

921. Nitro-steroids. Part IV.¹ Circular Dichroism and Conformation of Nitro-steroids

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The circular dichroism (c.d.) of 5α -steroids with 3β , 3α -, 4β -, 4α -, 6β -, 6α -, 7β -, 7α -, and 17β -nitro-groups and of 4β - and 4α -nitro- 5β -cholestane, as well as of some related compounds (*inter alia* geminal chloronitro- and dinitro-steroids), has been measured. A generalisation of the octant rule is suggested which is applicable to all optically active ${}^1A_1 \rightarrow {}^1A_2$ (point group C_{2v}) transitions. The Cotton effect of asymmetric axial nitrocyclohexanes is governed by the torsion angle of the nitro-group about the C-N bond; for equatorial nitrocyclohexanes with a torsion angle of 0 or 90° the sign of the Cotton effect is the opposite of that given by the octant rule for the corresponding ketones. The energetically most favoured conformation of an axial or equatorial nitro-group in a nitrocyclohexane without any other interfering substituents is that in which the torsion angle with respect to the geminal hydrogen atom is 90° . The Cotton effects of the *gem*-chloronitro-compounds support these rules. The high circular dichroism of two $\beta\gamma$ -unsaturated nitro-steroids is due to inherent dissymmetry of the chromophore.

THE nitro-group is a chromophore which exhibits a Cotton effect if the environment is dissymmetric. A summary of earlier optical rotatory dispersion (o.r.d.) work as well as some new measurements of nitro-steroids, undertaken for comparison of o.r.d. and circular dichroism (c.d.), has been published recently by Djerassi and his co-workers.² The Oxford authors (Part II) have now prepared a series of many different nitro-steroids and by examining these compounds it seems possible to correlate the Cotton effect and the conformation of the nitro-group in different positions.

It is generally assumed that the long-wavelength absorption of the nitro-group at about $280\text{ m}\mu$ is due to an $n \rightarrow \pi^*$ transition.³⁻⁷ The p_y -orbitals of the two oxygen atoms interfere with one another, thus giving rise to a symmetric (n_s) and an antisymmetric (n_a) combination (Figure 1). The corresponding transitions are of the type ${}^1A_1 \rightarrow {}^1B_1$ ($n_s \rightarrow \pi_3^*$) and ${}^1A_1 \rightarrow {}^1A_2$ ($n_a \rightarrow \pi_3^*$) (point group C_{2v}), the first being allowed, the second forbidden. As the overlap integral is very small in both, the allowed transition should give a low intensity band. The ketone $n \rightarrow \pi^*$ transition is of the type ${}^1A_1 \rightarrow {}^1A_2$: the $n_a \rightarrow \pi_3^*$ transition of the nitro-compounds is therefore said to correspond to the $280\text{ m}\mu$ band, the $n_s \rightarrow \pi_3^*$ transition occurring at shorter wavelength. Most authors assume the latter absorption to appear in the vacuum ultraviolet region, but a recent estimation by McEwen⁷ gives a blue shift of only about $10\text{ m}\mu$ relative to the $n_a \rightarrow \pi_3^*$ band.

This situation is now complicated by the appearance of another optically active band² near $350\text{ m}\mu$, which has not previously been detected by ultraviolet spectroscopy. With most of the nitro-compounds described in this Paper we also find this second circular dichroic band; the sign of its ellipticity is sometimes the same as, and sometimes the

¹ Part III, J. R. Bull, J. P. Jennings, W. Klyne, G. D. Meakins, P. M. Scopes, and G. Snatzke, *J.*, 1965, 3152. This Paper also formed Part V of the series "Circular Dichroism," by G. Snatzke and his co-workers. Part IV, G. Snatzke and D. Becher, *Tetrahedron*, 1964, **20**, 192.

² C. Djerassi, H. Wolf, and E. Bunnenberg, *J. Amer. Chem. Soc.*, 1963, **85**, 2835. I thank Professor C. Djerassi for sending me details of his work before publication.

³ F. A. Matsen, in A. Weissberger's "Technique of Organic Chemistry," Interscience Publishers, New York, 1965, vol. IX, p. 629. The treatment of the nitro-group follows that of the carboxylate iron by H. L. McMurry, *J. Chem. Phys.*, 1942, **10**, 655; W. West in A. Weissberger, *op. cit.*, 1960, vol. I, Part III, p. 1799. H. H. Jaffé and M. Orchin, "Theory and Application of Ultraviolet Spectroscopy," John Wiley and Sons, Inc., New York, 1962, p. 182.

⁴ S. Nagakura, *Mol. Phys.*, 1960, **3**, 152.

⁵ A. Balasubramanian and C. N. R. Rao, *Spectrochim. Acta*, 1962, **18**, 1337.

⁶ N. S. Bayliss and E. G. McRae, *J. Phys. Chem.*, 1954, **58**, 1006.

⁷ K. L. McEwen, *J. Chem. Phys.*, 1960, **32**, 1801.

opposite of that of the 280 m μ band. The occurrence of this new band could be explained by assuming either that it belongs to the $n_a \rightarrow \pi_3^*$ transition and that the $n_s \rightarrow \pi_3^*$ transition corresponds to the 280 m μ band, or that the d -orbitals are involved (the second possibility corresponding to the treatment of the Cotton effect of ketones by Moscovitz⁸). The first assumption seems less probable in that it does not take account of the striking similarity between the C=O and NO₂ absorption. However, the possibility that solvated or dimeric forms⁹ are involved cannot be excluded. In her calculation of the energy levels in nitromethane, McEwen⁷ assumed that the 280 m μ band arises from the allowed ${}^1A_1 \rightarrow {}^1B_1$ transition and gave the forbidden transition the oscillator strength of zero.

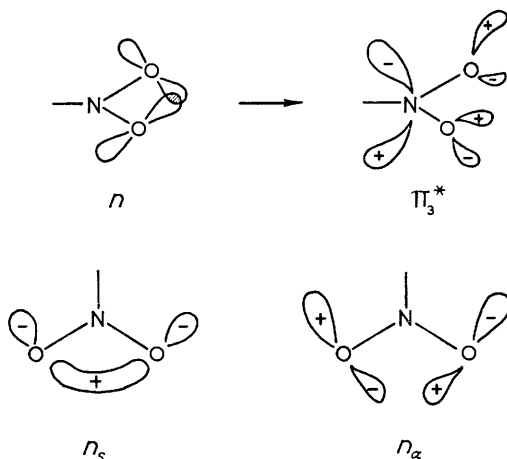


FIGURE 1. Orbitals involved in the $n \rightarrow \pi^*$ transition of nitro-compounds

The energy difference between the two $n \rightarrow \pi_3^*$ transitions is calculated to be as small as 0.15 eV; the ${}^1A_1 \rightarrow {}^1A_2$ band must then occur at about 270 m μ , in which case a separation of the two $n \rightarrow \pi_3^*$ bands in the spectrum seems improbable.

One characteristic feature of such $n \rightarrow \pi^*$ transitions is the blue shift of the maximum in going from non-polar to polar solvents,¹⁰ which is ascribed to different solvation of the ground and excited states. A small shift has indeed been noticed with simple nitroalkanes^{5,10,11} but not with nitro-steroids.^{1,2} This might be due to the semipolar character of the nitro-group, where both states have greater dipole moments, or to operation of the polarisation red shift.^{6,12}

The appearance of a Cotton effect requires an asymmetric molecule (no symmetry element), or at least a dissymmetric molecule (no alternating axis of symmetry). The NO₂ group belongs to the point group C_{2v} and therefore a c.d. is possible only when the rest of the molecule is optically active by itself or when it is attached asymmetrically to the chromophore. In both these cases, however, the free rotation around the C-N bond must be more or less restricted. Similarly, the strong Cotton effect of steroidal 20-ketones is ascribed to the adoption of one or more preferred conformations of the side-chain, and consideration of the amplitudes has been used to indicate these conformations in substituted pregnan-20-ones.¹³

⁸ A. Moscovitz, *Adv. Chem. Phys.*, 1962, **4**, 67.

⁹ In some solvents nitro-compounds do not obey Beer's law; P. A. D. de Maine, M. M. de Maine, and A. G. Goble, *Trans. Faraday Soc.*, 1957, **53**, 427.

¹⁰ H. McConnell, *J. Chem. Phys.*, 1952, **20**, 700.

¹¹ H. E. Ungnade and R. A. Smiley, *J. Org. Chem.*, 1956, **21**, 993; R. N. Haszeldine, *J.*, 1953, 2525.

¹² N.-S. Bayliss and E. G. McRae, *J. Phys. Chem.*, 1954, **58**, 1002.

¹³ C. Djerassi, I. Fornaguera, and O. Mancera, *J. Amer. Chem. Soc.*, 1959, **81**, 2382; J. Danilewicz and W. Klyne, *J.*, 1962, 4950, and unpublished work; P. Crabbé, *Tetrahedron*, 1963, **19**, 51; G. Snatzke, H. Pieper, and R. Tschesche, *ibid.*, 1964, **20**, 107, and unpublished work.

The Cotton effect of most of the saturated ketones can be interpreted on the basis of the octant rule,¹⁴ an understanding of which follows from theoretical calculations.⁸ If we assume that the basic principles of the octant rule hold with the nitro-compounds also, then it follows from the above symmetry considerations that the rule should be applied only to the $n_a \rightarrow \pi_3^*$ transition. As will be shown later, it is in fact the 280-m μ band which can be treated in this way.

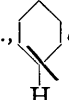
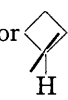
The analogy between ketones and nitro-compounds is further emphasised if we treat them together in a more general way. To this end the whole molecule is divided into

TABLE I
Possible elements of dissymmetry in cycloalkanes and nitrocycloalkanes

Sphere	$>C=O$	$\begin{array}{c} >C-NO_2 \\ \\ R \end{array}$
1	Chromophore itself	Chromophore itself
2	Ring containing the carbonyl group	Ring to which the NO_2 group is attached: (a) torsion of NO_2 relative to the ring (b) the ring itself
3	Substituents or condensed rings directly bonded to the second sphere	Substituents or condensed rings directly bonded to second sphere
4	More remote atoms	More remote atoms

"spheres," beginning with the chromophore and then progressing to the more remote atoms. For cycloalkanones this conception is illustrated in Table I. It may be postulated that the sphere with pronounced dissymmetry which is nearest to the chromophore mainly determines the Cotton effect and that the more remote ones have only minor influence. Thus in cyclohexanones with the ring in a chair conformation the third (and fourth) sphere determines the Cotton effect according to the octant rule.¹⁴ However, in cyclopentanones and those cyclohexanones whose carbonyl group forms the "point" of a twist conformation the dissymmetry of the ring (*i.e.*, the second sphere) governs the Cotton effect.¹⁵ With nonplanar $\alpha\beta$ -unsaturated¹⁶ and certain $\beta\gamma$ -unsaturated¹⁷ ketones the carbonyl group itself becomes dissymmetric, and here the first sphere does indeed determine the sign of the Cotton effect.

The analogous treatment of nitrocycloalkanes shown in Table I helps us to understand the c.d. of these compounds. The first, third, and fourth spheres have the same qualities as before. The second sphere of the nitro-compounds may become dissymmetric in two ways, either by deviation of the ring from a symmetrical (for cyclohexanes, chair) conformation or by torsion of the nitro-group in an asymmetrical manner, *i.e.*, to give an angle τ which is not 0 or 90°. The definition of τ by Klyne and Prelog¹⁸ is used. For a convenient notation τ (which can assume a value from -90 to +90°) is given as a sub-

script to "a" for an axial and "e" for an equatorial NO_2 group, *e.g.*,  a_{+45} or  e_{-20} .

For a nitro-group on a double bond the *a/e* differentiation no longer applies; in this case $\tau = 90^\circ$ corresponds to a planar conformation. The four possible symmetrical arrangements of a nitrocyclohexane, which will be the most stable ones in the absence of other

¹⁴ W. Moffitt, R. B. Woodward, A. Moscovitz, W. Klyne, and C. Djerassi, *J. Amer. Chem. Soc.*, 1961, **83**, 4013.

¹⁵ W. Klyne, *Tetrahedron*, 1961, **13**, 29; C. Djerassi and W. Klyne, *Proc. Nat. Acad. Sci. U.S.A.*, 1962, **48**, 1093.

¹⁶ $n \rightarrow \pi^*$ transition: (a) W. B. Whalley, *Chem. and Ind.*, 1962, 1024; (b) G. Snatzke, *Tetrahedron*, 1965, **21**, 413; $\pi \rightarrow \pi^*$ transition: (c) C. Djerassi, R. Records, E. Bunnenberg, K. Mislow, and A. Moscovitz, *J. Amer. Chem. Soc.*, 1962, **84**, 870.

¹⁷ See, *e.g.*, A. Moscovitz, K. Mislow, M. A. W. Glass, and C. Djerassi, *J. Amer. Chem. Soc.*, 1962, **84**, 1945; R. C. Cookson and J. Hudec, *J.*, 1962, 429.

¹⁸ W. Klyne and V. Prelog, *Experientia*, 1960, **16**, 521.

substituents, are shown in Figure 2. If one of them is adopted the third or fourth sphere must be dissymmetric to bring about a Cotton effect. Models of the Dreiding and Stuart-Briegleb type were used to estimate which kinds of dissymmetry were present.

Nitro-steroids with an Axial Nitro-group.—The c.d. of 4 β -nitro-5 α -cholestane (I) and its 6 β -analogue (IV) are enantiomeric (Figure 3); this striking symmetry with respect to the λ -axis holds for the secondary band also. Inspection of models shows that the nitro-group is almost completely "fixed," the hindrance to free rotation being introduced by

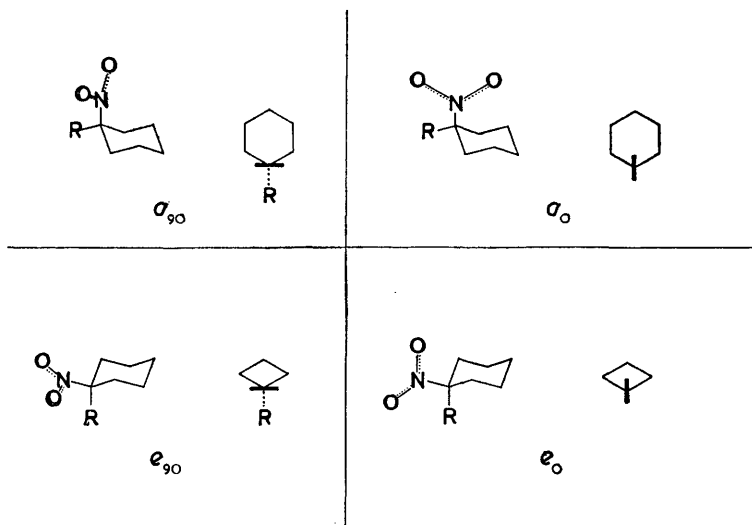
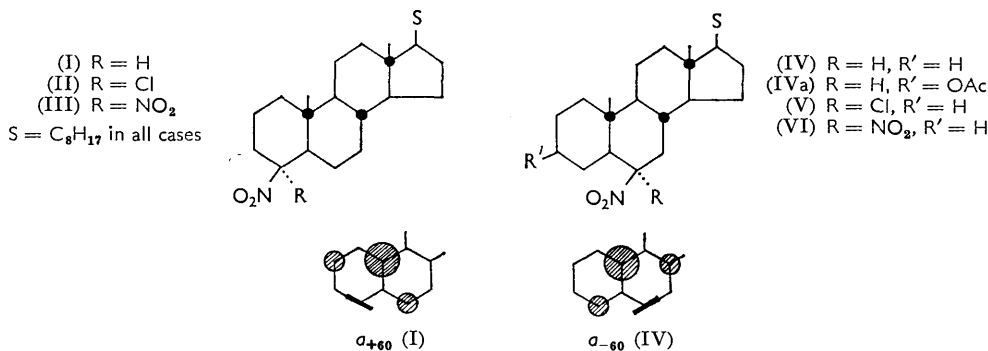


FIGURE 2. Symmetrical conformations of nitrocyclohexanes

the C-10 methyl group and the two axial hydrogen atoms [2 β -H and 6 β -H for (I) and 4 β -H and 8 β -H for (IV)]. The chromophore must therefore adopt the a_{+60} conformation in the first and the a_{-60} conformation in the second compound. Thus the second sphere is



asymmetric and should, according to the suggested generalisations, govern the Cotton effect. It follows from Figure 3 that with an axial nitro-compound a positive torsion angle, τ , leads to a positive c.d. and a negative τ to a negative effect: it also follows that different environments of the ring which bears the nitro-group have virtually no influence upon the magnitude of $\Delta\epsilon$. [The dichrogram of the 3 β -acetoxy-compound (IVa) is identical with that of compound (IV); see Experimental section.] Axial and equatorial nitro-steroids are treated separately, as in the compounds investigated the second sphere is dissymmetric for the first and symmetric for the latter. The rule given for the axial

compounds is possibly just a special form of the modified treatment given below. Application of this would also lead to the correct sign of the c.d., but the striking similarity between the curves of compounds (I) and (IV) is then lost.¹⁹

Rotation of the nitro-group in 4 α -nitro-5 β -cholestane (VII) is again severely restricted by steric interference from the 2 α -H, 7 α -H, and 9 α -H. The torsion angle, τ , is expected to be about -40° : a negative Cotton effect is therefore predicted, in agreement with the observed $\Delta\epsilon_{\text{max}}$ of -1.64 (Figure 3). The interactions on the rear side of ring A might also cause a small distortion of this ring. Free rotation of the nitro-group in 7 α -nitro-5 α -cholestane (VIII) is hindered by the 5 α -, 9 α -, 14 α -, and 15 α -hydrogens, but the situation differs from the previous cases in that three conformations can be adopted here by the

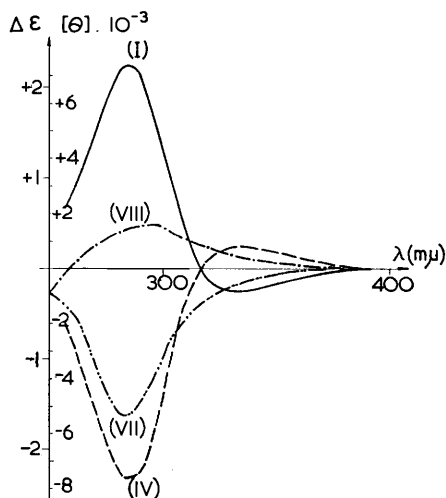
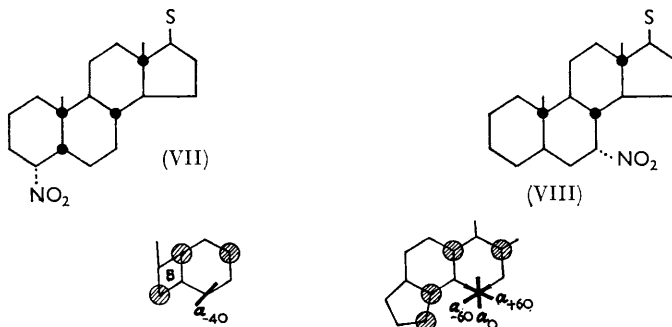


FIGURE 3. Circular dichroism of axial nitro-steroids (I), (IV), (VII), and (VIII)

nitro-group. The a_{+60} and a_{-60} conformations should give positive and negative effects, respectively, whereas for the a_0 conformation the third sphere is determinant. As the relative populations of these three conformations are unknown a prediction of the sign of

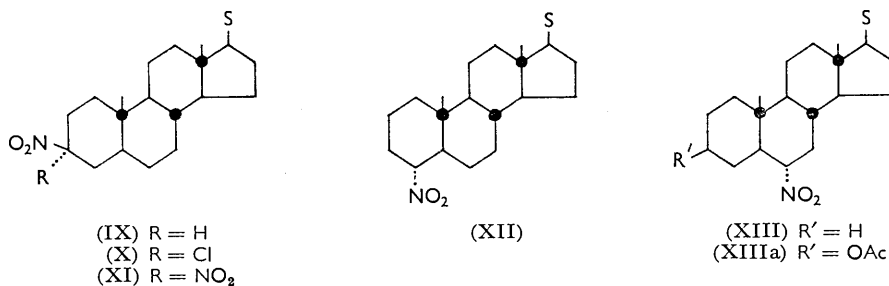


the c.d. is difficult. The a_{-60} conformation will be destabilised relative to the a_{+60} form by greater Pitzer strain and from these two forms a net positive c.d. is expected. From the measured value $\Delta\epsilon_{\text{max}}$ ($+0.48$; Figure 3) it appears either that the population of the a_0 conformation is quite small, or that its contribution to the Cotton effect is positive or very low. The other axial nitro-compound measured, 3 α -nitro-5 α -cholestane (XXVI), will be discussed later.

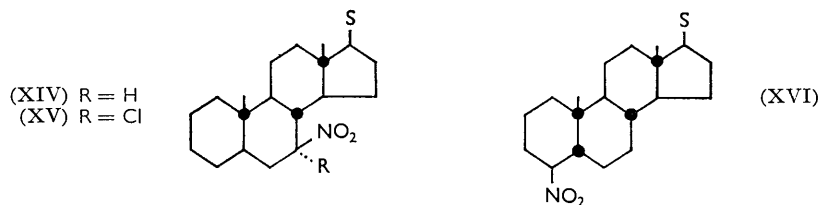
Nitro-steroids with an Equatorial Nitro-group.—With most of the compounds investigated the nitro-group is to some extent restricted in its rotation. This does not mean

¹⁹ I thank Professor Klyne for drawing my attention to this point.

that only one conformation is adopted by the nitro-group, but that the population of the most stable conformation is considerably higher than that of the others. The contributions of the latter to the c.d. largely cancel, and the compounds can be treated as having a fixed conformation which is adopted by only a certain percentage of the molecules.

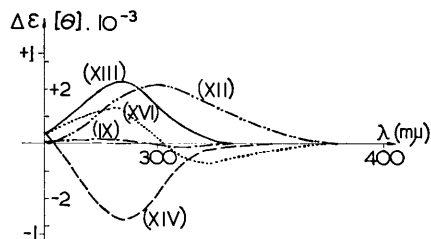


Molecular models show that in the equatorial nitro-steroids, (XII), (XIII), (XIV), and (XVI), the most stable conformation is always the e_0 : the alternative involves more unfavourable interactions. The degree of hindrance to free rotation is similar in compounds (XII), (XIII), and (XVI), but for 7 β -nitro-5 α -cholestane (XIV) the percentage of



“ effective active molecules ” is higher because its nitro-group is more nearly fixed.* The c.d. curves are shown in Figure 4. The most obvious difference from the corresponding axial compounds is that the curves for compounds (XII) and (XIII) are not of the enantiomeric type, though the relation of these two substances to one another is the same as that between compounds (I) and (IV). The 3 β -acetoxy-group of compound (XIIIa) has no influence (see Experimental section).

FIGURE 4. Circular dichroism of equatorial nitro-steroids (IX), (XII), (XIII), (XIV), and (XVI)



To rationalise these data we must resort to the general principles of the octant rule¹⁴ because in compounds (IX), (XII), (XIII), (XIV), and (XVI) the first and second spheres are symmetrical, and the spatial distribution of the atoms in the third (and fourth) spheres should therefore determine the Cotton effect. To apply a rule similar to the octant rule for ketones (which states that the sign of the contribution of an atom at point P (x, y, z) to the c.d. varies as the product $x \cdot y \cdot z$ of its co-ordinates), the following generalisation is suggested.

For an optically active transition with symmetry properties ${}^1A_1 \rightarrow {}^1A_2$ the contribution of an atom at point P(x, y, z) to the c.d. (or to the amplitude of the o.r.d.) reverses its sign if P is reflected relative to one of the two symmetry planes of the chromophore or to the

* Low-temperature circular dichroism measurements do not seem to support this.²¹

second nodal surface of the π^* orbital. As already stated in ref. 14 this nodal surface is not a plane. Whereas reflexion with respect to the symmetry planes will not alter the absolute magnitude of the contributions, this will certainly be the case for reflexions relative to the (x, y) surface. This will have only minor influence on the qualitative treatment of most of the investigated compounds. For the special case of the nitro-compounds we shall draw only one important inference from these considerations, viz. that the contribution of a substituent also reverses its sign if the group is rotated about the z -axis by 90° . In general the magnitude of the contribution will be altered by this rotation.

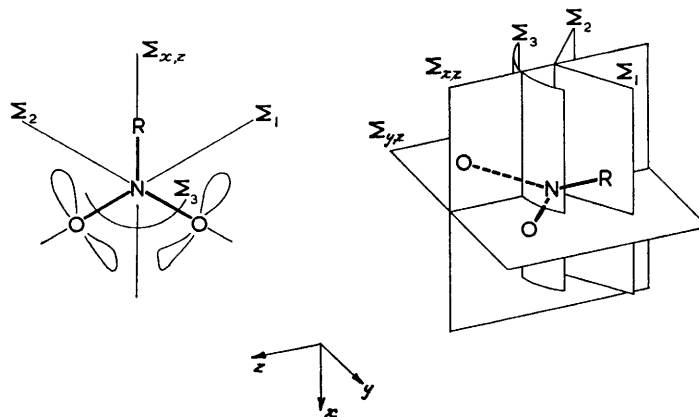


FIGURE 5. Nodal and symmetry surfaces of the $n_a \rightarrow \pi_3^*$ transition of nitro-compounds

With nitro-compounds $\Sigma_{x,z}$ and $\Sigma_{y,z}$ (Figure 5) are nodal as well as symmetry planes; Σ_3 is the third surface, which corresponds to the "plane" $\Sigma_{x,y}$ of ketones. The Σ_3 surface is definitely not planar for the nitro-chromophore. The two additional nodal planes, Σ_1 and Σ_2 , make the picture more complicated than for ketones, as we are not dealing with octants but with smaller sectors. On going through a nodal surface the c.d. contribution of an atom reverses its sign. As for $n_s \rightarrow \pi_3^*$ transition, $\Sigma_{x,z}$ is a symmetry, but not a nodal plane; atoms which are in left and right octants must then give contributions of the same sign, *i.e.*, the ${}^1A_1 \rightarrow {}^1B_1$ transition is not optically active. This supports the assumption that the 280-m μ band comes from an $n_a \rightarrow \pi_3^*$ transition. The same problem arises for acids, esters, and lactones; and Moscovitz, in collaboration with Klyne, Scopes, and Jennings, has suggested a similar treatment for these compounds.²⁰

Inspection of the octant projection (Figure 6) of compound (XII) shows that, apart from C-19, all the atoms which make some contribution to the Cotton effect are in the upper right octant. Since $\Delta\epsilon_{\max.} = +0.63$, atoms in this octant must give positive contributions; this is the reverse of the normal ketone rule. In the same way, a much modified "reversed octant" rule appears to offer a basis for consideration of Cotton effects in lactones.²⁰ To prove this assumption with the other compounds a "distance function" would be needed. As yet none is known and therefore a very simple one is advanced here for semi-quantitative estimations. C-Atoms within the third sphere are given the contribution 1, those within the fourth a value of $\frac{1}{2}$, and more remote ones a value of 0. Using 1 for the third, $\frac{1}{2}$ for the fourth, and $\frac{1}{4}$ for the fifth sphere does not essentially alter the result of this estimation. This treatment does not take into account the different distances from the nodal planes, but for an approximate estimation it should be as useful as the generally applied octant projections for ketones.¹⁴ Table 2 summarises the results and shows that the modified octant rule for equatorial nitro-steroids holds in the cases investigated.

²⁰ Cf. J. P. Jennings, W. Klyne, and P. M. Scopes, *Proc. Chem. Soc.*, 1964, 412.

It is not surprising that there is no proportionality between the estimated and the measured values but the relative high $\Delta\epsilon_{\max.}$ of (XIV) reflects the greater amount of steric hindrance in this nitro-steroid.

In 3 β -nitro-5 α -cholestane (IX) no atoms other than the four hydrogens at positions

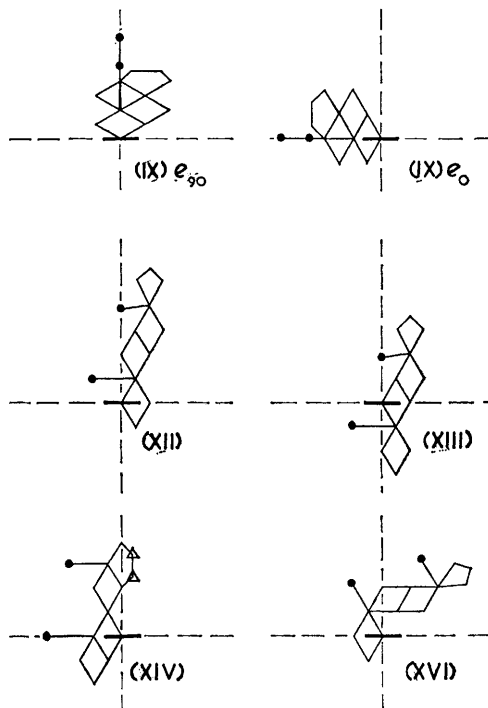


FIGURE 6. Octant projections of equatorial nitro-steroids

TABLE 2

Estimated contributions to the c.d. and observed $\Delta\epsilon_{\max.}$ -values for equatorial nitro-steroids

Compound	Sum of contributions	$\Delta\epsilon_{\max.}$	Compound	Sum of contributions	$\Delta\epsilon_{\max.}$
IX (e_0 conf.)	-2	+0.06	XIII	+3.5	+0.68
IX (e_{90} conf.)	+2		XIV	-2*	-0.84
XII	+4	+0.63	XVI	+4	+0.38

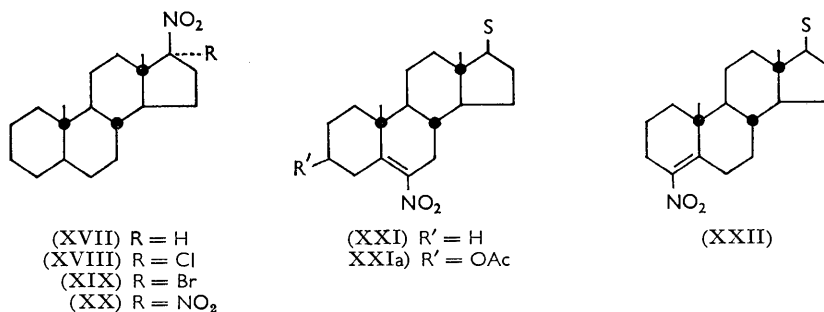
* This treatment takes into account the presence of C-15 and C-16 in a front octant of 7 β -nitro-5 α -cholestane (XIV).

2 and 4 are interfering with the nitro-group. This introduces only a very small hindrance to free rotation and on the basis of conformation analysis it is difficult to deduce the more stable of the two symmetrical conformations, e_0 and e_{90} . From Table 2 it follows that only the e_{90} form is consistent with the positive c.d. and therefore that this conformation is the energetically favoured one in (IX) and thus in all "unhindered" equatorial nitrocyclohexanes. This is supported by the c.d. of the corresponding chloronitro-compound (X) (see below) and by low-temperature measurements.²¹ The Cotton effect of 17 β -nitro-5 α -androstane (XVII) cannot be treated in a similar manner as the second sphere is

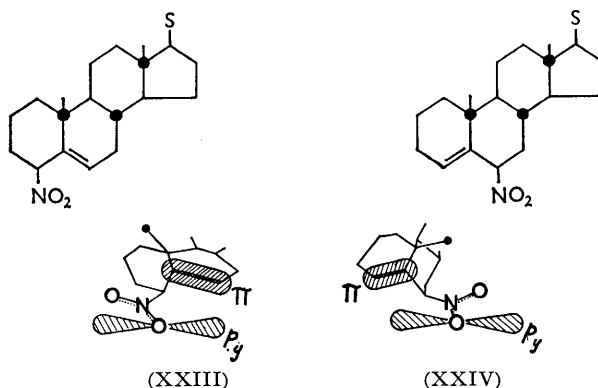
²¹ G. Snatzke, D. Becher, and J. R. Bull, *Tetrahedron*, 1964, **20**, 2443. In the meantime we have precisely measured the density variation with temperature of the solvent mixture used. All $\Delta\epsilon'$ -values (-188°) cited in the mentioned Paper should, therefore, be multiplied by 1.084. This does not essentially effect our discussion on the hindered rotation of the nitro-groups, however.

dissymmetric owing to the conformation of ring D, and the torsion angle ($\tau \neq 0^\circ, \neq 90^\circ$) is unknown.

$\alpha\beta$ - and $\beta\gamma$ -Unsaturated Nitro-steroids.—Conjugation of the nitro-group with a C=C double bond gives rise to intense ultraviolet absorption at about $260 \text{ m}\mu$, which has been



classified as a charge-transfer band.^{4,22} The c.d. (Figure 7) of 6-nitrocholest-5-ene (XXI)²³ reveals three optically active bands, those at $262 \text{ m}\mu$ (charge transfer), at $337 \text{ m}\mu$ ($n_a \rightarrow \pi_3^*$), and at $410 \text{ m}\mu$ (long-wavelength band). The second and third bands show pronounced bathochromic shifts due to conjugation. With 4-nitrocholest-4-ene (XXII) the charge transfer and the $n_a \rightarrow \pi_3^*$ band have the same sign, and no long wavelength band is



detectable. The enantiomeric relation of rings A and B in (XXI) and (XXII) is reflected in the opposite signs of their ${}^1A_1 \rightarrow {}^1A_2$ bands. While the sterically most stable conformation of the NO₂ group in these two compounds will have a torsion angle, $\tau \sim 0^\circ$, the most favourable conformation for full conjugation is, however, that with $\tau = 90^\circ$. It is therefore not possible to define the conformations adopted by these compounds. It is very interesting to compare the two $\beta\gamma$ -unsaturated compounds, 4 β -nitrocholest-5-ene (XXIII) and 6 β -nitrocholest-4-ene (XXIV), which are also of the enantiomeric type. Free rotation is hindered by the 19-methyl group, but not so severely as in the 5 α -dihydro-compounds. Nevertheless their $\Delta\epsilon$ -values are unusually high (Figure 7) and this points to an inherently dissymmetric chromophore.¹⁷ Thus, in these compounds the first sphere becomes dissymmetric, the π -cloud of the C=C double bond projecting to the right (XXIII) or the left (XXIV) upper octant. According to the rules for such chromophores^{16b} (XXIII) is expected to give a positive, and (XXIV) a negative c.d., and this is so. The long-wavelength band has the same sign as the main band in both cases.

²² S. Nagakura, *J. Chem. Phys.*, 1955, **23**, 1441.

²³ 6-Nitro- Δ^5 -androstene-3 β ,17 β -diol also shows these three bands (cf. ref. 3).

gem-Chloronitro- and Dinitro-steroids.—The *gem*-halogenonitro-compounds which were measured (II, V, X, XV, XVIII, XIX, and XXVI, Figures 8 and 9) all show at room temperature the same c.d. sign as the corresponding nitro-steroids. This holds even for the 350 m μ band with the exception of the 3-substituted compounds. A geminal chloro-atom will certainly destabilise the a_0 or e_0 conformation and tend to force the nitro-group into an a_{90} or e_{90} conformation. Using electron diffraction, Barss²⁴ found almost free rotation around the C-N bond in $\text{CCl}_3\cdot\text{NO}_2$. This is not in conflict with the assumption

FIGURE 7. Circular dichroism of unsaturated nitro-steroids (XXI), (XXII), (XXIII), and (XXIV)

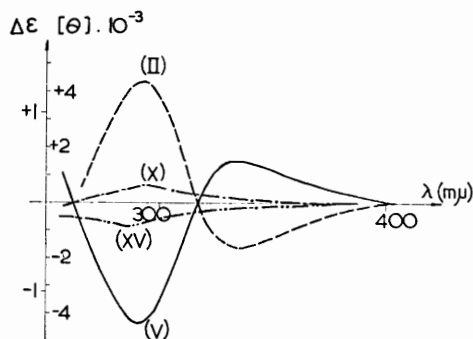
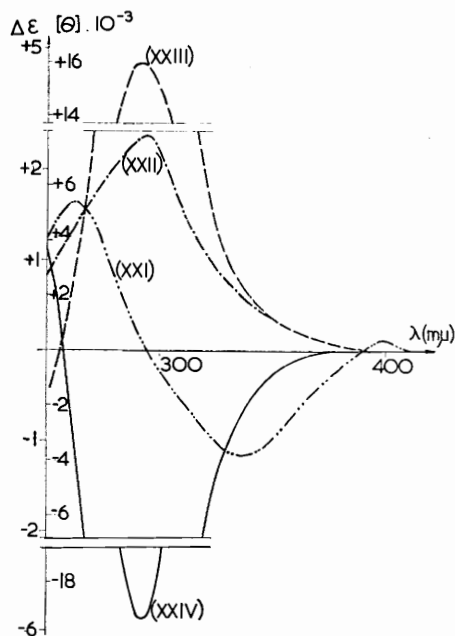


FIGURE 8. Circular dichroism of *gem*-chloro-nitro-steroids (II), (V), (X), and (XV)

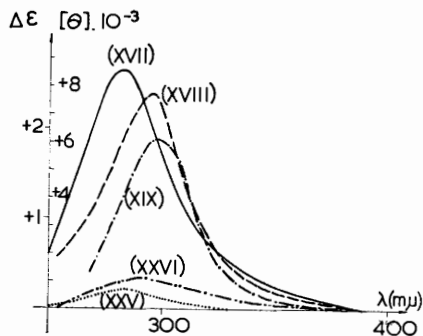


FIGURE 9. Circular dichroism of substituted 17 β -nitro-5 α -androstanes (XVII), (XVIII), and (XIX) and of substituted 3 α -nitro-5 α -cholestanes (XXV) and (XXVI)

that at room temperature and below²¹ the free rotation in substances of the asymmetric type $\text{RR}'\text{CCl}\cdot\text{NO}_2$ is more hindered by steric and field effects than rotation in $\text{RR}'\text{CHNO}_2$. For the 3 β -nitro-steroids this means that the population of the e_{90} conformation in (X) is higher than in the chlorine-free product (IX), thus enlarging the percentage of "effective

²⁴ W. M. Barss, *J. Chem. Phys.*, 1957, **27**, 1260.

active molecules" and therefore giving rise to a greater $\Delta\epsilon_{\max}$. If the e_0 conformation in (IX) had been favoured relative to the e_{90} form, then a change in the sign of the Cotton effect would have resulted (see the rule mentioned above regarding rotation by 90°).

In 4α -chloro- 4β -nitro- 5α -cholestane (II) and its 6-analogue (V) the torsion angle, τ , will be enlarged by the geminal chloro-atom to some extent, thus making the dissymmetry in the second sphere smaller than in the reference compounds. While $\Delta\epsilon_{\max}$ is therefore diminished for the main band, the $350\text{-m}\mu$ band becomes more intense, a result which cannot be explained at present. In 7α -chloro- 7β -nitro- 5α -cholestane (XV) the directing effects of

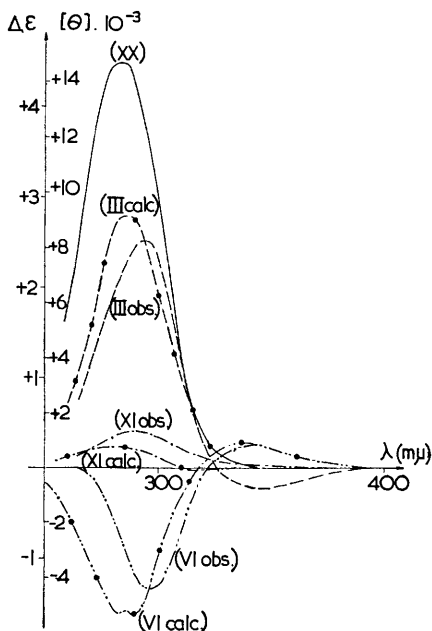


FIGURE 10. Observed and calculated circular dichroism of *gem*-dinitro-steroids (III), (VI), and (XI); c.d. of 17,17-dinitro- 5α -androsterane (XX)

the 15 -methylene group and the 7α -chloro-atom upon the nitro-group are opposed. This leads to a remarkable reduction in the magnitude of the c.d. and even to an inversion of the sign at low temperature (-188°). (This effect is discussed more thoroughly in ref. 21.) From the 3β -chloro- 3α -nitro- 5α -cholestane (XXVII) it is possible to determine the energetically most favourable conformation of the nitro-group in 3α -nitro- 5α -cholestane (XXV). In the latter compound there is very little restriction to free rotation, and conformation analysis is not helpful. However, the chlorine atom of (XXVI) will make the a_{90} conformation the preferred one for this compound and as both substances show the same (positive) c.d. sign (Figure 9) the preferred conformations must be similar in the two cases. For 3α -nitro- 5α -cholestane, and therefore for an unsubstituted axial nitrocyclohexane, the a_{90} conformation has the smallest Pitzer strain.

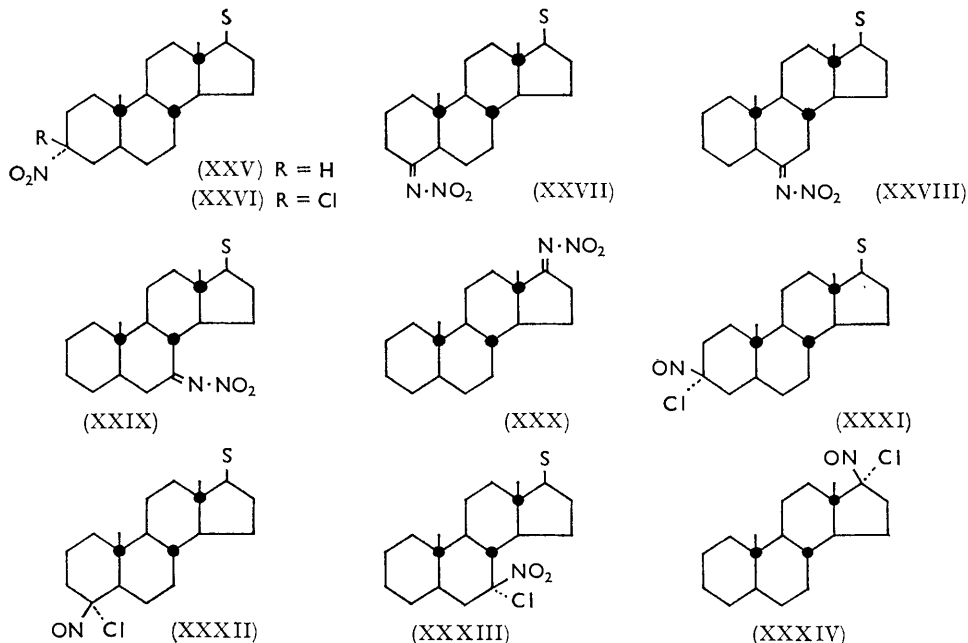
The geminally 17-substituted steroids strongly support these assumptions (Figure 9). Though the conformation of the 17β -nitro-group cannot be deduced in a simple way from the c.d., the ubiquitous reduction of $\Delta\epsilon_{\max}$ caused by substituting the 17α -hydrogen by chlorine and bromine can be easily explained. The larger the geminal substituent the more the torsion angle, τ , will approach 90° and thus diminish the dissymmetry of the second sphere. The o.r.d. curves given by Patchett and co-workers²⁵ for some 17α -substituted 17β -nitro-steroids cannot be used for comparison, as only the first extremum was reached.

According to Ungnade and Kissinger²⁶ the intensity of ultraviolet absorption of *gem*-

²⁵ A. A. Patchett, F. Hofmann, F. G. Giarrusse, H. Schwan, and G. F. Arth, *J. Org. Chem.*, 1962, **27**, 3822.

²⁶ H. E. Ungnade and L. W. Kissinger, *J. Org. Chem.*, 1957, **22**, 1088.

dinitro-compounds is about twice as great as that of mononitro-compounds, which suggests that one chromophore does not influence the ultraviolet absorption of the other to any extent. This need not be so for c.d. absorption because the two nitro-groups will mutually



influence their respective conformations. However, no pronounced vicinal effects are observed and Figure 10 shows that the deviation of the calculated from the found c.d. is surprisingly small.

FIGURE 11. Circular dichroism of "nitrimino-steroids" (XXVII), (XXVIII), (XXIX), and (XXX)

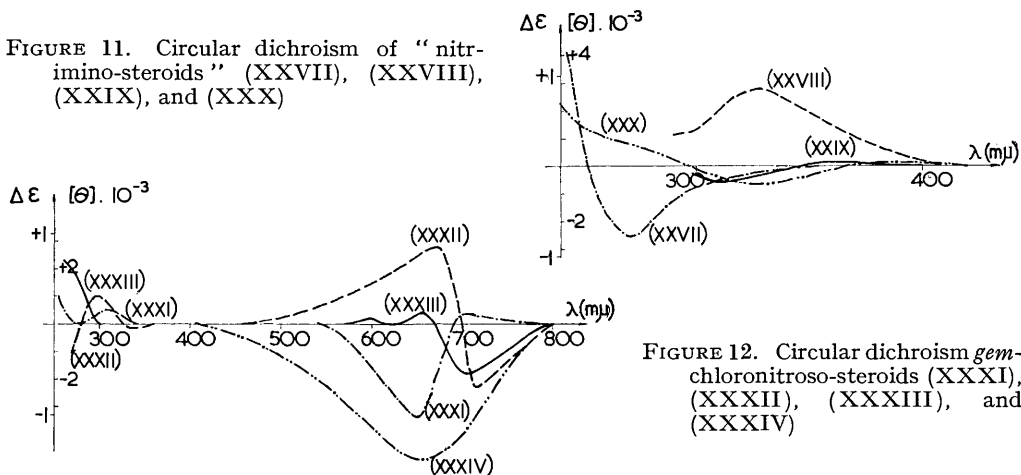


FIGURE 12. Circular dichroism *gem*-chloronitroso-steroids (XXXI), (XXXII), (XXXIII), and (XXXIV)

Some related compounds have been prepared by the Oxford authors in connection with their work on nitro-steroids. The c.d. of several "nitrimines" (XXVII—XXX) and *gem*-nitrosochlorides²⁷ (XXXI—XXXIV) are presented in Figures 11 and 12.

²⁷ The c.d. of the nitrosochlorides was kindly measured by courtesy of (a) Mr. W. Ungerer (Jouan S.A., Paris) and (b) Dr. E. Larsen (H. C. Ørsted-Institute, Copenhagen) on a new dichrograph with extended wavelength range.

The o.r.d. curves of most of these nitro-compounds have been measured at Westfield College, London (Klyne, Scopes, and Jennings) with a Bellingham & Stanley/Bendix-Ericsson polarimeter. The o.r.d. results and the detailed comparison of $a/\Delta\epsilon$ have been given in Part III of this series.¹

EXPERIMENTAL

The c.d. curves were measured in dioxan solution at 20° in a cell of 2-cm. pathlength with a Roussel-Jouan Dichrographe. The c.d. results are quoted as $\Delta\epsilon$ (λ in $m\mu$), the concentrations refer to mg./g. of dioxan. Molar ellipticities $[\theta]$ may be obtained by multiplying $\Delta\epsilon$ by 3300.²⁸⁻³⁰

4 β -Nitro-5 α -cholestane (I) ($c = 2.65$): 385 (0), 333 (-0.24), 317 (0), 284 (+2.25), 250 (+0.34).

4 α -Chloro-4 β -nitro-5 α -cholestane (II) ($c = 3.64$): 400 (0), 335 (-0.48), 317 (0), 293 (+1.34), 263 (+0.18).

4,4-Dinitro-5 α -cholestane (III) ($c = 1.99$): 392 (0), 345 (-0.22), 326 (0), 293 (+2.52), 266 (+0.86).

6 β -Nitro-5 α -cholestane (IV) ($c = 1.47$): 395 (0), 335 (+0.24), 317 (0), 284 (-2.34), 245 (-0.14).

3 β -Acetoxy-6 β -nitro-5 α -cholestane (IVa) ($c = 1.31$): 390 (0), 335 (+0.21), 318 (0), 284 (-2.45), 245 (-0.37).

6 α -Chloro-6 β -nitro-5 α -cholestane (V) ($c = 1.44$): 405 (0), 338 (+0.47), 317 (0), 290 (-1.37), 262 (0), 256 (+0.29).

6,6-Dinitro-5 α -cholestane (VI) ($c = 0.80$): 395 (0), 343 (+0.25), 322 (0), 296 (-1.35), 264 (0).

4 α -Nitro-5 β -cholestane (VII) ($c = 1.19$): 365 (0), 283 (-1.64), 246 (-0.15).

7 α -Nitro-5 α -cholestane (VIII) ($c = 1.63$): 390 (0), 293 (+0.48), 259 (0), 247 (-0.46).

3 β -Nitro-5 α -cholestane (IX) ($c = 2.85$): 345 (0), 310 (-0.03), 294 (0), 270 (+0.05), 243 (0).

3 α -Chloro-3 β -nitro-5 α -cholestane (X) ($c = 2.16$): 370 (0), 295 (+0.19), 262 (0), 250 (-0.03).

3,3-Dinitro-5 α -cholestane (XI) ($c = 1.75$): 375 (0), 289 (+0.39), 265 (+0.19).

4 α -Nitro-5 α -cholestane (XII) ($c = 3.07$): 380 (0), 300 (+0.63), 250 (0).

6 α -Nitro-5 α -cholestane (XIII) ($c = 1.12$): 330 (0), 284 (+0.68), 240 (+0.05).

3 β -Acetoxy-6 α -nitro-5 α -cholestane (XIIIa) ($c = 2.84$): 350 (0), 286 (+0.67), 245 (+0.06).

7 β -Nitro-5 α -cholestane (XIV) ($c = 3.80$): 365 (0), 285 (-0.84), 252 (0), 250 (+0.07).

7 α -Chloro-7 β -nitro-5 α -cholestane (XV) ($c = 3.67$): 390 (0), 285 (-0.24), 260 (-0.15).

4 β -Nitro-5 β -cholestane (XVI) ($c = 2.31$): 380 (0), 320 (-0.22), 302 (0), 280 (+0.38), 243 (+0.03).

17 β -Nitro-5 α -androstane (XVII) ($c = 1.54$): 390 (0), 282 (+2.67), 245 (+0.38).

17 α -Chloro-17 β -nitro-5 α -androstane (XVIII) ($c = 1.62$): 395 (0), 295 (+2.38), 264 (+0.55).

17 α -Bromo-17 β -nitro-5 α -androstane (XIX) ($c = 2.39$): 395 (0), 298 (+1.88), 270 (+0.46).

17,17-Dinitro-5 α -androstane (XX) ($c = 1.07$): 340 (0), 284 (+4.49), 260 (+1.78).

6-Nitrocholest-5-ene (XXI) ($c = 0.73$): 420 (0), 400 (+0.10), 390 (0); ($c = 0.27$): 337 (-1.17), 294 (0), 262 (+1.67), 240 (0).

3 β -Acetoxy-6-nitrocholest-5-ene (XXIa) ($c = 0.57$): 405 (0), 335 (-2.04), 296 (0), 291 (+0.36).

4-Nitrocholest-4-ene (XXII) ($c = 0.16$): 380 (0), 293 (+2.39), 276 (+2.00).

4 β -Nitrocholest-5-ene (XXIII) ($c = 1.52$): 400 (0), 293 (+4.87), 256 (0), 250 (-0.81).

6 β -Nitrocholest-4-ene (XXIV) ($c = 1.55$): 375 (0), 292 (-5.87), 257 (0), 248 (+1.33).

3 α -Nitro-5 α -cholestane (XXV) ($c = 2.36$): 330 (0), 283 (+0.20), 245 (+0.03).

3 β -Chloro-3 α -nitro-5 α -cholestane (XXVI) ($c = 1.98$): 395 (0), 290 (+0.33), 254 (0).

4-Nitrimino-5 α -cholestane (XXVII) ($c = 0.47$): 355 (0), 270 (-0.76), 252 (0), 243 (+1.26).

6-Nitrimino-5 α -cholestane (XXVIII) ($c = 1.55$): 410 (0), 327 (+0.83), 290 (+0.34).

7-Nitrimino-5 α -cholestane (XXIX) ($c = 3.03$): 400 (0), 360 (+0.03), 346 (0), 310 (-0.18), 298 (-0.07).

17-Nitrimino-5 α -androstane (XXX) ($c = 0.93$): 420 (0), about 390 (+0.04), 367 (0), 327 (-0.20), 296 (0); ($c = 0.34$): 240 (+0.68).

²⁸ The u.v. data of these compounds will be given in a forthcoming Paper of the Oxford authors.

²⁹ See, e.g., S. F. Mason, *Quart. Rev.*, 1963, **17**, 20.

³⁰ For nomenclature see C. Djerassi and E. Bunnenberg, *Proc. Chem. Soc.*, 1963, 299.

3 α -Chloro-3 β -nitroso-5 α -cholestane (XXXI) ($c = 0.73$): ^{27a} 800 (0), 704 (+0.11), 690 (0), 649 (-1.04), 540 (0); ($c = 0.66$): 340 (0), 308 (+0.17), 275 (0), 255 (+0.32).

4 α -Chloro-4 β -nitroso-5 α -cholestane (XXXII) ($c = 1.45$): ^{27a} 800 (0), 725 (-0.70), 700 (0), 674 (+0.84), 450 (0); ($c = 1.16$): 360 (0), 340 (-0.05), 324 (0), 297 (+0.30), 278 (0), 267 (-0.30).

7 α -Chloro-7 β -nitroso-5 α -cholestane (XXXIII) ($c = 1.94$): ^{27a} 800 (0), 705 (-0.54), 670 (0), 655 (+0.13), 625 (0), 598 (+0.06), 570 (0); ($c = 0.79$): 300 (0), 260 (+0.69).

17 α -Chloro-17 β -nitroso-5 α -androstane (XXXIV) ($c = 1.54$ in water): ^{27b} 800 (0), 656 (-1.49), 405 (0).

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