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CONFORMATIONAL ANALYSIS—XLIX

THE CONFORMATIONS OF THE ACETYL SIDE CHAINS OF SOME COMPOUNDS RELATED TO PREGNAN-20-ONE[1,2]

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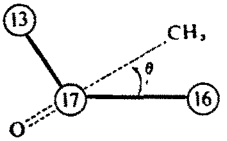
Abstract—The conformation of the side chains of pregnan-20-one, the 16β-methyl derivative, and the 17α-isomer of the former have been studied by conformational analysis and by the measurement of the dipole moments of the corresponding 3,20-diones. In each case the dipole moments are consistent with the predictions. Some of the difficulties involved in the interpretation of the Cotton effect curves of these compounds are pointed out.

INTRODUCTION

IN AN earlier paper[4] a determination of the conformation of the side chain of pregnan-20-one (I) was carried out utilizing the dipole moment of I, together with the dipole moments of cholestanone (II), and of pregnane-3,20-dione (III). It was calculated that the average angle between the dipoles in the latter compound was 133°. An alternative method for handling atomic polarization in the dipole moment calculations[5] leads to no change in the calculated angle. This angle between the dipoles corresponds to a dihedral angle θ (measured as in the Fig.) of about 210°.



17β-*Side Chains*

An examination of a Drieding model[6] shows that there do not appear to be serious interactions of the side chain with the rest of the system when θ has a value in the neighborhood of 210°, but for very different values of θ, there will always be at least one significant interaction. It was known that the Cotton effect curve for the system under discussion was strongly positive, and that fact was consistent with our conclusion. It was felt at the time that insufficient data were available to permit further conclusions to be drawn.

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[1] Paper XLVIII, N. L. Allinger, *Tetrahedron* **22**, 1367 (1966).

[2] This investigation was supported in part by U.S. Public Health Service Research Grant A-5836 from the National Institute of Arthritis and Metabolic Diseases.

[3] Recipient of a Predoctoral Fellowship from the Instituto Nacional de la Investigacion Cientifica, Mexico.

[4] N. L. Allinger and M. A. DaRooge, *J. Amer. Chem. Soc.* **83**, 4256 (1961).

[5] N. L. Allinger, J. Allinger and M. A. DaRooge, *J. Amer. Chem. Soc.* **86**, 4061 (1964).

[6] A. S. Dreiding, *Helv. Chim. Acta.* **42**, 1339 (1959).

More recently, additional data and speculations have appeared in the literature,[7–11] and while these tended generally to agree with the original conclusions, in certain cases they added additional points which are worth more careful consideration. In addition, we have examined the question of the conformation of the side chain when a 16β-methyl group was introduced into the ring, or when the normal 17β-side chain was replaced by the *iso* (or 17α) side chain. These latter two situations have already been studied by means of ORD and circular dichroism.[11,12]

DISCUSSION

Rakhit and Engel[7] looked at the conformation of the side chain in terms of four conformations, while Wellman and Djerassi[11] expanded this to a total of seven conformations. One can, of course, subdivide the problem into any number of conformations, but one should ask if this is the best approach. In the conformational analysis of ethane derivatives, one generally has to consider three conformers, as these correspond to distinct energy minima in simple cases.[13] Wellman and Djerassi[11] chose to discuss two conformations (which they refer to as VIa and VIIa) as *conformers* in equilibrium with a definite energy difference between them. The reader may interpret this to mean that there is also an energy barrier between these *conformations*, but no evidence for such a barrier was presented. Since the number and geometries of the energy minima are not known *a priori* in this case, a more exact way to formulate the problem at hand is not in terms of any specific number of conformations, but rather in terms of an energy function as the angle θ varies from 0 to 360°. This is easy enough to do in principle, but in practice there are certain difficulties involved. In certain cases, such energy functions can be arrived at reasonably well.[5,14]

To obtain reasonably good energy functions for the type of system under consideration at present, one would have to carry out much more laborious calculations, as the simplifications applied in the earlier cases are not very good approximations here. The problem should properly be treated by a full scale attack utilizing the Westheimer[15] method and minimizing the conformational energies with the aid of a computer.[16,17] While such calculations have been carried out in a few relatively simple cases, the present situation is a good deal more difficult, and its solution appears to be quite a ways in the future. The main difficulty in the present case stems from the fact

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[7] S. Rakhit, and C. R. Engel, *Canad. J. of Chem.* **40**, 2163 (1962).

[8] P. Crabbé, F. McCapra, F. Comer and A. I. Scott, *Tetrahedron* **20**, 2455 (1964).

[9] G. Snatzke, H. Pieper and R. Tschesche, *Tetrahedron* **20**, 107 (1964).

[10] (a) A. D. Cross and P. Crabbé, *J. Amer. Chem. Soc.* **86**, 1221 (1964);
(b) A. D. Cross and C. Beard, *J. Amer. Chem. Soc.* **86**, 5317 (1964);
(c) L. L. Smith and D. M. Teller, *J. Med. Chem.* **7**, 531 (1964).

[11] K. M. Wellman and C. Djerassi, *J. Amer. Chem. Soc.* **87**, 60 (1965).

[12] P. Crabbé, *Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry* p. 134. Holden-Day, San Francisco (1965).

[13] Customary usage is to limit the word "conformer" to arrangements corresponding to energy minima, whereas "conformation" implies no such restriction. Rotamer has been used with both meanings.

[14] N. L. Allinger, J. G. D. Carpenter and M. A. DaRooge, *J. Org. Chem.* **30**, 1423 (1965).

[15] E. L. Eliel, N. L. Allinger, S. J. Angyal and G. A. Morrison, *Conformational Analysis* p. 435. Interscience Division of J. Wiley, New York (1965).

[16] J. B. Hendrickson, *J. Amer. Chem. Soc.* **83**, 4537 (1961).

[17] K. B. Wiberg, *J. Amer. Chem. Soc.* **87**, 1070 (1965).

that there are quite a number of interactions involved which are known inaccurately, if at all. However, an examination of Dreiding models, together with our earlier experimental work, indicates that our original conclusions must be at least approximately correct, and the subsequent authors all agree on this point. We would now like to direct attention to the embellishments added by subsequent workers, and ask whether these are really convincing, either theoretically or experimentally, and we begin with the latter.

The 17β-acetyl chromophores generally have strong positive Cotton effects at room temperature,[11] and 5α-pregnan-3β-ol-20-one acetate has a rotational strength of $+11{\cdot}4 \times 10^{-40}$ cgs at 27°, which increases to $+13{\cdot}6 \times 10^{-40}$ cgs at $-192°$. This change was attributed[11] to an equilibrium between two conformers (which correspond to θ values of approximately 210° and 270°), and from these data, assuming a 1·1 kcal energy difference between the conformers, the rotational strength of each conformer was calculated and said to be in good agreement with expectations.

There are a number of points regarding the calculation described which require comment, and the Cotton effects will be considered first. The qualitative usefulness of Cotton effect curves has been tremendous,[12,18] but until they can be calculated quantitatively, one must use caution in making predictions about systems which contain groups in both positive and negative octants.[19] In this case it is clear the conformation with $\varepsilon = 210°$ should exhibit a strong positive Cotton effect. Most of the steriod is too remote from the carbonyl to have a significant effect, and the 18-methyl together with the D-ring are really going to determine the curve. When θ is 180°, all of the carbons not on nodal planes are in a positive octant, and the curve will unquestionably be positive. As θ increases above 180°, the 15-methylene appears to be lowered into a negative rear octant, but depending on the location of the surface perpendicular to the C=O bond, it may be in a positive front octant. As θ continues to increase to about 210°, C-15 tends back away from the oxygen, its position with respect to the nodal surface still in doubt. Simultaneously, C-14 moves from the upper left rear octant to the lower left rear, unless it has crossed the same undefined nodal surface at some point, and the 18-methyl is now lowering down into the carbonyl plane, and also leaning toward or into the front octant. Carbons 12, 13 and 14 probably will have an important effect, which is positive, but of unknown magnitude.

There are, then, at least six carbons contributing to the Cotton effect here, three of the contributions are known qualitatively, the others not at all. As θ continues to increase, because of the lack of knowledge of the one nodal surface, even the qualitative behavior to be predicted for the Cotton effect cannot be specified convincingly, until near $\theta = 360°$, when the important atoms all occupy a negative actant.

This case has been discussed in some detail, because we want to point out that the analysis of the situation is complicated, and the reliability of some of the conclusions drawn previously is somewhat less straightforward than might appear. The conclusions we would draw from the Cotton effect data are rather conservative; namely, the observed positive effect is consistent with the conformation proposed earlier, and the rather small change with temperature indicates that if the compound is a mixture

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[18] C. Djerassi, *Optical Rotatory Dispersion, Applications to Organic Chemistry.* McGraw-Hill, New York (1960).

[19] W. Moffitt, R. B. Woodward, A. Moscowitz, W. Klyne and C. Djerassi, *J. Amer. Chem. Soc.* **83**, 4013 (1961).

of conformers, either the other conformers are present in rather small amounts, or they have rotations similar to that of the principal conformer.

Next, we may examine the behavior expected of the compound on the basis of available theory. The most detailed analysis published previously[11] appears to be quite correct in so far as what was included, but leads to doubtful implications because of what was left out, and we will hence expand the analysis here to the limits of the available theory.

There are two problems which must be faced at the outset, which are the conformation of the 5-membered ring,[12,20] and the rotational barrier about a bond joining a carbonyl group to a tetrahedral carbon in a molecule of the acetone type. The former problem does not appear to seriously affect the conclusions, as one will calculate similar relative energies for possible conformers for any reasonable conformation of the 5 membered ring. The second problem, namely the rotational barrier in acetone, has been adequately solved, and it is now clear that the energy barrier is 0·8 kcal/mole high in acetone itself,[21] and the energy minimum is the conformation in which a hydrogen eclipses the oxygen.[22]

Beginning with the 21-methyl group eclipsed by the 16-methylene ($\theta = 0$), the *torsional energy* is 0·8 kcal/mole.[24] This value oscillates sinusoidally, reaching a minimum of zero at 60°, a maximum at 120° and so on (Table 1). Superimposed upon this function will be the various van der Waals interaction functions. These

TABLE 1. ESTIMATED INTERACTIONS IN 17β-21-KETO STEROIDS[b]

Interaction[a]	θ	0	30	60	90	120	150	180	210	240	270	300	330
C_{17}–C_{21}	Torsion	0·8	0·4	0	0·4	0·8	0·4	0	0·4	0·8	0·4	0	0·4
21Me | C_{16}		6·0	3·4	0·8	0·2	—	—	—	—	—	0·2	0·8	3·4
21Me | C_{13}		—	0·2	0·8	3·4	6·0	3·4	0·8	0·2	—	—	—	—
18Me | 21Me		—	0·4	1·6	3·7	3·7	0·8	0·2	0	—	—	—	—
O | 18Me		—	—	—	—	—	—	—	0·1	0·5	1·1	1·1	0·2
Pregnan-20-one		6·8	4·4	3·2	7·7	10·5	4·6	1·0	0·7	1·3	1·7	1·9	4·0
16βMe | 21Me		10	10	6·0	0·8	0·2	—	—	—	—	0·2	0·8	6·0
16βMe | O		—	—	—	—	—	0·2	1·6	1·6	0·5	—	—	—
16βMe-Pregnan-20-one		16·8	14·4	9·2	8·5	10·7	4·8	2·6	2·6	1·8	1·9	2·7	10·0

[a] When interaction with a carbon is mentioned, the energy includes also the interactions of the hydrogens attached to the carbon.

[b] If not otherwise specified the numbers given here are from Ref. 5 and 14.

[20a] F. V. Brutcher, T. Roberts, S. J. Barr and N. Pearson, *J. Amer. Chem. Soc.* **81,** 4915 (1959); [b] F. V. Brutcher and W. Bauer, *Ibid.* **84,** 2233, 2236 (1962).

[21] J. D. Swalen and C. C. Costain, *J. Chem. Phys.* **31,** 1562 (1959).

[22] This problem has been a worrisome one for many years (see Ref. 5 for a summary of the status of the problem at that time, and literature references). From the data reported by N. L. Allinger and F. M. Karkowski, *Tetrahedron Letters* 2171 (1965), the location of the energy minimum of the acetone barrier can be calculated to be as stated above.[23]

[23a] N. L. Allinger, H. M. Blatter, L. A. Freiberg and F. M. Karkowski, to be published; [b] N. L. Allinger and H. M. Blatter, *J. Amer. Chem. Soc.* **83,** 994 (1961).

[24] The van der Waals interaction between these two groups is considered separately.

include the 21-methyl group with: the 16-methylene, carbon 13, the 18-methyl and the oxygen atom with the 18-methyl. There are some additional small interactions which will not be considered here, as they complicate the problem and are not important at the energy minima. The interactions between the 21-methyl and the 16-methylene can be roughly approximated by a butane function, so that this interaction is taken to be 0·6 kcal at $\theta = 0$, diminishing to 0·8 kcal at $\theta = 60°$, to 0 at $\theta = 120°$, and then increasing again to 0·8 kcal at 300°. The numbers were connected by a simple cosine function. The interaction between the 21-methyl and C_{13} can be represented by similar function, with the maximum at $\theta = 120°$. The interaction between the 21-methyl and the 18-methyl is harder to specify accurately. The maximum should come around $\theta = 90°$ and should be similar to a 1,3 *syn*-axial dimethyl interaction,[25] with a value of 3·7 kcal/mole.[26] Judging from the distance between the methyl groups, this value should have fallen to less than 0·8 kcal at $\theta = 30°$ but more than 0·8 at 60°, and it should retain its maximum value to about $\theta = 120°$, and then fall to 0·8 kcal at $\theta = 150°$. The rest of the function is taken to be sinusoidal as previously. The interaction of the oxygen with 18-methyl has no very close analogy. Perhaps the value for the interaction between the oxygen and the methyl of equatorial 2-t-butylcyclohexanone (1·1 kcal/mole)[23] is as close as one can find. The rest of the curve is taken as proportional to the methyl/methyl curve, displaced appropriately.

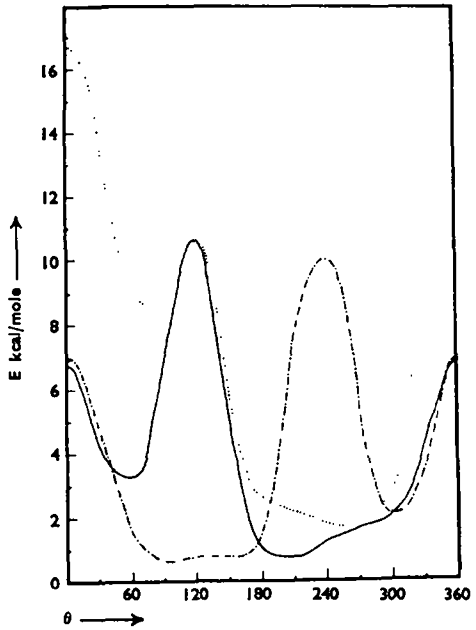

FIG. 1. The conformational energies of the 20-ketones as a function of θ: pregnan-20-one ———; 16β-methylpregnan-20-one·····; 17α-pregnan-20-one —·—·—.

These energy functions have been collected in Table 1. When they are totaled and the results plotted, Fig. 1 is obtained. It can be seen that an energy minimum

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[25] N. L. Allinger and M. A. Miller, *J. Amer. Chem. Soc.* **83**, 2145 (1961).

[26] When the energy is this large the molecule will not have this conformation to any significant extent, so a large error in this value is not serious.

exists near $\theta = 210°$, and a second one near $\theta = 60°$, the latter some 2·5 kcal/mol higher than the former. This energy difference is sufficient that, even allowing for inaccuracies in the calculation, one expects rather little of the high energy conformer at room temperature. Next, the shape of the curve in the range of $\theta = 210$ to 300° may be examined. This compound has been described[11] in terms of two conformers, with approximate values for θ of near 210 and 270°, but there seems to be no evidence for such a situation. There is rather a single conformer, which, as the vibrational degree of freedom in question is excited, oscillates more widely back and further over the indicated range. It is stressed that the errors inherent in this calculation do not allow one to put great confidence in the *quantitative* shape of this curve, but there seems to be no reason to suspect any *qualitative* error which would allow the existence of two separate conformers in this region.

Now, let us consider the dipole moment of pregnane-3,20-dione. The observed moment[4] corresponds to an angle of 133° between the dipoles. From models such an angle between the dipoles results for θ near either 90 or 210°. The former value can be clearly ruled out from Fig. 1, and the latter corresponds to our original conclusion.[4]

Having the conformation of the pregnan-20-one side chain reasonably well understood, we next turn to the 16β-methyl derivative. An examination of models shows that the additional methyl would be somewhat too close to the ketone oxygen at $\theta = 210°$ (about 2·2 Å), although if θ were increased to about 250° this distance would have increased to about 2·6 Å, at which distance the interaction is close to zero in 2-methylcyclohexanone.[23] It is hard to estimate the repulsion at $\theta = 210°$, but we have guessed that perhaps 1·6 kcal would be a reasonable number. Whatever the value is, it will obviously tend to force θ to increase from 210°, but probably not above 240–250°, at which point the repulsion of the 16β-methyl will become less than that of the 18-methyl. The interactions between the 21-methyl and the 16-methyl were deduced as previously, and the results are given in Table 1.

Introduction of the 16β-methyl into the system will lead to a qualitative shift as indicated in the Fig., although quantitatively uncertain. Whatever type of interaction is assumed between oxygen and methyl, the energy curve will show a single minimum between 240 and 270°. The dipole moment of 16β-methylpregnane-3,20-dione was then considered as an experimental test of these conclusions, and it was measured and found to have the value 2·66 D, just 0·3 D greater than in the absence of the 16-methyl. The dipole moment of the appropriate model compound, 16β-methylpregane-20-one was also determined, and it had the value 3·03 D, some 0·4 D larger than that of pregnane-20-one itself. The obvious conclusion was that the 16β-methyl had little effect on the conformation of the side chain. Quantitatively, the angle between the dipoles for 16β-methylpregnane-3,20-dione was calculated to be 128°, which differs slightly more than experimental error from pregnane-3,20-dione itself. This change in the angle between the dipoles corresponds to an increase of the order of 10–20° in θ, which is qualitatively similar to that predicted in Fig. 1. Clearly, only one conformer is expected. The introduction of the 16β-methyl group would lead to a large negative shift in the Cotton effect relative to the parent compound without any change in conformation, if the methyl were behind the nodal surface discussed earlier. Because of the number of atoms which have unknown effects, the assignment of positive and negative Cotton effects to two different conformers is unconvincing. It may well be that the potential curve (Fig. 1) is quite asymmetric near its minimum, and the Cotton effect may change drastically as the molecule is raised to torsionally excited levels. Such behavior might explain the observed results, but there are other possible explanations also, such as solvent effects. The feature of interest we would call attention to is not the difference in conformation caused by the introduction of the 16β-methyl, but rather the fact that this difference is so small.

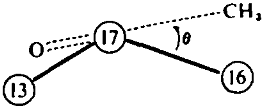
Finally, we have studied the conformation of the side chain in the 17α-series by measuring the dipole moment of 5β,17α-pregnane-3,20-dione. Interpretations of the ORD curves of 17α compounds have been given earlier,[11] but they involve the effects of several atoms distributed between positive and negative octants and for the same reasons mentioned above for the 17β isomer, are not convincing. In this system the oxygen must point over the D-ring, so that a very large dipole moment for the molecule is expected. The energy as a function θ can be calculated as before, the appropriate numbers are assembled in Table 2.

TABLE 2. ESTIMATED INTERACTIONS IN 17α,21-KETO-STEROIDS[a]

Interaction	θ	0	30	60	90	120	150	180	210	240	270	300	330
C_{17}–C_{21}	Torsion	0·8	0·4	0	0·4	0·8	0·4	0	0·4	0·8	0·4	0	0·4
21Me | C_{16}		6·0	3·4	0·8	0·2	—	—	—	—	—	0·2	0·8	3·4
21Me | C_{13}		—	—	—	—	—	0·2	0·8	3·4	6·0	3·4	0·8	0·2
21Me | C_{14}		—	—	—	—	—	—	—	—	0·2	0·6	0·2	—
21Me | C_{12}		—	—	—	—	—	0·2	0·8	3·7	3·0	1·2	0·2	—
O | C_{12}		0·2	1·1	0·5	—	—	—	—	—	—	—	—	—
Total		7·0	4·9	1·3	0·6	0·8	0·8	1·6	7·5	10·0	5·8	2·0	4·0

[a] If not otherwise stated, the numbers here are from Ref. 5 and 14.

Here calculation indicates the favorable arrangements have θ (measured as in the Fig.) variable from about 90 to 150° without significant energy change. There is another conformer with θ near 300°, but it appears to be sufficiently high in energy that one does not expect it to contribute much to the dipole moment at room temperature.



Having clear-cut predictions regarding the 17α side chain, the dipole moment of a 3,21-dione was considered, but only the 5β compound was available. While simple 5α-steroids present no problems regarding ring A, the conformational situation in ring A of the 3-keto-5β series has never been completely settled.[27] Nace and Turner[28] interpreted a dipole moment study of 5β-androstane-3,17-dione in terms of an appreciable amount of boat form in equilibrium with the chair. Since the dipole moment of a 3,12-dione was determined[29] and found to be just that calculated for ring A in the chair form, it seems now that the deviation of the experimental value

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[27] Ref. 15 p. 160.

[28] H. R. Nace and R. B. Turner, *J. Amer. Chem. Soc.* **75**, 4063 (1965).

[29] C. L. Neumann, Unpublished.

from that calculated for the chair by Nace and Turner is due to the D-ring having a somewhat different conformation than was attributed to it. Even if such a deformation occurs in the present case with C-17 tetrahedral, it will not significantly affect our conclusions.

Thus, the prediction is that 17α- side chain will have an average θ near 120°, which corresponds to an angle between the dipoles of about 40°. The necessary group moments should be obtained from 5β-cholestan-3-one (3·10 D) and 17α-pregan-20-one. We have used the value of the 17β-isomer (2·64 D) for the latter, which should introduce little error. The dipole moment of 5β,17α-pregane-3,20-dione was then measured and was found to have the value 5·16 ± 0·01 D. This value corresponds to an angle of 52° between the dipoles, which is in satisfactory agreement with the energy calculations. A single conformation, which undergoes a wide oscillation about the C-17–C-20 bond, thus seems to fit well with both theory and experiment.

EXPERIMENTAL

Microanalyses were due to Dr. A. Bernhardt, Max Planck Institut, Mühlheim (Germany). M.p.s were determined in capillary tubes with a "Mel-temp" apparatus. Rotations were taken between 16° and 22° with a 1 dm tube and sodium D-light. IR spectra were obtained with a Perkin–Elmer, Model 21, NaCl prism. UV absorption spectra were taken with a Beckman spectrophotometer, Model D.U., in EtOH solution.

3β-Hydroxy-16β-methylpregnan-20-one. Catalytic hydrogenation of 3β-hydroxy-16β-methylpregn-5-en-20-one[30] (1 g) in 200 ml AcOEt, with 10% Pd–C, gave quantitatively the saturated alcohol. After several recrystallizations from CH_2Cl_2–hexane, the analytical sample of *3β-hydroxy-16β-methylpregnan-20-one* was obtained: m.p. 190–191°; $[\alpha]_D$ +36° (C, 1; $CHCl_3$); λ_{max}^{KBr} 2·95 and 5·92 μ. (Found: C, 79·77; H, 10·45; O, 9·61. $C_{22}H_{36}O_2$ requires: C, 79·46; H, 10·92; O, 9·63.)

16β-Methylpregnane-3,20-dione. The above alcohol (1 g) was dissolved in 200 ml acetone (twice distilled over $KMnO_4$). To this solution, kept between 0–10°, 2 ml 8N chromic acid solution[31] was added with stirring. The mixture was then stirred for 10 additional minutes at room temp. Water was added and excess 10% Na_2CO_3aq. Further extraction with $CHCl_3$, followed by washing and drying over Na_2SO_4 afforded 950 mg crude diketone. Three recrystallizations from MeOH provided the analytical sample of *16β-methylpregnane-3,20-dione*: m.p. 187–189°; $[\alpha]_D$ +62° (*c*, 1; $CHCl_3$); λ_{max}^{EtOH} 286 mμ (log ε 1·81); λ_{max}^{KBr} 5·83, 5·85 μ. (Found: C, 79·81; H, 10·37; O, 9·86. $C_{22}H_{34}O_2$ requires: C, 79·95; H, 10·37; O, 9·68.)

16β-Methylpregnane-3,20-dione-3-cycloethylenethioketal. To a solution of 700 mg 16β-methyl-dihydro-progesterone in 30 ml AcOH, 1 ml BF_3-etherate and 1 ml ethanedithiol were added. This mixture was allowed to react for 12 hr at room temp. The crystalline precipitate which formed was filtered and dried (m.p. 192–194°; λ_{max}^{KBr} 5·86). This product was then purified by chromatography over 40 g silicagel. Elution with hexane–benzene (4–1) provided 550 mg of crystalline material. The pure sample was obtained after two crystallizations from CH_2Cl_2–methanol, and exhibited the following physical properties: m.p. 222–224°; $[\alpha]_D$ +25° (*c*, 1; $CHCl_3$); λ_{max}^{KBr} 5·87. (Found: C, 71·09; H, 9·50; S, 15·99. $C_{24}H_{38}OS_2$ requires: C, 70·89; H, 9·42; S, 15·77.)

16β-Methylpregnan-20-one. The thioketal (500 mg) was dissolved in 600 ml EtOH. To this solution 150 mg Raney Ni was added. The reaction mixture was then allowed to reflux gently for 24 hr. The solution was cooled, filtered and concentrated *in vacuo*, furnishing 350 mg of crystalline material (m.p. 129–133°). Chromatography over silica gel (40 g) gave, by elution with hexane–benzene (7–3), the pure 3-desoxy-20-keto-steroid. The analytical sample of *16β-methylpregnan-20-one*, obtained after three crystallizations from CH_2Cl_2–MeOH presented: m.p. 135–136°; $[\alpha]_D$ +49° (*c*, 0·5; $CHCl_3$); λ_{max}^{EtOH} 286–288 mμ (log ε 1·62); λ_{max}^{KBr} 5·85 μ. (Found: C, 83·37; H, 11·53; O, 5·29. $C_{22}H_{36}O$ requires: C, 83·47; H, 11·47; O, 5·05.)

[30a] R. E. Marker and H. M. Crooks, *J. Amer. Chem. Soc.* **64**, 1280 (1942);

[b] K. Heusler, J. Kebrle, C. Meystre, H. Ueberwasser, P. Wieland, G. Anner and A. Wettstein, *Helv. Chem. Acta* **42**, 2043 (1959).

[31] K. Bowden, I. M. Heilbron, E. R. H. Jones and B. C. L. Weedon, *J. Chem. Soc.* 39 (1946).

5β,17α-Pregnane-3,20-*dione*. This compound, prepared according to the technique of Butenandt and Fleischer[32] and Rubin and Blossey,[33] exhibited the following properties: m.p. 103–104°; $[\alpha]_D$ −79° (*c*, 0·2; dioxan); λ_{max}^{EtOH} 281–282 mμ (log ε 1·7); λ_{max}^{KBr} 5·86 and 5·88 (infl.). CD (*c*, 1·6; dioxan): $[\theta]_{293}$ −8877. (Found: C, 79·55; H, 10·06. $C_{21}H_{32}O_2$ requires: C, 79·70; H, 10·19.)

Dipole moments. The experimental dipole moments were determined at 25° in benzene solution using previously described apparatus,[34] and methods.[35] Molar refractivities were calculated from Tables[36] and atomic polarization was neglected.[5] The data are summarized in Table 3.

TABLE 3. DIPOLE MOMENT DATA

Compound	α	ε_1	d_1	β	P_{200}	μ(D)
16β-Methylpregnan-20-one	12·87	2·2748	0·8733	0·458	283·1	3·03 ± 0·12
16β-Methylpregnan-3,20-dione	10·46	2·2730	0·8730	0·883	239·6	2·66 ± 0·04
5β,17α-Pregnan-3,20-dione	35·57	2·2762	0·8733	0·763	636·1	5·16 ± 0·02

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