.33	60°, 60°



[a] From the peak width at half-height. [b] From one-half the peak width at half-height.

coupling of protons on trigonal carbon atoms joined by a single bond.

The angles corresponding to the observed coupling constants are listed in the fourth column of Table I. In the case of 3α-acetoxycholestane-2-one, the unresolved triplet of lines corresponds to the expected 60° angle between the coupling protons as illustrated in the Newman projection formula in the last column of Table I. In the case of the β-epimer a poorly resolved quartet of lines is observed with the same coupling constants as those found for the 2α-acetoxy compound. The calculated angles indicate a slight distortion from the perfect chair form of the cyclohexane ring as might be expected from the presence of the trigonal carbonyl group. Similar distortions are seen in the C_4-epimers.

The spectrum of 2β-acetoxycholestane-3-one was expected to exhibit a triplet of lines much like the 3α-acetoxy compound; however, the clearly resolved quartet of lines corresponds to angles in which the larger coupling constant corresponds to the smaller dihedral angle. Reversing the values in eq. 1 leads to an unlikely value for the angle between the geminal protons on carbon-1. Examination of Dreiding models indicates that a β-acetoxy group with the observed dihedral angles can be accommodated readily in the twist conformation[12] of the A-ring (see Fig. 2). This conformation, which is apparently favored over the chair due to a 1,3-diaxial interaction of the 2β-acetoxy group with the C_{19}-methyl group in the latter, was confirmed by optical rotatory dispersion measurements (see below).

In contrast with the case of 2β-acetoxycholestane-3-one, ring A of the isomeric 4β-acetoxy 3-ketone appears to prefer the chair to the twist conformation as shown by the normal n.m.r. and rotatory dispersion spectra. This difference may be attributable to the fact that the twist form of the latter isomer requires that the acetoxy group approach an eclipsed conformation with a methylene group (C_6), while in the former isomer the twist form finds the acetoxy group approaching an eclipsed arrangement with only a hydrogen atom (1β). This destabilization of the twist form of the 4β-isomer relative to the twist form of the 2β-isomer is evidently sufficient to overcome the unfavorable 1,3-diaxial interaction in the chair conformation of the 4β-isomer. The same argument serves to rationalize the conclusion reached by rotatory dispersion measurements that ring A of 2β-methylcholestane-3-one has departed from a chair conformation to a

(12) W. S. Johnson, V. J. Bauer, J. L. Margrave, M. A. Frisch, L. H. Dreger and W. N. Hubbard, *J. Am. Chem. Soc.*, **83**, 606 (1961).

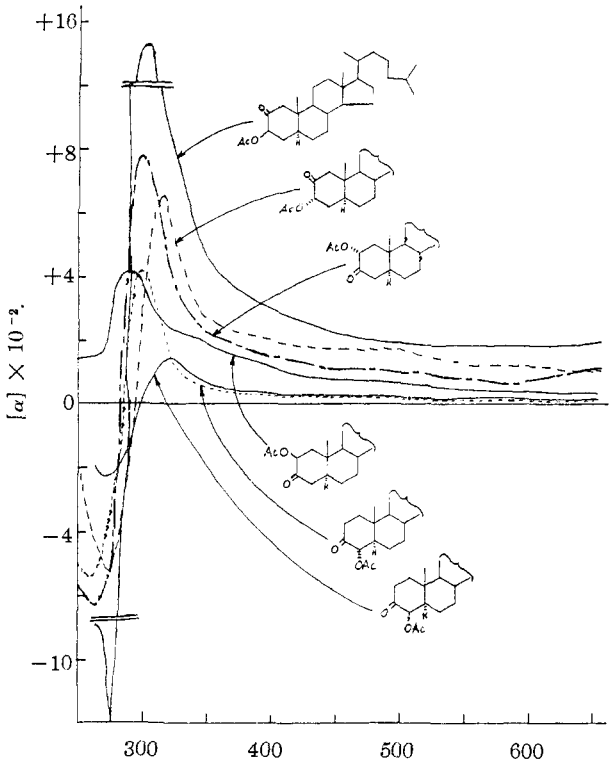


Fig. 3.

much greater extent than 4β-methylcholestane-3-one.[13]

Although mutually consistent results are obtained in the calculation of dihedral angles for these steroid acetoxy ketones by use of new values in the Karplus equation, it does not necessarily follow that this revised equation can be applied to the calculation of dihedral angles in other systems. Other factors which affect the coupling constants of adjacent protons are now under investigation It is known, for instance, that coupling constants observed in strained bicyclic systems[14] and in three- and four-membered rings[15] do not give mutually consistent values for calculated dihedral angles employing either the original Karplus equation or the revised form proposed here. We have observed, moreover, coupling constants of 4.8 and 12.5 c.p.s. in the case of 2α-bromo-3α-deutero-3β-hydroxycholestane, and constants of 4.5 and 12.5 c.p.s. in the case of 2α-bromocholestane-3-one ethylene thioketal which are in agreement with those recently reported by Musher.[10] Using the revised form of the Karplus equation, these values lead to unlikely geminal proton dihedral angles of *ca.* 106°. This equation therefore may be applicable only to six-membered rings containing a trigonal carbon atom adjacent to the bonds under consideration.

In a series of 11-keto-12-acetates of bile acids and sapogenins, a 15 mμ shift between the first extrema of the axial and equatorial epimers has been noted in the optical rotatory dispersion spectra, with the axial ketoacetate absorbing at the higher wave length.[16] In the rotatory dispersion spectra of the pair of acetoxy ketones epimeric at carbon-3 in the cholestane derivatives (see Fig. 3), the difference between the first extrema is 12 mμ and in the pair epimeric at carbon-4 the difference is 20 mμ, with that of the axial acetoxy ketone at the higher wave length in each case. The first extremum of the rotatory dispersion spectrum of 2β-acetoxycholestane-3-one, however, is not displaced to longer wave lengths relative to that of the 2α-epimer, but is shifted 15 mμ to *shorter* wave lengths with greatly decreased intensity. Such behavior is indicative of a major distortion of the A-ring in the β-acetate and is confirmatory evidence for the twist conformation calculated from the n.m.r. spectrum.

Chemical Shifts.—It has frequently been noted[1,3,17] that the n.m.r. absorption of equatorial protons on six-membered ring compounds exhibit chemical shifts that appear at lower fields than their axial counterparts. Inspection of Table I reveals that this rule is violated by two of the three pairs of acetoxy ketones under discussion here; the anomalous conformation of the 2β-acetate probably invalidates any conclusion regarding chemical shifts in the epimeric 2-acetoxy 3-ketones. Furthermore, no significant (>1 c.p.s.) difference was noted for the chemical shifts between the methyl protons in equatorial and axial acetates[18] in contrast to the behavior noted in the sugar acetates[1] and inositols.[3b] These discrepancies may be due to the increased rigidity of the steroid ring system which results in more severe non-bonded interactions[19] and/or the magnetic anisotropy effects introduced by the carbonyl group.

The spectra of the four acetoxy ketones having the carbonyl group at C_3 show chemical shifts for the C_{19}-methyl group of 9.11 τ in accord with the findings of Shoolery and Rogers[18] for other 3-keto steroids. It is interesting to note that the position of the resonance frequency of the C_{19}-methyl group is unaltered by the presence of the (axial) 4β-acetoxy group. This observation is in contrast with the down-field displacement of this absorption brought about by a 6β-methyl group.[19] The absorption at 9.32 τ for the C_{19}-methyl group in the spectra of the 3α- and 3β-acetoxy-2-ketones is the same as that found in 6-keto steroids.[20,21]

Acknowledgment.—We wish to express our thanks to Professor Carl Djerassi for the optical rotatory dispersion measurements. We also thank

(13) C. Djerassi, *et al.*, to be published.

(14) J. Meinwald and A. Lewis, *J. Am. Chem. Soc.*, **83**, 2769 (1961).

(15) F. S. Mortimer, *J. Mol. Spec.*, **5**, 199 (1960).

(16) C. Djerassi, O. Halpern, V. Halpern, O. Schindler and C. Tamm, *Helv. Chim. Acta*, **41**, 250 (1958).

(17) L. L. Smith, M. Marx, J. J. Garbarini, T. Foell, V. E. Origoni and J. J. Goodman, *J. Am. Chem. Soc.*, **82**, 4616 (1960); see footnote 41.

(18) J. N. Shoolery and M. T. Rogers, *J. Am. Chem. Soc.*, **80**, 5121 (1958), report that 2β-acetoxycholestane showed no shift of the acetoxy methyl resonance relative to eight equatorial acetates (3β- and 11α).

(19) G. Slomp, Jr., and B. R. McGarvey, *J. Am. Chem. Soc.*, **81**, 2200 (1959).

(20) L. F. Fieser, T. Coto and B. K. Bhattacharyya, *ibid.*, **82**, 1700 (1960).

(21) The magnitude and sign of the shielding of protons near a carbonyl group are a function of the orientation of the carbonyl group with respect to the shielded proton. For a lucid discussion, see L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959, p. 122.

the National Science Foundation, the U. S. Public Health Service, and the Allied Chemical Corp. for providing support for this study.

Experimental

Materials.—The preparation of the six acetoxy ketones has been previously described.[9b] The spectra were run on 20% solutions of the compounds in carbon disulfide containing 1% tetramethylsilane.

N.m.r. Spectra.—The Varian Associates V-4311 high-resolution NMR spectrometer with 12″ electromagnet system, operating at 60 mc., V-K3506 super stabilizer, and V-4365 field homogeneity control was employed. The positions of peaks were calibrated by the audiofrequency side band method[22] using a Hewlett–Packard 200-CD audio oscillator as well as graphical interpolation. The frequencies of the side bands were measured with a Hewlett–Packard 524-B electronic counter. Reported line positions are averages of six to ten spectra; the standard deviation was ±0.3 c.p.s.

Optical rotatory dispersion (Fig. 2) in methanol: **2α-acetoxycholestane-3-one.** (*c* 0.035): $[\alpha]_{650}$ +97°, $[\alpha]_{589}$ +63°, $[\alpha]_{305}$ +777°, $[\alpha]_{265}$ −628°; **2β-acetoxycholestane-3-one** (*c* 0.103): $[\alpha]_{650}$ +34°, $[\alpha]_{589}$ +43°, $[\alpha]_{290}$ +410°, $[\alpha]_{250}$ +140°; **4α-acetoxycholestane-3-one** (*c* 0.045): $[\alpha]_{650}$ −9°, $[\alpha]_{589}$ +18°, $[\alpha]_{300}$ +417°, $[\alpha]_{260}$ −543°; **4β-acetoxycholestane-3-one** (*c* 0.100): $[\alpha]_{650}$ +18°, $[\alpha]_{589}$ +18°, $[\alpha]_{320}$ + 164°, $[\alpha]_{270}$ − 218°; **3β-acetoxycholestane-2-one** (*c* 0.1775): $[\alpha]_{650}$ +158°, $[\alpha]_{589}$ +214°, $[\alpha]_{305}$ +1520°, $[\alpha]_{286}$ 0°, $[\alpha]_{270}$ −1200°, $[\alpha]_{265}$ −950°; **3α-acetoxycholestane-2-one** (*c* 0.105): $[\alpha]_{650}$ +95°, $[\alpha]_{589}$ +114°, $[\alpha]_{317}$ +647°, $[\alpha]_{296}$ 0°, $[\alpha]_{275}$ −525°, $[\alpha]_{260}$ −220°.

(22) J. T. Arnold and M. E. Packard, *J. Chem. Phys.*, **19**, 1608 (1951).

[CONTRIBUTION FROM THE BIOLOGICAL AND CHEMICAL RESEARCH DIVISIONS OF G. D. SEARLE AND CO., CHICAGO, ILL.]

Microbiological Transformations. VI. The Microbiological Aromatization of Steroids

BY R. M. DODSON[1] AND R. D. MUIR

RECEIVED JULY 5, 1961

4-Androstene-3,17-dione (I) was converted to 3-hydroxy-9,10-seco-1,3,5(10)-androstatriene-9,17-dione (III) by incubation with species of *Pseudomonas* and *Arthrobacter*. The structure of the 9,10-seco-phenol (III) was established by converting it, through a rational series of reactions, to 1-methoxy-4-methyl-1,3,5(10)-estratrien-17β-ol (X), which, in turn, had been prepared *via* the dienone–phenol rearrangement of 1,4-androstadiene-3,17-dione (II). This microbial aromatization of androstenedione (I) resembles, in many respects, the sequences postulated for the conversion of androgenic steroids to estrogens in mammals.

We have recently reported the microbiological conversion of 4-androstene-3,17-dione (I)[2] and of 9α-hydroxy-4-androstene-3,17-dione[2] to 3-hydroxy - 9,10 - seco - 1,3,5(10) - androstatriene - 9,17-dione (III) by fermentation of these compounds with species of *Pseudomonas*, Searle B20-184, and *Arthrobacter*, Searle B22–9, respectively. More recently, we have discovered that species of *Nocardia* and *Arthrobacter*, as well as other *Pseudomonas sp.* [Searle B40–324 (A.T.C.C. 13261) and Searle B40–327 (A.T.C.C. 13262)] also convert Δ^4-3-keto-steroids to the corresponding 9,10-seco-A-aromatic analogs. Because of the uniqueness of this conversion and the possibility that it closely parallels formation of estrogens from androgenic steroids in mammals,[3] we wish to describe in detail the preparation and proof of structure of 3-hydroxy-9,10-seco-1,3,5(10)-androstatriene-9,17-dione (III).[4]

Incubation of 4-androstene-3,17-dione with a species of *Pseudomonas*, B20–184, produced, besides very small quantities of 11α-hydroxy-4-androstene-3,17 - dione[5] and 7β - hydroxy - 4 - androstene-3,17-dione,[6] two different phenolic compounds. The first of these, III, m.p. 123.5–125°, was recognized as a phenol initially by its unique ultraviolet spectrum, $\lambda_{max}^{CH_3OH}$ 280 mμ (ε 2,320). It gave a positive Folin–Denis test,[7] was soluble in dilute alkali, was stable in dilute alkaline solution (under nitrogen) over long periods of time, and could be reprecipitated with carbon dioxide or acetic acid. The infrared spectrum of the compound showed the presence of a hydroxyl group (2.90 μ), a five-membered ring carbonyl group (5.76 μ), a six-membered ring carbonyl group (5.89 μ), and an aromatic ring, probably possessing an isolated hydrogen and two adjacent hydrogen atoms (6.22, 6.63, 11.45 and 12.21 μ).[8] Initial carbon and hydrogen analyses were close to both $C_{18}H_{22}O_3$ and $C_{19}H_{24}O_3$.

All possible structures with an intact steroid nucleus were quickly eliminated by the following reasoning: (1) It was assumed that two of the three oxygen atoms occupied positions corresponding to the positions of the two oxygen atoms in androstenedione. (2) It was assumed that no complex rearrangement had occurred and that the aromatic ring was formed by the breaking of the minimum number (one) of carbon–carbon bonds necessary to such formation. (3) The ultraviolet spectrum of III indicated the absence of a carbonyl group adjacent to the aromatic ring. (4) The ultraviolet spectrum of the dienediol triacetate VI indicated the absence of a carbonyl group beta to

(1) Department of Chemistry, University of Minnesota, Minneapolis 14, Minn.

(2) Preliminary communications of these results appeared in *J. Am. Chem. Soc.*, **80**, 5004, 6148 (1958); previous paper in this series: R. M. Dodson, A. H. Goldkamp and R. D. Muir, *ibid.*, **82**, 4026 (1960).

(3) (a) L. L. Engel, *Cancer*, **10**, 711 (1957); (b) A. S. Meyer, *Biochim. et Biophys. Acta*, **17**, 441 (1955); (c) K. T. Ryan, *J. Biol. Chem.*, **234**, 268 (1959); (d) J. E. Longchampt, C. Gual, M. Ehrenstein and R. I. Dorfman, *Endocrinol.*, **66**, 416 (1960).

(4) The preparation of the corresponding 9,10-seco-A-aromatic steroids from progesterone, 19-nor-4-androstene-3,17-dione and 3-(3-keto-17β-hydroxy-4-androsten-17α-yl)-propionic acid lactone will be reported later.

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