Tetrahedron, 1966, Vol. 22, pp. 2837 to 2844. Pergamon Press Ltd. Printed in Northern Ireland

CONFIGURATION AND PROPERTIES OF DL-$\Delta^{4,9}$-19-NOR-D-HOMOANDROSTADIENE-14α-OL-3,17A-DIONE

K. K. PIVNITSKY, N. N. GAIDAMOVICH and I. V. TORGOV

Institute for Chemistry of Natural Products,
USSR Academy of Sciences, Moscow, USSR

(*Received* 12 *June* 1965; *in revised form* 19 *January* 1966)

Abstract—The "natural" *anti-trans* configuration for DL-$\Delta^{4,9}$-19-nor-D-homoandrostadiene-14α-ol-3, 17a-dione (I) is based on conformational analysis and the rule of the additivity of structural factors affecting chemical shifts in the NMR spectra. Reduction of I with lithium in liquid ammonia followed by isomerization yields DL-14α-hydroxy-19-nor-D-homotestosterone (VII), while reduction with sodium borohydride affords 9,10-dehydro-VII in low yield.

THE synthesis of DL-$\Delta^{4,9}$-19-nor-D-homoandrostadiene-14α-ol-3,17a-dione (I) has been described and although the configuration of the asymmetric centers $C_{(8)}$ and $C_{(14)}$ was not clear,[1,2] it has been shown[2] that these centers are formed simultaneously during an aldol type of condensation. According to the published data[3] no definite stereochemical specifity has been observed in these condensations.

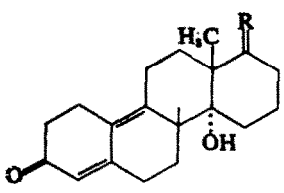
In contrast to ordinary steroids, the *cis* CD fused rings in isomers of hydroxydiketone (I) are capable of conformational conversion because ring B of these steroids has only one tetrahedral atom at the ring junction. Conformational analysis of the four possible isomers of hydroxydiketone (I) shows that only one stable conformation (we assume that all rings are in chair or halfchair form) is possible for each configuration.

Since asymmetrical atoms $C_{(13)}$ and $C_{(14)}$ have each four substituents of about the same size, the thermodynamic stability of an isomer will (in the first approximation) depend on the conformation at the third asymmetrical center, $C_{(8)}$, which carries substituents of different sizes. The isomer having the $C_{(7)}$–$C_{(8)}$ bond axial to ring C (in the most stable conformation) must therefore be labile from the thermodynamic point of view. This conclusion is irrefutable hence even the ability of rings A and B to undergo conformational conversion does not change the conformation of rings C and D although conformation of the $C_{(8)}$–$C_{(14)}$ bond to ring B is changed by this. Discussion of thermodynamic stability of the possible isomers of hydroxydiketone (I) is useful since the double bonds in $\Delta^{4,9}$-3-oxosteroids[4–9] as well as in other

[1] N. N. Gaidamovich and I. V. Torgov, *Isv. Acad. Nauk SSSR. Ser. Chim.* 1803 (1961).
[2] N. N. Gaidamovich and I. V. Torgov, *Steroids* 729 (1964).
[3] See for example W. S. Johnson, J. J. Korst, R. A. Clement and J. Dutta, *J. Amer. Chem. Soc.* **82**, 614 (1960) and Refs. cited therein.
[4] J. J. Brown and S. Bernstein, *Steroids* **I**, 113 (1963).
[5] Roussel-UCLAF, Fr.patent M1547 (1961); *Chem. Abstr.* **59**, 7619 (1963).
[6] Roussel-UCLAF, Brit. patent 919,434 (1963); *Chem. Abstr.* **59**, 4006 (1963).
[7] Roussel-UCLAF, Fr. patent 1,336,083 (1963); *Chem Abstr.* **60**, 3039 (1964).
[8] G. Nominé, R. Bucourt and M. Vignau (to Roussel-UCLAF), US patent 3,085,098 (1963) *Chem. Abstr.* **60**, 592 (1964).
[9] C. G. Bergstrom, R. T. Nicholson and R. M. Dodson, *J. Org. Chem.* **28**, 2633 (1963).

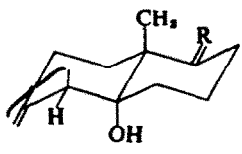
conjugated dienones[10] are mobile enough to realize the ionization and hence the epimerization of ε-carbon atoms (somewhat analogous epimerization see Ref. 11).

Conformational analysis and molecular models show that the $C_{(7)}$–$C_{(8)}$ bond is axial only in the *syn-trans* isomer of hydroxydiketone I (in preferred all-chair conformation; otherwise the ring C in this isomer must be in boat form) and therefore, this isomer is thermodynamically unstable. The hydroxydiketone (I) isomer obtained by us is undoubtedly thermodynamically stable since during preparation and isolation it

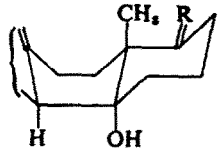


I R = O

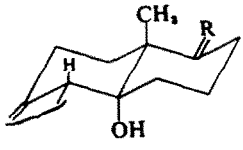
II R = H, OH



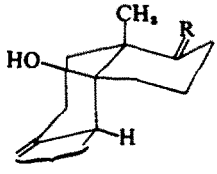
or



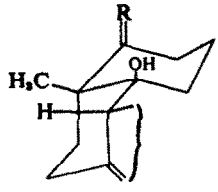
syn-trans



anti-trans



anti-cis



syn-cis

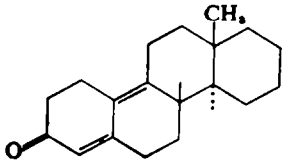
was treated by many epimerizing agents (e.g. heating with diethylamine in t-butanol and with *p*-toluenesulfonic acid in benzene, and prolonged contact with alumina[1,2]) and it can not, therefore, have the *syn-trans* configuration.

Further, the *anti-trans* configuration is supported by the NMR spectra of hydroxydiketone (I) and DL-$\Delta^{4,9}$-19-nor-D-homoandrostadiene-14α, 17aβ-diol-3-one (II) derived from I. The spectrum of hydroxydiketone (I) shows signals with chemical shift at 72·7 c/s (18-CH_3), 148 c/s (1,2-CH_2CH_2)[12] and 341 c/s (4-H). The spectrum of dihydroxyketone (II) is similar except that the 18-methyl group signal is shifted to 56·5 c/s. Based on the increments of substituents for the 18-methyl group signal in D-homosteroids calculated by us[12] and the published data (especially Zürcher's data[13]) it has been possible to calculate the expected positions of the angular methyl group signal in the spectra of stereoisomers of hydroxydiketone (I) and dihydroxyketone (II).

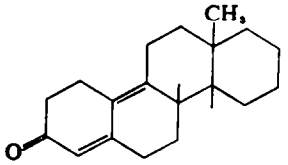
The position of the 18-methyl group signal in hypothetical $\Delta^{4,9}$-19-nor-D-homoandrostadiene-3-one (*anti-trans*, III) must be at 54·0 c/s.[12] The increment (for

[10] J. A. Zderic, A. Bowers, H. Carpio and C. Djerassi, *J. Amer. Chem. Soc.* **80**, 2596 (1958).
[11] G. Büchi, and H. J. E. Loewenthal, *Proc. Chem. Soc.* 280 (1962).
[12] K. K. Pivnitsky, and I. V. Torgov, *Tetrahedron* **22**, 1407 (1966).
[13] R. F. Zürcher, *Helv. Chim. Acta* **46**, 2054 (1963).

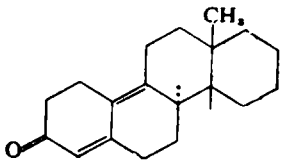
19-methyl group) of transition from *trans* to *cis* for a AB decaline system of steroids is +8 c/s.[13] When taking into consideration the rule of symmetry,* the same increment (for a 18-methyl group) is expected for a CD decaline system of D-homosteroids and, therefore, the chemical shift of the methyl group signal in *syn-cis* isomer (IV) should be 62·0 c/s. The situation is more complicated for the *anti-cis* isomer (V). In the parent 8α,14β-19-nor-D-homoandrostane the conversion of rings C and D has taken



III



IV



V

place and, therefore, the angular methyl group has an environment similar to that of the methyl group in 14β-19-nor-D-homoandrostane, and a chemical shift of 52·5 c/s may be taken in both cases. However, in contrast to other isomers the angular methyl group in ketone V is equatorial to ring C (and therefore is situated approximately in the plane of the ABC system), so the increment for $\Delta^{4,9}$-3-oxo-system (+9·5 c/s[12]) calculated for an angular methyl group axial to ring C must not be used in this case. The $\Delta^{4,9}$-3-oxo-grouping (towards 18-methyl group) is similar to the 3-carbonyl group (towards 19-methyl group) in situation, direction and value of effect and electron character. A comparison of increments of the 3-carbonyl group in 5α-steroids (angular methyl group is axial to ring A; +14·5 c/s[13]) and in 5β-steroids (angular methyl group is equatorial to ring A; +7·0 c/s[13]) shows that the effect of the substituent with such an electron character on the chemical shift of the signal from an equatorial methyl group is about half as strong as the analogous effect on an axial angular methyl group;[14] a diminishing effect should also be expected from the theoretical point of view. The increment of the $\Delta^{4,9}$-3-oxo-grouping for an equatorial methyl group at $C_{(13)}$ in ketone V may, therefore, be taken as +5 c/s and then the chemical shift of the 18-methyl group signal in *anti-cis*-dienone (V) will be 57·5 c/s.

When taking into account the equatorial or axial character of the 18-methyl group in ring D in III–V as well as the symmetry rule,[13,15] the value of the increment of the 17a-carbonyl group in III and V[16] can be taken as +21 c/s.[12] A similar increment in IV may be considered as almost equal to +13 c/s[13] of the 1-carbonyl group in 5β-steroids. As the interlocation of the 17a-hydroxyl group and angular methyl group in the dihydroxyketone (II) should be (independent of the stereochemistry of the parent hydroxydiketone I) similar to that in D-homosteroids of natural configuration (see Newman projection of possible stereoisomers of dihydroxyketone II along the bond

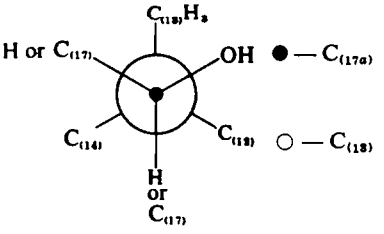
* For details see Ref. 12.

[14] Compare also the corresponding increments of carbonyl groups at $C_{(I)}$ (+22·5 and +13 c/s) and at $C_{(17)}$ (+10 and +5 c/s, for 18-methyl group).[13]

[15] E. R. Malinowski, M. S. Manhas, G. H. Müller and A. K. Bose, *Tetrahedron Letters* 1161 (1963).

[16] In contrast to the increment of 1-carbonyl group (for 19-CH_3) the increment of 12-carbonyl group (for 18-CH_3) does not depend on the type of ring fusion since in the latter case the angular methyl group does not change its conformation (related to the ring carrying carbonyl group) on altering fusion of the rings.

$C_{(17a)}$–$C_{(13)}$) the increments of all these hydroxyl groups must be identical, namely equal to +3 c/s.[12,17,18]



As the published data on the increments of 14-hydroxyl groups[13,19–21] for D-homosteroids has not been applied, it is better to use the increments of 5- and 9-hydroxyl groups (for 19-methyl group). The increment of the 5α-hydroxyl group is +3·5 c/s;[13] the value of +10 c/s[22,23] is probably exaggerated due to the presence of neighbouring 3- or 6-carbonyl groups in the compounds investigated.[24,25] The increment of the 9α-hydroxyl group is +8 c/s[13,20,21] and as there are no data on 5β-hydroxysteroids, one may consider the increment of the 5β-hydroxyl group synclinal to the 19-methyl group to be 5–7 c/s higher than the increment of the 5α-hydroxyl group periplanar to the 19-methyl group.[26,27] Therefore we consider the increment of

[17] The increments of both 17a α- and 17a β-hydroxyl groups should be within the limits of +1 – (+4) c/s[12,13] and therefore stereochemistry of dihydroxyketone (II) at $C_{(17a)}$ does not essentially alter the result of calculations.

[18] In contrast to the above discussed case of carbonyl group one should expect the increments of hydroxyl groups to depend only on an interlocation of hydroxyl and methyl groups but not on a conformational character of the latter. Compare increments of 17β-hydroxyl groups in 14α- and 14β-steroids (+2 and +1·5 c/s[13]).

[19] Y. Kawasoe, Y. Sato, M. Natsume, H. Hasegawa, J. Okamoto and K. Tsuda, *Chem. & Pharm. Bull. Tokyo* **11**, 338 (1962).

[20] E. Kondo and K. Tori, *J. Amer. Chem. Soc.* **86**, 736 (1964).

[21] K. Tori and E. Kondo, *Tetrahedron Letters* 645 (1963).

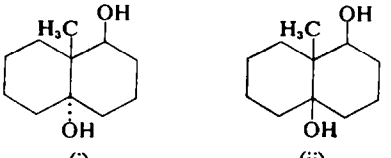
[22] J.-C. Jacquesy, J.-M. Lehn and J. Levissales, *Bull. Soc. chim. Fr.* 2444 (1961).

[23] K. Tori and T. Komeno, *Tetrahedron* **21**, 309 (1965).

[24] Note 33 in Ref. 13.

[25] A. D. Cross and I. T. Harrison, *J. Amer. Chem. Soc.* **85**, 3223 (1963).

[26] This is based on the general rules governing the deshielding effect of oxygen-containing substituents. See, for example, S. N. Ananchenko, V. N. Leonov, V. I. Zaretskii, N. S. Wulfson and I. V. Torgov, *Tetrahedron* **20**, 1279 (1964) and H. Gerlach and V. Prelog, *Liebigs Ann.* **669**, 121 (1963) and especially data from H. H. Westen, *Helv. Chim. Acta* **47**, 575 (1964). According to this data the transition from (i) to (ii) is accompanied with the shift of the angular methyl group



(i) (ii)

signal by +12·5 c/s. When taking into account the increment of change in ring fusion (+8 c/s) the changing of hydroxyl group configuration from α to β results in increasing its effect by the value of +4·5 c/s even in spite of the presence of intramolecular hydrogen bonding in (ii).

[27] It should be noted that the effect of 14-hydroxyl group changes in the direction opposite to the expected one when its configuration alters in normal, D-five-membered series.[19,21] Many explanations of this phenomenon may be put forward, but it is not possible to make a decision.

the 14α-hydroxyl group (periplanar to angular methyl group) in the *anti-trans* isomer to have the same value, +4-(+8) c/s, as in the case of periplanar 5α- and 9α-hydroxyl groups and the increment of synclinal 14β-hydroxyl groups in *anti-cis* and *syn-cis* isomers to be +9-(+15) c/s, as in the case of the 5β-hydroxyl group.

Based on this data, the expected positions of angular methyl group signals in the spectra of possible stereoisomers of hydroxydiketone (I) and dihydroxyketone (II) were calculated (Table 1).[28] These values may be exaggerated since hydrogen bonding is possible in any stereoisomer (hydrogen bond exists indeed in compounds I and II, see below) and then the rule of additivity of chemical shift increments becomes inexact and the calculated value of chemical shift turns out to be higher than the experimental value.[13]

TABLE 1. THE COMPARISON OF CALCULATED AND MEASURED CHEMICAL SHIFT VALUES

Compound	Expected chemical shift of signal from angular methyl group protons (c/s) for stereoisomer			Found chemical shift of this signal in synthetic isomer (c/s)
	anti-trans	*anti-cis*	*syn-cis*	
Hydroxydiketone I	79–83	88–93	84–90	72·7
Dihydroxyketone II	61–65	70–75	74–80	56·5

Taking into consideration the sentence described in the previous paragraph a comparison of the experimental data with the calculated ones given in Table 1 permits the conclusion that hydroxydiketone (I) and dihydroxyketone (II) have the *anti-trans* configuration.[29]

In order to obtain additional information on the stereochemistry and physicochemical properties of compounds I and II, their IR spectra were examined in the range 3200–3700 cm^{-1}. The spectrum of a $3 \cdot 10^{-3}$ mol/l. solution of hydroxydiketone (I) in CCl_4[30] displays a peak at 3578 cm^{-1} and dihydroxyketone (II) under analogous conditions manifest a peak at 3575 cm^{-1} with two peaks of less intensity at 3611 and 3630 cm^{-1}. Since the pattern of these spectra is not changed by further dilution, intramolecular hydrogen bonds should be present in compounds I and II. In each compound two types of hydrogen bonding are possible, namely, with π-electrons of $\Delta^{4,9}$-3-oxo-grouping[31–33] or with oxygen substituent at $C_{(17a)}$ (in the case of the hydroxyl group at $C_{(17a)}$ this realizes only in its suitable configuration).[30] A consideration of molecular models of stereoisomers of compounds I and II reveals that either

[28] Some approximate values that we ascribed to the increments of 17aβ-hydroxyl and 17a-carbonyl groups (as well as to the increment of transition to D-homosteroids[12]) do not effect the final result since we use only sums of these increments. This leads to algebraical annihilation of the primary approximation.

[29] This conclusion permits the real increment of the 14α-hydroxyl group in D-homosteroids by comparing the data of compounds I and II with those of corresponding 14-dehydroxy compounds described in Ref. 12. This increment is −1 c/s. However, the difference between this more exact increment and the above one (+4–8 c/s) does not decrease the validity of our calculations and conclusion. Obviously, this new increment has not been used in our calculations although its use would result in a better agreement with the calculation.

[30] F. Dalton, J. I. McDougall and G. D. Meakins, *J. Chem. Soc.* 4068 (1963).

[31] P. von R. Schleyer, C. Wintner, D. S. Trifan and R. Bacskai, *Tetrahedron Letters* No. 14, 1 (1959).

[32] F. Dalton, G. D. Meakins, J. H. Robinson and W. Zaharia, *J. Chem. Soc.* 1566 (1962).

[33] C. A. Grob and J. Hostynek, *Helv. Chim. Acta* **46**, 2209 (1963).

type of hydrogen bond may exist in any one isomer (Table 2). Since it is impossible to identify the type of a hydrogen bond[34] present it cannot be used for determination of configuration.

TABLE 2. POSSIBILITY OF A HYDROGEN BOND FORMATION IN ISOMERS OF COMPOUNDS I AND II

Possible isomer of I or II	*anti-trans*	*syn-trans*	*anti-cis*	*syn-cis*
Possibility of a hydrogen bond formation between 14-hydroxyl group and $\Delta^{4,9}$-3-oxo-grouping	+	−	+	−
oxygen function at C_{17a}	+	+	−	+

Concerning the chemical properties of hydroxydiketone (I), although isomerization to A-phenolsteroids has been described[35,36] for certain $\Delta^{4,9}$-3-oxo-steroids (namely with five-membered ring D and without 14-hydroxyl group) our attempts to aromatize hydroxydiketone (I) were unsuccessful. The compound remained unchanged after heating in ethanol with Pd/C[36] or on using Pd–black according to Brown.[37] Smith *et al.*[38] failed to carry out the aromatization of 14-dehydroxy-I, although he succeeded with the corresponding 17a-hydroxy derivative (14-dehydroxy-II).

Reduction of hydroxydiketone (I) with lithium in liquid ammonia proceeded as 1,6-addition to a dienone system together with simultaneous reduction of the saturated carbonyl group yielding DL-$\Delta^{5(10)}$-19-nor-D-homoandrostene-14α,17aβ-diol-3-one (VI). The β-configuration of the new hydroxyl group in the latter follows from the rule of equatorial alcohol formation on reduction of ketones with alkali metals in liquid ammonia[39] and from the presence of a peak of an equatorial hydroxyl group at 1018 cm^{-1} in the IR spectrum. Aqueous alcoholic alkali isomerizes the β,γ-unsaturated dihydroxyketone (VI) into the α,β-isomer, DL-Δ^{4}-19-nor-D-homoandrostene-14α, 17aβ-diol-3-one (14α-hydroxy-19-nor-D-homotestosterone) (VII). 9α- and 10β-configurations of asymmetric centers in compounds VI and VII are assumed in conformity with the rules of reduction of unsaturated ketones by alkali metals in liquid ammonia[40–43] and the thermodynamic control during isomerization of unsaturated ketones[44] (see also an example of inversion in γ-position[45]).

[34] Such hydrogen bonds are very weak and therefore the groups taking part in their formation (except hydroxyl group) are insignificantly influenced.[30] For example, in the spectrum of hydroxydiketone (I) peaks of 3- and 17a-carbonyl groups have normal positions—$\nu_{max}^{CHCl_3}$ 1657 and 1702 cm^{-1} as compared with $\nu_{max}^{CHCl_3}$ 1658 cm^{-1} for $\Delta^{1(9),5(10)}$-hexalone-2.[1] In addition, the positions of the peaks of carbonyl and 17a-hydroxyl groups in spectrum of dihydroxyketone II are $\nu_{max}^{CCl_4}$ 1678 and 3611, 3630 cm^{-1}.

[35] L. Velluz, G. Nominé and J. Mathieu, *Angew. Chem.* **72**, 725 (1960).

[36] R. Joly, J. Warnant, J. Jolly and A. Guillemette (to Roussel-UCLAF), Fr. patent 1,305,992 (1962); *Chem. Abstr.* **58**, 8001 (1963).

[37] H. C. Brown and C. A. Brown, *J. Amer. Chem. Soc.* **84**, 1494 (1962).

[38] G. H. Douglas, J. M. H. Graves, D. Hartley, G. A. Hughes, B. J. McLoughlin, J. Siddall and H. Smith, *J. Chem. Soc.* 5072 (1963).

[39] F. Sondheimer, O. Mancera, G. Rosenkranz and C. Djerassi, *J. Amer. Chem. Soc.* **75**, 1282 (1953).

[40] D. H. R. Barton and C. H Robinson, *J. Chem. Soc.* 3045 (1954).

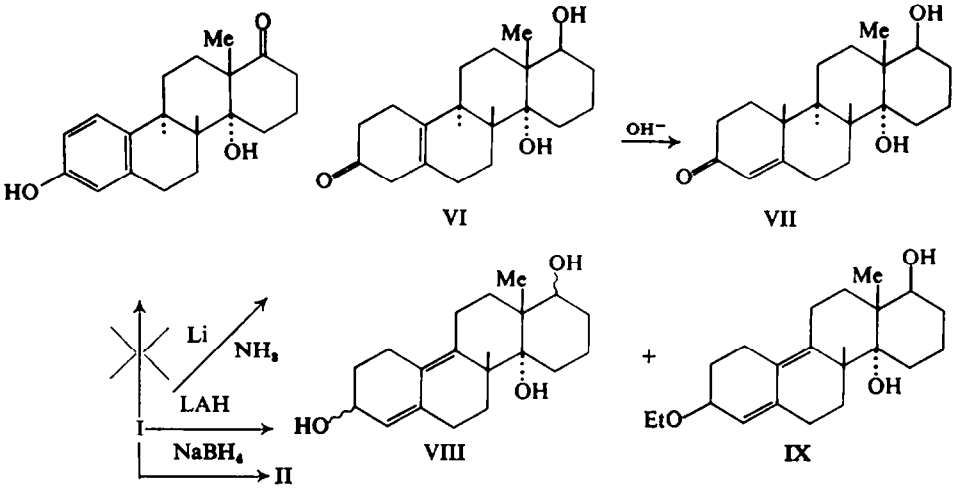
[41] A. J. Birch, H. Smith and R. E. Thornton, *J. Chem. Soc.* 1339 (1957).

[42] G. Stork and S. D. Darling, *J. Amer. Chem. Soc.* **86**, 1761 (1964).

[43] In this particular case both Barton's[40] and Stork's[42] rules lead to the same conclusion.

[44] O. Schindler, *Helv. Chim. Acta* **42**, 1955 (1959).

[45] H. J. Ringold, E. Batres and G. Rosenkranz, *J. Org. Chem.* **22**, 99 (1957).



Reduction of hydroxydiketone (I) with excess of $NaBH_4$ in ethanol, $LiBH_4$, LAH and $LiAlH(t\text{-}BuO)_3$ in tetrahydrofuran revealed that qualitatively identical mixtures of at least eight products were produced in each case. These mixtures consisted of the starting hydroxydiketone (I) and only two more polar substances together with substances of low polarity, which were the main products and the nature of which (except one example) was not investigated. The most polar substance in these mixtures was DL-$\Delta^{4,9}$-19-nor-D-homoandrostadiene-3ξ, 14α, 17ξ-triol (VIII) (probably a mixture of epimers at $C_{(3)}$ and $C_{(17a)}$) isolated in 40% yield after reduction of hydroxydiketone (I) with LAH. We also succeeded in isolating about 10% of a substance, $C_{21}H_{32}O_3$, which less polar than hydroxydiketone (I) was considered to be DL-$\Delta^{4,9}$-3β-ethoxy-19-nor-D-homoandrostadiene-14α, 17aβ-diol (IX) and this was confirmed by spectral data and chromatographic behaviour. Etherification of the allylic hydroxyl group could take place during crystallization from the ethanol–ether mixture. Reduction of hydroxydiketone (I) by $NaBH_4$ leads to dihydroxyketone (II; yield 16%) having an intermediate polarity between triol VIII and hydroxydiketone (I). The β-configuration at $C_{(17a)}$ is based on rules of reduction with complex metal hydrides[46] and by analogy.[47]

EXPERIMENTAL

For general instructions see Ref. 12. IR spectra were taken in Vaseline oil (unless otherwise stated) using Hilger H-800 or Zeiss UR-10 spectrometers.

DL-$\Delta^{5(10)}$-19-*Nor*-D-*homoandrostene*-14α, 17aβ-*diol*-3-*one* (VI).

A solution of I (830 mg) in 30 ml of dioxan–tetrahydrofuran mixture (1:1) was added during 10 min to a solution of Li (130 mg) in liquid ammonia (100 ml) at −70°. The mixture was kept for 10 min at −70° and then neutralized with dry NH_4Cl (5 g). After evaporation of ammonia the residue was diluted with water and extracted with CH_2Cl_2. The extract was washed with a sat brine, dried and evaporated. The residue was chromatographed on acid-washed alumina (II activity; 25 g). Elution with benzene–chloroform (1:1) yielded VI (338 mg, 40·5%) as colorless crystals, m.p. 160·5–161·5° (from hexane–benzene). The UV spectrum does not display an intense selective absorption in the range higher than 220 mμ; ν_{max} 3350 (OH), 1715 (C=O) and 1018 (C—OH) cm^{-1}. (Found: C, 75·3 H, 9·2. $C_{19}H_{28}O_2$ requires: C, 75·0 H, 9·3%).

[46] D. H. R. Barton, *J. Chem. Soc.* 1027 (1953).

[47] H. Heusser, P. T. Herzig, A. Fürst and P. A. Plattner, *Helv. Chim. Acta* 33, 1093 (1950).

DL-Δ^4-19-*Nor*-D-*homoandrostene*-14α, 17aβ-*diol*-3-*one* (VII).

Two drops of 40% ethanolic KOH were added to an ethanolic solution (10 ml) of VI (13·2 mg). After 2·5 hr at 20°, the mixture was neutralized with HClaq. Filtration and evaporation to dryness yielded VII (8·6 mg, 65·4%), m.p. 162·5–167°, λ_{max} 241 mμ (lg ε 4·01), ν_{max} 3400 (OH), 1679 and 1625 (C=C—C=O), 1019 (C—OH) cm^{-1}. A mixed m.p. with VI showed a strong depression.

Reduction of hydroxydiketone (I) *by complex metal hydrides.*

(a) *Reduction by* LAH. A solution of I (200 mg) in tetrahydrofuran (25 ml) was added dropwise to a suspension of LAH (62 mg) in tetrahydrofuran (15 ml) and the resulting jelly-like mixture was stirred for 18 hr. Two drops of EtOH and water (5 ml) then were added, an organic layer was separated and the water layer was extracted with CH_2Cl_2. After evaporation of the solvents, a light yellow oil (195 mg) was obtained which contained (according to the chromatographic data) a significant amount of starting I. This oil was again reduced with LAH (62 mg) and after the above-mentioned treatment the oil (172 mg) was shown to consist of 5 products, hydroxydiketone (I) being one of them. This oil was chromatographed in a layer of alumina (IV activity), 20 cm (start line) × 20 cm (run) × 1 mm (thickness) and development by ether. The detection was carried out by means of burning off with a thin red-hot wire (perpendicularly to a start line), as well as in UV light. A dark violet zone in UV light with R_f 0·6 was separated and eluted with CH_2Cl_2. Evaporation of the solution yielded a light yellow oil (51 mg) which was partly crystallized after keeping in EtOH–ether mixture. Ether IX (20 mg, 10%) was obtained with m.p. 187·5–190° (from EtOH), λ_{max} 249–250 mμ (lg ε 4·25), ν_{max} 3439 (OH), 1628 and 1580 (C=C—C=C), 1028 (C—OH) cm^{-1}. (Found: C, 75·5 H, 9·5. $C_{21}H_{32}O_2$ requires: C, 75·9 H, 9·7.) A dark violet zone with R_f 0·39 was separated and eluted with CH_2Cl_2. After evaporation, the resulting oil (38 mg) was crystallized by grinding with ether into starting hydroxydiketone (I) m.p. 200–204°. A dark violet zone in UV light situated close to the starting line was eluted by EtOH. Evaporation of the eluate yielded amorphous triol (VIII, 72 mg) which could not be crystallized, ν_{max} 3378 (OH), 1642 and 1570 (C=C—C=C) cm^{-1}.

(b) *Reduction by* $NaBH_4$. A solution of I (43 mg) and $NaBH_4$ (96 mg) in EtOH (10 ml) was stirred 80 min at 20°, diluted with a sat brine and extracted with $CHCl_3$. The extract was dried and evaporated. The residue (47 mg of yellow oil) was chromatographed on a layer of alumina (V activity), 25 cm (start line) × 20 cm (run) × 1 mm (thickness) and developed with ether. Five distinct dark-violet zones were seen in UV light. The zones were separated mechanically and eluted with ether. The first (from a start line) zone (2·5 mg) corresponded by R_f value to triol VIII, the third one (3 mg)—to the starting hydroxydiketone I, the fourth one (5·5 mg)—to ether IX, and the fifth one (26 mg)—to a mixture of compounds of unknown structure, λ_{max} 250 mμ, which separates in 4 spots by chromatography in a less polar system. The second (from a start line) zone (7 mg of yellow oil) corresponded to dihydroxyketone (II), λ_{max} 240–242 and 306–307 mμ, $\nu_{max}^{CCl_4}$ 1678 (C=C—C=C—C=O), 3575, 3611 and 3630 (OH) cm^{-1}, the NMR spectrum (see Theoretical section).