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STUDY OF THE COTTON EFFECT OF 16-SUBSTITUTED 20-KETO PREGNANE AND 17α-PREGNANE DERIVATIVES[1]

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Abstract—A study of the circular dichroism characteristics of various 16-substituted 20-keto pregnane and isopregnane derivatives has been made. The curves of the 16,17-*trans* compounds are similar to those of the 16-unsubstituted parent compounds. Modifications of functions in rings A and B have little effect, if any, on the circular dichroism maxima around 290 mμ. In the case of 16,17-*cis* compounds, both the configuration and the nature of the 16-substituent have an important bearing on the sign and intensity of the Cotton effect associated with the 17-acetyl side chain. The circular dichroism data for 16,17-epoxy-20-keto steroids are discussed.

IT HAS been shown previously that the nature of the Cotton effect associated with the 17α- and 17β-acetyl side chain is largely dependent on the stereochemistry of the 16-substituent of the steroid molecule.[2]

The present paper describes the examination of a series of 16-substituted 20-keto pregnane and isopregnane derivatives by both circular dichroism (C.D.)[3] and optical rotatory dispersion (O.R.D.)[4] methods.

Some previous observations[2,5] have been confirmed and information gained regarding the configurational and conformational factors responsible for the observed variations of the Cotton effect associated with the 17-acetyl side chain.

In Table 1 are shown the C.D. maxima associated with the acetyl side chain in various 16α-substituted 17β-acetyl steroids (I_{c_r}).[6] While little difference is observed in the positive Cotton effect of these compounds (I_{c_r}), it is worth noting that the positive

[1] This paper constitutes: [a] Steroids Part CCLXIV from the Research Laboratories, Syntex S.A. For Part CCLXIII, see J. A. Edwards, M. C. Calzada, L. C. Ibañez, M. E. Cabezas Rivera, R. Urquiza, L. Cardona, J. C. Orr and A. Bowers, *J. Org. Chem.*, in the press; [b] Circular Dichroism—III, in the British Columbia University Series.

[2] P. Crabbé, *Tetrahedron* **19**, 51 (1963).

[3] L. Velluz and M. Legrand, *Angew. Chem.* **73**, 603 (1961).

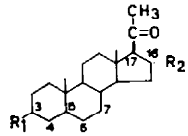
[4] C. Djerassi, *Optical Rotatory Dispersion: Applications to Organic Chemistry*. McGraw-Hill, New York (1960); W. Klyne in *Advances in Organic Chemistry* (Edited by R. A. Raphael, E. C. Taylor and H. Wynberg) Vol. I; p. 259. Interscience, New York (1960).

[5] W. A. Struck and R. L. Houtman, *J. Org. Chem.* **26**, 3883 (1961).

[6a] The minor variations observed in the Cotton effect of these substances could be attributed to changes of the nature of the substituent at C-16, as well as to experimental errors. It is relevant to point out that Velluz and Legrand[3] have reported that modifications in rings A and B of 20-keto steroids give small changes in the C.D. positive maximum associated with 17β-acetyl side chain.

[b] A similar observation has been made by G. Snatzke, H. Pieper and R. Tschesche, *Tetrahedron* **20**, 107 (1964).

TABLE 1



Compounds	Position of substituents			Circular dichroism maximum of 20-keto-group			Ref.
	3-R_1	4, 5, 6, and 7	16-R_2	λ_{max} (mμ)	$\Delta\varepsilon$	[θ]	
Ia	β OH	5α H	H	*ca.* 293	−3·50	+11,580	3
b	ketone	$\Delta^{1,4}$	H	292	−3·74	+12,320	3, 10
c	β OAc	Δ^5	O—CH_3	293	−3·50	+11,580	11
d	β OAc	5α H, Δ^7	O—CH_3	292	−3·00	+ 9,900	12
e	β OAc	5α H	O—H	293	+3·48	+11,500	13
f	β OH	Δ^5	C≡N	287	+4·52	+14,920	14
g	β OAc	Δ^5	C≡N	286	+4·57	+15,100	14
h	β OAc	5α H	C≡N	289	+4·40	+14,530	13
i	ketone	Δ^4	C≡N	287	+3·80	+12,560	14a
j	β OH	Δ^5	$CH(CH_3)_2$	293	+4·44	+14,680	15
k	β OH	Δ^5, 6 CH_3	$CH(CH_3)_2$	294	+5·00	+16,500	15
l	ketone	Δ^4, 6α CH_3	$CH(CH_3)_2$	293	−4·23	+14,000	15
m	β OAc	5α H	CH_3	292	+4·80	−15,850	16
n	β OH	Δ^5	$CH(CO_2H)_2$	290	+4·90	+16,200	17
o	β OAc	Δ^5	$CH(CO_2Et)_2$	292	+4·47	+14,750	14c
p	β OH	Δ^5	$CONH_2$	292	+5·00	+16,500	18
q	ketone	Δ^4	CO_2H	288	+3·70	+12,220	18
r	ketone	Δ^4	CO_2CH_3	288	+4·12	+13,600	18
s	ketone	Δ^4	$COCH_3$	290	−4·74	+15,680	18

maxima[7] of these substances are slightly higher than the reported value for the 17β-acetyl side chain of 3β-hydroxy-5α-pregnan-20-one (Ia).[3] Furthermore, when the 16α-substituent is a hydroxy group (I_e) or a methoxy function (Ic and Id), the positive Cotton effect is less than in the parent unsubstituted compound (Ia). Conversely, when the 16α-substituent is an amide, as in I_p, the positive maximum of the C.D. curve is greater.

[7] For circular dichroism nomenclature, see: C. Djerassi and E. Bunnenberg, *Proc. Chem. Soc.* 299 (1963).

[8] M. Legrand and J. Mathieu, *Bull. Soc. Chim. Fr.* 1679 (1961).

[9] For a comparative study of the applications of O.R.D. and C.D. in organic chemistry, see: P. Crabbé, *Tetrahedron* **20**, 1211 (1964).

[10] M. B. Rubin and E. C. Blossey, *J. Org. Chem.* in print. We are most grateful to Dr. Rubin for a preprint of his paper, as well as for providing us with very valuable samples.

[11] D. K. Fukushima and T. F. Gallagher, *J. Amer. Chem. Soc.* **73**, 196 (1951).

[12] This compound (I_d) was prepared by Mr. J. Iriarte, of these laboratories (Experimental).

[13] P. Crabbé, M. Pérez and G. Vera, *Canad. J. Chem.* **41**, 156 (1963).

[14a] J. Romo, *Tetrahedron* **3**, 37 (1958); [b] B. Ellis, V. Petrow and D. Wedlake, *J. Chem. Soc.* 3748 (1958); [c] R. H. Mazur and J. A. Cella, *Tetrahedron* **7**, 130 (1959); [d] see also Ref. 21.

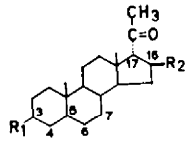
[15] F. von Werder, *Chem. Ber*, **95**, 773 (1962). We are pleased to thank Dr. von Werder for sending us samples of 16-isopropylpregnane derivatives.

[16a] 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. Chim. Acta* **42**, 2043 (1959).

[17] P. Crabbé, O. Halpern and J. Iriarte, unpublished results.

[18] P. Crabbé, L. M. Guerrero, J. Romo and F. Sanchez-Viesca, *Tetrahedron* **19**, 25 (1963).

TABLE 2



Compounds	Position of substituents			Circular dichroism maximum of 20-keto-group			Ref.
	3-R_1	4, 5, 6	16-R_2	λ_{max} (mμ)	Δε	[θ]	
IIa	β OAc	Δ^5	H	289	−2·70	−8,900	19
b	ketone	Δ^4	H	289	−2·30	−7,580	19
c	ketone	$\Delta^{1,4}$	H	292	−2·36	−7,780	10
d	β OH	Δ^5	CO_2H	289	−2·64	−8,700	14, 18
e	β OAc	Δ^5	CO_2H	289	−2·74	−9,030	18
f	β OAc	5α H	CO_2H	289	−2·80	−9,220	13
g	β OAc	Δ^5	CO_2CH_3	289	−2·89	−9,530	18
h	3,5α-cyclo	6β OH	CO_2CH_3	291	−2·94	−9,700	13
i	ketone	Δ^4	CO_2CH_3	292	−2·61	−8,580	18
j	β OH	Δ^5	CH_2OH	285	−2·66	−8,770	20
k	ketone	Δ^4	CH_2OH	292	−2·31	−7,610	20
l	ketone	Δ^4	CH_2OAc	292	−2·52	−8,250	20
m	β OAc	Δ^6	C≡N	286	−2·86	−9,410	21
n	ketone	Δ^4	CH_3	294	−2·58	−8,500	22
o	β OAc	5α H	$CONH_2$	290	−3·15	−10,390	13
p	β OAc	Δ^5	$CONH_2$	290	−3·18	−10,500	18
q	ketone	Δ^4	$CONH_2$	290	−3·13	−10,320	18
r	β OAc	Δ^5	$CONEt_2$	287	−3·33	−10,900	18
s	ketone	Δ^4	$COCH_3$	288	−4·18	−13,800	18
t	3,5α-cyclo	6-ketone	CO_2CH_3	291	−4·40	−14,530	13

From the results reported in Table 1 it is apparent that the intensity (Δε or [θ] value) of the positive maximum due to the 17β-acetyl side chain seems to be largely independent of the nature of the functions and substituents present in rings A and B.[6] For example, introduction of a new asymmetric center and a Δ^4-3-keto chromophore in compound I_j, to give I_1, leads to a C.D. curve which is simply the sum of both chromophores. Thus the C.D. maximum of I_1 at 293 mμ is very similar to that of the parent compound I_j. Although the same conclusion could be reached by O.R.D., this observation emphasizes the great selectivity shown by C.D. for which the Cotton effect depends mainly on the asymmetry in the immediate vicinity of the chromophore examined and is not affected by the background curve.[8,9] A consequence, discussed elsewhere,[9] is that asymmetric chromphores separated by as little as 20 mμ can frequently be resolved by C.D.

As far as the 16β-substituted 17α-acetyl steroids are concerned, it is apparent from Table 2 that these compounds exhibit a negative Cotton effect. Furthermore, the

[19a] A. Butenandt and L. Mamoli, *Ber. Dtsch. Chem. Ges.* **68**, 1847 (1935); [b] A. Butenandt, J. Schmidt-Thomé and H. Paul, *Ibid.* **72**, 1112 (1939); [c] D. M. Glick and H. Hirschmann, *J. Org. Chem.* **27**, 3212 (1962); [d] See also Ref. 10, and M. B. Rubin and E. C. Blossey, *Steroids* **1**, 453 (1963).

[20] P. Crabbé and J. Romo, *Bull. Soc. Chim. Belg.* **72**, 208 (1963).

[21a] P. Crabbé, J. Romo and L. Rodriguez-Hahn, *Bull. Soc. Chim. Fr.* 2675 (1963); [b] J. Romo, L. Rodriguez-Hahn, P. Joseph-Nathan, M. Martinez and P. Crabbé, *Ibid.* 1276 (1964).

[22] J. Romo, J. Lepe and M. Romero, *Bol. Inst. Quim., Mexico* **4**, 125 (1952).

intensity of the C.D. negative maximum,[7] associated with the 17α-acetyl side chain, is reminiscent of the negative Cotton effect of 17-isopregnenolone acetate (IIa).[19,23] The amides (II_{o-r}), as in the isomeric series I, show a stronger negative Cotton effect than the parent compounds.

In both *trans*-series (Tables 1 and 2), while the nature of the 16-substituent seems to exert little effect on the C.D. maximum associated with the 17-acetyl side chain, the size of this substituent changes quantitatively the Cotton effect.

The C.D. curves of the Δ^4-3-keto derivatives of these series (I and II) show better resolution of the Δ^4-3-keto and 20-keto bands than the corresponding O.R.D. curves[2].

This selectivity shown by C.D.[9] is exemplified by the curves of 16α-acetyl progesterone (I_s) and 16β-acetyl isoprogesterone (II_s)[18] (Fig. 1). In these curves the fine structure associated with the Δ^4-3-keto system is dissociated from the other chromophores. Furthermore, from the comparison of the C.D. curves of 16α-acetyl progesterone (I_s) with 16α-carbomethoxy progesterone (I_r), it is apparent (Fig. 1) that while the 16α-carbomethoxy grouping does not make any major contribution to the positive Cotton effect associated with the 17β-acetyl side chain (*vide supra*), the 16α-acetyl grouping of (I_s) enhances it considerably. Conversely, the negative maximum of the 17α-acetyl side chain of the isoprogesterone (II_s) is considerably increased by the 16β-acetyl grouping, but a 16β-carbomethoxy function, as in (II_l), exerts little, if any, effect (Fig. 1).

In Table 3 the C.D. data for the 17β-acetyl side chain of 16β-substituted steroids is reported. For some compounds ($III_{c,e,f,h,l}$) the molecular amplitude[24] of the optical rotatory dispersion curve is included and there is complete agreement between the C.D. and O.R.D. results obtained in these series.

Most of the *cis*-compounds (III_{c-j}) show a decrease of the positive Cotton effect of the 17β-acetyl side chain. Furthermore, as already observed in O.R.D. studies,[2] while the 16β-carbomethoxy function has little effect on the positive maximum, as in (III_c) and (III_d), some other 16β-substituents dramatically change the positive Cotton effect. In this respect the 16β-methyl derivatives (III_{g-j}) show the most profound modifications of the Cotton effect associated with the 17β-acetyl function.[6b,25] Thus the C.D. curves of the 16β-methyl derivatives (III_{g-i}) have a symmetrical shape, with weak positive and negative maxima, separated by 30 mμ (Fig. 1). However, in the C.D. curve of 16β-methyl progesterone (III_j) no positive maximum is observed (Fig. 1). The fine structure of the Δ^4-3-keto $n-\pi^*$ transitions predominates.

The molecular amplitude of the O.R.D. curves of compounds ($III_{e,f,h,l}$) is reported in Table 3. It is apparent that the amplitude (a) is considerably reduced in most of these compounds. For instance, for the 16α-cyano derivative (I_g) the amplitude is $a = +197$, while rotatory dispersion measurement of its 16β-cyano isomer (III_e) gives only $a = +93$. This result is in agreement with the dramatic decrease of the Cotton effect observed in C.D. The 16α-cyano ketone (I_g) shows a molecular ellipticity $[\theta] = +15{,}100$, but its 16β-isomer (III_e) shows $[\theta] = +7{,}360$. The same applies for the

[23] G. Amiard, M. Legrand, J. Mathieu, R. Heymès and T. van Thuong, *Bull. Soc. Chim. Fr.* 2417 (1961).

[24] C. Djerassi and W. Klyne, *J. Chem. Soc.* 4929 (1962); *Ibid.* 2390 (1963): see also Ref. 4.

[25] Similar findings have been made by J. C. Danilewicz and W. Klyne, *J. Chem. Soc.* in the press. We are most grateful to Prof. Klyne for communication of this manuscript, prior to publication.

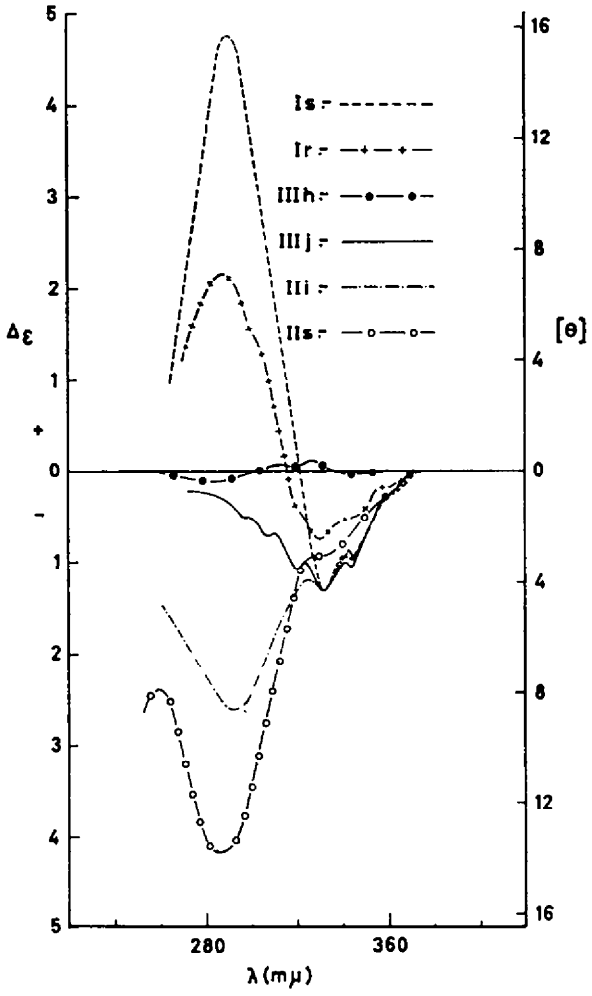


FIG. 1. Circular dichroism curves of 16α-carbomethoxy progesterone (Ir), 16α-acetyl progesterone (Is), 16β-carbomethoxy 17α-progesterone (IIi), 16β-acetyl 17α-progesterone (IIs), 3β-hydroxy 16β-methyl pregn-5-en-20-one (IIIh) and 16β-methyl progesterone (IIIj).

other *cis*-compounds, for example (III_f), (III_h) and (III_i) whose molecular amplitudes are given in Table 3.

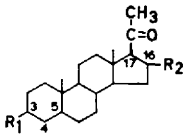
As far as the last group of stereochemical isomers is concerned, it was mentioned earlier[2] that the O.R.D. curves of 17α-acetyl steroid derivatives with a 16α-substituent (Table 4) show a stronger negative Cotton effect than their corresponding 16β-isomers (Table 2). Further investigation of this property confirmed the previous finding,[2] but also indicated the negative increment of the Cotton effect to be highly dependent on the nature and the size of the 16α-substituent. This is clearly shown by the C.D. negative maxima reported in Table 4 and by the O.R.D. results (see Experimental).

Marked changes of the O.R.D. amplitude and C.D. maximum are observed mainly for 16,17-*cis*-compounds belonging to the 16,17β-series (Table 3) and the 16,17α-series (Table 4). Various factors (conformation of ring D and acetyl side chain as well as electronic effects) seem to be responsible for these changes observed in the Cotton

effect associated with the 17-acetyl side chain. However, at present, a quantitative evaluation of the separate contribution of each of these factors to the Cotton effect is impossible. Furthermore, it is probable that the importance or quantitative influence of each factor varies from one compound to another.

It seems reasonable to assume that the conformation of the 17-acetyl side chain[26] is modified by the *nature* and the *size* of the *cis* substituent present at position 16.[21] Brutcher and Bauer[27] have discussed the possible conformations for the cyclopentane

TABLE 3



Compounds	Position of substituents			Circular dichroism maximum of 20-keto-group			Rotatory dispersion	Ref.
	3-R_1	4, 5	16-R_2	λ_{max} (mμ)	$\Delta\epsilon$	[θ]	a	
Ia	β OH	5α H	H	*ca.* 293	−3·50	+11,580		3
b	ketone	$\Delta^{1,4}$	H	292	+3·74	+12,320		3, 10
IIIc	β OAc	Δ^5	CO_2CH_3	290	+3·68	+12,150	−218	18
d	ketone	Δ^4	CO_2CH_3	290	+3·40	+11,220		18
e	β OAc	Δ^5	C≡N	290	+2·23	+7,360	+93	21
f	β OH	Δ^5	CO_2H	290	+1·40	+4,620	+68	18
g	β OAc	5α H	CH_3	321–307 271·5	+0·21 −0·26	−693 −859		16
h	β OH	Δ^5	CH_3	344 326 314 285	−0·034 +0·103 +0·062 −0·207	−112 +340 +205 −685	+8!	16
j	β OAc	Δ^5	CH_3	321 271	+0·22 −0·25	+726 +825	+4!	16
j	ketone	Δ^4	CH_3	307 296	−0·72 −0·49	−2,380 −1,618		16

ring D of a steroid. This concept has been emphasized in a recent N.M.R. examination of some 16-substituted pregnane derivatives.[28] In the present cases (compounds III_{c-j} and IV_{c-i}), it seems probable that the conformation of ring D, in at least some of these substances, is modified by the size or the nature of the C-16 substituent.[29] It is also very likely that changes of ring D conformation would alter the Cotton effect of the 20-carbonyl group. Finally, when the size of the 16-side chain is large, as in compounds ($IV_{c,e,f}$) for example,[30] it seems reasonable to assume that a part of the side

[26] The conformation of the 17β-acetyl side chain in the steroid molecule is known: [a] C. Djerassi, I. Fornaguera and O. Mancera, *J. Amer. Chem. Soc.* **81**, 2383 (1959); [b] N. L. Allinger and M. A. Da Rooge, *Ibid.* **83**, 4256 (1961); [c] S. Rakhit and Ch. R. Engel, *Canad. J. Chem.* **40**, 2163 (1962).

[27] F. V. Brutcher and W. Bauer, *J. Amer. Chem. Soc.* **84**, 2336 (1962).

[28] A. D. Cross and P. Crabbé, *J. Amer. Chem. Soc.* **86**, 1221 (1964); see also Ref. 21.

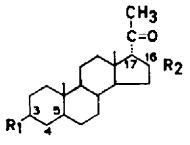
[29] Some recent NMR observations seem to support this hypothesis: A. D. Cross and C. Beard, private communication.

[30] The same applies for the O.R.D. curve of 16β-carbox-(N,N-diethyl-ethylenediamine)-amido-pregn-5-en-3β-ol-20-one-3-acetate methyl iodide.[2,18]

chain can make a positive or negative contribution to the Cotton effect, depending on its spatial orientation. This means that steric factors (conformation of acetyl side chain and ring D, interactions of 16-substituent and 20-carbonyl group), electronic factors (nature of the 16-substituent which could induce electrostatic attraction or repulsion with the 20-carbonyl) and also solvation of the 20-keto group[31] seem to be responsible for the dramatic changes observed both in the O.R.D. and C.D. curves of these substances (Table 3 and 4).

Comparison of the Cotton effect attributed to the 17β-acetyl side in a 16-unsubstituted compound (I_a) with the 16β-carboxy derivative (III_f) shows a decrease in

TABLE 4



Compounds	Position of substituents			Circular dichroism maximum of 20-keto-group			Ref.
	3-R_1	4, 5	16-R_2	λ_{max} (mμ)	$\Delta\varepsilon$	$[\theta]$	
IIa	β OAc	Δ^5	H	289	−2·70	−8,900	19
b	ketone	Δ^4	H	289	-2·30	−7,580	19
IVc	β OAc	Δ^5	$CH(CO_2Et)_2$	290	-2·30	−7,580	17
d	ketone	Δ^4	CH_3	303–289	−2·70	−8,900	10
e	β OAc	5α Cl	$CH(CO_2Et)_2$	286	−3·00	−9,900	17
f	β OH	Δ^5	$CH(CO_2H)_2$	285	−3·06	−10,100	17
g	β OAc	5α H	CO_2CH_3	290	−3·85	−12,710	13
h	β OAc	Δ^5	CO_2CH_3	292	−4·06	−13,390	18
i	ketone	Δ^4	CO_2CH_3	292	−3·54	−11,690	18

intensity. This could be attributed to reorientation of the 20-carbonyl axis[26] of the 17β-acetyl side chain in the latter compound, due to electronic repulsion exercised by the *cis*-16-carboxy grouping on the 20-carbonyl function. The 16β-methyl 20-keto pregnane case seems to be different. In these compounds (III_{g-j}), there is probably a steric interaction between the 16β-methyl group and the 20-carbonyl function. This could induce a modification not only of the 17-acetyl conformation but also of ring D conformation (*vide supra*).[27,29]

The C.D. curve of compound (III_h) (Fig. 1) is reminiscent of the C.D. curve of D-homoandrostane-17a-one[32] and of some (2,2,1) bicyclo heptanones.[31d] The C.D. curve of (III_h) changes sign in a region associated with *only one* optically active n–π* transition.[33] This curve is the mirror image of the C.D. curves of lanost-8-ene-3-one and other terpenic ketones,[34] as well as of a ketone obtained by degradation of

[31] See for example: [a] K. M. Wellman, E. Bunnenberg and C. Djerassi, *J. Amer. Chem. Soc.* **85**, 1870 (1963); [b] A. Moscowitz, K. M. Wellman and C. Djerassi, *Proc. Natl. Acad. Sci.*, U.S. **50**, 799 (1963); [c] A. Moscowitz, K. M. Wellman and C. Djerassi, *J. Amer. Chem. Soc.* **85**, 3515 (1963); [d] Ch. Coulombeau and A. Rassat, *Bull. Soc. Chim. Fr.* 2673 (1963); [e] K. M. Wellman, R. Records, E. Bunnenberg and C. Djerassi, *J. Amer. Chem. Soc.* **86**, 492 (1964).

[32] S. Bory, M. Fétizon and P. Laszlo, *Bull. Soc. Chim. Fr.* 2310 (1963).

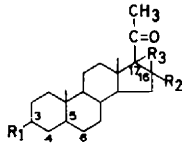
[33] S. F. Mason, *Quart. Rev.* **17**, 20 (1963).

[34] P. Witz, H. Herrmann, J. M. Lehn and G. Ourisson, *Bull. Soc. Chim. Fr.* 1101 (1963).

isoagathic acid,[32] and of various 1-keto steroids.[31e,32] In these cases, the C.D. curve is probably a composite of *almost* equal positive and negative contributions due to various conformations of the 17-acetyl group, possible solvation of the 20-ketone and/or changes of ring D conformation. The proper discussion of the relative importance of these effects awaits the results of low-temperature C.D. measurements of these compounds, now in progress.

In Table 5, the C.D. maximum of some 20-keto, 16,17-epoxy and cyclopropyl derivatives is reported. The Cotton effect of these α,β-epoxy 20-ketones and α,β-cyclopropyl 20-ketones is characterized by a low intensity. Furthermore, as mentioned

TABLE 5



Compounds	Position of substituents				Circular dichroism maximum of 20-keto-group			Ref.
	3-R_1	4, 5	R_2	R_3	λ_{max} (mμ)	Δε	[θ]	
Va	β OH	5α H	16β H	α-epoxy	300	−0·38	−1,250	13
b	β OAc	Δ⁵	16β H	α-epoxy	296–306	−0·33	−1,090	37
c	β THP	Δ⁵	16β H	α-epoxy	302	−0·38	−1,250	38
d	β OH	Δ⁵	16β H	α-cyclopropyl	278	+0·92	+3,030	39
e	β OH	Δ⁵	16β CH_3	α-epoxy	304	+2·13	+7,020	40
f	β OH	Δ⁵	16α H	β-epoxy	306–314	−0·16	−528	41

earlier,[35] the Cotton effect of α,β-epoxy-cyclohexanones and α,β-cyclopropyl-cyclohexanones seems to follow an "inverted" Octant Rule.[36] Since the above mentioned substances (Table 5) are not cyclohexanone derivatives the problem is still more complicated. Nevertheless, it seems that apart from the probably modified ring D and acetyl side chain conformations, the specific electronic properties associated with the epoxy and cyclopropyl function have a direct bearing on the Cotton effect of the 20-keto grouping. Incidently, in such compounds (Va–Vf) the conformation of the side chain is more rigid than in 17-unsubstituted pregnane derivatives. Furthermore, it is worth while to mention that when the cyclopropane ring is *adjacent* to the cyclohexanone system, as in the diketo steroid (II_t) (Table 2), the cyclopropane ring does not seem to disturb the Cotton effect of the 6-hetone.[13] Indeed, the observed Cotton effect of (II_t) is the arithmetic sum of a 6-keto and a 20-keto function in a 17α-acetyl steroid.

From this study, various conclusions can be drawn. The intensity of the positive

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

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or negative C.D. maximum of the 16,17-*trans*-substituted steroids (Tables 1 and 2) seems to be largely independent of the nature of the 16-substituent, with the exception of the carboxamido group which enhances the Cotton effect. The 16α-substituted 20-keto pregnane derivatives show a C.D. positive maximum slightly higher than the 16-unsubstituted 20-keto pergnane derivatives. Furthermore, the Cotton effect associated with the 17-acetyl side chain in these compounds (Tables 1 and 2) seems to be independent of the nature of substituents and unsaturation in rings A and B. O.R.D. and C.D. examination of 16,17-*cis*-steroids (Tables 3 and 4) indicates that in most cases the *cis*-substitution pattern makes a negative contribution to the Cotton effect. The positive Cotton effect is decreased in most 16,17β-*cis* compounds listed in Table 3 and the negative Cotton effect is increased in most 16,17α-*cis* compounds listed in Table 4.

EXPERIMENTAL

The C.D. curves were obtained at the University of British Columbia, with an apparatus described in Ref. 42, and with a Roussel-Jouan Dichrograph, at the University of Strasburg, through the courtesy of Professor G. Ourisson. The C.D. curves were obtained in dioxane solution, at room temp, with concs ca. 0·1. The position of C.D. maxima as well as the wavelengths at which $[\theta] = 0$ are reported; s refers to a shoulder; Γ is the band-width at half maximum and Γ/2 is reported when the band is not well isolated.[7]

The O.R.D. curves[4] were obtained with a Bellingham and Stanley Spectropolarimeter, at the University of London, through the kind cooperation of Professor W. Klyne, and at Syntex with a Rudolph Spectropolarimeter.

Pregna-1, 4-*diene*-3, 20-*dione* (1b)[8,10]: C.D.: $[\theta]_{332}$ O; $[\theta]_{376}$ −195; $[\theta]_{362}$ −776; $[\theta]_{345}$ −1,356; $[\theta]_{333}$ −1,280, $[\theta]_{292}$ +12,320; $[\theta]_{268}$ +7,440.

3β-*Hydroxy* 16β-*methoxy pregn*-5-*en*-20-*one* 3-*acetate* (Ic):[11] C.D.: $[\theta]_{330}$ O; $[\theta]_{293}$ +11,580; $[\theta]_{250}$ O. Γ = 39 mμ.

3β-*Hydroxy* 16α-*methoxy* 5α-*pregn*-7-*en*-20-*one* 3-*acetate* (Id):[12] A solution of 450 mg 3β-hydroxy 5α-pregn-7,16 dien-20-one 3-acetate[43] in 200 ml dry methanol was saturated with hydrogen chloride.[11] The reaction mixture was poured into water, extracted with ether and washed with water. After drying and evaporation of the solvent a crystalline material was obtained, m.p. 120–130°, which was acetylated with acetic anhydride in pyridine solution at room temp overnight. Acetate (Id) was obtained (365 mg), m.p. 149–150°. Further crystallization from acetone–hexane afforded the analytical sample of 3β-*hydroxy* 16α-*methoxy* 5α-*pregn*-7-*en*-20-*one* 3-*acetate* (Id); m.p. 151–152·5°; $[\alpha]_D$ −9° (*c*, 0·4; $CHCl_3$); C.D.: $[\theta]_{326}$ O; $[\theta]_{315}$ +2,640 (s); $[\theta]_{292}$ +9,900; $[\theta]_{287}$ +9,580 (s); $[\theta]_{267}$ −660. Γ = 34 mμ. λ_{max}^{EtOH} 236 mμ (log ε 3·57) and 302 mμ (log ε 2·64); ν_{max}^{KBr} 1730, 1710 and 1250 cm^{-1}. (Found: C, 74·57; H, 9·50. $C_{24}H_{36}O_4$ requires: C, 74·19; H, 9·34%).

3β,16α-*Dihydroxy* 5α-*pregnan*-20-*one* 3-*acetate* (Ie):[13] C.D.: $[\theta]_{326}$ O; $[\theta]_{293}$ −11,500; $[\theta]_{255}$ −1,180. Γ = 35 mμ.

3β-*Hydroxy* 16α-*cyano pregn*-5-*en*-20-*one* (If):[14] C.D.: $[\theta]_{324}$ O; $[\theta]_{287}$ +14,920; $[\theta]_{238}$ O. Γ = 39 mμ.

3β-*Hydroxy* 16α-*cyano pregn*-5-*en*-20-*one* 3-*acetate* (Ig):[14] C.D.: $[\theta]_{328}$ O; $[\theta]_{286}$ −15,100; $[\theta]_{235}$ O. Γ = 39 mμ.

3β-*Hydroxy* 16α-*cyano* 5α-*pregnan*-20-*one* 3-*acetate* (Ih):[13] C.D.: $[\theta]_{330}$ O; $[\theta]_{295}$ +13,850 (s); $[\theta]_{259}$ +14,530; $[\theta]_{250}$ +990. Γ = 39 mμ.

16α-*Cyano progesterone* (Ii):[14a] C.D.: $[\theta]_{370}$ O; $[\theta]_{362}$ −923; $[\theta]_{345}$ −2,180; $[\theta]_{332}$ −2,900; $[\theta]_{318}$ O; $[\theta]_{308}$ −9,560 (s); $[\theta]_{295}$ +12,090; $[\theta]_{287}$ +12,560; $[\theta]_{281}$ +11,550 (s); $[\theta]_{270}$ +7,920.

3β-*Hydroxy* 16α-*isopropyl pregn*-5-*en*-20-*one* (Ij):[15] C.D.: $[\theta]_{334}$ +468; $[\theta]_{293}$ +14,680; $[\theta]_{266}$ +4,420. Γ = 37 mμ.

[42] A. I. Scott, F. McCapra, F. Comer, S. A. Sutherland, D. W. Young, G. A. Sim and G. Ferguson, *Tetrahedron* **20**, 1339 (1964).

[43a] C. Djerassi, J. Romo and G. Rosenkranz, *J. Org. Chem.* **16**, 754 (1951); [b] W. V. Ruyle, E. M. Chamberlin, J. M. Chemerda, G. E. Sita, L. M. Aliminosa and R. L. Erickson, *J. Amer. Chem. Soc.* **74**, 5929 (1952).

3β-Hydroxy 6-methyl 16α-isopropyl pregn-5-en-20-one (Ik):[15] C.D.: $[\theta]_{330}$ O; $[\theta]_{304}$ +16,500; $[\theta]_{291}$ +16,300 (s); $[\theta]_{267}$ +3,400. Γ = 37 mμ.

6α-Methyl 16α-isopropyl progesterone (I_1):[15] C.D.: $[\theta]_{372}$ O; $[\theta]_{360}$ −1,950; $[\theta]_{343}$ −3,585; $[\theta]_{331}$ −4,770; $[\theta]_{293}$ +14,000; $[\theta]_{265}$ +4,660.

3β-Hydroxy 16α-methyl 5α-pregnan-20-one 3-acetate (Im):[16] C.D.: $[\theta]_{330}$ O; $[\theta]_{303}$ +12,880 (s); $[\theta]_{292}$ +15,850; $[\theta]_{288}$ +15,500 (s); $[\theta]_{269}$ +6,930. Γ = 39 mμ.

3β-Hydroxy 16α-dicarboxymethyl pregn-5-en-20-one (In):[17] C.D.: $[\theta]_{324}$ O; $[\theta]_{305}$ +8,080 (s); $[\theta]_{290}$ +16,200; $[\theta]_{264}$ +3,460. Γ = 34 mμ.

3β-Hydroxy 16α-dicarbethoxymethyl pregn-5-en-20-one 3-acetate (Io):[14c] C.D.: $[\theta]_{332}$ O; $[\theta]_{292}$ +14,750; $[\theta]_{248}$ +680. Γ = 39 mμ.

3β-Hydroxy 16α-carboxamido pregn-5-en-20-one (Ip):[18] C.D.: $[\theta]_{332}$ O; $[\theta]_{292}$ +16,500; $[\theta]_{240}$ O. Γ = 39 mμ.

16α-Carboxy progesterone (Iq):[18] C.D.: $[\theta]_{370}$ O; $[\theta]_{362}$ −990 (s); $[\theta]_{344}$ −2,442 (s); $[\theta]_{330}$ −3,760; $[\theta]_{316}$ O; $[\theta]_{301}$ +9,040 (s); $[\theta]_{288}$ +12,220; $[\theta]_{274}$ +8,580.

16α-Carbomethoxy progesterone (Ir):[18] C.D. (Fig. I): $[\theta]_{370}$ −627; $[\theta]_{360}$ −1,190 (s); $[\theta]_{343}$ −3,630 (s); $[\theta]_{330}$ −4,950 (s); $[\theta]_{323}$ −3,300 (s); $[\theta]_{316}$ O; $[\theta]_{301}$ +9,900 (s) $[\theta]_{288}$ +13,600; $[\theta]_{270}$ +7,800.

16α-Acetyl progesterone (Is):[18] C.D. (Fig. I): $[\theta]_{374}$ O; $[\theta]_{360}$ −1,020; $[\theta]_{345}$ −3,210; $[\theta]_{332}$ −4,270; $[\theta]_{290}$ +15,680; $[\theta]_{262}$ +6,180.

3β-Hydroxy 17α-pregn-5-en-20-one 3-acetate (IIa):[19] C.D.: $[\theta]_{334}$ O; $[\theta]_{303}$ −6,670 (s); $[\theta]_{298}$ −8,900; $[\theta]_{279}$ −6,800 (s); $[\theta]_{256}$ −1,320. Γ = 40 mμ.

17α-Progesterone (IIb):[19] C.D.: $[\theta]_{374}$ O; $[\theta]_{360}$ −990 (s); $[\theta]_{346}$ −2,975; $[\theta]_{331}$ −3,830; $[\theta]_{303}$ −673 (s); $[\theta]_{295}$ −7,460 (s); $[\theta]_{289}$ −7,580; $[\theta]_{270}$ −3,470.

1-Dehydro 17α-progesterone (IIc):[10] C.D.: $[\theta]_{360}$ −932; $[\theta]_{324}$ −1,165; $[\theta]_{292}$ −7,780; $[\theta]_{266}$ −1,180.

3β-Hydroxy 16α-carboxy 17α-pregn-5-en-20-one (IId):[14,18] C.D.: $[\theta]_{328}$ O; $[\theta]_{319}$ −1,090 (s); $[\theta]_{309}$ −5,940 (s); $[\theta]_{295}$ −7,260 (s); $[\theta]_{289}$ −8,700; $[\theta]_{280}$ −7,090 (s); $[\theta]_{250}$ −1,090. Γ = 37 mμ.

3β-Hydroxy 16β-carboxy 17α-pregn-5-en-20-one 3-acetate (IIe):[18] C.D.: $[\theta]_{324}$ O; $[\theta]_{307}$ −413 (s); $[\theta]_{294}$ −8,440 (s); $[\theta]_{289}$ −9,030; $[\theta]_{285}$ −8,550 (s); $[\theta]_{262}$ −3,300 (s); $[\theta]_{250}$ −792. Γ = 38 mμ.

3β-Hydroxy 16β-carboxy 5α, 17α-pregnan-20-one 3-acetate (IIf):[13] C.D.: $[\theta]_{328}$ O; $[\theta]_{317}$ −1,024 (s); $[\theta]_{289}$ −9,220; $[\theta]_{260}$ −858. Γ = 39 mμ.

3β-Hydroxy 16β-carbomethoxy 17α-pregn-5-en-20-one 3-acetate (IIg):[18] C.D.: $[\theta]_{327}$ O; $[\theta]_{289}$ −9,530; $[\theta]_{255}$ −1,650. Γ = 38 mμ.

3,5α-Cyclo 6β-hydroxy 16β-carbomethoxy 17α-pregnan-20-one (IIh):[13] C.D.: $[\theta]_{328}$ O: $[\theta]_{321}$ −627 (s); $[\theta]_{302}$ −5,940 (s): $[\theta]_{291}$ −9,700; $[\theta]_{288}$ −9,070 (s); $[\theta]_{260}$ −1,090. Γ = 39 mμ.

16β-Carbomethoxy 17α-progesterone (IIi):[18] C.D. (Fig. I): $[\theta]_{380}$ O; $[\theta]_{359}$ −1,012 (s); $[\theta]_{345}$ −3,130; $[\theta]_{332}$ −4,280; $[\theta]_{292}$ −8,580; $[\theta]_{260}$ −3,150.

3β-Hydroxy 16β-hydroxymethyl 17α-pregn-5-en-20-one (IIj):[20] C.D.: $[\theta]_{324}$ O; $[\theta]_{286}$ −8,770; $[\theta]_{251}$ −1,618. Γ = 36 mμ.

16β-Hydroxymethyl 17α-progesterone (IIk):[20] C.D.: $[\theta]_{374}$ O; $[\theta]_{359}$ −970 (s); $[\theta]_{345}$ −2,910; $[\theta]_{332}$ −3,920; $[\theta]_{292}$ −7,610; $[\theta]_{268}$ −3,850.

16β-Hydroxymethyl 17α-progesterone acetate (IIl):[20] C.D.: $[\theta]_{276}$ O; $[\theta]_{359}$ −1,072 (s); $[\theta]_{345}$ −3,270; $[\theta]_{332}$ −4,370; $[\theta]_{292}$ −8,250; $[\theta]_{262}$ −1,020.

3β-Hydroxy 16β-cyano 17α-pregn-5-en-20-one 3-acetate (IIm):[21] C.D.: $[\theta]_{324}$ O; $[\theta]_{286}$ −9,410; $[\theta]_{271}$ −6,600. Γ/2 = 17 mμ.

16β-Methyl 17α-progesterone (IIn):[22] C.D.: $[\theta]_{378}$ O; $[\theta]_{360}$ −1,135 (s); $[\theta]_{346}$ −3,320; $[\theta]_{333}$ −4,640; $[\theta]_{318}$ −6,000; $[\theta]_{294}$ −8,500; $[\theta]_{260}$ −2,900.

3β-Hydroxy 16β-carboxamido 5α,17α-pregnan-20-one 3-acetate (IIo):[13] C.D.: $[\theta]_{328}$ O; $[\theta]_{290}$ −10,390; $[\theta]_{250}$ −860. Γ = 37 mμ.

3β-Hydroxy 16β-carboxamido 17α-pregn-5-en-20-one 3-acetate (IIp):[18] C.D.: $[\theta]_{334}$ O; $[\theta]_{290}$ −10,500; $[\theta]_{284}$ −9,800 (s); $[\theta]_{244}$ −750. Γ = 40 mμ.

16β-Carboxamido 17α-progesterone (IIq):[18] C.D.: $[\theta]_{378}$ O; $[\theta]_{364}$ −860 (s); $[\theta]_{345}$ −3,380; $[\theta]_{332}$ −4,400; $[\theta]_{290}$ −10,320; $[\theta]_{262}$ −4,060.

3β-Hydroxy 16β-carbox [diethylamido] 17α-pregn-5-en-20-one 3-acetate (IIr):[18] C.D.: $[\theta]_{327}$ O; $[\theta]_{294}$ −9,900 (s); $[\theta]_{287}$ −10,900; $[\theta]_{276}$ −1,300. Γ = 43 mμ.

16β-Acetyl 17α-progesterone (IIs):[18] C.D. (Fig. I): $[\theta]_{378}$ O; $[\theta]_{360}$ −1,030; $[\theta]_{330}$ −3,090; $[\theta]_{288}$ −13,800; $[\theta]_{264}$ −7,680.

3,5α-*Cyclo* 16β-*carbomethoxy* 17α-*pregnane*-6,20-*dione* (IIt):[12] C.D.: $[\theta]_{328}$ O; $[\theta]_{291}$ −14,530; $[\theta]_{260}$ −2,970. Γ = 37 mμ.

3β-*Hydroxy* 16β-*carbomethoxy pregn*-5-*en*-20-*one* 3-*acetate* (IIIc):[18] C.D.: $[\theta]_{335}$ O; $[\theta]_{298}$ + 11,650(s); $[\theta]_{290}$ + 12,150; $[\theta]_{248}$ + 1,460. Γ = 43 mμ. R.D.: cf. Ref. 2. Some quantitative variations in the R.D. amplitude as well as in the C.D. intensity have been observed in different solvents. This property is currently being examined by C.D. low temperature measurements.

16β-*Carbomethoxy progesterone* (IIId):[18] C.D.: $[\theta]_{370}$ −627; $[\theta]_{350}$ −1,452; $[\theta]_{346}$ −3,170; $[\theta]_{332}$ −4,320; $[\theta]_{323}$ −2,505 (s); $[\theta]_{317}$ O; $[\theta]_{297}$ +10,340 (s); $[\theta]_{290}$ +11,220; $[\theta]_{270}$ +5,940.

3β-*Hydroxy* 16β-*cyano pregn*-5-*en*-20-*one* 3-*acetate* (IIIe):[21] C.D.: $[\theta]_{343}$ O; $[\theta]_{290}$ +7,360; $[\theta]_{239}$ O. Γ = 41 mμ. R.D.: (C, 0·02; CH_3OH): $[\Phi]_{700}$ +96°; $[\Phi]_{589}$ + 120°; $[\Phi]_{316}$ +3,570°; $[\Phi]_{270}$ −5,790°; $[\Phi]_{267.5}$ −5,600°.

3β-*Hydroxy* 16β-*carboxy pregn*-5-*en*-20-*one* (IIIf):[18] C.D.: $[\theta]_{328}$ O; $[\theta]_{290}$ +4,620; $[\theta]_{250}$ +205. Γ = 39 mμ. R.D.: cf. Ref. 2,

3β-*Hydroxy* 16β-*methyl* 5α-*pregnan*-20-*one* 3-*acetate* (IIIg):[16] C.D.: $[\theta]_{360}$ O; $[\theta]_{321-307}$ +693; $[\theta]_{297}$ O; $[\theta]_{271}$ +870 (s).

3β-*Hydroxy* 16β-*methyl pregn*-5-*en*-20-*one* (IIIh):[16] C.D. (Fig. I): $[\theta]_{360}$ O; $[\theta]_{344}$ −112; $[\theta]_{334}$ O; $[\theta]_{326}$ −340; $[\theta]_{320}$ +200; $[\theta]_{314}$ +205; $[\theta]_{308}$ O; $[\theta]_{285}$ −685; $[\theta]_{260}$ −385. R.D. (C, 0·1; Dioxane): $[\Phi]_{700}$ 0°; $[\Phi]_{589}$ −26°; $[\Phi]_{325}$ +76°; $[\Phi]_{320}$ −310°; $[\Phi]_{312.5}$ −488°; $[\Phi]_{307.5}$ −700°.

3β-*Hydroxy* 16β-*methyl pregn*-5-*en*-20-*one* 3-*acetate* (IIIi):[16] C.D.: $[\theta]_{342}$ O; $[\theta]_{321}$ +726; $[\theta]_{313}$ +584 (s); $[\theta]_{301}$ O; $[\theta]_{271}$ −825 (s). R.D. (C, 0·1; CH_3OH): $[\Phi]_{700}$ 0°; $[\Phi]_{589}$ −54°; $[\Phi]_{315}$ +158°; $[\Phi]_{307.5}$ −228°; $[\Phi]_{302.5}$ −264°.

16β-*Methyl progesterone* (IIIj):[16] C.D. (Fig. I): $[\theta]_{350}$ O; $[\theta]_{330}$ −926 (s); $[\theta]_{344}$ −3,480; $[\theta]_{332}$ −4,240; $[\theta]_{320}$ −3,540; $[\theta]_{307}$ −2,380; $[\theta]_{296}$ −1,618; $[\theta]_{268}$ −780.

3β-*Hydroxy* 16α-*dicarbethoxymethyl* 17α-*pregn*-5-*en*-20-*one* 3-*acetate* (IVc):[17] C.D.: $[\theta]_{324}$ O; $[\theta]_{290}$ −7,580; $[\theta]_{254}$ −1,750. Γ = 39 mμ. R.D. (C, 0·05; CH_3OH): $[\Phi]_{700}$ −212°; $[\Phi]_{589}$ −253°; $[\Phi]_{302.5}$ −5,900°; $[\Phi]_{260}$ +3,790°; $[\Phi]_{250}$ +3,310°.

16α-*Methyl* 17α-*progesterone* (IVd):[10] C.D.: $[\theta]_{370}$ O; $[\theta]_{340}$ −4,230 (s); $[\theta]_{325}$ −5,870 (s); $[\theta]_{314}$ −7,980 (s); $[\theta]_{303-289}$ −8,900; $[\theta]_{269}$ −3,770.

3β-*Hydroxy* 16α-*dicarbethoxymethyl* 5α-*chloro*, 17α-*pregnan*-20-*one* 3-*acetate* (IVe):[17] C.D.: $[\theta]_{324}$ O; $[\theta]_{286}$ −9,900; $[\theta]_{267}$ −5,810. Γ/2 = 18·5 mμ. R.D. (C, 0·1; CH_3OH): $[\Phi]_{700}$ −194°; $[\Phi]_{589}$ −298°; $[\Phi]_{300}$ −5,640°; $[\Phi]_{257.5}$ +4,120°; $[\Phi]_{252.5}$ +4,030°.

3β-*Hydroxy* 16α-*dicarboxymethyl* 17α-*pregn*-5-*en*-20-*one* (IVf):[17] C.D.: $[\theta]_{320}$ −1,560; $[\theta]_{285}$ −10,000; $[\theta]_{266}$ −5,900. Γ/2 = 18 mμ. R.D. (C, 0·06; CH_3OH): $[\Phi]_{700}$ −185°; $[\Phi]_{589}$ −408°; $[\Phi]_{300}$ −6,400°; $[\Phi]_{260}$ +3,660°; $[\Phi]_{250}$ +3,220°.

3β-*Hydroxy* 16α-*carbomethoxy* 5α,17α-*pregnan*-20-*one* 3-*acetate* (IVg):[18] C.D.: $[\theta]_{330}$ O; $[\theta]_{301}$ −9,660 (s); $[\theta]_{290}$ −12,710; $[\theta]_{277}$ −9,230 (s); $[\theta]_{250}$ −1,090. Γ = 37 mμ. D.R.: cf. Ref. 13.

3β-*Hydroxy* 16α-*carbomethoxy* 17α-*pregn*-5-*en*-20-*one* 3-*acetate* (IVh):[18] C.D.: $[\theta]_{321}$ −759; $[\theta]_{293}$ −13,390; $[\theta]_{287}$ −13,300 (s); $[\theta]_{251}$ −2,210. Γ = 39 mμ. D.R.: cf. Ref. 2.

16β-*Carbomethoxy* 17α-*progesterone* (IVi):[18] C.D.: $[\theta]_{370}$ O; $[\theta]_{350}$ −1,050; $[\theta]_{346}$ −3,270; $[\theta]_{331}$ −4,440; $[\theta]_{293}$ −11,690; $[\theta]_{263}$ −3,300. D.R.: cf. Ref. 2.

3β-*Hydroxy* 16,17α-*epoxy* 5α-*pregnan*-20-one (Va):[13] C.D.: $[\theta]_{334}$ O; $[\theta]_{300}$ −1,250; $[\theta]_{276}$ −429. Γ = 33 mμ.

3β-*Hydroxy* 16,17α-*epoxy pregn*-5-en-20-*one* 3-*acetate* (Vb):[37] C.D.: $[\theta]_{336}$ O; $[\theta]_{306-296}$ −1,090; $[\theta]_{266}$ −462. Γ = 55 mμ.

3β-*Hydroxy* 16,17α-*epoxy pregn*-5-*en*-20-*one* 3-*tetrahydro pyranyl ether* (Vc):[38] C.D.: $[\theta]_{336}$ O; $[\theta]_{314}$ −1,155 (s); $[\theta]_{302}$ −1,250; $[\theta]_{286}$ −958 (s); $[\theta]_{268}$ −462. Γ = 47 mμ.

3β-*Hydroxy* 16,17α-*cyclopropyl pregn*-5-*en*-20-*one* (Vd):[39] C.D.: $[\theta]_{297}$ +495; $[\theta]_{289}$ +1,587 (s); $[\theta]_{278}$ +3,030; $[\theta]_{265}$ −1,587. Γ/2 = 13 mμ.

3β-*Hydroxy* 16β-*methyl* 16,17α-*epoxy-pregn*-5-*en*-20-*one* (Ve):[40] C.D.: $[\theta]_{340}$ O; $[\theta]_{326}$ +3,238 (s); $[\theta]_{313}$ +6,240 (s); $[\theta]_{304}$ +7,020; $[\theta]_{288}$ +260. Γ = 42 mμ.

3β-*Hydroxy* 16,17β-*epoxy pregn*-5-*en*-20-*one* (Vf):[41] C.D.: $[\theta]_{330}$ −33; $[\theta]_{314-306}$ −528; $[\theta]_{292}$ −33. Γ = 22 mμ.

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