Circular Dichroism of Nitrate Esters: A Planar Symmetry Rule for the Nitrato Chromophore[1]

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Conformational analysis of nitrate esters based on X-ray and spectroscopic data showed the nitrato group to be coplanar with the α carbon atom and, in the preferred rotamer, the nitro moiety to be antiperiplanar to the β carbon atom. Three optically active absorption bands not apparent in the isotropic electronic spectra were resolved in the circular dichroism spectra. Band I (270 nm) reflected nitrato group libration changing sign and magnitude with changes in temperature and solvent polarity. Differences in rotatory strength of band III (210 nm) for *cis*- and *trans*-dinitrates indicated transition moment coupling. A planar symmetry rule for chromophores in the C_s point group correlated the molecular geometry and sign of band II for 42 nitrate esters: when the lowest-energy rotamer of the nitrate ester is viewed down the O—C bond with the nitro group uppermost rotatory contributions to band II (230 nm) are positive for perturbing atoms to the right and negative for those to the left of the nitrato symmetry plane.

L'analyse conformationnelle des esters nitriques, basée sur les données de la spectroscopie et des rayons-X, montre que le groupe nitrate est coplanaire avec l'atome de carbone en α et que, dans le rotamère privilégié, le fragment nitro est antipériplanaire à l'atome de carbone en β. Trois bandes d'absorption optiquement actives, non apparentes sur le spectre électronique isotrope, ont été résolues dans le spectre de dichroisme circulaire. La bande I (270 nm) reflète la vibration du groupe nitro et change de signe et d'amplitude lorsque la température et la polarité du solvant changent. Les différences dans le pouvoir rotatoire de la bande III (210 nm) pour les dinitrates *cis* et *trans* indiquent un couplage du moment de transition. Une règle de symétrie plane pour les chromophores du groupe C_s relie la géometrie moléculaire au signe de la bande II pour 42 esters nitriques: lorsque le rotamère de plus basse énergie de l'ester nitrique est regardé le long de la liaison O—C avec le groupe nitro, les contributions rotatoires décisives pour la bande II (230 nm) sont positives lorsque les atomes sont situés à droite du plan de symétrie du nitrate et négatives lorsqu'ils sont à gauche.

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Introduction

A correlation of the absolute configuration (chirality) of nitrate esters with their accessible c.d. spectra was sought in the present work. Such a symmetry rule (1, 2) would permit assignment of unknown configurations and contribute to understanding of the bonding, electronic spectra, and conformational equilibria of these explosive and physiologically reactive compounds.

Early o.r.d. spectra of hexose nitrates (3–7) included background rotation due to other chromophores and only the transition of the nitrato group at 270 nm (band I) was identified with the aid of c.d. spectra (5, 6). The sign of band I was positive for nitrato groups in α- (or D) configuration and negative for those with β- (or L) configuration in α-glucosides, the signs being reversed for the corresponding β-anomers. Band I was reported to be red-shifted by steric crowding of the chromophore and to decrease in rotatory strength with location on the hexose chain in the order C-2 > C-3 > C-4 > C-5. It was also concluded from o.r.d. data that (*R*)- and (*S*)-α-nitrato-carboxylic acids showed positive and negative Cotton effects, respectively, at *ca.* 265 nm (5).

Our preliminary c.d. studies on a series of 1,4;3,6-dianhydrohexitol nitrates (8) revealed a new transition at 230 nm (band II) which was positive for *endo*-(*R*)- and negative for *exo*-(*S*)-nitrato groups at locations 4 and 8 on the *cis*-2,6-dioxabicyclo[3.3.0]octane skeleton. In this series of nitrates the sign of band I was positive throughout and was insensitive to changes in configuration at the α-carbon atom.

A third dichroitic band at 210 nm (band III) was detected in nitrato steroids (9). Exciton splitting as the source of band III was considered improbable since its rotatory strength varied independently of that of band II. Although the sign patterns of bands I–III were characteristic

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[1] Taken in part from the thesis submitted by R. E. Barton in partial fulfilment of the requirements for the Ph.D. degree. This is Part III of a series on stereochemistry of nitrate esters. For part II, see ref. 24.

of location on the steroid skeleton, rotational mobility of the nitrato group precluded complete configurational analysis (9).

A fourth nitrato absorption band at 200 nm (band IV, ε 5800) was found in the isotropic spectrum of ethyl nitrate (10) but has not so far been reported in c.d. spectra. Band I has been identified with the $n \rightarrow \pi^*$ transition (11), and bands III and IV with the $\pi \rightarrow \pi^*$ transition (10) of the nitrato chromophore whereas the identity of the transition associated with band II is unknown.

The nitrato group, —ONO_2, with four coplanar atoms (12–16) belongs to the C_s point group with symmetry elements E and σ. The molecular orbitals of the nitro moiety probably resemble those of the nitroalkanes (17, 18); however, there is uncertainty concerning participation of the alkoxyl oxygen in π bonding (16). The scatter of the available values for the RO—NO_2 bond length (1.36 to 1.53 Å) (13–16) leaves open the question of electron delocalization over the entire —ONO_2 group.

From the C_s character table the pseudoscalar part of the —ONO_2 potential is the A'' representation and hence, according to Schellman's analysis (2), there should exist a planar symmetry rule for nitrate esters based on the symmetry plane. This approach specifies only the minimum number of spatial regions in which perturbing groups generate rotational strength (19); other nodal surfaces not determined by symmetry may lead to further spatial subdivisions. In view of the uncertainty in the bonding and orbitals in —ONO_2, however, only a planar rule was considered as a first approximation. The problem was then to establish the most probable position of σ in the molecular framework; once this was known examination of molecular models would reveal the distribution of polarizable groups with respect to the fiducial plane for comparison with c.d. spectra.

The investigation involved the following steps: (*a*) synthesis of model nitrate esters with known configurations and restricted molecular conformations, (*b*) measurement of isotropic and c.d. spectra to establish the preferred conformations, (*c*) analysis of the c.d. spectra in terms of the molecular geometry in an attempt to assign rotatory contributions from spatial regions of the intramolecular environment, and (*d*) generalization of the pictorial model through tests on nitrate esters with more varied patterns and degrees of substitution and greater degrees of molecular flexibility.

Experimental

Circular dichroism spectra were taken on JASCO J5 and J20 spectrophotometers calibrated for wavelength and dichroic absorption with 5α-cholestan-3-one in 1,4-dioxan ($\Delta\varepsilon + 1.13$ at 295 nm (20)). Low temperature measurements (21) were corrected for volume contraction from published solvent data (22). Ultraviolet spectra were run on a Cary 15 spectrophotometer with slit widths less than 1 mm and absorbance below 1.0. All solvents were of spectral grade or were purified by standard procedures to give satisfactory ultraviolet absorption spectra.

The nitrate esters were synthesized from the corresponding chiral alcohols (Table 3) (7, 24, 28–32) either with anhydrous nitric acid in acetic acid – acetic anhydride at 0° (23, 24) or via the corresponding chloroformate and silver nitrate (25) and were purified by distillation (*ca.* 0.5 Torr) or chromatography on columns of silica gel developed with chloroform (26). Purification was monitored by t.l.c. (26) and by the u.v., c.d., n.m.r., (27) and i.r. (24) spectra which agreed with the constitutional assignments. Elemental analyses of new nitrate esters are shown in Table 1.

Results and Discussion

The isotropic electronic absorption spectra of the nitrate esters in solvents of different polarity showed no maxima; however, the molar extinction coefficients of the band envelope were measured at wavelengths corresponding to bands I–IV (Table 2). These were generally larger in acetonitrile than in cyclohexane at 270 and 230 nm and the reverse was true at 210 and 200 nm. This trend of ε with solvent polarity was confirmed in the u.v. spectra of (−)-menthyl nitrate (**19**) in four additional solvents and suggested the presence of different unresolved transitions.

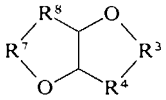
Oxolanyl Nitrates (1–11)

The restricted, approximately V-shaped conformation of the fused oxolane rings in the parent 4,8-dihydroxy-*cis*-2,6-dioxabicyclo[3.3.0]octanes (**1–4**, **8–10**) is known from X-ray data (14) and has been shown by n.m.r. measurements not to be significantly altered by intramolecular hydrogen bonding or esterification (28). The restricted nonplanar conformation of oxolan-2-one (**6**, **7**) was established by microwave spectroscopy (29).

The barrier to rotation on the O—C bond in methyl nitrate is 2.3 kcal mol^{-1} and to rotation on the O—N bond, 9.1 kcal mol^{-1} (16), the

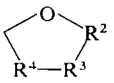
TABLE 1. Analyses of nitrate esters

		Analysis (%)					
		Calculated			Found		
Nitrate ester	Melting point/boiling point	C	H	N	C	H	N
3-Nitrato-4,4-dimethyl-oxolan-2-one (**7**)	90°/0.5 mm	41.14	5.18	8.00	41.28	5.16	8.07
3,4-Dinitratooxolane (**11**)	43.7°	24.75	3.12	14.43	24.78	3.01	14.58
2-*exo*,3-*exo*-Dinitrato-bornane (**15**)	73.8–75.0°	46.15	6.20	10.77	46.31	6.25	10.65
1-Nitrato-2-isopropyl-5-methylcyclohexane (**19**)	62.5–63.0°/0.5 mm	59.67	9.52	6.96	59.39	9.72	6.92
1-Nitrato-2-methyl-5-isopropylcyclohexane (**21**)	82–90°/1 mm	59.67	9.52	6.96	59.99	9.70	6.91
1-Nitrato-2-methylene-5-isopropylcyclohexane (**23**)	60–74°/1 mm	60.28	8.60	7.03	60.15	8.51	7.10
1-Nitrato-3-methylcyclo-hexane (**24**)	48–53°/1 mm	52.81	8.23	8.80	52.92	8.20	8.85



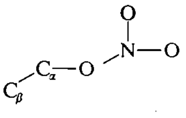
	R^3	R^4	R^7	R^8
1	CH_2	$CHONO_2$(*endo*)	CH_2	CHOH(*exo*)
2	CH_2	$CHONO_2$(*exo*)	CH_2	CHOH(*endo*)
3	CH_2	$CHONO_2$(*endo*)	CH_2	CHOH(*endo*)
4	CH_2	$CHONO_2$(*exo*)	CH_2	CHOH(*exo*)
5	CHR*	$CHONO_2$(*exo*)	$C(CH_3)_2$	O
8	CH_2	$CHONO_2$(*exo*)	CH_2	$CHONO_2$(*exo*)
9	CH_2	$CHONO_2$(*endo*)	CH_2	$CHONO_2$(*endo*)
10	CH_2	$CHONO_2$(*endo*)	CH_2	$CHONO_2$(*exo*)

R* = 1,3-dioxa-2,2-dimethyl-4-cyclopentyl

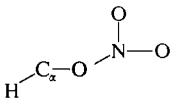


	R^2	R^3	R^4
6	C=O	$CHONO_2(\beta)$	$C(CH_3)_2$
7	C=O	$CHONO_2(\alpha)$	$C(CH_3)_2$
11	CH_2	$CHONO_2(\alpha)$	$CHONO_2(\beta)$

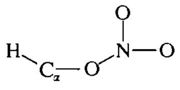
former value being comparable to the barriers restricting overall molecular rotation in various solvents (30). Our calculations from the atom coordinates of six nitrate ester groups in different chemical and crystal environments (12–15) showed that the carbon atom α to the nitrato group lies in or close to the symmetry plane of the group in every case as was also found for methyl nitrate by microwave spectroscopy (16).



anti-C_β



anti-H



syn-H

The *endo*-nitrato groups at C-4 of the 2,6-dioxabicyclo[3.3.0]octane skeleton (14) was found to be also coplanar with the methylene β carbon atom, C-3, and to be antiperiplanar to it on the O—C bond (rotamer *anti*-C_β). This conformation brings the *endo*-nitrato group into proximity with the oxygen atom in the ad-

TABLE 2. Ultraviolet absorption of nitrate esters at 25°

Nitrate ester	Solvent	ε(mol l^{-1} cm^{-1})*			
		270 nm	230 nm	210 nm	200 nm
7	CH_3CN	25	670	2100	3400
	C_6H_{12}	25	642	2200	3600
11†	CH_3CN	28	700	4700	7700
	C_6H_{12}	28	550	5200	8900
12	CH_3CN	37	1100	3800	4500
	C_6H_{12}	30	830	3900	5100
13	CH_3CN	34	1140	3800	4400
	C_6H_{12}	26	800	3900	4100
14	CH_3CN	60	1600	3200	4100
	C_6H_{12}	37	1200	3200	4400
15†	CH_3CN	65	1700	5900	7600
	C_6H_{12}	58	1300	6700	9700
17†	CH_3CN	52	1400	5100	6700
	C_6H_{12}	47	1200	6000	8700
18†	CH_3CN	59	1860	7200	9500
	C_6H_{12}	50	1260	7400	9900
19	CH_3CN	30	940	3900	4900
	C_6H_{12}	25	650	3800	5300
23	CH_3CN	38	860	3900	7700
24	CH_3CN	28	336		
25	CH_3CN	35			

*At four selected points on the smoothly rising absorption envelope.
†Dinitrate esters.

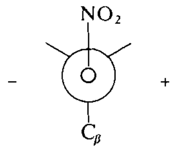
jacent ring (O....N 2.85 Å (14)) in compounds **1**, **3**, **9**, and **10** and causes an increase in the symmetric stretching frequency of the NO_2 group in acetonitrile solutions (24). The *exo*-nitrato group in compounds **2**, **4**, **8**, and **10**, on the other hand, does not show this frequency shift and cannot interact with the oxygen atom of the adjacent ring. Models show that rotamer *anti*-C_β, C_β=CH_2 is probably also preferred for the *exo*-nitrato group but with a somewhat greater degree of librational freedom. Rotamer *anti*-H is precluded by steric hindrance from the oxolane ring and rotamer *syn*-H may be ruled out on the basis of the microwave spectrum of methyl nitrate which showed the methyl hydrogens to be staggered with respect to the nearest oxygen of the NO_2 group (16). Models permitted selection of *anti*-C_β as the preferred rotamer in compounds **5**, **6**, **7**, and **11** (Table 4) with the choice of C_β being governed by steric crowding.

The sign of c.d. band I was found to be dependent on nitrato rotamer populations for other nitrate esters (*vide infra*) but did not change for compounds **6**–**11** on going from acetonitrile to cyclohexane as solvent (Table 3) thus confirming that rotamer *anti*-C_β persists in these solutions. The positive sign of band II for **7** distinguished it from the negative lactone band observed for the parent hydroxylactone (31). The rotatory strength of band II increased moderately ($I^{+5}_{-90} = -47\%$ (32)) and that of band I was drastically decreased ($I^{+5}_{-90} = +150\%$) on cooling a methanol solution of **7**. This result suggested that partial rotation (libration) of the nitrato group on the O—C bond alters an interaction of the lactone and nitrato chromophores.

Resolution of band II for the oxolanyl dinitrate, **11**, was achieved through variation of solvent and temperature. In nonpolar solvents it apparently was hidden under bands I and III but in polar solvents a negative peak appeared near 238 nm (Fig. 1). In methanol solution the intensity of both bands I and II decreased with temperature and in EPA solution band I passed through a minimum negative value between −115° and −145°. These results are most readily understood as due to libration of nitrato rotamers leading to interaction of contiguous nitrato groups (13, 27) in the less polar solvents (24) and at the lower temperatures. In the absence of this attractive interaction in polar solvents the dihedral angle between the planes of the nitrato groups in **11** would increase to approximately 180° to give the rotamer conformation shown in Table 4.

The sign of band II was characteristic of the configuration of the nitrate esters **1**–**11** and was found to depend on the distribution of perturbing atoms with respect to the plane of the nitrato group according to the following rule

When the nitrate ester in the anti-C_β conformation is viewed down the O—C bond with the NO_2 group uppermost the rotatory contribution to band II is positive for atoms lying to the right of the plane of the nitrato group and is negative for atoms to the left of that plane.



In applying the rule only atoms other than hydrogen were counted and atoms lying in the

TABLE 3. Circular dichroism spectra of nitrate esters*

Nitrate Ester			$[\theta]_{\max} \times 10^{-3}$		
Formula	Configuration	Parent alcohol	Band I (270 nm)	Band II (230 nm)	Band III (200–210 nm)
1	1*R*4*R*5*R*8*S*	D-Isosorbide(24)	+2.41	+11.0	
2	1*R*4*S*5*R*8*R*	D-Isosorbide(24)	+0.10	−1.91	
3	1*R*4*R*5*R*8*R*	D-Isommanide(24)	+1.82	+10.3	
4	1*R*4*S*5*R*8*S*	L-Isoidide(24)	+0.40	−2.08	
5	1*R*3*R*4*S*5*R*(4*R*)	1,2;5,6-di-*O*-Isopropylidene-α-D-glucose (6, 8)	+0.59	−4.13	+1.66
6	3*S*	L-Pantolactone	−0.60(−0.50)	−6.50(−3.50)	+17.0(+7.0)
7	3*R*	D-Pantolactone	+0.60(−0.48)	+6.50(+3.50)	−17.0(−6.2)
8†	1*R*4*S*5*R*8*S*	L-Isoidide(23)	+0.43(+0.15)	−4.46(−1.35)	+19.8
9†	1*R*4*R*5*R*8*R*	D-Isommanide(23)	+2.48(+2.97)	+18.4(+16.2)	−1.18
10†	1*R*4*S*5*R*8*R*	D-Isosorbide(23)	+1.58(+1.75)	+7.26(+8.42)	−6.84
11†	3*S*4*S*	L-Threitan	−0.52(−0.69)	−0.57§	+16.0(+16.0)
12	1*R*2*R*4*R*	Isoborneol(28)	+0.13(−0.09)	−1.65‖	−2.20(−1.80)
13	1*S*2*R*4*S*	Borneol(28)	−0.26(−0.25)	−3.30(−3.40)	+2.90
14	1*R*2*R*4*S*	D-α-Fenchol(28)	−0.74(−0.48)	+11.2(+10.5)	−12.7(−9.8)
15†	1*R*2*S*3*R*4*S*	Camphane-2,3-diol	−0.59(−0.43)	−0.30‖	+0.92
16†	1*R*2*S*3*S*4*S*	Camphane-2,3-diol	+0.10	−5.10	+7.20
17†	1*R*2*R*3*S*4*S*	Camphane-2,3-diol	+0.40(+0.30)	+4.10(+3.60)	−2.00
18†	1*R*2*R*3*R*4*S*	Camphane-2,3-diol	+0.20(−0.15)	+9.00(+7.10)	−9.00
19‡	1*R*2*S*5*R*	Menthol	+1.23(+0.91)	−3.26(−3.23)	+7.30(+5.80)
20‡	1*R*2*R*5*R*	Carvomenthol	+0.63	−0.87	+5.00
21	1*S*2*S*5*R*	Isocarvomenthol	+0.06(−0.03)	+0.87(+1.10)	
22	1*R*5*R*	*p*-Menth-1(7)-ene-2-ol	+0.92	+0.25‖	+9.20
23	1*S*5*R*	*p*-Menth-1(7)-ene-2-ol	−0.61(−1.09)	+6.40(+6.34)	−12.0(−9.30)
24‡	1*R*3*S*	3-Methylcyclohexanol	+0.07(+0.01)	+0.06(+0.20)	
25‡	1*S*3*S*	3-Methylcyclohexanol	+0.03(−0.01)	−0.07(−0.04)	
26‡	2*R*	Lactic acid	−0.22	+0.36	−2.30
27‡	2*S*	Diethyl malate(7)	+0.17	−2.10	+4.00
28†	2*R*3*R*	Diethyl tartrate(7)	+0.44	+0.66	−11.00

*At 30° in acetonitrile solution. Numbers in parentheses refer to solution in cyclohexane.

†Dinitrate esters.

‡Additional bands for **19**: 320 nm, −0.010(−0.018); **20**: 318 nm, −0.009; **24**: 298 nm, −0.004; **25**: 292 nm, (−0.004); **26**: 292 nm, +0.022; **27**: 310 nm, −0.010.

§At 238 nm in polar solvents.

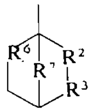
‖Estimated from unresolved bands.

C_s plane were considered to make no rotatory contribution. For dinitrates the distribution of the perturbing atoms was examined for each nitrato group in turn and the algebraic sum of their contributions was used to predict the sign of band II. In Table 4 colums 2 and 3 show the *anti*-C_β rotamer conformations by means of the location numbers for the carbon atoms α and β to the nitrato groups. The distribution of perturbing atoms is shown in column 4 as left-of-plane, in-plane, and right-of-plane, respectively. For dinitrate **10** where the atom distributions for the *endo*- and *exo*-groups are equal and opposite a positive sign for band II was predicted from the greater magnitude of the positive band of the *endo*-group.

The agreement of predicted and observed signs is consistent with the known configurations and the conformational analysis, and permits extension of the symmetry rule to both vicinal and non-vicinal dinitrates.

Alkylbicyclo[2.2.1]heptyl Nitrates (12–18)

The rigid bridged bicyclic skeleton sterically hinders rotation of the nitrato group in this series. Models show that both *endo*- and *exo*-nitrato groups at C-2 are restricted to libration of about ±45° from the conformer *anti*-C_β with C_β = C-1. The C-3 nitrato group in the dinitrates also adopts rotamer *anti*-C_β with C_β = C-2 (Table 4). Nitrato group librational freedom decreases in the order **13** > **12** > **14** for the



	R^2	R^3	R^6	R^7
12	$CHONO_2$(*exo*)	CH_2	CH_2	$C(CH_3)_2$
13	CH_2	CH_2	$CHONO_2$(*endo*)	$C(CH_3)_2$
14	$CHONO_2$(*endo*)	$C(CH_3)_2$	CH_2	CH_2
15	$CHONO_2$(*exo*)	$CHONO_2$(*exo*)	CH_2	$C(CH_3)_2$
16	$CHONO_2$(*exo*)	$CHONO_2$(*endo*)	CH_2	$C(CH_3)_2$
17	$CHONO_2$(*endo*)	$CHONO_2$(*endo*)	CH_2	$C(CH_3)_2$
18	$CHONO_2$(*endo*)	$CHONO_2$(*exo*)	CH_2	$C(CH_3)_2$

TABLE 4. Conformations and chirality of nitrate esters **1–28**

Compound	Conformation*		Perturbing atoms†	Sign of band II	
	C_α	C_β		Predicted	Observed
1	4	3	0/6/7	+	+
2	4	3	7/6/0	–	–
3	4	3	0/6/7	+	+
4	4	3	7/6/0	–	–
5	4	3	8/6/7‡	–	–
6	3	4	4/7/1	–	–
7	3	4	1/7/4	+	+
8	4,8	3,7	10/6/0,10/6/0	–	–
9	4,8	3,7	0/6/10,0/6/10	+	+
10	4,8	3,7	10/6/0,0/6/10	+ §	+
11	3,4	4,3	4/6/3,4/6/3	–	–
12	2	1	6/6/2	–	–
13	2	1	6/7/1	–	–
14	2	1	1/6/7	+	+
15	2,3	1,2	10/6/2,8/7/3	–	–
16	2,3	1,2	10/6/2,4/7/7	–	–
17	2,3	1,2	1/7/10,3/8/7	+	+
18	2,3	1,2	1/7/10,8/6/4	+	+
19	1	2	4/7/3	–	–
20	1	2	6/7/1	–	–
21	1	2	1/10/3	+	+
22	1	6	1/6/7	+	+
23	1	2	0/7/7	+	+
24	1	2	1/6/7	+	+
25	1	6	5/6/0	–	–
26	2‖	3‖	0/6/3	+	+
27	2‖	3‖	5/11/0	–	–
28	2,3‖	3,2‖	4/11/5,4/11/5	+	+

*$Anti$-C_β, C_α and C_β are identified by location numbers of carbon atoms in formulae **1** to **28**

†Numbers of nonhydrogen atoms left/in plane/right of plane of nitrate group.

‡Rotation of the substituent on C-3 would reduce the + value.

§Assigned from the relative rotatory strengths of *endo* (+) and *exo* (–) bands.

‖Assigned on the basis of the planar chirality rule.

mononitrates and **17** > **18** > **16** > **15** for the dinitrates.

The intensity of the isotropic absorption envelope at 230 nm (Table 2) increased with steric hindrance for the mononitrates, and, among the dinitrates, the most sterically hindered, **15**, had the largest ε value at this wavelength.

The sign of c.d. band I was reversed with change of solvent for nitrates **12** and **18** (Table 3). It was positive for compound **12** in four solvents and negative in seven. The rotatory

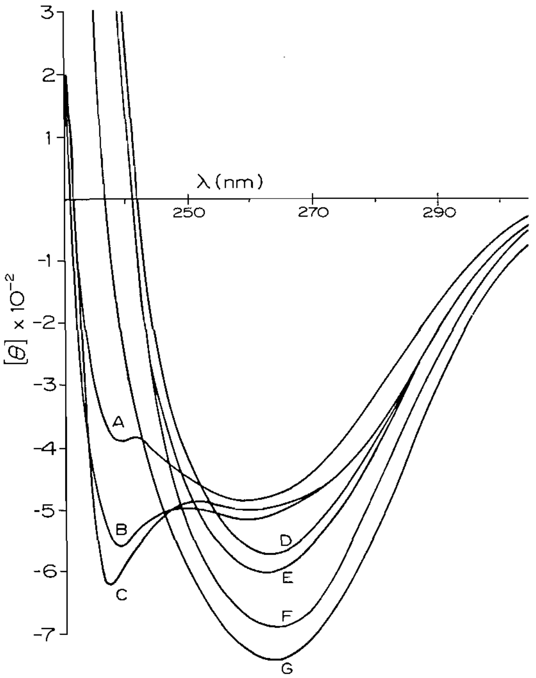


FIG. 1. Effect of solvent on the c.d. spectrum of L-threitan dinitrate (**11**). *A*, 2,2,2-trifluoroethanol; *B*, acetonitrile; *C*, methanol; *D*, pentane; *E*, heptane; *F*, cyclohexanes; *G*, tetrahydrofuran/cyclohexane (14:86, v/v).

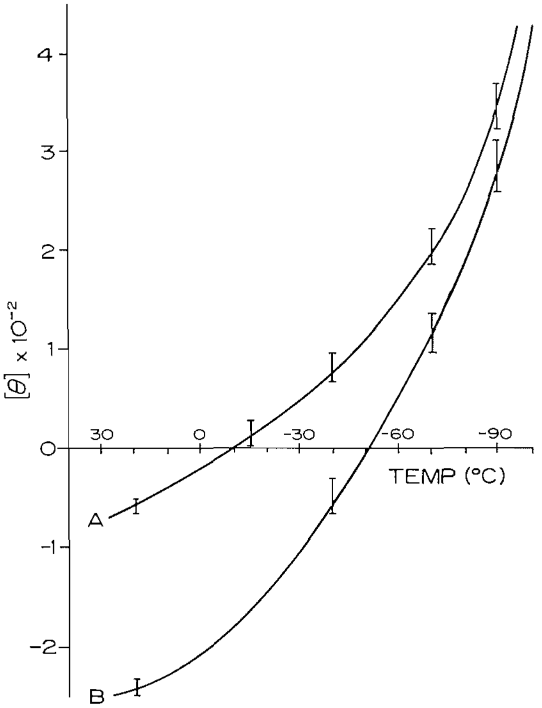


FIG. 2. Effect of temperature on band I (*A*) for isobornyl nitrate (**12**) and (*B*) for bornyl nitrate (**13**) in methanol.

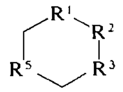
strength of band I for compound **14** showed no correlation with the usual solvent parameters of refractive index, dipole moment, dielectric constant, *Z*-value, or the relation $K - 1/K + 2$ (33) of the eleven solvents. On cooling methanol solutions of **12**–**18**, band I showed no appreciable change in frequency but reversed sign for compounds **12**, **13**, (Fig. 2), **16**, and **17** and increased in intensity for **14**. Similar temperature effects were observed in other solvents, the smallest changes being observed for a chloroform solution of **13** and for a methanol solution of **15**. Varying the concentration of **12** from 0.036 to 0.1 *M* in methanol did not appreciably alter the molecular ellipticity *vs.* temperature plot for band I (Fig. 2).

The intensity of band III for the *trans*-dinitrates **16** and **18** was 5–8 times greater than for the *cis*-dinitrates **15** and **17** in acetonitrile solutions whereas the magnitudes of band II showed only 2-fold differences between the *cis*- and *trans*-isomers (Table 3). Since band III is a strong transition ($\varepsilon > 10^3$) and therefore probably allowed, electric dipole – electric dipole transition coupling could be expected (2, 34) which would lead to the observed lower rotatory strength for the approximately parallel *cis*-nitrato groups as compared to the more nearly orthogonal *trans*-nitrato groups (34, 35). The exciton splitting would not be evident because of overlap with band II.

The sign of band II was not altered by changes in solvent or temperature and, on application of the planar symmetry rule, was again found to be a reliable indicator of the molecular configuration (Table 4).

Alkylcyclohexyl Nitrates (19–25)

Conformational freedom in these nitrate esters includes the possibility of ring inversion as well as nitrato group rotation. The parent alcohols of **19** and **20** have *ca.* 100% and that of **21** *ca.* 70% population of the conformer with equatorial hydroxyl at 25° (36). Since cyclohexyl nitrate is 73% equatorial (37) and cyclohexanol 65% equatorial (38) at 25°, ring conformations with equatorial nitrato groups would be expected to predominate in compounds **19**, **20**, **22**,



	R^1	R^2	R^3	R^5
19	$CHONO_2$(e)	$CHCH(CH_3)_2$(e)	CH_2	$CHCH_3$(e)
20	$CHONO_2$(e)	$CHCH_3$(e)	CH_2	$CHCH(CH_3)_2$(e)
21	$CHONO_2$(e)	$CHCH_3$(e)	CH_2	$CHCH(CH_3)_2$(a)
22	$CHONO_2$(e)	$C{=}CH_2$	CH_2	$CHCH(CH_3)_2$(e)
23	$CHONO_2$(a)	$C{=}CH_2$	CH_2	$CHCH(CH_3)_2$(e)
24	$CHONO_2$(e)	CH_2	$CHCH_3$(e)	CH_2
25	$CHONO_2$(a)	CH_2	$CHCH_3$(e)	CH_2

and **24**. All substituents in compounds **21**, **23**, and **25** cannot be equatorial; however, estimates from conformational free energy differences for these groups (39) suggest that the nitrato group would be equatorial in **21** and axial in **23** and **25**. Similar estimates for the related methyl ethers correctly predicted axial and equatorial methoxyl groups (40). The n.m.r. spectrum of **23** indicated an axial nitrato group since the α-proton resonance, a distorted triplet, had a half-height band width of 10 Hz. This ring conformation of **23** also permitted maximum separation of the π orbitals of the exocyclic double bond and the nitrato group. The preferred ring conformations in this series are shown in formulae **19**–**25**.

The preferred nitrato rotamer was also *anti*-C_β in this series with C_β = C-2 for **19**–**21** and **23**, and C_β = C-6 for **22**, **24**, and **25** (Table 4). Ring inversion in **23** and **25** did not alter the rotamer preference.

The c.d. spectra of nitrates **19**–**25** showed bands I–III and, in addition, very weak new bands appeared in the region 292–320 nm (Table 3) which did not correspond to any previously reported nitrate ester transitions. Similar bands were found in the spectra of the acyclic nitrates **26** and **27** but not in those of more conformationally rigid nitrates. The new band was negative for compound **19** in 15 different solvents and as the neat liquid ($[\theta]_{max}$ − 6.4 to − 18 at 322 ± 2 nm). Its intensity rapidly approached zero as the temperature of a methanol solution was lowered to −90° while that of bands I and II increased more slowly. These results suggest that the new band may be a component of the n–π^* transition, similar to the 350 nm band of nitro-compounds (17), or that it may be the resultant of partially-overlapped, oppositely-signed 270 nm bands from different conformers. In the latter case the conformers probably arise from nitrato group libration rather than from ring inversion since the energy barrier for the latter process is estimated to be *ca.* 4.4 kcal mol^{-1} for **19** and **20** and (+)-3-methyl-cyclohexyl nitrate (**24**), which could be expected to have a larger population of the axial conformer, had the weakest of these bands near 298 nm (Table 3).

Band I was even more sensitive to changes in temperature and solvent polarity for **19**–**25** than for the more conformationally rigid nitrate esters. It was positive in acetonitrile solution for all members of the series except **23** and changed sign for compounds **21** and **25** on going to cyclohexane solutions. It appeared at 270 ± 2 nm for compound **19** in 15 different solvents, as the vapor, and as the neat liquid, and was most intense in highly polar solvents such as hexafluoroisopropanol ($[\theta]_{max}$ + 1590) and weakest in cyclohexane (Table 3). There was no clear correlation of the molecular ellipticity of band I with the usual solvent parameters (33), and, as noted above, it increased linearly in magnitude with decreasing temperature.

Nitrates **22** and **23** showed greater intensity in band III than other members of the series and this might be attributed to transition moment coupling of the olefinic and nitrato chromophores.

Again in this series band II was relatively insensitive to changes in solvent and temperature showing no change in sign or wavelength and only ±3% differences in $[\theta]_{max}$ among eight solvents and an increase of only 13% in $[\theta]_{max}$ between +30° and −90° for compound **19**. Band II for compound **22** was partially obscured by band III but was clearly positive in sign. The agreement between the observed signs of band II and those predicted by the planar rule from

TABLE 5. Conformations and chirality of steroid nitrates

Nitrate	Conformations*		Perturbing atoms†	Sign of band II	
	C_α	C_β		Predicted	Observed (8,9)
3β-Cholesteryl	3	4	0/6/25	+	+
3β-Acetoxycholestane-6-one-5α-yl	5	10	8/7/21	+	+
3β,6β-Diacetoxycholestane-5α-yl	5	10	8/7/29	+	+
6α-Fluoro-21-acetoxy-16α-methyl-1,4-pregnadiene-3,20-dione-11α-yl	11	9	15/8/10	–	–
3α,17β-Diacetoxy-5β-androstane-11β-yl	11	9	11/7/13	+	+
6α-Fluoro-21-acetoxy-16-methyl-1,4-pregnadiene-3,20-dione-11β-yl	11	9	8/8/17	+	+
4-Androstene-3-one-17β-yl	17	13	4/10/10	+	+
17α-Ethynyl-4-estrene-3-one-17β-yl	17	13	6/10/9	+	+
5α-Androstane-3β-ol-17β-yl	17	13	4/10/10	+	+
5α-Androstane-3-one-17β-yl	17	13	4/10/10	+	+
3β-Acetoxy-5α-androstane-17β-yl	17	13	4/13/10	+	+
19-*nor*-4-Pregnene-3,20-dione-17α-yl	17	16	3/6/17	+	+
4-Pregnene-3,20-dione-17α-yl	17	16	3/6/18	+	+
21-Acetoxy-4-pregnene-3,20-dione-17α-yl	17	16	7/6/18	+	+

**Anti*-C_β, C_α, and C_β are identified by carbon atom location numbers.

†Numbers of nonhydrogen atoms left/in plane/right of plane of nitrato group.

the preferred conformations was excellent (Table 4).

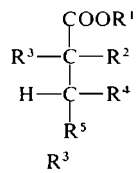
Steroid Nitrates

The planar rule was further tested on 20 nitrate esters of secondary steroid alcohols for which the nitrato c.d. bands have previously been reported (8, 9). The conformational analyses followed the procedure outlined above, the results, and the predicted and observed signs of band II are shown in Table 5. Agreement between observed and predicted signs for fourteen of these steroidal nitrates is very good. Six cholestane and androstane derivatives with 3α- or 3β-nitrato groups (compounds numbered **1–6** by Snatzke and co-workers (9)) could not be conformationally analyzed since molecular models showed no preference for one nitrato rotamer in the 3-position on ring A. Conformational lability is suggested by the absence of a detectable band I in the spectra of the 3-equatorial nitrates and the weakly negative band I found for the axial chromophores (7). The conformational preference of this nitrato group probably could be determined through variable temperature and solvent studies. The rule could not be applied to the c.d. spectra of hexose nitrates published by Tsuzuki *et al.* (5, 6) since only band I has been reported.

Acyclic Nitrates (26–28)

Since no skeletal constraint was apparent from models of these compounds, the planar symmetry rule was applied to predict molecular conformations.

Rotamer *anti*-C_β was assumed to predominate and selection of C_β as methyl, methylene, and methine carbons, respectively, in compounds **26–28** yielded agreement of predicted and observed signs for band II (Table 4). Nitrates **26** and **27** gave bands I–III and an additional, weak, long wavelength bands at 292 nm and 310 nm respectively which, as noted earlier, may be due to the presence of different rotamers in solution. The additional band did not appear



$$\begin{array}{c} COOR^1 \\ | \\ R^3—C—R^2 \\ | \\ H—C—R^4 \\ | \\ R^5 \end{array}$$

	R^1	R^2	R^3	R^4	R^5
26	H	ONO_2	H	H	H
27	C_2H_5	H	ONO_2	H	$COOC_2H_5$
28	C_2H_5	H	ONO_2	ONO_2	$COOC_2H_5$

in the spectrum of the dinitrate of diethyl-L-tartrate (**28**). The o.r.d. data for **26–28** which suggested that nitrates of α-D-hydroxy acids have positive Cotton effects while those of α-L-hydroxy acids have negative Cotton effects (7) probably reflected the sign of band III only since the weaker bands I and II would have been obscured in the background rotation.

The acyclic nitrate esters of the primary steroid alcohols, 3β-acetoxy-5α-cholestane-19-ol and 3β-acetoxy-5β-cholestane-19-ol (9) when assigned *anti*-C_β conformations (C_α = C-19, C_β = C-10) showed a further degree of conformational freedom, namely rotation on the C_α—C_β bond. Assignment of the conformation with C-9 antiperiplanar to the nitrato group gave agreement of the predicted (+) and observed (+) signs for band II whereas similar assignments for C-1 or C-5 were less favored according to the molecular models of these compounds and predicted (+) and (−) signs for band II, respectively.

In general the application of the symmetry rule to the acyclic nitrate esters led to molecular conformations which appeared to be plausible from molecular models.

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