Tetrahedron: Asymmetry Vol. 2, No. 5, pp. 381-387, 1991
Printed in Great Britain

0957-4166/91 $3.00+.00
Pergamon Press plc

CIRCULAR DICHROISM XCIV: CHIROPTICAL PROPERTIES OF STEREOISOMERIC CONJUGATED OXIMES, PART II[1]

Jadwiga Frelek,[a] Günther Snatzke,[b]* and Wojciech J. Szczepek[c]

[a] Institute of Organic Chemistry, Polish Academy of Sciences
PL-012-224 Warszawa, Kasprzaka 44

[b] Chair of Structural Chemistry, Ruhr-University Bochum
D W-4630 Bochum 1, POB 10 21 48

[c] Department of Chemistry, Warsaw University
PL-02-093 Warszawa, Pasteura 1

(*Received* 9 *April* 1991)

Abstract: - Some oximes and oxime acetates of transoidal cholestenones have been synthesized. In three cases of stable syn/anti pairs of oximes both stereoisomers could be separated. The CD-spectra of all compounds have been measured. All syn-isomers show an additional CD band around 280 nm, which does not exist for anti-oximes.

The O-benzyl and O-isopropyl substituted oximes of 6-membered transoid steroidal enones[1,2] usually show the long wavelength Cotton effect around 300 nm (band I). Compared to the sign of the principal CE (band II) this CE is of opposite sign for the syn-, or of the same sign for the anti-isomers. It should be stressed, that all stereomers studied so far by us were syn-Z or anti-E isomers. In continuation of our studies of the oxime chromophore we have, therefore, synthesized a series of oximes derived from easily available transoidal cholestenones. The oximes and oxime acetates were obtained by the standard procedure.[3] Of them we could separate three syn/anti pairs, *viz.* compounds **2/3**, **6/8**, and **10/11**.

The configuration of these new oximes was established by comparison of their ^{1}H NMR spectra with those of the parent enones. In the case of the syn-oximes we have observed a strong deshielding effect[4,5] for the α-olefinic proton (from +0.62 to +0.88 ppm) caused by the syn-oriented oxime hydroxyl group, and a considerable shielding effect for the β-olefinic proton (ca. -0.6 ppm). The α-olefinic proton of anti-oximes was weakly or moderately deshielded (from +0.05 to +0.38 ppm), but the β-olefinic proton remained still strongly shielded (ca. -0.7 ppm). In comparison to the chemical shift of the corresponding protons in the parent oximes acetylation

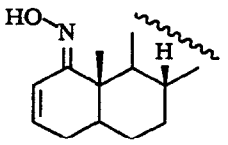
of the hydroxyl of the oxime introduces a positive shift for the α-olefinic proton of anti-oxime acetates (ca. +0.2 ppm), and for the β-olefinic proton of syn- and anti-oximes. A negative shift of the α-olefinic proton is found for syn-oxime acetates (ca. -0.1 ppm).

Independent support about the syn/anti geometry of the oximes could be deduced from the value of the chemical shift of the α'-proton[3] which lies in, or is very close to, the plane of the oxime group. The signal of the methine H or of one proton from a methylene moiety in α-position to the oxime appeared at 3.34 (for **11**) or 2.77 to 3.03 ppm for anti-oximes and their acetates. In syn-oximes the corresponding signal is well separated only for the proton from the methine group (δ = 2.48 for **10**) because of the weak deshielding effect caused by the electron lone pair of the nitrogen. We have also found another regularity: in all cases the R_f-values of anti-oximes were higher than those of the corresponding syn-oximes.

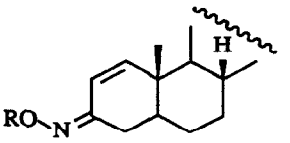
The CD-data of the oximes and their acetates are collected in Table 1. The principal CD band (band II) of oximes of steroidal transoid enones, associated with the $\pi \rightarrow \pi^*$ transition, appears between 227 - 237 nm for syn-, and between 236 - 259 nm for anti-oximes. The sign of this Cotton effect is the same for stereoisomeric syn/anti oximes (*cf.* the pairs **2/4**, **6/8**, **7/9**, and **10/11**). The second short-wavelength band (band III) is found between 199 - 213 nm (except for compound 3) or 221 - 231 nm for syn and anti oximes, respectively. In all cases band II and band III have opposite signs. At shorter wavelenghts another band is present (band IV), which is always detectable in the CD-curves of the anti-oximes, but only occasionally in those of the syn-oximes.

All syn-oximes and their acetates show the long-wavelength CD band (band I) in the 263 - 282 nm region, which is of opposite sign to the principal Cotton effect, and which corresponds to the $n \rightarrow \pi^*$ transition. The magnitudes of this Cotton effect vary from 0.07 to 1.29 $\Delta\epsilon$-units, and are much higher than those of O-benzyloximes (0.02 - 0.32) or O-isopropyloximes (0.08 - 0.20).[1,2] For anti-oximes band I does either not appear at all, or it is overlapped by the principal band, which shows a red shift (ca. 11 - 16 nm in relation to the isomeric syn-oxime). In case of a weak CE I of same sign as CE II it must be overlapped by the latter if it is strong, and will, therefore, not be detectable. Such a possibility is well illustrated in Figure 1, which shows the CD curves for syn-oxime **10** and anti-oxime **11**.

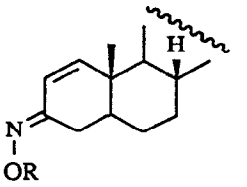
Besides these some compounds give an additional CD-band. Thus the oxime acetates **7** and **9** of 4-cholesten-3-one show very small CEs of opposite signs around 330 nm, and oxime **12** and its acetate **13** give an additional negative CD around 300 nm. The origin of these Cotton effects is unknown, but it is sure that they are not caused by traces of the corre-



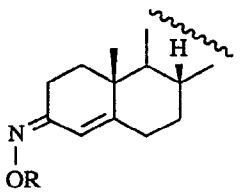
1



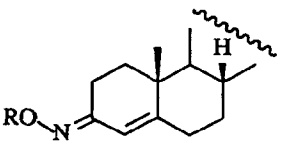
2 R = H
3 R = Ac



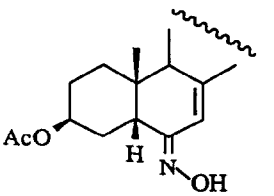
4 R = H
5 R = Ac



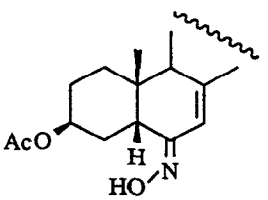
6 R = H
7 R = Ac



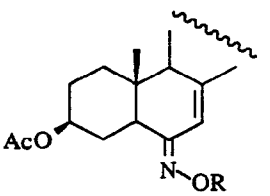
8 R = H
9 R = Ac



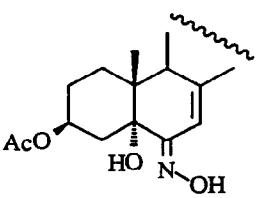
10



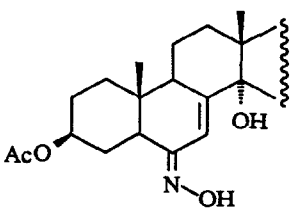
11



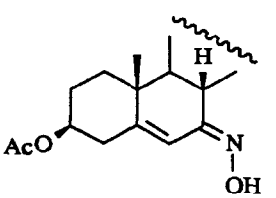
12 R = H
13 R = Ac



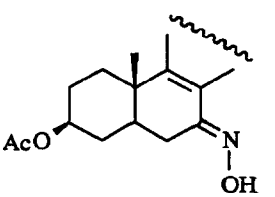
14



15



16



17

sponding conjugated enone.

EXPERIMENTAL

Melting points were determined on a Boetius micro-melting point apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 241 polarimeter in chloroform solution, concentrations are given in g/100 ml. IR-spectra were recorded on a UR-20 spectrometer in KBr (wave numbers, main bands are cited in cm^{-1}). ^1H NMR were taken on a Bruker AM-500, Bruker AM-400, Tesla BS 567, or Bruker AM-80 in $CDCl_3$. CD spectra were recorded with a modified ISA-JOBIN-YVON Dichrographe Mark III in acetonitrile. Column chromatography was performed on Kieselgel 60, 70-230 mesh, Merck.

The oximes and oxime acetates were synthesized from the known α,β-unsaturated ketones according to the earlier reported procedure.[1] The isolated products had the following data:

(1E)-1-Hydroxyimino-5α-cholest-2-ene (**1**): m.p. 157-159°C (hexane). - IR: 3320, 3050, 1650, 960, 938, 790. - ^1H NMR (80): 0.68 (s, 3H, 18-Me), 0.98 (s, 3H, 19-Me), 6.08 (m, 3-H), 6.65 (m, 2-H), 7.39 (s, NOH). Lit.[6]: m.p. 155°C (methanol). - ^1H NMR: 0.68 (s, 3H, 18-Me), 0.95 (s, 3H, 19-Me), 6.10 (m, 2-H), 6.65 (m, 3-H).

(3Z)-3-Hydroxyimino-5α-cholest-1-ene (**2**): m.p. 149-153°C (methanol). - $[\alpha]_D$ +29.1 (c=0.2). - IR: 3270, 3060, 1637, 974, 786. - ^1H NMR (500): 0.68 (s, 3H, 18-Me), 0.91 (s, 3H, 19-Me), 2.17 (dd, J=15.9 and 3 Hz, 4α-H), 2.32 (dd, J=15.9 and 13.9 Hz, 4β-H), 6.49 (d, J=10.4 Hz, 1-H), 6.66 (d, J=10.4 Hz, 2-H), 7.74 (br m, NOH). Lit.[5]: ^1H NMR (the spectrum was taken from a mixture of 3*Z* and 3*E* isomers): 6.42 (1-H), 6.56 (2-H).

(3Z)-3-Acetoxyimino-5α-cholest-1-ene (**3**): m.p. 73-76°C (hexane). - IR: 1780, 1630, 1208, 1004, 934, 886, 788. - ^1H NMR (80): 0.66 (s, 3H, 18-Me), 0.92 (s, 3H, 19-Me), 2.16 (NOAc), 6.57 (d, J= 10.1 Hz, 2-H), 6.67 (d, J=10.1 Hz, 1-H).

$C_{29}H_{47}NO_2$ (441.7)	calcd.	C 78.86	H 10.73	N 3.17
	found	C 78.91	H 10.63	N 3.24.

(3E)-3-Hydroxyimino-5α-cholest-1-ene (**4**): m.p. 156-160°C (methanol). - IR: 3280, 978, 965, 939, 775. - ^1H NMR (100): 0.68 (s, 3H, 18-Me), 0.87 (s, 3H, 19-Me), 2.80 (dd, J=18 and 3.5 Hz, 4α-H), 5.97 (d, J=9.9 Hz, 2-H), 6.43 (d, J=9.9 Hz, 1-H). Lit.[5]: m.p. 149-150°C (methanol). - ^1H NMR: 0.68 (s, 3H, 18-Me), 0.87 (s, 3H, 19-Me), 6.00 (2-H), 6.42 (1-H).

(3E)-3-Acetoxyimino-5α-cholest-1-ene (**5**): m.p. 149-150°C (hexane). - IR: 3060, 1773, 1625, 1590, 1300, 1230, 1010, 960, 896, 800. - ^1H NMR (400): 0.65 (s, 3H, 18-Me), 0.86 (s, 3H, 19-Me), 2.16 (NOAc), 2.77 (dd, J=18.1 and 4.2 Hz, 4α-H), 6.14 (d, J=10 Hz, 2-H), 6.64 (d, J=10 Hz, 1-H). Lit.[5]: m.p. 159-162°C (acetone). - ^1H NMR: 0.67 (s, 3H, 18-Me), 0.88 (s, 3H, 19-Me), 6.18 (2-H), 6.68 (1-H).

(3Z)-3-Hydroxyimino-cholest-4-ene (**6**): m.p. 81-83°C (hexane-ether). - $[\alpha]_D$ +165.8 (c=0.6). - IR: 3290, 1650, 950, 914, 876. - ^1H NMR (400): 0.69 (s, 3H, 18-Me), 1.07 (s, 3H, 19-Me), 6.44 (d, J=1.5 Hz, 4-H). Lit.[3]: ^1H NMR (the spectrum was taken from a mixture of 3*Z* and 3*E* isomers): 6.48 (4-H).

(3Z)-3-Acetoxyimino-cholest-4-ene (**7**): m.p. 97-99°C (hexane). - $[\alpha]_D$ +165.8 (c=0.3). - IR: 1768, 1632, 1210, 1000, 936, 880, 863. - ^1H NMR (400): 0.67 (s, 3H, 18-Me), 1.09 (s, 3H, 19-Me), 2.20 (NOAc), 6.33 (s, 4-H).

$C_{29}H_{47}NO_2$ (441.7)	calcd.	C 78.86	H 10.73	N 3.17

found C 78.99 H 10.57 N 3.28.

(3E)-3-Hydroxyimino-cholest-4-ene (8): m.p. 162-165°C (methanol). - $[\alpha]_D$ +76.5 (c=0.4). - IR: 3280, 1644, 1000, 974, 935, 870, 856. - ^{1}H NMR (400): 0.67 (s, 3H, 18-Me), 1.03 (s, 3H, 19-Me), 3.03 (d, J=17.1 Hz, 2α-H), 5.75 (d, J=1.4 Hz, 4-H). Lit.[3]: m.p. 62/152°C. - ^{1}H NMR: 5.77 (4-H).

(3E)-3-Acetoxyimino-cholest-4-ene (9): m.p. 72-75°C (hexane). - $[\alpha]_D$ +107.9 (c=0.9). - IR: 1778, 1642, 1605, 1220, 1005, 948, 910, 858. - ^{1}H NMR (400): 0.66 (s, 3H, 18-Me), 1.04 (s, 3H, 19-Me), 2.14 (NOAc), 2.98 (d, J=17.4 Hz, 2α-H), 5.93 (s, 4-H).

$C_{29}H_{47}NO_2$ (441.7) calcd. C 78.86 H 10.73 N 3.17
found C 78.72 H 10.90 N 3.23.

(6E)-6-Hydroxyimino-5β-cholest-7-en-3β-ol 3-acetate (10): m.p. 174-178°C (ethanol). - IR: 3455, 1716, 1637, 1280, 1236, 1160, 1032, 1000, 917. - ^{1}H NMR (400): 0.57 (s, 3H, 18-Me), 0.88 (s, 3H, 19-Me), 2.07 (OAc), 2.48 (dd, J=12.9 and 3.2 Hz, 5β-H), 5.07 (nm, 3α-H), 6.33 (nm, 7-H).

$C_{29}H_{47}NO_3$ (457.7) calcd. C 76.10 H 10.35 N 3.06
found C 76.17 H 10.29 N 3.11.

(6Z)-6-Hydroxyimino-5β-cholest-7-en-3β-ol 3-acetate (11): m.p. 210-214°C (hexane). - $[\alpha]_D$ -42.0 (c=0.4). - IR: 3410, 1730, 1640, 1270, 1234, 1160, 1030, 970, 948, 930, 908, 868. - ^{1}H NMR (400): 0.56 (s, 3H, 18-Me), 0.91 (s, 3H, 19-Me), 2.08 (OAc), 3.34 (dd, J=12.9 and 3.2 Hz, 5β-H), 5.06 (nm, 3α-H), 6.05 (nm, 7-H).

$C_{29}H_{47}NO_3$ (457.7) calcd. C 76.10 H 10.35 N 3.06
found C 76.02 H 10.44 N 2.98.

(6E)-6-Hydroxyimino-5α-cholest-7-en-3β-ol 3-acetate (12): m.p. 223-225°C (acetone). - $[\alpha]_D$ -120.5 (c=0.4). - IR: 3390, 1717, 1638, 1280, 1040, 945, 930. - ^{1}H NMR (80): 0.57 (s, 3H, 18-Me), 0.83 (s, 3H, 19-Me), 2.02 (OAc), 4.73 (br m, 3α-H), 6.37 (nm, 7-H), 7.68 (s, NOH).

$C_{29}H_{47}NO_3$ (457.7) calcd. C 76.10 H 10.35 N 3.06
found C 75.97 H 10.29 N 3.12.

(6E)-6-Acetoxyimino-5α-cholest-7-en-3β-ol 3-acetate (13): m.p. 136.5-138°C (methanol). - $[\alpha]_D$ -126.8 (c=0.8). - IR: 1775, 1740, 1632, 1250, 1225, 1205, 1041, 942, 930, 885. - ^{1}H NMR (80): 0.57 (s, 3H, 18-Me), 0.81 (s, 3H, 19-Me), 2.01 (3-OAc), 2.06 (NOAc), 4.73 (br m, 3α-H), 6.24 (nm, 7-H).

$C_{31}H_{49}NO_4$ (499.7) calcd. C 74.51 H 9.88 N 2.80
found C 74.39 H 10.01 N 2.76.

(6E)-6-Hydroxyimino-5α-cholest-7-en-3β,5-diol 3-acetate (14): m.p. 223-227°C (decomp., from acetone-hexane). - $[\alpha]_D$ -132.3 (c=0.4). - IR: 3600-3050, 1735, 1640, 1260, 1160, 1050, 1027, 978, 950, 926, 874. - ^{1}H NMR (500): 0.59 (s, 3H, 18-Me), 0.88 (s, 3H, 19-Me), 2.03 (OAc), 5.13 (br m, 3α-H), 6.24 (t, J=2.1 Hz, 7-H), 8.11 (s, NOH).

$C_{29}H_{47}NO_4$ (473.7) calcd. C 73.53 H 10.00 N 2.96
found C 73.76 H 9.89 N 2.88.

(6E)-6-Hydroxyimino-5α-cholest-7-en-3β,14α-diol 3-acetate (15): m.p. 253-256°C (acetone). - $[\alpha]_D$ -56.5 (c=0.4). - IR: 3500-3320, 1716, 1645, 1285, 1044, 940, 924, 910, 860. - ^{1}H NMR (500): 0.69 (s, 3H, 18-Me), 0.81 (s, 3H, 19-Me), 2.04 (OAc), 2.29 (dd, J=12.1 and 3.5 Hz, 5α-H), 2.48 (m, 9α-H), 4.73 (br m, 3α-H), 6.63 (d, J=2.7 Hz, 7-H), 8.00 (s, NOH).

$C_{29}H_{47}NO_4$ (473.7) calcd. C 73.53 H 10.00 N 2.96
found C 73.48 H 10.15 N 3.04.

(7Z)-7-Hydroxyimino-cholest-5-en-3β-ol 3-acetate (16): m.p. 189.5-191°C (acetone). - IR: 3470, 1725, 1648, 1270, 1040, 958, 920, 905, 873,

717. - ^{1}H NMR (80): 0.67 (s, 3H, 18-Me), 1.10 (s, 3H, 19-Me), 2.02 (OAc), 4.68 (br m, 3α-H), 6.57 (s, 6-H), 6.98 (s, NOH, disappeared after D_2O addition). Lit.[7]: m.p. 191°C. - Lit.[8]: ^{1}H NMR 0.70 (s, 3H, 18-Me), 1.13 (s, 3H, 19-Me), 2.05 (OAc), 4.70 (3α-H), 6.61 (6-H).

(7E)-7-Hydroxyimino-5α-cholest-8-en-3β-ol 3-acetate (**17**): m.p. 138-140°C (methanol). - $[\alpha]_D$ -51.3 (c=0.4). - IR: 3470, 1730, 1273, 1037, 915. - ^{1}H NMR (80): 0.59 (s, 3H, 18-Me), 1.05 (s, 3H, 19-Me), 2.02 (OAc), 3.02 (br d, J=12 Hz, 6α-H), 4.78 (br m, 3α-H and NOH).

$C_{29}H_{47}NO_3$ (457.7) calcd. C 76.10 H 10.35 N 3.06
found C 75.95 H 10.42 N 3.11.

Table 1: CD-data of the conjugated oximes in acetonitrile.
$\Delta\epsilon$ (λ[nm])

Comp. No.	E/Z	Addit. Band	Band I	Band II	Band III	Band IV
			syn-oximes			
1	E		-0.13(275)	+22.8(227)		+3(195)
2	Z		+0.9 (270)	- 3.2(237)	+5 (213)	
3	Z		+0.92(267)		+4.0(227)[a]	-6(202)[a]
6	Z		-0.35(280)	+12.6(235)	-4 (211)	+2(193)
7	Z	+0.02(333)	-0.41(277)	+13.5(236)[a]		+7(212)[a]
10	E		+0.46(281)	-19.8(234)	+6 (205)	
10[d]	E		+0.66(282)	-17.5(236)	+4 (207)	
12	E	-0.03(300)	+0.39(279)	-28.9(232)	+3 (203)	
13	E	-0.11(296)	+0.07(280)	-27.1(234)	+10 (199)	
14	E		+0.62(276)	-24.6(237)	+10 (200)	
14[d]	E		+0.83(275)	-27.9(237)		
15	E		+0.85(274)	-10.7(235)		
16	Z		+0.41(279)	-19.0(234)		-6(196)
			anti-oximes			
4	E			- 6.20(249)	+17.7(224)	-2(199)
5	E			- 5.65(254)	+17.9(226)	-7(199)
8	E			+11.7 (246)	- 6.8(221)	-3(197)
9	E	-0.02(329)		+14.0 (250)	- 4.1(224)	-4(199)
11	Z			-18.6 (250)		+10(190)
11[d]	Z			-18.41(251)		
17	E			+13.29(259)	-25.2(231)	+5(203)

[a] Assignment of band on basis of sign and not on wavelength
[d] Measurement of solution in dioxane

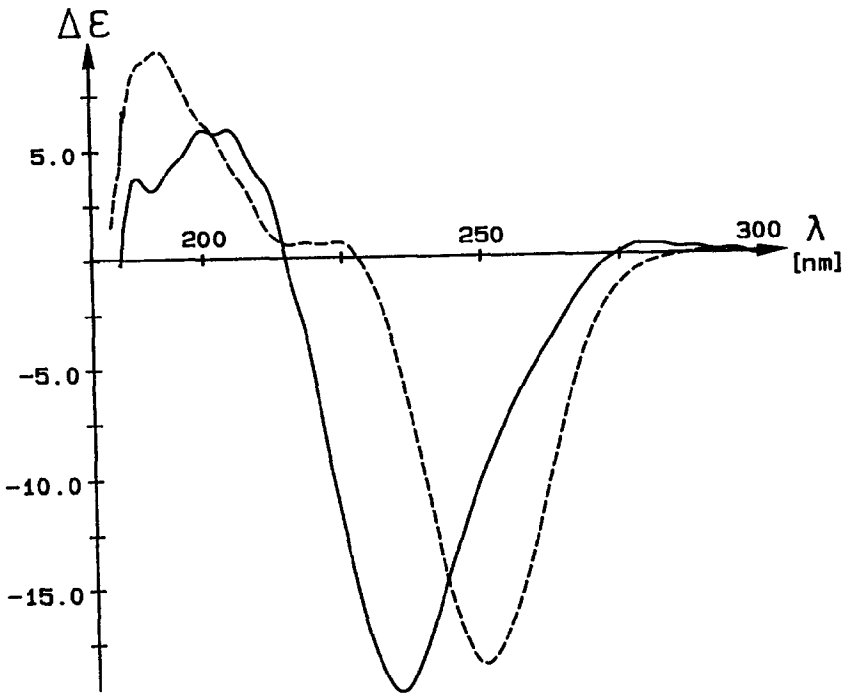


Figure 1: CD of **10** (——) and 11 (----), acetonitrile solution.

ACKNOWLEDGEMENTS

G.S. thanks the DFG, FONDS der Chemie, and HOECHST AG, J.F. and W.J. Szcz. PAN and DFG for valuable financial support. We all thank Prof. Duddeck for many NMR-spectra and Ing. U. Wagner for valuable technical assistance.

REFERENCES

1. J. Frelek, L. Huang, F. Kerek, G. Snatzke, and W.J. Szczepek, *Liebigs Ann.Chem.* (1991) 89.
2. A. Bodor, D. Breazu, J. Miklos, B. Demian, and F. Kerek, *Tetrahedron* 36 (1980) 1785.
3. H. Duddeck, J. Frelek, W.J. Szczepek, and W.J. Rodewald, *Bull.Chem. Soc.Ethiop.* 1 (1987) 18.
4. C.W. Shoppee, R. Lack, and B.C. Newman, *J.Chem.Soc.* (1964) 3388.
5. C.W. Shoppee, R. Lack, R.N. Mirrington, and L.R. Smith, *J.Chem.Soc.* (1965) 5868.
6. Ch. Marazano and P. Longevialle, *Bull.Soc.Chim.Fr.* (1975) 1307.
7. B. Matkovics, Zs. Tegyey, G. Gondos, and Z. Balaspiri, *Microchem.J* 13 (1968) 502.
8. C.G. Francisco, D. Melian, J.A. Salazar, and E. Suarez, *J.Chem.Soc., Perkin Trans.I* (1982) 923.