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Sylvestrene Nitrosochloride and Derived Amino Oximes*

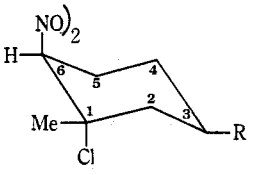
Douglas J. Brecknell,[A] *Raymond M. Carman*,[A] *Bakthan Singaram*[B] *and James Verghese*[B]

[A] Department of Chemistry, University of Queensland, St. Lucia, Qld. 4067.
[B] Department of Chemistry, Christian Medical College, Vellore 632002, India.

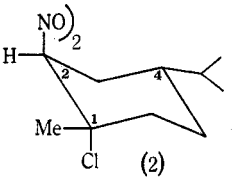
Abstract

Configurational and conformational effects in amino oximes derived from sylvestrene (*m*-mentha-6,8-diene) nitrosochloride are discussed in terms of o.r.d. and ^{1}H n.m.r. observations.

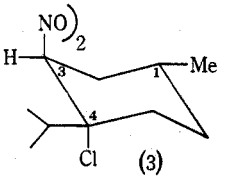
(+)-Sylvestrene nitrosochloride, known since 1888,[1] was recently[2] assigned structure (1a) (without stereochemical implications). With benzylamine,[3,4] piperidine[4] and aniline[4] it affords crystalline 'nitrolamines' which yield corresponding chloro derivatives by the addition of hydrogen chloride.[4,5] The structure and stereochemistry of these derivatives has now been reinvestigated.



(1a) R = MeC═CH$_2$
(1b) R = CClMe$_2$



(2)



(3)

The nitrosochloride is assigned stereostructure (1a). The proton under the nitroso group is clearly equatorial, showing only small ^{1}H n.m.r. couplings to the adjacent C5 protons. The C1 stereochemistry is more difficult to determine. The C1 methyl and C6 proton show ^{1}H n.m.r. field positions (δ 1·67 and 5·68) similar to the C1 methyl and C2 proton of *p*-menth-1-ene nitrosochloride (2)[6] (δ 1·68 and 5·73). Compound (2) shows a C2 equatorial proton the spectral shape, coupling and chemical shift of which are similar to those of the analogous C3 proton (δ 5·70) of *p*-menth-3-

* Part XLVII in the series 'Studies in Terpenes' of the Indian Group; Part XLVI, *Indian J. Chem.*, in press.

[1] Wallach, O., *Justus Liebigs Ann. Chem.*, 1888, **245**, 241.
[2] Mathew, C. P., and Verghese, J., *Indian J. Chem.*, 1964, **2**, 457.
[3] Wallach, O., *Justus Liebigs Ann. Chem.*, 1889, **252**, 106.
[4] Bardyshev, I. I., and Balashov, N. N., *Dokl. Akad. Nauk B. SSR*, 1967, **11**, 133.
[5] Wallach, O., and Conrady, E., *Justus Liebigs Ann. Chem.*, 1889, **252**, 141.
[6] Carman, R. M., and Verghese, J., *Aust. J. Chem.*, to be published: 'Amino oximes from *p*-menth-1-ene and from limonene'.

ene nitrosochloride (3)[6] in which the C 4 isopropyl group is likely to be in the equatorial position. Therefore the chlorine atom in compounds (1a), (2) and (3) exerts a similar effect upon the adjacent equatorial proton in each case and is positioned axially in all three compounds. Thus the addition of nitrosyl chloride has occurred *trans* diaxially in all these examples. This is in accord with recent literature reports[7] that the addition is normally *trans* across a double bond although instances of *cis* addition have been recorded.[8–10]

Addition of hydrogen chloride to nitrosochloride (1a) yields the chloro derivative (1b) with a consistent ^{1}H n.m.r. spectrum. Compounds (1a,b) and (2) [but unfortunately not (3) which was only available in optically inactive (*meso* or racemic?) form] all show the same o.r.d. curve; this suggests that the stereochemistry about the N–N dimer system is the same in each case.

Treatment of compound (1a) with primary amines led to a series of amino oximes (4a–h) and (5). Subsequent hydrochlorination of these amino oximes gave chloro derivatives (6a–f) and (7a). Nitrosation of the amino oximes (4) gave *N*-nitroso derivatives (8a–e). Reaction of compound (1a) with secondary amines did not afford pure products, but chloro derivatives (7b,c) were isolated when these reaction mixtures were hydrochlorinated. Only crystalline products are discussed subsequently.

As in previous work,[11,12] some interesting configurational and conformational effects were observed in the amino oximes. All products are written with the C=N bond in the more stable (*E*) configuration,[13] and no evidence of (*Z*) isomers was obtained. The reaction from nitrosochloride (1a) to amino oxime is pictured[12] as proceeding through the nitrosoene (9) in which the configuration at C 1 has been destroyed, so that either axial [(4), (6), (8)] or equatorial [(5), (7)] amino groups result depending upon the relative stabilities of the products.

The configurations are determined mostly from ^{1}H n.m.r. data (Table 1). As in former studies,[11,12] the methyl group adjacent to the oxime group is deshielded when it lies equatorially and in the plane of the C=N double bond, while the axial methyl in (7b) and (7c) falls at much higher field. *N*-Nitrosation of the secondary amines leading to (8a–e) causes a considerable shift to H 5*ax*, which also suggests that the amine and H 5*ax* are proximal.

The o.r.d. curves are listed in Table 1 and presented in Fig. 1. Compounds (4a–g) and (6a–d) group together as a family, with some enhancement of values associated with the benzylamines (4g) and (6d). The curves all show a plain positive slope, consistent with the results of Crabbé[14] who demonstrated that oximes show curves of the same sign as those of the corresponding ketone. In the examples listed above the amino group always falls into a positive quadrant. The *N*-nitroso products (8a–e) showed a similar family of positive curves, with minor perturbations superimposed between 436 and 334 nm due to the *N*-nitroso group. The similarity of all these curves suggests similar stereochemistry within the families.

[7] Rogic, M. M., Demmin, T. R., Fuhrmann, R., and Koff, F. W., *J. Am. Chem. Soc.*, 1975, **97**, 3241.
[8] Meinwald, J., Meinwald, Y. C., and Baker, T. N., *J. Am. Chem. Soc.*, 1964, **86**, 4074.
[9] Fieser, L. F., and Fieser, M., 'Current Topics in Organic Chemistry' Vol. 1, p. 86 (Reinhold: New York 1964).
[10] Bell, K. H., *Aust. J. Chem.*, 1971, **24**, 1089.
[11] Carman, R. M., Singaram, B., and Verghese, J., *Aust. J. Chem.*, 1974, **27**, 453.
[12] Carman, R. M., Singaram, B., and Verghese, J., *Aust. J. Chem.*, 1974, **27**, 909.
[13] Lyle, G. G., and Barrera, R. M., *J. Org. Chem.*, 1964, **29**, 3311.
[14] Crabbé, P., and Pinelo, L., *Chem. Ind. (London)*, 1966, 158.

The o.r.d. of the equatorial tertiary amines (7b–c) also showed plain positive curves, of reduced amplitude. The amino group now lies in the sector-dividing plane, while the methyl falls into a positive quadrant.

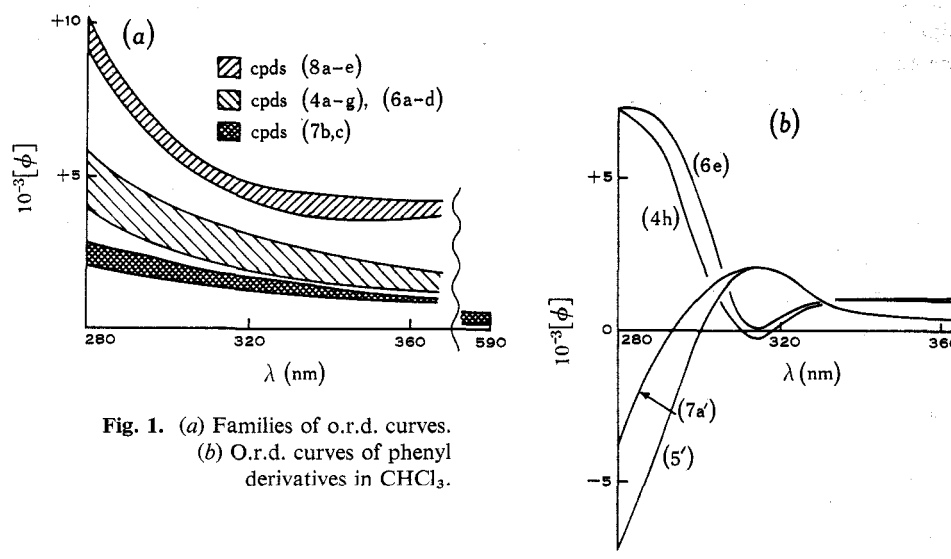


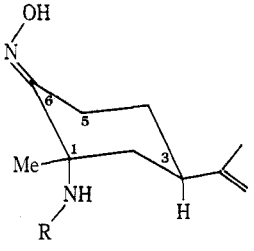
Fig. 1. (*a*) Families of o.r.d. curves. (*b*) O.r.d. curves of phenyl derivatives in $CHCl_3$.

The stereochemistry of the phenylamino compounds (4h), (5), (6e) and (7a) proved to be more troublesome. Two isomers (4h) and (5) are formed when aniline reacts with compound (1a). On hydrochlorination (4h) gives (6e), and (5) gives (7a). In order that two isomers should form, the conformational preferences between axial methyl, equatorial phenylamino and equatorial phenylamino, axial methyl, when they are vicinal to an oxime group, must be small. In the general case it seems that dipole–dipole repulsions between the oxime and amine groups force the amine into an axial position unless the amine is large (tertiary) when 1,3-diaxial interactions predominate and allow the eclipsed equatorial amine conformation to become the more stable arrangement. In the special case of the phenylamines (4h) and (5) these effects almost balance. Compounds (4h) and (6e) show ^1H n.m.r. spectra compatible with the conformations as drawn, and they give negative Cotton effect curves due to a phenylamino transition superimposed upon the strong positive background of conformationally analogous oximes. The *p*-tolylamino derivative (6f) also fits this series. The remaining isomers (5) and (7a) must then be epimeric with (4h) and (6e) at C 1. However, compound (5) shows in the ^1H n.m.r. spectrum an equatorial C 1 methyl eclipsed by the oxime, at the same field position as given by isomer (4h). Furthermore the o.r.d. curve of (5), expected to show a positive Cotton effect due to the phenylamino group superimposed upon a plain positive curve due to the oximo group with a methyl in a positive quadrant, in fact showed a positive Cotton effect superimposed upon a strong negative curve. The boat conformation (5′)* (or some minor twist form of (5′)) is the only arrangement which allows a plain negative curve, a positive phenylamino Cotton effect and the eclipsed methyl/oxime groups, and we propose that compound (5) exists in chloroform as conformer (5′). The other possible conformer, with the axial isopropyl group (5″), is rejected on grounds that isomer (5″) is expected to be much less

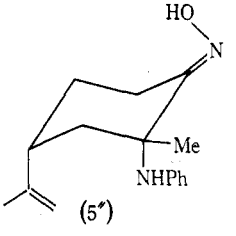
* Numbers are primed to indicate a conformer of the unprimed structure.

stable than isomer (4h) due to the adverse 1,3-diaxial isopropyl/phenylamino interaction.

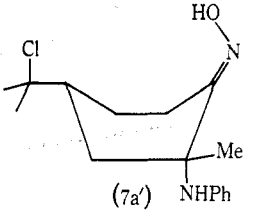
Hydrochloride (7a) likewise is assigned conformation (7a′), at least in solution. These boat conformers (5′) and (7a′) appear to minimize the phenylamino/oxime dipole–dipole repulsion without introducing any other prohibitive interactions. When the amino group becomes larger, as in the tertiary amines, the equatorial requirements of the large group dominate and the chair conformers (7b) and (7c) are adopted.



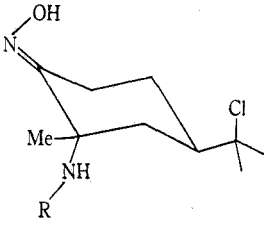
(4a) R = Me
(4b) R = Et
(4c) R = Pr
(4d) R = $CH_2CH{=}CH_2$
(4e) R = Bu
(4f) R = cyclohexyl
(4g) R = $PhCH_2$
(4h) R = Ph



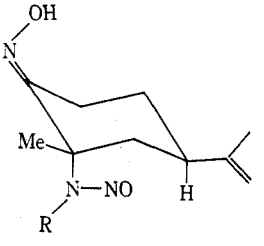
(5′)



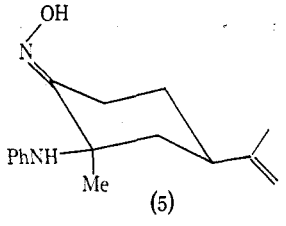
(7a′)



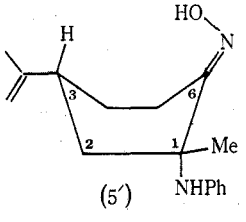
(6a) R = Pr
(6b) R = Bu
(6c) R = cyclohexyl
(6d) R = $PhCH_2$
(6e) R = Ph
(6f) R = p-MeC_6H_4



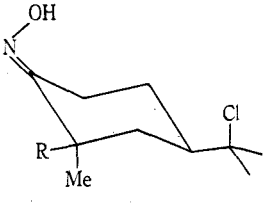
(8a) R = Me
(8b) R = Et
(8c) R = Pr
(8d) R = Bu
(8e) R = pentyl



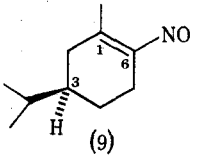
(5)



(5′)



(7a) R = PhNH
(7b) R = piperidyl
(7c) R = Et_2N



(9)

It is interesting to note that the axial C 3 proton of (4a–h) and of (8a–e), which is visible in the ^1H n.m.r. spectra of these isomers because it is in an allylic position, moves upfield considerably in compound (5′), consistent with the C 3 proton in (5′) being shielded due to its position above the plane of the oxime double bond.

^1H n.m.r. spectra in benzene solution confirm the structures. Normally, in the (4), (6) and (7) series and also in 1-substituted amino-*p*-menthan-2-one oximes,[6] benzene causes only very small shifts in the field position of the C 1 methyl whether it is

Table 1. ^{1}H n.m.r. and o.r.d. data

Molecular rotations were measured in $CHCl_3$ and are positive, unless otherwise specified

Compound	^{1}H n.m.r. δ values in $CDCl_3$ solution								Molecular rotations [ϕ] at λ (nm)									
	H 5*eq*	H 5*ax*	H 3	C 1–Me	C 8–Me	H 9	H 2*ax*	H 2*eq*	589	436	365	334	313	302	297	289	280	265
(4a)	3·37	1·9	2·52	1·24	1·70	4·68	1·42	[A]	350	750	1300	1800	2400	2800	3000	3400	4200	6200
(4b)	3·37	1·9	2·5?	1·27	1·72	4·69	1·40	[A]	380	840	1400	2000	2500	3000	3300	3700	4500	6600
(4c)	3·37	2·0	2·5?	1·26	1·71	4·70	1·42	[A]	410	870	1500	2000	2600	3100	3300	3700	4600	6800
(4d)	3·38	2·0	2·61	1·29	1·71	4·70	1·47	[A]	420	880	1500	2000	2700	3100	3400	3800	4600	6700
(4e)	3·39	2·0	2·55?	1·26	1·72	4·71	1·42	[A]	430	900	1500	2100	2800	3300	3600	4000	4900	7300
(4f)	3·37	2·13	2·5?	1·29	1·71	4·71	1·42		340	670	1200	1600	2100	2600	2700	3100	3900	6000
(4g)	3·4?	2·10	2·64	1·39	1·70	4·72	1·47	[A]	480	1000	1700	2400	3100	3600	3900	4500	5400	
(4h)	3·36	2·12	2·72	1·48	1·74	4·75	1·64?	[A]	360	710	1020	1010	−170	1800	3600	6300	7200	
(6a)	3·33	1·9		1·28	—1·55—		1·42?		440	860	1500	2100	2700	3100	3400	3800	4700	7200
(6b)	3·32	1·9		1·27	—1·55—		1·40?		380	770	1300	1800	2400	2700	3000	3400	4100	6100
(6c)	3·34	1·9		1·30	—1·56—		1·42?		360	750	1300	1700	2300	2600	2900	3300	4100	6400
(6d)	3·38	2·1		1·40	—1·56—				520	1100	1900	2600	3400	3900	4200	4800	5800	
(6e)	3·36	2·1		1·50	1·56	1·63	1·62?	[B]	380	770	1120	1030	100	3500	5300	7100	7200	5900
(6f)	3·36	2·1		1·46	1·57	1·63	1·62?		320	620	830	550	1600	4600	5100	5800	5400	
(8a)	3·50	1·7	2·43	1·54	1·72	4·70	1·7?	3·0	480	800	3900	4500	5100	5900	6400	7500	9500	14600
(8b)	3·5	1·7	2·46	1·57	1·73	4·72	1·7	2·98	540	980	4100	3900	4900	5900	6600	7700	9600	
(8c)	3·5	1·7	2·43	1·54	1·70	4·72	1·7?	2·98	560	1000	4200	4100	5000	6100	6800	8000	10000	
(8d)	3·5	1·7	2·48	1·57	1·73	4·72	1·6	3·01	490	890	3700	3650	4600	5500	6100	7300	9100	14300
(8e)	3·5	1·7	2·48	1·57	1·72	4·72		2·98	530	930	3900	3850	4900	5900	6600	7800	10200	
(5′)	3·39	2·1	<2·35	1·51	1·72	4·70			110	210	400	680	2100	650	−1300	−4100	−7200	
(7a′)	3·34	2·0	<2·2	1·51	—1·56—			[C]	150	280	450	740	2100	1400	480	−850	−3700	
(7b)	3·26	2·2		1·05	1·51	1·58	1·16		270	530	840	1100	1400	1600	1700	1800	2000	2400
(7c)	3·30	2·2		1·12	1·55	1·62	1·2?		310	670	1100	1500	1800	2100	2300	2600	2800	3900

[A] δ 1·9–2·0, H 2*eq*, H 4. [B] δ 1·9–2·4, H 2*eq*, H 4. [C] δ 1·9–2·2, H 2*eq*, H 4.

axial or equatorial. Downfield shifts of δ 0–0·1 are common. Compound (4h) in benzene showed the C 1 methyl at δ 1·53, a typical downfield shift of only 0·05 ppm. However, compound (5′) in benzene gave the C 1 methyl at δ 1·26, an abnormal upfield shift of 0·26 ppm, and taking the methyl more into the region expected for the axial methyl, equatorial phenylamino conformer (5). The spectrum of (4h) in benzene separated H 5*eq* (doublet of triplets), H 3*ax* (triplet of triplets) and H 5*ax* (triplet of doublets), with couplings showing clearly the axial nature of H 3. Compound (5′) in benzene gave an unresolved four-proton singlet from which couplings were unattainable at δ 1·95, but with H 3 and H 5*ax* at higher field than in (4h). These results all support conformer (5′) for compound (5) in chloroform solution, with the equilibrium being perhaps displaced toward (5) in benzene. A similar upfield shift in benzene was noted for the C 1 methyl of (7a′).

The o.r.d. curves of all the compounds were essentially the same in benzene as in chloroform. The exception was compound (5′) which showed a much reduced amplitude in benzene. This result is again consistent with a displacement of conformation, in a conformationally labile system, due to solvent effects.

Experimental

Melting points are in open capillary and are uncorrected. O.r.d. data in $CHCl_3$ are recorded in Table 1 and in Fig. 1. ^{1}H n.m.r. data for $CDCl_3$ solutions are given in Table 1. All compounds listed showed $J_{5ax,5eq}$ of $-12 \rightarrow -14$ Hz, with $J_{5eq,4ax} \approx J_{5eq,4eq} \approx 3$ Hz. H 3 when visible was a triplet of triplets with $J_{3ax,4ax} \approx J_{3ax,2ax} \approx 12$ Hz and $J_{3ax,4eq} \approx J_{3ax,2eq} \approx 3$ Hz. Peaks assigned to H 2*ax* were sometimes apparent as a triplet with $J_{2ax,2eq} \approx J_{2ax,3ax} \approx 12$ Hz but often one or more lines were obscured under methyl peaks. Peaks quoted to only one decimal place were obtained by decoupling exploration. Peaks listed with a question mark were partly obscured. In all cases the amino side chain gave the expected ^{1}H n.m.r. pattern, which often obscured ring protons. I.r. spectra are in Nujol mulls.

(+)-*Sylvestrene Nitrosochloride* (*1a*)

Hydrochloric acid (conc., 11·3 ml) was added dropwise over 90 min to a vigorously stirred solution of (+)-sylvestrene[15] (6·3 g) and isopentyl nitrite (7·5 ml) at -5 to $-10°$. The slush was triturated with cold methanol (3 × 10 ml), filtered, and precipitated thrice from chloroform (8 ml) with methanol (40 ml) giving bis[(1*S*,3*R*,6*S*)-1-chloro-6-nitroso-*m*-menth-8-ene] (1a) (3·2 g), m.p. 115–116° (lit.[4,16] 110–111°, 114–115°) (Found: C, 59·5; H, 7·7; Cl, 17·6; N, 7·0. Calc. for $C_{20}H_{32}Cl_2N_2O_2$: C, 59·5; H, 8·0; Cl, 17·6; N, 6·9%). N.m.r. δ ($CDCl_3$): 1·67, s, C 1–Me; 1·76, s, C 8–Me; 4·77, br s, $W_{h/2}$ 4 Hz, H 9; 5·68, br d, J 4 Hz, $W_{h/2}$ 7 Hz, H 6. Irradiation at δ 2·46 located one H 5 and reduced H 6 to a singlet. N.m.r. δ (C_6D_6): 1·54, 1·68, two s, Me; 4·80, fine m, $W_{h/2}$ 7 Hz, H 9; 5·78, fine m, $W_{h/2}$ 7 Hz, H 6. Irradiation at δ 2·14 sharpened up H 6. Irradiation at δ 5·78 located H 5*eq* as a sextet at δ 2·14, J 15·5, 4·5, 4·5. O.r.d. ($CHCl_3$, [ϕ] based on dimeric structure): $[\phi]_{589}$ +1360, $[\phi]_{436}$ +2900, $[\phi]_{405}$ +3500, $[\phi]_{365}$ +2900, $[\phi]_{334}$ +18000, $[\phi]_{313}$ +33000, $[\phi]_{302}$ +9600, $[\phi]_{297}$ −1000, $[\phi]_{289}$ −9100, $[\phi]_{280}$ −16000, $[\phi]_{265}$ −15000, $[\phi]_{254}$ −10000. I.r.: 1635, 1212, 1175, 1150, 885 cm^{-1}. U.v. λ_{max} (EtOH): 225 nm (ε 1330).

Chloro Nitrosochloride (*1b*)

Hydrogen chloride was passed for 2 h into compound (1a) (1 g) in ethanol (15 ml) at −10°. After a further hour, the mixture was poured onto ice to give *bis*[(*1S,3R,6S*)-*1,8-dichloro-6-nitroso*-*m*-*menthane*] (1b) (380 mg), m.p. 126–127° (from light petroleum) (Found: C, 50·4; H, 7·3; Cl, 30·1; N, 6·2, 5·7. $C_{20}H_{34}Cl_4N_2O_2$ requires C, 50·4; H, 7·4; Cl, 29·8; N, 5·9%). N.m.r. δ ($CDCl_3$): 1·57, 1·65, 1·65, three Me s; 5·68, br d, J 4 Hz, $W_{h/2}$ 8 Hz, H 6. O.r.d. ($CHCl_3$, [ϕ] based on dimeric

[15] Johny, K. P., and Verghese, J., *Indian J. Chem.*, 1972, **10**, 792.
[16] Johny, K. P., and Verghese, J., *Perfum. Essent. Oil Rec.*, 1968, **59**, 875.

structure): $[\phi]_{589}$ +1330, $[\phi]_{436}$ +2900, $[\phi]_{405}$ +3500, $[\phi]_{365}$ +3000, $[\phi]_{334}$ +15000, $[\phi]_{313}$ +29000, $[\phi]_{302}$ +14000, $[\phi]_{297}$ +4300, $[\phi]_{289}$ −14000, $[\phi]_{280}$ −16000, $[\phi]_{265}$ −11000, $[\phi]_{254}$ −5700. I.r.: 1230, 1219, 1202 cm^{-1}.

Sylvestrene Amino Oximes (4a–g)

These compounds, with the exception of (4b), were prepared as described previously[12] for the substituted amino oximes of γ-terpinene nitrosochloride. The nitrosochloride (1a) in ethanol was warmed with the amine and cooled. If crystals did not form, the mixture was acidified with hydrochloric acid (dil.), filtered, and the filtrate basified with ammonia. All recrystallizations are from ethanol.

(A) (*1S,3R*)-*1-Methylamino*-m-*menth-8-en-6-one oxime* (4a), m.p. 95° (Found: C, 67·2; H, 10·2; N, 14·1. $C_{11}H_{20}N_2O$ requires C, 67·3; H, 10·3; N, 14·3%). N.m.r. ($CDCl_3$) as in Table 1 plus δ 2·22, s, NMe. N.m.r. δ (C_6H_6): 1·32, s, C 1–Me; 1·59, s, C 8–Me; 2·11, s, NMe; 2·47, br t, *J c.* 12 Hz, H 3*ax*; 3·58, br d, *J c.* 12 Hz, H 5*eq*. O.r.d. (C_6H_6): $[\phi]_{589}$ +360, $[\phi]_{436}$ +730, $[\phi]_{365}$ +1200, $[\phi]_{334}$ +1700, $[\phi]_{313}$ +2200, $[\phi]_{302}$ +2500, $[\phi]_{297}$ +2700, $[\phi]_{289}$ +3200, $[\phi]_{280}$ +3700. I.r.: 3175, 1645, 935, 885, 775 cm^{-1}.

(B) (*1S,3R*)-*1-Ethylamino*-m-*menth-8-en-6-one oxime* (4b), m.p. 81,° was obtained by refluxing the reagents for 30 min (Found: C, 68·6; H, 10·2, 10·9; N, 13·0. $C_{12}H_{22}N_2O$ requires C, 68·5; H, 10·5; N, 13·3%). N.m.r. as in Table 1 plus δ 1·09, t, *J* 7 Hz and δ 2·46, m, ethylamino group; 10, vbr, NOH. I.r.: 3175, 3080, 1642, 946, 882, 782 cm^{-1}.

(C) (*1S,3R*)-*1-Propylamino*-m-*menth-8-en-6-one oxime* (4c), m.p. 79° (Found: C, 69·7; H, 10·8; N, 12·5. $C_{13}H_{24}N_2O$ requires C, 69·6; H, 10·8; N, 12·5%). N.m.r. ($CHCl_3$) as in Table 1 plus δ 0·91, 3H, t, *J* 7 Hz, δ 1·43, 2H and δ 2·36, 2H, m, propylamino; 9·6, vbr, NOH. N.m.r. δ (C_6H_6): 0·79, t, *J* 7 Hz; 1·4, 2H, and 2·5, 2H, m, side chain; 1·35, s, C 1–Me; 1·57, s, C 8–Me; 3·57, br d, *J* 13 Hz, H 5*eq*; 4·69, s, H 9. O.r.d. (C_6H_6): $[\phi]_{589}$ +380, $[\phi]_{436}$ +790, $[\phi]_{365}$ +1300, $[\phi]_{334}$ +1800, $[\phi]_{313}$ +2200, $[\phi]_{302}$ +2600, $[\phi]_{297}$ +2800, $[\phi]_{289}$ +3200, $[\phi]_{280}$ +3600. I.r.: 3300, 1640, 930br, 890 cm^{-1}.

(D) (*1S,3R*)-*1-Allylamino*-m-*menth-8-en-6-one oxime* (4d), m.p. 79–80° (Found: C, 69·9; H, 10·0; N, 12·6. $C_{13}H_{22}N_2O$ requires C, 70·2; H, 10·0; N, 12·6%). N.m.r. ($CHCl_3$) as in Table 1 plus δ 3·09, octet, 2H, H 1 of allyl; 5·08, three broad lines, 2H, H 3 of allyl; 5·87, eight lines of a 12-line system, 1H, H 2 of allyl, in which $J_{1,2} \approx J_{1',2} \approx 6$ Hz, $J_{2,3}+J_{2,3'} = 27$ Hz, $J_{3,3'}$ small, $J_{1,1'}$ 14 Hz, $\delta_{1,1'}$ 27 Hz, $\delta_{3,3'}$ 11 Hz; 9·9, vbr, NOH. Irradiation at δ 5·87 converted the δ 3·09 system into an AB quartet with J_{AB} 14 Hz, δ_{AB} 27 Hz. N.m.r. δ (C_6H_6): 1·30, ob t, *J* 12–14 Hz, H 2*ax*; 1·32, s, C 1–Me; 1·55, s, C 8–Me; 2·04, dd, $J_{2ax,2eq}$ 14 Hz, $J_{2eq,3ax}$ 4 Hz, H 2*eq*; 2·53, br t, $J_{2ax,3ax} \approx J_{3ax,4ax} \approx 12$ Hz, $J_{3ax,2eq}$ and $J_{3ax,4eq}$ small, H 3*ax*; 3·01, octet, NCH_2; 3·54, d, $J_{5eq,5ax}$ 12 Hz, H 5*eq*; 4·68, unres d, H 9; 5·0, three lines, 2H and 5·78, eight lines, 1H, side chain vinyls. I.r.: 3300, 1640, 945br, 895 cm^{-1}.

(E) (*1S,3R*)-*1-Butylamino*-m-*menth-8-en-6-one oxime* (4e), m.p. 58° (Found: C, 70·7; H, 11·0; N, 11·7. $C_{14}H_{26}N_2O$ requires C, 70·5; H, 11·0; N, 11·8%). N.m.r. as in Table 1 plus δ 0·91, dist t; 1·4, br; and 2·4, m, butyl group; 10, br, NOH. I.r.: 3160, 3050, 1640, 945, 885, 780 cm^{-1}.

(F) (*1S,3R*)-*1-Cyclohexylamino*-m-*menth-8-en-6-one oxime* (4f), m.p. 126–127° (Found: C, 72·4; H, 10·7; N, 10·7. $C_{16}H_{28}N_2O$ requires C, 72·7; H, 10·7; N, 10·6%). N.m.r. as in Table 1 plus δ 1·2, 1·6, 2·5, cyclohexyl. I.r.: 3330–3100, 1645, 930, 890, 790, 775 cm^{-1}.

(G) (1*S*,3*R*)-1-Benzylamino-*m*-menth-8-en-6-one oxime (4g), m.p. 71° (lit. m.p. 71–73°,[3] 230–231°;[4] $[\phi]_{589}$ +506,[5] +232[4]) (Found: C, 74·7; H, 8·9; N, 10·0. Calc. for $C_{17}H_{24}N_2O$: C, 75·0; H, 8·9; N, 10·3%). N.m.r. ($CDCl_3$) as in Table 1 plus δ 3·61, AB q, *J* 13 Hz and δ 7·28, 5H, benzylic group; 9·96, br, NOH. N.m.r. δ (C_6D_6): 1·33, t, *J* 13 Hz, H 2*ax*; 1·39, s, C 1–Me; 1·55, s, C 8–Me; 2·03, td, *J* 13, 13, 4 Hz, H 5*ax*; 2·53, tt, *J* 13, 13, 2, 2 Hz, H 3*ax*; 3·58, br d, *J c.* 13 Hz, H 5*eq*, superimposed upon 3·54, AB q, *J* 12 Hz, benzylic protons; 4·7, fine q, $W_{h/2}$ 9 Hz, H 9; 7·23, 5H, aromatic; 10·4, br, NOH. I.r.: 3320–3040, 1645, 930, 888, 755, 695 cm^{-1}.

The Phenylamino Oximes (4h) and (5')

Sylvestrene nitrosochloride (1a) (2g), aniline (2 ml) and ethanol (3 ml) were warmed to a clear solution, cooled to −5° and acidified with hydrochloric acid (conc., 5 ml). The precipitate was filtered off, washed successively with ethanol (3 ml) and ether (5 ml), then basified with ammonia (0·88, 6 ml). Recrystallization (ethanol) gave (*1S,3R*)-*1-phenylamino*-m-*menth-8-en-6-one oxime* (4h)

(650 mg), m.p. 120° (lit.[4] m.p. 146–147°, $[\phi]_{589}$ +211) (Found: C, 74·1; H, 8·8; N, 11·0. $C_{16}H_{22}N_2O$ requires C, 74·4; H, 8·6; N, 10·8%). N.m.r. ($CDCl_3$) as in Table 1 plus δ 6·73, m, *meta* and *para* protons; 7·12, overlapping d, *J* 7 Hz, *ortho* protons; 9·44, s, NOH. N.m.r. δ (C_6H_6): 1·52, 1·54, s, C 1 and C 8 methyls, superimposed upon 1·4–1·8, m, 4H, H 2 and H 4; 2·06, td, *J* 13, 13, 4 Hz, H 5*ax*; 2·52, tt, *J* 13, 12, 3, 3 Hz, H 3*ax*; 3·18, s, NH; 3·50, dt, *J* 13, 2, 2 Hz, H 5*eq*; 4·66, 4·72, two br s, H 9; 9·94, s, NOH. O.r.d. ($CHCl_3$) see Table 1 plus $[\phi]_{405}$ +840, $[\phi]_{320}$ +630, $[\phi]_{308}$ +100. O.r.d. (C_6H_6): $[\phi]_{589}$ +360, $[\phi]_{436}$ +730, $[\phi]_{405}$ +830, $[\phi]_{365}$ +1090, $[\phi]_{334}$ +1130, $[\phi]_{320}$ +180, $[\phi]_{313}$ −130, $[\phi]_{302}$ +1800, $[\phi]_{297}$ +3600, $[\phi]_{289}$ +5400, $[\phi]_{280}$ +6200. I.r.: 3355, 1642, 1605, 1500, 940, 928, 890, 760 cm^{-1}. λ_{max} (EtOH): 247·5 nm (ε 15000).

The filtrate from the above preparation was stored with excess ammonia (8 ml) for 12 h at −5°. The precipitate was dissolved in benzene (2 ml), diluted with light petroleum (10 ml) and stored at −5° for 24 h to give (*1*R,*3*R)-*1-phenylamino*-m-*menth-8-en-6-one oxime* (5) as (5′) (100 mg), m.p. 132° (from 80% ethanol) (Found: C, 74·5; H, 8·7; N, 10·5. $C_{16}H_{22}N_2O$ requires C, 74·4; H, 8·6; N, 10·8%). N.m.r. ($CDCl_3$) as in Table 1 plus two sharp *c.* 1H peaks at δ 1·96 and 2·04; 4·5, br, NH; 6·65, 3H, t and 7·08, 2H, overlapping doublets, *J* 7 Hz, phenyl; 8·0, NOH. The δ 3·39 system (H 5*eq*) was a broad doublet, $J_{5ax,5eq}$ 14 Hz, with each band of $W_{h/2}$ 8–9 Hz. N.m.r. δ (C_6H_6): 1·26, s, C 1–Me; 1·48, s, C 8–Me; 1·95, s, 2H; 3·42, br d, *J* 14 Hz with each band of $W_{h/2}$ 8–9 Hz, H 5*eq*; 4·63, br s, H 9; and with H 5*ax* and H 3*ax* both δ <2·0. O.r.d. ($CHCl_3$) as in Table 1 with $[\phi]_{308}$ +2200. O.r.d. (C_6H_6): $[\phi]_{589}$ +62, $[\phi]_{436}$ +150, $[\phi]_{365}$ +230, $[\phi]_{334}$ +320, $[\phi]_{313}$ +650, $[\phi]_{302}$ +320, $[\phi]_{297}$ −260, $[\phi]_{289}$ −650, $[\phi]_{280}$ −1900. O.r.d. (MeOH): $[\phi]_{589}$ +90, $[\phi]_{436}$ +160, $[\phi]_{365}$ +280, $[\phi]_{334}$ +470, $[\phi]_{313}$ +1400, $[\phi]_{302}$ +700, $[\phi]_{297}$ −470, $[\phi]_{289}$ −2000, $[\phi]_{280}$ −3900, $[\phi]_{265}$ −6200. I.r.: 3320–3050, 1640, 1605, 1500, 965, 935, 760 cm^{-1}.

Chloro Derivatives (6a–f) and (7a–c)

Hydrogen chloride was bubbled (30 min) through the appropriate amino oxime (4) in methanol at −5°. The mixture was poured onto ice, basified with ammonia, and the precipitate recrystallized from ethanol.

(A) (*1*S,*3*R)-*8-Chloro-1-propylamino*-m-*menthan-6-one oxime* (6a), m.p. 107° (Found: C, 60·0; H, 9·8; Cl, 13·2, 13·2; N, 10·5. $C_{13}H_{25}ClN_2O$ requires C, 59·9; H, 9·7; Cl, 13·6; N, 10·7%). N.m.r. ($CDCl_3$) as in Table 1 together with propyl peaks at δ 0·91, t, *J* 7 Hz and δ 2·45, m, 2H. N.m.r. δ (C_6H_6): 0·77, t, *J* 7 Hz, propyl Me; 1·27, 1·31, 1·34, three s, Me; 3·54, br d, *J* 12 Hz, H 5*eq*. I.r.: 3180, 3070, 1130, 1110, 932, 810, 790 cm^{-1}.

(B) (*1*S,*3*R)-*1-Butylamino-8-chloro*-m-*menthan-6-one oxime* (6b), m.p. 117° (Found: C, 61·4; H, 9·9; Cl, 12·6; N, 10·2. $C_{14}H_{27}ClN_2O$ requires C, 61·2; H, 9·9; Cl, 12·9; N, 10·2%). N.m.r. as in Table 1 together with butyl peaks including δ 0·89, distorted t, 3H. I.r.: 3300, 3170, 3060, 1112, 930, 812, 790 cm^{-1}.

(C) (*1*S,*3*R)-*8-Chloro-1-cyclohexylamino*-m-*menthan-6-one oxime* (6c), m.p. 152° (Found: C, 64·1; H, 10·0; Cl, 12·1; N, 9·3. $C_{16}H_{29}ClN_2O$ requires C, 63·9; H, 9·7; Cl, 11·8; N, 9·3%). N.m.r. as in Table 1 together with cyclohexyl protons. I.r.: 3300–3060, 930, 810, 790 cm^{-1}.

(D) (*1*S,*3*R)-*1-Benzylamino-8-chloro*-m-*menthan-6-one oxime* (6d), m.p. 130° (lit. m.p.[4] 243–244°; $[\phi]_{589}$ +301,[4] +245[5]) (Found: C, 66·3; H, 8·4; Cl, 11·4; N, 9·0. $C_{17}H_{25}ClN_2O$ requires C, 66·1; H, 8·2; Cl, 11·5; N, 9·1%). N.m.r. ($CDCl_3$) as in Table 1 plus δ 3·6, AB q, *J* 12 Hz, benzylic; 7·30, fine m, 5H, phenyl. N.m.r. δ (C_6H_6): 1·26, s, chloroisopropyl methyls; 1·37, s, C 1–Me; 3·52, 3H complex of AB benzylic protons superimposed upon br d, H 5*eq*. I.r.: 3300–3030, 1500, 1110, 942, 930, 815, 758, 740, 695 cm^{-1}.

(E) (1*S*,3*R*)-8-Chloro-1-phenylamino-*m*-menthan-6-one oxime (6e), m.p. 138–139° (lit.[4] m.p. 138–139°, $[\phi]_{589}$ +476) (Found: C, 65·5; H, 8·0; Cl, 12·0; N, 9·3. Calc. for $C_{16}H_{23}ClN_2O$: C, 65·2; H, 7·9; Cl, 12·0; N, 9·5%). N.m.r. ($CDCl_3$) as in Table 1 plus 6·74, t(?), 3H and 7·12 overlapping doublets, *J* 7 Hz, 2H, phenyl; 9·3, NOH. N.m.r. δ (C_6H_6): 1·15 and 1·25, s, chloroisopropyl methyls; 1·53, s, C 1–Me; 2·08, br d, *J* 12 Hz, q, H 2*eq*?; 3·2, NH; 3·48, br d, *J* 13 Hz, H 5*eq*; 9·4, NOH. O.r.d. (C_6H_6): $[\phi]_{589}$ +400, $[\phi]_{436}$ +800, $[\phi]_{365}$ +1200, $[\phi]_{334}$ +1120, $[\phi]_{313}$ +180, $[\phi]_{302}$ +2700, $[\phi]_{297}$ +5300, $[\phi]_{289}$ +7400, $[\phi]_{280}$ +8000. I.r.: 3350, 1605, 1500, 930, 860 cm^{-1}.

(F) (*1*S,*3*R)-*8-Chloro-1*-p-*tolylamino*-m-*menthan-6-one oxime* (6f), m.p. 142° (Found: C, 66·3; H, 8·1; Cl, 11·5; N, 9·0. $C_{17}H_{25}ClN_2O$ requires C, 66·1; H, 8·2; Cl, 11·5; N, 9·1%). N.m.r. as in Table 1 with δ 2·24, s, aromatic Me; 6·62, 6·94, two 2H, d, *J* 8 Hz, aromatic; 9·1, NOH. O.r.d. ($CHCl_3$) as in Table 1 plus $[\phi]_{405}$ +730. O.r.d. (C_6H_6): $[\phi]_{589}$ +290, $[\phi]_{436}$ +560, $[\phi]_{405}$

+660, $[\phi]_{365}$ +740, $[\phi]_{334}$ +460, $[\phi]_{325}$ +300, $[\phi]_{313}$ +1050, $[\phi]_{302}$ +4300, $[\phi]_{297}$ +5200, $[\phi]_{289}$ +6500, $[\phi]_{280}$ +5500. I.r.: 3240, 1615, 1515, 920, 810 cm^{-1}.

(G) (*1R,3R*)-*8-Chloro-1-phenylamino*-m-*menthan-6-one oxime* (7a) as (7a′), m.p. 136–137° and depressing the m.p. of (6e) (Found: C, 65·0; H, 7·9; Cl, 11·4, 11·5; N, 9·7. $C_{16}H_{23}ClN_2O$ requires C, 65·2; H, 7·9; Cl, 12·0; N, 9·5%). N.m.r. ($CDCl_3$) as in Table 1 plus δ 6·67 and 7·12, 3H and 2H, phenyl. N.m.r. δ (C_6H_6): 1·18, 1·18, 1·25, s, methyls; 3·31, br d, *J* 13 Hz, H 5*eq*. O.r.d. ($CHCl_3$) as in Table 1 with $[\phi]_{308}$ +2400. O.r.d. (C_6H_6): $[\phi]_{589}$ +118, $[\phi]_{436}$ +240, $[\phi]_{365}$ +440, $[\phi]_{334}$ +810, $[\phi]_{313}$ +2100, $[\phi]_{302}$ +1030, $[\phi]_{297}$ −290, $[\phi]_{289}$ −2100, $[\phi]_{280}$ −4700. I.r.: 3310, 1604, 1495, 960, 742, 680 cm^{-1}, and different from compound (6e).

(H) (*1R,3R*)-*8-Chloro-1*-N-*piperidyl*-m-*menthan-6-one oxime* (7b), m.p. 134° (Found: C, 62·8; H, 9·5; Cl, 12·1; N, 9·7. $C_{15}H_{27}ClN_2O$ requires C, 62·8; H, 9·5; Cl, 12·4; N, 9·8%). N.m.r. ($CDCl_3$) as in Table 1 plus δ 9·58, NOH. N.m.r. δ (C_6H_6): 1·17, 1·23, 1·32, s, methyls; 3·54, br d, *J* 11 Hz, H 5*eq*; 9·6, NOH. O.r.d. (C_6H_6): $[\phi]_{589}$ +252, $[\phi]_{436}$ +560, $[\phi]_{365}$ +880, $[\phi]_{334}$ +1200, $[\phi]_{313}$ +1500, $[\phi]_{302}$ +1700, $[\phi]_{297}$ +1800, $[\phi]_{289}$ +2000, $[\phi]_{280}$ +2200. I.r.: 3270, 1120, 940, 775 cm^{-1}.

(I) (*1R,3R*)-*8-Chloro-1-diethylamino*-m-*menthan-6-one oxime* (7c), m.p. 117–118° (Found: C, 61·2; H, 9·9; Cl, 12·6; N, 9·8. $C_{14}H_{27}ClN_2O$ requires C, 61·2; H, 9·9; Cl, 12·9; N, 10·2%). N.m.r. as in Table 1 plus δ 1·06, t, *J* 7 Hz, 6H and δ 2·5, m, 4H, ethyl groups; 9·56, NOH. N.m.r. δ (C_6H_6): 0·95, 6H, t, *J* 7 Hz, ethyls; 1·19, 1·25, 1·36, three s, methyls; 1·83, br d, *J c.* 14 Hz, H 2*eq*?; 2·4, m, 2H, CH_2N, superimposed upon other protons; 3·57, dt, *J* 13, 3, 3 Hz, H 5*eq*; 10·3, s, NOH. Decoupling experiments placed H 5*ax* at δ 2·05, one H 4 proton at δ 1·6 and H 2*ax*? at δ 0·95. I.r.: 3250, 1208, 1110, 933, 765 cm^{-1}. The compound slowly decomposed with loss of hydrogen chloride.

The N-*Nitroso Derivatives* (*8a–e*)

N-Nitrosation of relevant secondary amines was accomplished by the procedure described previously.[12] The n.m.r. spectra of the products gave H 3*ax* as a broad triplet with $J_{3ax,2ax} \approx J_{3ax,4ax} \approx$ 12 Hz. H 2*eq* was apparent as a broad doublet with $J_{2eq,2ax}$ *c.* 13 Hz.

(A) (*1S,3R*)-*1*-(N-*Nitrosomethylamino*)-m-*menth-8-en-6-one oxime* (8a), m.p. 126–127° (Found: C, 58·3; H, 8·4; N, 18·5. $C_{11}H_{19}N_3O_2$ requires C, 58·6; H, 8·5; N, 18·7%). N.m.r. as in Table 1 plus δ 2·93, s, NMe; 9·24, NOH. O.r.d. as in Table 1 plus $[\phi]_{405}$ +310 (min.). I.r.: 3350, 1640, 1412, 1298, 1150, 960, 938, 890 cm^{-1}.

(B) (*1S,3R*)-*1*-(N-*Nitrosoethylamino*)-m-*menth-8-en-6-one oxime* (8b), m.p. 139° (Found: C, 60·2; H, 8·9; N, 17·4. $C_{12}H_{21}N_3O_2$ requires C, 60·2; H, 8·8; N, 17·6%). N.m.r. as in Table 1 plus δ 1·08, t, *J* 7 Hz and 3·50, m, 2H, ethyl; 9·3, NOH. O.r.d. as in Table 1 plus $[\phi]_{405}$ +590 (min.). I.r.: 3280, 1642, 1310, 1270, 1245, 1140, 955, 935, 895, 820 cm^{-1}. λ_{max} (EtOH): 233 nm (ε 7800).

(C) (*1S,3R*)-*1*-(N-*Nitrosopropylamino*)-m-*menth-8-en-6-one oxime* (8c), m.p. 151° (Found: C, 61·6; H, 9·1; N, 16·5. $C_{13}H_{23}N_3O_2$ requires C, 61·6; H, 9·2; N, 16·6%). N.m.r. as in Table 1 plus δ 0·86, t, *J* 7 Hz, 3H; 1·5, m, 2H, propyl; 9·3, NOH. O.r.d. as in Table 1 plus $[\phi]_{405}$ +640 (min.). I.r.: 3340, 1640, 1242, 1140, 1105, 1050, 955, 935, 885 cm^{-1}.

(D) (*1S,3R*)-*1*-(N-*Nitrosobutylamino*)-m-*menth-8-en-6-one oxime* (8d), m.p. 140° (Found: C, 62·6; H, 9·4; N, 15·8. $C_{14}H_{25}N_3O_2$ requires C, 62·9; H, 9·4; N, 15·7%). N.m.r. as in Table 1 plus δ 0·92, dist t, 3H; 1·4, br s; 3·48, br s, 2H, butyl; 9·4, NOH. O.r.d. as in Table 1 plus $[\phi]_{405}$ +530 (min.). I.r.: 3250, 1640, 1240, 1205, 955, 930, 885 cm^{-1}.

(E) (*1S,3R*)-*1*-(N-*Nitrosopentylamino*)-m-*menth-8-en-6-one oxime* (8e), m.p. 130° (Found: C, 64·3; H, 9·7; N, 14·8. $C_{15}H_{27}N_3O_2$ requires C, 64·0; H, 9·7; N, 14·9%). N.m.r. as in Table 1 plus side chain peaks including δ 0·88, dist t, 3H, and 3·4, m, 2H; 9·4, NOH. O.r.d. as in Table 1 plus $[\phi]_{405}$ +560 (min.). I.r.: 3340, 1640, 954, 890 cm^{-1}.

Nitrosation of the phenylamino derivatives (4h) and (5) gave brown oils.

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