The couple is polarographically reversible in hydrochloric acid giving an oxidation potential (thermodynamic convention) for the reaction $Np(III) \rightleftarrows Np(IV) + e^-$ of -0.142 ± 0.005 volt. The hydrogen ion independence of the couple between 0.1 and 1.0 molar hydrochloric acid is interpreted as supporting the conclusion that the neptunium(III) and neptunium(IV) ions are Np^{+3} (hydrated) and Np^{+4}(hydrated) in non-complexing acid media.

The neptunium(III)–neptunium(IV) couple is polarographically irreversible in perchloric acid. The difference in polarographic behavior of the tri-positive and tetra-positive ions of neptunium and uranium in perchlorate media is discussed.

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CONTRIBUTION FROM THE SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH AND THE DIVISION OF CHEMISTRY OF THE NATIONAL RESEARCH COUNCIL OF CANADA[1]

Studies in Steroid Metabolism. IX. Further Observations on the Infrared Absorption Spectra of Ketosteroids and Steroid Esters

BY R. NORMAN JONES, P. HUMPHRIES AND KONRAD DOBRINER

It has been reported in previous publications[2,3] that the frequency of the carbonyl stretching vibration in the infrared spectra of steroids is characteristic of the type of carbonyl group present and of its location in the molecule. These observations have been applied to the elucidation of the structure of steroids isolated from urine.[4,5] During the past year the spectra of an additional one hundred and eighty steroids have been examined. The results of these measurements, which are reported in this paper, confirm and extend the correlations between spectra and structure previously established.

In Table I are listed the frequencies of the carbonyl stretching maxima of additional compounds of types discussed previously.[2,3] These data are in good agreement with those reported earlier and call for no detailed comment.

TABLE I

CARBON–OXYGEN DOUBLE BOND STRETCHING VIBRATIONS IN STEROIDS, NEW DATA SUPPORTING PREVIOUSLY ASSIGNED FREQUENCIES

(All measurements in solution in carbon disulfide[a]).

In the compounds described here, the configuration of the 17-hydroxyl group is designated β if it is the same as that in testosterone. This is the *inverse* of the convention employed in the previous publications in this series (references 2, 3, 5, 10). The sources of the individual compounds are indicated by superscripts to footnotes at the end of the table. In some cases derivatives (acetates, methyl esters, or epoxides) were prepared at the Sloan-Kettering Institute; this is indicated by an asterisk following the reference to the donor of the original compound.

Non-Carbonyl Compounds.—The following showed no absorption bands between 1650 and 1800 cm.$^{-1}$: estranol-17β,[12] estranediol-3,17β,[12] $\Delta^{5,7,9}$-estratrienol-17β,[12] $\Delta^{1,3,5:10}$-1-methylestratrienediol-3,17β,[3] $\Delta^{1,3,5:10}$-1-methyl-17-(1-methylheptyl)-estratrienol-3,[3] Δ^5-androstenol-3β,[23] Δ^{16}-androstenol-3α,[19] Δ^{16}-etiocholenol-3α,[19] Δ^{16}-etiocholenol-3β,[19] uranediol-3β,11,[12,17] Δ^5-cholestene,[7] $\Delta^{2,4}$-cholestadiene,[5] ergostane,[7] $\Delta^{8:14}$-ergostene,[7] Δ^{22}-ergostene,[1] lumisterol,[7] vitamin D_2,[11] Δ^7-5-isoergostenol-3α,[1] Δ^{22}-5-isoergostene,[1] $\Delta^{7,22}$-5-isoergostadiene.[1]

Monocarbonyl Compounds

I. 3-Ketones. (1716–1719 cm.$^{-1}$).—Allopregnanone-3,[21] allopregnanediol-17α,20-one-3,[21] uranol-11-one-3,[12] tigogenone,[18] $\Delta^{8:14}$-ergostenone-3,[1] Δ^{22}-ergostenone-3.[1]

II. 7-Ketones (1710–1713 cm.$^{-1}$).—Pregnanone-7,[21] cholestanone-7.[7]

III. 17-Ketones (1742–1745 cm.$^{-1}$).—3-Methoxy-(*dl*)-isoequilenin,[10] equilenone-17,[10] isoequilenone-17,[10,26] $\Delta^{1,3,5:10}$-3-methoxyestratrienone-17,[3] $\Delta^{1,3,5:10}$-1-methylestratrienol-3-one-17,[3] $\Delta^{1,3,5:10}$-3-methoxy 1-methylestratrienone-17,[3] 9,11-epoxyetiocholanol-3α-one-17.[22*]

IV. 20-Ketones (1706–1710 cm.$^{-1}$).—$\Delta^{1,3,5:10}$-3-Methoxy-17-acetyl-estratriene,[3] pregnanol-3β-one-20,[12] $\Delta^{(2 \text{ or } 3),11}$-pregnadienone-20,[21] allopregnanone-20.[21]

V. 3-Acyl Esters (1735–1739 cm.$^{-1}$).—$\Delta^{1,3,5:10}$-17-Ethynylestratrienediol-3,17-acetate-3,[9] androstanol-3α-acetate,[23*] androstanol-3β-acetate,[23*] Δ^5-androstenol-3β-acetate,[23*] Δ^5-17-ethynylandrostenediol-3β,17-acetate-3,[9] Δ^{16}-androstenol-3α-acetate,[19*] Δ^{16}-etiocholenol-3α-acetate,[19*] Δ^{16}-etiocholenol-3β-acetate,[19*] pregnanol-3β-acetate,[12*] Δ^{23}-3α-acetoxy-24,24′-diphenylcholene,[5] ergostanol-3β acetate,[7] lumistanol-3β-acetate,[7] lumisteryl acetate.[7]

VI. 17-Acyl Esters (1737–1742 cm.$^{-1}$).—$\Delta^{1,3,5:10}$-1-Methylestratrienediol-3,17β-acetate-17,[3] androstanol-17β-acetate,[17*,23*] $\Delta^{3,5}$-androstadienol-17β-acetate,[27] etiocholanediol-3α,17α-acetate-17.[5,14]

VII. Alkyl Esters of Steroid Carboxylic Acids (1737–1742 cm.$^{-1}$).—$\Delta^{1,3,5:10}$-3-Methoxy-17-carbomethoxy-estratriene,[3] etioallocholanic acid M.E.,[15] 3α-hydroxyetiocholanic acid M.E.,[13*] 3β-hydroxyetioallocholanic acid M.E.,[15] Δ^5-3β-hydroxyetiocholenic acid M.E.,[2,15] Δ^{11}-3α-hydroxyetiocholenic acid M.E.,[13*] 3α-hydroxybisnorcholanic acid M.E.,[13] Δ^{11}-3α-hydroxybisnorcholenic acid M.E.,[13] Δ^{11}-3α-hydroxynorcholenic acid M.E.,[13,24] cholanic acid M.E.,[24] 3α,12α-dihydroxycholanic acid E.E.,[24] Δ^5-3β-hydroxycholenic acid M.E.,[5] Δ^{11}-3α,9α-epoxycholenic acid M.E.,[13,24]

VIII. 3-Aryl Esters (1719–1724 cm.$^{-1}$).—Δ^5-Cholestenol-3β-benzoate,[4] Δ^5-cholestenediol-3β,4β-benzoate-3,[4,16] 5α,6α-dichlorocholestanol-3β-benzoate,[1] 5α,6β-dichlorocholestanol-3β-benzoate.[1]

IX. $\Delta^{3,5}$-Diene-ol-3 Acyl Ester (1754–1758 cm.$^{-1}$).—$\Delta^{3,5}$-Cholestadienol-3β-acetate.[24]

Dicarbonyl Compounds

X. Δ^4-3,11-Diketones (1674–1677:1710 cm.$^{-1}$).—Δ^4-Urenedione-3,11.[12]

XI. 3,17-Diketones (1719:1742–1745 cm.$^{-1}$).—Estranedione-3,17.[12]

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(1) Published as Contribution No. 2066 from The Laboratories of The National Research Council of Canada.

(2) Jones, Williams, Whalen and Dobriner, THIS JOURNAL, **70**, 2024 (1948).

(3) Jones, Humphries and Dobriner, *ibid.*, **71**, 241 (1949).

(4) Dobriner, *Acta de L'Union Internationale Contre le Cancer*, **6**, 315 (1948).

(5) Jones and Dobriner, *Vitamins and Hormones*, **7**, 294 (1949).

TABLE I (*Continued*)

XII. Δ^4-3,17-Diketones (1674–1677:1742–1745 cm.$^{-1}$).—Δ^4-Estrenedione-3,17.[12]

XIII. 3,20-Diketones (1706–1710:1716–1719 cm.$^{-1}$).—Δ^{11}-Pregnenedione-3,20.[21]

XIV. Diacyl Esters (1735–1742 cm.$^{-1}$).—Androstanediol-3β,17α-diacetate,[23*] Δ^5-androstenediol-3β,17α-diacetate,[23*] etiocholanediol-3α,17β-diacetate,[14*] etiocholanetriol-3α,11,17-diacetate-3,17,[22] allopregnanediol-3β,20α-diacetate,[12*,17*] allopregnanediol-3β,20β-diacetate,[16] Δ^5-pregnenediol-3,20-diacetate,[12*] Δ^{16}-allopregnenediol-3β,20β-diacetate,[17*] Δ^5,3β-acetoxyetiocholenic acid M.E.,[15] 3α-hydroxy-12α-acetoxyetiocholanic acid M.E.,[21] 3α,12α-dihydroxy-7α-acetoxyetiocholanic acid M.E.,[15] 3α-acetoxy-11α,12α-epoxycholanic acid M.E.,[5,24] Δ^5-3β-acetoxycholenic acid M.E.,[5] $\Delta^{9:11}$-3α-acetoxycholenic acid M.E.,[23,24] Δ^{11}-3α-acetoxycholenic acid M.E.,[5,24] Δ^{11}-3β-acetoxycholenic acid M.E.[24]

XV. Phenolic Diacetates (1739–1742:1764–1767 cm.$^{-1}$).—$\Delta^{1,3,5:10}$-1-Methylestratrienediol-3,17-diacetate,[3] $\Delta^{1,3,5:10}$-1-methyl-17-carbomethoxyestratrienol-3-acetate.[3]

XVI. 3-Ketoesters (1719:1739–1742 cm.$^{-1}$).—$\Delta^{3,11}$-3-Ketocholadienic acid M.E.,[24] Δ^{11}-3-ketocholenic acid M.E.[24]

XVII. 12-Ketoesters (1706–1710:1739–1742 cm.$^{-1}$).—$\Delta^{(3 \text{ or } 4)}$-12-Ketocholenic acid M.E.[24]

XVIII. $\Delta^{9:11}$-12-Ketoesters (1680–1684:1739–1742 cm.$^{-1}$).—$\Delta^{9:11}$-3α-Hydroxy-12-ketocholenic acid M.E.[13]

XIX. 17-Ketoesters (1737–1745 cm.$^{-1}$).—5α,6α-Epoxyandrostanol-3β-one-17-acetate,[5,16] 5β,6β-epoxyandrostanol-3β-one-17-acetate,[5,16] etiocholanediol-3α,11β-one-17-acetate-3,[22*] i-androstanol-6-one-17-acetate.[1a]

XX. 20-Ketoesters (1706–1710: 1737–1742 cm.$^{-1}$).—Allopregnanol-3α-one-20-acetate,[5] pregnanediol-3α,11β-one-20 acetate-3.[21*]

XXI. 21-Acetoxy-20-ketones (1729–1732:1754–1758 cm.$^{-1}$).—$\Delta^{1,3,5:10}$-3-Methoxy-17-(2-acetoxyacetyl)-estratriene,[3] $\Delta^{1,3,5:10}$-1-methyl-3-methoxy-17-(2-acetoxyacetyl)-estratriene,[3] allopregnanediol-3β, 21-one-20-acetate-21,[21] pregnanediol-3α,21-one-20-acetate-21,[21] pregnanediol-3β,21-one-20-acetate-21.[21]

Polycarbonyl Compounds

XXII. Polyketones[b].—$\Delta^{9:11}$-Allopregnenetrione-3,12,-20 (1726, 1710, 1680),[21] uranetrione-3,11,20 (1713).[12]

XXIII. Polyesters (1737–1742 cm.$^{-1}$).—Androstanetriol-2,3,17-triacetate,[12*] Δ^4-androstenetriol-3β,4,17β-triacetate,[12*] allopregnanetriol-3α,16,20-triacetate,[6*,12*] pregnanetriol-3α,16,20-triacetate,[17*] Δ^5-pregnenetriol-3β,20,21-triacetate,[17*] 3α-succinoxy-7α-acetoxy-12α-hydroxyetiocholanic acid M.E.,[15] 3α-hydroxy-7α,12α-diacetoxyetiocholanic acid M.E.,[15] 3α,7α,12α-triacetoxyetiocholanic acid M.E.[15]

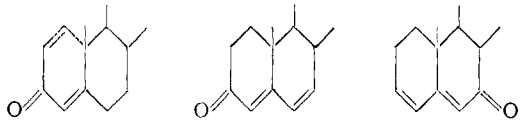
XXIV. Polyketoesters.[b]—$\Delta^{5,16}$-Pregnadienediol-2,3β-one-20-diacetate (1670, 1746),[17] 3-keto-12-acetoxycholanic acid M.E. (1719, 1742),[3] 3-keto-7α,12α-diacetoxyetiocholanic acid M.E. (1719, 1742),[15] 7-keto-3α-succinoxy-12α-hydroxyetiocholanic acid M.E. (1719, 1742),[15] 7-keto-3α,6α,12α-triacetoxycholanic acid M.E. (1743),[5] 12-keto-3α-succinoxy-7α-acetoxyetiocholanic acid M.E. (1723, 1742),[15] 3,6-diketoallocholanic acid M.E. (1718, 1742),[5] 3,12-diketo-7α-acetoxyetiocholanic acid M.E. (1723, 1742),[15] 11,12-diketonorcholanic acid M.E. (1726, 1743).[15]

[a] M.E. and E.E. designated methyl ester and ethyl ester, respectively. [b] The positions of the absorption maxima (cm.$^{-1}$) of the individual compounds are indicated after the name.

(1) D. H. R. Barton, Imperial College, London, England. (1a) D. H. R. Barton, Imperial College, London, England and W. Klyne, Postgraduate Medical School, London, England.
(2) B. J. Brent, Organon Inc., Orange, N. J.
(3) C. Djerassi and C. R. Scholz, Ciba Pharmaceutical Products, Inc., Summit, N. J.
(4) D. Fukushima, Sloan-Kettering Inst., New York, N. Y.
(5) T. F. Gallagher, Sloan-Kettering Inst., New York, N. Y.
(6) G. A. Grant, Ayerst, McKenna and Harrison Ltd., Montreal, P. Q.
(7) Sir I. M. Heilbron, Imperial College, London, England.
(8) R. F. Jacobsen, Worcester Foundation for Experimental Biology, Shrewsbury, Mass.
(9) J. R. Jamieson and E. Lozinski, Charles E. Frosst and Co., Montreal, P. Q.
(10) W. S. Johnson, University of Wisconsin, Madison, Wis.
(11) E. R. H. Jones, Victoria University, Manchester, England.
(12) O. Kamm, Parke, Davis and Co., Detroit, Mich.
(13) E. C. Kendall, Mayo Clinic, Rochester, Minn.
(14) T. H. Kritchevsky, Sloan-Kettering Inst., New York, N. Y.
(15) A. Lardon and T. Reichstein, University, Basel, Switzerland.
(16) S. Lieberman, Sloan-Kettering Inst., New York, N. Y.
(17) R. E. Marker, Pennsylvania State College, State College, Pa.
(18) C. R. Noller, Stanford University, Palo Alto, Calif.
(19) V. Prelog, Eidg. Tech., Hochschule, Zurich, Switzerland.
(20) D. A. Prins, Cleveland Clinic, Cleveland, Ohio.
(21) T. Reichstein, University, Basel, Switzerland.
(22) L. H. Sarett, Merck and Co., Rahway, N. J.
(23) C. R. Scholz, Ciba Pharmaceutical Products Inc., Summit, N. J.
(24) R. Turner, Harvard University, Cambridge, Mass.
(25) W. W. Westerfeld, Syracuse University, Syracuse, N. Y.
(26) A. L. Wilds, University of Wisconsin, Madison, Wis.
(27) J. Wolfe, Harvard University, Cambridge, Mass.

Measurements on New Types of Carbonyl Functions

In **Δ^1-3-ketones**, the maximum at 1680–1684 cm.$^{-1}$ is sensibly higher than that of the Δ^4-3 ketone group at 1674–1677 cm.$^{-1}$. In the **$\Delta^{1,4}$-dieneone-3** system (I) the maximum is displaced down to 1663 cm.$^{-1}$ by the introduction of the second conjugated double bond,[6] and is in the same range as the two linear dieneone groupings II and III previously considered.[2,5]



I II III

(6) The behavior of the carbonyl vibration bands in the Δ^4-one-3 and $\Delta^{1,4}$-dieneone-3 systems shows an interesting difference from the behavior of these conjugated systems as ultraviolet chromophores. In the ultraviolet spectrum, the Δ^1-3-ketone, the Δ^4-3-ketone and the cross conjugated $\Delta^{1,4}$-dieneone-3 systems all exhibit absorption maxima in a narrow wave length range between 2300 and 2400 Å. (ether solution).[7,8] The small variations within the range can be attributed to secondary effects of carbon substituents on the ethylenic double bonds.[9] In the linear dieneones II and III the maxima are displaced down to the neighborhood of 2800 Å. Thus, both the Δ^1- and the Δ^4-double bonds appear to exert a reinforcing influence in displacing the C=O stretching vibration further into the infrared, but their influence on the electronic excitation of the C=O groups is independent or mildly antagonistic.

(7) Dannenberg, *Abhandlungen Preuss. Akad. Wiss. Mathnaturw. Klasse*, Nr. 21 (1939).
(8) Wilds and Djerassi, THIS JOURNAL, **68**, 1712 (1946).
(9) Woodward *ibid.*, **63**, 1123 (1941); **64**, 76 (1942).

In all the conjugated unsaturated ketones, additional intense absorption bands occur between 1580 and 1630 cm.$^{-1}$ associated with the stretching vibration of the C=C bonds[10] and the different structures may be readily distinguished from one another if the positions of these bands are also taken into consideration.

Free Carboxylic Acids.—Four steroid carboxylic acids have been examined (Table II) and a maximum attributable to the carboxylic acid group[11] is observed between 1703 and 1710 cm.$^{-1}$. This figure agrees well with measurements on a series of straight chain fatty acids[12,13] which have a maximum at 1708 cm.$^{-1}$.

TABLE II

CARBON–OXYGEN DOUBLE BOND STRETCHING VIBRATIONS IN CARBONYL GROUPS OF TYPES NOT PREVIOUSLY INVESTIGATED

Compound[a]	Position of max.[b] cm.$^{-1}$ (CS_2)	Source[a]
A. Δ^1-3-Ketones		
Δ^1-Androstenol-17β-one-3	1684	3
Δ^1-Androstenol-17β-one-3-hexahydrobenzoate	1684, 1739	3
Δ^1-Androstenedione-3,17	1680, 1745	3
Δ^1-Cholestenone-3	1680	3
B. $\Delta^{1,4}$-Dieneone-3		
$\Delta^{1,4}$-Androstadienol-17β-one-3	1666	3, 26
$\Delta^{1,4}$-Cholestadiene-one-3	1666 ± 1	3, 26
$\Delta^{1,4}$-Androstadienedione-3,17	1663, 1745	3
$\Delta^{1,4}$-Androstadienol-17β-one-3 hexahydrobenzoate	1663, 1735	3, 26
$\Delta^{1,4}$-3-Ketoetiocholadienic acid M. E.	1663, 1743	3
C. Carboxylic Acids		
$\Delta^{1,3,5:10}$-1-Methyl-3-hydroxy-17-carboxyestratriene	1703, 1748[W]	3
$\Delta^{1,3,5:10}$-1-methyl-3-methoxy-17-carboxyestratriene	1704, 1750[W]	3
Etioallocholanic acid	1703, 1754[W]	15
Cholanic acid	1710	5, 24
D. δ-Lactones[c]		
Estrololactone acetate-3 (IV)	1742, 1767	8, 25
Isoandrololactone acetate-3β (V)	1742	8, 20
Etiocholanololactone acetate-3β (VI)	1742	20
E. γ-Lactones		
Δ^5-20-(Spiro-2-oxa-3-oxocyclopentano)-pregnenol-3β-acetate (VII)	1738, 1780	2
Δ^5-20-(Spiro-2-oxa-3-oxocyclopentano)-pregnenol-3β-benzoate (VIII)	1718, 1777	2
F. *p*-Toluenesulfonate Esters[d] of:		
Cholestanol-3β	No max.	5
Androstanol-3α-one-17	1742	14
Etiocholanol-3α-one-17	1742	14
G. 20-Acyl Esters		
Pregnanediol-3α,20α-monoacetate-20	1735	5
Allopregnanol-20α-one-3-acetate	1735	12
H. 6-Ketosteroids		
Cholestanol-3β-one-6	1714	17
6-Keto-3α-acetoxyallocholanic acid M. E.	1713 ± 1, 1740	5
-3α-*p*-toluenesulfonoxyallocholanic acid M. E.	1714 ± 1, 1742	5
-3α-hydroxycholanic acid M. E.	1706 ± 1, 1740	5
-3α-acetoxycholanic acid M. E.	1708 ± 1, 1740	5
I. Δ^4-Enedione-3,6		
Δ^4-Androstenol-17β-dione-3,6-acetate	1686, 1700, 1743	5
J. 2-Bromo-3-ketones		
2-Bromocholestanone-3	1735 ± 1	3, 26
-androstanol-17β-one-3	1735 ± 1	3
-androstanol-17β-one-3 hexahydrobenzoate	1739	3
-androstanedione-3,17	1734 ± 1, 1745	3
-3-ketoetioallocholanic acid M. E.	1739	3
K. 4-Bromo-3-ketones		
4-Bromo-coprostanone-3	1735	3
-3-keto-12-acetoxycholanic acid M. E.	1742	3
L. 2,2-Dibromo-3-ketones		
2,2-Dibromo-cholestanone-3	1737 ± 1	3
-androstanol-17β-one-3-acetate	1739	3
-androstanol-17β-one-3 hexahydrobenzoate	1739	3, 26
-3-ketoetioallocholanic acid M.E.	1739	3
M. 2,4-Dibromo-3-ketones		
2,4-Dibromo-cholestanone-3	1756 ± 1	3, 26
-androstanol-17β-one-3-acetate	1742, 1758	3
-androstanol-17β-one-3 hexahydrobenzoate	1739, 1758	3, 26
-3-ketoetioallocholanic acid M. E.	1742, 1758	3
N. Δ^4-2-Bromo-3-ketones		
Δ^4-2-Bromo-androstenol-17β-one-3 hexahydrobenzoate	1697, 1739	3
-3-ketoetioallocholenic acid M. E.	1697, 1742	3
O. Δ^1-2-Bromo-3-ketones		
Δ^1-2-Bromo-cholestenone-3	1697	3
-androstenol-17β-one-3 hexahydrobenzoate	1697, 1735	3
-3-ketoetioallocholenic acid M. E.	1697, 1742	3

(10) Jones, Humphries, Packard and Dobriner, THIS JOURNAL, **72**, 86 (1950).

(11) It is uncertain what significance should be attached to the weak component bands noted in the spectra of three of these carboxylic acids at 1754–1748 cm.$^{-1}$. In the vapor spectra of simple carboxylic acids, multiple absorption bands have been recorded in this region of the spectrum.[14]

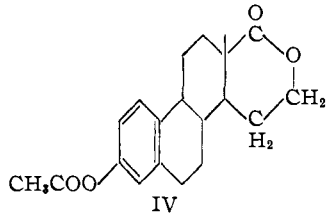
(12) Jones, Canadian Chem. and Process Industry, March, 1946.

(13) Jones, Royal Society of Canada, Vancouver Meeting, 1948.

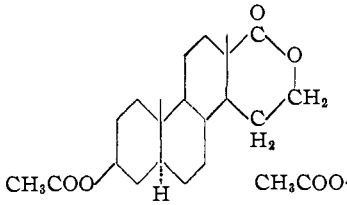
(14) Hartwell, Richards and Thompson, *J. Chem. Soc.*, 1437 (1948).

[a,b] See footnotes to Table I. [c] These compounds are named according to the system used by Jacobsen (*J. Biol. Chem.*, 171, 61, 71 (1947)). [d] See also section H of this Table.

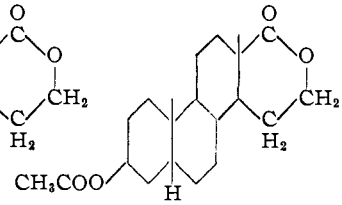
Lactones.—Three compounds, IV–VI, containing the δ-lactone structure in ring D have been examined. In IV bands are present at 1742 and 1767 cm.$^{-1}$; the latter is undoubtedly associated with the 3-phenolic acetate group, so that the 1742 cm.$^{-1}$ band must be assigned to the carbonyl of the lactone; in V and VI the single peak observed at 1742 cm.$^{-1}$ is in accord with this, since the carbonyl of the 3-acetate group also absorbs at 1742 cm.$^{-1}$. It appears that the carbonyl group of the δ-lactone absorbs in the frequency range common to the 17-ketone, the acyl acetate and the carbomethoxy group.[2,5]



IV

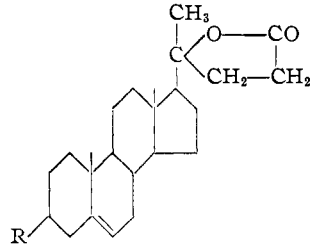


V



VI

In compounds VII and VIII a γ-lactone group is present on the side chain, and the absorption bands is at 1777–1780 cm.$^{-1}$. This is the highest frequency yet observed in a steroid carbonyl group. It is also in accord with the observation that the carbonyl group in a pentacyclic ring absorbs at a higher frequency than in a hexacyclic ring.



VII, R = —OCOCH$_3$
VIII, R = —OCOC$_6$H$_5$

Steroid Esters of *p*-Toluenesulfonic Acid.—In cholesterol-3β-*p*-toluenesulfonate, no bands occur between 1650 and 1800 cm.$^{-1}$, and in the two other steroid *p*-toluenesulfonate esters only the absorption bands expected of the carbonyl groups in the molecule are observed. It may therefore be inferred that esterification of a steroid alcohol with *p*-toluenesulfonyl chloride does not produce any new absorption bands in this region of the spectrum. Advantage may be taken of this for the identification of steroid alcohols which are insoluble in carbon disulfide or carbon tetrachloride. Conversion to a sulfonate ester or to a thioacetate may in some cases be preferable to acetylation as a means of rendering the compound soluble, since it avoids the introduction of an additional carbonyl group.[15]

Ester Carbonyl Groups.—Previous measurements on acyl esters of steroid alcohols included acetates, propionates and hemisuccinates. Several hexahydrobenzoates esters have now been measured (Table II) and the carbonyl maximum was observed at 1735–1739 cm.$^{-1}$.

Secondary Factors Influencing the Position of the C=O Stretching Vibration.—The evidence presented in this and the previous papers indicates that the frequency of the C=O stretching vibration of steroids, in carbon disulfide solution, is characteristic of the nature and location of the carbonyl group in the molecule. The only exceptions hitherto observed have been in certain dicarbonyl compounds in which the two carbonyl groups are separated by not more than two carbon atoms.[3,5] Under these conditions the bands are displaced to higher frequencies. Additional instances of the effects of the neighboring structure have now been noted in 6-ketosteroids, and in ketosteroids brominated on the carbon atoms alpha to the carbonyl group.

6-Ketosteroids.—Five 6-ketosteroids are included in Table II. Of these, two are derived from cholane, and three from allocholane. In the cholane derivatives the maximum at 1706–1708 cm.$^{-1}$ must be attributed to the 6-ketone group, since the other maxima are accounted for by the other carbonyl groups in the molecule. In the allocholane derivatives the corresponding maximum occurs at 1714 cm.$^{-1}$. It seems reasonable to associate this shift in frequency with the stereochemical inversion at the adjacent 5-position, which must result in a change in the force field in the neighborhood of the 6-ketone. None of the ketosteroids hitherto examined have involved carbonyl groups adjacent to a center of stereochemical inversion, except for the 17-ketosteroids, and in these the configuration at 13 has always been the same. It might be expected that inversion of the methyl group at 13 would produce a similar effect on the 17-ketone band. As yet no such compounds have been available to us.

Effects of α-Bromination.—A variety of 3-ketosteroids containing one or two bromine atoms at position 2 and 4 have recently been examined.[9,16] The results of measurements on these compounds are given in Table II.[17]

Previous work[2] has established that the nonconjugated 3-ketone group normally gives a maximum at 1715–1719 cm.$^{-1}$. The introduction

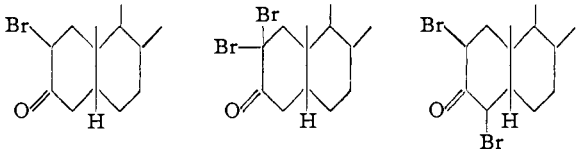
(15) The benzenesulfonate esters of the estrogens have been utilized as soluble derivatives by Carol, Molitor and Haenni (*J. Am. Pharm. Soc., Sci. Edit.*, **37**, 173 (1948)).

(16) Djerassi and Scholz, THIS JOURNAL, **70**, 1911 (1948), and earlier publications.

(17) We wish to thank Dr. A. L. Wilds of the University of Wisconsin and Drs. C. Djerassi and C. R. Scholz of Ciba Pharmaceutical Products Co. for the gift of this extensive collection of compounds.

of a single bromine atom either at position 2 or 4 displaces this maximum to 1735 cm.$^{-1}$. A displacement of the carbonyl maximum to a higher frequency on halogenation of the alpha carbon atom is well known and has been investigated extensively in Raman spectra.[18]

In the 2,4-dibromo-3-ketones, the introduction of the second bromine atom displaces the absorption band to a still higher frequency (1758 cm.$^{-1}$), the frequency increment for the second bromine atom being approximately the same as that for the first. In the 2,2-dibromo-3-ketones however it is curious to note that the introduction of the second bromine atom has a negligible effect, thus 2-bromocholestanone-3 (IX) and 2,2-dibromocholestanone-3 (X) both absorb at 1735–1739 cm.$^{-1}$, while 2,4-dibromocholestanone-3 (XI) absorbs at 1756 cm.$^{-1}$.



IX X XI

Displacement of the carbonyl absorption band to higher frequency on halogenation of the alpha carbon atom has been attributed to suppression of the carbonyl bond polarization by the halogen atom with an increase in the double bond character of the carbonyl linkage.[14] If this is the sole factor involved, it is not easy to understand why the second halogen atom has such a small effect when introduced onto the same alpha carbon atom, but an equal augmentative effect when placed on the alpha carbon atom on the opposite side of the carbonyl group. In the series of methyl esters of monochloro-, dichloro and trichloroacetic acids, Gillette[19] has reported that the frequency of the carbonyl group is displaced progressively to higher frequencies as the degree of chlorine substitution increases.

Table II also includes measurements on 2-bromo derivatives of Δ^1-3-ketones and Δ^4-3-ketones, in both of which the alpha bromine atom displaces the carbonyl band upward by about 20 cm.$^{-1}$.[20]

Experimental

The spectra were determined in carbon disulfide solution using Perkin–Elmer models 12a and 12b spectrometers with sodium chloride and calcium fluoride prisms. Full details of the experimental techniques have been given previously.[2,21]

(18) Cheng, *Z. physik. Chem.*, **B24**, 293 (1934).

(19) Gillette, THIS JOURNAL, **58**, 1143 (1936).

(20) In one dibrominated 17-ketosteroid, believed to be 16,16'-dibromoandrostanol-3β-one-17, a maximum was observed at 1764 cm.$^{-1}$. This would be consistent with the proposed structure if it be assumed that in the D-ring two bromine atoms on the carbon atom alpha to the 17-ketone group also raise its frequency by 20 cm.$^{-1}$.

(21) Dobriner, Leiberman, Rhoads, Jones, Williams and Barnes, *J. Biol. Chem.*, **172**, 297 (1948).

Most of the measurements were made with a sodium chloride prism and are accurate to ±3 cm.$^{-1}$. The frequency of several of the maxima were also checked at higher dispersion with a

TABLE III

POSITIONS OF CHARACTERISTIC CARBONYL MAXIMA ARRANGED IN ORDER OF DECREASING FREQUENCY

Carbon disulfide solution.

Position of max., cm.$^{-1}$	Carbonyl type	Number of compounds examined
1780–1777	γ-Lactone	2
1770	Naphtholic 3-acetate	1
1767–1764	Phenolic 3-acetate	4
1758–1756	2,4-Dibromo-3-ketone	4
1758–1756[a]	21-Acetoxy-20-ketone	12
1754	Δ^{14}-17-Ketone	2
1754	$\Delta^{3,5}$-Diene-ol-3-acetate (enol ester)	2
1754[a]	11,17-Diketone	5
1749	16-Ketone	1
1745–1742	17-Ketone	21
1742	δ-Lactone	3
1742	Methyl esters of cholanic, norcholanic and bisnorcholanic acids	30
1742–1739[a]	12-Ketoetiocholanic acid M. E.	3
1742–1737	17-Acetate and propionate esters	13
1739–1737	M. E.'s of etiocholanic and etioallocholanic acids	12
1739–1735	3-Acetate and propionate esters	32
1739–1735	17-Hexahydrobenzoate ester	5
1737	2,2-Dibromo-3-ketone	1
1735	20-Acetate ester	2
1735	2-Bromo-3-ketone	3
1735	4-Bromo-3-ketone	1
1732–1729[a]	21-Acetoxy-20-ketone	12
1726	11,12-Diketone	3
1724–1719	Benzoate esters	11
1723[a]	12-Ketoetiocholanic aid M. E.	3
1723	3,6-Diketone	2
1719–1715	3-Ketone	24
1719–1713[a]	11,17-Diketone	5
1719–1713	7-Ketone	7
1716	Δ^{15}-17-Ketone	2
1716–1710	11-Ketone	24
1714–1713	6-Ketone (allocholane series)	3
1710–1706	12-Ketone	3
1710–1706	20-Ketone	30
1710–1703	Carboxylic acid	4
1708–1706	6-Ketone (cholane series)	2
1697	Δ^1-2-Bromo-3-ketone	3
1697	Δ^4-2-Bromo-3-ketone	2
1686	Δ^4-Enedione-3,6	1
1684–1680	Δ^1-3-Ketone	4
1684–1680	$\Delta^{9:11}$-12-Ketone	4
1677–1674	Δ^4-3-Ketone	20
1670–1666	Δ^{16}-20-Ketone	5
1669–1666	$\Delta^{4,6}$-Dieneone-3	2
1666–1663	$\Delta^{1,4}$-Dieneone-3	5
1663	$\Delta^{3,5}$-Dieneone-7	1

[a] These structures give rise to two maxima, both of which are listed in the table.

calcium fluoride prism and the higher accuracy of these data (± 1 cm.$^{-1}$) is indicated in Table II.

Comments

The observations presented here supplement and substantiate the general conclusions developed in the previous publications and do not necessitate an extensive discussion. It may be considered firmly established that for complex molecules in solution the stretching vibration of the carbonyl group is influenced only by the molecular structure in its immediate vicinity. Unless the carbonyl group forms part of a conjugated system this influence normally does not extend beyond one carbon atom. Two carbonyl groups only interact on one another if they are separated by not more than two saturated linkages, and if such interaction occurs it causes a displacement of both the absorption bands to higher frequencies.[3] In this paper it has also been shown that the carbonyl stretching band is considerably disturbed by introduction of an alpha bromine atom. The situation in the 6-ketosteroids is also of interest, since it suggests that a carbon atom adjacent to a center of stereochemical inversion may be influenced by the steric configuration at that point. In cyclic ketones the position of the carbonyl band is also influenced by the ring size.

These correlations between structure and infrared absorption spectra are summarized in Table III. They parallel observations on the stretching frequency of the carbon–carbon double bond, which are reported separately,[10] and are proving of considerable value in the elucidation of the structure of ketosteroids. In certain instances it has been possible by this means to recognize and locate the carbonyl functions in newly isolated steroids where the quantities of material available are of the order of 25 to 50 micrograms.

Acknowledgments.—The authors wish to thank the several investigators listed individually in a footnote to Table I who kindly made available many of the compounds. The technical assistance of Miss E. Packard and Mr. D. Keir is also gratefully acknowledged.

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Summary

Measurements of the position of the carbonyl stretching vibration in the infrared spectra of carbon disulfide solutions of an additional 180 steroids are reported. The compounds include steroid carboxylic acids, γ-lactones, δ-lactones, p-toluenesulfonate esters, 6-ketosteroids and a variety of α-brominated 3-ketosteroids. The results substantiate the previously reported observation that the position of the maximum of this absorption band is characteristic for the type of carbonyl group and its position in the steroid molecule.

These correlations between structure and infrared absorption spectra are being utilized in the determination of the structure of new steroids isolated from urine.

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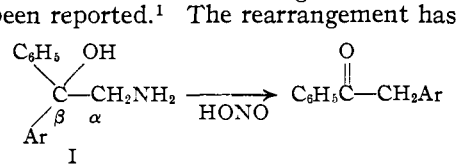
Stereospecificity in the Rearrangement of Amino Alcohols

BY PETER I. POLLAK AND DAVID Y. CURTIN

The rearrangement with nitrous acid of a number of amino alcohols with the general formula (I) has been reported.[1] The rearrangement has generally been assumed to be closely related to the pinacol rearrangement and the "relative migratory aptitudes" suggested by this series of rearrangements are at least qualitatively in the order obtained by Bachmann, Moser and Ferguson[2] in the acid-catalyzed rearrangement of a series of symmetrically substituted tetraphenylethylene glycols. For instance, in each case p-tolyl, p-anisyl and 1-naphthyl have been reported to migrate faster than phenyl.



I

In striking contrast to the results obtained with the series of amino alcohols above were those reported[3] with a series of compounds (II) differing from series (I) only in the presence of an additional phenyl on the α-carbon. Here, for example, phenyl was reported to migrate faster than p-anisyl or p-tolyl.

(1) (a) Luce, *Compt. rend.*, **180**, 145 (1925); (b) McKenzie, Mills and Myles, *Ber.*, **68**, 904 (1930); (c) Orekhoff and Roger, *Compt. rend.*, **180**, 70 (1925); Tiffeneau, Orekhoff and Roger, *Bull. soc. chim. France*, **49**, 1757 (1931).

(2) Bachmann and Moser, THIS JOURNAL, **54**, 1124 (1932); Bachmann and Ferguson, *ibid.*, **56**, 2081 (1934).

(3) (a) McKenzie and Mills, *Ber.*, **62**, 1784 (1929); (b) McKenzie and Wood, *ibid.*, **71**, 358 (1938).